
MAGNETIC NAVIGATION IN PERCUTANEOUS CARDIAC INTERVENTION
MARK PATTERSON

Magnetic Navigation in Percutaneous Cardiac Intervention

Mark Simon Patterson

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Magnetic Navigation in Percutaneous Cardiac Intervention

Magneet navigatie in percutaan cardiale interventie

Thesis

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Background, history and system description

CHAPTER 1

Introduction

INTRODUCTION

Magnetic navigation is the use of a magnetic field to re-orientate a magnetically-enabled wire or device. The field is directed by external magnets that are moved by a computer-controlled system. This technology could improve percutaneous coronary interventional procedures as it improves 3 specific and complementary capabilities, namely precise tip adjustability, computer-enhanced, image-guided tip orientation, and computer–enhanced image processing.

Although this technology is relatively new, it already appears that this system can equal, and even improve on, current conventional wire technique. The current usability, combined with the exciting potential of future developments, could result in a formidable adjunct to PCI.

This thesis deals with the early use of the system, development of different strategies for the exploitation of the unique novel features that the system has. Specifically it will describe a number of areas.

1. Background, history and system description

The aim of this introduction is to provide a brief description of the background of magnetic procedures with respect to Stereotaxis Inc, and a description of the magnetic moment, and a short description of the current system together with the specially-produced wires.

2. Feasibility in phantom models, and initial system development

This section deals with aspects related to feasibility of use, validation of the software, and initial experience in different clinical situations and finally with the potential use in treating one of the sequelae of coronary disease i.e. poor left ventricular function by the possible delivery of cardiac stem cells.

3. Initial experience in clinical practice and illustrative case reports

This section deals with the clinical use in percutaneous coronary intervention concentrating on the initial patient studies.

4. Investigation of benefits in subgroups

This section concentrates on particular subsets of coronary intervention patients and the specific hypotheses that can be drawn from these.

BACKGROUND, HISTORY AND SYSTEM DESCRIPTION

In vivo magnetic navigation for delivering medical therapies is a small but not new field. Vascular studies using magnetic navigation first began over 50 years ago when Tillander used magnetic fields to guide an articulated steel-tip catheter in rabbit aortae (1,2). After these initial investigations, small external permanent magnets were used to stereotactically direct iron particles for thrombosis of intracranial aneurysms (3-5). Later, rotating electromagnets were used, enabling better control (6). The first human use was for neonatal heart catheterization in 1991 for the diagnosis of anomalous congenital cardiac drainage (7).

Stereotaxis Inc. officially started as a company in 1991 with an initial goal of enhancing wire passage in neurosurgical procedures. In the case of Stereotaxis, much of the initial academically-driven work was dedicated solely to hyperthermia therapies of deep-seated brain tumors. The system has been through a number of iterations of magnet configurations. Some of the previous system configurations are shown below - the Telstar family – Tristar, Unistar and Pullstar, together with the current system, Niobe®.

The Stereotaxis Niobe® magnet control system represents the commercial realization of magnetically-targeted therapy to the heart. The system received regulatory approval for human clinical use in cardiac electrophysiology and interventional neuroradiology in 2000, and for interventional cardiology in 2003.

While previous systems were only suitable for relatively large vessels or chambers because of the size of the catheter magnets required, the development of magnets of ≤0.014", see figure 1.5, the standard diameter of coronary guidewires, has allowed application to Interventional Cardiology.

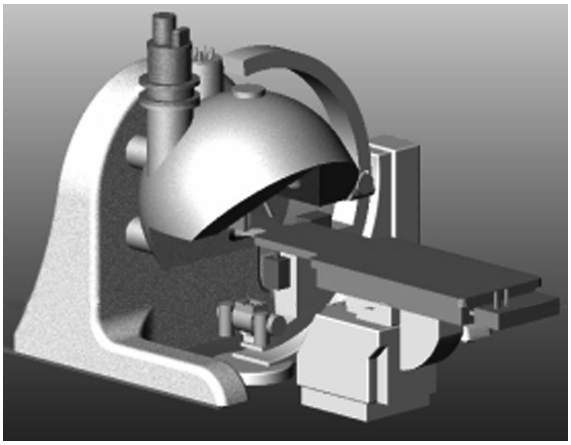

Figure 1. The Tristar configuration had a superconducting magnet with an open field and was electrically controlled. *See this figue in color in the Appendix page 373.*

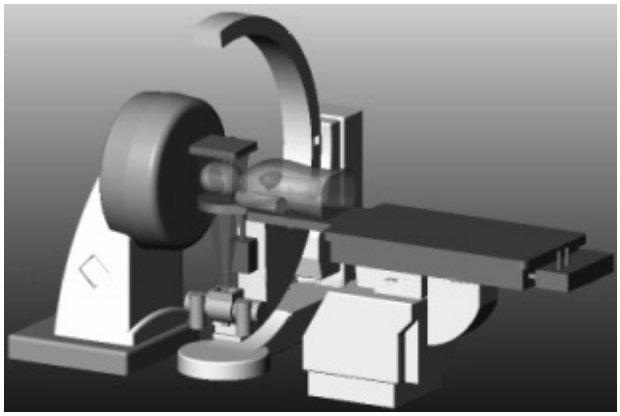

Figure 2. The Unistar configuration had a permanent magnet that had a lower field strength but was less expensive and was mechanically controlled. *See this figue in color in the Appendix page 373.*

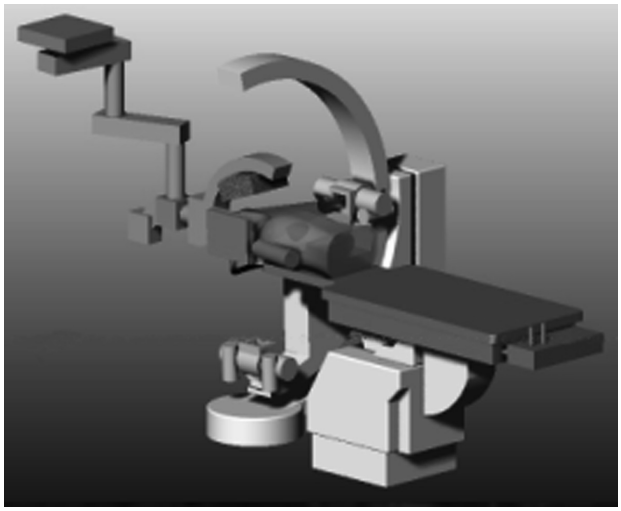

Figure 3. The Pullstar configuration was a permanent magnet that gave a gradient field for low cost aneurysm treatment. This was manually controlled. *See this figue in color in the Appendix page 374.*

The Stereotaxis Niobe® magnet control system is an advanced cardiology instrument control system for use in a hospital's interventional surgical suite to enhance the treatment of coronary artery disease and arrhythmias. The Magnetic Navigation System is designed to enable physicians to complete complex interventional procedures by providing image guided delivery of catheters and guidewires through the blood vessels and chambers of the heart to treatment sites. This is achieved using computer-controlled, externally applied magnetic fields that govern the attitude of the working tip of the catheter or guidewire, with the aim of improving navigation and potentially leading to shorter procedure times and reduced x-ray exposure and contrast media use.

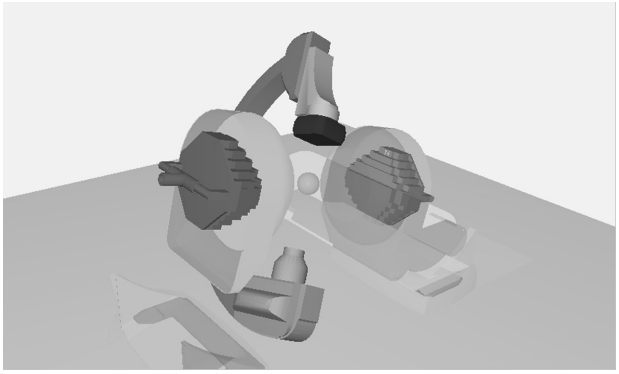

Figure 4. The Niobe® configuration has 2 permanent magnets on mechanically controlled positioners at either side of the patient. *See this figue in color in the Appendix page 374.*

The current system is a combination of the Niobe® Stereotaxis magnet control system that controls the magnet movements and is controlled by the Navigant™ Work Station. The development of this system has been enabled by the availability of low-cost modern magnetic materials combined with the use of digital imaging plates that are minimally affected by magnetic fields.

Two large neodymium-iron-boron (Nd-B-Fe) magnets are mounted on mechanical positioners that produce an interacting magnetic field. Magnetic moment is exerted upon a magnet when the applied field is offset from a magnet's principal magnetization axis, and this moment causes the magnet to align with the external field.

The current list price for the Stereotaxis system is $1.9 million. The size of a typical modern Stereotaxis interventional suite is 770 square feet (72 square meters). The cost of magnetic shielding generally ranges from $50,000–$100,000 and consists of minimal common steel shielding in the walls, ceiling and floor.

There is a range of magnetically enabled Stereotaxis 0.014" guidewires, see figure 1.5, that are priced at a marginal premium over conventional wires. All other PCI equipment is standard and compatible with the Stereotaxis guidewires and MNS.

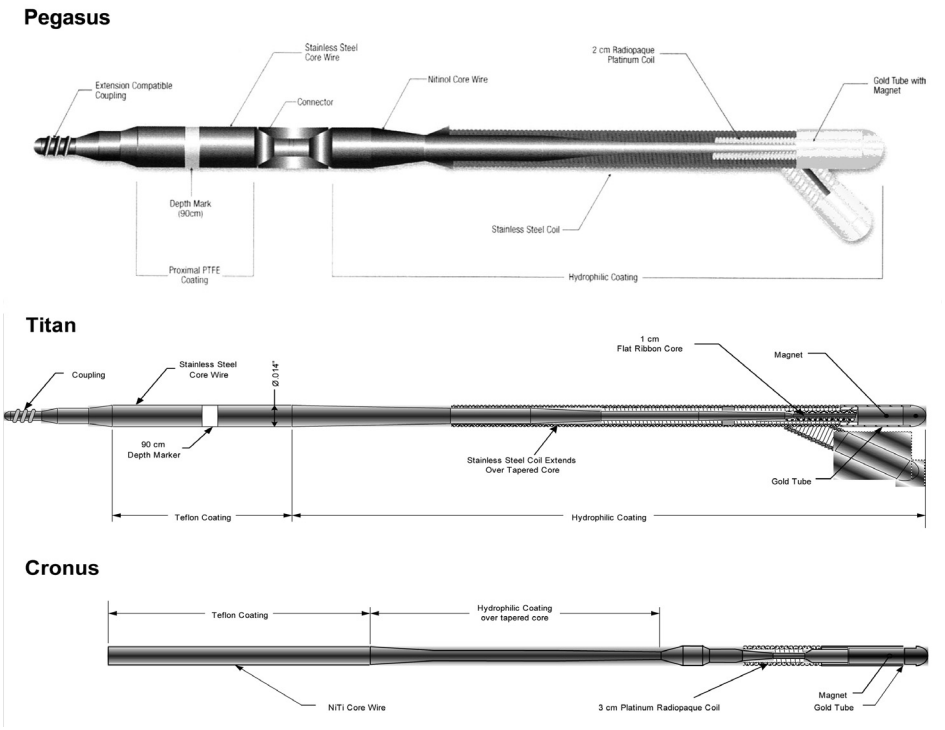

Figure 5. The structure of the current magnetic wires. *See this figue in color in the Appendix page 375.*

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CHAPTER 2

Magnetic Navigation in Percutaneous Coronary Intervention

MAGNETIC NAVIGATION IN PERCUTANEOUS CORONARY INTERVENTION

Magnetic navigation is the use of adjustable magnetic fields to precisely direct wires and equipment for clinical applications. It is a recently developed option that is now available for interventional cardiology. Procedures are based on the production of a three-dimensional reconstruction of the vessel lumen from standard angiographic images. Knowledge of the positions of the table and image intensifier during angiography allows calculation of the vessel coordinates in real space within the patient's chest. The applied magnetic field can be changed at any time to redirect the wire tip in order to improve navigation through complex and tortuous anatomy. The digital information of the coronary reconstruction can be used in further novel ways. Firstly, the integration of multislice computerized tomography images adds information about the path of the previous lumen of chronic total occlusions. Secondly, the computed center-line of the reconstructed vessel can be superimposed onto the live fluoroscopy images as a three-dimensional guide. The combination of improved navigation together with the other available system features may improve time, contrast, and material usage in a range of coronary lesions. Future potential developments include improvements in equipment and software, and potential therapeutic strategies under consideration include the use of equipment to perform remote control procedures, and the integration of the system to improve bone marrow–derived stem cell delivery.

INTRODUCTION

The field of interventional cardiology has been characterized by the rapid introduction and uptake of new treatments and devices such as stents (1), clopidogrel (2) drug-eluting stents (3), bivalirudin (4) and new guidewire technology. These new technologies have driven the continuously increasing total number of percutaneous coronary interventions (PCI) (5). A recent promising development is the use of a magnetic navigation system (MNS) to steer a guidewire through coronary arteries. This technology is already accepted for the performance of electrophysiological studies (6–9) and has tested favorably in neurosurgery both in animal models (10) and in humans (11). Interventional coronary procedures present more of a moving target when compared with neurosurgery and require smaller magnets when compared with electrophysiology. The combination of smaller wire tip magnets together with new software and imaging features has made the MNS available as a new platform for PCI. Magnetic navigation allows a magnetically enabled wire tip to be pointed in any orientation. This allows the adjustment and readjustment of the direction of the wire tip in vivo whenever needed. In addition, the system produces three-dimensional images, integrates information with multislice computerized tomography (MSCT), and is able to use this three-dimensional information superimposed on live fluoroscopy. The potential areas where such a system

provides new options include challenging and tortuous anatomy, chronic total occlusions (CTOs), reduction in time, contrast, and materials, and remote control PCI. This article reviews a brief history of magnetic procedures, the current status, some future possibilities, and some limitations within the area of non-electrophysiological cardiac interventions.

The System

The magnetic navigation system (Niobe®, Stereotaxis, St. Louis, Missouri) has been developed for use with digital coronary angiography. The system consists of two permanent magnets, mounted on mechanical positioners, on either side of the fluoroscopy table (see Fig. 1).

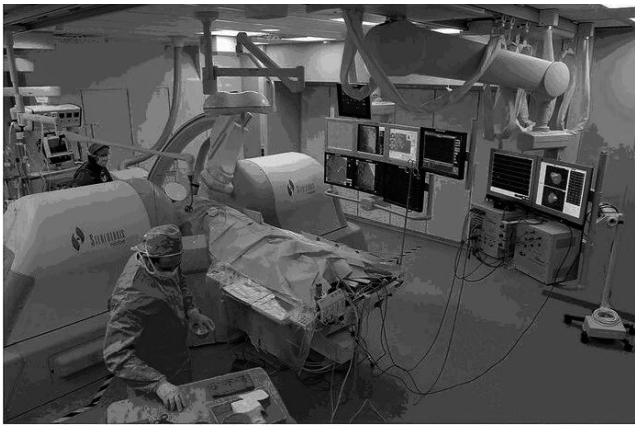

Figure 1. Magnetic navigation system is shown with the magnets in position on either side of the patient. *See this figue in color in the Appendix page 375.*

These magnets produce an interacting magnetic field to produce an approximately spherical 15 cm uniform magnetic field of 0.08 T. The magnets move along three different coordinates and rotate about the z axis, move toward or away from the navigation volume along the z axis, and tilt about an axis located just behind the magnet. This allows the direction of the applied magnetic field vector to be orientated in 360° in all planes. The three-dimensional location of the X-ray image is known from the positions of the image intensifier, angiography system, and table. A three-dimensional reconstruction is created from the angiographic images using dedicated reconstruction software (CardiOp-B, Paieon Medical Inc., Rosh Ha'ayin, Israel). This reconstruction is used by the MNS to give three-dimensional coordinates that are localized in real space (within the chest of a patient during a procedure). This provides two new abilities. Firstly, the three-dimensional model allows the computation of the orientations of the magnetic field needed for alignment with the center-line at every point of the virtual coronary artery. Secondly, the three-dimensional coordinates are known in real space and this provides the data for the MNS to change the magnetic field vector, and therefore the

resulting magnetic moment on the wire tip, at every location in the vessel. The magnetic moment is equal to the product of the strength of the applied magnetic field, the cross-sectional area of the tip magnet, and the sine of the angle of the magnet direction relative to the applied magnetic field. The result is control of the direction of the wire tip, *in vivo,* without the need for a preshaped wire tip angle. There is a recently introduced and broadened range of dedicated, magnetically enabled wires (Titan™ series) for PCI available for use with the MNS.

History

The use of magnets to control an intravascular catheter was first reported in 1951 (12) while the first human use was a neonatal heart catheterization in 1991 for the diagnosis of anomalous congenital cardiac drainage (13). The current MNS has been developed over the past 15 years. Previous systems were only suitable for relatively large vessels because of the size of the catheter magnets required. The current system now has tiny magnets (≤0.014″) and is the most widely used. This system received regulatory approval for human clinical use in cardiac electrophysiology and interventional neuroradiology in 2000, and for interventional cardiology in 2003. It has been shown to be feasible in neurosurgery (10,11) and is a well-accepted technique in electrophysiology (6–9).

CURRENT STATUS

Navigation.

The core feature of the system is the ability to alter the direction of the wire tip within a patient during a procedure to give improved wire tip control compared to conventional procedures. First, the ability to precisely direct the wire tip means that the wire can be redirected and readjusted throughout the procedure to configurations that exactly suit the angulations and direction of the vessel, or alternatively used in a precisely defined probing pattern to interrogate the vessel ahead. This ability is not affected by friction on the shaft of the wire that can impair manipulation in tortuous vessels. Second, it overcomes the problem of a conventional tip that can become damaged and misshapen during a procedure and so impair manipulation. Finally, the passage of the wire is guided by the magnetic vector rather then rotational manipulation and this may reduce wire entanglement. This problem sometimes occurs in bifurcation procedures where wires can become intertwined with manual manipulation and prevent passage of materials. These abilities mean that the lesion can be approached, and navigated through, with a straight tip. A straight tip may reduce the chance of the wire tip impacting against the vessel wall or unintentionally navigating into side branches. A major goal in the development of this system has been to enable the successful passage of the

wire through vessels that prove challenging to conventional guidewires. In this context, two situations are particularly relevant: firstly, tortuous and/or heavily calcified vessels where a conventional guidewire loses manipulability as described above; secondly, CTOs where the path of the vessel is not visible and the required tip direction is unclear.

Difficult Anatomy

This technology has been examined in a number of different situations with regards to difficult lesions. Passage of a wire to distal segments of in vitro phantoms was not only successful but, in addition, fluoroscopy times were found to be significantly reduced (14). This potentially reduces radiation exposure both to patients and personnel. The system has been shown to be feasible for PCI *in vivo* (15,16), and furthermore, both of these studies showed that the magnetically enabled wire was capable of crossing lesions where a conventional wire had failed. In addition to normal PCI, MNS can support other specialist intracoronary procedures such as percutaneous alcohol septal ablation (17).

These navigational advantages are enhanced by a range of imaging possibilities including the three-dimensional lumenogram, the bull's-eye view, and the endoluminal view (see Figs. 2 and 5). In addition, the MNS has dedicated ranges of magnetically enabled guidewires (the Titan™ and Cronus® ranges) that vary in stiffness, magnet length, and tip angulation to tailor the system to each individual coronary artery. These 0.014" wires are entirely compatible with all current standard PCI equipment and standard access sites, both radial and femoral. The combination of precise navigation and additional imaging options available may reduce time, contrast, fluoroscopy, and material use.

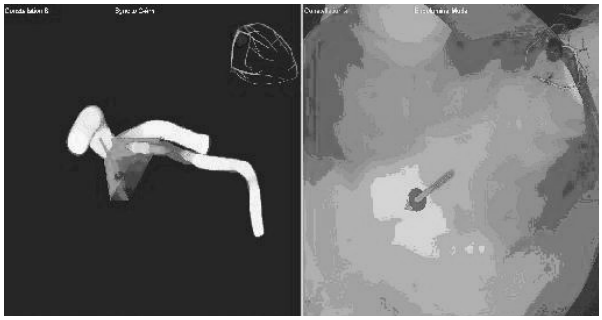

Figure 2. This shows the three-dimensional reconstruction in the left panel and the endoluminal view of the LAD/diagonal bifurcation in the right panel. Note that these are live, moving, real-time images during a procedure. *See this figue in color in the Appendix page 376.*

Figure 3. The left panel shows 64-slice cardiac MSCT with vessels; a tissue attenuation line is seen in the RCA after the RV branch. The right panel shows a post-processed image of the vessel that more clearly shows the 30-mm occlusion. *See this figue in color in the Appendix page 376.*

CTOs and MSCT Integration

A second lesion type that continues to be vexing is the CTO. Success rates for PCI of CTOs are around 65% to 80%, depending on the technique used and presence of other diseases such as diabetes (18–21).

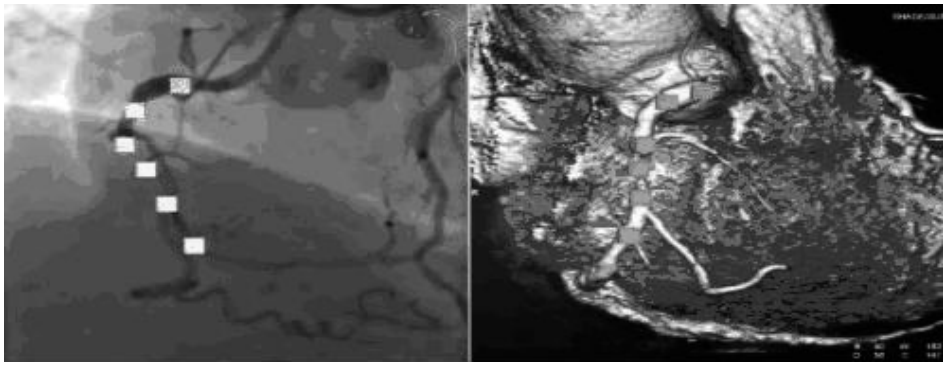

Figure 4. The fluoroscopy image is marked on the system with dots ready for three-dimensional integration in the left panel with the MSCT marked with dots for integration in the right panel. These give the specific three-dimensional coordinates that allow integration of the two modalities (see Fig. 5). *See this figue in color in the Appendix page 376.*

A number of strategies have been suggested to facilitate the treatment of CTOs, e.g., intracoronary thrombolytic infusion (22), the use of tapered tip guidewires (20), imaging with (16-slice) MSCT (23) and the use of a laser guidewire (24). The ability to precisely steer and change the orientation of the wire tip may be crucially important in avoiding wire exit,

and may hold a major advantage in comparison with a conventional wire that has a fixed, unchangeable angulation. However, with regard to CTOs, the MNS has a further major advantage as it can also integrate 64-slice MSCT images (see Figs. 3–5). This imaging technique can identify both a distal vessel that is filled via collaterals and also show a tissue attenuation line (the scarred tissue of the original vessel lumen). This imaging allows a path to be visualized and then synchronized with the MNS (see Figs. 3–5) to direct the wire tip along the previous vessel lumen (or at least the scar tissue) to the distal vessel. These features have helped the success of the MNS in the initial experience of CTO procedures (25).

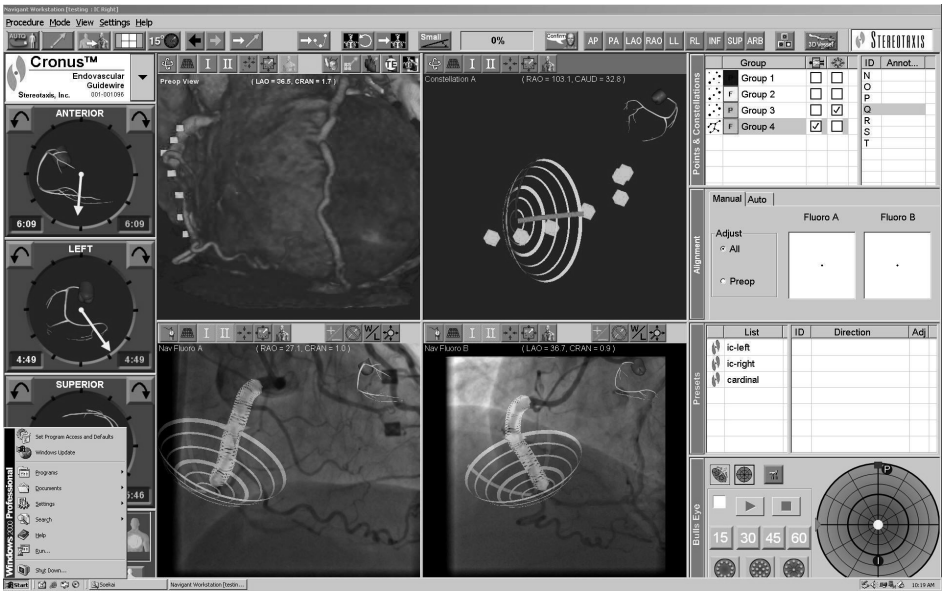

Figure 5. The Stereotaxis screen is shown with the integrated MSCT image and reconstruction made. In the upper panels the green dots indicate where attenuated tissue of previous vessel was seen on the MSCT, while the lower panels show fluoroscopy images with a superimposed three-dimensional reconstruction that follows the path identified by the MSCT. *See this figue in color in the Appendix page 377.*

Future Developments

The MNS is a flexible system and, as well as improvements in the areas described above, it can be expected that the current capabilities will be extended and further potential strategies will be discovered. This system is a platform that adds new abilities to conventional PCI. Some possibilities in both strategy and equipment currently under consideration are described below.

Newer and Improved Equipment

The newest system available offers tilting magnets for better imaging (the older system limits RAO and LAO projections to approximately 30° because of the magnets) and software upgrades. In addition, the current range of wires is being increased. A new intermediate-grade wire will increase the range of stiffness of the wires and a new blended nitinol-stainless steel wire may offer improved flexibility with memory. Further potential wire developments include coil magnet and multimagnet configurations of the wire tip that may offer increased flexibility within tortuous anatomy and better deformation in extremely tortuous segments.

Contrast Reduction

A further feature of the MNS is the ability to project a white line overlay onto the fluoroscopy screen. This can be used as a guide for wire passage and enables the operator to pass the wire with minimal or no use of contrast (26) (see Fig. 6). Contrast-induced renal dysfunction, and the dialysis needed in some cases, remains a cause of morbidity and mortality in procedures involving intravascular contrast (27). While some medical manoeuvres, such as fluid (28) N-acetyl-cysteine (29) and theophylline (30) administration, may confer some protection, evidence suggests that limiting intravascular contrast load to 100 mL may be a cutoff dose for the development of acute renal failure requiring dialysis (27). The ability to pass the wire without contrast may allow such a goal to be reached in patients with pre-existing renal problems.

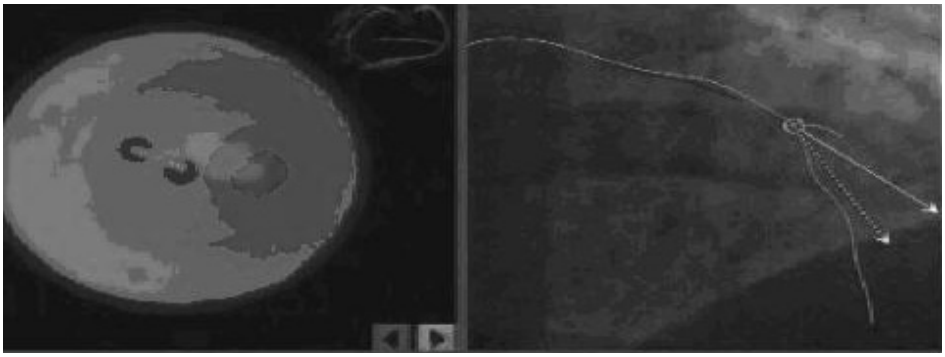

Figure 6. The left panel shows the endoluminal view that is synchronized with the position of the marker on the fluoroscopy screen. The right panel shows the fluoroscopy screen with the white line overlay, the dashed line is the desired vector, and the solid line is the applied vector (in this example the desired vector has just been moved and the applied vector is in the process of moving to that position). Note that these are live, moving, real-time images during a procedure. *See this figue in color in the Appendix page 377.*

Chronic Total Occlusions

In addition to the advantages described above for the treatment of CTOs, the ongoing development of a magnetically enabled radio frequency ablating wire may be highly advantageous. This will combine the current advantages of highly adjustable steering, the identification of the missing section of the vessel (shown by MSCT integration), and the ability to ablate intervening scar tissue.

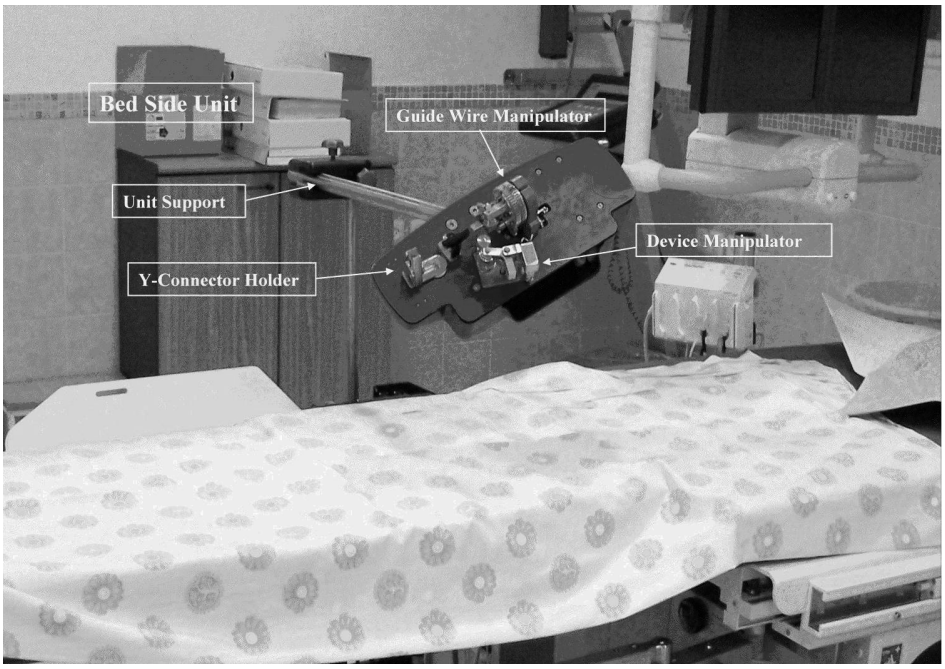

Figure 7. The Remote Navigation system® is shown in a catheterization suite. (Courtesy of T. Wenderow, CEO, Navicath Ltd.). *See this figue in color in the Appendix page 378.*

Remote Control

A further new concept in PCI is the ability to remotely control the delivery system. Remote control equipment (see Fig. 7) in the form of the Remote Navigation System® (Navicath Ltd., Haifa, Israel) has been successfully tested in both *in vitro* and *in vivo* models (31). This successful testing in models was mirrored by the successful use in the majority of a series of clinical PCI cases (32). Remote control procedures have already been shown to be possible in electrophysiology (6). Such remote control procedures have the advantages of more exact movement of wires. Wire advancement by a remote system could potentially be integrated with the MNS to advance the wire and change the magnetic vector in tandem thereby enabling robotic procedures. Theoretically such movements could even be gated

to the ECG to advance the tip and this might overcome some of the limitations of the static three-dimensional reconstruction. This combination would add the advantages of improved wire control to those of remote control procedures with reduction of irradiation of personnel and the reduction of collateral problems such as back pains from wearing lead coats.

Stem Cell Therapy

Stem cell therapy presents another possibility for MNS that may give both precisely directed delivery and also utilize integration with other forms of imaging. Intramyocardial injections of bone marrow–derived stem cells have been shown to have a potential for improving regional and global left ventricular function (33). However, delivery of stem cells to the correct areas has remained inexact with relatively crude methods of identifying where the injections are to be placed on delivery and where they have been placed on restudy. The identification of infarcted areas on MSCT (34) may add a further tool that can be integrated into the MNS for such target localization. The MNS gives highly precise three dimensional control and, with the possible development of a magnetically enabled injection catheter, the current MSCT integration may help localization of the infarct area to give a more tailored delivery. The combination of such localization techniques with the mapping abilities of systems like the recently developed NOGA® XP Cardiac Navigation System (Biosense Webster Inc./Biologics Delivery System Group, Diamond Bar, CA; Cordis Corporation) may give complementary information and result in more exact delivery. Integration of other digitized information from sources such as three-dimensional intracardiac echocardiography or magnetic resonance imaging could give functional data on improvements in wall segment motion.

LIMITATIONS

This new system has a number of weaknesses that may be considered in terms of software, hardware, strategy, and general limitations.

Software

The MNS software has many useful features; however, some aspects remain limited. Reconstructions are static images with no variation with respiration and heart motion, there is a restricted range of forward advancement along the virtual vessel to 1–5 mm per touch of the screen, and the alignment can be problematic. Vessel reconstructions are restricted to two branches and are based on angiography films alone resulting in limited resolution. Reconstructions of the exact vessel borders and hazy lesions may have poor definition leading to underestimation of stenoses and difficulty with sharp, short lesions.

Hardware

The equipment has some physical limitations such as the length of the wire tip magnet, which, with a standard of 3 mm, may hinder advancement in extremely tortuous and narrowed segments. In addition, the integration of other imaging modalities directly into the system remains incompletely explored.

Strategy

Strategies for using this system in the performance of PCI are under development and these will depend on the indication for the procedure. The system remains relatively new with limited operator experience and current strategies utilize ad hoc reconstruction of the vessel, which may be time-consuming during a procedure. The timing of the reconstruction may have an impact on image quality and readiness for use in procedures. The usefulness of the center-line overlay for the minimization of the contrast load is not yet clarified.

General

As a whole, currently, the system functions well. However, this system is still in further development and further refinements are expected. Furthermore, this system is an aid in the performance of PCI, so should problems occur or, in the worst-case scenario, the system fails, then standard PCI can be performed.

CONCLUSION

The MNS is a new platform for PCI that gives the operator more precise control of wire tip direction as well as broadening imaging and integration abilities. This system facilitates navigation for difficult vessels and CTOs, it gives useful control of direction derived from MSCT integration, and it may lead to a reduction in irradiation and discomfort to operators, personnel, and patients. For the future, the versatility of the system indicates further possible avenues for investigation such as reductions in contrast and irradiation, and navigable ablation and injection capabilities. Further investigation and development is under way.

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CHAPTER 3

Technology Insight: magnetic navigation in coronary interventions

SUMMARY

Magnetic navigation is rapidly emerging as a useful technology in the field of interventional cardiology. Precise control of the direction of a guide wire or a device in three-dimensional space offers a means to access vessels and areas of the heart that are often challenging to access with conventional methods. In this comprehensive Review, we detail the development of magnetic navigation technology and how this tool has been adapted for use during percutaneous coronary intervention. We aim to provide an up-to-date analysis of what is currently possible with this technology and an insight into what the future holds, particularly with respect to chronic occluded arteries and cell transplantation.

INTRODUCTION

The growth of interventional cardiology has led to numerous technological developments (1) the development of metallic and biodegradable stents that elute novel bioactive molecules (2); specialized guidewires with subtle differences for accessing different types of lesion (3); and various new pharmacological agents (4). One area that has not seen substantial progress thus far is the technology used to precisely guide a wire across a lesion. In most instances, crossing a lesion still relies heavily on both the skills of the interventional cardiologist performing the procedure and the mechanical properties of the guidewire. The Niobe® Magnetic Navigation System (MNS; Stereotaxis Inc., St Louis, MO) is a novel technology that can precisely control the tip of a magnetically enabled wire or device *in vivo* (5). Preliminary data suggest that the MNS could be useful in tortuous vessels or in complex lesions such as bifurcations, in which the initial bend placed on the wire might not be ideal for crossing tandem lesions (6). Magnetic navigation also means the wire is less likely to deviate into side branches, therefore, reducing radiation exposure and the amount of contrast required (7). The combination of dedicated magnetically enabled devices with three-dimensional (3D) imaging methodologies such as multislice CT (MSCT) and the NOGA® mapping system (Cordis Corporation, Miami Lakes, FL), can increase the accuracy in targeting chronic total occlusions (CTOs) and stem-cell implantation. To date, the transition of this technology into interventional cardiology has been slow. In many centers the MNS was first used in cardiac electrophysiological procedures, for which the benefits are well established; only now are centers extending the use of this technology to the interventional setting, despite the obvious advantages that the MNS offers. This somewhat cautionary approach stems from the fact that no randomized clinical trials have currently compared the MNS with older, more-established techniques. This issue clearly needs addressing, with future developments in both the software and hardware designs being investigated in timely clinical trials. At present, the expenses incurred in setting up an MNS will also influence its popularity. This Review discusses some of the major technological developments in the context of interventional cardiology and provides an insight into what is currently possible and what might be possible with this novel technology in the future.

Early developments

Vascular studies using magnetic navigation first began over 50 years ago when Llander (8), and later Tillander (9), used magnetic fields to guide an articulated steel-tip catheter in rabbit aorta. After these initial investigations, small external permanent magnets were used to stereotactically direct iron particles for thrombosis of intracranial aneurysms (10-12), later, rotating electromagnets were used, enabling better control (13). In 1991, Ram and Meyer performed the first magnetically guided angiography in a human. They successfully used a

magnetized catheter controlled with external permanent magnets in a neonate with anatomically complex congenital heart disease (14).

Despite initial success, further development was hampered by low field strengths, the need for large magnets and the lack of precise 3D control (15,16). In order for stereotactic localization and computer-controlled vector guidance to be possible, considerable advances in both medical physics and magnet design were required (17). Further advancements in these areas and the use of MRI coregistered with real-time fluoroscopy enabled the navigation of both a small object in a canine brain (18) and magnetically enabled catheters in pig brains (19). These experiments led to the MNS first being used in interventional radiology and cardiac electrophysiology, and now in interventional cardiology (20–22). Across these disciplines there are now more than 100 systems installed worldwide. It should be noted, however, that applying this technology in interventional cardiology presents a greater challenge than in more established indications such as neurosurgery. Unlike the brain, the heart is a dynamic structure, and the patient's chest moves with respiration.

The Niobe® magnetic navigation system

Navigation hardware

The Niobe® MNS (Figure 1A) has four key components: two permanent adjustable magnets mounted on mechanical frames situated at either side of the fluoroscopy table; navigation software (Navigant®, Stereotaxis, St Louis, MO) to control the magnets by creating a virtual roadmap and magnetic vectors after imaging data are gathered; a real-time fluoroscopy system to display a virtual map of the live image; and finally, a sterile touch-screen monitor for controlling the system, ideally placed at the operating table. In the second-generation system, Niobe® II, the mechanical frames enabling the magnets to be positioned were adapted to allow the magnets to translate or tilt about their axes. This tilting action enabled more angiographic projections— the previous version of Niobe® had limited right anterior oblique and left anterior oblique views because of the bulkiness of the magnets. The majority of systems are integrated with a modified C-arm flat-panel detector fluoroscopic imaging suite (AXIOM Artis *d*FC; Siemens AG, Malvern, PA), but there are systems that can also incorporate biplane fluoroscopic imaging and rotational angiography.

Biplane fluoroscopy has the advantage of reducing the amount of contrast used during image acquisition, but once the images are transferred into the Navigant® software the lateral C-arm must be stored in order for the magnets to be positioned. Rotational angiography, on the other hand, enables a 3D image to be generated directly from a single acquisition. When the patient is correctly positioned and isocentered, the magnets interact to produce a spherical magnetic field 15 cm in diameter and uniformly of 0.08 Tesla—the 'magnetic volume'. Within this volume any applied magnetic vector can precisely direct a 2–3 mm magnet mounted on the tip of a wire (Figure 1B) or steerable device so that a full 360° rotation can

be achieved. Clinically approved devices include guidewire and electrophysiological ablation catheters; other devices currently in development include coronary and peripheral ablative radiofrequency wires, multidirectional probing catheters, and catheters fitted with needles that are designed for cell implantation.

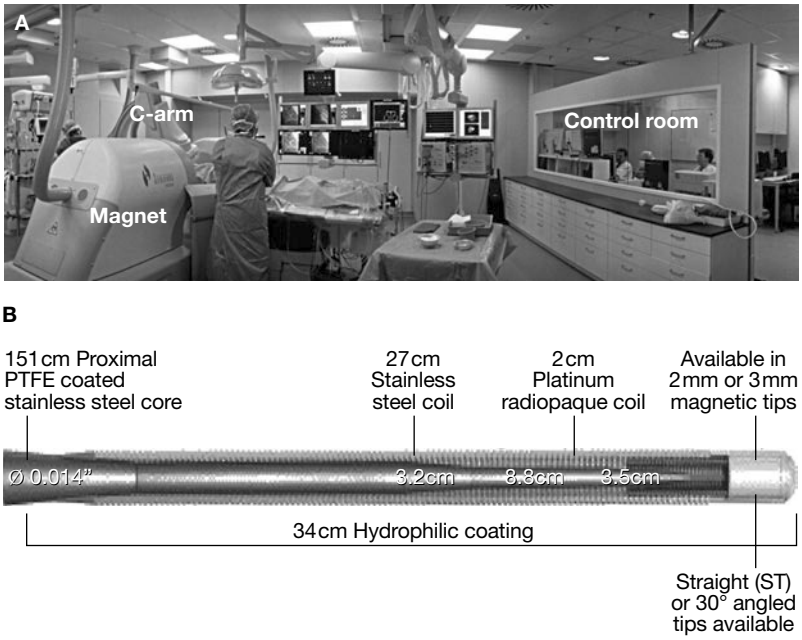

Figure 1. The Niobe® Magnetic Navigation System. (**A**) A typical magnetic navigation system set-up showing the magnets, C-arm and the control room. (**B**) The Titan® magnetic navigation wire showing the 2 or 3 mm magnet located at its tip.

Navigation software

Free-mode navigation Magnetic navigation is performed by presetting a magnetic vector using the touch-screen monitor. Following programming, the vector is displayed as a dotted line on the live fluoroscopy image, and the permanent magnets—illustrated by a solid vector line—move to align a magnetic field to this vector. Wire advancement is controlled manually to follow a desired incremental distance and is guided by either two-dimensional (2D) or 3D software features in Navigant®. The 2D navigational modes include the use of preset navigational vectors that are adapted to a particular coronary anatomy. This software also allows the user to create new presets if necessary, for example in patients who have vascular anomalies or to target coronary artery bypass grafts. Other approaches include the 'bulls eye view', which allows navigation around a central axis, and is, hence, a particularly useful technique for CTOs. The 3D Navisphere® program (Stereotaxis, Inc., St Louis, MO) is a spherical navigation object that contains regularly spaced polar lines (e.g. latitude and longitude lines). The aim of this program is to improve recognition of the 3D structure of the coronary

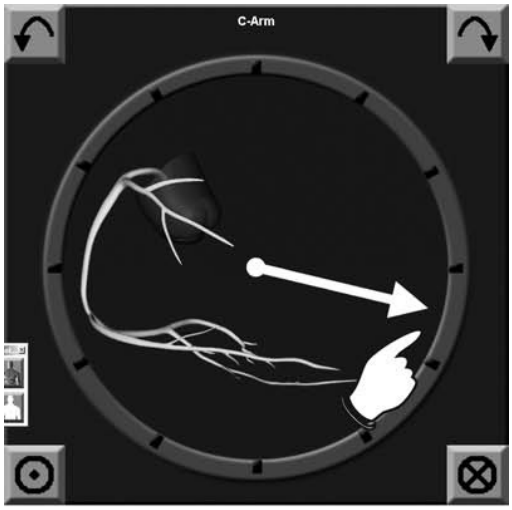

Figure 2. The clockface navigational mode. By touching the perimeter the vector moves in that direction; controls for anterior and posterior movements are at the edges.

artery tree. Navigation is also feasible through the 'clock face' mode, which mimics the dial of a clock (Figure 2). This technique permits fast navigation relative to other techniques, but does require some understanding of the spatial coronary anatomy. Direct anatomical navigation is possible by directly introducing a fluoroscopic image in Navigant®; however, 2D image representation of a 3D structure has obvious limitations. True-vessel navigation uses an accurate 3D representation of the coronary artery. Navigant® software can create such a virtual map from two X-ray images provided that they are 30° apart. This program uses a feature called constellations to map identical points on both images, thus, generating a 3D navigational path or 'centerline' through the vessel lumen (Figure 3A). Alignment of the centerline with the live fluoroscopy image is required for navigation. A 3D representation of the coronary anatomy and centerline can also be created from two fluoroscopic images using the CardiOp-B® software (Paieon Inc., New York, NY; Figures 3 and 4). The advantage of using this program is that it can limit vascular foreshortening (23) and improve the accuracy of quantitative coronary angiography measurements (24,25). Using this software, navigational vectors can be directed through a virtual representation of the vessel lumen, so subtle changes in the vessel morphology can be accentuated (Figure 3C) (26). A 3D road map can also be created from an MSCT dataset. The importance of MSCT in interventional cardiology stems from its ability to detect early-stage coronary artery disease (27,28), identify vascular anomalies and provide information on coronary plaques composition (29). Using Navigant®, the vessels can be isolated from the dataset and a 3D volume-rendered reconstructed MSCT image can be incorporated into the virtual roadmap for magnetic navigation (Figure 4B). The mapping of points along the vessel is used to create a virtual lumen and a centerline (Figure 4D), which is coregistered and aligned to the fluoroscopic image for navigation. The ability of

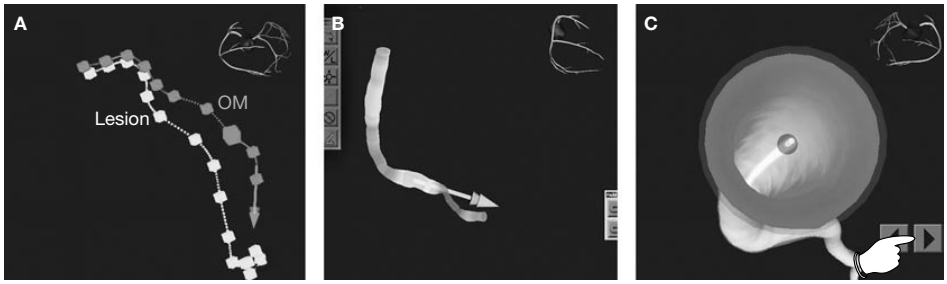

Figure 3. True-vessel navigation using an accurate three-dimensional representation of the coronary artery. (**A**) A constellation road map created from two-dimensional X-ray images; chosen points are depicted by squares along the navigational path. (**B**) Navigation using a three-dimensional reconstruction created with the CardiOp®-B software. (**C**) Navigation by means of the endoluminal view. Abbreviation: OM, obtuse marginal branch.

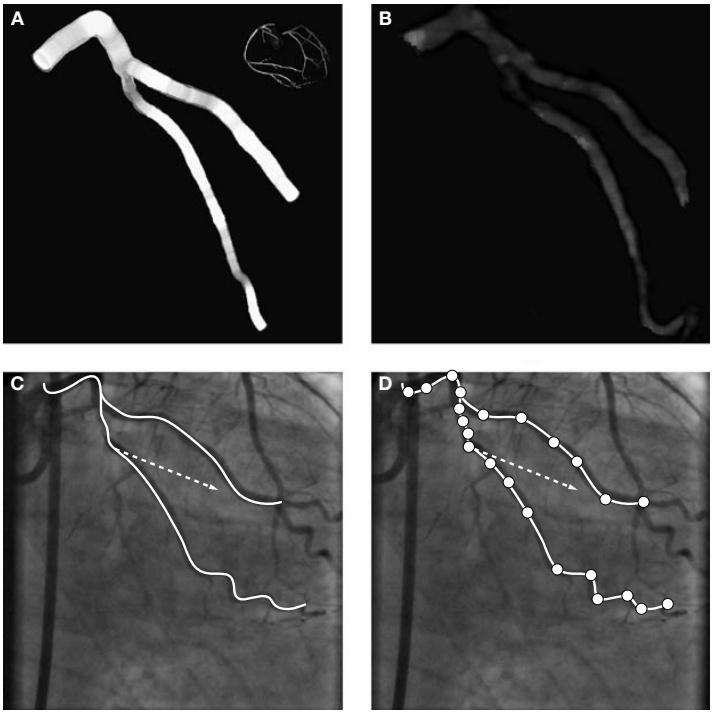

Figure 4. Three-dimensional representation of the coronary artery. (**A**) A threedimensional reconstruction of the artery using the CardiOp®-B software. (**B**) The same arteries extracted from a multislice CT data set (**C** and **D**), displayed as navigational centerlines with a directional vector on the live fluoroscopic images.

MSCT to 'fill in' the occluded vessel segments that are not seen angiographically means that it is a useful tool for navigating through CTOs (Figure 5A), with newer versions of Navigant® able to show both the endoluminal view and the multiplaner reconstructed cross-sections (Figure 5B).

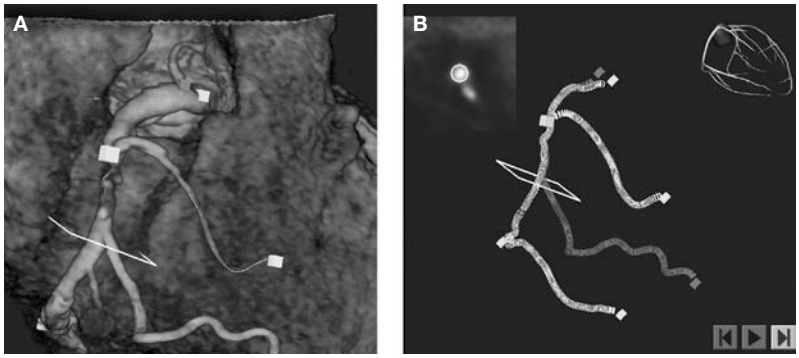

Figure 5. Using the Navigant® system the multislice CT data set can be used to create: (**A**) a road map of a chronic total occlusion not seen angiographically and (**B**) cross-sections along the map.

The MNS and intervention: What is currently possible?

Patent coronary arteries

Tortuous and severely angulated coronary arteries are associated with reduced procedural success rates and a raised incidence of CABG surgery (30). A guidewire must be maneuvered without causing complications such as dissection or perforation. Several phantom studies in hepatic celiac arteries and the cerebral arteries have demonstrated higher procedural success using the MNS than with manual manipulation, and shown that the MNS is easier, more accurate and faster even when used by inexperienced operators (31–33). Studies in a coronary phantom, however, reported longer crossing times with the MNS than with a standard wire, although fluoroscopic times were significantly reduced (34). The longer crossing times could have been related to the use of first generation Cronus® (Stereotaxis Inc., St Louis, MO) magnetic wires—subsequent generations have been easier to track. Indeed, a recent 2D phantom study using five increasingly tortuous vessel models found that as vessel complexity increased the newer generation wires—Titan® and Pegasus® (Stereotaxis Inc., St Louis, MO)—were significantly better in reducing both the crossing and fluoroscopy times than were conventional wires (35). Moreover, in some of the phantom models, prior experience of magnetic navigation was not a prerequisite for successful crossing. Overall wire usage was significantly reduced with the MNS. A seminal paper by Atmakuri *et al.* showed the effectiveness of magnetic navigation during percutaneous coronary intervention (PCI) in native coronary arteries that would have been difficult to cross with conventional methods because of severe tortuousity (36). In this study of 68 lesions in 59 patients, successful MNS crossings were achieved in 85% of cases. More importantly perhaps, magnetically guided intervention was successful in 9 (63%) of the 13 patients in whom PCI with a conventional wire had previously failed. The procedural success rates for magnetically guided intervention as the primary intervention and following failed conventional PCI ('secondary' intervention) were 84% and 62%, respectively, with longer median fluoroscopy and crossing times observed in second-

ary procedures. Similar success was reported in a study of 21 consecutive diseased coronary arteries, although guidewire navigation with the MNS was found to be slower than manual navigation (37). The patients enrolled in this study did, however, have simple, straightforward lesions indicating that the MNS could be more suitable for use in complex coronary lesions and as a secondary procedure following failed conventional wire placement. This theory is exemplified further by the successful results seen when the MNS was used following an unsuccessful alcohol septal ablation that failed because of severe angulation (130°) (38) and when used to cross a crushed stent of a bifurcation that was complicated by dissection (39). At present it is not clear how wide the applicability of magnetic-assisted navigation is likely to be in patent vessels. In order to evaluate this issue, our group has been assessing prolonged conventional crossing times to characterize the lesions and vessels that might be appropriate for magnetic navigation.

Occluded coronary arteries

CTOs have been described as one of the last frontiers in interventional cardiology (40). Despite advances in technology and the development of specialized devices and dedicated wires, the rate of successful crossings is still unsatisfactory (41). An attractive strategy for treatment of CTOs was postulated by Serruys in 2006 (1). The first stage of this strategy involves magnetic navigation to steer a guidewire through the occlusion. Second, optical coherence tomography, intravascular ultrasonography or MSCT cross sections are employed to 'look forward' within the vessel to ensure that the wire is ideally positioned in the true lumen. Finally, ablative power at the tip of the wire is used to recanalize the CTO (42). The first successful study to demonstrate the feasibility of MSCT angiography and magnetic-enabled PCI used a system that 'looked forward' at the occlusion—the bull's eye view—making the search pattern for microchannels through the occlusion more uniform by avoiding repetitions (43). Although mapping the occluded segments was easily accomplished, the bulky 2–3 mm magnetic tips used were a notable limitation. Furthermore, the fact that navigation was performed using a fixed roadmap (centerline) rather than a dynamic one gated to the electrocardiogram meant that there was discordance between the live fluoroscopy image and the centerline—another limitation. Ordinarily, when navigating through a patent vessel this discordance is not a problem as the wire is contained within the vessel's lumen, so that when the heart moves with each beat the wire can still follow the trajectory of the predetermined vectors. In CTOs, however, the lack of a patent lumen means that as the heart moves, the tip of the wire can be perpendicular to the vascular wall and when pushed can protrude. Hence, it is of paramount importance to develop technologies that allow dynamic road mapping (centerline) to be superimposed on the live fluoroscopy image, especially when considering magnetic enabled radiofrequency ablation. Paieon Inc. is developing a dynamic road-mapping system based on their software that can recognize systolic and diastolic phases on fluoroscopic images. This system might have a role in patent vessels or those with subtotal

occlusion, but not necessarily in CTOs because contrast media is needed to demarcate the vessel contours. Much more appealing are methods aimed at electrocardiographic phase gating of the MSCT derived centerline to the live fluoroscopic image following alignment to recognizable landmarks such as spinous processes and the catheter tip. This technique ensures that at a designated point in the cardiac cycle both the centreline and the live fluoroscopic image of the vessel are superimposed, enabling safe advancement of the ablating wire. Development of the magnetic enabled wire with radiofrequency ablation functionality is nearing completion (Figure 6). This device is composed of a 0.014 inch wire with a small radiofrequency electrode at its tip and three small magnets embedded proximally.

An external generator supplies the radiofrequency energy needed for ablation. A safety and feasibility pilot study of this wire in 'within stent' CTOs is planned for early 2008 at the Thoraxcenter, Rotterdam, The Netherlands.

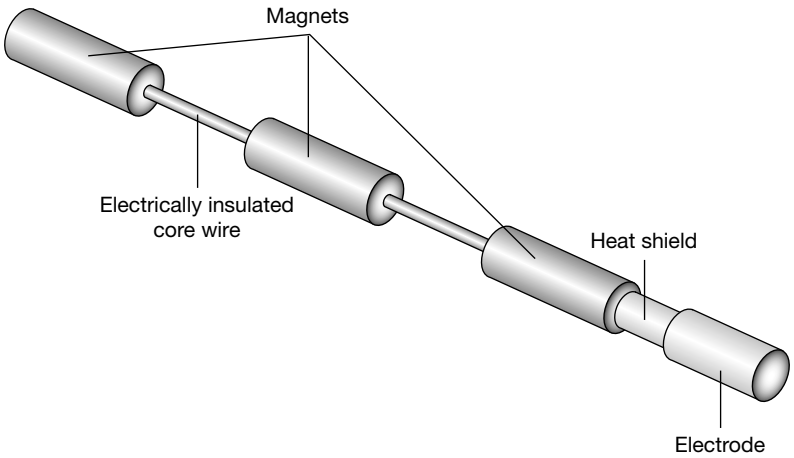

Figure 6. A diagrammatic representation of the magnetically enabled radiofrequency ablating wire for chronic total occlusions.

Stem-cell injection

Intramyocardial injection of bone-marrow derived stem cells is a novel technology that has the potential to induce myocardial regeneration and improvement in left ventricular function (44). Currently, electromechanically guided injection is the preferred mode of delivery in patients with chronic myocardial ischemia (45). Indeed, clinical studies have shown that transendocardial injections of stem cells using the NOGA® mapping system are feasible and safe (46). In this system, once the mapping electrode makes a good contact with the myocardium and the operator recognizes the appropriate electrical signal strengths, stem cells are injected through a needle linked to the device. One major drawback with this system is the difficulty of reaching remote areas of the left ventricle with manual manipulation of the catheter. This drawback can be addressed by using the magnetically enabled MNS-guided

NOGA® electromechanical mapping catheter (Stereotaxis Inc.; Figure 7). The guiding can be performed remotely to reduce operator radiation exposure. Moreover, the magnetic momentum at the catheter tip precludes the need for shaft support, allowing the use of a softer catheter that is less likely to penetrate the myocardium and cause a perforation. By using MSCT or MRI to identify the infarcted area, relevant data can be integrated into Navigant® to further augment the accuracy of target localization. A recent animal study showed the preclinical feasibility of Stereotaxis-compatible NOGASTAR mapping and MYOSTAR® injection catheters (Cordis Corporation, Miami Lakes, FL) both equipped with a small permanent magnet at the tip (47). Remote NOGA® mapping was possible with a computer-controlled catheter advancement system (Cardiodrive unit; Stereotaxis Inc., St Louis, MO). The introduction of the NOGA® map into Navigant® provided 3D vectors for the navigation of a magnetically enabled MYOSTAR® catheter. The combination of these technologies resulted in a 95.8% success rate of magnetic-guided injection of mesenchymal precursor cells into the myocardium. When labelled, cells were detected in all but one segment on histology.

Figure 7. A diagrammatic representation of magnetically enabled cell injection catheter following an automatic map in the myocardium.

What does the future hold?

Magnetic navigation is still in the developmental phase and as such will not revolutionize the way we currently perform PCI. By considering magnetic navigation as an adjunct technique to current practices, however, this technique could be used to beneficial effect in clinical situations that are technically difficult or associated with low procedural success. The development of both software and hardware is, therefore, in the context of adjunct therapy. More powerful magnetic fields (i.e. 0.1–0.12 Tesla, increased from the current 0.08) and software upgrades to further improve the precision of wire control are in development. In

terms of CTOs, future developments include dynamic road mapping and appropriate gating of the MSCT images with real-time fluoroscopic images. In addition, alignment between angiographically determined 3D reconstructed non-occluded segments and the occluded sections obtained through MSCT will be more accurate. Moreover, as MSCT cross-section analysis provides important information on plaque composition and can accurately identify the vessel's border—a 'true' centerline can be reconstructed by 'stacking' the gated cross sections if the center of each cross section (Figure 5B) is determined precisely. Incorporation of this idea in future versions of the Navigant® software is being contemplated, so that a gated wire can be advanced in a frame-like fashion to ensure central wire transit. The unwarranted complexity of several MNS workstations, which can slow processing speed, will be reduced in the future by a new single-screen user interface (Odyssey™ Network Solutions, Stereotaxis, St Louis, MO) that links diagnostic information from several sources. To further improve the speed of navigation without compromising safety there will, however, need to be improvements in alignment of the centerline to the real-time fluoroscopy image, possibly through dynamic electrocardiographic gating. This improvement would allow the operator to drag the vector with confidence, instead of using 1–5 mm jumps along the centerline. With this development, the MNS could then compete with conventional wires in all lesions, not just complex cases. New advances in material science have permitted the development of several guidewires with variable degrees of support and flexibility, tailored to individual coronary lesions.

The newest generation in wire design—the Pegasus®—is made from a nitinol–stainless steel composite for improved flexibility with minimal deformity. Future wire-related developments will include magnets that can change the stiffness of the wire to improve the delivery of a device, multimagnet configurations to enable smoother transition across the tip, and wires with the ability to feedback their position in space. The ability to accurately identify a wire's position can be useful when combined with a robotic wire advancement system. To date, such systems have been successfully employed in electrophysiological procedures (48,49) but have not yet been extended to MNS-guided PCI. A stand-alone remote navigation system (CorPath®, Corindus Ltd, Haifa, Israel) for wire advancement and stent deployment using a joystick to control the wire's axial (i.e. advance, retract) and rotational movements has been shown to be feasible (50), which opens the possibility of linking such a device to the MNS to achieve full automation.

LIMITATIONS

Even though the concept of directional wire guidance has been effectively realized, the areas in which the system offers a clear advantage over current approaches still need to be identified, which explains the slow market penetration in interventional cardiology. In addition,

apart from a few institutional registries, there are limited data on this new technology. The lack of randomized, controlled trials makes comparisons with existing technologies purely speculative. Furthermore, new operators experience a learning phase before achieving an adequate level of competence, irrespective of whether they are a physician or technical staff. Similarly, as the software develops, there is a need for continuing educational updates or seminars to ensure that operators are kept abreast of new developments. At present, the main limitation with the software remains the alignment of the virtual image to the real-time image. There is also a need for dynamic road mapping of the vessel; at present operators navigate through a static image. The 3D-reconstruction packages used still have limitations with respect to accuracies in tracing the vascular contours from which the central path for navigation is ultimately derived. The physical limitations of magnets attached to the wire tip could hinder advancement in extremely tortuous vessels, highlighting the importance of the multimagnet design that offers a smoother transition. Ultimately, the success of 3D magnetic-enabled procedures still depends heavily on the time it takes to prepare the road map. The time taken can vary enormously depending on the vessel characteristics and must, therefore, be taken into account during procedural planning. The 2D navigation approach is quicker; however, the level of accuracy is compromised.

CONCLUSIONS

Magnetic navigation in coronary intervention is rapidly evolving. State-of-the-art magnetic devices are now competing with conventional non-magnetically enabled wires and devices. These technological advances are creating new roles for stereotactic magnetic navigation, which in the future will include a wider range of invasive cardiac procedures.

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CHAPTER 4

Magnetically supported percutaneous coronary interventions

SECTION 1: MAGNETIC NAVIGATION

Magnetic navigation is the use of a magnetic field to re-orientate a magnetically-enabled wire or device. The field is directed by external magnets that are moved by a computer-controlled system. Each function of the system is designed to improve wire steering. This young technology could improve percutaneous coronary interventional procedures as it gives an unprecedented improvement in 3 specific and complementary capabilities, namely precise tip adjustability, computer-enhanced, image-guided tip orientation, and computer–enhanced image processing. This chapter will explore the benefits that revolve around these three capabilities.

Although this technology is relatively new, it already appears that this system can equal, and even improve on, current conventional wire technique. The efficacy of this system is becoming evident at a point in time that is relatively soon after its regulatory approval. The current usability, combined with the exciting potential of future developments, could result in a formidable adjunct to PCI.

The System

The Stereotaxis Niobe® magnet control system is an advanced cardiology instrument control system for use in a hospital interventional suite. It is designed to enable physicians to complete more complex interventional procedures by providing image guided delivery of catheters and guidewires through the blood vessels and chambers of the heart to treatment sites, see figure 1.

The current system combines the Navigant™ Work Station that runs the computer software control for the Stereotaxis Niobe® magnet positioning system. This magnet positioning systems moves two large neodymium-iron-boron (Nd-B-Fe) magnets mounted on mechanical positioners, see figure 1. These result in an interacting magnetic field that produces a predictable vector at their midpoint. Magnetic moment is generated on a magnet when the applied field is offset from a magnet's principal magnetisation axis and this causes the magnet to align with the external field. The computer-controlled, externally-applied, magnetic field aligns a magnet on the working tip of the catheter or guidewire to govern the tip direction. The system obtained regulatory approval for use in humans in 2003.

The current list price for the Stereotaxis system is $1.9 million. The size of a typical modern Stereotaxis interventional suite is 770 square feet (72 square meters). The cost of magnetic shielding generally ranges from $50,000–$100,000 and consists of minimal common steel shielding in the walls, ceiling and floor. There is a range of magnetically enabled Stereotaxis 0.014" guidewires, see figure 2, that are priced at a marginal premium over conventional

wires. All other PCI equipment is standard and compatible with the Stereotaxis guidewires and MNS.

Figure 1. System in position for PCI. M indicates magnets in tilt position for better lateral movement of the image intensifier. T indicates touch screen interface to give real-time instruction to the MNS. S indicates in-lab main screen monitor. *See this figue in color in the Appendix page 378.*

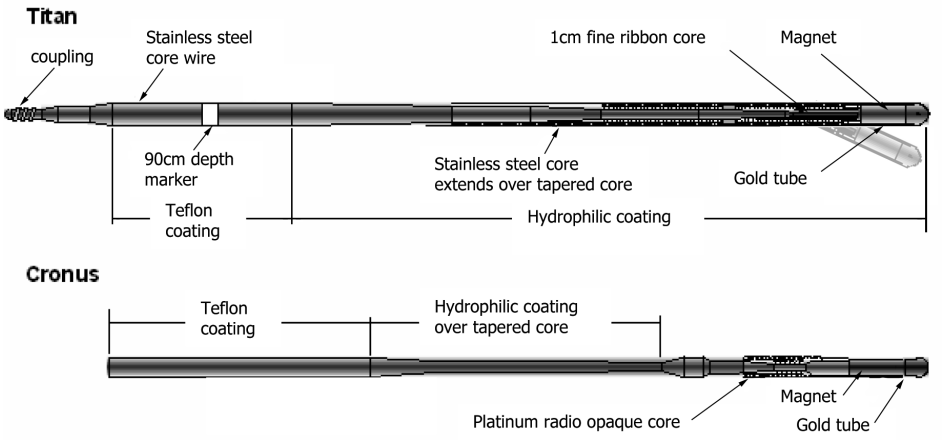

Figure 2. Schematic of the structure of the Titan Soft Support and Cronus wires. *See this figue in color in the Appendix.*

Limitations of conventional manual wire manipulation

Traditionally 2D fluoroscopic images are interpreted using the training and anatomical knowledge of the physician to estimate and probe for the correct wire orientation to enable passage of the wire or device through a vessel. The tip of a conventional wire has a fixed angulation that is shaped before insertion. This tip is manipulated at a distance of approximately 1m by rotating the part of the wire that is external to the guiding catheter. Conventional manual wire manipulation is therefore a process of trial and error that is inherently limited by a number of problems.

First the wire direction is judged from the 2D image seen on a fluoroscopy screen image that is seldom at exactly 90° to the coronary vessel and therefore susceptible to foreshortening. Foreshortening can become problematic by hiding angulations and even the entire lesion.

Second, rotation of the shaft to redirect the fixed tip, seen in 2D, is imprecise as it is not possible to judge whether the tip is pointing into or out of the screen. While steering is generally easy in straightforward coronary anatomy, difficulty may occur in the multiple bends of a tortuous, calcified vessel that increases deformation of the wire, affecting wire rotation and therefore control.

Third, the conventional tip angle cannot be varied in cases where anatomy varies from straight segments to highly angulated segments and back again, thus a compromise tip angle has to be made. In simple anatomy this angle is often not crucial, and the wire can be passed distally easily. However in tortuous vessels with multiple angles, this compromise angle may not be suitable for all angles and this may result in the tip pointing inappropriately into the vessel wall.

These factors combine in tortuous and difficult anatomy to restrict wire delivery, increase use of irradiation, equipment and contrast and, in the worst case scenario, reduce procedural success.

Abilities provided by the MNS

Magnetic navigation in percutaneous coronary intervention provides an unprecedented versatility that revolves around a number of capabilities.

Precise tip adjustability

As the magnetic field steers the front-end of the wire, the angulation of the tip can be exactly varied to the required angulation. This means that the tip can be kept co-axial to the vessel when crossing a straight segment and then directed at specific angles for tortuous bends or sharply angulated sidebranches. This control may help to prevent inadvertent sidebranch can-

nulation, facilitate the passage of extreme angulations or avoid dislodgement of friable material loosely attached to the wall e.g. in degenerated vein grafts or thrombus in acute lesions.

In addition, the magnetic field acts to stabilise the tip and tends to keep the tip pointing in the specified direction. This may reduce prolapse when resistance at the tip is encountered. This stabilisation of the tip at a certain angulation may improve the chance of the tip cleanly entering a tight lesion or a sidebranch.

Computer-enhanced, image-guided tip orientation

Orientation of the magnetic field in 3 dimensions is automatically achieved with the use of computer control. In practice this is done by using the preset vectors (standard 3D vectors derived from the average 3D direction of the coronary segment in 50 CT scans) or alternatively a patient-specific model from individually created 3 dimensional reconstructions of the patient's coronary arteries. This means that 3D information is integrated by the computer-adjusted magnetic field direction control to produce precise steering of the tip. Such 3D information may facilitate navigation in cases where the complexity may not be obvious on a 2D fluoroscopy screen.

Computer-enhanced image processing

The use of computers allows the production of digitalised images of the coronary arteries in great detail. These reconstructions can be made with the patient on the table or from previously acquired images. The fact that these images are digital allows post-processing that results in new ways to use the information giving new clinical applications such as the white-line overlay or the integration of MSCT.

The production of a patient-specific, tailored vessel reconstruction is performed with dedicated reconstruction packages such as the Cardi-Op B™ software, (Paieon Medical Inc., Rosh Ha'ayin, Israel) integrated in the Navigant™ Work Station, and the 3DCA software on

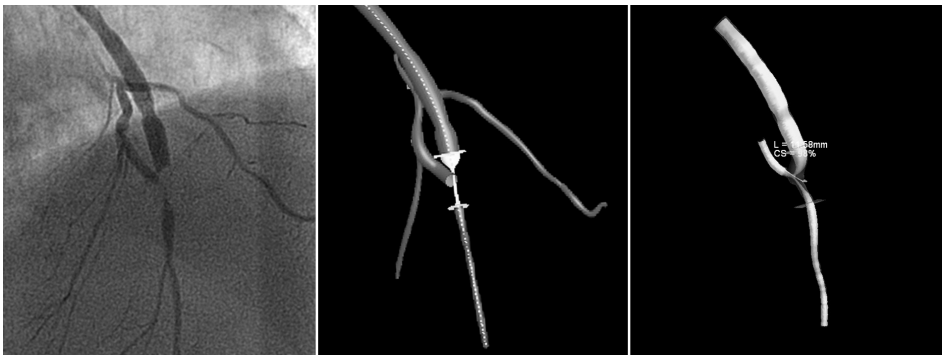

Figure 3. A severe lesion involving an anastomosis of a saphenous vein graft on a LAD. The left panel shows the angiographic image, the panel in the middle shows the Philips reconstruction and the right panel shows the Paeion reconstruction. *See this figue in color in the Appendix page 379.*

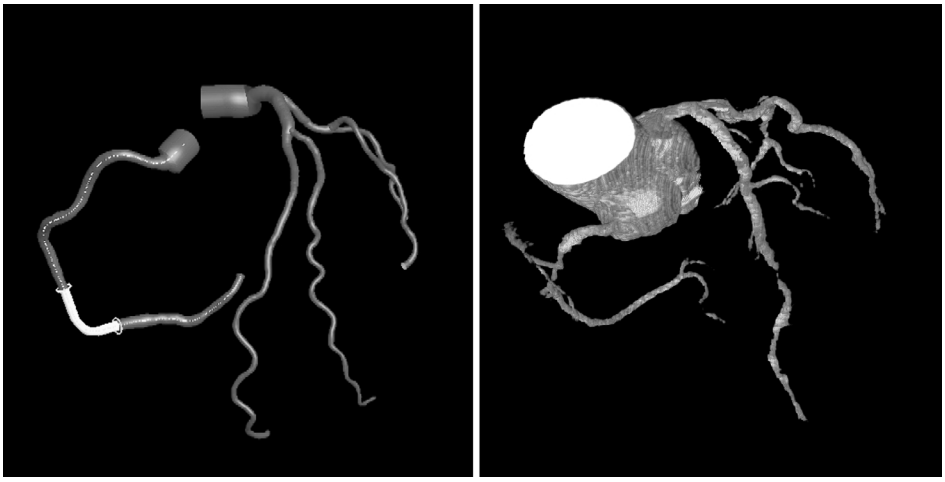

Figure 4. The left panel shows the coronary tree as extracted from MSCT by the Philips 3DCA system while the right panel shows the vessels extracted directly from CT by the Siemens package. *See this figue in color in the Appendix page 379.*

the stand-alone Interventional Tools workstation (Philips Medical Systems, Eindhoven, The Netherlands) (see figure 3). Both systems perform the reconstruction by triangulating points from 2 static images at different angulations at least 30° apart, but differ in that the Paieon system uses frames from 2 separate contrast injections at separate angles while the Philips system uses 2 frames from a single rotational acquisition. Frames are normally chosen in diastole to minimise movement artefact.

Current applications of post-processing

Computed centre-line

This is derived from the calculated center-line of the reconstruction and is currently used in two ways.

First, the centre-line provides the patient-specific 3D trajectory of the vessel that is the basis for the magnetic field direction control used by the Niobe® system. The system sets the magnet positions to produce this magnetic field direction and therefore the direction that the tip of the magnetic wire will align itself to. The reconstruction therefore gives not only an individual reconstruction but also an individualized 3D direction for every point along that reconstruction.

Second, the centre-line is the basis of a white-line overlay that is projected onto the fluoroscopy screen. As the MNS has the data on the angulation and position of the image intensifier and table, this white-line overlay is orientated at the appropriate angulation for the fluoroscopic view and changes in real-time as the image intensifier moves. This gives the operator a permanently visible roadmap on the fluoroscopy screen that automatically adjusts to the angle of view to which he can compare either the shape of the wire or the contrast image.

MSCT integration

The introduction of patient-specific information from non-invasive, off-table investigations has obvious advantages. The use of MSCT can provide a complete coronary tree model for use during the procedure. With cardiac MSCT becoming both more accurate and more available in the ER for diagnosis, the possibility of reducing the on-table procedural burden of time and contrast use becomes more realistic.

This benefit not only applies to patent vessels but may be more valuable in the area of chronic total occlusion (CTO). First, MSCT can visualise the distal section of an occluded vessel to enable the wire to be steered in that direction. Second, the trajectory of the occluded segment may be visible. Third, information regarding the consistency of an occlusion or the surrounding tissue may be obtained e.g. for the extent of calcification. This information may be valuable in assessing the chance of success, choosing the strategy needed or directing the wire. However, the true benefit in CTO may only be realised when the loop can be fully closed with accurate tip localisation and dynamic mapping.

Summary of potential advantages

The system therefore gives a number of theoretical specific advantages to the PCI procedure that can be coupled with specific functionalities.

Navigation

Tip adjustment	- the ability to bend and direct the tip as requested, even to extreme angulations.
Front-end steering	- the avoidance of friction affecting manipulation.
Precision direction	- for steering along a path or for probing patterns.
3D orientation	- the ability to reliably use the third dimension during wire passage.
Wire stabilization	- the exact selection and maintenance of a direction along a vessel or into a sidebranch.
Lack of tip rotation	- tip direction becomes independent of friction on the shaft and the tip movements become more controlled
MSCT integration	- Computer-enhanced patient-specific 3D information.

Operator

White-line overlay	- a patient-specific visual map projected directly on the fluoroscopy screen
Endoluminal view	- an 'internal' view of the vessel that can be useful for sidebranch orientation.
MSCT integration	- missing vessel segments, extra-luminal details.

Procedure

Reduced irradiation - reduced irradiation may occur from better navigation,

Reduced contrast - contrast-sparing strategies using of diagnostic angiography films or MSCT for navigation.

Shorter procedures - quicker and more efficient procedures not only benefit the patient but also the operator for example less irradiation or less time wearing protective lead coats

CONCLUSION

The system has a number of new capabilities that may bring advantages to a PCI procedure. Individually a specific advantage may not play a crucial role in each and every procedure but together may allow for smoother and less troubled wire passage. Ultimately magnetic navigation could potentially increase efficiency, reduce procedure time, facilitate the application of advanced technologies, decrease irradiation of the operators and thus better use hospital resources to lower overall hospital costs. The following section will review the current literature to assess whether there is support for these theoretical benefits and whether this is translated into a clinical benefit.

SECTION 2: LESSONS FROM THE LITERATURE

Publications to date fall into a number of categories

Reviews

These articles have introduced and given an overview of the technology (1,2). They have generally explored the currently evolving technique, describing the potential methods of utilisation and the situations where these may become useful. They have also introduced and previewed up-coming features and technology and speculated about the new areas where this technology may extend to the future such as remotely controlled procedures or stem cell injection.

Phantom studies

These studies have looked at the use of the magnetic navigation in artificial phantoms to assess manoeuvrability and indicate which vessels might benefit the most. The earliest study used a 3 dimensional phantom with channels representing the LAD, Cx and RCA (3). It was

performed soon after regulatory approval, and with an early version of the software at a time when operators had had minimal experience with the system. It compared the speed (procedure time) and the amount of radiation (fluoroscopy time) needed to pass a wire, either conventional or magnetic, to a particular coronary segment. In most segments this early iteration of the system did not show improvement in navigating most segments but only suggested benefit in distal lesions such as the RDP with reductions in procedure time and fluoroscopy time. An additional part of the study examined the use of the system in stented bifurcations and suggested an advantage.

A later study used a 2 dimensional Perspex® model with 3 and 2mm channels to compare the effectiveness of conventional and magnetic wires in increasingly tortuous trajectories as well as comparing Interventionalists with different levels of experience (4). This study showed that, while there was no significant advantage in more straightforward trajectories, magnetic navigation improved wire passage in the more tortuous trajectories. Furthermore in inexperienced hands the improved success rate was maintained in more complex lesions. This improved success rate was associated with a reduction in the number of wires needed to complete complex trajectories properly.

In conclusion, these phantom studies suggest a number of benefits and give some indication as to the areas where magnetic navigation may be particularly advantageous. First, there appeared to be particular benefit in tortuous trajectories with the suggestion that this technology may help in the treatment of bifurcation lesions. Second, there appeared to be improvement across all levels of experience. Third, there was a reduction in equipment use. However, phantom studies have the limitations of their artificial nature exemplified by their lack of movement, absence of stenoses, and an unnatural surface for wire passage and conclusions need to be drawn with caution and preferably should be mirrored by the findings of clinical studies.

Case reports

The use of magnetic navigation has been described in a number of specific cases. Such case reports not only describe the feasibility of using the system in particular circumstances but also showcase the capabilities of the system.

An early case report demonstrated the ability to complete failed conventional procedures. In this case, a primary PCI had been performed conventionally but the bifurcation stenting procedure could not be completed with a kissing balloon dilatation as conventional wires would not cross into the sidebranch despite prolonged attempts (5). Attempts to cannulate the sidebranch conventionally had produced an angiographically visible perivascular dissection parallel to the sidebranch. A further attempt to cannulate the sidebranch was performed later in the magnetic catheterisation suite. Here it proved relatively simple to cannulate the sidebranch and perform a kissing balloon dilatation. This led to a good angiographic result

with obliteration of the perivascular dissection. This case not only demonstrated the ability to complete a case that could not be finished conventionally but also exemplified a possible advantage in bifurcation lesions where wire passage through the side of the stent was required, echoing the results of phantom studies.

It is clear that such navigation might be useful in complicated emergency procedures and this message was reinforced in a further primary PCI case (6). In this primary PCI case procedure, material was more evident on one side of the vessel while crossing the lesion. The magnetic field was orientated to direct the wire away from the material. In addition, once flow was re-established, a bifurcation was seen. A bifurcation procedure was performed without incident. In this case the ability to steer the wire away from friable material and to steer without wire rotation (that would sweep around the circumference of a vessel and possibly dislodge material) could be an advantage in procedures where embolisation might be a risk such as primary PCI or diseased SVGs. In addition, the bifurcation proved easy to treat, again reinforcing a message about crossing a stent in a bifurcation.

A further demonstration of use in complex anatomy was described in a case that had proved resistant to conventional technique (7). In this case 2 previous conventional procedures had failed despite the use of 5 catheters and 7 guidewires. A patient-specific 3D reconstruction was made from on-table angiography to give a tailored path from the LMS via the Cx to a remnant section of open vein graft and then on to the posterior descending branch of the RCA that filled retrogradely. While this did not prove to be a simple procedure, as it required an over-the-wire balloon and a support wire, it demonstrates the ability of the system to successfully navigate an extremely tortuous trajectory. In addition it also cautions that, while the wire may reach distal territories, new strategies to allow delivery of angioplasty materials may be needed.

The system has also been described in a difficult case of alcohol septal ablation to cannulate the septal when conventional wires had failed (8). As it can occasionally prove problematic to enter septal branches, magnetic navigation may help to cross these extreme angulations. In this case there was a retroflexed 130° angulation of the origin of the septal artery that a number of conventional wires had failed to properly cannulate due to prolapse when attempting to advance more deeply. This case again demonstrates the ability of the system to navigate a single acute angulation that was impossible with conventional wires.

In conclusion these case studies demonstrate a number of points. They parallel the message from phantom studies regarding the usefulness of the system in bifurcation procedures, extreme angulations, and complex, tortuous anatomy. They show that the system is clinically useful in failed conventional cases, in primary PCI, and in cases where extreme care is necessary to avoid embolisation. However case reports are limited in that they are uncontrolled anecdotal reports that may have involved other factors than just the complexity of the lesion.

Technical reports

There are a number of reports investigating the performance of technical aspects of the system predominantly focussing on the accuracy of the measuring ability of the system (9,10).

These technical papers have both looked at the accuracy of calculated measurements of the dimensions of the reconstructions. In the first study, 22 angiographic images of precision-drilled plexiglass phantoms in pigs were compared both by the 3D reconstruction software (CardiOp-B™) and standard 2D software (CAAS II™). This showed that while there was good agreement of the 2 systems, underestimation was greater in the 3D system. A second study compared the 3D measurements with a newer 2D measurement system and showed a similar superiority of the 2D system. These results are not entirely surprising as the 3D reconstruction has been in development for a much shorter time than the 2D and in addition, it is important to realise that the 3D reconstruction software has been primarily designed to provide reconstructions rather than measurements. However the reports identify the interest in the potential of such 3D imaging technology and the emphasis on continued development of this software.

Feasibility studies

The feasibility of the system has been described by a number of centres and at various stages since the system obtained regulatory approval (11-14). A very early study examined general feasibility of passage of a wire in 68 lesions in 59 patients (11). This study describes some of the very first experience and, even at this early stage, showed a reasonable success rate of 88% in crossing the lesion. Many of these procedures were completed with a conventional wire but it was noted that in 4 procedures the conventional wire failed and the magnetic wire succeeded, and that 3 of these failures were through the side of a stent into a jailed sidebranch, again paralleling results from the phantom and case studies. A second study at the same institution, also performed soon after system acquisition, compared crossing with a magnetic wire and then crossing-over to a conventional wire in 21 lesions (12). This study included lesions described as having relatively simple and straightforward characteristics. The patients included were among the first 70 patients attempted at that institution. While on one hand, this study found significantly longer crossing times, more fluoroscopy and greater contrast use, on the other hand it showed a success rate for the magnetic wire of 90%. These latter 2 studies both used the first generation of magnetic wires and an early version of the navigation software and did not demonstrate a clear benefit.

A further study looked at a more difficult group of patients who were judged as difficult or impossible for conventional technique (primary attempt group, n = 46) or had failed conventionally (secondary attempt group, n = 13) (13). This study showed a reasonable success rate

of 84% in the difficult (primary) group and a rate of 62%, well over half, in the conventional failure (secondary) group.

A further feasibility study has shown the initial experience of a center soon after system installation on a less-selected group of patients more representative of daily practice (14). The success rates were again reasonably high at 86%. However an important note was highlighting of a problem with complex subtotal stenoses.

In conclusion, these feasibility studies show that the system is useable and gives reasonable success rates soon after system installation. However, there was no evidence of a clear superiority shown in these studies. However there has been some improvement with the newer generation of wires, newer software and more experience.

Comparative studies

The OLVG Registry (15) study provides the first large single centre patient series describing the results obtained using magnetic navigation for PCI. This patient series included every patient treated by magnetic navigation from day 1. The procedures were examined by subdividing the first 320 patients into groups of 80 to examine issues such as a learning curve, and comparing the total group with historical controls. This center was deliberately organised with a small group of staff highly familiar with the system in order to examine issues related to optimisation of the start-up of system use.

In this fairly complex group of patients, success rates were high at 92% and procedural parameters were at least within the limits of usual practice. This study clearly showed a learning curve with improvements of over 50% in fluoroscopy time between the first group of 80 patients and the latest of the groups. An estimate of a learning curve of approximately 100 procedures was felt to be needed under these circumstances (small, dedicated team, routine use of the system in terms of regularity and use in all patient groups). This improvement appeared to be across the board with reduction in procedure and fluoroscopy times and less contrast use. The system had a high initial success rates and was highly applicable and safe in day-to-day practice. The system was used with the both transradial and femoral approaches.

An important point is the identification of inferior results in certain lesion types, such as CTO or severely eccentric tortuous lesions, and such lesions frequently needed to cross-over to dedicated angioplasty wires.

The comparison with historical controls showed no significant difference in fluoroscopy and procedural times but a reduction in contrast use. Moreover, in the MNS group significantly more lesions per patient were treated, while procedural and fluoroscopy times were within the same range as the single lesion stent control group.

In conclusion the system was shown to be feasible, effective and there appeared to be reduction in contrast, irradiation and consumables that was particularly evident in complex

cases. A learning curve was demonstrated that has implications for the use of the system in other institutions.

Further analysis of this registry looked at particular sub groups with case matching to provide further insights into the effects. Cases have been matched for age, gender and vessel segment. In these case-matched groups, simple elective single vessel disease cases show a benefit with a reduction in contrast but no significant reduction in procedural or fluoroscopy time. However, complex cases show a significant improvement of all three of these parameters. The implications of this, if confirmed by randomised control trials, could be significant with two particular points of interest. First, the ability to reduce contrast even in simple cases may have implications for procedures in groups at risk of contrast-induced nephropathy. Second, this demonstrated a greater advantage in complex anatomy, not just in terms of success or failure but also in reduction in time, irradiation and contrast. This suggests that this technology may give particular improvement in the performance of complex, difficult cases.

Stem cell injection

A possible development in stem cell delivery by intramyocardial injection may result from use of a magnetically-enabled, dedicated injection catheter, see figure 5 (1,15,17). This catheter has been shown to be effective in cell injection and accurate in targeting predefined segments (16). The use of magnetic navigation may not only improve accuracy of delivery but may also enable better identification of suitable target areas as it allows easy, simultaneous electromechanical mapping with a combination of information derived on both movement (longitudinal linear shortening) and also electrical activity (unipolar voltage).

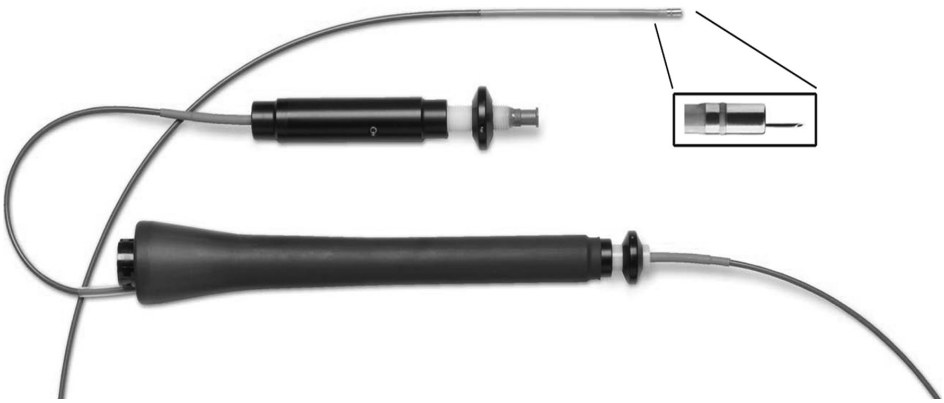

Figure 5. Stem cell delivery catheter combined with better electromechanical measurements. *See this figue in color in the Appendix page 379.*

Identification of difficult lesions

An important issue that emerges from review of the literature is the need for identification of the most appropriate lesions for magnetic navigation. A system that is based upon the 3D morphology of the vessel from 3D reconstruction has been described (18). This examined the time needed to cross a lesion using a conventional wire and correlated this to various anatomical factors. A registry of procedures (awaiting publication) suggests that there was indeed a trend towards less influence on crossing times times in vessels/lesions having high complexity scores. The ability to predict difficulty and a method of classifying and comparing complex procedures may help to define the patient population that would help derive the greatest benefit.

Summary of points from the literature

The system is both feasible and useable for clinical use in PCI.

Particular anatomy appears to derive particular benefit. These are tortuous segments, extreme angulation and bifurcations especially when crossing into sidebranches through a stent. These attributes clearly relate to complex or failed cases.

The literature indicates that use of magnetic navigation in such lesions may lead to benefit in terms of procedural time, fluoroscopy time and contrast use.

There appears to be a learning curve that may be optimised by the use of an defined, small group of users that regularly perform procedures. In addition early experience should not concentrate solely on difficult cases.

There may be a wider range of diverse clinical indications that may benefit from this technology such as alcohol septal ablaton or the delivery of stem cells.

LIMITATIONS

Procedural

Initial use of the system can be time consuming due to of a lack of familiarity with what is a complex system that requires the isocenter position, moving the magnets into the correct position, and time to reconstruct. However, once there is an established routine, these manoeuvres become fluid and quick.

Care is suggested with intracardiac devices such as pacemakers and AICDs as the magnetic field may affect function. While no problems have been described thus far, the effect of a magnetic field on the device should be ascertained beforehand e.g. fixed rate pacing for pacemakers or inhibition of shock delivery for AICDs. Settings should be checked before and

monitoring should be in place when the patient is brought into the magnetic field. A further device check is advisable after the procedure.

Software

The angiographic reconstructions still have a number of weaknesses. First, the reconstructions produced are susceptible to error if the diagnostic images are of poor quality. Angiographic images that are foreshortened in one or both views may severely underestimate the true angulation, a problem that is not infrequently seen in reconstructions of the LMS where the wire may not get enough angulation to turn into the appropriate major vessel. Second, the precision of the reconstructions is marginal. As seen with the technical reports, dedicated systems for measurement perform better then the systems used for navigation, this may have consequences and influence the accuracy of the models and therefore the accuracy of navigation. Third, the reconstructions are static and normally taken from diastolic frames. This has repercussions on passage of the wire at other phases of the cardiac cycle as the diastolic direction may be different to the direction in systole for the same point in the vessel.

On a minor level, the WLO is static and may exhibit a distracting scissoring of the WLO and the fluoroscopic image.

The software is constantly under development to optimize ergonomics.

Hardware

Wires

The wire-tip is a solid magnet that is 3 or 2mm long. Clearly, this does not have the flexibility of conventional wires that have a long history of development. This mainly leads to two problems:

Narrow channel angle grip

If calcium or tough scar tissue is present in an angulation it may prevent deflection of the tip and maintain an orientation that directs the tip into the vessel wall and into the intimal layer. It can be physically impossible for the solid inflexible wire tip to pass through a narrow, highly angulated channel, see figure 6. This may explain the results in sub-total and chronic total lesions that may involve sharp turns in calcified scarred tissue on a microscopic level.

Wire lock

The solid wire tip can become trapped behind stent struts or calcium. Traction on the wire will lead to a kink at the junction of wire and magnet and the wire becomes 'locked', see figure 7. At this point the risk of wire fracture becomes high. The problem can be avoided by

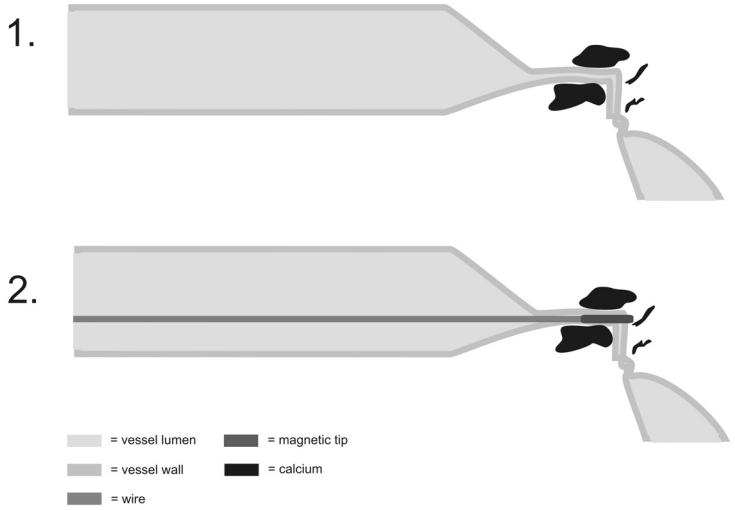

Figure 6. Schematic showing the wire tip attempting to turn a tight bend and being forced into the vessel wall.

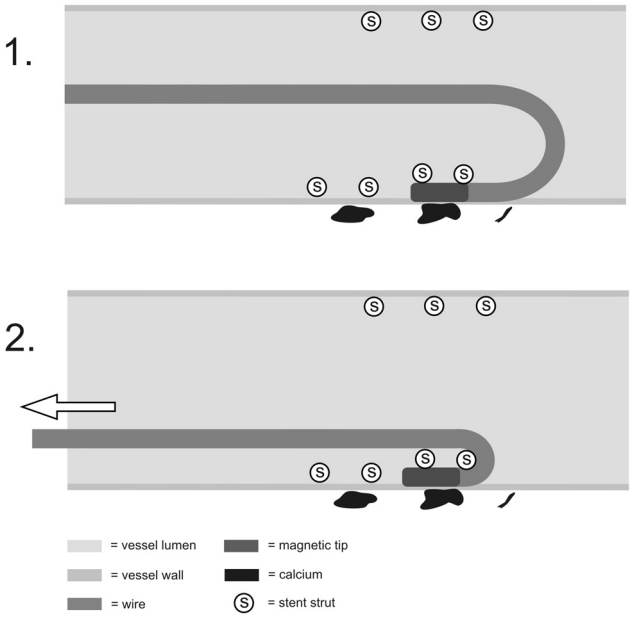

Figure 7. The two stage process of wire lock

ensuring correct tip orientation during the procedure and can be reversed by advancing the wire tip, possibly supported with a balloon to free the tip.

A range of new wires such as the Pegasus and multi-magnet wires may alleviate these problems.

Magnets

The magnetic field direction control is achieved by the movement of heavy solid external magnets on the positioners. The inertia of these magnets means that the response time is slow and, for example, is one factor against the development of dynamic roadmaps.

CONCLUSION

New technology frequently suffers from slow uptake. This technology is relatively new with limited market penetration due to a combination of factors. This has resulted in this technology for PCI being restricted to a few pioneer institutions and results from factors such as the limited amount of evidence that is currently available due to the limited time since regulatory approval combined with the system cost and the investment in time and effort to learn the technique.

SECTION 3: FUTURE DEVELOPMENT

Clinical

Data is now accumulating from studies as to the possible clinical advantages of using the system and strategies to enhance the learning curve are developing (14). More data is needed from randomised trials to convincingly show benefit and to identify which strategies, anatomy and patient groups can benefit the most. Methods for identifying, classifying and comparing complex procedures need further development

Technological

Future directions for research should include improvements in the software design and advancements in the hardware such as wire technology, RF ablation wire see figure 9 and remote control equipment, see figure 9.

Software developments include newer versions of the Navigant™ software. In particular, ease of use of current functions and improvements in integration are planned.

Hardware projects in development include a magnetically controllable RF wire for hard and tough lesions, figure 8 remote control system, figure 9 and the Odyssey screen, figure 10.

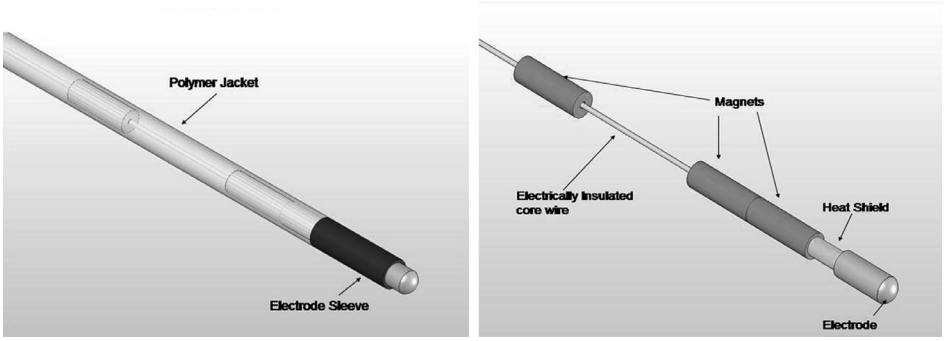

Figure 8. Magnetically controllable RF wire for hard and tough lesions. *See this figue in color in the Appendix page 380.*

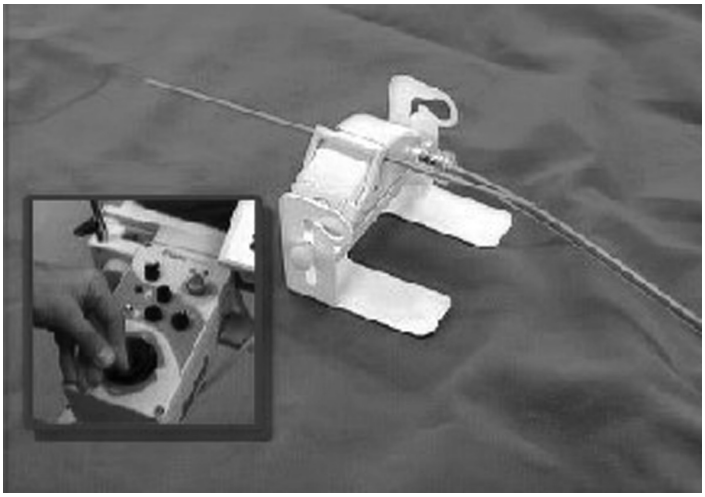

Figure 9. Remote control system. *See this figue in color in the Appendix page 380.*

Figure 10. Odyssey screen. *See this figue in color in the Appendix page 380.*

SECTION 4: CONCLUSION

This new technology combines precise tip control, with image guided steering and the flexibility of computer enhancement. The 3D reconstruction of a virtual coronary artery can be performed in real-time while the patient is on the table during an interventional procedure. These images may not only give a better appreciation of the anatomy with regards to tortuosity but also give a volume-rendered model with the computer-calculated magnetic field direction control that allow magnetic navigation. These individualised, scale models supply the directions for deflecting the wire as it passes through the vessel.

The current advantages of this system in PCI include precise tip orientation, image-guided computer control and computer-enhanced image-processing. The current literature shows that there may be advantages of the system compared to conventional technique. Specifically, vessels with severe angulation(s), tortuousity, and particularly bifurcations that involve crossing stent struts may derive the greatest benefit. However, sub-total calcified lesions may prove less attractive with the current wire configuration. Identifying the appropriate classes of lesion may reinforce the benefit with respect to time, irradiation and contrast use that could have knock on effects on complications (such as contrast-induced renal dysfunction), the complexity of procedures (such as particularly complex or failed conventional procedures and on new areas of intervention).

This new technology could transform the practice of interventional procedures with the introduction of computer enhanced imaging and guidance that revolves particularly around the production of 3D models.

ACKNOWLEDGEMENT

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PART II

Feasibility in phantom models, and initial system development

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Eurointervention 2007;3(1):100-108.

CHAPTER 5

In vivo validation of a novel three-dimensional quantitative coronary angiography system (CardiOp-B™): comparison with a conventional two-dimensional system (CAAS II™) and with special reference to optical coherence tomography

ABSTRACT

Aims: To validate a novel 3-D QCA system (CardiOp-B™) and compare the 2-D (CAAS II™) and 3-D systems in *in vivo* experimental settings. The phantom lumen diameters were also assessed *ex vivo* by optical coherence tomography (OCT). The accuracy of the 3-D system has not been appreciated.

Methods and results: Precision-drilled plexiglass phantoms with 5 different luminal diameters that ranged from 0.5 to 1.9 mm were percutaneously inserted into the coronary arteries in four Yorkshire pigs. Twentytwo angiographic images of the artificial phantom coronary artery stenoses in the pigs were acquired as an in vivo validation test. Quantitative assessments of the minimum and mean lumen diameters were performed using both QCA systems. Ex vivo images of the same phantom lumens were also taken and measured using OCT. Both of the 2-D and 3-D QCA systems significantly underestimated the actual phantom lumen diameters with the exception of measurements taken in the lateral projection at isocenter using the 2-D QCA systems. This underestimation was more significant in the 3-D system (accuracy of 0.19 at isocenter; 0.23 by catheter calibration). There was good agreement between the two QCA systems. OCT measured the ex vivo lumen diameter of plexiglass phantoms precisely.

Conclusions: The accuracy of the luminal diameter measurements with the current 2-D system was still superior to the 3-D system. Further development and validation studies under various conditions are warranted. The excellent results achieved by OCT with the *ex vivo* images indicate its potential as an intravascular quantitative imaging tool for future clinical practice.

INTRODUCTION

The field of quantitative coronary angiography (QCA) has undergone substantial improvement since the first automated QCA developments took place 1980's (1). Two major clinical applications have stimulated this improvement: 1) the on-line use during coronary intervention procedures in catheterisation laboratories; 2) the use as an angiographic endpoint for the assessment of stent or pharmacological treatments in experimental and clinical trials. On the other hand, the use of two-dimensional (2-D) interpretation of lesion or vessel anatomy and the lack of information about the vessel wall (other than for calcification) are well known limitations of current angiography and are situations where intravascular ultrasound (IVUS) can provide supplemental information. Development of online three-dimensional (3-D) vessel reconstruction systems based on angiography may be a solution to the former limitation. The concept of 3-D reconstruction of coronary tree was postulated as early as the 1980's (2). The routine use of a 3-D quantitative angiography system in the catheterisation laboratory could be a major improvement in interventional cardiology. Recently, a novel 3-D visualisation and quantitative analysis software system (CardiOp-B™, Paieon Medical Inc., Rosh Ha'ayin, Israel) has been introduced. This newly developed software system uses the detected vessel contours in two projections during coronary angiography to visualise a 3-D reconstruction of an arterial segment. Quantitative results are presented based on the reconstruction. Its utility and potential advantage over 2-D QCA systems has been reported (3,4). However, to date there have been no studies determining the accuracy of the 3-D quantitative angiographic technique by the *in vivo* measurement of precisely known vessel lumens. Our group has implemented *in vivo* validation techniques using radiolucent cylindrical plexiglass or polyamide stenosis phantoms with precision-drilled eccentric lumens in the field of quantitative angiographic analysis (5-7). The aim of this study was to validate a novel 3-D QCA system (CardiOp-B™) and compare the 2-D and 3-D systems in *in vivo* experimental settings that simulated a diagnostic coronary angiogram. Aside from the primary objective, we also tested the accuracy of optical coherence tomography (OCT), a light-based imaging modality with a high resolution (10 μm), in the ex vivo measurement of lumen diameter using the same plexiglass phantoms. This additional examination was performed in order to investigate its potential as a quantitative intravascular imaging modality in the future.

METHODS

This study was conducted according to the guidelines of the American Heart Association on animal use in research and was approved by the ethics committee on animal experimentation of the Erasmus Medical Center.

Plexiglas stenosis phantoms

The stenosis phantoms were manufactured at the workshop of the Erasmus Medical Center. The phantom stenoses that were used consist of radiolucent plexiglass (acrylate) and polyamide cylinders that have had precision-drilled circular lumens of 499 (aimed to be 0.5mm), 707 (0.7 mm), 982 (1.0 mm), 1,367 (1.4 mm) and 1,921 μm (1.9 mm) in diameter (Figure 1). The outer diameters of the cylinders are 3.0 or 3.5 mm; the mean lengths of phantoms are 8.28, 7.96, 7.85, 8.01, and 7.38 mm in 0.5, 0.7, 1.0, 1.4, 1.9 mm diameter phantoms, respectively. Optical calibration of the stenosis channels using 40 fold magnification gives a tolerance of 0.003 mm. A second 1.3 mm diameter lumen, parallel to the stenosis lumen, has been drilled in the cylinders to enable their attachment to the tip of 4 Fr Fogarty catheters (Vermed, Neuilly en Thelle, France). The lumens of the Fogarty catheters contained a removable metallic stylet that aided the intracoronary insertion of the phantoms as well as their positioning in the radiographic isocenter. Details of our experimental approach to QCA validation have been previously described (5-7).

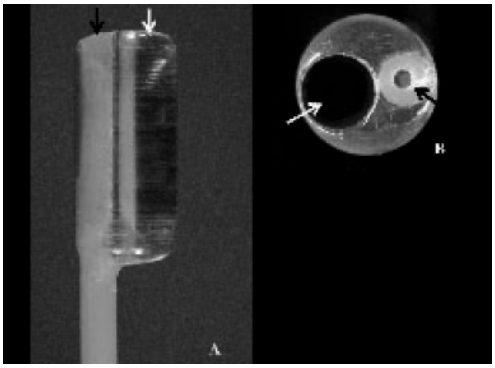

Figure 1. A: The magnified tip of one of the Fogarty catheters used for mounting the phantom. Note the transparent radiolucent cylinder connected to the tip of the catheter with a channel of 1.9 mm diameter (white arrow) and the catheter lumen used for insertion of removable metallic stylet (black arrow). B: The catheter tip photographed perpendicularly to the long axis of the phantom lumen. Note the almost perfect circular aspect of the precision-drilled lumen (diameter 1.9 mm, white arrow). The catheter lumen used for insertion of metallic stylet is indicated with a black arrow. *See this figue in color in the Appendix page 381.*

Animal preparation

Four Yorkshire pigs (average weight, 40 to 45 kg) were pretreated with intramuscular ketamine (20 mg/kg) and intravenous etomidate (5 mg/kg). The animals were then intubated and ventilated with a mixture of oxygen and isoflurane. Anaesthesia was maintained with a continuous intravenous infusion of pentobarbital (5-20 mg/kg/hour). 12 Fr introducer sheaths were inserted into both carotid arteries to allow the sequential insertion of the guid-

ing catheter and phantoms. Jugular access was used for the administration of medication and fluid. An intravenous bolus (10,000 IU/l) followed by a continuous infusion of heparin was given.

In vivo image acquisition of stenosis phantoms by fluoroscopy

The digital angiograms were obtained with a biplane cine angiographic system (Axiom Artis™, Siemens, Forchheim, Germany) that employs a matrix size of 1,024 x 1,024 pixels. The radiographic system settings used were the same (kVp, mA, ms) in all projections. All phantoms were imaged in two projections simultaneously. After engaging the 6 Fr guiding catheter (Mach 1™, Boston Scientific Corp., Natick, MA, USA) in either the left or right coronary artery, intracoronary isosorbide-dinitrate (1 mg) was administered. The first angiogram was then performed for orientation purposes. The phantoms were wedged in the coronary arteries and positioned in the Xray isocenter using the tip of the metal wire as a marker. The wire was removed prior to angiography. Coronary angiography was performed by manual injection of contrast medium (Visipaque™ 320 mg I/ml, Amersham Health B.V., Eindhoven, The Netherlands). The ventilator was disconnected transiently during contrast injection to minimise the effect of diaphragmatic movement on angiographic images.

Calibration

Two different calibration methods were used during off-line analysis.

1) Calibration at the isocenter: this method was performed using an automatic isocentric calibration - this is one of the calibration options of the biplane angiographic system. The calculated calibration factor is used for 2-D and 3-D QCA analyses by entering the number in millimetres in the manual calibration mode;

2) Conventional catheter calibration: the non-tapering part of the tip of each 6 Fr guiding catheter filled with contrast was used as a reference.

Quantitative angiographic analysis of ex vivo and in vivo phantom images

The off-line measurement of the minimum lumen diameter (MLD) and the mean lumen diameter (mean LD) were performed by 2-D QCA (CAAS II™ version V2.0.1, Pie Medical Imaging, Maastricht, The Netherlands) as well as by 3-D QCA system (CardiOp-B™ version 1671017, Paieon Medical Inc.). For in vivo analysis, an end diastolic cine frame was selected. Manual edge correction is an option available in both systems, but this was intentionally never allowed in the present analyses. In the 2-D system, a restriction option was applied in order to correct for an unsatisfactorily detected contour in one image. This option is not technically a manual correction, but offers users the possibility of excluding parts of the image of the

detection by restricting the area of interest. For the one measurement with the 3-D system, the automatically determined stenotic segment was manually corrected to avoid the measurement of the MLD at the site of a discrete intraluminal filling defect. Minimum values as well as mean values were determined as the diameters of the stenosis phantom lumens. Each angiographic image that was analysed or calibrated (for catheter calibration) was designated specifically by the number of the frame count so that all of the analyses using both QCA systems were performed upon identical images.

2-D QCA system

The diameter of the stenosis phantoms was calculated with an automatic contour detection technique. The user is able to define a number of centreline points within the vessel segment. The frontal and the lateral images are analysed separately. The mean LD of the phantom lumen is obtained with the CAAS II™ system from a user defined region of interest (ROI) where the two vessel contours are considered to be parallel (Figure 2).

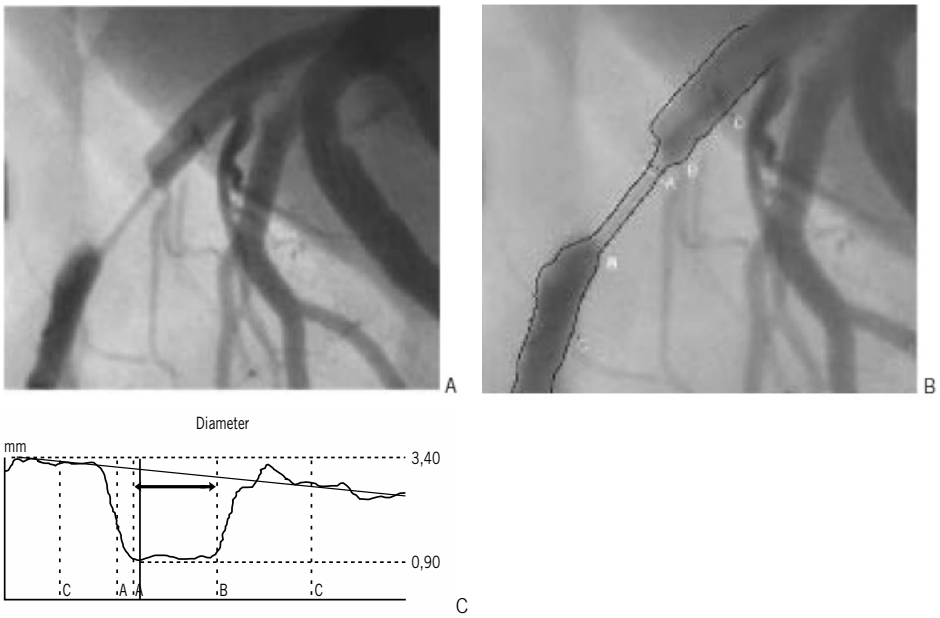

Figure 2. Angiographic visualisation of the artificial coronary obstruction produced by a 1.0 mm stenosis phantom in the left anterior descending artery (A) with subsequent quantitative measurement of luminal diameter by 2-D QCA system (CAAS II™) (B, C). The bidirectional arrow indicates the region of interest for mean luminal diameter (C). *See this figue in color in the Appendix.*

3-D QCA system

This system uses the contours detected in the frontal and lateral images in combination with the projection data in the DICOM format into a 3-D reconstruction of an arterial segment. The two acquired images that are used for reconstruction must differ by an angle of at least 30 degrees. In this study, two orthogonal views, simultaneously acquired by the biplane system, were used for reconstructing a 3-D vessel image. If calibration was performed in one view, further calibration was not requested in the second corresponding view. To perform quantitative analysis, the user is requested to mark three points: proximal and distal reference points and point within the stenosis. The severity of the stenosis is indicated by the colour given by the computer to the reconstructed segment that varies from white (healthy vessel) to dark red (99% cross-sectional area stenosis) (Figure 3). The minimum luminal diameter values are automatically given as one of the default quantitative data. As mean LD within the user-defined ROI is not automatically supplied in this system, we obtained the values using a text import wizard of MS Excel 2003. The current version of 3-D QCA system does not provide quantitative degree of vessel curvature and bifurcation angle between main and side branch.

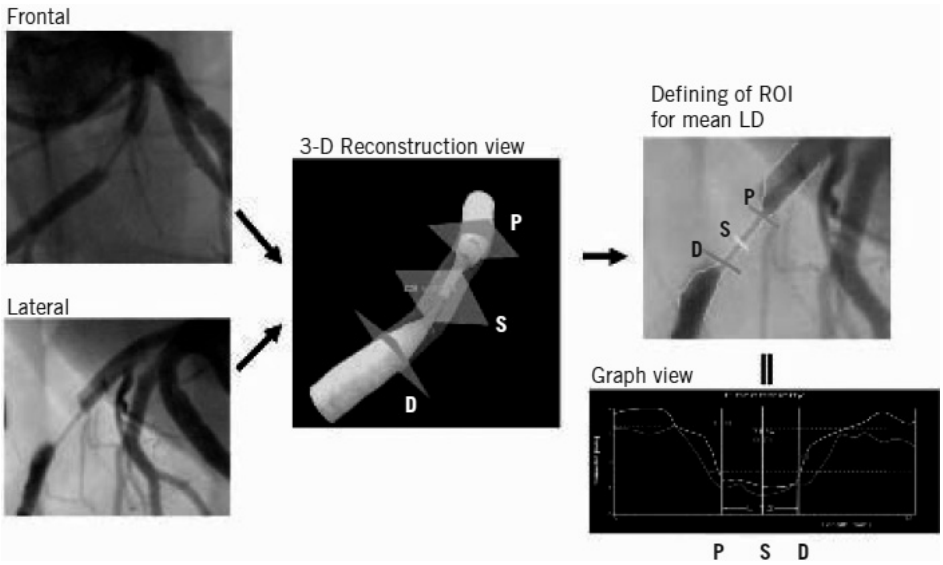

Figure 3. Illustration of the 3-D reconstruction process by CardiOp-B™. Color-coded 3-D reconstruction of coronary artery with artificial stenotic segment (3-D Reconstruction view) is derived from 2 orthogonal views (Frontal and Lateral). The 3-D colour varies according to the severity of stenosis ranging from white (healthy vessel) to dark red (99% cross-sectional area stenosis). The squares in pale blue, yellow and green denote proximal reference point (P), most stenotic point (S) and distal reference point (D) of the target lesion, respectively. The region of interest (ROI) for calculation of mean luminal diameter can be manually defined by moving the proximal (P) and distal (D) points (Definition of ROI for mean LD; Graph view). *See this figue in color in the Appendix page 381.*

Ex vivo image acquisition of stenosis phantoms by OCT

We prepared a fluid mixture containing 90% degassed water and 10% ethanol as an ex vivo replacement for blood. The room temperature was kept at 22 °C. These conditions are similar to those required for the preparation for an ex vivo validation of intravascular ultrasound (8,9). The OCT wire was inserted into the five differently sized phantom lumens. Images were obtained with the M2 OCT imaging system (Lightlab Imaging, inc.). The M2 OCT system uses a 1,310-nm broadband light source to produce images with an axial resolution of 15 µm and a lateral resolution of 25 µm by the principle of interferometry. The M2 uses the ImageWire™ imaging probe to deliver light to the tissue and collect the returning signals. The ImageWire™ consists of 0.006-inch (0.15 mm) fiberoptic core, inside a sheath with a maximum o.d. of 0.019 inch (0.48 mm).

OCT image analysis

The images were stored for off-line analysis in the OCT system computer. The analysis was performed using proprietary software from Lightlab Imaging, Inc. with a mouse based interface. The system was calibrated to the reflection of the OCT imaging wire that is the standard calibration technique for this system. Lumen diameter and lumen area in each of the 5 phantoms were measured.

Intra- and inter-observer variability assessment

Two independent observers, who were blinded to the real phantom diameters, assessed reproducibility by measuring the minimum and mean luminal diameter using each of the two QCA systems. In the *ex vivo* cases imaged by OCT, only the cross sectional diameter was analysed and used for evaluation of reproducibility. These examinations by two observers were performed on different days. One of the two observers performed second measurements on different days for assessment of individual reproducibility.

Statistical analysis

The individual values for minimum and mean luminal diameter obtained by both QCA systems were compared with the corresponding values of the phantom by paired t test (two-tailed). Additionally, the data were plotted against the actual phantom diameter values and a linear regression analysis was applied. The mean differences between measured luminal diameters and the corresponding phantom dimensions were computed and considered to be an index of the accuracy of the measurements, while the standard deviation of the differences was defined as an index of precision. The relative standard deviation was calculated

(precision / mean of measured diameter value x 100) to assess the degree to which the sets of diameter data points varied. In order to determine the agreement between 2-D and 3-D QCA systems, Bland-Altman analysis was performed (10). Statistical analyses were performed with SPSS 12.0.1 for Windows (SPSS Inc., Chicago, IL, USA). A p value < 0.05 was considered statistically significant.

RESULTS

Thirty coronary angiographic images were acquired after intracoronary insertion of the stenosis phantoms. Three images were excluded from the QCA analysis because of extreme foreshortening of the stenosis segment in frontal views. Five images that had insufficient arterial filling using the 0.5 or 0.7 mm phantoms were also excluded. The remaining 22 images were used for the diameter measurements using both QCA systems. In vivo intra- and inter-observer variability of the 2 QCA systems and ex vivo OCT was calculated in all the 22 analysable images (1). Satisfactory reproducibility was noted in all of the two QCA systems and OCT.

Table 1. Intra- and inter-observer variability of lumen diameter.

	Intra-observer				Inter-observer			
	Diff.	r	Intercept	Slope	Diff.	r	Intercept	Slope
Ex vivo analysis								
OCT lumen diameter	0.03±0.02	1.000	–0.01	0.99	0.00±0.05	0.996	0.04	0.97
In vivo analysis								
2-D QCA system								
Isocentric								
Frontal MLD	–0.01±0.03	0.997	–0.01	1.01	0.02±0.11	0.969	-0.02	1.00
Lateral MLD	0.00±0.03	0.998	0.00	1.00	0.06±0.09	0.985	0.03	0.92
Frontal mean LD	–0.01±0.03	0.998	–0.02	1.01	0.02±0.08	0.982	-0.02	1.00
Lateral mean LD	0.01±0.05	0.993	0.02	1.00	0.06±0.08	0.986	0.03	0.93
Catheter								
Frontal MLD	–0.01±0.06	0.991	0.05	0.94	0.00±0.10	0.972	0.01	0.99
Lateral MLD	0.02±0.05	0.993	0.00	1.02	–0.03±0.09	0.983	0.01	1.02
Frontal mean LD	–0.01±0.08	0.981	0.06	0.93	0.00±0.07	0.984	0.00	1.00
Lateral mean LD	0.00±0.05	0.991	0.04	0.97	–0.02±0.07	0.989	0.00	1.02
3-D QCA system								
Isocentric								
MLD	0.01±0.03	0.997	0.01	1.00	0.01±0.09	0.973	0.06	0.95
Mean LD	0.00±0.03	0.997	–0.04	0.97	0.03±0.06	0.988	0.11	0.93
Catheter								
MLD	0.00±0.06	0.986	–0.02	1.03	0.01±0.08	0.973	0.09	0.92
Mean LD	–0.01±0.05	0.994	–0.05	1.04	0.03±0.09	0.972	0.11	0.92

LD = luminal diameter; MLD = minimum luminal diameter; OCT = optical coherence tomography; QCA = quantitative coronary angiography

In vivo assessment of luminal diameter by 2-D and 3-D QCA

The comparative results of the actual phantom lumen diameter and the dimensional values derived from both QCA systems are shown in Table 2 along with Figures 4 and 5.

Table 2. Summary of *in vivo* validation results of 2-D and 3-D QCA systems (CardiOp-B™) (22 observations)

	Measured diameter (mm)	Accuracy	Precision	Relative SD* (%)	Correlation	SEE	Intercept	Slope	p-value of paired t test
2-D QCA									
Isocentric									
Frontal MLD	1.07	0.10	0.12	11.1	0.968	0.11	0.04	0.88	0.001
Lateral MLD	1.06	0.10	0.08	7.9	0.985	0.07	0.00	0.91	< 0.0001
Frontal mean LD	1.19	–0.03	0.09	7.9	0.983	0.08	0.17	0.88	0.17
Lateral mean LD	1.15	0.01	0.09	7.6	0.987	0.07	0.13	0.88	0.43
Catheter									
Frontal MLD	0.98	0.18	0.12	12.4	0.971	0.10	0.01	0.83	< 0.0001
Lateral MLD	1.01	0.16	0.11	11.2	0.977	0.09	0.03	0.84	< 0.0001
Frontal mean LD	1.09	0.07	0.11	9.9	0.980	0.08	0.11	0.84	0.005
Lateral mean LD	1.10	0.06	0.10	9.2	0.984	0.07	0.12	0.84	0.009
3-D QCA									
Isocentric									
MLD	0.98	0.19	0.13	13.7	0.966	0.10	0.04	0.80	< 0.0001
Mean LD	1.04	0.13	0.10	9.4	0.985	0.07	0.05	0.85	< 0.0001
Catheter									
MLD	0.93	0.23	0.14	15. 2	0.970	0.09	0.05	0.76	< 0.0001
Mean LD	0.99	0.18	0.13	11.4	0.984	0.07	0.05	0.80	< 0.0001

* (precision/mean of measured diameter value) x 100
LD = luminal diameter; MLD = minimum luminal diameter; OCT, QCA = quantitative coronary angiography; SD = standard deviation

In both systems, accuracy was better with isocentric calibration compared to catheter calibration. Mean luminal diameter measurements yielded better accuracy than minimum values in any of the dimensional measurements. Among the 8 methods of diameter measurements in the 2-D QCA, mean luminal diameter by isocentric calibration in lateral view proved to have the best accuracy (0.01 mm). Both systems significantly underestimated the actual phantom diameter values, except for minimum and mean diameters in the lateral view with isocentric calibration. There was again good correlation between luminal diameter measurements and phantom actual diameter values with both QCA systems (r=0.961 ~ 0.987). However, the 2-D QCA system demonstrated better values of accuracy than the 3-D system in diameter measurements regardless of the calibration option.

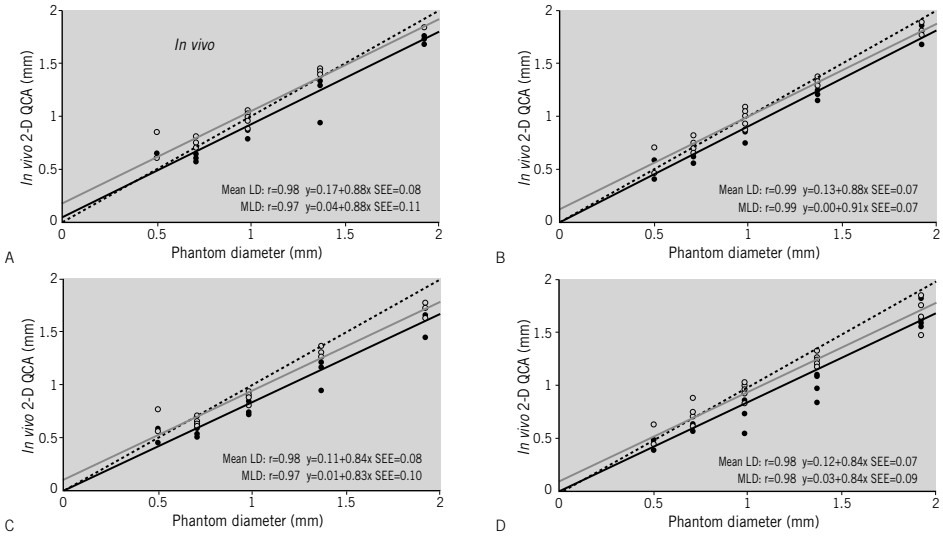

Figure 4. Two-dimensional QCA assessment of minimum (continuous black lines) and mean luminal diameter (continuous grey lines) with calibration at the isocenter in frontal (A) and lateral views (B) and with catheter calibration in frontal (C) and lateral views (D). The dashed lines indicate the line of identity.

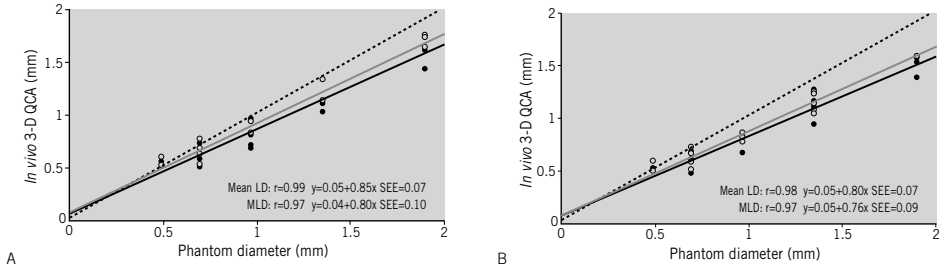

Figure 5. Three-dimensional QCA assessment of minimum (continuous black lines) and mean luminal diameter (continuous grey lines) with calibration at the isocenter (A) and with catheter calibration (B). The dashed lines indicate the line of identity. *See this figue in color in the Appendix page 382.*

Agreement between 2-D and 3-D QCA systems

A direct comparison between the 2-D (frontal views) and the 3-D QCA systems is shown in Figure 6. The two systems demonstrate good correlations in diameter measurements (r=0.947 isocenter, minimum; r=0.982, isocenter, mean; r=0.940, catheter, minimum; r=0.976, catheter, mean). The plot of differences between both systems demonstrates satisfactory agreement over the entire range of phantom sizes. This proved to be true for calibration at the isocenter as well as for catheter calibration (Figure 6).

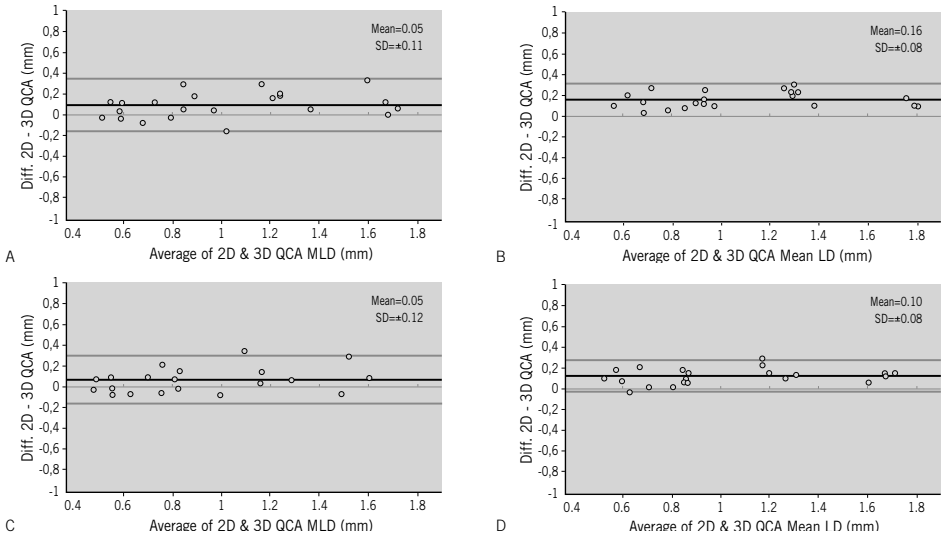

Figure 6. Bland-Altman plots of the differences between the minimum and mean luminal diameter measurements acquired by the 2 systems versus means of the measurements. A: minimum diameter with calibration at the isocenter. B: mean diameter with calibration at the isocenter. C: minimum diameter with catheter calibration. D: mean diameter with catheter calibration. The data from the frontal view are used as 2-D QCA measurements. *See this figue in color in the Appendix page 383.*

Ex vivo assessment of luminal diameter by OCT

Figure 7A depicts the linear regression analysis of comparison between actual phantom luminal diameter versus ex vivo diameter values derived from OCT. OCT-based dimensional values proved to correlate extremely well with the real luminal diameter (accuracy= – 0.03, precision=0.02, relative standard deviation=1.8%, r=1.000, intercept=0.01, slope=1.02). OCT clearly visualised the circular lumen of plexiglass phantom (Figure 7B).

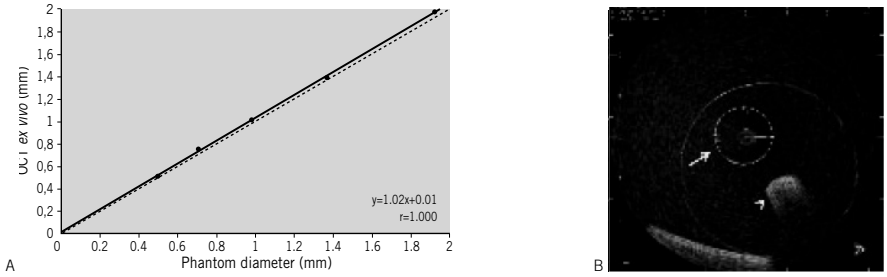

Figure 7. A: Linear regression analysis of the phantom lumen diameter versus the cross-sectional luminal diameter measured with OCT. B: Representative OCT images of the stenosis phantom with 1.4-mm lumen. Arrow: 1.4-mm lumen for measurement; arrow head: lumen for guidewire. *See this figue in color in the Appendix page 383.*

DISCUSSION

The results of the present study indicate the following three findings: 1) the 3-D QCA system significantly underestimated actual phantom diameter values compared to the 2-D system; 2) the 3-D QCA system showed a good agreement with the 2-D QCA system; 3) the values of the ex vivo diameter measurements by OCT were almost identical to the actual phantom diameter values. As the number of coronary interventions has increased over the years, the complexity of target lesions has increased concomitantly. Development of a 3-D visualisation and quantitative analysis system has been encouraged by the increasing need to better understand the true vessel structure and the spatial orientation of complex features and to quantify vessel morphology more precisely. There is a growing interest in applying this new technology as an additional imaging tool in interventional cardiology. Recently, the feasibility and potential superiority of 3-D QCA system in the measurement of 38 coronary lesions was reported by comparing it with a 2-D QCA system (Medview™, Medcon Telemedicine Technology, Tel Aviv, Israel) (3). However, this 3-D QCA system should be evaluated in comparison with the largely validated conventional 2-D QCA systems (5,7,11,12). Moreover, the accuracy or limitations of this system can only be appreciated by measuring in vivo vessels of known lumen dimensions. This is especially important since the accuracy of the reconstruction is not only the basis for quantitative results but also for producing a correctly visualised image. In theory the 3-D quantitative analysis should fully correct for foreshortening and out-of-plane magnification differences. Systematic underestimation of luminal diameter measurements was noted for both QCA systems and this was more significant in the 3-D system. The image acquisition was performed by hand injection of contrast and this may result in less radiographic opacity of stenotic segment compared to mechanical injection. Consequently automated detection of vessel boundaries might have been affected leading to smaller diameter values than expected having been derived. However, even with mechanical contrast injection, the angiographic examination of these high-grade stenosis phantoms cannot always be satisfactory because of possible intraluminal thrombus that results from the reduced blood flow or from the presence of intraluminal cellular debris collected during the insertion of the phantoms. The values of the both QCA systems with catheter calibration were smaller than those obtained with calibration at isocenter. This might be explained by an out-of-plane magnification phenomenon: a greater distance between the image intensifier and the catheter tip than between the image intensifier and the isocenter that would result in a smaller calibration factor (13,14). In the 2-D QCA system, lateral views showed better accuracy and precision than frontal views. Foreshortened images were more frequently observed in frontal views than in lateral views. Accordingly, suboptimal contour detection of frontal images might have occurred. Although theoretically the 3-D reconstruction should enable the correction of foreshortening and out-of-plane magnification errors, these improvements could not be identified in the present analysis. OCT is a novel imaging modality that provides

intravascular images that have a resolution of approximately 10 - 20 µm. This 10-fold greater resolution in comparison with IVUS enables visualisation of microscopic structures within the coronary arteries (15,16). In vivo dimensional and volumetric measurements of implanted coronary stents have shown that OCT can produce accurate results that are comparable to IVUS (17). Post-mortem analysis suggested that OCT can measure the intima-media thickness more accurately than IVUS (18). Currently OCT is regarded as a modality that may surpass the performance of angiography or IVUS after stent implantation (19,20). The present study provided *ex vivo* validation of OCT with respect to diameter measurements. Unfortunately, we could not compare OCT to IVUS because the IVUS catheter could not cross phantom lumens smaller than 1.0 mm. Furthermore in vivo examination would most likely prove difficult in these high-grade stenoses as the presence of a wire itself might result in the rapid development of intolerable ischaemic changes for the animals even before the induction of further ischaemia by the OCT occlusion balloon.

LIMITATIONS

This validation test using concentric cylindrical phantoms was originally designed to test 2-D QCA systems (5,7,11,12). The use of phantoms with a regular circular lumen does not allow the assessment of asymmetry. Here the use of reconstruction from two projections included in one 3-D result supplies information of lesion asymmetry more precisely than that available from 2-D analysis. Since the precise and validated eccentric phantoms were not readily available, we decided to conduct the present study with previously established approach using concentric phantoms (5,7,11,12). The 3-D reconstruction is based on two imaged diameters that results in an oval cross section where the 2-D analysis is based on one image results in a single diameter to be used for a circular cross section. However, densitometric analysis available in the 2-D QCA system can provide estimates for cross sectional areas in complex lesions (21,22). Our results were based on a series of small-size (< 2 mm) lumen phantoms. From a clinical point of view, validation tests using larger-size (> 2.25 ~ 2.5 mm) phantoms might be more relevant to investigate whether this 3D system is useful as a tool to determine the optimal device size, or to confirm the acute post-procedural results during the interventional procedures.

CONCLUSIONS

The minimum and mean luminal diameter measured with the 3-D QCA system underestimated the true phantom lumen diameter more than 2-D QCA. However, since there was a strong correlation with the 2-D QCA system, this system could be a useful alternative in

clinical practice. OCT precisely measured the lumen diameter of plexiglass phantoms in this ex vivo experimental setting. In addition to its usefulness in the quantitative assessment of coronary plaque, this imaging tool could be developed further as a reliable device for intravascular quantitative assessment with the advancement of less invasive preparation for the image acquisition.

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CHAPTER 6

A Randomised Controlled Study Comparing Conventional and Magnetic Guidewires in a Two-Dimensional Branching Tortuous Phantom Simulating Angulated Coronary Vessels

ABSTRACT

Objectives: To directly compare the magnetic navigation system (MNS) guidewires with conventional guidewires in branching tortuous phantoms with operators of varying MNS and percutaneous coronary intervention experience.

Background: Vessel tortuosity, angulation, and side branches remain limiting factors in coronary interventions. The MNS addresses these limitations by precisely directing the tip of a magnetised guidewire in vivo aided by two permanent adjustable external magnets.

Methods: Crossing and fluoroscopy times of six operators were evaluated in five tortuous Perspex™ phantom vessels in three consecutive attempts. Standard guidewire (SG) usage was unrestricted. Two second generation magnetic guidewires (MG) were used. Failure was noted if the cross was unsuccessful within 5 min.

Results: The magnetic navigation was vastly superior to SG techniques with increasingly tortuous phantoms. It dramatically decreased both the crossing and fluoroscopy times with maximal reduction from 201.7 ± 111 to 36.4 ± 13 sec, $P < 0.001$ and 204.7 ± 24 to 47.2 ± 19 sec, $P < 0.001$, respectively. The MNS had a 98.8% procedural success rate compared to 68% with SG techniques. Moreover it considerably limited the amount of wire usage from 5.5 to 1.3. Operators with prior MG experience performed significantly better than those without, except in the simplest phantom where the difference was non significant (33.8 ± 13 sec vs. 41.7 ± 17 sec, $P = 0.2$).

Conclusion: MNS significantly reduces both the crossing and fluoroscopy times in tortuous coronary phantom models achieving excellent success rates with dramatic reductions in guidewire usage. Operators with prior MNS experience had an advantage over the inexperienced.

INTRODUCTION

The tortuosity and side branches in a coronary tree can determine the procedural outcome of a percutaneous coronary intervention (PCI) (1). An appropriate guidewire that manoeuvres easily through a tortuous segment or side branch can avoid complications such as a dissection or a perforation. The success in crossing a lesion depends both on the appropriate shape at the tip of the guidewire and the manual dexterity of the operator. As such the tip of a guidewire may require reshaping several times during an interventional procedure in a process of trial and error. Additionally, the frictional contact of a preshaped wire on the vascular wall can limit the amount of torque transmitted by the operator leading to wire prolapse. As complexity increases these standard coronary guidewire limitations can often lead to longer procedural and fluoroscopy times together with the use of higher contrast loads (2). The magnetic navigation system (MNS) with its steerable wire can potentially address some of the above limitations (3). In a random set of patients who underwent PCI, both the procedural and fluoroscopy times were significantly reduced (4) and confirmed results obtained in a non tortuous coronary vessel phantom (5). To address tortuosity, more complex and tortuous anatomy phantom models of the hepatic, celiac arteries (6), and the cerebral arteries (7) have been previously used to compare MNS with standard techniques but thus far no comparison has been made with tortuous coronary phantoms by practicing interventional cardiologist.

In this randomised study we assessed the efficacy of the MNS guidewires with conventional guidewires in phantom vessels with varying degrees of angulation and reduction in vessel's calibre so as to mimic a coronary trunk and its' side branch. Our aims were to determine: (a) the crossing time to reach to a fixed point on the phantom using magnetic navigation in comparison to manual manipulation of the wire in the hands of interventional cardiologists with varying MNS experience, (b) to determine if there is a reduction in fluoroscopy time, (c) and to assess the procedural success and wire usage between the two different approaches for each of the phantom vessels evaluated.

Materials and Methods

The Magnetic Navigation System The Stereotaxis Niobe® II MNS (Stereotaxis, St. Louis, MO) has two permanent adjustable magnets that can be rotated, translated, or tilted to produce a uniform magnetic field of 0.08 T. This field precisely directs a tiny magnet mounted on the tip of a guidewire by changing its' magnetic moment and allows fine control of the orientation of the tip of the guidewire in space. The system is integrated with a modified C-arm flat-panel detector fluoroscopic imaging suite (AXIOM Artis dFC, Siemens Medical Solutions, Forchheim, Germany) for angiographic imaging. A three-dimensional (3D) virtual vessel roadmap can be created from two angiographic images provided that they are 30° apart by using reconstruction software (CardiOp-B, Paieon Medical, Rosh Ha'ayin, Israel). As our

phantom models were two-dimensional (2D) we chose the alternative 2D mode displayed as a "clock-face" on a touch screen monitor (Fig. 1). In this 2D navigation mode touching the screen at a particular point results in the Navigant software calculating a vector that directs a magnetic field to align the wire tip in the desired direction. The advantage of this technology is that it allows a full 360° omni directional rotation of the tip of the wire at anytime during the procedure, in vivo, without the need for a preshaping wire's tip.

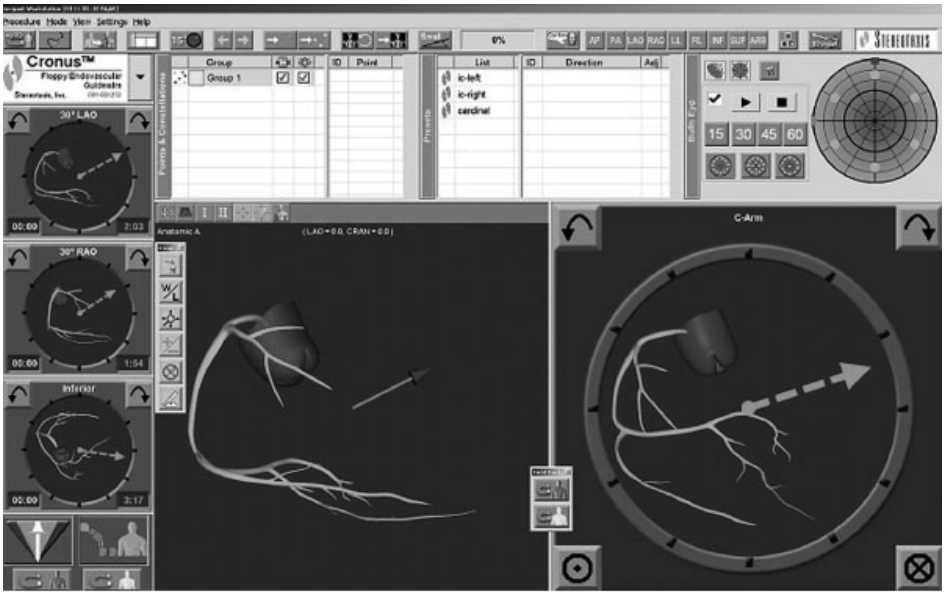

Figure 1. The "clockface" navigation system. *See this figue in color in the Appendix page 384.*

The Guidewires

The Titan™ Soft Support coronary guidewire (Stereotaxis, St. Louis, MO) is a 180 cm moderate support, hydrophilic coated wire with a diameter of 0.014 in./0.36 mm having a flexible 2-cm distal coiled tip that has a 2 or 3 mm gold cup neodymium-iron-boron magnet attached. The Pegasus™ guidewire is similar to the Titan Soft Support coronary guidewire apart from its more hydrophilic nitinol coating. The conventional wires used in the study were PT Graphix™ Intermediate, Choice™ PT Floppy (Boston Scientific, Miami, FL), Miracle bros™3G (Abbott Vascular Devices, Redwood, CA) and high torque BMW (Guidant, Santa Clara CA).

The Phantom

The phantom is a Perspex™ model with 3 and 2 mm channels simulating five different tortuous vessels with varying degrees of difficulty graded 1–5 due to increasing angulations and

side branches (Fig. 2). In the least tortuous phantom A both the magnetic (MG) and standard (SG) guidewires were required to traverse a 120° turn followed by a right angle bend in a simulated vessel of 3 mm calibre. This was in contrast to the most challenging and tortuous simulated vessel (phantom E) where a 3 mm vessel gave rise to a 2 mm side branch at a right angle and then made a sharp 120° turn. To simulate tissue lubricity the phantoms were wetted with a mixture of soap and diluted contrast.

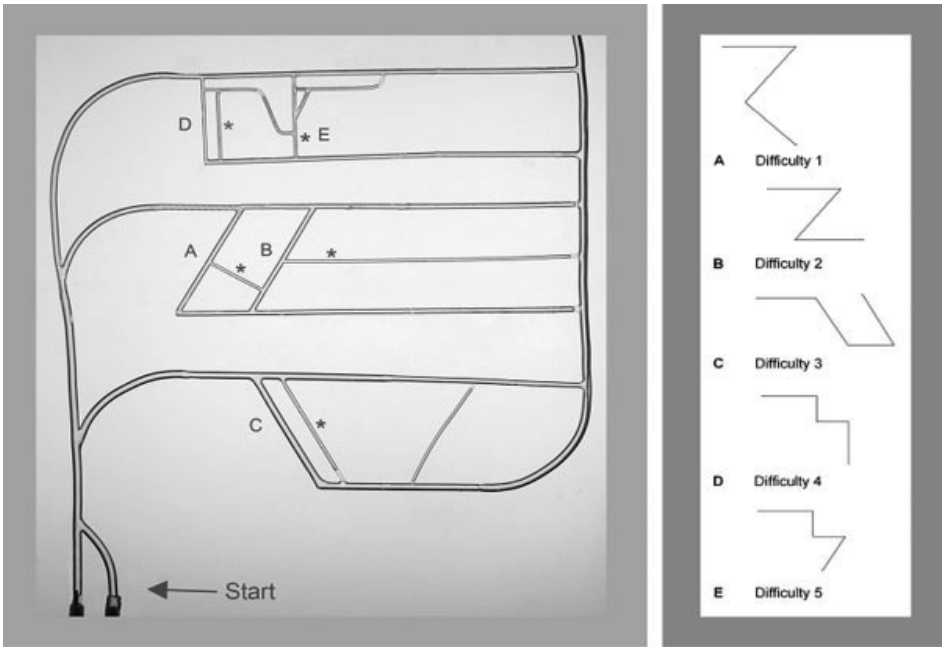

Figure 2. The phantom A–E with diagramatic representation of the level of difficulty. The angles and "vessel" caliber are as follows: (A) 3 mm, 120° turn into a 3 mm, 90° turn; (B) 3 mm, 120° turn into a 3 mm, 90° turn; (C) 3 mm, 60° turn into a 3 mm, 120 turn and then into a 60° turn to a 2 mm vessel; (D) 3 mm, 90° into a 2 mm followed by a 90° turn; (E) 3 mm, 90° into a 2 mm followed by a 120° turn. The "arrow" indicates the starting point and the asterisk (*) show the end of each phantom run. *See this figue in color in the Appendix page 384.*

The Procedure

The phantom model was fitted with a 6 French diagnostic catheter, filled with 20% contrast solution and placed in the magnetic field of the MNS. Six interventional cardiologists from our institution were divided into three groups depending on their level of experience with magnetic navigation and SG techniques. In the group 1, operators 1 and 2 had the most MNS experienced with each having performed more than 35 magnetic aided cases. Group 2 (operators 3 and 4) had moderate MNS experience with less than 35 cases and group 3 had MNS inexperienced operators (operators 5 and 6) and they were also the most junior of all the conventional interventionalists. The operators were randomly assigned to start with either a

SG of their choice or one of the two 2nd-generation magnetically enabled wires. Operators had to manipulate their guidewire past a fixed point along the simulated phantom vessel (A–E). The crossing and fluoroscopy times were measured when the wire positioned at the tip of the catheter passed a predetermined fixed point on the phantom (Fig. 2). Recordings for both the MG and SG were triplicated for each simulated phantom vessel and an average crossing and fluoroscopy time was determined for each group of operators. To compensate for any deterioration in the guidewire's tip or wire performance during the procedure the operators were allowed to exchange a damaged wire for a new or different guidewire as many times as deemed necessary so as to achieve a successful cross within 5 min. If the vessel was not crossed during this 5-min period then the attempt was classed as unsuccessful due to a time failure. Each time failure was recorded as 300 sec for both the crossing and fluoroscopy times. However, it must be stressed, that this value was in fact an underestimation of the time it would have taken if the operator had eventually crossed the simulated vessel.

Statistics

As the crossing times and fluoroscopic exposure times were continuous variables they are presented as means and standard deviation. T-test and one-way ANOVA (Bonferoni) were used to determine if there were significant differences in the procedural time and fluoroscopic times. Analyses were performed using SPSS 11.5 for Windows (SPSS, Chicago, IL). P value <0.05 was considered statistically significant.

RESULTS

Crossing and Fluoroscopy Times in Phantoms A–E

Overall, the MG was vastly superior to the SG in both the crossing and fluoroscopy times (Fig. 3). The SG was faster than the MG in phantom A (41.8 ± 26 sec vs. 47.9 ± 20 sec, P = 0.3) however the difference was not significant (Fig. 3A). In phantom B, the average MG crossing time was shorter than the SG (49.3 ± 23 sec vs. 76.5 ± 65 sec, P = 0.1) but was significantly less in the more tortuous phantoms C and D with dramatic reductions in crossing times from 201.7 ± 111 to 36.4 ± 13 sec, P < 0.001 and 204.7 ± 24 to 47.2 ± 19 sec, P < 0.001, respectively. Similar results were observed with the most angulated phantom E where it was greatly superior in manipulating through a 2 mm side branch (89.1 ± 65 sec vs. 247.3 ± 82 sec, P < 0.001). In the majority of cases the trend of fluoroscopy times (Fig. 3B) closely mimicked that observed in the crossing times. As such, phantom A had longer fluoroscopy times with the MG (47.7 ± 23 sec vs. 72.0 ± 58 sec, P = 0.1) and phantom B had longer fluoroscopy times with the SG (47.7 ± 23 sec vs. 72 ± 58 sec, P = 0.1). With increasing complexity (phantoms C–E) there were both

significant and dramatic reductions in fluoroscopy times similar to that reported with the crossing times.

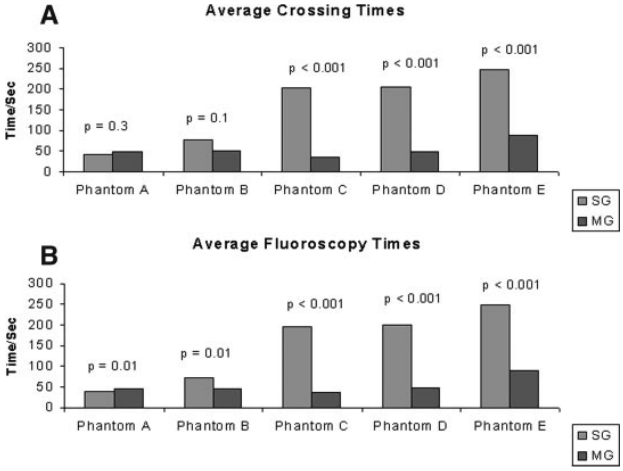

Figure 3. (A) The average crossing times/sec obtained using SG and MG for all operators with phantoms A–E. (SG, standard guidewire; MG, magnetic guidewire). (B) The average fluoroscopy times/sec obtained using SG and MG for all operators with phantoms A–E. (SG, standard guidewire; MG, magnetic guidewire). *See this figue in color in the Appendix page 385.*

Sub-Group Analysis of Crossing Times in Phantoms A–E

On the subgroup analysis of the operator performances (Fig. 4), in the simplest phantom A the most MNS experienced operators (group 1) were significantly faster (28.5 ± 9 sec vs. 60.7 ± 18 sec, $P < 0.007$) than those inexperienced (group 3). This was not surprising as the inexperienced group needed to get acquainted with the equipment. The overall decrease performance of the MG to the SG (41.8 ± 26 sec vs. 47.9 ± 20 sec, $P = 0.3$) was thus due to the longer times attained by groups 2 and 3 since group 1 was faster with the MG (28.5 sec vs. 32.8 sec). In phantom B, group 1 performances with the MG were also significantly faster than group 3 (26.2 ± 4 sec vs. 53.7 ± 13 sec, $P = 0.025$) but there was no significant difference observed between groups 2 and 3 (68.0 ± 24 sec vs. 53.7 ± 13 sec, $P = 0.4$). Of note in this phantom, both groups 1 and 3 times with the SG were more than twice that of MG (64.7 and 112.8 sec vs. 26.2 and 53.7 sec, respectively) with the intermediate experienced group 2 having no significant difference with either wire (MG, 68.0 sec and SG, 52.0 sec). As the tortuosity and branching increased (phantoms C–E) there was a dramatic difference between the MG and SG performances amongst all the groups (Fig. 4).

In phantom C there was no significant difference between all the MG users regardless of previous MNS experience and in phantom D only group 1 remained significantly faster than group 3 (39.5 ± 12 sec vs. 62.7 ± 21 sec, $P = 0.008$). With the conventional wire technique a similar

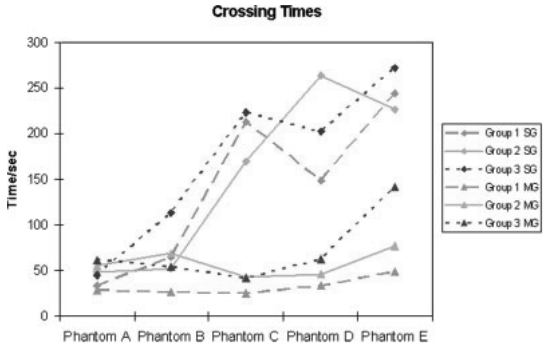

Figure 4. The average crossing times/sec obtained using SG and MG for groups 1–3, operators with phantoms A–E. (SG, standard guidewire; MG, magnetic guidewire). *See this figue in color in the Appendix page 385.*

trend was observed with no significant differences between the senior (groups 1 and 2) and the junior (group 3) operators in both phantoms C (190.8 ± 113 sec vs. 223.7 ± 112 sec, P = 0.6) and phantom D (205.9 ± 106 sec vs. 202.3 ± 109 sec, P = 0.9). This trend continued in phantom E where groups 1 and 3 had non significant time differences (244.2 ± 99 sec vs. 271.5 ± 70 sec, P = 0.9) with the SG and group 1 still being significantly faster with the MG than group 3 (48.8 ± 12 sec vs. 141.5 ± 85 sec, P = 0.03). Overall, the operators with previous MNS experience (groups 1 and 2) performed better (62.8 ± 31 sec vs. 141.5 ± 85 sec, P = 0.01) in this phantom.

Procedural Success and Wire Usage in Phantom A–E

There were 100% successful crossings in phantoms A and B with both the MG and SG (Fig. 5A). In phantom C and D, the procedural success with the SG was (10/18) 56% and (9/18) 50%, respectively as compared to a 100% success with the MG. The success of the SG in the most tortuous phantom E was only (8/18) 33% and the MG (17/18) 94%. The one failure with the MG was observed in an operator with no prior MNS experience. Up to eight SG were used by operator 1 with a 60% overall success rate (9/15 successful crossings), to manipulate through all the phantoms (Fig. 5B). In contrast, a maximum of two MG (operator 5) were used for the same task with a 93% success rate (14/15 successful crossings). The overall ratio of SG to MG usage was found to be 5.5 SG to 1.3 MG.

DISCUSSION

MNS is an established technique in cardiac electrophysiological procedures (8,9) and is emerging as a powerful tool in interventional cardiology (10). The results in crossing simple and straight forward lesions has been equivocal (4) but importantly it has been successfully

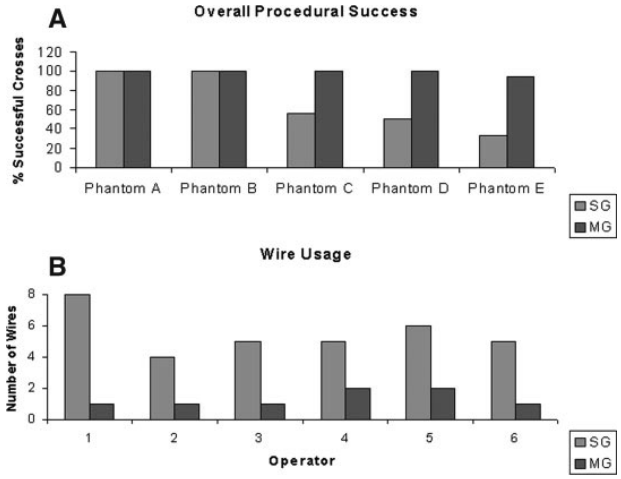

Figure 5. (A) The overall procedural success using SG and MG for phantoms A–E. (SG, standard guidewire; MG, magnetic guidewire). (B) The SG and MG usage in operators 1–6 for phantoms A–E. (SG, standard guidewire; MG, magnetic guidewire). *See this figue in color in the Appendix page 385.*

used to cross coronary lesions that failed with SG techniques (2,11). In the modified ACC/AHA lesion classification lesions with severe angulation (>90°) and extreme proximal tortuosity are known to have lower procedural success rates (12). In addition, PCI on tortuous vessels with side branches also have a higher incidence of emergency coronary artery surgery (13) and greater radiation exposure to both the operator and the patient (14). By precisely guiding a wire in a full 360° rotation MNS may offer a potential solution to address the tortuosity reportedly encountered in 24% of all PCI cases (15). Moreover, because the tip of the magnetic wire is oriented only when needed there is potentially less trauma to the vessel wall and less wire prolapse (16). Our study aimed to assess the MNS guidewires and conventional wires in phantom models mimicking angulations and tortuosity with side branches seen in a PCI setting. We realized that phantom models are not wholly equivalent to what is encountered in the reality of the catheterization laboratory. However, they do play a vital role in the comparative assessment of different techniques and training. This is primarily because any confounding factors such as variation in coronary anatomy or external influences such as voluntary and involuntary movement of a patient can be effectively excluded. As such it therefore justifies previous phantoms experiments used to comparatively assess MNS with conventional techniques (5–7,17). Our results unequivocally demonstrate that magnetic navigation is vastly superior to SG techniques in phantom models with increasing tortuosity and side branches. The MNS dramatically reduced both crossing and fluoroscopy times with a 98.8% procedural success rate compared to a 68% with SG techniques. Moreover it considerably limited the amount of wire usage from 5.5 to 1.3. The only phantom where it was not superior was in the least tortuous phantom A. This was not surprising as the angulations in this phantom were non-acute and the side branch was of similar caliber to the main vessel, confirming

previous results in simple phantom models (4). Even though the MG was slower than the SG in phantom A, it must be stressed that the differences between the two wires were not statistically significant. With more demanding angulations and smaller side branches the dominance of MG prevailed with a highly significant reduction in crossing and fluoroscopy times over the SG. The importance of this finding is that it unambiguously demonstrates that a novel technology can be tailored to address a definitive problem encountered by the interventional cardiologist. It clearly shows that for simple angulations there is no net gain with MNS but as the angulation and complexity increases then the MG is far more attractive due to its ability to redirect the tip of the wire in situ (6). Remarkably, the most dramatic difference of the MG over the SG was noted in phantoms of intermediate tortuosity (phantoms C and D). These two phantoms were created to mimic a 3 mm giving rise to a 2 mm side branch with increasing angulations. The calibre of the side branches at the angulations of 60°, 90°, and 120° turns is not too dissimilar to those usually encountered in the normal coronary tree. Importantly, in these phantoms there were no significant differences between the operators regardless of previous MNS experience apart from those most and inexperienced in phantom D. This is in contrast to previously published data on a neurosurgical phantom where the MNS was more accurate and faster in the hands of the least experienced investigators (7). Although this is indeed the case for the total number of operators with experience compared with no MNS experience, if the data was further analyzed to look at the difference between the most experienced and those with no experience then the results would not be too dissimilar to our findings, suggesting that the most experienced have a slight advantage over the inexperienced. This was further illustrated in the most tortuous phantom E where the significant difference between the two groups persisted and is exemplified by the only MNS failure occurring with an operator having no prior MNS experience. This suggests that with a very tortuous vessel prior knowledge on the MG behaviour might be advantageous and substantiates the results of the SG, where all the operators had prior experience with these wires and hence there was no significant difference between the most and least experienced operators.

LIMITATION

Our study was limited by the fact that 2D phantoms were not representative of the 3D characteristics of ordinary coronary arteries. In addition, these 2D models were limited to "clockface" navigation rather than the more precise 3D reconstruction software. The phantoms also employed static road mapping for wire progression rather than the transient dynamic road mapping used in patients.

CONCLUSION

MNS is an emerging tool in interventional cardiology and has been successfully employed to cross lesions that failed with conventional techniques. In our phantom study we have unequivocally shown that a MG is vastly superior to a SG with dramatic reductions in crossing and fluoroscopy times in phantom models that mimic coronary arteries with increasing tortuosity and side branches. As the complexity of the phantoms increased operators with prior MNS experience performed better than those with no previous MNS exposure. There was an outstanding procedural success with the MNS (98.8% vs. 68%) together with a clear reduction in guidewire usage (5.5 vs. 1.3).

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CHAPTER 7

First Direct In Vivo Comparison of Two Commercially Available Three-Dimensional Quantitative Coronary Angiography Systems

ABSTRACT

Aim: The in vivo comparison of the accuracy of two 3-dimensional quantitative coronary angiography (QCA) systems.

Methods: Precision-drilled plexiglass phantoms with five different luminal diameters (0.5–1.9 mm) were percutaneously inserted into the coronary arteries of four Yorkshire pigs. Twenty-one angiographic images of these stenotic phantoms were acquired for in vivo validation testing. Quantitative assessments of the minimum, maximum, and mean luminal diameters together with the minimum luminal area were determined using two 3D QCA systems, the CardiOp-B® and CAAS 5.

Results: The CardiOp-B system significantly underestimated the minimum luminal diameter MLD whilst both systems significantly overestimated the maximum luminal diameter at the minimal luminal area (MLA) over the phantom's true value. The CAAS 5 system had a greater degree of accuracy/mm (mean difference = 0.01 vs. 0.03) and precision/mm (SD = 0.09 vs. 0.23) than the CardiOp-B in assessing the minimal LD. An increased precision/mm (SD 5 0.01 vs. 0.29) and accuracy/mm (mean difference = 0.03 vs. 0.11) in the mean LD was observed with the CAAS 5. In comparing the MLA/mm the CAAS 5 was more precise/mm2 (SD = 0.14 vs. 0.55) and accurate/mm2 (mean difference = 0.12 vs. 0.02) to the true phantom MLA compared to the CardiOp-B system.

Conclusions: In a 21 phantom study, the CAAS 5 3D QCA system had a greater degree of accuracy and precision in both the luminal and area measurements than the CardiOp-B 3D QCA system.

INTRODUCTION

In the percutaneous treatment of coronary artery disease the on-line two-dimensional quantitative angiography (QCA) is often the chosen method to determine both the vessel length and size to guide stent implantation (1). There are, however, several limitations with this technique as depending on the angiographic views the vessels can appear foreshortened or overlapped resulting in inaccurate measurements (2). Moreover, in tortuous vessels this can lead to an underestimation of the appropriate length of stent required to cover the lesion (3). Recently, a novel method, the three-dimensional (3D) reconstruction of standard coronary angiography using an algorithm integrating single-plane images has been validated (4). This technology is aimed at providing a solution to many of the limitations inherent with 2D QCA. In addition, the enhanced accuracy in determining the lesion length and luminal diameter the 3D reconstructed image can be incorporated in a designated navigation software (Navigant® Stereotaxis, St Louis, MO) to enable magnetically aided guidewires to precisely transit through the vessel lumen (5). The accuracy of the luminal diameter can be crucial for a successful wire transit to avoid vascular wall trauma or plaque disruption (6). The potential benefits of this 3D QCA technology has led two companies Paieon Medical, Rosh Ha'ayin, Israel and Pie Medical Imaging, Maastricht, the Netherlands to develop the CardiOp-B and CAAS 5 systems, respectively. Both systems are similar in using two angiographic images to reconstruct a 3D image but in the current version of the CardiOp-B the calibration standard is performed manually whilst in the CAAS 5 system it is automated. The aim of this study was to compare the accuracy of the detection of a luminal stenosis using two 3D QCA systems in vivo using radiolucent cylindrical plexiglass or polyamide stenotic phantoms with precision-drilled eccentric lumens implanted in porcine coronary arteries (7).

METHODS

The ethics committee on animal experimentation at the Erasmus Medical Center, Rotterdam, NL approved the study that was conducted in accordance to the guidelines of the American Heart Association on animal use in research.

Preparation and Insertion of the Stenotic Phantoms

The stenotic phantoms (Fig. 1) were precisely engineered by the Department of Bioengineering at the Erasmus Medical Center. Radiolucent plexiglass (acrylate) and polyacrylamide cylinders of diameters 3.0 or 3.5 mm and length of 8.28, 7.96, 7.85, 8.01, and 7.38 mm were precision-drilled to have circular lumens of 499 (aimed to be 0.5 mm), 707 (0.7 mm), 982 (1.0 mm), 1,367 (1.4 mm), and 1,921 (1.9 mm) lm in diameter, respectively. This accuracy calibrated optically at

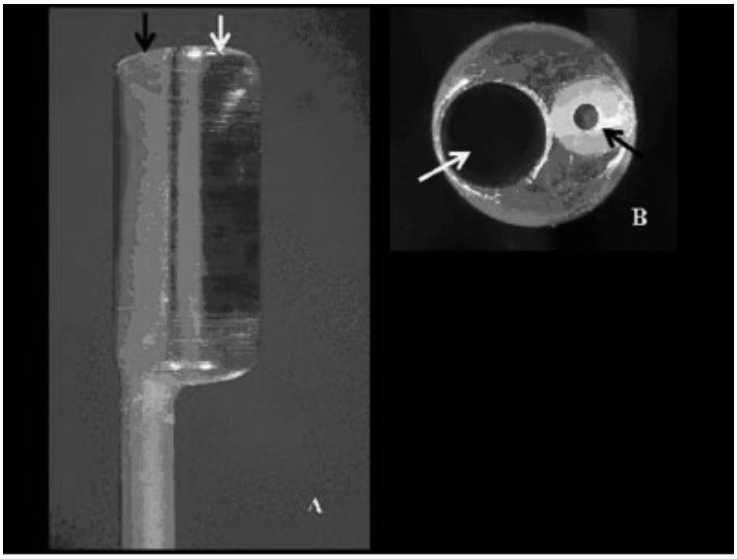

Figure 1. The magnified tip of one of the Fogarty catheters view along its long (A) and short axis (B) with a transparent radiolucent cylinder (phantom) having a channel of 1.9 mm diameter (white arrow) and the catheter lumen used for insertion of removable metallic stylet (black arrow) to aid positioning. *See this figue in color in the Appendix page 381.*

40-fold magnification achieved a maximum tolerance of 0.003 mm. A second 1.3 mm diameter lumen was drilled parallel to the stenosis lumen to attach to the tip of 4-Fr Fogarty catheters (Vermed, Neuilly en Thelle, France) to facilitate the intracoronary insertion and positioning of the phantoms. Four Yorkshire pigs (average weight, 40–45 kg) were pretreated with intramuscular ketamine (20 mg/kg) and intravenous etomidate (5 mg/kg). The animals were then intubated and ventilated with a mixture of oxygen and isoflurane. Anesthesia was maintained with a continuous intravenous infusion of pentobarbital (5–20 mg/kg/ hr). About 12-Fr introducer sheaths were inserted into both carotid arteries to allow the sequential insertion of the guiding catheter and the phantoms. Jugular access was used for the administration of medication and fluids. An intravenous bolus (10,000 IU/l) followed by a continuous infusion of heparin was given. Following the experiments, the animals were humanely euthanized.

In Vivo Image Acquisition of Stenosis Phantoms by Fluoroscopy

Biplane cine angiographic system (Axiom Artis™, Siemens, Forchheim, Germany) was used to create digital angiograms of matrix size of 1024 X 1024 pixels. Identical radiographic imaging settings were employed (kVp, mA, ms) in the two projections used to image each phantom to maintain consistency. Following intubation of the left or right coronary artery with a 6-Fr guiding catheter (Mach 1TM, Boston Scientific, Natick, MA) intracoronary isosorbide-dinitrate (1 mg) was administered and an angiogram was made to aid orientation of the phantom in the

vessel. The phantoms were wedged in the coronary arteries and positioned in the X-ray isocenter using the tip of a metal wire marker placed on the Fogarty catheter. Coronary angiography was performed by manual injection of contrast medium (Visipaque™ 320 mg I/ml, Amersham Health B.V., Eindhoven, The Netherlands). The ventilator was disconnected transiently during contrast injection to minimize the effect of diaphragmatic movement on angiographic images.

Three Dimensional QCA Analyses of In Vivo Phantom Images

In total, 21 readings were made in 21 different arteries; four arteries had phantoms of diameters 1.9 mm, six arteries had phantoms of 1.4 mm, six arteries had 1 mm diameter phantoms, four arteries had 0.7 mm phantoms, and one artery had a 0.5 mm phantom. The in vivo analysis of each phantom was performed in end-diastole on the same number of the frame count and was ECG gated so that all of the analyses using both QCA systems were performed on identical images. Calibration of the CardiOp-B system was done manually using the conventional catheter calibration of the nontapering part of the tip of each 6-Fr guiding catheter filled with contrast. The CAAS 5 system performs an automatic calibration based on the DICOM information in the image. Once calibrated, the two orthogonal views (at least 30° apart) that were simultaneously acquired in the biplane system were then used to reconstruct the 3D vessel image (Fig. 2). This was achieved by marking three points in the CardiOp-B system: proximally, distally, and at the stenosis on the two angiographic images. In the CAAS 5, this was done by defining a common image point (a landmark common to both images), and two points distal and proximal to the stenotic region (8). The software then created automatic contour detection and if this was inaccurate then finer adjustments were made to the edge detection manually in the CardiOp-B system and the restriction option, an algorithm that excludes gross image artifacts such as the diagnostic catheter was applied in the CAAS 5 system. The restriction option is therefore not a manual edge correction but instead it offers users the possibility of excluding parts of the image of the detection by restricting the area of interest.

Following contour detection and corrections/restrictions if required, the 3D reconstruction of the artery was automatically created. The software determined the minimum luminal area (MLA) and the pixel size at each position in the 3D space. Based on the position of the MLA and the known pixel size, the minimum luminal diameter (MLD) for each of the angiographic images was automatically calculated. Assuming a noncircular shape at the MLA then there will be two MLD values (maximum and minimum LD) obtained, the smallest representing the absolute MLD. The mean luminal diameter was based on the values in between the borders of a predetermined segment in the phantom (Fig. 2). Along the centerline in between this segment, the diameter at each scanline was taken and divided by the total number of scanlines to automatically afford the mean LD. The following data was therefore compared, the minimum LD (MLD) and the maximum LD at the MLA, together with the minimum luminal area MLA and the mean LD over the region of interest (ROI) in each 3D QCA system to that of the

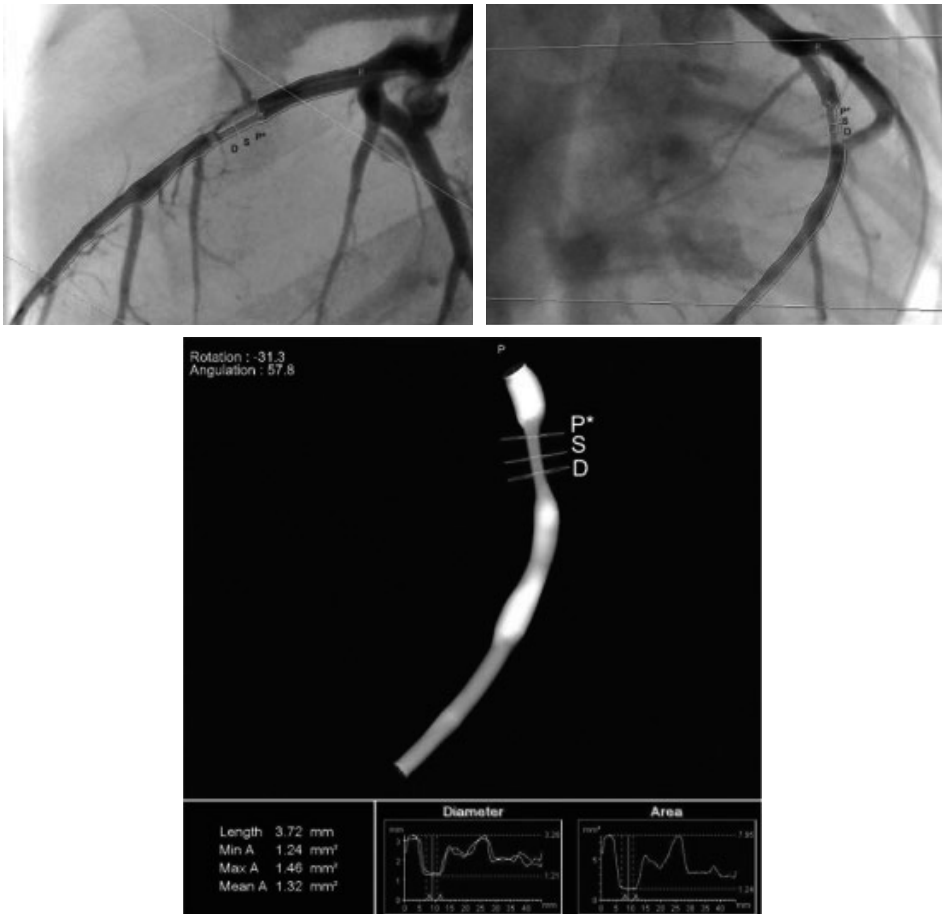

Figure 2. The 3D reconstruction of a phantom derived from two orthogonal views (frontal and lateral) using the CASS 5 system. The 3D color varies according to the severity of stenosis ranging from white (healthy vessel) to dark red (99% crosssectional area stenosis). The yellow squares denote proximal reference point (P*), most stenotic point (S), and distal reference point (D) of the target lesion, respectively. The region of interest (ROI) for calculation of mean luminal diameter can be manually defined by moving the proximal (P*) and distal (D) points (Definition of ROI for mean LD; Graph view). *See this figue in color in the Appendix page 386.*

phantom models. We purposely chose to perform only one measurement per phantom given the primary interest in the relative accuracy and precision of both techniques, instead of an assessment of the intra- and inter-observer variability of the QCA techniques. Expert users from both the Pie Medical and Paieon companies were used to perform the measurements.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation and compared using the Wilcoxon signed-rank test. Categorical variables are expressed as counts and percentages. The

mean of the differences between measurements and phantom dimensions of both systems was computed and considered to be an index of the accuracy of the measurements, while the standard deviation of the differences was defined as an index of precision. Bland–Altman plots (9) were used to assess the agreement between both 3D QCA systems and the phantom models. Pearson's correlation was used to determine the degree of correlation between the measurements. Statistical analyses were performed with SPSS 12.0.1 for Windows (SPSS, Chicago, IL). A P value < 0.05 was considered statistically significant.

RESULTS

Comparison of Minimum LD with Phantom "True" Values

In this study the CardiOp-B system had only one manual adjustment to correct the detected contour whilst six adjustments were used in the CAAS 5 system to restrict the contours to the region of interest. Overall, the comparison of both 3 D QCA systems with the true LD noted in the 21 phantom models revealed a closer association with the CAAS 5 system than in the CardiOp-B (Table I).

Table 1. Comparison of the Two 3D QCA Systems (CardiOp-B® and CAAS 5) Accuracy, Precision, and the Correlation to the True Luminal Diameter of the 21 Stenotic Phantoms

	Accuracy	Precision	Correlation	Slope	Intercept	P value
CardiOp-B® vs. phantoms						
Min LD (MLD)	0.03	0.23	0.87	0.87	0.15	0.03
Max LD	0.24	0.40	0.78	0.86	0.23	0.001
Mean LD	0.11	0.29	0.84	1.02	0.08	0.31
MLA	0.12	0.55	0.87	1.09	0.01	0.74
CAAS 5 vs. phantoms						
Min LD (MLD)	0.01	0.09	0.99	0.92	0.06	0.26
Max LD	0.06	0.11	0.97	1.12	0.10	0.015
Mean LD	0.03	0.10	0.98	0.87	0.19	0.39
MLA	0.02	0.14	0.99	0.91	0.13	0.95

Accuracy = mean differences between recorded measurements and the phantom; Precision = standard deviation and P value is derived from the recorded measurements and the phantom.

The CardiOp-B system significantly underestimated the minimum LD (MLD) whilst both systems significantly overestimated the maximum LD at the MLA over the true value. In assessing the MLD, the CAAS 5 system had a greater degree of accuracy/mm (mean difference = 0.01 vs. 0.03) and precision/mm (SD = 0.09 vs. 0.23) compared with that observed with the CardiOp-B system. The Bland–Altman plots of the MLD (Fig. 3a and b) showed that both systems had one outlier

reading beyond 2 SD. This value was, however, smaller in the CAAS 5 system resulting in a better overall correlation to that of the phantom's actual diameter (r = 0.99 vs. 0.87) and influencing the degree of precision. Notably, in the CardiOp-B system 11/21 (52%) of the measurements laid outside ± 10% of the true phantom LD compared with 3/21 (14%) of the measurements derived using the CAAS 5 system. Table I and Fig. 3a and b compares min LD (MLD) in both systems.

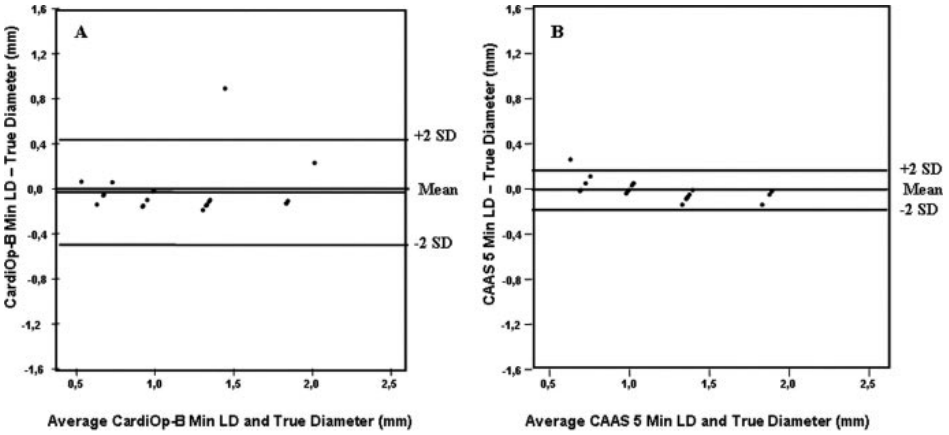

Figure 3. Bland–Altman plots of the minimal LD (a) CardiOp-B® with the phantoms (b) CAAS 5 with the phantoms.

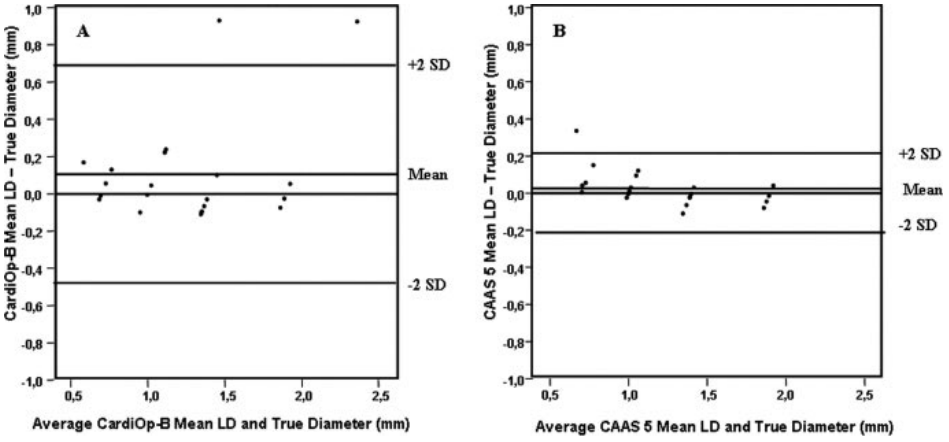

Figure 4. Bland–Altman plots of the MLD (a) CardiOp-B® with the phantoms (b) CAAS 5 with the phantoms.

Comparison of Mean LD with Phantom "True" Values

There was no significant difference observed when the mean LD in either system was compared with the luminal diameter of the phantoms (Table I). The Bland–Altman plots revealed two observations outside ± 2 SD range in the CardiOp-B analysis compared with only one

observation noted in the CAAS 5 system (Fig. 4a and b). As observed with the minimum LD values there was an increased precision/mm (SD = 0.10 vs. 0.29) and accuracy/mm (mean difference = 0.03 vs. 0.11) with the CAAS 5 mean LD values with the latter having a closer correlation with the true value (r = 0.98 vs. 0.84). Figure 4a and b compares mean LD in both systems.

Comparison of Minimal Luminal Area with Phantom "True" Values

The Bland–Altman plots of the MLA further demonstrated higher precision/mm^2 (SD = 0.14 vs. 0.55) and accuracy/mm^2 (mean difference = 0.02 vs. 0.12) with the CAAS 5 (Fig. 5a and b). Moreover, in the CardiOp-B system 14/21 (67%) of the measurements laid outside ± 10% of the true phantom MLA compared with 7/21 (33%) of the measurements derived using the CAAS 5 system. Consequently, the Pearson coefficient demonstrated a closer correlation with the CAAS 5 than the CardiOp-B system (r = 0.99 vs. 0.87). Figure 5a and b compares mean LD in both systems.

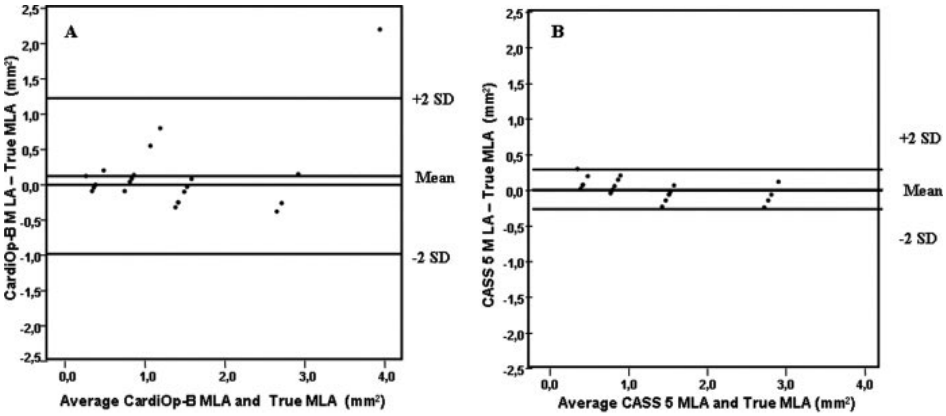

Figure 5. Bland–Altman plots of the MLA (a) CardiOp-B® with the phantoms (b) CAAS 5 with the phantoms.

DISCUSSION

3D QCA has been shown in phantom models (10) as well as in stented vessel segments (11), and complex lesions like bifurcations (12) to have a closer correlation to the true vessel's dimensions than 2D QCA. Moreover in conventional angiography, overlapping vessel can impair the optimal visualization of a lesion and if the lesion is eccentric then it may be missed altogether (13). In the formulation of a 3D QCA, the system uses a 3D computer-based modelling algorithm to integrate the 2D projections, identify key vessel features like bifurcations and the centreline, calculate and display the vessel's cross-sectional contours that are subse-

quently "filled in" to create the virtual vessel. Both the CardiOp-B system and CAAS 5 system adopt this system when generating the reconstructed vessel but there are subtle differences between the 2 programs that may influence the degree of accuracy. The CardiOp-B system utilizes a manual guide catheter mode calibration method in contrast to the CAAS 5 system that uses an automatic calibration at the region of interest (ROI). With the manual method, the catheter size in French or mm has to be inputted for system recognition and calibration. This is an established method that has been shown to have greater precision than the equivalent 2D measurements with respect to the minimal lesion diameter ($P < 0.005$), minimal lesion area ($P < 0.05$), and lesion length ($P < 0.01$) (4). However, it has been reported that because the catheter may not be in the same plane as the ROI that this method of calibration can give rise to differences in magnification and measurements and influence the accuracy (13). In addition, the way in which the contour is drawn on the 2D angiographic image also highlights an important difference that may also influence the accuracy and precision between the two systems. Both the CardiOp-B and CAAS 5 systems have the ability to manually correct the generated contours if they are adjudged to be inaccurate. Although this is subjective, in this paired comparative study contour adjustment had to be performed on one of the 21 phantom models in the CardiOpB as the detected contour deviated significantly from the vessel's edge. In the rest of the models, edge detection was adjudged satisfactory. No edge corrections were needed in the CAAS 5 but the catheter had to be excluded from the ROI on six occasions. Because the edge detection is used to deduce the measurement, the less manual correction needed then greater is the accuracy of the automated system.

The aim of this study was to evaluate the accuracy and precision of both the CAAS 5 and CardiOp-B 3D QCA system with respect to precisely engineered stenotic phantoms in vivo. The rational was that in addition to evaluating precision in measurements, the importance of the study stems from the demand to accurately determine the luminal diameter so that a precise endoluminal road map of a vessel can be achieved for magnetic navigation when the 3D reconstructed image is incorporated in the Navigant software (14). The lack of accuracy may result in the guidewire exiting from the vessel lumen to cause a perforation. The results demonstrated good overall correlation of the minimal LD and maximum LD at the MLA together with the mean LD and MLA in each system to the true values of the phantoms. However in the CardiOp-B system, the range of these correlations were slightly less (0.78–0.87) compared with the CAAS 5 system (0.97– 0.99). In addition, systematic underestimation of luminal diameter measurements has been previously reported for the CardiOp-B system QCA system (11).

In assessing the minimum LD (MLD), greater precision and accuracy was observed with the CAAS 5 arguably because of two observations in the CardiOp- B system varying markedly from the true value (Δ min LD 47% and 25%) in comparison to one observation (Δ min LD 34%) in the CAAS 5 system. However, what is important to note is that in terms of the accuracy is that 11/21 (52%) of the measurements laid outside ± 10% of the true phantom LD

using the CardiOp- B system compared with 3/21 (14%) of the measurements derived using the CAAS 5 system. This was also mirrored with the MLA measurements where two thirds of the values in the CardiOp-B system 14/ 21 laid outside ± 10% of the true phantom MLA compared with one third (7/21) with the CAAS 5 system. The result highlights the perceived superiority of automatic isocenter calibration together with improved edge detection (15). Despite the variability in 3D QCA measurements in both systems, we should remain appreciative of the fact that this novel technology creates a 3-dimensional coronary map and as such has widespread application to both scientific research and clinical practice. By doing so, it solves many of the limitations currently observed with 2D QCA and unlike other imaging modalities like multislice computed tomography and magnetic resonance imaging it can provide absolute measurements of coronary luminal diameter and lengths in real time. It is therefore hopeful that the findings of our study will stimulate further research in this exciting new imaging field.

LIMITATIONS

This study is the first direct comparison of two commercially available 3D QCA systems. The study was, however, limited by the relatively small sample size of 21 phantom models. This was due to difficulties in obtaining more animal models. The concentric phantoms used in this study do not represent natural coronary lesions, as they do not allow the assessment of asymmetry. It is better to use eccentric phantoms but precise and validated eccentric phantoms were not available. The validation tests with these cylindrical concentric phantoms were, however, used by our group recently to test 2D and 3D QCA systems (10).

CONCLUSION

In a 21 phantom study, the CAAS 5 3D QCA system had a greater degree of accuracy and precision in both the luminal and area measurements than the CardiOp- B 3D QCA system. Further development and validation studies are warranted in order for this novel technology to be increasingly adopted in routine clinical practice.

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CHAPTER 8

Rotational coronary sinus venography and magnetic navigation to facilitate LV lead placement in cardiac resynchronization therapy

ABSTRACT

This report demonstrates the production and use of a 3D reconstruction of a coronary sinus from a single injection rotational angiogram. The detailed virtual model enabled easy magnetic navigation of a wire for device placement in cardiac resynchronization therapy.

INTRODUCTION

The use of the magnetic navigation system (MNS: Stereotaxis, St Louis, Missouri, USA) in electrophysiology is now well established. This system has been described in detail previously (1,2). Using computer-controlled movements of the magnets, a 15-20 cm uniform magnetic field volume can be directed in 360º in all planes to deflect a magnetic wire tip precisely. This control is coupled with an ability to reconstruct a patient-specific vessel and provide image-guided navigation for each and every section of the vessel. A 3D model can be produced that enables magnetic field direction control from the computer generated image. Published reports have shown the clinical utility of the MNS in routine electrophysiology catheter ablation procedures, including specific reports describing its use in atrial fibrillation (3,4), atrioventricular nodal reentrant tachycardia (5), atrioventricular reentrant tachycardia (6), right ventricular outflow tract tachycardia (7), parahisian accessory pathways (8), and more complex arrhythmia ablation procedures such as ventricular tachycardia (9).

Recent studies indicate its usefulness in CRT to facilitate the placement of left ventricular leads in cardiac resynchronization therapy device implantation procedures (10,11). This report demonstrates the feasibility of producing an on-table, real-time coronary sinus reconstruction to facilitate lead placement in a cardiac vein. This virtual coronary sinus was produced with a single contrast injection and the use of rotational angiography.

CASE REPORT

A 76 year old lady with poor left ventricular function due to ischaemic heart disease was admitted for cardiac resynchronization therapy and ICD implantation. She had previously undergone CABG and had had a DDD pacemaker implanted for Mobitz II heart block.

An old atrial active fixation lead was successfully extracted while the old ventricular tined lead was left *in situ*. An Endotak Reliance SG active fixation shock lead (Guidant) was placed in the RV apex and a Capsure Fix active fixation lead (Medtronic) in the RA. The coronary sinus (CS) was cannulated using a CS guiding catheter. The table was put in the isocenter position, the CS was occluded using a balloon catheter, and 20 ml of diluted contrast used to perform rotational venography. A 3D virtual coronary sinus was reconstructed using *3DCA* software (Philips Medical Systems, Eindhoven, The Netherlands), see figure 1. This model was imported into the MNS, see figure 3. A Titan™ 3mm angled Soft Support wire passed on the first attempt using navigation based on the model into a side branch of the great cardiac vein. An Easytrack 3 lead (Guidant) passed easily over this. A Contak Renewel 4 RF (VVED-CRT; Guidant) was implanted. All checks were satisfactory at implantation and at follow-up.

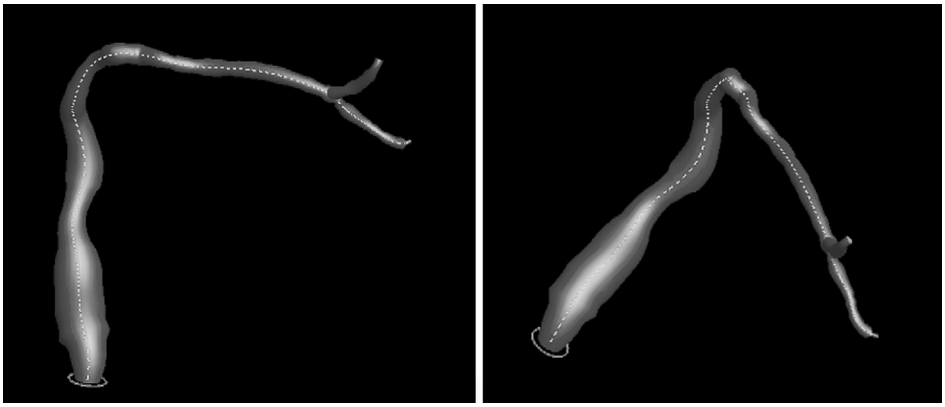

Figure 1. The reconstruction of the coronary sinus in 2 views, the left panel shows AP and the right panel shows LAO 30°.

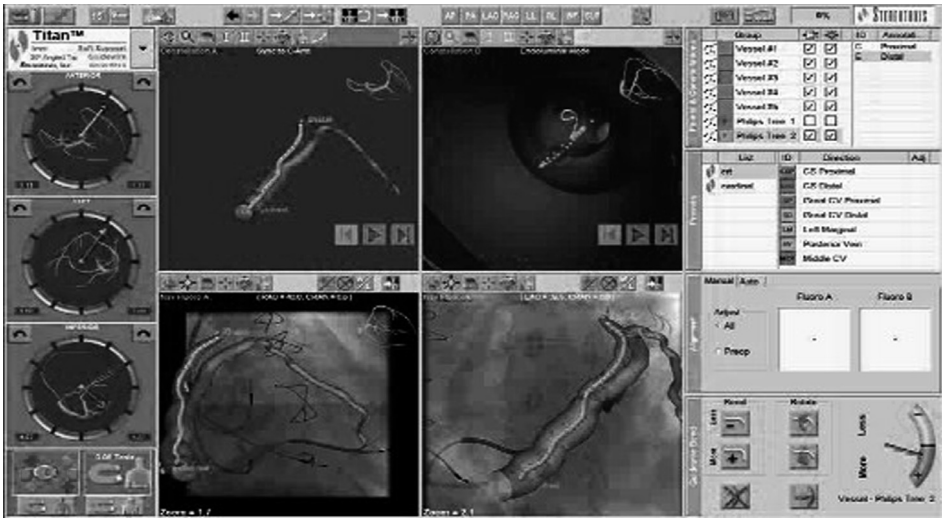

Figure 2. The Stereotaxis screen; The upper panels show the model (upper right) and the endoluminal view (left upper) while the lower panels show the model superimposed on stills of the fluoroscopy.

Discussion

CRT is an important technique in reducing morbidity and improving patient well-being. Cardiac resynchronization therapy (CRT) improves quality of life and prolongs survival in appropriate patients with QRS prolongation or left ventricular (LV) dysynchrony (12-15). However a number of difficulties may hamper lead placement in CRT procedures such as difficulty in obtaining coronary sinus (CS) access, efficiently selecting CS branch vessels, maintaining lead stability, and avoiding both phrenic nerve stimulation and lead dislodgement (16-20).

Feasibility studies suggest that the MNS without full 3D reconstruction appears to be at least as good as manual technique (10,11). The rotational venogram provides a number of possible benefits that may facilitate lead placement in CRT. The production of a patient-specific 3D model supplies the vectors required for image-guided steering of the wire along the length of the vessel, see figure 3. In addition, this 3D model supplies a white line overlay (of the centre-line of the model) that automatically adjusts to the view on the fluoroscopy screen. This acts as a guide to wire positioning. This technique has two clear advantages for contrast use and procedure time for 2 reasons. First, a patient-specific 3D model of the coronary sinus and its branches is produced from a single injection of contrast, thus reducing contrast and time. Second, the use of the patient-specific vectors should facilitate wire placement and re-positioning potentially leading to reduced contrast use and procedure times.

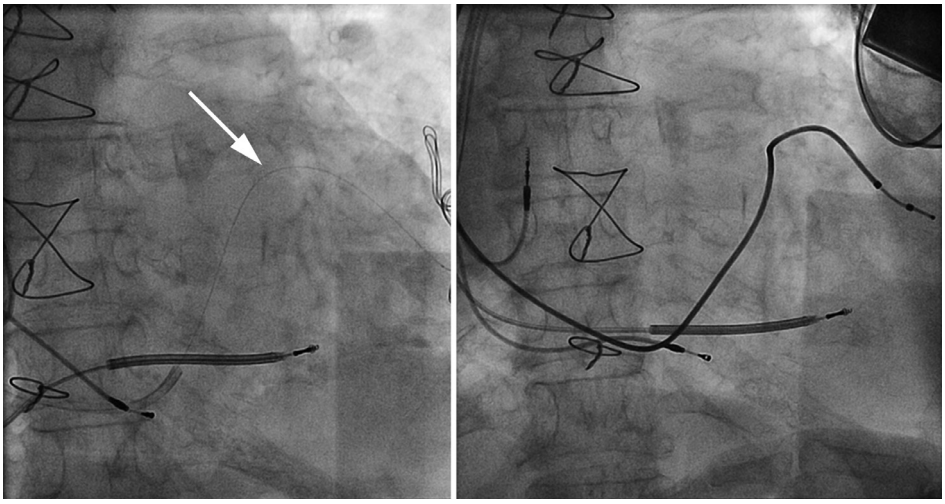

Figure 3. The left panel shows the wire passed distally, while the right panel shows the final result with implanted pacing lead and device.

CONCLUSION

The combination of improved navigation and a reduced burden to the patient and operator may be facilitated by such easy on-table 3D reconstruction as it allows computer generated image guidance of magnetic field direction control and better wire steering. This may lead to faster wire placement by facilitating wire delivery to a target sidebranch and also easier repositioning should unsatisfactory lead stability or phrenic pacing occur. This will lead ultimately to limitation of contrast load, radiation time, and procedure times.

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CHAPTER 9

Magnetically Supported Procedures and Cardiac Regeneration

INTRODUCTION

Cardiac failure secondary to ischaemic heart disease is a leading cause of morbidity and mortality. Infarction leads to cell loss by oxidative stress and reperfusion injury. Chronic ischaemia and myocyte loss produces progressive expansion of the infarct area, fibrous replacement of the myocardium and predisposes to dilation of the left ventricle, a major factor in survival. Progenitor/stem cell therapy has potential for promoting structural and functional repair of the myocardium. Progenitor/stem cells may stimulate either angiogenesis by the release of growth factors and anti-apoptotic factors (including Akt, VEGF and FGF), and/or vasodilation (by VEGF) with an increase in iNOS bioavailability that may help maintain cell viability and encourage blood flow. More controversially, progenitor/stem cells from the bone marrow, circulating blood or embryonically-derived, may lead to myocardial cell regeneration. However to date, improvements in cardiac function and structure have been modest. Current delivery techniques include 2-D angiographically guided endocardial injection and catheter based intracoronary release. However, these techniques have general limitations that include imprecise on-table identification of the best areas to target, poor ability in targeting a specific area, and mediocre identification of the treated area at follow-up. In addition, intracoronary release has specific drawbacks such as induction of ischaemia, or the 'shedding' of cells into the general circulation. Two particular clinical settings that appear particularly appropriate for progenitor/stem cell therapy are those of recent anterior myocardial infarction that results in reduced LV function and of chronic, ischaemic, dilated cardiomyopathy. The development and integration of electromechanical mapping technology, NOGA® XP (Biologics Delivery Systems™, Cordis Corporation, Diamond Bar, CA, USA) with the development of a magnetically navigable injection catheter, the MyoStar™ injection catheter (Biologics Delivery Systems™), could transform cell delivery. This article will review the principles of magnetic navigation with the forthcoming technology; consider how localisation, delivery and follow-up might potentially be improved compared with current techniques; discuss the relevance to two of the clinical settings that might derive the most benefit; and mention the possibilities of improved percutaneous revascularisation that might be used to optimise the local milieu for progenitor/stem cell survival. The purpose of this article is to suggest and speculate upon how this technology might allow integration of the real-time visualisation of target tissue with site directed deliverability in order to reduce procedure times and irradiation, and to simultaneously improve efficacy and follow-up.

MAGNETIC NAVIGATION SYSTEM

The magnetic navigation system (Niobe®, Stereotaxis, St. Louis, MO, USA) consists of two adjustable permanent magnets on either side of the fluoroscopy table (see Figure 1).

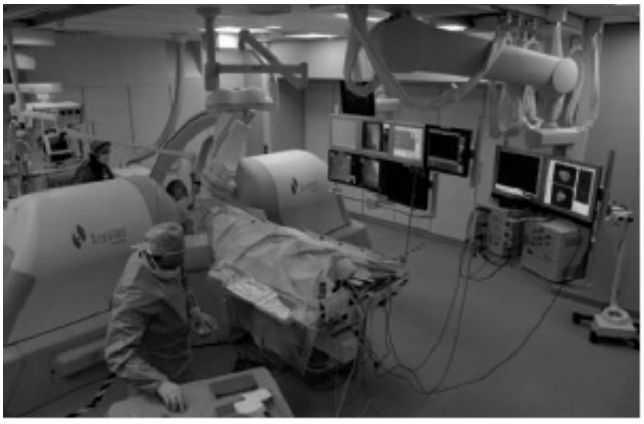

Figure 1. Magnetic navigation system is shown with the magnets in position on either side of the patient. *See this figue in color in the Appendix page 375.*

In essence the system does three things. Firstly, the system operates using a 3-D reconstruction that is either produced from angiographic images (as in the case of coronary arteries) or, alternatively, an imported 3-D reconstruction from an external system e.g. NOGA® XP. Secondly, the spatial orientation and location of this reconstruction is matched to the real-life patient's internal cardiac anatomy; i.e. coronary artery or cardiac chamber. Thirdly, the model gives the real-time, on-line vectors to direct an external magnetic field to orientate a magnet on an intravascular device to match the direction required for navigation through the 3-D reconstruction. The result is the ability to use 3-D information in real-time in patient therapy.

The magnetic navigation system has been described in detail previously. Briefly, the interacting magnetic field produces a 15 cm uniform magnetic field of 0.08 Tesla that can be increased to 0.1 Tesla. Computer controlled movements of the magnets allow redirection of this externally applied magnetic field vector in 360° in all planes. For cardiac chambers a 3-D volume rendered reconstruction is imported and aligned for navigation. For coronary artery use, the 2-D locations of points on X-ray images are known in relation to the image intensifier, angiography system and table and this allows production of a 3-D reconstruction from 2 views separated by at least 30°. The result is real-time, on-table localisation of the reconstruction within the chest of a patient during a procedure to allow direction of therapy. Adjustment of the magnetic vectors from the model synchronised to the X-ray system adjusts tip-magnet direction in the patient to produce deflection of the wire. This gives reproducibly precise steering of the tip of the intravascular device and this steering is independent of the factors that can restrict conventional procedures such as poor transmission of manipulation.

NEW TECHNOLOGY FOR PROGENITOR/STEM CELL DELIVERY

Previous methods for endocardial stem cell delivery had several drawbacks in identification, cell delivery and therapy. Identification of the sites for injections was poor and depended on strategies such as marking acetate sheets overlaid on the X-ray screen, delivery was time-consuming with poor targeting, and follow-up was hampered by imprecise knowledge of where the injections had been and therefore depended on generalised LV measurements rather then the region of interest. The magnetic navigation system can integrate other 3-D volume rendered information such as MSCT, MRI or the NOGA® XP mapping system, see Figure 2, to give precise steering/direction of injections. Infarct localisation is possible by current techniques such as MSCT, which is capable of identifying infarcted areas of myocardium, and integration can provide a 3-D volume rendered map of the damaged myocardium. However this information is not real-time and was of limited use in treating the patient on the table. New technology is under current development. The NOGA® XP mapping system gives information on the functional and electrical properties of the myocardium simultaneously with real-time, precise localisation by producing a map of the left ventricle (see Figure 2).

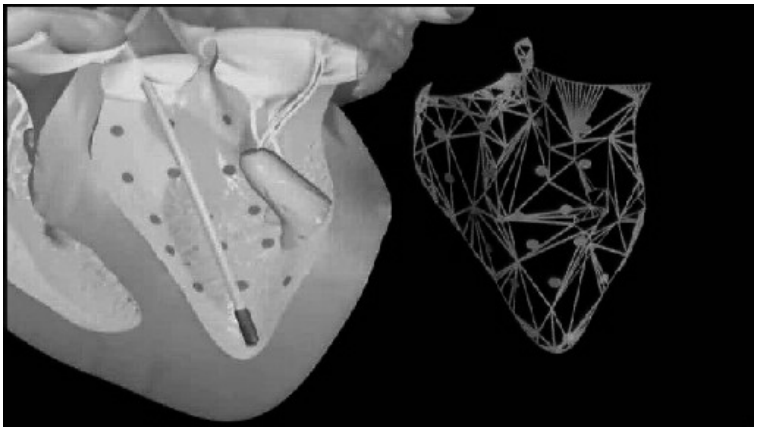

Figure 2. Graphic showing reconstruction of LV mapping. *See this figue in color in the Appendix page 386.*

This may allow differentiation between the extent of the infarct and peri-infarct regions as well as giving valuable information for followup. This, together with the MyoStar™ injection catheter to allow magnetically enabled cell delivery (see Figure 3) may not only allow areas to be identified by electrical and mechanical mapping measurements but also deliver injections of cell therapy. Potentially, this could give several major advantages. Firstly, integration of real-time electromechanical mapping would give a real-time, on-table 3-D LV map for exact localisation. Secondly, electromechanical mapping may discriminate between viable and non-viable infarcted areas e.g. identifying electrically active but non-contractile areas such as stunned myocardium. Therefore this combination of detection methods could enable

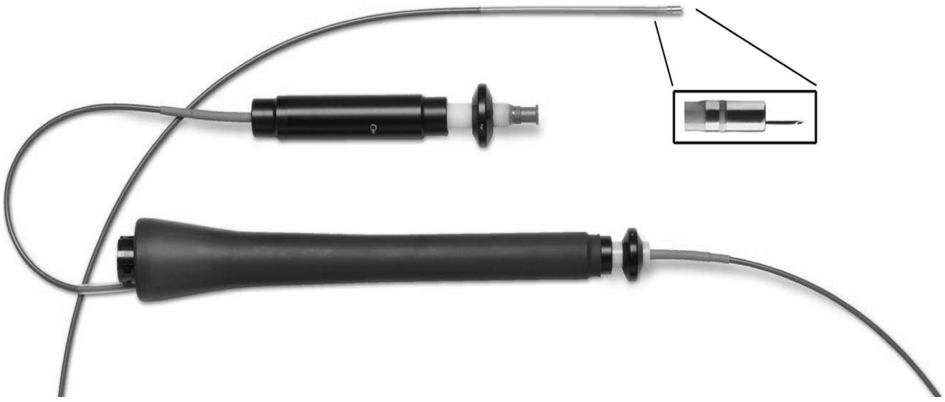

Figure 3. MYOSTAR™ injection catheter to have electromechanical guidance provided by the NOGA® XP. *See this figue in color in the Appendix page 379.*

new strategies that tailor delivery of cell therapy to particular areas. Thirdly, a magnetically navigable injection catheter could precisely direct cell injection and simultaneously integrate spatial and electrical information. Fourthly, an electromechanical map could aid follow-up both to identify the region on the map that was previously treated, and also to give quantifiable information for specific locations on the map. Definable delivery of stem cells would allow investigation of specific locations or patterns of cell delivery. As different parts of an infarcted area may have discordant electrical and mechanical properties, with intact electrical but poor mechanical activity, this may allow identification of stunned myocardium in penumbral regions that might derive particular benefit from stem cell injection. Additionally, current estimates of the resolution of the new system suggest that this could localise positions to within 1 mm that would represent a major improvement. An idea of the type of the information that may be available with this system for diagnosis and follow-up is seen in Figure 4.

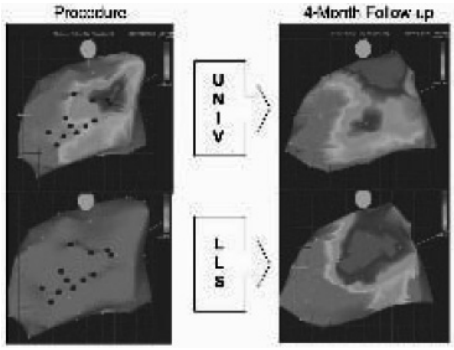

Figure 4. NOGA™ electrical (UNIV, at top) and mechanical (LLS, at bottom) maps from a human patient in the stem cell treatment group. The maps on the left are those performed at the time of injection and maps at right are those at four month follow-up. An area of viability, showing normal electrical activity, can be noted on the upper right map. The maps on the right show improvement in both electrical and mechanical function. LLS = linear local shortening; UNIV = unipolar voltage. *See this figue in color in the Appendix page 387.*

LIMITATIONS OF CURRENT CELL DELIVERY TECHNIQUES

The strategy of endocardial injection has suffered from a number of limitations. The current technique of LV angiography gives mediocre localisation as the entire LV volume is seen only in 2-D pictures from different views. This technique gives little idea of the location of the watershed or penumbral area that might contain stunned rather then necrotic cells. Injection sites, and particularly areas that might be particularly susceptible to improvement with cell therapy, are poorly identifiable in real-time, and are difficult to access with current equipment. Intracoronary injection has been the other widely used technique and has its own limitations. Release of cells depends on haematogenous spread, and this may be poor in areas that are poorly revascularised or are still occluded, therefore reducing the effectiveness in these areas. This inhomogeneous delivery may prevent delivery to salvageable areas that have competitive flow from a neighbouring territory that is, however, insufficient for long-term survival. As intracoronary injection often uses occlusion of the proximal vessel this results in further ischaemic insult with further, possibly irreversible, damage and cell loss and reduced perfusion pressure leading to collapse of pinched microvasculature. Additionally, loss of cells that do pass through the microvasculature into the general circulation, also known as 'shedding', may lead to the drawback of these progenitor cells reaching areas where conditions favourable for angiogenesis are present but clinically unwanted, e.g. neoplastic neovascularisation or ischaemic areas such as retinopathy.

IMPLICATIONS FOR THE CLINICAL SITUATION OF CELL DELIVERY

Two particular situations may be particularly appropriate for treatment of cell therapy; these are recent anterior infarction with significant LV impairment and non-revascularisable chronic ischaemic cardiomyopathy. While these situations have some similarity such as extensive cell loss and unattractiveness for cardiothoracic surgery, there are specific reasons why precisely directed endocardial injection may hold particular advantages. These have advantages over and above the general advantages of improved diagnosis with two modalities, precise site-directed delivery and follow-up discussed above.

The purpose of using cell therapy in the treatment of recent acute MI is to prevent maladaptation or remodelling and so preserve LV contractile function and thus exercise tolerance. This group may be the most effective group to treat with cell therapy in order to maximise myocardial cell salvage. As discussed above, endocardial injection may be advantageous over intracoronary delivery as it delivers cells to areas that have a restricted or absent blood supply. This direct delivery via the endocardium overcomes the problem of tissue swelling related to ischaemic damage that may cause pinching of the microvasculature to reduce haematogenous delivery to peripheral sections of the infarct territory, i.e. to the penumbral areas

that may be particularly suitable for salvage. In addition, endocardial injection decreases shedding of cells into the circulation since cells are injected within the tissue thus placing decreased numbers of cells into the bloodstream. In the treatment of chronic heart failure there has already been tissue loss and often this is combined with severe ischaemic coronary disease. Cell therapy aims to reverse the chronic changes by improving the vascular bed and salvaging as much myocardium as possible. This situation would particularly benefit from addition of new myocardial cells, although the ability to produce new myocytes remains controversial. Precise delivery to electrically and mechanical definable areas could allow uniform coverage or other distributions to target specific areas. In addition the risk of perforation of a thin myocardium may be minimised by use of electrical signals via the adjustable and retractable needle providing exact depth control together with monitoring of the ECG for reverse potentials.

REVASCULARISATION

A further option enabled by the magnetic navigation system is the ability to treat complex coronary disease. As the predominant cause of LV dysfunction is ischaemic heart disease, the partial or complete recovery of the native coronary circulation may encourage both recovery of native myocytes and provide a milieu for better uptake and differentiation of stem cells.

The ability of the system to support PCI has been demonstrated in a number of scenarios from simple to complex lesions and evidence suggests that this system may be particularly advantageous in more difficult anatomy and is capable of successfully treating CTO's. The integration of MSCT data (see Figure 5) allows the missing segment of the vessel to be judged (see Figure 6) and the superimposition of this data by co-registration gives an indication of the pathway.

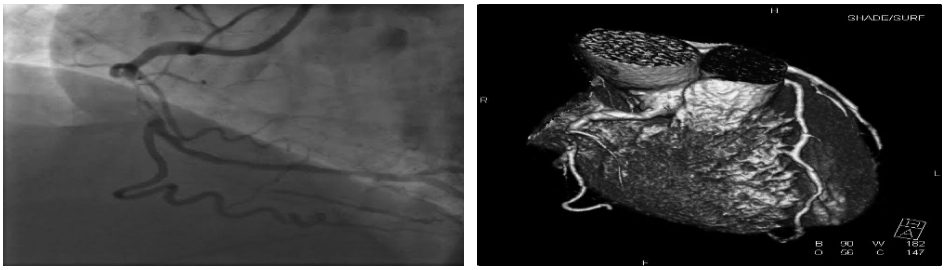

Figure 5. The panel on the left shows the raw data from angiography and the panel on the right shows the reconstructed MSCT. *See this figue in color in the Appendix page 387.*

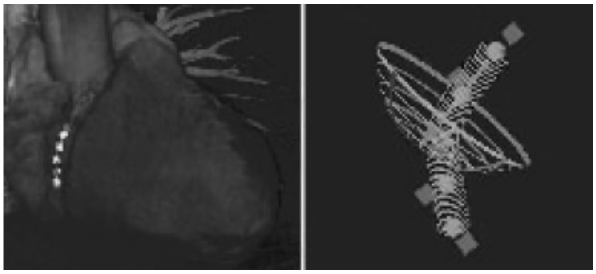

Figure 6. The panel on the left shows the co-registered points applied to the MSCT image that was imported into Navigant and the panel on the right shows the computer reconstructed pathway that is derived from CT and projected onto the reconstruction in Navigant. *See this figue in color in the Appendix page 387.*

CONCLUSION

Magnetic navigation may aid the performance of cardiac stem cell transplantation by allowing integration of spatially localised, 3-D volume rendered information with real-time tissue visualisation in multiple modalities to give site directed deliverability to reduce procedure times and irradiation, and improve efficacy simultaneously.

The development of the NOGA® XP system and the magnetically navigable MyoStar™ injection catheter may lead to improved detection of non-functional myocardium, better delivery and more precise follow-up.

ACKNOWLEDGEMENT

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CHAPTER 10

First experience with remote left ventricular mapping and transendocardial cell injection with a novel integrated magnetic navigation-guided electromechanical mapping system

ABSTRACT

Aims: The purpose of this preclinical feasibility study was to evaluate a novel integrated platform in which magnetic navigation is used to remotely guide electromechanical mapping of the left ventricle (LV) and transendocardial cell injections. Using an integrated remote system would greatly facilitate intramyocardial delivery of stem cells for treating ischaemic heart disease.

Methods and results: We used the computer-controlled Stereotaxis magnetic navigation system to guide the NOGA electromechanical mapping system in mapping viable myocardium in the LV of seven pigs. We then tested the feasibility of this system to perform transendocardial injections in three of the pigs and to deliver mesenchymal precursor cells (MPCs) to targeted myocardial segments in four of the pigs. The success or failure of each injection was determined by myocardial contrast staining in the first group and by histopathologic analysis in the last group. The mean time (±SD) spent mapping the LV for each pig was 49.3±10.6 min. The success rate for transendocardial injections was 94.4%, as indicated by myocardial contrast staining. There was a 95.8% success rate for targeted injections of MPCs, and 4',6-diamidino-2-phenylindole-labeled MPCs were detected in all but one segment of one pig. No epicardial haemorrhage or injury was observed, although there was some venous drainage.

Conclusions: The integrated Stereotaxis/NOGA system has excellent remote navigability inside the LV cavity while sparing the operator from radiation exposure. This system also allows transendocardial cell injections to be performed with a high success rate. Further studies are needed to define the safety profile of this system for clinical use.

INTRODUCTION

Recent studies have suggested that the heart has an intrinsic ability to regenerate after injury (1-3). This new finding has stimulated research on stem cell therapy for ischaemic heart disease (4-7). Preliminary preclinical data have shown that intramyocardial delivery of stem cells results in better cell retention than do intracoronary or retrograde injections through the coronary venous sinus (8). Electromechanically guided injection is the currently preferred mode of delivery in patients with chronic myocardial ischaemia. Using the NOGA electromechanical mapping (EMM) system to deliver transendocardial injections has been shown in clinical studies to be feasible and safe (4,5,9,10). The capability to perform online assessment of myocardial ischaemia and viability using unipolar voltage mapping has also been previously described (11-13). Segments of myocardium with unipolar voltage less than 6.9 mV are associated with transmural scarring on MRI, with a sensitivity of 93% and specificity of 88% (12). The ability of the NOGA system to obtain a detailed map of the LV cavity with 1-mm precision, combined with its ability to differentiate viable from non-viable myocardium, permits the accurate targeting of cell delivery to ischaemic or viable myocardium. The Stereotaxis magnetic navigation system (MNS) comprises two magnets that can be oriented to generate a 0.08-T directional magnetic field. This new system has had good preliminary safety results in patients with complex anatomy undergoing percutaneous coronary interventions (14). The safety and feasibility of this system for guiding electrophysiology catheters for diagnostic and interventional procedures has also been shown (15,16). Integrating the NOGA EMM system with the Stereotaxis MNS would allow remote navigation inside the left ventricular (LV) cavity. In theory, the electromagnetic force exerted at the catheter tip would preclude the need for support from its shaft, thus allowing for the use of a softer catheter that is less likely to penetrate the myocardium and cause perforation. The new catheter also allows for transendocardial injections in remote areas of the LV not easily reached with the current manually directed catheters. This remote navigation capability of this system would also avoid excessive mapping times and undue exposure of the operator to radiation. The purpose of this preclinical feasibility study was to evaluate a novel integrated Stereotaxis MNS-guided NOGA EMM system for remote mapping and stem cell injections. We used a porcine model to test the ability of this system to construct a LV electromechanical map and to deliver transendocardial injections to various myocardial segments.

METHODS

Stereotaxis MNS-guided NOGA EMM system

The MNS (Niobe®, Stereotaxis, St. Louis, MO, USA) consists of two computer-controlled permanent magnets, located in a fixed housing apparatus, that can be manoeuvred relative to each other to create a directional magnetic field (16). The apparatus is located on either side of the fluoroscopy table (AXIOM Artis, Siemens, Malvern, PA, USA) and can be adjusted to the patient's body position. While in the "navigate" position, the magnets create a relatively uniform magnetic field (0.08 T) of approximately 15 cm in diameter inside the patient's chest. The Stereotaxis-compatible NogaStar® mapping and MyoStar® injection catheters (Biologics Delivery Systems, Cordis Corporation, Diamond Bar, CA, USA) are equipped with a small permanent magnet positioned at the tip that aligns itself with the direction of the externally controlled magnetic field, thereby enabling the catheter to be steered effectively. Changing the orientation of the outer magnets relative to each other changes the orientation of the magnetic field, leading to deflection of the catheter (17) (Figure 1). All magnetic field vectors can be stored and, if necessary, reapplied while the magnetic catheter is navigated automatically. In addition, a computer controlled catheter advancer system (Cardiodrive unit, Stereotaxis, St. Louis, MO) is used to allow truly remote catheter navigation without the need for manual manipulation after the catheter has been inserted into the ascending aorta. The video workstation (Navigant II, Stereotaxis, St. Louis, MO, USA), in conjunction with the Cardiodrive unit, allows precise orientation of the catheter by 1° increments and by 1-mm steps in advancement and retraction. The system is controlled by joystick or mouse and allows remote control of the injection catheter from inside the control room, away from radiation sources. The NOGA system enables users to identify viable myocardium by assess-

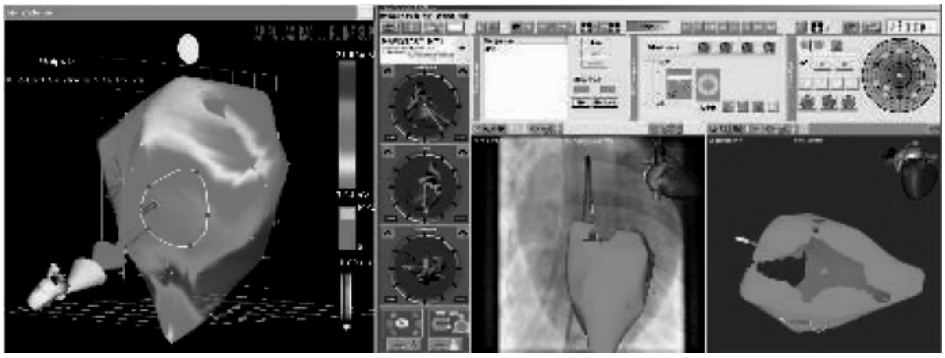

Figure 1. Mapping the LV cavity with the NogaStar® catheter. Left: unipolar voltage map of the LV cavity, showing the Stereotaxis-compatible NogaStar® catheter, the vector of the catheter position (green), and the directional vector (yellow) created by the magnetic field. Right: Navigant II screen showing integration of the fluoroscopy image and the endocardial map. *See this figue in color in the Appendix page 388.*

ing unipolar voltage (12). Thus, integrating the NOGA XP (Microsoft Windows platform) with the Stereotaxis MNS would allow for remote LV navigation and targeted stem cell delivery into viable ischaemic myocardium. The integration of the two systems at the level of the user interface is achieved by simply placing a three dimensional vector into the NOGA map that can be moved by clicking and dragging a computer mouse. Catheter movement tracks the orientation of the vector. No catheter manipulation is required.

Animals

This study was reviewed and approved by the Institutional Animal Care and Use Committee of Washington University (St. Louis, MO, USA) and met the criteria of the National Institutes of Health and American Heart Association for animal research. Seven healthy adult domestic pigs of either sex, weighing between 30 and 55 kg, were subjected to cutdown exposure of the femoral artery for catheter insertion, performance of the EMM procedure, and transendocardial injections.

Remote electromechanical mapping procedure

In brief, general anaesthesia was induced with intravenous pentothal (17 mg/kg) and maintained with isoflurane (1.5% to 2.25%) in each pig. The pig's right femoral artery was then exposed, an 8F introducer was positioned, and the NogaStar® catheter was manually advanced into the ascending aorta. The Cardiodrive unit was used to advance the catheter though the aortic valve into the LV cavity while orienting the magnetic field vector posterosuperiorly to bend the catheter tip against the valve leaflets. After the catheter entered the LV cavity, the vector was redirected to the apex, and the catheter was advanced until it contacted the endocardial surface. Electromechanical mapping was performed by orienting the vector and advancing or retracting the catheter with the Cardiodrive unit until a complete map of the LV cavity was acquired.

Transendocardial injections

The prototype magnetic injection catheter (Stereotaxis-compatible MyoStar®) was evaluated for its navigational characteristics, magnetic deflection capabilities, and the amount of push force exerted by the catheter tip. In a previous study, a prototype injection catheter showed good success in navigating a Stereotaxis small heart phantom; the catheter was able to reach all targets of interest in the LV via the retrograde approach. The injection catheter prototype catheter tip could also be deflected by 150° when the unsupported (or freely deflectable) length was 5 cm. This is comparable to the tip deflection of 132° obtained with the MyoStar® catheter with a similar free length. The push force exerted by the injection prototype catheter

just before the catheter tip buckles, unaided by any magnetic field, was 70 g when the unsupported length was 4.5 cm. Under similar conditions, the tip force exerted by the MyoStar® catheter overloaded the test gauge (> 100 g) without any buckling of the catheter tip. The maximum tip force exerted by the prototype catheter decreases progressively as the tip is bent in response to the applied magnetic field. This will likely contribute to added safety during transendocardial injections in regard to avoiding myocardial perforation (Figure 2). Before performing the transendocardial injections, we manually divided the EMM into a polar map with 13 segments, excluding the most basal segment of the heart (Figure 3). The NogaStar® catheter was replaced with the MyoStar® catheter, and the needle length was set at 5 mm. Phase I of the study tested the feasibility of using the integrated Stereotaxis/NOGA system to perform transendocardial injections.

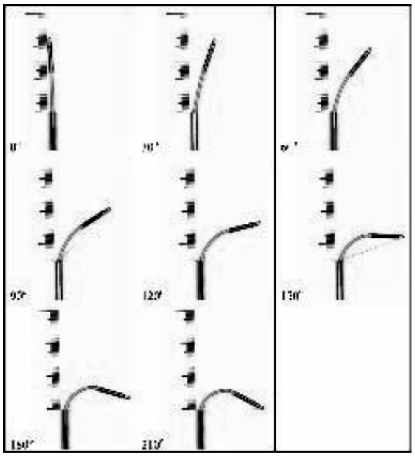

Figure 2. Magnetic deflection of the prototype catheter. Images show magnetic deflection of a prototype catheter in various directions in a 0.08-T field when the catheter is extended 4.5 cm from rigid support. *See this figue in color in the Appendix page 388.*

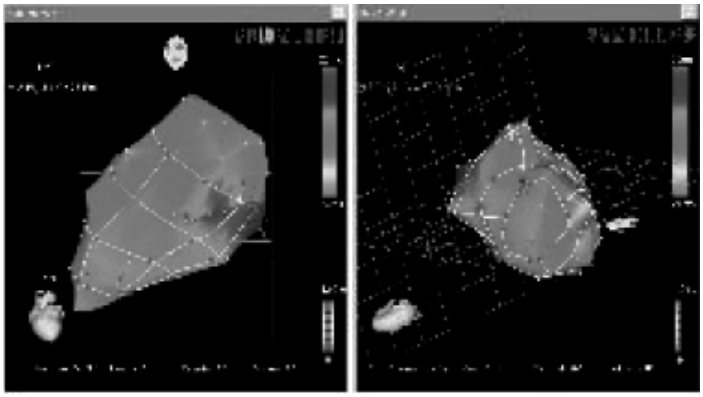

Figure 3. Manually reconstructed polar map from one representative animal of phase I of the study. The basal segments were excluded. *See this figue in color in the Appendix page 388.*

In three pigs, each of the 13 predefined segments was targeted and injected with 0.2 ml of isosmolar contrast medium (iodixanol [Visipaque], Amersham Health, Princeton, NJ, USA). Each segment received three injections of contrast medium. In the second animal the apical segments received an additional nine injections. The presence of contrast stained myocardium by fluoroscopy confirmed the success or failure of each transendocardial injection. For each injection, the catheter angle relative to the endocardial surface was recorded as well as the force exerted by the catheter tip against the endocardium (measured as quartiles from 0 (minimum force) to 4 (maximum force), and the presence of premature ventricular contraction (PVC) upon needle exposure. Phase II of the study tested the ability of the integrated Stereotaxis/NOGA system to deliver bone marrow derived allogeneic mesenchymal precursor cells (MPCs; Angioblast Systems) to targeted segments. The first stem cell-injected animal received unlabelled MPCs and the three animals that followed were injected with 150 million 4',6-diamidino-2-phenylindole (DAPI)-labeled MPCs diluted in 4.8 cc of phosphate buffered saline. In all four animals the injections were targeted to the mid-ventricular segments (anterior, anteroseptal, inferoseptal, inferior, inferolateral, and anterolateral). Four stem cell injections of 0.2 cc were delivered to each predefined segment. As in phase I, we recorded for each injection the catheter angle relative to the endocardial surface, the force exerted against the endocardium (measured as quartiles from 0 to 4), and the presence of PVC upon needle exposure. The pigs were euthanised after the procedure, and their hearts were sent for histopathologic analysis.

Histopathologic analysis

After each animal was euthanised, the aortas and hearts were rapidly excised. Shortly after excision, the pericardial sac of each phase I and II study animal was examined for signs of effusion, and each heart was evaluated for epicardial haemorrhage or injury. Additionally, in the phase II animals, each heart was also evaluated for the presence of DAPI-labelled cells as follows. The heart was perfusion-fixed and then sliced into 1-cm-thick sections (bread-loaf technique). Each slice was photographed on both sides. A portion of the slices was then placed in 10% buffered formalin for immediate histological evaluation, and the other portion was frozen in Tissue Tek optimal cutting temperature compound (Sakura Finetek USA, Torrance, CA, USA) and stored at – 80°C for subsequent histologic analysis. The histopathology slides were correlated with the correspondent injected segment to detect DAPI-labeled MPCs by fluorescence microscopy. Needle tracks were identified, and the depth of each injection (vertical distance from the endocardial surface) was calculated.

Statistical analysis

Descriptive statistics were performed using SPSS software (standard version 11.0, SPSS). Numerical variables are reported as mean±SD. Categorical data are reported as proportions.

RESULTS

The integrated Stereotaxis/NOGA system was used to perform remote EMM and transendocardial injections in seven pigs. The weight of the animals, the number of map points per animal, and the time spent for the mapping and injection procedures are summarised in Table 1.

Table 1. Animal weights and procedure times.

Pig #	Weight (kg)	Number of mapping points	Total mapping time (min)	Total injection time (min)
1	55.0	65	60	143
2	40.0	56	45	80
3	52.0	67	60	60
4	45.0	59	55	60
5	55.0	79	50	45
6	54.5	57	45	35
7	29.5	38	30	36
Mean	47.3	60.1	49.3	65.6
SD	9.7	12.5	10.6	37.6

The mean mapping time (±SD) was 49.3±10.6 min per animal, or 49.4±6.3 s per mapping point.

Phase I: injection feasibility

A total of 126 0.2-ml injections of iodinated contrast dye were performed. One hundred and nineteen injections (94.4%) were successful; that is, they resulted in myocardial contrast staining. The presence of PVC upon needle exposure predicted successful transendocardial injection with a sensitivity of 98% and a specificity of 71%. The catheter angle relative to the endocardial surface varied from < 30° to 90°, and the force exerted against the endocardium varied on a scale of 0 to 4. Transendocardial injections had a high rate of success regardless of the catheter angle and force (Table 2).

Table 2. Success rates of intramyocardial injections by catheter angle and force exerted against endocardium.

	Myocardial staining		Success
	Present	Absent	rate (%)
Catheter angle (degrees)			
<30	21	1	95.5
30-59	54	2	96.4
60-89	39	3	92.9
90	5	1	83.3
Total	119	7	94.4

Venous drainage, defined as contrast staining of the vein, was observed in 50 (39.7%) of the 126 injections. Histopathologic analysis revealed no evidence of pericardial effusion, epicardial haemorrhage, or injury.

Phase II: Stem cell injection feasibility

A total of 96 injections of MPCs were performed. In the first animal injected with unlabelled MPCs, the presence of MPC clusters and corresponding needle tracks in the myocardium was confirmed by gross microscopy (Figure 4). In the remaining three animals that received transendocardial injections of DAPI-labelled MPCs, the presence of MPCs was assessed under fluorescence microscopy. The depth of the injections was also assessed at higher magnification. MPCs were detected in 23 of the 24 injected segments for each animal, comprising a success rate of 95.8% (Figure 5). Histopathologic analysis revealed no evidence of pericardial effusion. In each animal, needle tracks could be identified in 18 of the 24 injected segments. In 16.7% of injected segments, the needle track length reached the entire thickness of the correspondent myocardial segment. The remaining needle tracks identified injections with a mean depth of 53.5±17.3% of the LV wall thickness. The only injected segment (out of 24 injected segments) that did not contain injected cells was the mid-inferior segment of pig #7. In this pig, DAPI-labelled cells were found at the epicardial surface, and small petechiae were found in the mid-anterior segment (Figure 6). This pig had a substantially lower body weight, a lower heart weight (235 g), and thinner LV walls than did the other animals.

Figure 4. Transendocardial injections of unlabelled MPCs. (A) Several needle tracks (arrows) and an area of micro-haemorrhage (box) in the subepicardial space. (B) Distribution of MPCs along a needle track, with concomitant haemorrhage (red areas). (C) Cluster of MPCs at higher magnification. *See this figue in color in the Appendix page 389.*

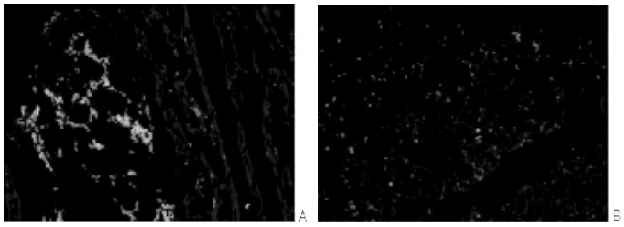

Figure 5. Frozen sections of an injected myocardial segment imaged under fluorescence microscopy (blue, DAPI-labelled nuclei; green, α- sarcomeric actinin). A. Small cell cluster corresponding to an injection site. B. DAPI-labelled MSCs dispersed throughout the apex. Magnification: x20. *See this figue in color in the Appendix page 389.*

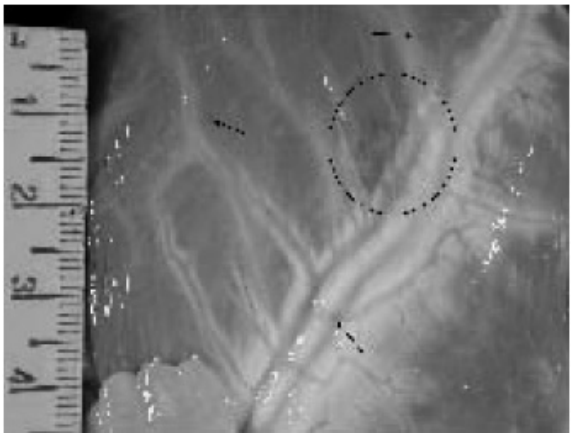

Figure 6. Small petechiae (arrow and circled area) in the anterior wall of pig #7. *See this figue in color in the Appendix page 389.*

DISCUSSION

This initial preclinical experience provides preliminary evidence of the feasibility of remote EMM, transendocardial injections, and LV cavity navigation with the integrated Stereotaxis MNS guided NOGA system. The new Stereotaxis-compatible mapping (NogaStar®) and injection (MyoStar®) catheters have demonstrated excellent capacity for intraventricular navigation, being able to reach every endocardial segment needed to construct an electromechanical map and successfully perform endocardial injections. Furthermore, this system preserved navigation precision and map quality while sparing the operator from exposure to radiation during the procedure. Magnetically driven navigation has important advantages over conventional catheter manipulation inside the LV. Because the force driving the catheter and holding it stable against the endocardium is exerted on the tip of the magnetically guided catheter, its shaft does not need to provide backup support and is flexible enough to allow the movement guided by the magnetic field. This feature permits the catheter to bend at acute angles to reach remote segments while keeping a stable position after needle exposure. This allows for easy mapping and injection of LV segments, such as the high anterior wall, that are extremely difficult to reach with conventional catheter techniques. The excellent navigability of the catheter and the magnetic force holding it against the myocardium could explain the high success rate of our transendocardial injections (Figure 7) regardless of the catheter angle or its force against the endocardium. In addition, the softer shaft of the magnetically guided catheter may help prevent cardiac perforation. The present study offers new insights into transendocardial injections. First, we found that the presence of a PVC upon needle extension can be used to guide transendocardial injections. In the first set of transendocardial injections, the presence of PVC predicted the success of the injections with high sensitivity. Second, a substantial number of contrast injections (nearly 40%) resulted in some degree of

drainage by the coronary venous system. This phenomenon could influence retention rates after delivery of cells though this route, so transendocardial delivery strategies may need to be optimised to limit venous delivery of cells.

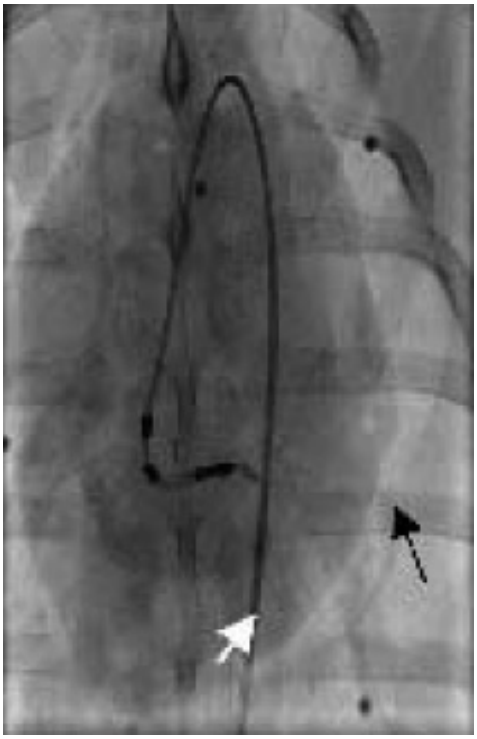

Figure 7. Image from fluoroscopy of a transendocardial injection, showing the acute angle made by the catheter. Myocardial staining confirms the intramyocardial position of the needle. Vein drainage is evident (arrow).

Study limitations

Because of the small number of animals and the constant needle length used in this study, the full safety profile of this new catheter navigation system could not be established. Although there was no histopathologic evidence of pericardial effusion, injected cells were found in the epicardium of one pig, which also had petechiae in the epicardial surface. Further preclinical studies specifically designed to assess safety should be performed before this system is used for transendocardial injections in patients. The success rates with this new catheter may have been overestimated because of the small number of animals used, although we did perform a large number of injections that were well distributed throughout the LV. In addition, the success rates achieved with this new catheter have not been compared head-to-head with those achieved with conventional manual navigation.

CONCLUSIONS

The integrated Stereotaxis MNS-guided NOGA EMM system can be used for remote navigation inside the LV cavity and allows the performance of transendocardial injections with a high success rate. The feasibility of this system for transendocardial cell delivery was confirmed by histopathologic analysis. More studies are needed to define the safety profile of this system.

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PART III

Initial experience in clinical practice and illustrative case reports

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CHAPTER 11

Use of the Stereotaxis Niobe® Magnetic Navigation System for Percutaneous Coronary Intervention: Results From 350 Consecutive Patients

ABSTRACT

Objective: The Stereotaxis Niobe® magnetic navigation system (MNS; Stereotaxis, St. Louis, MO) facilitates precise vector based navigation of magnetically-enabled guidewires for percutaneous coronary intervention (PCI) by using two permanent magnets located on opposite sides of the patient table to produce a controllable magnetic field. The objective of this study is to describe the results of a large patient series using this system, to compare the results with a historical control group, and to detail the MNS learning curve.

Methods: We prospectively collected data on 439 lesions in 350 consecutive PCI patients using the MNS predominantly using the radial approach. All data were entered into a customized database to capture the key parameters and then compared with a previously collected stent registry from the same center.

Results: In 410/439 lesions (93%) the wire crossed the lesion successfully using the MNS. Twenty-five of the 35 failures were chronic total occlusions. No wire perforations or dissections occurred in this population. Lesion crossing time was 81 ± 168 sec (mean ± SD), and fluoroscopy time was 64 ± 123 sec. A clear learning curve was evident after the first 80 patients. Contrast use was reduced when compared with a historical control group. Procedural and fluoroscopy times were similar.

Conclusions: Use of the MNS may enable the successful performance of more complex procedures in the cardiac catheterization laboratory with an improvement in time efficiency.

INTRODUCTION

Percutaneous coronary intervention (PCI) has become the standard of care for the treatment of ischemic lesions of the coronary arteries. While the success rates of PCI are generally excellent, there exists a subset of procedures that are either difficult or impossible to complete due to a myriad of factors, such as complex angulations or recalcitrant disease processes. Recently, a magnetic navigation system (MNS) has been developed for the precise steering of endovascular devices. Use of the MNS in cardiology procedures is becoming increasingly established. Several published reports have shown the clinical utility of the MNS in routine electrophysiology catheter ablation procedures, including specific reports describing its use in atrioventricular nodal reentrant tachycardia (1), atrioventricular re-entrant tachycardia (2), right ventricular outflow tract tachycardia (3), and parahisian accessory pathways (4). Additional studies have demonstrated the ability of the system to add benefit to more complex arrhythmia ablation procedures such as ventricular tachycardia (5) and atrial fibrillation (6,7), and to facilitate the placement of left ventricular leads in cardiac resynchronization therapy device implantation procedures (8).

With the advent of the magnetically enabled wires and the advanced software tools for interventional cardiology, investigators have reported their initial experiences on the use of MNS in routine (9,10) and complex (11) PCI procedures. Case studies have been published on the use of MNS in complex interventions such as alcohol septal ablation (12) and crushed stent crossing (13), and an animal study has been published detailing its potential utility in left ventricular transendocardial cellular injection (14). Recently an exhaustive review of the use of this technology in PCI has been published, including a description of several future concepts and developments (15). To date, however, no extensive clinical series on the use or learning curve of MNS in a large series of PCI patients has been published in the literature.

The objective of the present study is to detail the results of PCI with the MNS in a large consecutive patient series, to compare these results with a similar historical cohort, and to describe the learning curve associated with this system.

METHODS

Patient Population

Three-hundred and fifty consecutive patients with 439 lesions underwent PCI at our hospital using the MNS. All patients undergoing PCI were treated via the right radial approach unless contraindicated. Patient data was prospectively collected and entered into a custom-designed PCI database.

Medication and PCI

Patients were pretreated with aspirin (600 mg Aspegic i.v.), clopidogrel (600 mg plavix p.o.) and heparin (100 IU per kg). Patients were orally sedated with oxazepam 5 mg. Choice of type of guide catheter, balloon catheter and stents was left to the discretion of the operator.

Magnetic Navigation System

The Niobe MNS (Stereotaxis, Saint Louis, MO), is a fully integrated system (workstation and magnet control equipment) for navigating proprietary catheters and guidewires that have very small magnets placed at their distal tips. The orientation of these devices is controlled by precise manipulation of the field generated by two large neodymium–iron–boron magnets that are mounted on mechanical positioners on either side of the patient. Rotation and translation of these magnets maintain a net magnetic field of 0.08-T within a 20-cm diameter sphere in the patient's upper thorax. These magnets are permanent and can be stowed and retracted away from the patient when not in use.

The MNS is fully integrated at our center with the Integris Allura FD10 cardiovascular imaging system (Philips Medical Systems, Eindhoven, The Netherlands) as shown in Fig. 1. The operator interfaces with the system via the Navigant™ navigation work station (NWS) software interface ("NWS," Stereotaxis, St. Louis, MO). The NWS has several features that are specifically engineered for interventional cardiology procedures. These features include 3D preoperative navigation that allows the user to import and coregister standard digital imaging and communication in medicine images and perform "point and click" navigation on the imported image. In addition, the NaviView software (CardiOp-B, Paieon Medical, Rosh Ha'ayin, Israel) allows use of angiographic images from the procedure to generate a 3D vessel reconstruction that can also be used for "point and click" navigation (Fig. 2).

Fig. 1. The Stereotaxis Niobe MNS. The magnet positioners are on either side of the patient table, with the Philips Integris Allura FD10 Single plane C-arm fluoroscopy machine in the center. *See this figue in color in the Appendix page 390.*

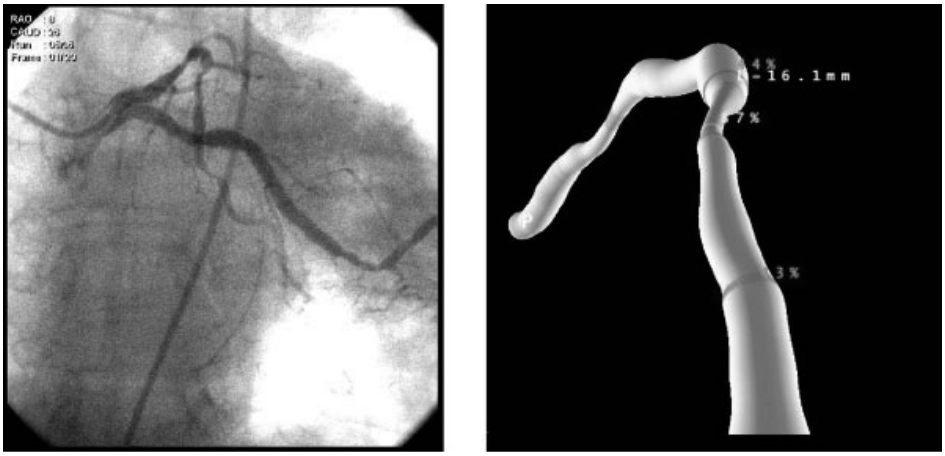

Fig. 2. NaviView Feature. This three-dimensional reconstruction was created from the fluoroscopic angiogram as shown using the NaviView software feature (powered by the Paieon software). *See this figue in color in the Appendix page 390.*

In our centre, there was no standard protocol for choice of wire and navigation technique (2D mode, 3D mode, or a combination of these), although 3D mode navigation was predominantly used in patients with more complex pathology.

Magnetically Enabled Wires

A series of magnetically enabled disposable guide wires that are custom designed to integrate with and be precisely navigated by the MNS are available in a variety of sizes and a range of stiffness. For this study, we utilized the Titan™ Guidewires, a family of endovascular guidewires specifically designed to be more flexible and steerable for navigation in small, angulated vessels and the Assert™ Endovascular Guidewire, a magnetically controlled wire with a stiffer (2.29 g), more pushable tip engineered for crossing difficult coronary lesions. A schematic of a Titan Guidewire is shown in Fig. 3.

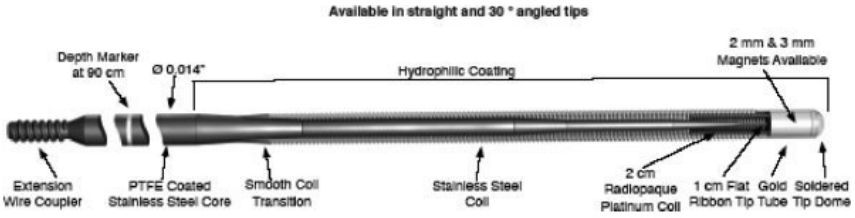

Fig. 3. Titan™ Guidwires. This schematic shows the basic design features of the magnetically enabled Titan Endovascular Guidewires. *See this figue in color in the Appendix page 390.*

Historical Control Group

Thousand four hundred and seventy seven patients underwent single vessel single lesion coronary stent implantation in our center between March 2001 and December 2002. Data were prospectively stored in a dedicated database.

After matching for senior operators, for 6F guide use and for an equal distribution of elective PCI and primary PCI, 385 patients remained for comparison with the MNS group. No major changes in PCI protocols were introduced (except for use of the MNS) that could influence procedural time, fluoroscopy time and contrast use between 2001 and 2007. The basic technique involved transradial direct stenting via 6F guides, just as in the present protocol. The same operators and nursing staff were involved in these interventions.

Learning Curve Evaluation

An early analysis of the results in the first 80 patients (99 lesions) was compared with the total outcome and with three consecutive groups of 80 patients. The parameters used to describe a learning curve were time and fluoroscopy time required to cross a lesion, total procedural time, total fluoroscopy time and success rates.

Statistical Analysis

Continuous variables are expressed by mean ± SD and were compared by the unpaired two-tailed student's t-test. Proportions were compared with the Chi-square test. A P-value < 0.05 was considered to be statistically significant. All data was analyzed using Primer of Biostatistics software (Stanton A. Glantz, Mc.Graw-Hill, San Francisco).

Definitions

To facilitate the interpretation of the data collected in this study, the following standard definitions were used:

- *Time to cross lesion*: Time (sec) required to advance the wire from the tip of the guide catheter to a point well distal to the target lesion.
- *Fluoroscopy time to cross lesion*: Fluoroscopy time (sec) required to advance the wire from the tip of the guide catheter to a point well distal to the target lesion.
- *Contrast used to cross a lesion*: Amount of contrast (in ml) required to advance the wire to a point well distal to the lesion.
- *Procedural time*: Time from the start of the puncture to complete removal of the final guide catheter.

- *Fluoroscopy time*: Fluoroscopy time from start of puncture to complete removal of the final guide catheter.
- *Contrast use*: Total amount of contrast used during the procedure.

Vessel and lesion tortuosity, calcification, and lesion eccentricity were graded on a semi quantitative scale, varying from none, moderate to severe.

RESULTS

From 20 September 2006 to 1 May 2007, 350 consecutive patients assigned to two operators (FK and MP) underwent PCI with the MNS. In 335 patients (95.7%) the radial approach was used. Patient characteristics and angiographic data of the MNS group and the control group are summarized in Tables 1–4, respectively.

Table I. Patient characteristics1

	MNS group (n = 350)		Control group (n = 385)		
	N	SD/Percentage	N	SD/Percentage	P-value
Age (years)	62.9	11.6	62.5	11.9	NS
Male	26.5	75.7	29.1	75.6	NS
Diabetes mellitus	62	17.7	44	11.4	0.02
Family history	111	31.7	98	25.5	NS
Current smoker	87	24.8	102	26.5	NS
Hypertension	138	39.4	146	37.9	NS
Cholesterol	95	27.1	145	37.6	0.003
AP CCS 0–1	11	3.2	11	2.9	NS
AP CCS 2	63	18	27	7.0	<0.001
AP CCS 3	159	45.4	133	34.5	0.003
AP CCS 4	117	33.4	214	55.6	<0.001
Previous PCI	115	32.8	66	17.1	<0.001
Previous MI	74	21.2	107	27.8	0.05
Previous CABG	43	12.3	31	8.1	NS
Stable AP	214	61.1	161	41.8	<0.001
Unstable AP	77	22	145	37.7	<0.001
Primary PCI	46	13.1	50	13.0	NS
Other	13	3.8	29	7.5	NS

AP, angina pectoris; CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; MI, myocardial infarction

Although 52.6% of patients had multivessel disease, a single vessel was treated in 82.6% of patients. A total of 439 lesions were treated in the 350 patients (mean of 1.25 lesions per patient).

Vessel and lesion specifications, including QCA data (n = 439) are displayed in Table 3. Mean lesion length was 18.3 ± 13.3 mm (mean ± SD). TIMI 3 flow was present in 301 vessels (68.6%). More complex lesions (type B2 and C) were found in 68.8%. Severe tortuosity

Table 2. Patient Characteristics

	MNS group (n 5 350)		Control group (n 5 385)		
	N	Percentage	N	Percentage	P-value
1 Vessel disease	166	47.4	205	53.2	NS
2 Vessel disease	125	35.7	105	27.3	0.02
3 Vessel disease	59	16.9	75	19.5	NS
1 Lesion treated	290	82.6	385	100	<0.001
2 Lesions treated	57	16.3	0	0	<0.001
3 Lesions treated	3	0. 8	0	0	<0.001
Radial	335	95.7	359	93.2	NS

Table 3. Lesion Characteristics

	MNS group (n 5 439)		Control group (n 5 385)		
Vessels	N	Percentage	N	Percentage	P-value
RCA	111	25.4	93	24.2	NS
LM	4	0.9	10	2.6	NS
LAD/D/AL	211	48.1	206	53.5	NS
CX	58	13.2	52	13.5	NS
OM	40	9.1	10	2.6	<0.001
VBG	15	3.4	14	3.6	NS
QCA	Mean	SD	Mean	SD	P-value
RD (mm)	2.61	0.59	2.84	0.57	<0.001
MLD (mm)	0.54	0.48	0.61	0.47	0.04
DS (%)	79.2	17.6	77.7	16.0	NS
Length (mm)	18.3	13.3	–	–	–
Flow	N	Percentage	N	Percentage	P-value
TIMI 0	68	15.5	76	19.7	NS
TIMI 1	26	5.9	26	6.8	NS
TIMI 2	44	10	34	8.8	NS
TIMI 3	301	68.6	249	64.7	NS

AL, anterolateral branch; CX, circumflex coronary artery; D, diagonal; LAD, left anterior descending; LM, left main stem; OM, obtuse marginal; RCA, right coronary artery; VBG, venous bypass graft; DS, diameter stenosis; MLD, minimal luminal diameter; RD, reference diameter.

Table 4. Lesion Characteristics

	MNS group (n 5 439)		Control group (n 5 385)		
Type	N	Percentage	N	Percentage	P-value
Type A/B1	137	31.2	138	35.8	NS
Type B2	99	22.6	88	22.9	NS
Type C	203	46.2	159	41.3	NS
Pathology	N	Percentage		Not assessed	
Tortuosity+++	49	11.2	-	-	-
Calcified+++	74	16.8	-	-	-
Eccentric+++	169	38.5	-	-	-

(11.2%), calcifications (16.8%) and eccentricity (38.5%) were seen in 11.2, 16.8, and 38.5% of lesions, respectively.

Out of 439 lesions, 404 could be crossed with MNS (92%). Of the 35 failed attempts to cross, 25 were chronic total occlusion (CTO) (71.4%). Following a failed attempt, 30 attempts were made with conventional wires without MNS (85.7%). Of these, 14 (46.6%) were successful. Totally 49 CTO's have been attempted with varying techniques (2D 49%; 3D 51%). In all instances the lesion could be reached. However, only 24 (49%) CTO's were successfully crossed with a magnetic wire. In 20 out of the 25 failed attempts (80%), the procedure was continued with conventional wires, of which 9 (45%) could finally cross the lesion. The mean total number of coronary wires used was 1.5 ± 0.8.

Final procedural success was obtained in 410 of the 439 lesions giving a success rate of 93.4%. No wire perforations and dissections occurred. Time to cross the lesion (n = 410) was 81 ± 168 sec (range 1–2,160 sec) and fluoroscopy time was 64 ± 123 sec (range 1–1,581 sec). Time to cross A and B1 type lesions (n = 136) was 51 ± 94 sec, whereas in type B2 and C lesions (n = 5 268) this took 96 ± 194 sec [P = 0.01]. Fluoroscopy times to cross lesions were 41 ± 73 and 76 ± 141 sec, respectively [P = 0.008]. All type A and B1 lesions could be crossed and all failed attempts to cross (n = 35) were found in type B2 and C lesions [P < 0.001].

In the first 3 months of MNS use (80 patients and 99 lesions crossed) these times were 142 ± 272 (range 4–2,160 sec) and 109 ± 202 sec (range 4–1,581 sec), respectively [P = 0.005]. When divided into groups of 80 patients, a trend to a reduction in times was obvious (Fig. 4).

Total procedural and fluoroscopy times were 33.9 ± 19.3 (range 7.5–138 min) and 9.2 ± 7.6 min (range 1.2–56 min), respectively. In the first 80 patients these values were 37.4 ± 17.1 (range 12–94) [P = 0.05] and 11.0 ± 9.5 min (range 2.3–56) [P = 0.01] (Fig. 5).

The mean amount of contrast agent required to cross the lesion was 5.4 ± 12.0 ml. No contrast was used in 51% of patients and 0–10 cc of contrast was used in 36.1% of lesions. Total amount of contrast used was 138 ± 91 ml (range 20–600 ml). In the first 80 procedures total contrast consumption was 153 ± 98 (range 30–600 ml) [P = 0.19].

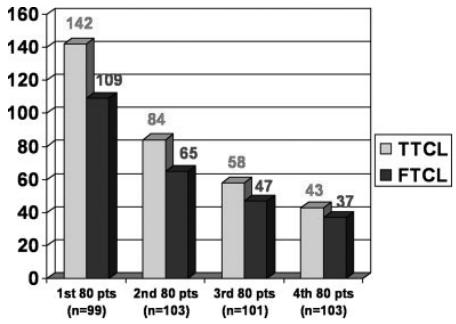

Fig. 4. Decreasing times in seconds (mean ± SD) to cross lesion and fluoroscopy times in four consecutive groups of 80 patients. *See this figue in color in the Appendix page 391.*

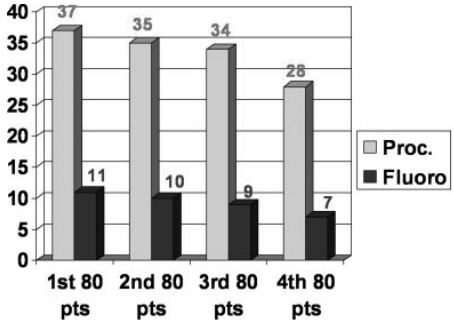

Fig. 5. Decreasing procedural and fluoroscopy times in minutes (mean ± SD) in four consecutive groups of 80 patients. *See this figue in color in the Appendix page 391.*

Significantly more lesions were treated in the MNS group (1.25 ± vs. 1.0 ± 0; P < 0.001). Despite this difference in favor of the control group, procedural and fluoroscopy times were similar: 34.3 ± 20.4 [NS] and 10.2 ± 8.3 min [NS], respectively. More contrast was used in the control group when compared with the MNS group, with a mean of 212 ± 112 ml [P < 0.001].

DISCUSSION

This study provides the first large single center patient series describing the results obtained using MNS for PCI. In this fairly complex group of patients, success rates were high and procedural parameters were at least within the limits usual in our practice. Moreover, in the MNS group significantly more lesions per patient were treated, while procedural and fluoroscopy times were within the same range as the single lesion stent control group. Inevitably there were differences between the study population and the historical control group (Tables 1– 3).

However, factors influencing outcome have been matched to the greatest extent possible. Operator experience, use of transradial approach, use of 6F guides, coronary stenting and patient acuity were considered to be the most influencing parameters. Actually, the MNS group was less favorable (1.25 lesion per patient), since the control group only contained single vessel stenting (1 lesion per patient). In addition, in the control group all lesions could be crossed by the wire, while in the MNS group this was just the target issue.

Recently data were published on an evaluation of fluoroscopy times and correlation of outcomes after single vessel PCI (16) In 9,650 patients treated at a single center from 2000 to 2004, procedural and fluoroscopy times were 81.6 ± 60.6 and 18.3 ± 12.2 min, respectively. The procedural data from our current series compare quite favorably with these data, as well. The fact that currently most failures in our practice occurred in patients with CTO and that only 49% of CTO's could be crossed by use of magnetic wires alone, are not due to navigation problems but rather are due to shortcomings in wire technology. Since MNS for PCI is a young

technique, these magnetically enabled wires do not yet have all specifications required to deal with very tortuous, calcified, and totally occluded lesions. However, improvement in wire technology is imminent and should help to increase the success rates for CTO. In addition, the 3D reconstruction software tools are currently being improved. The ability to reconstruct the complete vessel with the lesion in a more detailed fashion may allow further refinement of navigation. We decided to obtain MNS in our PCI practice because the technique offers a wide scale of both current and future advantages. The combination of several visualization techniques with fluoroscopy, means that success rates might be improved in complex situations with shorter procedural times and with the use of fewer disposable materials. In addition, the technique offers the possibility of reducing contrast agent usage, which obviously is of great value, especially in the diabetic population. Faced with a growing population of patients with complex coronary pathology, these issues are becoming of practical and economic importance. Once the system was installed in our center, a core group of two cardiologists, three nurses and one technician were designated to use the system to concentrate knowledge and experience and to become independent from the support team of Stereotaxis. In a later phase, this group will train the other members of the interventional group to expand PCI practice by MNS. One may argue that MNS is not required for simple pathology and this is recognized by our group. However, by treating a large consecutive group of patients with the MNS, operators, nurses, and technical staff became thoroughly familiar with the system and its technical options in a relatively short period of time and this resulted in a steep decrease in learning time. In comparison with the first 80 patients, all of our procedural parameters significantly improved. Once the operator and staff become experienced with the system, the MNS can be used in very complex situations as well, which will lead to optimal success rates. With continuously improving hardware and software and wire technology, it is our conviction that the MNS will become a standard tool in future catheterization laboratories.

Study Limitations

The main caveat of this study is the lack of a contemporary control group or of a randomized assignment of patients. We sought to mitigate this shortcoming by limiting our comparison group with a consecutive series of single vessel single lesion PCI patients done at the same center by a senior interventional team using the same basic techniques (transradial stenting via 6F guides). Although not as rigorous as a prospective, randomized, controlled trial, we believe that the similarities between the two groups offer a valid comparison that will be of value to the interventional community.

CONCLUSION

Magnetic navigation is highly applicable, safe, and successful in day-to-day practice. When adequate proficiency is achieved, no additional time is added to the procedure when compared with conventional methods.

Use of the MNS was associated with a reduction in contrast use, when compared with a matched historical control group at our center. Future directions for research should include advancements in wire technology and improvements in the software design.

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CHAPTER 12

A Randomized Comparison of the Magnetic Navigation System Versus Conventional Percutaneous Coronary Intervention

ABSTRACT

Objective: A randomized comparison of the magnetic navigation system (MNS) to conventional guidewire techniques in percutaneous coronary interventions.

Background: The MNS precisely directs a magnetized guidewire in vivo using two permanent external magnets.

Methods: A total of 111 consecutive patients were enrolled. Crossing success, crossing-/fluoroscopy times, and contrast usage were directly compared. Lesions were classified according to the AHA/ACC criteria. Three tertiles of vessel/ lesion complexity (low (<5), medium (6–10) and high (>10)) were defined using 3D reconstructions and angiographic information.

Results: The crossing success for magnetic and the conventional wires were 93.3 and 95.6%, respectively. Crossing and fluoroscopy times were longer with the magnetic wires (72.9 ± 50.3 sec vs. 58.1 ± 47.2 sec, $P < 0.001$ and 66.2 ± 44.1 sec vs. 55.2 ± 44.4 sec, $P = 0.03$, respectively). In vessels with low and medium complexity the magnetic wires had significantly longer times ($P < 0.001$) but for those with high scores (>10) a trend towards shorter times was observed. The MNS resulted in a small but significant reduction in contrast usage (2.3 ± 3.5 ml vs. 4.5 ± 4.4 ml, $P < 0.001$). Moreover by superimposing a virtual roadmap of the vessel on the live fluoroscopy image 48% of the lesions were crossed without requiring contrast agents with the MNS.

Conclusion: The MNS has comparable crossing success to conventional PCI. It is relatively slower but there is a trend to support a potential advantage in more complex vessels. By simultaneously employing a virtual roadmap there is a small but significant reduction in contrast usage.

INTRODUCTION

Magnetic navigation is an innovative technology that can accurately control the positioning of a guidewire or a catheter in vivo (1). To accomplish this, a small (2–3 mm) magnet embedded at the tip of the wire or catheter is reoriented by a predetermined and rapidly updated external magnetic field. The field is generated by two permanent external (0.08 Tesla) magnets that can rotate, tilt, or translate on movable positioners (2). Within this field a magnetic vector is created through computer driven software to direct the tip of the device (the magnetically enabled wire or catheter). The advantage of in vivo control has been previously demonstrated in cardiac electrophysiological procedures whereby inaccessible pathways can be effectively targeted, even remotely (3). In percutaneous coronary intervention (PCI) the initial bend placed on the wire to engage the target vessel might not be ideally suited to cross the target lesion. As such, preliminary studies in patients with complex lesions and tortuous vessels have shown an advantage with magnetic assisted intervention (MAI) in cases that failed with conventional PCI (4). However, to date the only randomized direct comparison of the magnetic navigation system (MNS) to conventional approaches was performed in increasingly tortuous phantom models where it was suggested that the MNS might be advantageous (5). To further assess the implication of this novel technology to PCI, it is necessary to include randomized comparisons in native coronary lesions. Areas that warrant investigation include evaluating procedural success, crossing/fluoroscopy times together with contrast media usage. It is perceived that for some of these parameters the MNS may be advantageous as reorienting the wire in situ and the navigational road map created from a 3D reconstructed image—superimposed on real-time fluoroscopy— may indirectly influence the procedure (6). To assess the performance of the MNS we performed the first direct randomized comparison with conventional wire technique in patients presenting with stable and unstable angina.

MATERIALS AND METHODS

Patient Selection and Definitions

In a 12-month-period commencing September 2006, 111 consecutive patients admitted with stable and unstable angina were single-blinded randomized to cross the culprit lesion twice, either using a conventional or a magnetically-enabled guidewire. All patients were appropriately informed about the procedure and gave their consent. Angina was defined according to the Canadian Cardiovascular Society and Braunwald classification, respectively (7,8). Patients were excluded if they were haemodynamically unstable or had contraindications for magnetic-assisted intervention (MAI) such as a pacemaker. The objectives of the study were the direct evaluation of the crossing success, crossing/ fluoroscopy times, and contrast

usage. This was assessed by measuring the time (sec) and contrast media (ml) required to cross the lesion having first placed the guidewire at the tip of a guiding catheter engaged at the ostium and following the wire passage distal to the lesion. The wire was then withdrawn and the comparative wire was then used to coincide with the start and end position of the first wire. Lesions not crossed within 6 min with either wire were labeled as wire failures as previously defined by our published phantom studies (5). Included within the 6 min was the time taken for wires to be removed from the catheter and reshaped to achieve a successful crossing. Wires that were damaged in crossing could be exchanged for a similar or different conventional or magnetically enabled wire if necessary. The operators (four in total) had unrestricted access to the choice of either magnetic or conventional guidewires and were interventional cardiologists who were also trained in MAI procedures. The crossing success of each wire was defined as the amount/percentage of successful crossings within 6 min. The procedural success was defined as successful crossings without time restrictions using the complementary technique having failed with the first wire technique to cross within 6 min.

The MNS

The Niobe® II MNS (Stereotaxis, St. Louis, M. USA) integrated with a modified C-arm flat-panel detector-fluoroscopic imaging suite (AXIOM Artis dFC, Siemens Medical Solutions, Forchheim, Germany) for angiographic imaging was used throughout this study. The system allows two different modes for navigation by using either 2-dimensional (2D) such as in the "clockface" method (Fig. 1A) or 3-dimensional (3D) maps of the coronary artery (1). In this study navigation was performed using a 3-dimensional reconstructed (3DRC) virtual vessel roadmap generated from two angiographic images 30° apart (CardiOp-B, Paieon Medical, Rosh Ha'ayin, Israel) (Fig. 1B). The 3DRC was first coregistered with the fluoroscopic image (Fig. 1C) and a navigational pathway created through the lumen of the 3DRC (Fig. 1D). This pathway was then displayed as a fixed centreline on the real-time fluoroscopic image. The operator was then able to manually advance the navigational vectors associated with this centreline at a predetermined distance (1–9 mm) by pressing the advance/go button on the touch screen monitor. In cases of complex 3DRC the navigation was performed using the 2D "clock face" model. In this model navigational vectors are displayed in a circle that looks like the face of a 12-hr clock on the touch screen monitor. By pressing points around the perimeter of the circle/clock, the software (Navigant®) calculates vectors to redirect the magnetic field and realign the wire tip to the chosen direction (Fig. 1A). In both the 2D and 3D navigational modes the operator manually advances the guidewire once the vector reaches the desired position. As training with the magnetic system requires both an understanding of the software and the hardware on average a novice needs at least 12 hr of practical training to be fully acquainted with all the techniques and tools. In our department, which is a leading center that evaluates the MNS to PCI we feel that after 35 magnetic cases the operator can

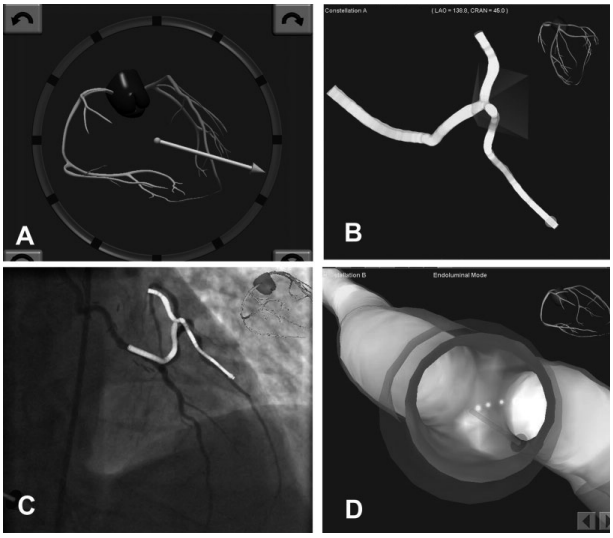

Figure 1. (A) The clockface navigational mode showing a vector depicted by an arrow that can be repositioned by selecting points around the perimeter of the clock; (B) a 3-dimensional reconstruction of a coronary bypass graft to the native left anterior decending artery and (C) the registration with the fluoroscopic image; (D) navigating at the bifurcation of the virtual reconstructed graft showing a navigational pathway through the lumen.

be called an experienced user. In addition, one trained technician is required to operate the system from a control viewing room in the catheterization laboratory.

The Guidewires

The conventional wires used in the study were PT Graphix™ Intermediate, Choice™ PT Floppy (Boston Scientific Corp. Miami, FL), Whisper (Abbott Vascular Devices, Redwood, CA) and high torque BMW (Guidant Corp, Santa Clara, CA). The magnetic guidewires used were all 180-cm-long Titan™ Soft Support wires with a 2-mm angled or 3-mm long straight magnetic tips attached to a 0.014 in./0.36-mm stainless steel core (Stereotaxis, St. Louis, MO. USA).

Lesions and Vessel Characterizations

Lesions were defined as type A, B1, B2, and C in accordance with the American College of Cardiology/American Heart Association ACC/AHA classifications (9). Type A lesions were generally discrete (<10-mm length), concentric, readily accessible nonangulated lesions with little or no calcification and did not involve the ostium or major side branches. Type B1-lesions were longer (10–20 mm), or eccentric, or with moderate tortuosity and angulation (45°–90°). These lesions might have moderate to heavy calcification and could involve the ostium or a bifurcation. Lesions classed as type B2 had more than one B1 criteria.

Type C lesions were diffusely diseased (>2 cm in length) with extreme tortuosity and angulations (>90º). When involving a complex bifurcation there is a potential risk of losing the side branch. Given the limitations of the AHA/ACC classification, namely in not considering the vessel characteristics which may influence the ability to get a wire across our group has developed a simple score system for predicting prolonged crossing times to select patients who would benefit from MAI (10). The score takes into consideration the angulation of the proximal segment, the number of bends to reach the lesion, total vessel angulation, length, calcification, number of sidebranches, and if there is a stent proximal to the lesion. It also incorporates the following lesion characteristics: side-branch in the lesion or within 10 mm of the lesion, lesion angulation and calcification, the lesion length and the length of lesion more than 80% diameter stenosis, and also if the lesion is due to instent restenosis (Table 1) (11).

Table I. A Scoring System Based on Vessel and Lesion Characteristics

Vessel characteristics	Score ()
1st turn (Aorta-Prox vessel angulation)	(0): <90°, (1): 90° –135°, (2): >135°
Turns (number) before lesion	1 turn = 1, 2 turns = 2 etc, max (5)
5 worst angulations	(0): <45°, (1): 45° –90°, (2): 90° –135°, (3): 135° –180°, (4): >180°
End to end length ostium-lesion/mm	(0): <50 mm (1): 50–100 mm, (2): >100 mm
Visible calcification	(0): none, (1): mild, (2): severe
Visible side branch before lesion	max (2)
Stent before lesion	(0): no, (1): yes
Lesion characteristics	
Side branch within 10mm	(0): no, (1): yes
Side branch in lesion	(0): no, (1): yes
Lesion angulation	(0): <45°, (1): 45–90°, (2): 90–135°, (3): 135–180°, (4): >180°
Lesion calcified	(0): no, (1): yes
Lesion length/mm	(0): <10 mm, (1): 10–20 mm, (2): >20 mm
Length/mm of >80% stenosis	(0): <1 mm, (1): 1–3 mm, (2): 3–10 mm, (3): >10 mm
Through a stent	(0): no, (1): yes (1stent), (2): yes (through struts)
Specific morphological abnormality, e.g. aneurysms, fistula etc.	(0): no, (1): yes for each max 6

The vessel angulations and turns defined as a change in angulation of >45° were determined using the virtual 3DRC images created in the CardiOp-B® and integrated in the Navigant. This scoring system was used to define three tertiles of vessels taking into account the lesion characteristics: low (<5), medium (6–10), and high (>10) so that the performances of the wires in relation to the vascular anatomy could be evaluated.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation. Parametric student *t* test was used to determine if there were significant differences between the parameters assessed using the two techniques. Spearman nonparametric correlation was used to define a trend

between the crossing/fluoroscopy times, contrast media usage, and lesion/vessel type. Analyses were performed using SPSS 11.5 for Windows (SPSS, Chicago, IL). P value < 0.05 was considered statistically significant. Scatter plot distribution was examined correlating complexity score with crossing/fluoroscopy times and contrast media usage for both the magnetic and the conventional wires.

RESULTS

In 93% of the cases magnetic navigation was performed with a 3-dimensional reconstructed (3DRC) virtual vessel roadmap superimposed on the real time fluoroscopy image. The "clock face" technique was used for the remaining cases. In the 111 patients having 165 lesions there were 7 magnetic wire and 3 conventional wire failures corresponding to a crossing success within 6 min of 93.3 and 95.6%, respectively. In addition, in another four cases (four lesions) both wires failed in the same patient within 6 min. In three of these, the lesions were eventually crossed successfully (one magnetically and two conventionally). In one case where both wires failed, the patient proceeded to coronary arterial bypass surgery. The overall procedural success in this study was 99.3% with 91.5% of the lesions crossed within 6 min.

Table 2. Patient characteristics

	(N): Patients	%
Patient characteristics		
Age/years	64.4	(45–90)a
Sex	(male)	74.2%
Non/Unknown Smoker	(N = 68)	66.0%
Ex-smoker	(N = 28)	27.2%
Current Smoker	(N = 7	6.8%
Diabetes	(N = 23)	22.3%
Insulin	(N = 4)	3.9%
Hyperlipidaemia	(N = 65)	63.1%
Hypertension	(N = 49)	47.6%
Family History	(N = 47)	45.6%
Indication		
Stable Angina	(N = 78)	75.7%
Unstable Angina	(N = 25)	24.3%
Previous PCI	(N = 30)	29.1%
CABG	(N = 7)	6.8%
Diseased vessel		
1 Vessel Disease	(N = 49)	47.6%
2 Vessel Disease	(N = 43)	41.7%
3 Vessel Disease	(N = 11)	10.7%
Renal dysfunction (Creatinine > 100lmol/l)	(N = 10)	9.7%

[a]Range

The direct comparison of successful crossing in the same vessel was performed in 151 lesions (151 vessels) corresponding to 103 patients. The patient characteristics are shown in Table 2.

The average age of the patients was 64.4 years with three quarters being male. Over one fifth were diabetic, with 3.9% on insulin and almost two-thirds were hyperlipidaemic. Three quarters of the patients presented with stable angina. Nearly, one third of the patients had previous PCI with 6.8% having prior surgery. There was a similar distribution of single and multi-vessel disease within the total population. In 9.7% of the patients a creatinine >100 lmol/l was observed. Lesions classified according to the AHA/ACC criteria were 15 Type A (10%), 30 Type B1 (20%), 95 Type B2 (63%), and 11 Type C (7%). The LAD was targeted in 60 patients (40%), followed by the RCA (N = 29, 19%), then the diagonal (N = 26, 17%), the LCx (N = 25, 16%), marginalis (N = 9, 6%), and the ramus intermediate (N ± 2, 1%).

Crossing and Fluoroscopy Times

Overall the crossing times (sec) with the magnetically enabled wires were longer than the conventional standard wire approach (72.9 ± 50.3 sec vs. 58.1 ± 47.2 sec, P < 0.001) especially in AHA/ACC B2 lesions (P < 0.01) (Table 3).

Table 3. Crossing Times in Lesions Classified According to the AHA/ACC Criteria

	A	B1	B2	C	A + B1	B2 + C	All
	n = 15 (10%)	n = 30 (20%)	n = 95 (63%)	n = 11 (7%)	n = 45 (30%)	n = 106 (70%)	N = 151
Crossing time/sec							
Magnet	61.8 ± 42.4	62.5 ± 41.5	74.3 ± 53.4	105 ± 38.3	62.3 ± 42.8	77.4 ± 52.9	72.9 ± 50.3
Standard	46.5 ± 33.7	51.7 ± 30.8	59.7 ± 54.2	76.5 ± 19.8	50.0 ± 31.9	61.5 ± 52.0	58.1 ± 47.2
P value	0.15	0.72	0.01	0.06	0.02	0.002	<0.001
Fluoroscopy time/sec							
Magnet	54.0 ± 22.7	55.3 ± 33.5	69.9 ± 48.9	79.8 ± 23.6	54.9 ± 30.3	71.0 ± 47.9	66.2 ± 44.1
Standard	44.3 ± 37.4	50.0 ± 28.6	56.9 ± 50.9	71.7 ± 18.2	48.1 ± 30.4	58.2 ± 48.8	55.2 ± 44.4
P value	0.27	0.34	0.13	0.40	0.14	0.009	0.03

The crossing times proportionally increased with the lesion complexity (Fig. 2A). Simpler type A and B1 lesions were quicker to cross with either wire than the more complex B2 and C lesions, but subanalyses of the crossing times revealed that the magnetic wires were significantly slower than the conventional wire in both groups. In the group consisting of type A and B1 lesions the times for magnetic wires compared to the conventional wires were (62.3 ± 42.8 sec vs. 50.0 ± 31.9 sec, P = 0.02) and in the group containing the lesions B2 and C the times were (77.4 ± 52.9 sec vs. 61.5 ± 52.0 sec, P < 0.002, respectively). In a comparative assessment of the fluoroscopy times, the conventional approach with the standard wires were overall superior to the magnetic wires although the difference was less (66.2 ± 44.1 vs. 55.2 ± 44.4 sec, P < 0.03) compared with the crossing times (Table 3 and Fig 2B).

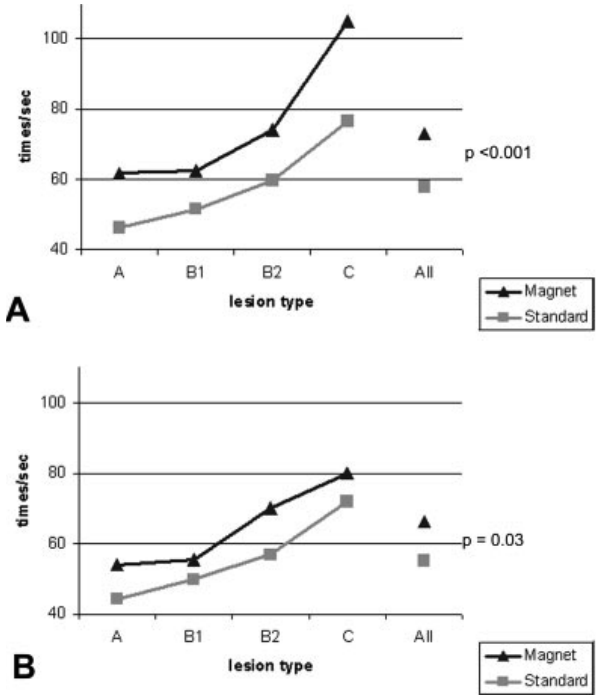

Figure 2. Relationship of (A) Crossing and (B) Fluoroscopy times of both the conventional and magnetic wires to the lesion subtypes.

The Relationship of the Crossing and Fluoroscopy Times to the complexity score.

Scatter plots were performed and correlation of the complexity scores were performed for both the crossing and fluoroscopy times with the standard conventional and magnetic wires. Although there was no obvious correlation seen, a lower slope and R^2 was observed with the magnetic group. This may suggest that the magnetic wire had less of an influence on both the crossing and fluoroscopy times in vessels/lesions having high complexity scores—(standard conventional wire's slope and correlation coefficient of the crossing times/sec with complexity score was 7.5 and 0.2, respectively; magnetic wire's slope and correlation coefficient of the crossing times/sec with complexity score was 4.3 and 0.06, respectively; similarly, standard conventional wire's slope and correlation coefficient of the fluoroscopy times/sec with complexity score was 7.2 and 0.21, respectively; magnetic wire's slope and correlation coefficient of the fluoroscopy times/sec with complexity score was 4.0 and 0.07, respectively). When the complexity scores were subgrouped into tertiles of less than 5 and from 6 to 10 the crossing and fluoroscopy times were significantly prolonged ($P < 0.001$) with the magnetic wires compared to the conventional standard wires (Fig. 3). Interestingly, for the tertile greater than 10 both the crossing and fluoroscopy times with the magnetic wire were shorter than that observed with conventional wires although they were not significant (P values of 0.24 and 0.21, respectively).

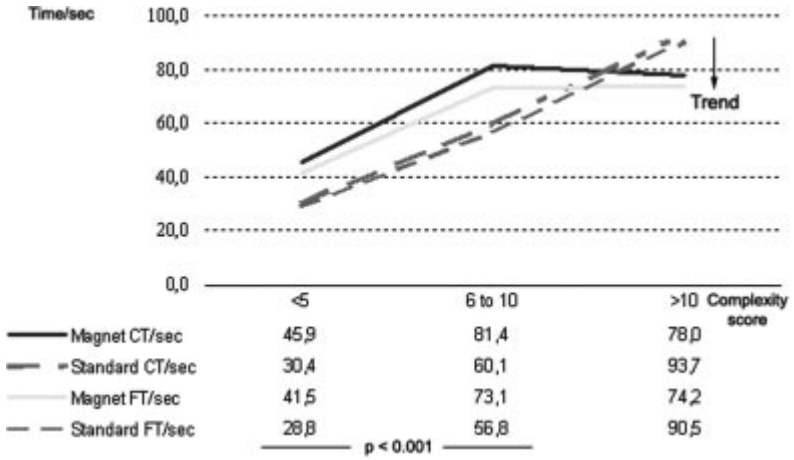

Figure 3. Relationship of the crossing and fluoroscopy times to the complexity score per tertile (FT = fluoroscopy time; CT = crossing time).

Crossing Times and the Minimum Luminal Diameters

Regardless of the studied vessel's minimum luminal diameters (MLD) the magnetic wire was slower. In vessels with a MLD > 2 mm the magnetic wire crossing times/sec compared to the standard conventional wires were 52.8 ± 42.9 sec vs. 34.2 ± 20.2 sec, $P < 0.03$. Similarly, in vessels having MLDs of 1–2 mm and < 1 mm the crossing times/sec were 74.1 ± 52.7 sec vs. 56.9 ± 46.1 sec, $P < 0.004$ and 75.8 ± 49.6 sec vs. 63.7 ± 51.1 sec, $P < 0.05$ respective to that of the standard conventional wires.

Contrast Media Usage

The Spearman nonparametric correlation test demonstrated a positive trend between contrast media usage and lesion complexity with the conventional wire technique ($P = 0.025$). This increase in contrast media usage was eliminated when the MNS was employed ($P = 0.63$) with the Spearman nonparametric correlation for trend. Type A lesions showed no significant difference in contrast usage (ml) in crossing with either the magnetic or conventional wire (1.5 ± 1.8 vs. 1.9 ± 2.3 $P = 0.59$, respectively) (Fig. 4). As lesion complexity increased significantly less contrast (ml) was needed with the MNS:- Type B1 (2.5 ± 3.2 vs. 4.0 ± 2.6, $P = 0.01$); Type B2 (2.3 ± 3.8 vs. 4.9 ± 4.9, $P < 0.001$); Type C (2.9 ± 3.4 vs. 5.9 ± 4.9, $P = 0.03$).

Overall, the MNS gave a small but significant reduction in contrast usage (2.3 ± 3.5 vs. 4.5 ± 4.4, $P < 0.001$) relative to the conventional technique. Interestingly, no contrast was required when crossing in 72 lesions (48%) with the MNS and in 31 lesions (21%) with the conventional approach (Table 4).

Table 4. The Lesions Crossed Using Zero Contrast

	Number of lesions crossed without contrast	
	Magnetic wire	Conventional wire
Lesion type	72	31
Type A	8	7
Type B1	14	3
Type B2	47	19
Type C	3	2

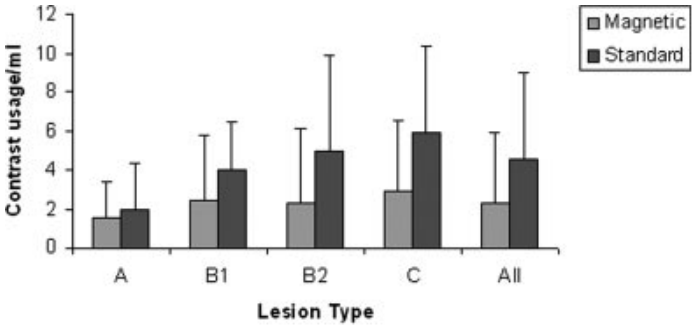

Figure 4. Comparative contrast usage based on lesion type.

Moreover, regardless of the vessel crossed, the MNS required less contrast than the conventional wire and this was also observed with increasing complexity scores (Fig. 5). Vessels with scores >10 complex vessels had the largest reduction, 7.0 vs. 2.6 ml. Vessels with scores 6–10 had almost a two-fold reduction (2.7 vs. 4.9 ml) and those with scores of less than 5 had a limited reduction of 1.0 ml. As observed with the crossing and fluoroscopy times a lower slope was recorded with the magnetic wire when the complexity scores were correlated with contrast usage, Fig. 6.

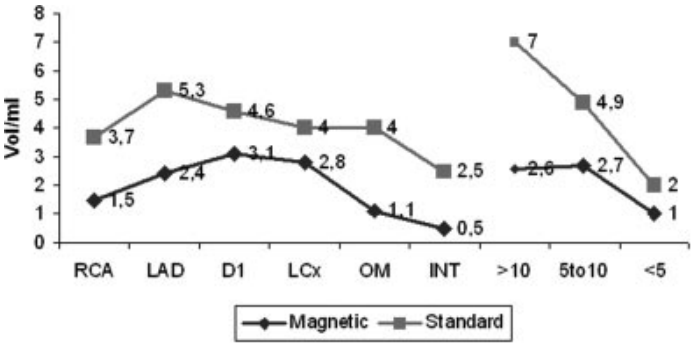

Figure 5. Comparative contrast usage based on vessel type and complexity score.

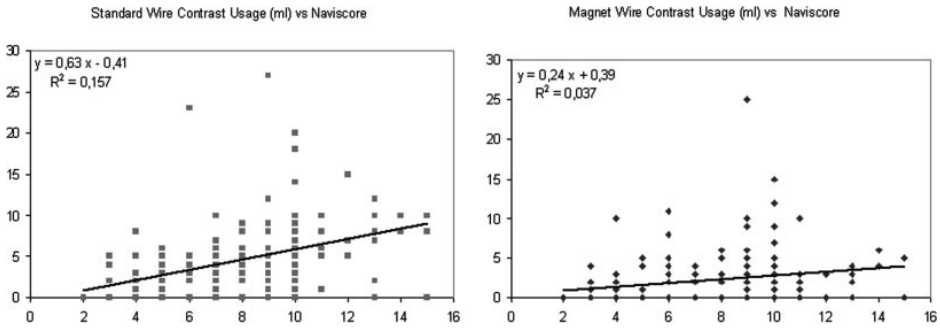

Figure 6. The scatter plot relationship between contrast and all the complexity scores.

DISCUSSION

The application of the MNS to PCI is a promising technology (12). There are now over 100 systems installed in catheterization laboratories worldwide. The system has advantages over traditional PCI techniques with its ability to redirect a magnetized guidewire in situ. This has been shown to be useful in situations where the ability to cross a lesion with a standard wire failed and in coronary phantom models with increasing tortuosity (5). Even though there is clearly an advantage in precisely controlling the tip of a guidewire, the interventional community has been slow to adopt MNS. There are several reasons why there maybe reservations:

(a) the presence of a rigid 2- to 3-mm-long magnet at the tip of the wire can compromise the performance achievable with conventional wires,
(b) many conventional wires have achieved a level of sophistication having evolved over several generations to enhance both their trackability and device deliverability,
(c) the "ocular-hand coordination" seems currently unbeatable because of the delay in responsiveness in the MNS hardware—the speed in moving the large external magnets to align to the desired vectors,
(d) there is a steep learning curve that must be reached by both the interventionalist and skilled technical staff (6,13),
(e) together with the additional financial costings for both the MNS and staff training,
(f) moreover, any gain in crossing time might be compromised by the preparation of the MNS case although in some clinical scenarios this may prove to be beneficial long term e.g. MSCT cointegration for CTO,
(g) but more importantly, there is little randomized data to support the use of the MNS to PCI. Some of these limitations are currently being addressed with newer generations of wire design together with software updates that can offer automated navigational vector advancement—but many of them are yet to be resolved (14). In this first randomized study di-

rectly comparing the performance of the MNS to conventional PCI techniques we exclusively assessed one system (technique) versus the other. In some studies a "hybrid" approach can be contemplated whereby the magnetic wire is used initially as a conventional wire technique until a problem of crossing is encountered at which point the external magnets are engaged and then the MNS utilized to facilitate the crossing of the wire through the lesion/vessel (13). This approach was discussed but not acted upon to keep the data independent and "clean" for both techniques. Overall the crossing success of the magnetic wires was comparable to that of the standard guidewires (93.3% vs. 95.6%). Analysis of the four cases that failed to cross with both wires within 6 min was in two of the cases subtotal occlusions that failed with the magnetic wires and was eventually crossed with conventional wires. The case that failed with the conventional wire and was crossed with the magnetic wire was in a vessel with an acute angulation. The only case where both wires failed after numerous attempts the patient had an aneurysmal swelling that led into a pinpoint occlusion.

It was not surprising that overall the crossing and fluoroscopy times were longer with the magnetic wire. This is partly because of limitations with the software available at the time of the study that required manual updates of the navigational vectors. This had to be performed by pressing an advancing icon on the touch screen monitor. It meant that the operator had a time delay prior to advancing the magnetic guidewire as the system updated. Newer versions of the software are being developed to address this limitation. But despite this limitation the only significant difference was seen in AHA/ACC B2 lesions as in these cases the operators generally chose smaller incremental distances for the vector to follow. Larger incremental distances were often used in type A and B1 lesions so the differences between the two techniques were less apparent. In type C lesions, the magnetic wire was not significantly slower due to observed limitations with conventional wire techniques in these lesion subtypes (15). In general, the fluoroscopy times were less than the crossing times because manipulations such as reshaping the conventional wire did not require fluoroscopy but was still being timed. Consequently, no significant differences in fluoroscopy times observed between the two systems. The ACC/AHA criteria was however developed almost 20 years ago using 11 simple angiographic factors to define a lesion complexity in the comparison with the outcomes of PCI (16). It is based solely on the lesion and does not take into account the complexity of the vessel as a whole, which can sometimes influence the procedural outcome. In an attempt to circumvent this several other grading systems exist but they are generally based on simple angiographic features and hence fail to take into account the 3-dimensional (3-D) nature of the coronary tree (17,18). Moreover, visual estimates from angiographic images are known to have poor inter-observer reproducibility (19). By employing dedicated 3D software more detailed information can be used to define a complexity scoring systems based on both the vessel and lesion characteristics (11). Using this approach and dividing the scores in tertiles of low (5 or less), medium (between 6 and 10), and high complexity (greater than 10) a positive trend for the magnetic wire was observed for crossing and fluoroscopy times in the

high complexity group. Both the magnetic wire crossing and fluoroscopy times significantly increased over the conventional methods used in vessels with low and medium complexity scores. But with high complex scores lower times were recorded with the magnetic wire (78.0 vs. 93.7 sec and 74.2 vs. 90.5 sec, respectively). This trend does however support anecdotal clinical reports that in selected cases with increased complexity the MNS can be advantageous (20,21). Attempts however to further subcategorize the population with the high complexity scores were unsuccessful because of the size of the study.

To assess measurable differences between the two techniques we quantitatively recorded the amount of contrast media used to cross the lesion. We appreciated the fact that this volume is relatively small in comparison to the total amounts traditionally used in an entire procedure. Nevertheless when assessed as a measurable difference between the two techniques the MNS did reduce the amount of contrast used to cross a lesion primarily because it integrates a 3-dimensional roadmap to provide a visual clue to the position of the wire on the fluoroscopic image. As a result the significant difference between contrast and lesion complexity observed with the conventional wire was effectively eliminated with the MNS. In vessels with complexity scores > 10, there was almost a three fold reduction in amount of contrast used. Moreover 48% of the lesions were crossed without the need of contrast as a direct effect of following a superimposed road map on the live fluoroscopy image. This is an important finding in support of developing technologies aimed at reducing contrast usage that can ultimately affect clinical consequence such as contrast-induced nephropathy (CIN). Already the use of an overlay created from an MSCT cointegration with the MNS can aid the visualization of CTOs, which may limit the need for retrograde contrast media injection (14). Contrast usage has also been reduced by using 3D reconstruction (3DRC) software to correctly define the optimum angiographic projections needed for stent deployment (22,23). In addition some technologies can accurately localize a wire/device—global positioning—within the coronary artery (24). If these technologies were amalgamated with more sophisticated magnetic wires such as Stereotaxis's multi-magnet design having three smaller 1-mm interspaced magnets at the tip and furthermore is integrated with a system for automatic wire advancement then an entirely new approach to conventional PCI and contrast usage would be effectively realized (1,25). But for every emerging technology there is a limited period for it to be adopted so it is important that the current limitations and reservations be addressed if the MNS is to succeed in the competitive area of PCI.

LIMITATIONS

The 3DRC used in this study was time-consuming and took up to 30 min to complete. The production of the reconstruction required angiography of a suitable standard and this was not always possible from standard views due to foreshortening or overlapping. A static road map

created from the 3DRC image was superimposed on a dynamic real-time image for magnetic navigation. Only patent vessels were included, as the re-crossing of totally occluded vessels by the comparative wire was avoided because of inherent clinical risk. There were a number of operators and types of wires and this, together with no selection of the target vessel segment, may have led to heterogeneity. The lesion score was also not externally validated. In addition, this study examines only one specific aspect of the PCI related to crossing of lesions and does not address other necessary elements such as the passage and deployment of the balloon and stent. Lastly, this study was performed at a University specialist tertiary referral unit and the case mix might be different to that seen elsewhere.

CONCLUSION

The MNS has a comparable crossing success to conventional PCI techniques in crossing lesions as defined by the ACC/AHA criteria. The longer crossing and fluoroscopy times reflect limitations in manually updating the navigational vectors on the roadmap displayed on the live fluoroscopic image. In defining the vessel complexity taking into account the full 3-dimensional characteristics a positive trend was found in support of using MNS in more complex vascular lesions/anatomies. Moreover the incorporation of the 3DRC navigational pathway with the MNS offered a small but significant reduction in the amount of contrast needed to cross a target lesion when compared to a conventional wire approach. Nearly half of the cases required no contrast agent to guide the magnetic wire transit within the vessel.

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CHAPTER 13

Magnetic Wire Lock: prevention and correction to avoid Wire Fracture

ABSTRACT

This report illustrates an undescribed mechanism of causing magnetic angioplasty wire fracture and goes on to describe how to avoid it occurring and how to correct it should it occur. The cause is the transition point in the wire between a flexible wire shaft and the inflexible magnetic tip of a magnetically enabled wire. In the first stage of the problem, the wire becomes trapped in a doubled-back position. Subsequently traction causes the second stage that kinks the wire and hooks behind a structure, in this case a stent, causing magnetic wire lock. Further traction has a high chance of wire fracture. Correction, although challenging, remains possible before wire fracture occurs. While there is no intrinsic problem with the technology, attention to this problem by the operator will reduce its occurrence and therefore its sequelae.

INTRODUCTION

The fracture of a coronary angioplasty wire can potentially lead to serious consequences such as thrombosis, perforation or death (1). Fortunately wire fracture occurs infrequently with a published rate of 0.02% of procedures (2). A variety of mechanisms have been described previously (2-10). The newly evolving technique of magnetic navigation provides new abilities that may be advantageous in percutaneous coronary intervention (11-13) but these wires have a certain structure that may require special attention in order to avoid problems.

The Niobe® II magnetic navigation system (Stereotaxis, St Louis, Missouri, USA) has been described in detail previously (11-13). It produces a 15-20 cm spherical volume with a uniform magnetic field that is centered on the heart of the patient and can be reliably and reproducibly directed in 360° in all planes. Selecting the 3D direction on the computer screen, leads to movement of the 2 external magnets to give a precisely directed magnetic field vector that will actively deflect the magnetic wire tip resulting in reproducibly precise steering. This active steering may give easier and 'cleaner' wire passage through complex anatomy (13), give 3D guidance of the wire from computer generated models, and allow integration of other information from investigations such as MSCT (11).

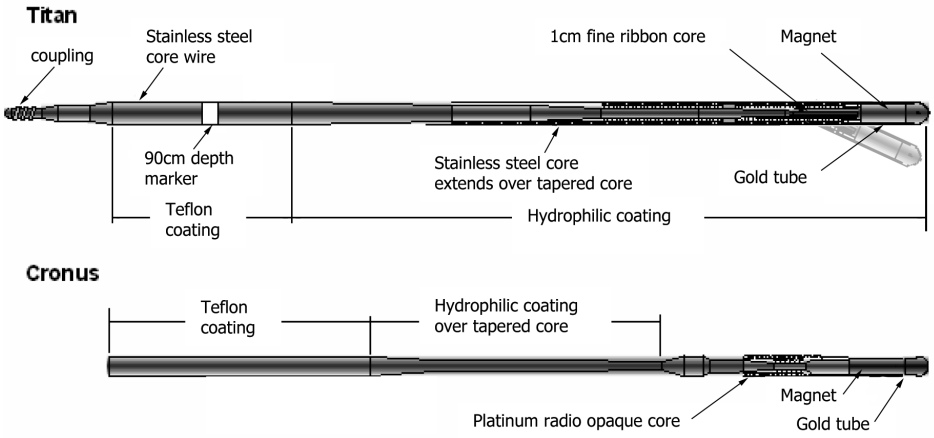

Figure 1. The structure of currently available magnetic wires with their solid magnetic tip.

Magnetically enabled wires have a tiny solid magnet at the tip made of neodymium-iron-boron, see figure 1, to allow them to be actively steered by an external magnetic field. Currently all magnetic wires are manufactured under instruction from, and marketed by, Stereotaxis. The transition between the flexible wire and the inflexible tip predisposes to the occurrence of a two-stage process of wire entrapment leading to magnetic wire lock (MWL). The first stage is the entrapment of the wire in a doubled-back position, see figure 2. At this point the wire is only loosely fixed behind the structure. The second stage results from

proximal traction with the wire-tip fixed that leads to kinking of the wire, leaving it hooked behind the stent struts, see figure 2. Further traction has a high chance of wire fracture.

This report aims to illustrate this problem, emphasize its avoidance and suggest a corrective strategy.

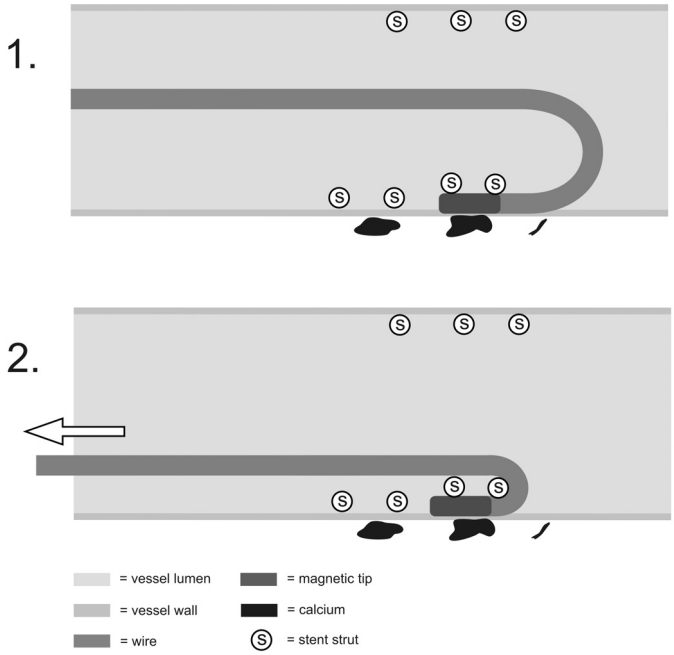

Figure 2. Diagrammatic representation of MWL, 1 denotes the double-backed wire with the tip caught between two stent struts (stent strut denoted by "s"). 2 shows the acute angle caused by traction at the transition point between shaft and magnet—the wire is now locked.

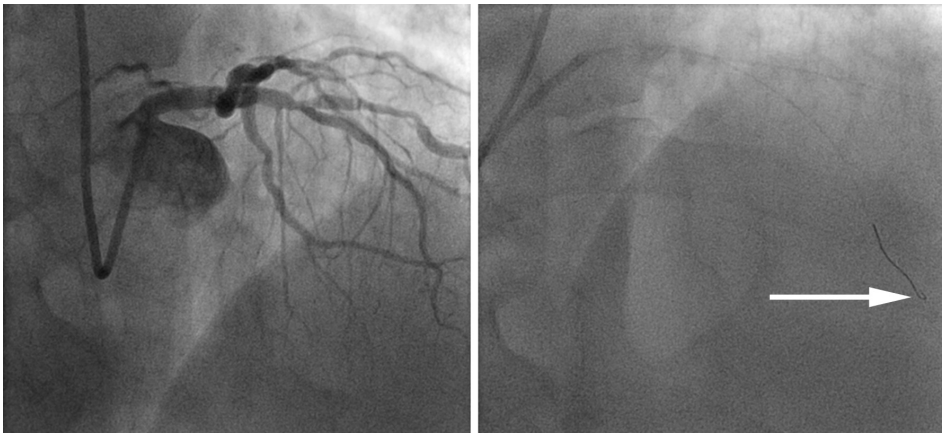

Figure 3. The left panel shows the bifurcation lesion affecting the LAD and diagonal, the right panel shows the wires in place, the magnetic wire can be seen at this point to be doubled back (arrowed).

CASE REPORT

Case 1 – Magnetic wire lock leading to wire fracture

A 57 year old male presented with stable Canadian Cardiovascular Society grade II angina pectoris despite treatment with triple medication. Angiography showed a significant bifurcation lesion involving the Left Anterior Descending artery (LAD) and a large diagonal, see figure 3. A Titan™ 3 mm angled Soft Support wire (Stereotaxis, St Louis, Missouri, USA) was placed into the diagonal and a second into the LAD, see figure 3. Two overlapping drug eluting stents were deployed in the diagonal with the proximal end in the LAD. The wire from the diagonal was placed easily into the LAD. However, on withdrawal of the wire from the LAD, the solid tip of the wire became trapped behind the stent at the bifurcation, see figure 4. The

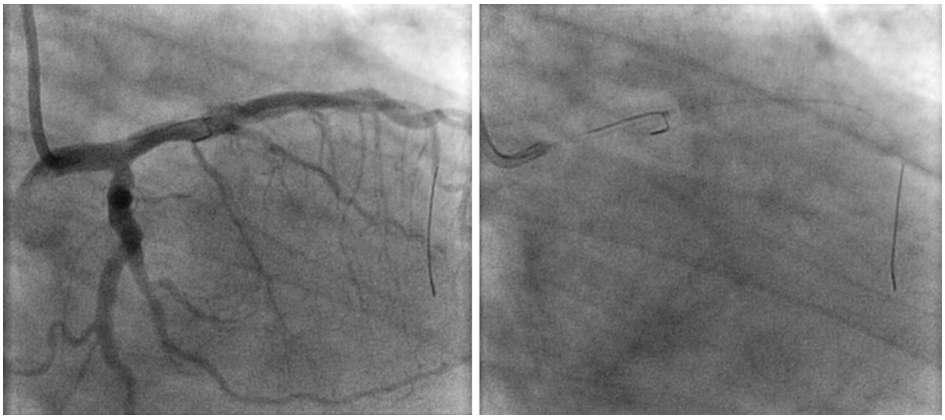

Figure 4. These panels show the wire tip caught in the stent, the left panel shows the appearance with contrast, and the right without.

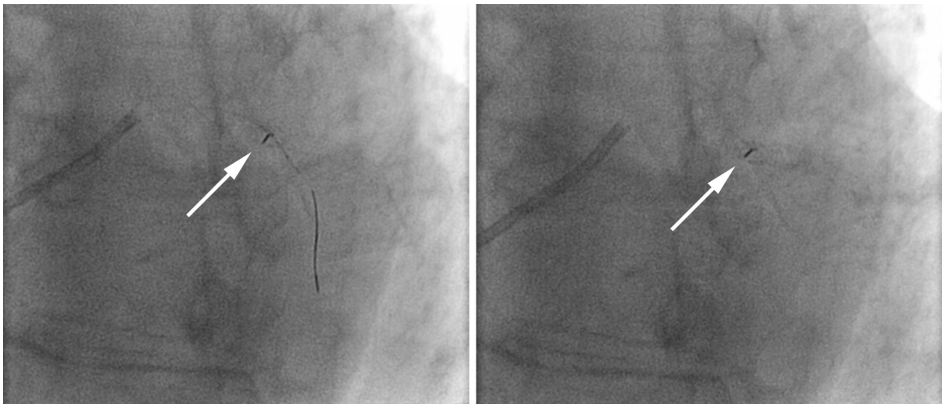

Figure 5. The left panel shows both wires before withdrawal, and the right panel shows only the fractured wire tip (arrowed) in LAD.

wire could not be advanced and, with further traction, the wire unravelled and broke, see figure 5. The patient remained asymptomatic and was treated conservatively.

Case 2 – Correction of magnetic wire lock

A 66 year old man presented with Canadian Cardiovascular Society grade III angina pectoris. A MIBI scan showed ischaemia both anteriorly and laterally. Angiography showed an occluded circumflex artery (Cx) and a bifurcation lesion of the LAD/diagonal. The patient was scheduled for a staged attempt to reopen the Cx and, if successful, to then undergo treatment of the bifurcation lesion. The occluded Cx was successfully recanalized using magnetic navigation. 1 week later he was scheduled for a procedure to the bifurcation lesion of the LAD and the diagonal, see figure 6. Two Titan™ 3 mm angled Soft Support wires were placed in the LAD and diagonal. On inflation of the LAD stent the wires were correctly orientated, see figure 6. However, when exchanging the wires, the wire in the diagonal became trapped, see figure 7, with a curve of the wire visible (arrowed in figure). The wire could not be advanced. A 1.5mm Maverick was advanced to support the wire just proximal to stent. At this point the wire was successfully advanced. By the use of careful manipulation and reorientation of the magnetic field, the wire was straightened and withdrawn. The procedure was completed with a further stent into the diagonal and the final result after kissing balloons was completely satisfactory, see figure 8.

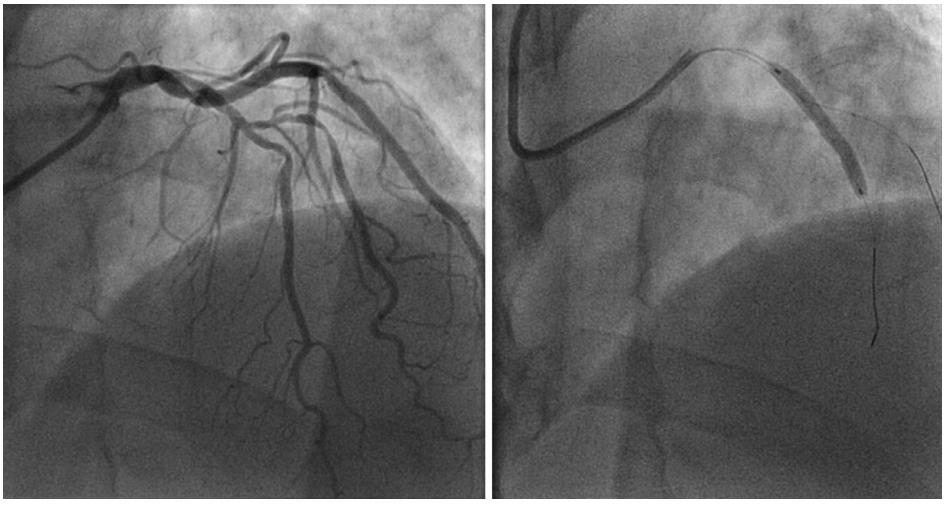

Figure 6. The left panel shows the bifurcation before intervention, the right panel shows the stent placement in the LAD when the wires were correctly orientated.

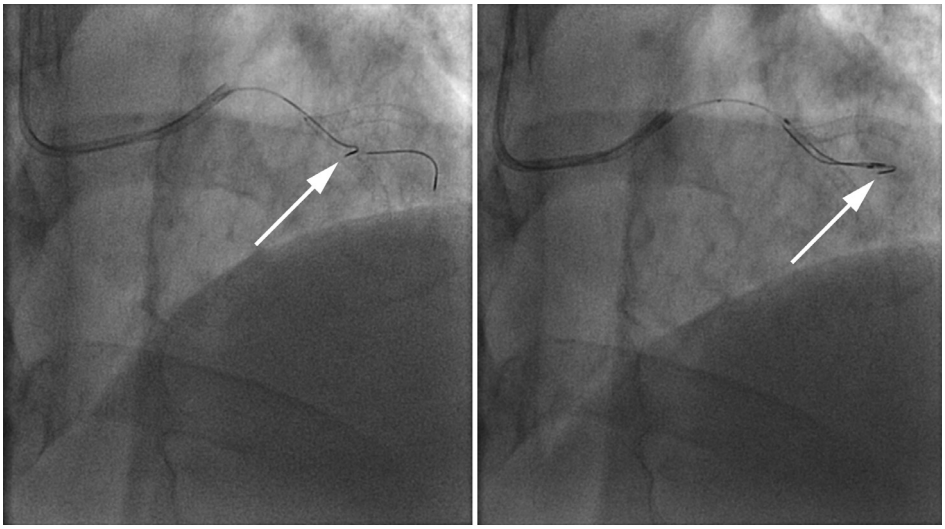

Figure 7. The left panel shows the doubled back wire tip at the stent (arrowed), the left panel shows the wire tip pushed forward clear of the stent (arrowed) before being straightened.

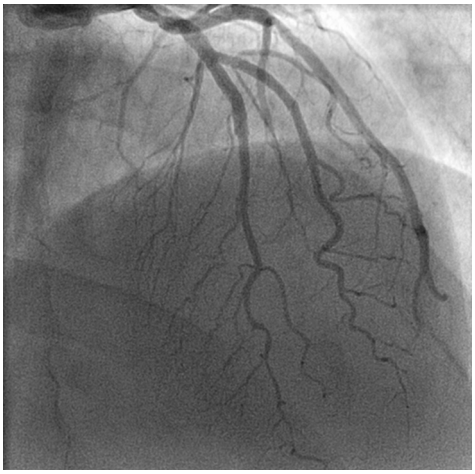

Figure 8. Final result.

DISCUSSION

The occurrence of wire fracture is infrequent (1). A range of causal mechanisms have been postulated including entrapment in the vessel wall (2-4), transection by a device (5-8), or metal fatigue due to repetitive strain (9). This range of causal mechanisms is mirrored by a range of management strategies that include, first, conservative (2), second, retrieval by wires (10,14), by grabbing devices (2,15), or by snares (16-18), or third, surgery (19,20). The management strategy chosen depends on factors such as the location of the wire, the clinical

scenario and the knowledge of possible management strategies, and requires a balanced view of the pros and cons of each strategy.

With a magnetic wire, the transition between the flexible shaft of the wire and the solid inflexible tip magnet can act as a hinge point. MWL appears to occur as a 2-stage process. The first stage of MWL is entrapment of the tip behind the stent in a doubled-back position, see figure 2. This may only loosely fix the tip of the wire and at this point it may be relatively simple to advance the wire. The second stage depends on traction on the wire producing a sharp kink in the wire, leaving it effectively hooked behind the stent struts, locking it in place, see figure 2.

Avoidance of MWL should be the initial strategy by ensuring that the magnet does not fold back on the shaft of the wire. If the wire tip does become doubled before reaching a distal enough position for stent placement, further advancement should be stopped, and either by retraction of the shaft or by manipulation of the magnetic field, the tip should be returned to the proper orientation for further advancement.

Correction of the problem in the first stage.

If the wire is in the process of being pulled back and the wire becomes doubled back on itself, retraction should be stopped before the kink in the wire occurs and a strategy to straighten the tip pursued.

Correction of the problem in the second stage.

If the wire has been pulled back and the wire has become kinked, there are a number of further strategies that are possible. Attempts should be made to re-advance the wire. If this is unsuccessful by simply pushing the wire, then support on the wire shaft can be increased by advancing an over-the-wire balloon up to the stent. The wire is supported within the lumen of the balloon catheter and behind the stent. This may allow the tip to be pushed forward. This solution, that proved effective in this case, is only one of several possible strategies for treating this problem and other strategies should be considered and applied as appropriate.

Ongoing advances in the wire design, such as the use of nitinol in the new Pegasus™ wires, or a flexible, multi-magnet tip, should be pursued in order to reduce this problem.

CONCLUSIONS

This case demonstrates a previously undescribed two stage mechanism of MWL that led to wire fracture and demonstrates one possible strategy for treating it. While no intrinsic defect exists, a quirk in the current design leaves it vulnerable to this problem. The use of magnetic

wires requires a different approach and different awareness from the operator. Identification of this problem, together with strategies to prevent or manage it, will reduce its occurrence and sequelae.

ACKNOWLEDGEMENT

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PART IV

Investigation of benefits in subgroups

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CHAPTER 14

Integration of 3D reconstruction in the SELection criteria for Excessive Crossing Times for Magnetically Supported Percutaneous Coronary Intervention. SELECT-MP

ABSTRACT

Aims: To develop a clinical prediction rule based on 3D reconstruction of coronary arteries that would prospectively identify lesions that are difficult to cross and could benefit from magnetic navigation.

Methods and results: The coronary anatomy of a cohort of 120 lesions that had undergone percutaneous coronary intervention (derivation set) was analysed using 3D reconstruction for vessel and lesion characteristics. The crossing time was the total clock time to reach a satisfactory distal position after leaving the guiding catheter. Multivariable logistic regression and linear shrinkage with bootstrapping were used to develop a clinical prediction rule that dichotomised cases into easy or difficult (prolonged crossing time). A value of 6 was the best cut-off value. This clinical prediction rule was applied to a second independent cohort of patients (validation set) where crossing time was measured. The bootstrapped c-statistic of the model was 0.82 indicating excellent discrimination.

Conclusions: 3D reconstruction helped to develop a simple, accurate clinical prediction rule to identify difficult cases for conventional wires and in whom magnetic navigation may be preferable.

INTRODUCTION

Currently the majority of percutaneous coronary intervention (PCI) procedures are performed satisfactorily with conventional wires. However, there is a proportion of PCI procedures where difficulty, or sometimes failure, occurs. As equipment improves and PCI extends into more difficult territories, e.g. smaller, more tortuous, heavily calcified and more distal lesions, there will be an increasing challenge to manual dexterity. The recently introduced magnetic navigation system (MNS) from Stereotaxis uses a magnetic field to precisely steer the wire that can take direction from a 3D model of the vessel created from angiographic images, and may be of benefit in such problematic procedures (1). Improved wire delivery may lead to reduced procedural time and complications (2-4).

However, there is no specific method of identifying those cases where passing the lesion with a wire, or 'crossing', is difficult. The currently available range of lesion classification systems (5-9) is aimed at predicting complications and these have relatively modest accuracies. We have investigated a simple, specific, measurable and crucial part of the PCI procedure, the time to pass the wire from the guiding catheter to a position distal to the culprit lesion. Such prediction may have a number of major benefits.

First, better guidance for operators in the assessment of the difficulty of a particular case may help better risk-benefit decision-making.

Second, it may allow selection of patients who have difficult morphology for an alternate technique such as magnetic navigation. A clinical prediction rule (CPR) may be a useful method of ultimately comparing magnetic navigation or other navigation technologies to conventional wire manipulation.

The aims of this study were two-fold. First, the development of a simple CPR to predict difficult lesions to cross with a conventional wire. Second, the validation of this CPR in lesions that had undergone angioplasty.

METHODS

Patient selection

Derivation set

The crossing times of a cohort of 425 consecutive lesions that had elective and semi-urgent PCI performed with a conventional wire at a single centre were noted. Lesions that were excluded from analysis consisted of occluded vessels where a reconstruction could not be produced due to inadequate vessel flow (TIMI flow of 2 or less) such as primary PCI, acute coronary syndrome (ACS), and chronic total occlusion (CTO). ACS patients were generally not excluded. In addition, lesions where special techniques had been used, such as biplane

angiography or magnetic navigation, were excluded. Several strategies were undertaken in order to reduce possible bias.

The crossing times of the patients were consecutively measured and the times were analysed to show the boundaries of the tertiles (Figure 1). The patient data were left unsorted when separated into the three groups of 40 lesions. The films of each of these groups were examined consecutively and the inclusion for analysis was determined by a coin toss. The person analysing the films and performing reconstructions was completely blinded to the crossing time. The derivation set comprised of these three groups and the CPR was developed from this.

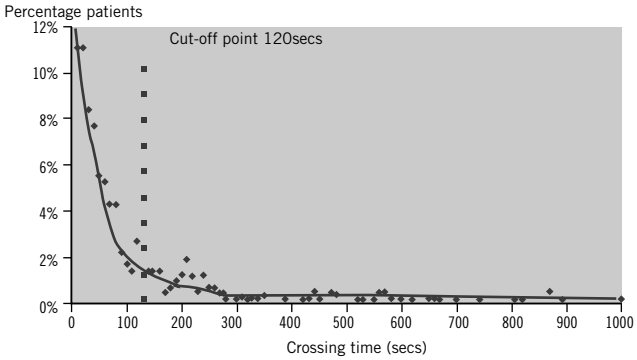

Figure 1. Graph showing distribution of the total population. *See this figue in color in the Appendix page 391.*

Validation set

The CPR was validated in a second cohort of 415 lesions, the validation set. The same exclusion criteria and strategies were used as in the derivation set. Sixteen lesions were randomly selected from each tertile of the crossing times for further analysis. In order to blind the analysis, the analyst had no knowledge of the results of the crossing time.

Magnetic navigation system

The MNS (Navigant, Stereotaxis, St Louis, MO, USA) has dedicated 3D reconstruction software (CardiOp-B, Paieon Medical Inc., Rosh Ha'ayin, Israel) that produces a virtual model of the entire vessel. With the reconstruction package it is possible to take 2 angiographic views and identify the vessel edges. The reconstructions were performed from suitable films where 2 separate films at suitable angulations (of >40°). As the angles of the image intensifier and the position of the table are known, it is possible to triangulate the position of each point of the vessel and make a 3D reconstruction of the vessel that is volume-rendered (Figure 2). All measurements can be made from diagnostic angiography films of suitable quality. There were 3, 2 and 6 films that were not suitable for analysis in the shortest, middle and longest tertiles respectively –the average inability to produce a reconstruction was therefore

approximately 10% of the total, but with a trend increasing in more complex morphology. To produce as accurate and reproducible reconstructions as possible, the images were routinely taken in diastole (on or just before the QRS complex). The software has functions that allow measurement of length, diameter and area stenosis with respect to the calculated reference diameter at that point. The model can then be imported into the Navigant program where the angulation of each bend can be measured. The bends were assessed visually and then measured to see whether they fitted the following definition. A bend was considered to be an angulation of 45° within 10 vessel diameters (for the purpose of this analysis a standard vessel diameter was considered to be 3 mm therefore a bend had to occur within 30 mm).

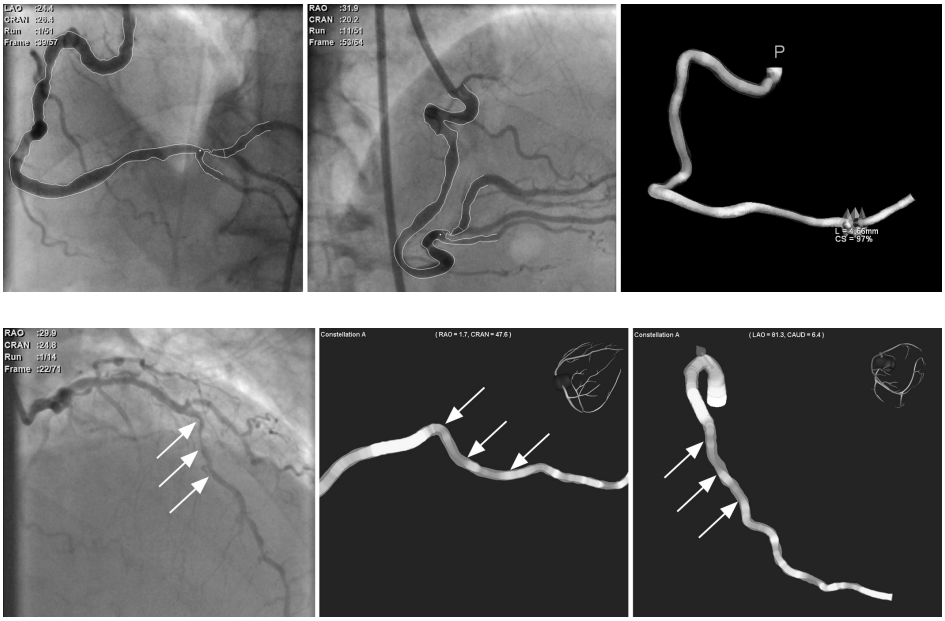

Figure 2. The upper panels: The left 2 panels show separate angiographic angulations with edges detected and the right panel shows a 2D image of the 3D reconstruction. The lower panels: The left panel shows the angiographic view of the LAD, the middle and right panels show the reconstruction in different views with the angles shown by the 3D reconstruction arrowed. *See this figue in color in the Appendix page 392.*

Definition of crossing time

A prolonged crossing time was defined as the absolute time (in seconds) from the initial entry of the wire into the coronary system, out of the guiding catheter, until crossing and reaching a suitable position distal to the target culprit lesion in the coronary artery. The crossing time includes the time required for any and all procedural manoeuvres once the wire has initially left the tip of the guiding catheter, such as the time required to remove and re-shape the conventional wire, re-engagement of the catheter should prolapse occur, or to pass a balloon for support, and implies the placement of the wire in a satisfactory final position for device

delivery. This was a registry where no special techniques of passing a wire were used, and therefore the operators should have been performing normally. A total of 9 interventional cardiologists were involved in these procedures. While a competitive element may have occurred within an operator's mind, the data once collected was only available to one person. This data was not, and has never been, shown in a fashion that would compare one operator with another and while operators may well have tried to perform their best, this is felt to be an advantage with the 'best' crossing times recorded.

The relevant hypothesized anatomical factors encountered with conventional angioplasty guidewires can be divided into vessel and lesion characteristics, see appendix 1. We imposed an arbitrary maximum to each factor in order to prevent any specific factor from dominating the grading system.

Vessel characteristics

Number of bends before the lesion (Vb) (Figure 3)

Each bend causes deformation of the wire resulting in friction. A greater number of bends leads to increased friction resulting in more difficultly in manipulating the wire. The maximum score is 5.

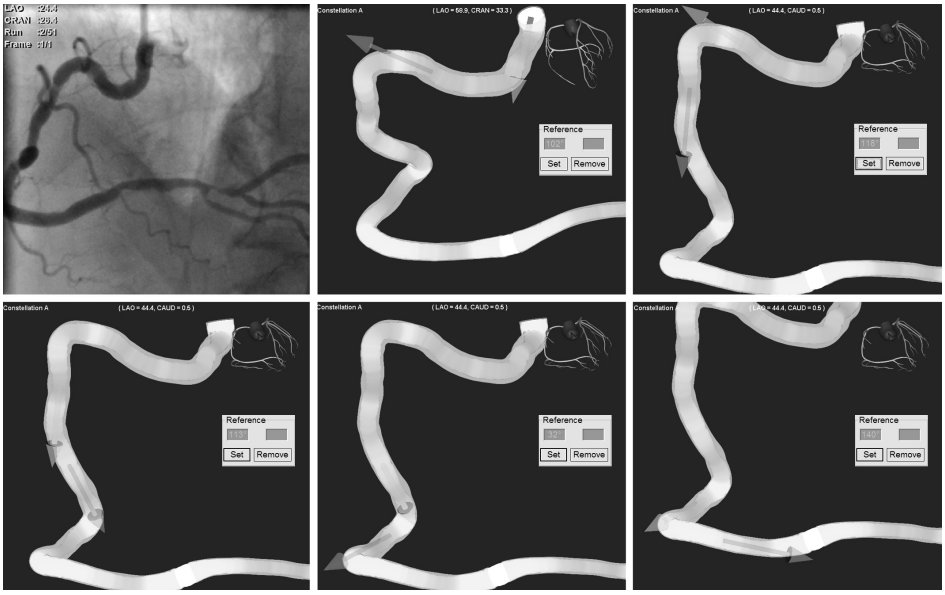

Figure 3. Identification of the bends in a vessel and measurement of each angle (possible in the Navigant program). *See this figue in color in the Appendix page 392.*

The total angulation of the 5 worst bends (Vta) (Figure 3)

The greater the cumulative angle, the more the wire is deformed along its course. This results in more friction and produces increased difficulty during manipulation. This has been dichotomised to above 45° (= 1) and below 45° (= 0). The maximum score per bend is 1, maximum number of bends is 5.

End-to-end length from the ostium to the lesion (Vl) (Figure 4)

The more distal the lesion is from the ostium, then the greater the chance of encountering problematic bends that impair manipulation, and also the longer the time required to physically pass the wire. This is divided into shorter than 50 mm (=0), between 50 and 100 mm (=1) and greater then 100 mm (=2). The maximum is 2.

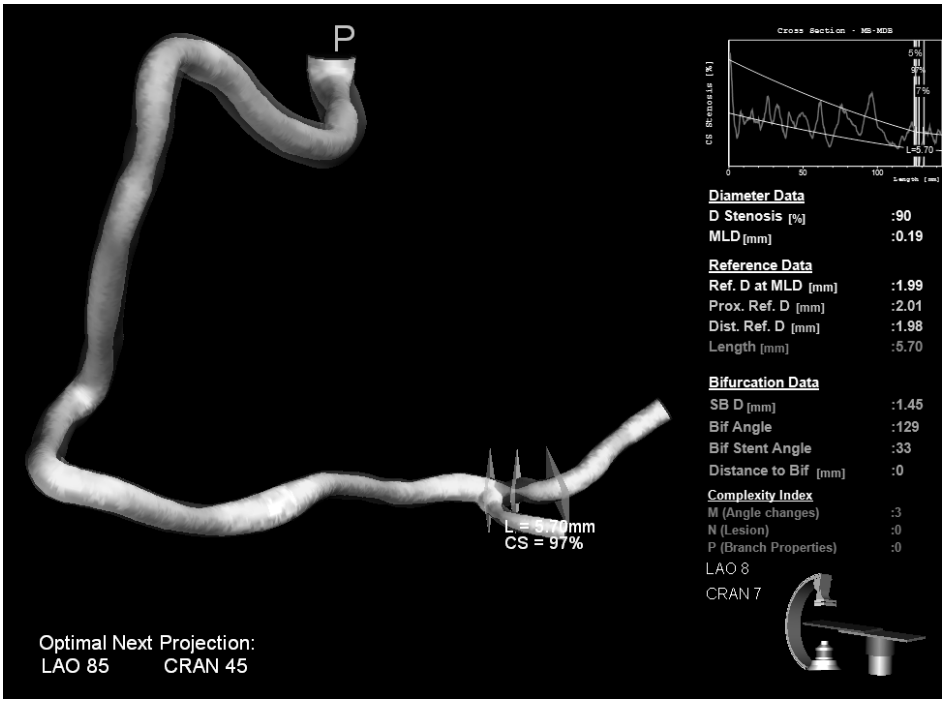

Figure 4. The measurement of the length from the vessel ostium to the lesion in CardiOp-B (green square indicates proximal marking point and blue square indicates distal marking point). *See this figue in color in the Appendix page 393.*

Vessel calcification (Vc)

Calcium may increase friction as the vessel becomes more rigid and less deformable and does not conform to the wire. The frictive effect of a specific angle will be accentuated if deformation cannot occur. The complete angiographic absence of calcium scores 0, mild calcification is 1 and severe calcification is 2. The maximum is 2.

Visible side-branches before lesion (Vsb) (Figure 5)

Visible side-branches result in a greater chance of taking a wrong bend. This is dichotomised to 0 or 1.

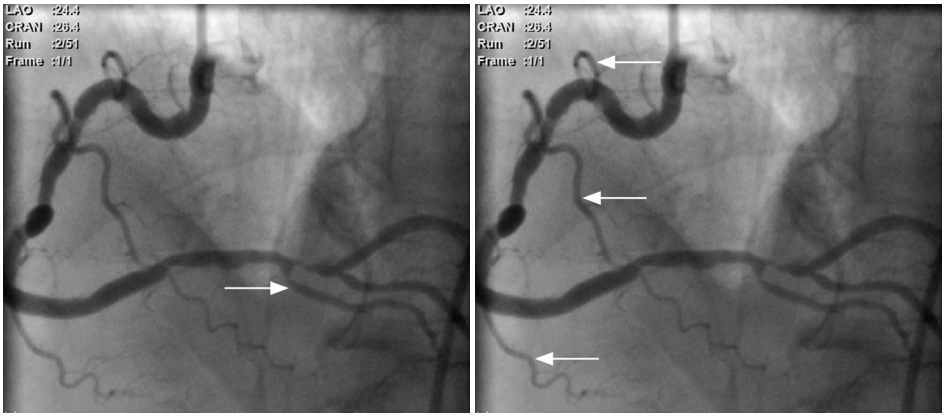

Figure 5. The left panel shows visible side-branches (arrowed) greater then 1 mm before the lesion with the right panel showing a branch just before the lesion (within 10 mm). *See this figue in color in the Appendix page 393.*

Lesion factors

Luminal lesion characteristics such as complex and intricate 3D form or tight lesions with little space for manoeuvre affect how quickly and easily a wire can pass. Navigation through complex, intricate, and/or tight lesions may involve a variety of angles that cannot be easily be traversed by a conventional guide-wire with a fixed bend as it has a specific angle of approach.

Lesion characteristics

Side-branches within 10 mm (Lbb) (Figure 5)

Side-branches within 10 mm of the lesion increase difficultly because, on the approach to a lesion finer control is necessary, the fixed wire-tip angle needed for bends now may have more of a predisposition for side-branches. This is dichotomised to 0 or 1.

Side-branches in lesion (Lsb)

When the angulated wire tip has to pass through a stenosis, there is a greater chance that the tip will be pushed against the wall and this increases the chance of selecting side-branches. The lesion angulation will affect the friction of the wire passing through the lesion. This is dichotomised to 0 for <45° or 1 for > 45°.

Lesion calcification (Lc)

Calcium makes the lesion rigid and reduces deformability, therefore producing more friction. This is dichotomised to 0 or 1.

Lesion length (Ll) (Figure 6)

Longer lesions produce more friction on the wire. This factor has been divided into <10 mm (=0), between 10 and 20 mm (=1) and greater then 20 mm (=2). The maximum is 2.

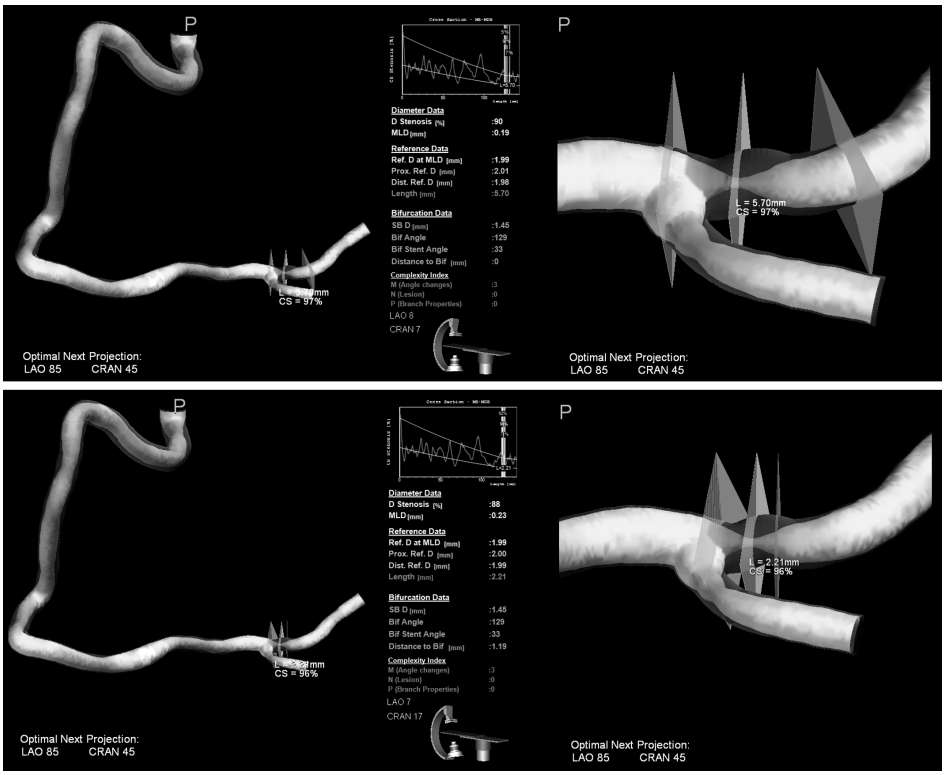

Figure 6. The top panels show the measurement of the lesion length (green square indicates proximal marking point and blue square indicates distal marking point). The lower panel shows the segment greater than 80% measured in CardiOp-B (green square indicates proximal marking point and blue square indicates distal marking point) *See this figue in color in the Appendix page 394.*

Length of severe (greater than 80% area) stenosis (Lss) (Figure 6)

Tighter lesions have greater contact with the wire and this magnifies the effect of bends leading to a greater chance of the wire being forced against the wall. This is dichotomised to into 0 for <3 mm and 1 for >3 mm.

Statistical analysis

A prolonged crossing time, Pct, was dichotomised with an arbitrary cut-off value of 120 seconds based on the observed crossing times (Figure 1). By the design of the study, one-third of the lesions had the presence of a long crossing time and two-thirds had a normal crossing time.

Statistical modelling

The association between each prognostic factor and the presence or absence of a long crossing time was studied by univariate logistic regression analysis. We applied a stepwise backward selection process (p=0.100) to select the predictors for the final model. A key problem of regression modelling in small data sets is that the regression coefficients are overestimated for predictive purposes. We calculated a linear shrinkage factor for the regression coefficients with bootstrapping (11). The difference between performance in the bootstrap samples and the original sample is an estimate of the optimism in the apparent performance (miscalibration). This difference is averaged to obtain a stable estimate of the optimism. 'Shrunk' coefficients were calculated by multiplication of the standard coefficients with the shrinkage factor, which might take values between 0 and 1. The final model was transformed into a CPR. Regression coefficients were rounded to the nearest integer. A score was obtained for each individual lesion by assigning points for each variable and adding the results.

Predictive performance

The prognostic ability of the model, i.e. the power to discriminate between subjects with and without a long crossing time, was estimated with c-statistic. The c-statistic, provides a quantitative summary of the discriminative ability of a predictive model. A value of 0.5 indicates that the model does not have any discriminatory ability, and a value of 1.0 represents perfect discrimination.

Calibration refers to whether prediction models agree with the observed probabilities and was assessed with the Hosmer- Lemeshow statistic. Statistical analyses were performed with SPSS and S-plus software (MathSoft, Inc., Seattle WA, USA: version 2000).

RESULTS

The mean age was 65 years and 74% of patients were male. All baseline characteristics in the derivation set and the validation set were generally similar although there were more unstable patients in the validation subset (Table 1).

Table 1. Patient characteristics for test and validation groups.

Baseline patient characteristics	(N=120)	(N=48)	*P value*
Age-yr	65.9±10.6	65.5±10.4	0.8
Male sex-no.(%)	74.3	73.3	0.9
Diabetes mellitus-no.(%)	25.7	35.6	0.2
Hypertension-no.(%)	55.7	60.5	0.6
Hypercholesterolemia-no.(%)	94.8	94.8	0.9
History of smoking cigarettes-no.(%)	18.6	11.6	0.3
Previous PCI-no.(%)	32.4	42.2	0.3
Previous CABG-no.(%)	7.6	6.7	0.8
Previous myocardial infarction-no.(%)	38.8	46.7	0.4
Clinical presentation			0.05
Stable angina pectoris	62.1	46.7	
Unstable angina pectoris	37.9	53.3	
CCS class			
I	5.0	5.3	1.0
II	38.3	36.8	
III	53.3	52.6	
IV	3.3	5.3	
LVEF			0.6
Good	76.3	66.7	
Moderate	15.8	27.8	
Poor	7.9	5.6	
Vessel disease			0.5
1VD	43.0	31.3	
2VD	30.8	35.5	
3VD	23.4	33.3	

The vessel location of the culprit lesion is shown in Table 2.

Table 2. Distribution of vessel location of culprit lesion.

Vessel analysed	Number	Percentage
Vessel – first tertile		
LAD	15	37.5
Cx	13	32.5
RCA	12	30
Vessel – second tertile		
LAD	18	45
Cx	14	35
RCA	8	20
Vessel – third tertile		
LAD	10	25.0
Cx	15	37.5
RCA	14	35

There was a spread of values for the crossing times showing that 15% of lesions could still not be crossed at 5 minutes (310 s) and 10% by 8 min (480 s) (Figure 1). The CPR was derived after applying logistic regression to the sample from the derivation group (results of univariate and multivariate analysis shown in Tables 3 and 4) to provide a relative estimate of crossing complexity:

Pct=1*Vb+1*(Vl=1)+2*(Vl=2)+2*Vc+1*Lbb)+1*(Ll=1)+2*(Ll=2)

(N.B. abbreviations refer to morphological factors, see appendix 1)

This dichotomises cases into easy and difficult (prolonged crossing time). Pct is an integer and a value of 6 was found to be the best cut-off value.

Table 3. Results of univariate analysis.

	Coefficient	P value
Vessel characteristics		
Number of bends before lesion (Vb)	0.73	<0.001
The total angulation of the 5 worst bends (Vta)	0.58	0.177
End to end length from the ostium to the lesion (Vl)		
50-100	1.18	0.009
>100	1.55	0.045
Vessel calcification (Vc)	2.03	<0.001
Visible side-branches before lesion (Vsb)	1.08	0.017
Lesion characteristics		
Side-branches within 10mm (Lbb)	0.01	0.985
Side-branches in lesion (Lsb)	0.58	0.163
Lesion angulation (La)	1.00	0.013
Lesion calcification (Lc)	0.98	0.013
Lesion length (Ll)	0.75	0.055
Length of severe (> 80% diameter) stenosis (Lss)	1.01	0.013

Table 4. Multivariate predictors of the crossing times in the derivation set.

	ß coefficient	Odds ratio	P-value
Bends to lesion, (Vb)	1.0278	5.06 (1.54-16.66)	<0.001
(end to length from the ostium to lesion (Vl) 50-100mm	1.0495	0.44 (0.12-1.63)	0.119
>100mm	2.7242	3.75 (0.38-37.13)	0.018
Vessel calcification (Vc)	2.9004	9.85 (2.52-38.42)	<0.001
Side-branches in lesion (Lbb)	1.0622	2.31 (0.78-6.89)	0.057
Lesion length (Ll) 10-20	0.8377	0.52 (0.15-1.76)	0.018
>20	2.0567	2.62 (0.68-10.01)	0.004

The c-index of the standard model was 0.88 and 0.83 for the shrunk model used for the CPR. Calibration with the Hosmer-Lemeshow test gave a non-significant p-value. This CPR was then applied to the results from the validation cohort. The c-statistic derived from this group was 0.82 showing good discrimination.

DISCUSSION

We have developed a clinical prediction rule (CPR) that examines the whole vessel that is undergoing PCI and is able to predict which vessels will require more time to cross. The CPR integrates the use of a 3D reconstruction developed from a combination of lesion and vessel characteristics to give a relative estimate of crossing complexity. It will allow an assessment of the importance of physical factors on wire passage and whether difficult wire passage is related to increased complication rates. This is directly applicable to the decision process of selecting a patient for a magnetically navigated procedure. This system is fundamentally different from previous classification systems that were developed for the prediction of procedural success and complications. The ACC/AHA guidelines for lesion grading were developed in 1988 (5), modified in 1990 (6) and use 11 simple angiographic factors to help take into account lesion complexity in the comparison of the outcomes of PCI. Further systems, such as the SCAI (7), the Mayo Risk Score (8) or the SYNTAX score (9), were subsequently developed in order to improve this predictive ability further. However, the discriminatory power was lower than expected (6,12) A number of possible reasons may help to explain this shortcoming. First, previous grading systems use a number of coronary factors that have generally been simple, angiographically-defined lesion characteristics. Use of such simple lesion characteristics may underestimate both the lesion complexity itself and also the importance of the rest of the vessel in successfully crossing with a wire. Second, while these factors have a great deal of merit in their simplicity, they are visual estimates from angiographic images and these are known to have poor interobserver reproducibility (13-15). Third, some systems include clinical factors, either as an endpoint or in their grading, that are frequently complex and multi-factorial. Difficulty in crossing an individual coronary lesion, especially if wire passage itself results in a clinical complication such as dissection, may only be indirectly related to the poor clinical state of an acutely sick patient or to the pre-existing clinical diseases. Conversely, a poor clinical state or pre-existing disease may be more closely associated with a complication than the adverse coronary anatomy. Therefore the use of clinical factors, either the pre-existing clinical diseases or the resultant clinical complication, may obscure a clear answer.

A number of factors have been investigated in previous studies. These indicate that increasing complexity of a lesion is associated with an increasing incidence of complications (7,16) and that some anatomical factors of the vessel, such as tortuosity, lesion length or angulation, are associated with decreased success of stent passage (17-19). The introduction and use of new 3D imaging technology enables a more complete anatomical analysis of the vessel and lesion in a new way. In order to give the clearest idea of factors that might influence passage of the wire we analysed the entire vessel as well as the target lesion. This approach has not been used before. All the measurements required for the CPR can be obtained from adequate diagnostic angiography films. The CPR can be applied in a matter

of minutes and is therefore applicable in general practice. This system is completely independent of the clinical factors that, while important in the broad clinical outcome, are either only loosely related, or even irrelevant, to the passage of a wire through a coronary artery. The analysis aimed to reflect these factors by defining the anatomy of both the coronary vessel and lesion. There are a number of advantages of this system. First, it uses a 3D reconstruction to identify and measure specific vessel factors and to give hard numbers to predict a single, clearly definable endpoint. Second, it examines the anatomy of the entire vessel, a factor that is clearly crucial to the delivery of a wire. Third, it is independent of the clinical factors that obscure the importance of physical factors. Fourth, it has clear applicability in choosing patients who might benefit from a magnetically navigated procedure. There are a number of limitations. Currently the reconstruction is time-consuming and can take up to 30 minutes to complete. The production of the reconstruction requires angiography of a suitable standard and is not always possible from standard views due to foreshortening or overlapping. The reconstruction that is produced is static and the impact of movement on the measured factors, such as angulation, is unknown. The use of the software does require some practice and some manual correction is often needed. This was deliberately kept to a minimum. After analysis some factors were not incorporated into the CPR. There may be a variety of reasons for this. Some factors occurred infrequently, such as the presence of a stent. The infrequent occurrence therefore may not reflect the unimportance of the factor but the effect of a small sample size e.g. few patients with stents. Another possible reason for a particular factor not showing significance is the variability of the factor itself. Side-branches may be cannulated without intention during procedures but this may only occur with side-branches that come off at a certain angle and not all as measured in this analysis. Therefore, in general, these factors may play some role, but this may only occur in specific circumstances, or occasionally, and will need further investigation to identify any additional benefit. More generally, there was unselected use of wires and no selection of operators. The limitations of this model therefore also relate to individual operators, techniques and equipment. There were a number of operators and types of wires and this, together with no selection of the target vessel segment, may have led to heterogeneity. In addition, this study examines only one specific aspect of the PCI and deliberately does not address other necessary elements such as the passage and deployment of the balloon and stent. Lastly, this study was performed at a university specialist tertiary referral unit and the case mix might be different to that seen elsewhere.

Despite such limitations, the system could prove useful in application. The ability to predict difficult cases may allow consideration for alternative strategies. In this context, the ability of the MNS to precisely direct the tip of a wire has a clear potential for improving the treatment of patients identified in this way as suggested in the study in this issue of EuroIntervention (20). However the system could potentially be used in other ways. As the number of MNS in an institution is normally limited to one, reconstruction could be performed on selected

subsets of patients. Identification of the patients who would most benefit would be not only beneficial for patients but would maximise efficiency. Alternatively, an automated system would also allow all patients to be screened in addition to possibly improving reproducibility.

This CPR will be valuable in several ways. First, to identify which anatomical factors are predominant by prospectively identifying difficult cases. Second, this may be a crucial tool in deciding whether a patient should undergo a conventional procedure or rather will benefit from magnetic navigation.

CONCLUSION

Previous classification systems have been of significant clinical use but relatively modest predictive ability due to a reliance on few lesion features and no vessel features, inclusion of clinical features with indirect relevance to the procedure, and the use of broad clinical endpoints. This study shows an accurate clinical prediction rule can be developed that uses the 3D reconstruction software of the magnetic navigation system to aid identification of difficult lesions for guide-wire placement on the basis of specific coronary analysis. It provides only five measurable, anatomical variables and has a simple but crucial endpoint. This clinical prediction rule is a good predictor of prolonged crossing time (c-statistic of 0.82) and may provide a more accurate and prospective method of predicting difficult procedures in which magnetic navigation might be a better option than the conventional techniques.

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Appendix

Grading factors	range of values
Number of bends before lesion (Vb) max 5	(0-5)
The total angulation of the 5 worst bends (Vta) 0:<45,1>45	(0-1)
End-to-end length from the ostium to the lesion (Vl) 0:<50mm, 1:50-100, 2:>10	(0-2)
Vessel calcification (Vc) 0:none, 1:yes	(0-1)
Visible side-branches before lesion (Vsb) 0 or 1	(0-1)
Lesion characteristics	
Side-branches within 10 mm (Lbb) 0:no, 1:yes	(0-1)
Side-branches in lesion (Lsb) 0:no, 1:yes	(0-1)
Lesion angulation (La) 0:<45,1:>45	(0-1)
Lesion calcification (Lc) 0:no, 1:yes	(0-1)
Lesion length (Ll) 0:<10, 1:10-20, 2:>20	(0-2)
Length of severe (> 80% diameter) stenosis (Lss) 0:<3mm, 1:>3mm	(0-1)

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CHAPTER 15

Comparison of Magnetically Navigated and Conventional Wire Percutaneous Coronary Intervention of a Single Discrete Stenosis

ABSTRACT

Objective: The objective of this study is to compare magnetic guidewire navigation in percutaneous coronary intervention (MPCI) to conventional percutaneous coronary intervention (CPCI) for the elective treatment of a single discrete stenosis.

Background: Magnetic navigation actively steers an angioplasty wire-tip and may improve PCI procedures, but it is not known whether the intricacy and increased preparation necessary for using the system negatively influences the performance of simple procedures in terms of time and contrast use.

Methods: The procedures of 44 patients (mean age 65 ± 10 year) undergoing elective single vessel MPCI of a single discrete stenosis were matched for age, gender, and lesion location with 44 concurrent patients (mean age 65 ± 10 year) undergoing CPCI. The major endpoint was procedural time.

Results: Technical success was defined as an intraluminal wire position distal to the stenosis. Procedural outcome, contrast use, and costs were evaluated. Clinical demographics and angiographic characteristics of the two groups were similar, except for a higher incidence of previous MI and class III angina pectoris in the conventional group. The technical success rate was high and identical in both groups (97.7%). Procedural and fluoroscopy times were not significantly different for MPCI compared to CPCI (21.0 ± 14.5 min vs. 24.7 ± 14.0 min; 4.9 ± 4.8 min vs. 7.3 ± 10.3 min, P = NS). There was a significant reduction in median contrast use (60 ml/patient (41–100) vs. 100 ml/patient (64–130); P = 0.006].

Conclusion: Magnetic navigation does not increase procedural time, irradiation, equipment use, or cost compared to conventional PCI of a single discrete stenosis. It proved feasible, yielding high rates of procedural success with less contrast use.

INTRODUCTION

Magnetic navigation uses two computer-controlled magnets to produce an adjustable magnetic field to precisely deflect a tip-mounted magnet on an angioplasty wire. This gives the fundamentally new ability of actively controlling the "front-end" of the wire. The precise steering of a wire-tip has a number of potential advantages including maintenance of a coaxial vessel orientation, more accurate sidebranch cannulation, and a reduction in problems inherent with conventional wires such as entanglement in two wire procedures. Percutaneous coronary intervention (PCI) using magnetic navigation appears to be feasible for all lesion types (1–5). However, while reports in both phantom (3) and humans (6,7) have reported benefit, the advantages for different and specific patient subgroups remain undefined. Importantly, magnetic guidewire navigation PCI (MPCI) requires both time for system preparation and also familiarity for efficient use. Therefore, it remains unclear as to whether the burden of the more extensive preparation and performance of this wire technique prolongs procedure time or rather is compensated for by smoother, less troubled and "cleaner" wire passage and thus a more efficient procedure. This clearly has implications on the use of this technique, for example, whether it should be restricted to the most difficult cases. Patients who are treated by elective PCI of a single discrete stenosis form a relatively simple and homogeneous group in whom the anatomy is known from preceding diagnostic angiography and there is generally a low occurrence of complicating factors such as the presence of thrombus or suboptimal hemodynamic condition. On the other hand, time-consuming techniques or technology would be most likely to have an impact on these procedures. Therefore, we examined the procedural outcomes of patients having MPCI for elective treatment of a single discrete stenosis and compared them with those of concurrent matched control patients undergoing conventional guidewire navigation PCI (CPCI) to assess whether the procedures are comparable in terms of time, irradiation, or contrast use.

MATERIALS AND METHODS

Selection of Patients and Age-Matched Controls

Between January 2007 and May 2007, 375 patients underwent elective single lesion PCI in our center. From this patient group, 68 patients had undergone elective single vessel MPCI for elective treatment of a single discrete stenosis that would require a maximum of two stents. An attempt was made to match all of these patients for gender, age (± 5 years), and intracoronary location of the lesion with concurrent patients undergoing elective CPCI. The conventional cases were taken from the general catheterization database that has single vessel disease as an input parameter. The films were individually reviewed to ensure that

only single, discrete lesions were chosen and that no other investigation such as contrast angiography, IVUS, or FFR had been performed on the target or other vessel. Gender and coronary segment were matched and then patients were matched by the closest age.

Exclusion criteria for both groups were diagnostic revisualization of another vessel/lesion during the procedure, performance of another diagnostic procedure such as fractional flow reserve measurement, the use of intravascular ultrasound, multiple lesions in the target vessel, multi-vessel PCI, bifurcation lesions, acute and chronic total occlusions, or a previous failed conventional attempt for the same target lesion. It was possible to match 44 suitable MPCI patients for age, gender, and coronary segment with 44 control patients who had undergone CPCI.

The Magnetic Navigation System

The Niobe® II magnetic navigation system (MNS; Stereotaxis, St Louis, MO) has been described in detail previously (1–3). The MNS is fully integrated at our center with the Integris Allura FD10 cardiovascular imaging system (Philips Medical Systems, Eindhoven, The Netherlands) as shown in Fig. 1. The operator interfaces with the system using a touch screen to the Navigant™ Work Station software (Stereotaxis, St Louis, MO). A 15–20 cm uniform spherical

Figure 1. The Niobe® Magnetic Navigation System position for PCI. M indicates magnets in tilt position for better lateral movement of the image intensifier. T indicates touch screen interface to give real-time instruction to the MNS. S indicates in-lab main screen monitor. C indicates the controls for magnet deployment. *See this figue in color in the Appendix page 394.*

magnetic field volume is produced that is centered on the heart of the patient and can be reliably and reproducibly directed at 360^0 in all planes. Selecting a 3D direction on the computer screen (see Fig. 2) leads to movement of the two external magnets to give a precisely directed magnetic field vector that will actively deflect the magnetic wire tip resulting in reproducibly precise steering.

The current list price for the Stereotaxis MNS is $1.9 million. The size of a typical modern magnetically enabled catheterization suite is 770 ft^2 (72 m^2). The cost of magnetic shielding generally ranges from $50,000 to $100,000 and consists of minimal common steel shielding in the walls, ceiling, and floor.

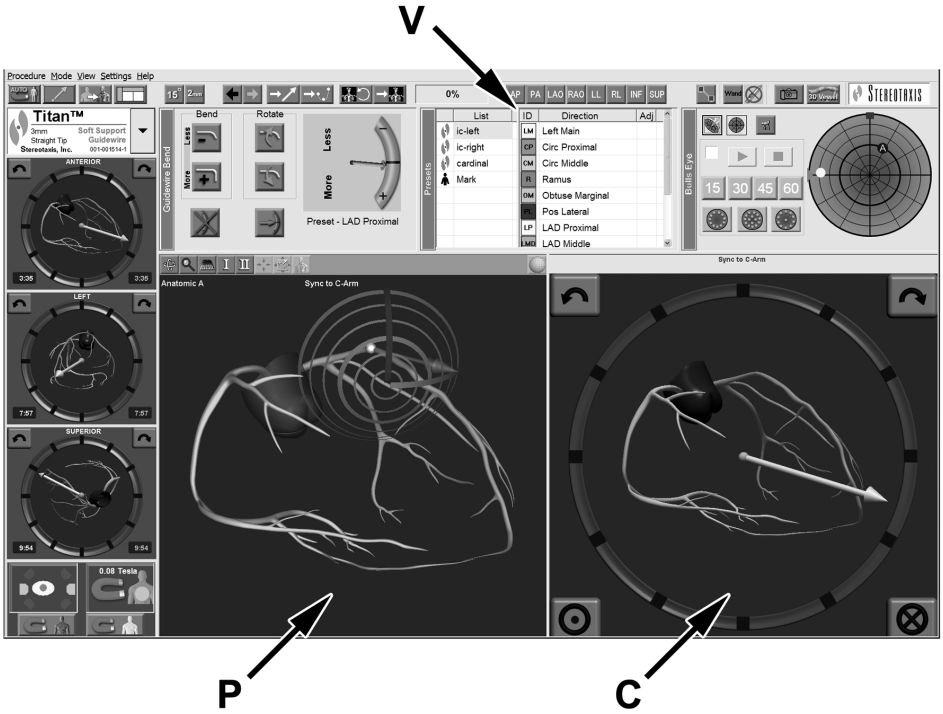

Figure 2. The screen of the Navigant™ workstation (2.11 version); the panel (P) shows virtual coronary tree of the preset navigation with the list of preset vectors (V) seen above. The panel (C) shows the 2D clock face. *See this figue in color in the Appendix page 395.*

Magnetically Enabled Wires

A series of magnetically enabled disposable guide wires that are custom-designed for use with the MNS are available in a variety of sizes and in a range of stiffness. For this comparison, the Titan™ guidewires were used (see Fig. 3). These are specifically designed to be more flexible and steerable for magnetic navigation. These are 180 cm moderate support, hydrophilic coated wires with a diameter of 0.014 in./0.36 mm having a flexible 2-cm distal coiled tip at the end of which is a gold cup attached to a 2 or 3 mm neodymium-iron-boron magnet.

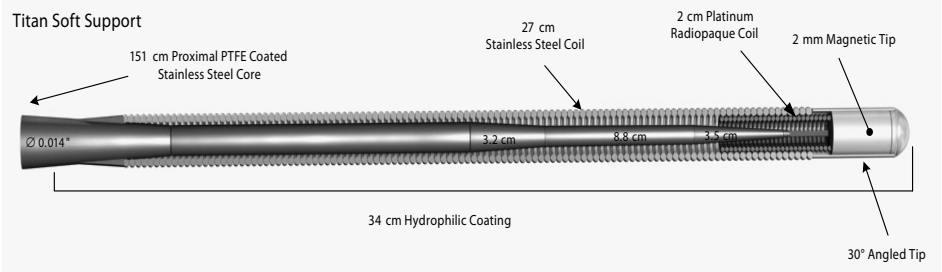

Figure 3. The structure of Titan™ Soft Support magnet wire. *See this figue in color in the Appendix page 395.*

PCI Procedure

All patients gave informed consent to the proposed procedure. The inner diameter of all 6-Fr guides was 0.70". The choice of guiding catheter and equipment was left entirely to the discretion of the operator and followed routine practice as did the use of drug-eluting stents, bare metal stents, and the use of glycoprotein IIb/IIIa receptor antagonists. There were no restrictions on the operators' choice of conventional wire. The angioplasty wires for magnetic procedures were the standard magnetically enabled wires supplied by the company (see previous paragraph). The interventional staff consisted of five senior operators. Three have greater than 10 years experience and two less than that; CPCI procedures were performed by all five operators, while MPCI procedures were performed by two of the five operators, one with greater than 10 years experience and one with less than 10 years. There were nine conventional patients (~20%) treated by the two operators who performed the magnetic procedures. The data have been taken from either the general catheterization database or from a registry of all the magnetic procedures. An arbitrary time period was selected for this comparison after a 3-month lead-in period for familiarization with the MNS to reflect normal working practice. Aspirin, 500 mg i.v., and clopidogrel, 600 mg, were given to all patients. Weight-adjusted unfractionated heparin, 100 IU/kg, was given as an intravenous bolus at the beginning of the procedure. The approach for access was via the radial artery or, in case of contraindication, the femoral artery.

Angiographic Variables

All angiograms were stored in a computer database and analyzed off-line by an independent observer, using CAAS 2003 Camtronics (Phillips Medical Systems). Lesion types were graded according to the ACC/AHA lesion classification (8).

Definition of End Points

The major endpoint was the amount of time required to complete the procedure. Procedural duration was measured from the time of sheath insertion until the removal of the guiding catheter at the end of the procedure. Secondary endpoints were fluoroscopy time, total procedural time, total contrast use, number of wires, number of balloons and stents, technical success, major adverse cardiac events, and procedural costs. Technical success was defined as an intraluminal wire position distal to the stenoses. Procedural success was defined as (1) TIMI grade III flow (9), (2) <30% residual stenosis, and (3) absence of clinical events during the procedure (death, acute stent thrombosis, myocardial infarction, emergency coronary artery bypass grafting, and stroke). Fluoroscopy times were automatically recorded by the Poly Diagnost (C2) Digital Cardiac Imaging System (Phillips Medical Systems). Procedural costs included the materials and laboratory and staff time. Laboratory and staff time were calculated by multiplying the procedural time + 30 min by 17 euro/ min; the latter figure was based on time-tested cost estimates, obtained from a large data set collected by a company linked to the Erasmus University Hospital of Rotterdam, the Netherlands. Materials included in the cost analysis were coronary guidewires, angioplasty balloons, premounted bare-metal or drug-eluting stents, and angiographic contrast agent.

Statistical Analysis

For comparison of continuous variables between the two groups, the unpaired two-tailed Student's t-test was used or, for the median of the contrast use (as for skewed data), the Mann–Whitney *U*-test. Comparison of categorical variables between the two groups was performed using the Chi-square test or, in case of a minimum expected count less than five, the Fisher exact test. Continuous variables were expressed as mean ± SD for nonskewed data; medians were expressed as 95% CI for skewed data. Categorical data were expressed as numbers of patients and percentage of patients. A P value less than 0.05 was considered statistically significant. Statistical tests were carried out with the SPSS 14.0 statistical software package.

RESULTS

Baseline Demographics

Forty-four consecutive patients having MPCI for elective treatment of a discrete single lesion were compared to 44 matched control patients having CPCI. Baseline clinical characteristics (Table I) were similar in both groups, although a previous history of MI and also angina CCS-

class III occurred more frequently in the CPCI group. Baseline angiographic variables were equally distributed in both groups (Table 1).

Table 1. Baseline Characteristics

Characteristics	Magnetic PCI (N = 44)	Conventional PCI(N = 44)	P value
Age (year)	65±10	65±10	0.99
Male sex	70.5	70.5	1.00
Diabetes mellitus	22.7	12.5	0.22
Hypertension	43.2	51.3	0.53
Hypercholesterolemia	29.5	37.5	0.44
Family history of CAD	25	25	1.00
History of smoking cigarettes	27.3	30	0.78
Previous PCI	34.1	43.2	0.38
Previous CABG	22.7	9.1	0.08
Previous myocardial infarction	6.8	34.1	0.002
CCS anginal class			
I	5.3	0	0.50
II	36.8	12.5	0.03
III	52.6	87.5	0.002
IV	2.6	0	1.00
Vessel disease			
1VD	61.4	54.5	0.52
2VD	29.5	29.5	1.00
3VD	9.1	16.3	0.31
Target lesion location			
Left anterior descending artery (LAD)			
Prox LAD	31.8	31.8	1.00
Mid LAD	20.5	20.5	1.00
First diagonal	2.3	2.3	1.00
Left circumflex artery (CX)			
Obtuse marginal	9.1	9.1	1.00
Prox CX	6.8	6.8	1.00
Right coronary artery (RCA)			
Prox RCA	9.1	9.1	1.00
Mid RCA	15.9	15.9	1.00
Dist RCA	4.5	4.5	1.00
ACC/AHA lesion class			
A	22.7	18.2	0.60
B1	36.4	31.8	0.65
B2	13.6	18.2	0.56
C	27.3	31.8	0.64

For age mean ± SD is given and for all other cases percentage of patients are given. CAD = coronary artery disease; CCS = Canadian Cardiovascular Society.

The intracoronary segment locations were, by design, equally distributed in both groups.

Procedural Outcome

Vascular access was successful via the radial approach in 100% of the magnetic procedures and in 97.7% of the conventional procedures. Procedural and fluoroscopy times were not significantly different (MPCI:CPCI, 21.0 ± 14.5 vs. 24.7 ± 14.0, P = 0.23, 4.9 ± 4.8 vs. 7.3 ± 10.3, P = 0.16, respectively), and overall technical and procedural success was high (97.7%) in both groups (Table 2).

Table 2. Procedural Outcome

Variable	Magnetic PCI (N ¼ 44)	Conventional PCI (N ¼ 44)	P value
Technical success	97.7	97.7	1.00
Procedural success	97.7	97.7	1.00
Successful radial approach	100	97.7	1.00
Successful second access femoral approach	0	2.3	1.00
Dissection	4.5	6.8	1.00
Stent length per patient, mm	20.1 ± 8.0	19.4 ± 7.8	0.69
Stent diameter per patient, mm	3.0 ± 0.4	3.0 ± 0.5	0.57
No. of stents implanted per patient	1.3 ± 0.8	1.5 ± 0.8	0.42
No. of drug-eluting stents implanted per patient	0.7 ± 0.9	0.8 ± 0.9	0.36
No. of bare-metal stents implanted per patient	0.7 ± 0.6	0.6 ± 0.9	0.78
No. of balloons used per patient	0.6 ± 1.0	0.6 ± 0.8	1.00
No. of wires implanted per patient	1.1 ± 0.3	1.3 ± 0.6	0.20
Procedural duration, min	21.0 ± 14.5	24.7 ± 14.0	0.23
Fluoroscopy time, min	4.9 ± 4.8	7.3 ± 10.3	0.16
Contrast consumption (median), ml	60 (41–100)	100 (64-130)	0.006
Procedural costs, euro	2,786 ± 1,859	3,148 ± 1,636	0.36

The results are presented either as the percentage value of the group or as the mean value ± one standard deviation.

The median contrast use was marginally but significantly reduced when comparing MPCI and CPCI [60 ml/patient (41–100) vs. 100 ml/patient (64–130); P = 0.006].

Material Consumption and Costs

The data for the MPCI patients who could not be matched was compared to the data of those successfully matched, and no significant difference was found between these groups. MPCI did not significantly increase procedural duration, and there was no increased use of wires, balloons, and stents (DES or BMS) in either group but rather there was a trend to reduction in all these parameters. MPCI did not result in significantly increased procedural costs compared to CPCI.

DISCUSSION

Magnetic navigation has been shown to be applicable and feasible in interventional cardiology (1–7). However, it has been unclear as to whether the more intricate nature of the procedure, in particular with respect to the time needed for preparation, might limit the technique to more difficult cases. The system adds a further level of complexity to PCI procedures. Specifically, the system must be isocentered on the heart of each patient before the magnets can be brought in; there is time required to get the magnets to their working position; sometimes the position of the patient must be altered to allow the magnets to come close enough to the working position; and the system may limit the position of the image intensifier, so alternative angulations must be sought. Additionally, it can be time consuming creating and preparing 3D reconstructions if these are used, especially with inexperienced users. All these maneuvers take time that may delay the procedure and thus reduce overall efficiency.

In contrast, once in position and with an experienced operator, this new technique gives the operator several new and definable capabilities that may aid smoother, less troubled, and "cleaner" wire passage. As conventional wires are steered by turning the distal angled tip, there is a tendency to deviate from a central, co-axial path in the vessel, and there may be poor maneuverability if severe proximal tortuosity is present and impairs wire rotation. The active front-end steering of the MNS suffers from no such problems. First, active tip adjustment of the wire gives the ability to bend and direct the tip as required, whether this is to maintain the tip coaxially in the vessel or to steer around bends or into sidebranches. Second, the automatic inclusion of 3D information, whether by using the clock-face, the presets, or 3D reconstruction from patient images, routinely adds the use of the third dimension during wire passage. Third, this "front-end" method of steering could facilitate some aspects of wire passage. Additionally, the system avoids some problems inherent in conventional technique. The minimization of tip rotation leads to a reduced chance of wire entanglement in procedures where multiple wires are used, and also the magnetic field tends to maintain the tip direction and help stabilize the wire. Individually, a specific advantage may not play a crucial role in each and every procedure but together they may facilitate better procedures. The patient group selected for this comparison was restricted to simple procedures, where forethought could be given to factors such as strategy, catheter choice, and the working position of the image intensifier. The lesions themselves were not complicated by severe calcification, poor- or no-flow or thrombus and were suitable for stent placement. While complications and problems can arise in any PCI procedure, it was hoped that this group would have minimal untoward events and this is indeed reflected in the short procedure times and low contrast use. On the other hand, use of time-consuming technology would be most marked in these patients. This comparison was performed relatively soon after acquisition of the system (after a 3-month lead-in period) when the system had been used relatively intensively to establish a set routine. This comparison indicates that there is no disadvantage

in using the MNS, as MPCI procedures can be performed safely and efficiently, as defined by procedural time, fluoroscopy time, and contrast use, which is at least equivalent to CPCI. Indeed, these nonrandomized results show a trend to reduced procedural parameters with a significant reduction in the median contrast use.

Study Limitations

This comparison has the limitations associated with retrospective cohort studies in that procedures were not randomized. Factors influencing outcome have been matched to the greatest extent possible, but the use of concurrent patients left a third of the possible MPCI patients unmatched. Concurrent patients have been used rather than historical controls to minimize differences in routine catheterization procedure to the greatest possible extent. However, the increased incidence of previous myocardial infarction and CCS III angina in conventional patient baseline characteristics may suggest that there was more extensive disease, although this possibility is contradicted by the statistical equivalence of the AHA/ACC grading for both groups. The limitations of the magnet navigation system technology are discussed above. In addition, only two out of five CPCI operators performed MPCIs and, although all five operators are experienced operators and there was proportionately more experience in the CPCI group, operator bias cannot be excluded.

CONCLUSION

In conclusion, magnetic navigation PCI appears to give no disadvantage in terms of procedural time or success, irradiation, contrast use or cost in routine elective PCI of a single discrete stenosis. The use of this technology, which may initially appear complex and intricate, is associated with equivalent or possibly even a marginal improvement in the simplest of PCI procedures when compared with CPCI. Randomized controlled trials are warranted to further investigate the use in this population.

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CHAPTER 16

Magnetically navigated percutaneous coronary intervention in distal and/or complex lesions may improve procedural outcome and material consumption

ABSTRACT

Aims: Comparison of magnetic guidewire navigation in percutaneous coronary intervention (magnetic PCI) across distal and /or complex lesions versus conventional navigation (conventional PCI).

Methods and results: Forty-seven consecutive patients (age 61 ± 10yr) undergoing elective single vessel magnetic PCI for distal and/or complex lesions were matched by age and lesion location with 45 patients undergoing conventional PCI (age 63 ± 10yr). Technical success rate was defined as an intraluminal wire position distal to the stenosis. Procedural outcome and costs were evaluated. Baseline demographics and angiographic characteristics of the two groups were similar. The technical success rate did not differ between magnetic and conventional PCI (95.7 vs 97.8%; p=1.00). Significantly shorter procedural and fluoroscopy time were observed for magnetic compared to conventional PCI (29.9 ± 17.6 vs 41.1±21 min, p=0.007; 7.5 ± 7.3 vs 16.1 ± 22.4 min, p=0.02 respectively). Less contrast was used in the magnetic PCI group (58 ml/patient; P=0.02). These advantages resulted in a mean estimated saving of 1400 euro per patient (P<0.001). Advantages of procedural outcome were even more pronounced in the ACC/AHA lesion class C subgroup.

Conclusions: Magnetic compared to conventional PCI is an attractive novel technique that proved to be feasible and safe and might be faster in distal and especially complex lesions.

INTRODUCTION

Magnetic guidewire navigation in percutaneous coronary intervention (magnetic PCI) is a new technique for steering the front end of an angioplasty wire using a tip-mounted magnet. This technique has been shown to be both feasible and practical (1-5). Magnetic PCI has proved suitable for all lesion types (2-4). Studies in both phantoms and humans have suggested potential benefits for magnetic PCI (3,4,6). However, the advantages for different patient subgroups remains undefined.

Magnetic PCI is based on the production of a 2 or 3-dimensional reconstruction of the vessel lumen from standard angiographic images. Knowledge of the positions of the table and image intensifier during angiography allows calculation of the vessel coordinates in real space within the patient's chest. The applied magnetic field can be changed at any time to redirect the wire tip that may improve navigation through complex and tortuous anatomy. Magnetic PCI could also result in less wire deviation into side-branches (7). Benefits of magnetic PCI are complete omnidirectional guidewire navigation, precise direction of wires using navigational vectors within an adjustable magnetic field and increased accuracy by integrating 3-dimensional imaging modalities and 3-dimensional virtual reconstruction software (7). These characteristics of magnetic PCI could potentially result in reduced procedural and fluoroscopy duration and lower material and contrast consumption especially when it is used in patients with distal and complex lesions (5,8). In addition, lower contrast consumption could possibly result in less contrast induced nephropathy (9). For these reasons, the procedural outcomes of patients having magnetic PCI for distal lesions, with special attention to complex lesions, was compared to concurrent matched control patients undergoing conventional guidewire navigation PCI (conventional PCI).

METHODS

Selection of patients

Between January 2007 and May 2007, 375 patients underwent single lesion PCI in the Amsterdam Department for Interventional Cardiology, a large regional tertiary centre. From this patient group, 47 consecutive eligible participants having elective single vessel magnetic PCI for distal and/or complex lesions were included. Distal lesions were defined as all coronary segments except for segment 1, 2, 5, 6 and 11 according to the modified ACC/AHA coronary segment classification. Selected magnetic PCI patients were matched by age, gender and coronary segment with 45 control patients having conventional PCI in the same time period.

Exclusion criteria were simple proximal lesions, multivessel PCI, previous failed conventional PCI for the same target lesion, diagnostic review of another vessel in a staged procedure

or inclusion of another diagnostic procedure such as fractional flow reserve measurement or the use of intravascular ultrasound. An ACC/AHA lesion class type C subgroup was defined in both groups. All patients gave informed consent to the proposed procedure.

Magnetic navigation system

The Niobe® Magnetic Navigation System (MNS, Stereotaxis Inc., St Louis, MO, USA), is a fully integrated system (workstation and magnet control equipment) for navigating proprietary catheters and guidewires that have very small magnets at their distal tips. The orientation of these devices is controlled precisely by manipulation of the field generated by two adjustable large neodymium-iron-boron magnets that are mounted on mechanical positioners on either side of the patient. Rotation and translation of these magnets maintain a net magnetic field of 0.08-Tesla within a 20 cm diameter spherical field in the patient's upper thorax. These permanent magnets are stowed and retracted away from the patient when not in use.

The MNS is fully integrated at our centre with the Integris Allura FD10 cardiovascular imaging system (Philips Medical Systems, Eindhoven, The Netherlands) as shown in Figure 1. The Constellation software included in the Stereotaxis MNS was seldom used for navigation. Most of the cases were performed with either free-style (2D clockwise navigation) or full 3D reconstruction. The operator interfaces with the system via the Navigant™ Navigation Work Station software interface (NWS, Stereotaxis Inc., St. Louis, MO, USA). The NWS has several features that are specifically engineered for interventional cardiology procedures; these features include: 3-dimensional (3D) preoperative navigation that allows the user to import and co-register standard angiographic images and perform "point and click" navigation on the imported image. In addition, the NaviView software (CardiOp-B, Paieon Medical, Rosh Ha'ayin, Israel) allows use of angiographic images from the procedure to generate a 3D vessel reconstruction that can also be used for "point and click" navigation (Figure 2). In our centre, choice of wire and navigation technique (2D mode, 3D mode, or a combination of these) was left to the discretion of the operator.

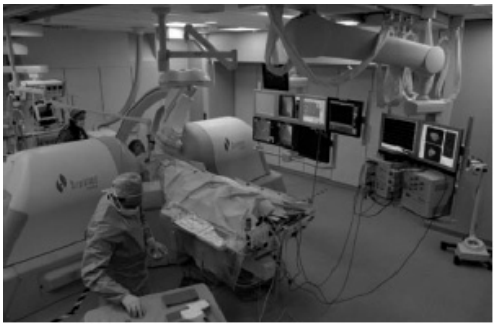

Figure 1. The Niobe® Magnetic Navigation System. A typical magnetic navigation system set-up showing the magnets and C-arm. *See this figue in color in the Appendix page 375.*

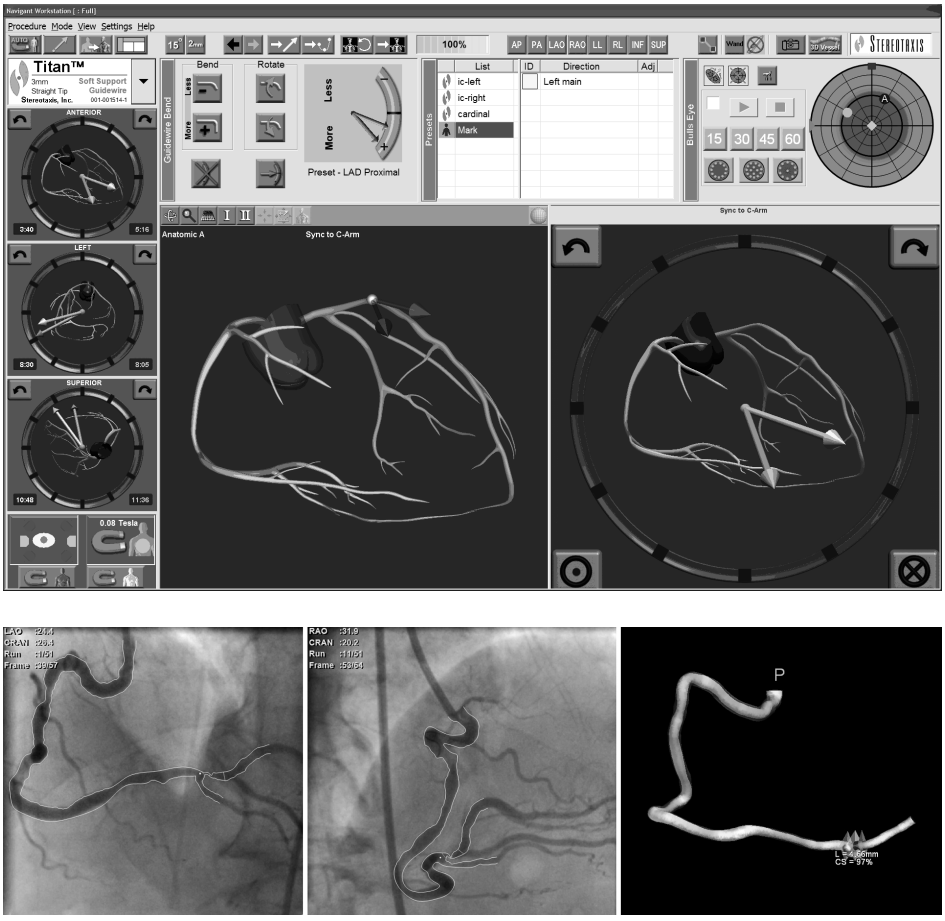

Figure 2. This 3-D reconstruction was created from the fluoroscopic angiogram as shown using the NaviView software feature. *See this figue in color in the Appendix page 396.*

Magnetically enabled wires

A series of magnetically enabled disposable guide wires that are custom designed to integrate with, and be precisely navigated by, the MNS are available in a variety of sizes and a range of stiffness. For this study, we utilised the Titan™ guidewires that are specifically designed to be more flexible and steerable for magnetic navigation. A schematic of a Titan guidewire is shown in Figure 3.

PCI procedure

The interventional staff of the Onze Lieve Vrouwe Gasthuis includes five experienced operators. Conventional PCI procedures were assigned to all 5 operators whereas magnetic PCI

procedures were assigned to 2 of the 5 experienced operators. Aspergic, 500 mg i.v., was administered before, and clopidogrel, 600mg, was administered after the procedure to all patients. Weight adjusted unfractionated heparin, 100 IU/kg, was given as an intravenous bolus at the beginning of the procedure. The use of glycoprotein IIb/IIIa receptor antagonists was left at the operators` discretion. The approach for access was predominantly the transradial technique or, in case of contraindication, the transfemoral approach. The choice of the guiding catheter and equipment was left at the operators' discretion and followed routine practice. The angioplasty wires for magnetic PCI were the standard magnetically enabled wires supplied by the company described above. There was no restriction on the operators' choice of conventional wires. Drug-eluting and bare metal stents were chosen at the operators' discretion.

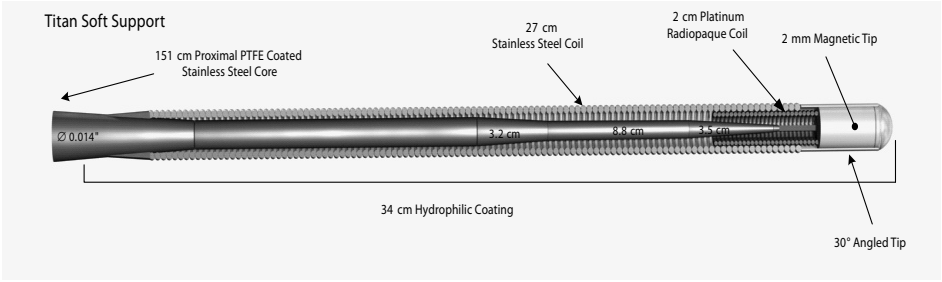

Figure 3. The Titan® magnetic navigation wire with the 2mm magnet located at its tip. *See this figue in color in the Appendix page 395.*

Angiographic variables

All angiograms were stored in a computer database and analysed off-line, using CAAS 2003 Camtronics (Philips Medical System, Eindhoven, The Netherlands), and analysed by an independent observer. Vessel and lesion characteristics have an impact on the performance of the PCI procedure as shown by a study in this issue (9). The angulation of the first turn of the vessel is defined as the first angle within the first 30 mm of the vessel in which the catheter is engaged. It is the angle from the ostium at the aorta into the beginning of proximal left anterior descending artery, beginning of proximal circumflex artery, or the first angle into the right coronary artery. The possible grading is <45° (i.e. mild bend), 45°-90° (i.e. moderate bend), 90°-135° (i.e. severe bend) and 135°-180° (i.e. extremely severe bend). The number of turns before the target lesion was noted. The total cumulative angulation of the 5 worst turns was also noted, using the same grading as above. End-to-end length from the ostium to the lesion was measured using quantitative coronary angiography. The number of visible sidebranches before the lesion, presence of a stent before a lesion, presence of sidebranches within 10 mm of the lesion, sidebranches in the lesion, presence of vessel and lesion calcification were noted. Lesion types were graded according to the ACC/AHA lesion classification

(10). Specific morphological abnormalities were also noted (e.g. aneurysm, dissection flap, AV malformation).

Endpoint definitions

Endpoints of this study were to compare procedural outcome in both groups (e.g. technical success, procedural and fluoroscopy duration, contrast and material consumption). Technical success was defined as an intraluminal wire position distal to the stenoses. Procedural success was defined as 1) TIMI grade III flow (11), 2) <30% residual stenosis, and 3) absence of clinical events during the procedure (death, acute stent thrombosis, myocardial infarction, emergency coronary artery bypass grafting and stroke). Procedural duration was measured from the time of sheath insertion until the removal of the guiding catheter at the end of the procedure. In case 3D reconstruction was used, procedural duration for magnetic PCI included 3D reconstruction time (±5 min). Fluoroscopy times were automatically recorded by the Poly Diagnost (C2) Digital Cardiac Imaging System (Philips). Additional endpoints were the occurrence of dissection, stent length and diameter per patient, contrast usage and material consumption. Estimated procedural costs included the materials and laboratory and staff time. Laboratory and staff time were calculated by multiplying the procedural time + 30 minutes by 17 €/minute; the latter figure was based on time-tested cost estimates, obtained from a large data set collected by Cardialysis, a company linked to the university hospital of Rotterdam, the Netherlands. Materials included in the cost analysis were coronary guidewires, angioplasty balloons, premounted bare metal or drug-eluting stents and angiographic contrast agent.

Statistical analysis

For comparison of continuous variables between the treatment groups, the unpaired two-tailed student's t test was used or, in the case of skewed data, the Mann-Whitney U-test. Comparison of categorical variables between the 2 groups was performed using the Chi-square test, or in case of a minimum expected count less than 5, the Fisher exact test. Continuous variables were expressed as mean ± SD. Categorical data were expressed as numbers of patients and percentage of patients. Spearman rank correlation testing (coefficient Rs) was performed to identify variables related to procedural duration, fluoroscopy time and contrast usage. Among the variables identified, step-down linear regression was performed until all remaining variables were significant, to reveal predictors of procedural duration, fluoroscopy time and contrast usage (12). A P value less than 0.05 was considered statistically significant. Statistical tests were carried out with the SPSS 14.0 statistical software package (Chicago, IL, USA).

RESULTS

Baseline demographics

Forty-seven consecutive patients having magnetic PCI for distal and/or complex lesions were compared to 45 matched control patients having conventional PCI. Baseline clinical charac-

Table 1. Baseline clinical characteristics.

Characteristics	Magnetic PCI (N=47)	Conventional PCI (N=45)	P Value
Age-yr	61±10	63±10	0.35
Male sex	31 (66)	31 (68.9)	0.76
Diabetes mellitus	7 (14.9)	9 (20.0)	0.52
Hypertension	24 (51.1)	20 (44.4)	0.53
Hypercholesterolaemia	18 (38.3)	18 (40)	0.87
Family history of CAD	18 (38.3)	12 (26.7)	0.23
History of smoking cigarettes	13 (27.1)	8 (17.8)	0.26
Previous PCI	23 (48.9)	26 (57.8)	0.40
Previous CABG	3 (6.4)	3 (6.7)	1.00
Previous myocardial infarction	14 (29.8)	16 (35.6)	0.56
Clinical presentation			
Stable angina pectoris	30 (63.8)	28 (62.2)	0.87
Unstable angina pectoris	17 (36.2)	18 (40)	0.71
CCS* anginal class			
I	0	0	–
II	7 (14.9)	13 (28.9)	0.10
III	25 (53.2)	25 (55.6)	0.82
IV	15 (31.9)	7 (15.6)	0.07
Vessel disease			
1VD	18 (38.3)	18 (40)	0.87
2VD	20 (42.6)	16 (35.6)	0.49
3VD	9 (19.1)	11 (24.4)	0.54
Target lesion location			
Left anterior descending artery (LAD)	24 (51.1)	22 (48.9)	0.84
Mid LAD	20 (42.6)	13 (28.9)	0.17
Distal LAD	2 (4.3)	3 (6.7)	0.67
1st diagonal	2 (4.3)	4 (8.9)	0.43
2nd diagonal	0	2 (4.4)	0.24
Left circumflex artery (CX)	14 (29.8)	13 (28.9)	0.93
Obtuse marginal	8 (17)	11 (24.4)	0.38
Distal CX	5 (10.6)	2 (4.4)	0.44
Left posterior lateral	1(2.1)	0	1.00
Right coronary artery (RCA)	9 (19.1)	10 (22.2)	0.72
Distal RCA	5 (10.6)	8 (17.8)	0.33
Right descending posterior	2 (4.3)	1 (2.2)	1.00
Right posterior lateral	2 (4.3)	1 (2.2)	1.00

For age means ±SD are given, and in all other cases number of patients with percentages (within parenthesis). CAD: coronary artery disease. CCS: Canadian Cardiovascular Society.

teristics (Table 1) did not differ significantly between groups, although angina CCS-class IV tended to occur more frequently in the magnetic PCI group.

Table 2. Baseline angiographic variables. Presented are the number of patients with percentages (within parentheses), and in some cases means ±SD.

Variable	Magnetic PCI (N=47)	Conventional PCI (N=45)	P value
Target vessel characteristics			
Angulation 1st turn (aorta to proximal vessel)			
< 45°	10 (21.3)	4 (8.9)	0.10
45°–90°	32 (68.1)	35 (77.8)	0.30
90°–135°	5 (10.6)	5 (11.1)	1.00
135°–180°	0	1 (2.2)	0.49
No. of turns before lesion	2.3±1.5	2.4±1.4	0.79
Angulation of the 5 worst turns			
< 45°	9 (19.1)	3 (6.7)	0.08
45°–90°	27 (57.4)	27 (60)	0.80
90°–135°	10 (21.3)	12 (26.7)	0.55
135°–180°	1 (2.1)	3 (6.7)	0.36
End to end length from ostium to lesion (mm)	50.7±31.2	50.2±32.2	0.94
No. of visible side-branches before lesion	3.9±2.2	3.6±1.5	0.46
Stent before lesion	5 (10.6)	6 (13.3)	0.76
Target lesion characteristics			
No. of side-branches within 10 mm of lesion			
0	0	1 (2.2)	0.49
1	41 (87.2)	42 (93.3)	0.49
2	6 (12.8)	2 (4.4)	0.27
No. of side-branches in lesion			
0	0	1 (2.2)	0.49
1	36 (76.6)	32 (71.1)	0.55
2	11 (23.4)	12 (26.7)	0.72
Lesion angulation			
< 45°	40 (85.1)	30 (66.7)	0.04
45°–90°	6 (12.8)	13 (28.9)	0.06
90°–135°	1 (2.1)	2 (4.4)	0.61
135°–180°	0	0	–
Lesion calcification	20 (42.6)	18 (40)	0.80
Through stent	4 (8.5)	4 (8.9)	1.00
Specific morphologic abnormality (e.g. aneurysmal, shelf, dissection flap, AV malformation)	2 (4.3)	0	0.50
ACC/AHA lesion class			
A	3 (6.4	) 8 (17.8)	0.09
B1	10 (21.3)	12 (26.7)	0.55
B2	12 (25.5)	12 (26.7)	0.90
C	22 (46.8)	13 (28.9)	0.08

No.=number

Most of the baseline angiographic variables (Table 2) were equally distributed between both treatment groups, although the percentage of type C ACC/AHA lesions tended to be higher in the magnetic PCI group (46.6% vs 28.9%; P=0.08).

The number of included chronic total occlusions in the magnetic PCI (6.4%) and conventional PCI group (2.2%) were low and did not differ significantly between groups. The occurrence of severe vessel or lesion angulation (90°-180°) was similar between groups.

Procedural outcome

Successful vascular access was obtained via the radial approach in 97% and in the remainder via the femoral artery. Overall technical and procedural success was high (up to 98%) and similar in both groups (Table 3).

Table 3. Procedural outcome of all distal and/ or complex lesions. Presented are the number of patients with percentages (within parentheses) or in other cases means ±SD.

Variable	Magnetic PCI (N=47)	Conventional PCI (N=45)	P value
Technical success	45 (95.7)	44 (97.8)	1.00
Procedural success	44 (93.6)	44 (97.8)	0.62
Successful radial approach	46 (97.9)	43 (95.6)	0.61
Successful 2nd access femoral approach	1 (2.1)	2 (4.4)	1.00
Dissection	4 (8.5)	3 (6.7)	1.00
Stent length per patient (mm)	21.1±6.8	19.2±7.6	0.22
Stent diameter per patient (mm)	2.9±0.4	2.7±0.4	0.08
No. of stents implanted per patient	1.3±0.9 1	.9±1.1	0.005
No. of drug-eluting stents implanted per patient	0.6±0.9 1.	4±1.1	<0.001
No. of bare-metal stents implanted per patient	0.7±0.8	0.5±0.7	0.14
No. of balloons used per patient	0.9±1.1	1.4±1.3	0.05
No. of wires implanted per patient	1.5±0.8	1.3±0.7	0.38
Procedural duration-min	29.9±17.6	41.1±21	0.007
Fluoroscopy time-min	7.5±7.3	16.1±22.4	0.02
Contrast consumption-ml	122±82	180±147	0.02
Material costs in Euros	2030±1547	3514±2106	<0.001
Procedural costs in Euros	3323±1806	4723±2288	0.002

No.= number.

One serious clinical event occurred in the magnetic PCI group (acute bare-metal stent thrombosis) and one in the conventional PCI group (side branch occlusion). All technical failure cases were type C ACC /AHA lesions. Technical and procedural success was high (up to 92%) in the type C ACC/AHA lesion subgroup (Table 4).

Table 4. Procedural outcome of type C ACC/AHA lesion class subgroup. Presented are the number of patients with percentages (within parentheses) or in other cases means ±SD.

Variable	Magnetic PCI (N=22)	Conventional PCI (N=13)	P value
Technical success	20 (90.9)	12 (92.3)	1.00
Procedural success	20 (90.9)	12 (92.3)	1.00
Procedural duration-min	31.3±15.7	55.5±23.1	0.001
Fluoroscopy time-min	9.0±6.9	28.6±34.4	0.01
Contrast consumption-ml	147±91	214±85	0.04
Procedural costs in Euros	3994±2070	6781±2693	0.002

Significantly shorter procedural and fluoroscopy times and lower contrast consumption were observed in favour of magnetic PCI (Table 3). In multivariate analysis, among 12 demographic, clinical and angiographic variables tested, magnetic PCI (P<0.001) and absence of ACC/AHA lesion type C (P=0.01) were independent predictors for shorter procedural duration. Among 14 demographic, clinical and angiographic variables tested, magnetic PCI (P=0.01), absence of target lesion location in the distal left anterior descending artery (P<0.0001) and absence of 3-vessel disease (P=0.04) were independent predictors of shorter fluoroscopy duration. Among 14 demographic, clinical and angiographic variables tested, magnetic PCI (P=0.008), absence of a previous myocardial infarction (P=0.006), absence of severe vessel or lesion angulation (<135°; P<0.001) and absence of type C ACC/AHA lesion (P=0.02) were independent predictors for lower contrast consumption. Advantages in procedural outcome for the magnetic PCI group were even more pronounced in the type C ACC/AHA lesion subgroup (Table 4).

Material consumption and cost estimation

Magnetic PCI was associated on average with an 11 minute reduction in procedural duration (P=0.007) and reduced usage of angiographic contrast agent (58 ml/patient; P=0.02). Significantly more stents and balloons, as well as drug-eluting stents per patient, were implanted in the conventional PCI group (Table 3). Therefore magnetic PCI resulted in significantly lower material and procedural costs compared to conventional PCI, representing a mean procedural saving of 1400 € per patient (P<0.002). Costs remained significantly lower for magnetic PCI when corrected for the difference in number of drug-eluting stents used (€2727± €1190 vs €3301± €1395, P=0.04).

The type C ACC/AHA lesion subgroup was larger in the magnetic PCI group (Table 2). In this subgroup magnetic PCI had even more pronounced savings (Table 4) in procedural duration (difference, i.e. delta, with conventional PCI: 24 min), fluoroscopy time (Δ: 20 min), contrast consumption (Δ: 67 ml) and procedural costs (Δ: €2787).

DISCUSSION

Magnetic PCI is a promising technique in cardiac electrophysiological procedures (13,14) and is emerging as a powerful tool in interventional cardiology (1-6). Phantom studies have suggested that magnetic PCI provides more benefit in distal and tortuous lesions and may be expected to provide greater advantage in complex procedures (3,4). Therefore, we compared in the clinical setting the efficacy of elective single vessel magnetic PCI in distal and more specifically complex lesions to matched controls using conventional PCI. Our study indicates that magnetic PCI might be superior to conventional PCI for procedural duration, fluoroscopy time, contrast usage and costs. The high technical and procedural success rates were similar between groups. It is noteworthy that this group of procedures was challenging as is indicated by the time-consuming procedures and high incidence of type C ACC/AHA lesions. The incidence of type C ACC/AHA lesion, an independent predictor for worse procedural outcome, was significantly higher in the magnetic PCI compared to the conventional PCI group. Therefore the procedural advantage of magnetic PCI could have been more pronounced if ACC/AHA lesions had been equally distributed among groups. It is noteworthy that magnetic PCI was an independent predictor for shorter procedural and fluoroscopy times and lower contrast consumption. The significantly lower procedural duration, fluoroscopy time, contrast usage, number of stents and balloons used resulted in significantly lower procedural costs with a mean saving of 1400 euro per patient. However, one should bear in mind that the acquisition of the Stereotaxis Magnetic Navigation System is highly expensive (±€1.4 million). At least one thousand patients should be treated with magnetic PCI to compensate for these expenses. The benefit in procedural outcome for magnetic PCI is even more pronounced in patients having magnetic PCI for type C ACC/AHA lesions (Table 4). In complex lesions magnetic PCI resulted in a 44% reduction of procedural duration, 69% reduction in fluoroscopy duration, 31% reduction in contrast consumption and a 41% reduction in costs. Treatment of these complex lesions is generally more problematic due to the difficulty in steering and pushing a guidewire through them. As the Magnetic Navigation System provides precise, computerised control of the working tip of a guidewire, it can enable physicians to more easily locate small openings in, and to advance a guidewire across, these lesions. The possible benefit in procedural outcome for magnetic PCI revolves around key abilities of the system. First, magnetic PCI procedures incorporate 3D information (presets, constellation and reconstruction). The automatic 3D alignment of the magnetic tip with the chosen vector, rather than manual steering by estimation from the 2D fluoroscopy screen, improves coaxialisation of the guidewire tip in the vessel. This can help to orientate the guidewire tip in order to pass a vessel angulation, or into a desired branch, and this may reduce incorrect selection of a side-branch, a problem that is inherent with the bent and non-coaxial tip of a conventional wire. This reorientation can be performed within the patient at any time during the procedure meaning that the wire tip is actively steered. This steering is independent of

factors in the proximal section of the vessel such as tortuosity or calcium that may impair the rotation and manipulation of a conventional wire that is needed to steer the tip. The result is that the operator is not forced to use a single fixed bend that may not be appropriate to each and every bend of a coronary vessel, lesion and side-branch.

Second, the use of a computer enables the introduction of features that give added value and were previously unavailable during PCI. An example is the white line overlay map on the fluoroscopy screen, which is a further progression as compared to the use of a separate still image on a 2nd screen or 'roadmap'. The white line overlays the trajectory of the vessel on the fluoroscopy screen, as calculated from the virtual vessel, and is automatically reorientated on the screen as the viewing angle of the x-ray image intensifier is changed. This white line overlay acts as a guide and assists wire placement. This may explain the reduced procedural duration, fluoroscopy time and contrast usage observed in the current study.

In addition to efficient and successful procedures, economic and practical advantages, magnetic PCI results in a substantial reduction in x-ray exposure to physicians, staff and patients as well as potential reduction in contrast induced nephropathy especially in diabetic and hypertensive patients (15,16). This study has limitations associated with cohort studies in that procedures were not randomised. Selection bias could have occurred. As shown in Table 3, stent diameter tended to be larger and the number of stents and balloons implanted per patient were lower for the magnetic PCI group. These findings suggest that relatively larger vessels and shorter lesions were treated in the magnetic PCI group that could in part explain the shorter procedural and fluoroscopy duration and cost advantage in the magnetic PCI group. Only two out of five operators performed the magnetic PCIs in the current study after a short learning curve, which has been described earlier (6). Operator bias could also have affected outcome. One operator, who performed a large part (±43%) of the conventional PCIs in this study, used significantly more drug eluting stents per patient compared to the other operators. This could in part explain the higher usage of drug-eluting stents and higher costs in the conventional PCI group. Nevertheless all operators were experienced and multivariate analysis showed that the operator was not a predictor for outcome. In this respect a randomised trial should be performed. However, a randomised trial may also raise objections. It is not possible to blind the performing physician to the type of procedure. All operators should use both techniques in order to eliminate differences in operator skills and speed and the risk of competition between operators with consequences for the quality of the procedure. On the other hand bias could occur in favour of magnetic PCI when all operators perform magnetic as well as conventional PCIs.

Another limitation related to magnetic PCI is that certain aspects of the procedure can be time consuming such as obtaining the isocenter position and moving the magnets into the correct position or time to reconstruct. However, with familiarity, these manoeuvres become quick. In addition the choice of magnetic compared to conventional PCI wires is limited especially for flexible wires. This might complicate difficult procedures such as heavily

calcified chronic total occlusions. In addition, manipulation of the Titan guidewire in severely angulated lesions could be difficult due to the rigidity of the 2 to 3 mm magnet located at the tip of the guidewire.

In conclusion, magnetic PCI is an attractive novel technique, which proved to be safe and may result in improved procedural outcome in distal and/or complex lesions. A randomised trial is needed for proper comparisons.

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CHAPTER 17

Magnetic Navigation System Used Successfully to Cross a Crushed Stent in a Bifurcation that Failed With Conventional Wires

ABSTRACT

Bifurcation lesions can be technically demanding to manage, and even in the era of drug eluting stents, their procedural success is variable. The use of the crush technique followed by "kissing" balloon postdilatation has been shown to improve the overall outcome. However, crossing the crushed stent is essential to allow performance of a final dilatation with "kissing" balloons and is regarded as the main Achilles' heel of this technique. In this report, we describe the first reported, planned procedure to use a magnetic navigation system to steer a wire through the crushed stent to use "kissing" balloons that had previously failed with conventional wires.

INTRODUCTION

Coronary bifurcation lesions are a challenging and frequent problem encountered in patients undergoing percutaneous coronary interventions (1). Their overall longterm success rate is variable but has improved since the introduction of drug eluting stents (DES). A number of stenting techniques are employed in the management of these lesions and they include T-, V-, Y-stenting, the "culotte" and the "crush" technique (2). The latter is a technique that ensures complete coverage of the side branch ostium so as to ensure drug delivery to minimize restenosis at this site (3). This involves wiring both the main vessel and side branch. The proximal part of the stent that is deployed in the side branch protrudes into the main vessel and is crushed with another stent that is deployed in the main vessel (4). Crucial to the success of this technique is the use of "kissing" balloons to ensure complete apposition of both DES to the vessel wall (5). To do this a wire must cross the crushed stent overlying the ostium of the side branch (6). In certain cases this can be difficult and may result in a prolonged procedure with possible complications such as contrast nephropathy and increased radiation exposure. The magnetic navigation system (MNS) can be utilized to steer a wire through the stents' struts to address this limitation of the "crush" technique (7). The MNS has previously been successfully used in chronic total occlusions and in vessels with tortuous anatomy but has not so far been reported as an aid to bifurcation stenting (8–10).

We report a planned procedure to use magnetic navigation with an appropriate wire to cross a crushed stent where previous attempts with conventional wires had failed in the emergency setting. This was followed by "kissing" balloon dilatation and led to procedural success in a patient with a bifurcation lesion.

THE MAGNETIC NAVIGATION SYSTEM

The MNS has been shown to be effective in neurosurgical and cardiac electrophysiological procedures (11,12). In percutaneous coronary intervention it is a platform that offers a powerful tool to aid navigation of a guidewire through complex coronary anatomy (13). The Stereotaxis Niobe® MNS has two permanent magnets that can be moved (rotated, translated, or tilted) to produce a uniform magnetic field of 0.08 Tesla within the patient's chest. This field is used to precisely direct a tiny magnet mounted on the tip of a guidewire by changing its magnetic moment. This allows fine control of the orientation of the tip of the guidewire in space. The Titan™ Soft Support coronary guidewire used in this case is a 180-cm moderate support, hydrophilic coated wire with a diameter of 0.014 in./0.36 mm and has a flexible 2 cm distal coiled tip at the endof which is a gold cup attached to a neodymium-iron-boron 2- or 3-mm magnet.

A three-dimensional virtual vessel roadmap is created from the angiographic images using reconstruction software (CardiOp-B, Paieon Medical, Rosh Ha'ayin, Israel). The system

computes a navigation plan from the reconstructed virtual path that supplies all the vectors required to navigate through the coronary artery. By touching a point of interest on this virtual map that is displayed on a touch screen monitor, the Navigant software calculates the best vector and directs the magnetic field to align the wire tip with that direction. This can be performed at anytime during the procedure, in vivo, and without the need for a preshaped wire tip angle.

CASE REPORT

The patient was a 58-year-old man who presented with an anterior ST elevation MI. His risk factors included being a non-insulin-dependent diabetic and being on treatment for hypertension.

The Primary PCI

Angiography revealed an occluded LAD that, once open, showed a bifurcation lesion at LAD/D1. This was managed by placing PT Graphix wires into each vessel. A Taxus Liberte 3.0 x 16 mm stent in the LAD was used to crush the proximal end of a Taxus Liberte 2.5 x 12 mm stent in the diagonal. Both stents were deployed without predilatation of the lesion at 16 atmospheres. To perform the "kissing" balloon technique it was necessary to cross the crushed stents' struts to gain entry into the diagonal. This was unsuccessful despite the various techniques employed, such as an over the wire balloon (OTW), to support the wire or by changing the angle of the wire tip manually. When a stiffer wire (PT Graphix Super Support) was used, it did not enter the true lumen but went subintimally. This was apparent after dilatation with a Maverick 1.5 x 15 mm OTW balloon as it resulted in a dissection at the proximal end of the deployed stent in the diagonal (Fig. 1A and B). Consequently, it was even more imperative to use "kissing" balloons in this case to fully appose the diagonal stent against the dissected vessel so as to improve the overall outcome.

Attempts were made to finish the procedure and, having tried to cross the stent struts for almost an hour, and in the presence of TIMI 3 flow down both the LAD and D1, the operator elected to leave the sheath in situ and use magnetic navigation in the morning.

The Magnetic Navigation Assisted PCI

The left coronary artery was cannulated with a Mach 1 CLS 3.5 6F guide catheter. The first attempt was with another PT Graphix intermediate wire but this again preferentially chose to follow the tract of dissection, outside the stent before re-entering the true lumen. Therefore, a three-dimensional virtual vessel roadmap was created from the angiographic images by

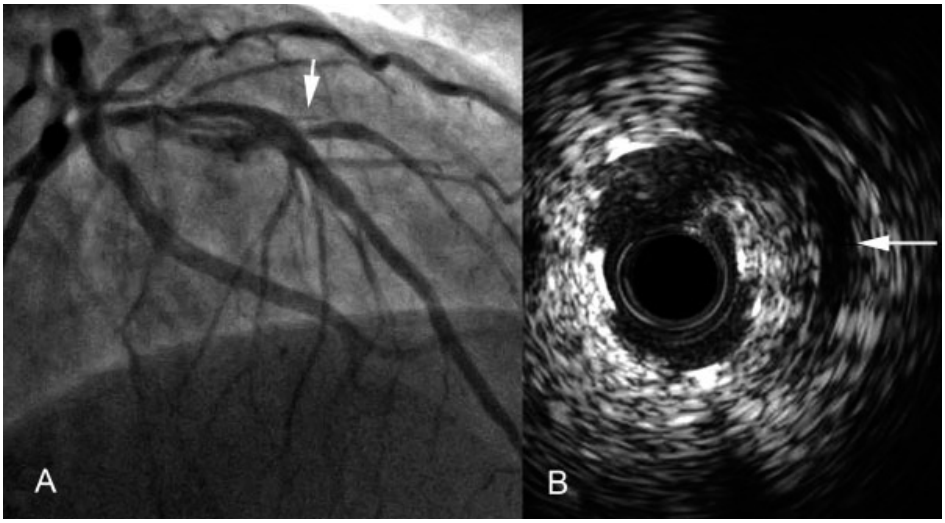

Figure 1. (A) The results of crushing the proximal end of the stent in D1 with a stent in the LAD and a dissection of D1 (arrowed) created iatrogenically by inflating a balloon between the D1 stent and the vessel wall. (B) An IVUS image of the deployed crushed stent showing the dissection (arrowed).

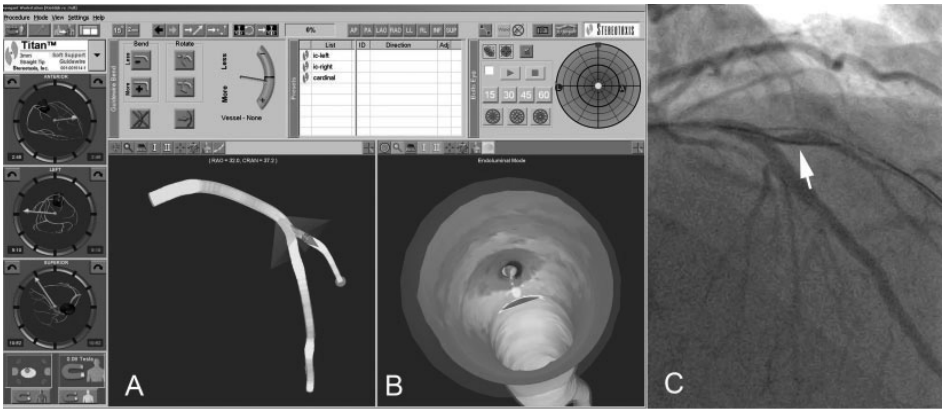

Figure 2. The 3D reconstruction (A) and the endoluminal view of the LAD/diagonal bifurcation (B). The magnetically guided Titan™ Soft Support wire (arrowed) successfully crosses the stent strut into the true lumen and the Graphix Intermediate wire preferentially chose the false lumen of the dissection (C). *See this figue in color in the Appendix page 396.*

using reconstruction software (Fig. 2A). A vector was then created that navigated a Titan™ Soft Support angled magnetic tip wire between the crushed stents' struts and avoid the false lumen (Fig. 2C). Subsequent use of "kissing" balloons, Maverick 2.5x15 mm in the diagonal and Maverick 3.0x15 mm in the LAD at 16 atmospheres (Fig. 3A), resulted in full apposition of the diagonal stent (Fig. 3B). The patient tolerated the procedure well and his cardiovascular status was stable as monitored via an arterial line.

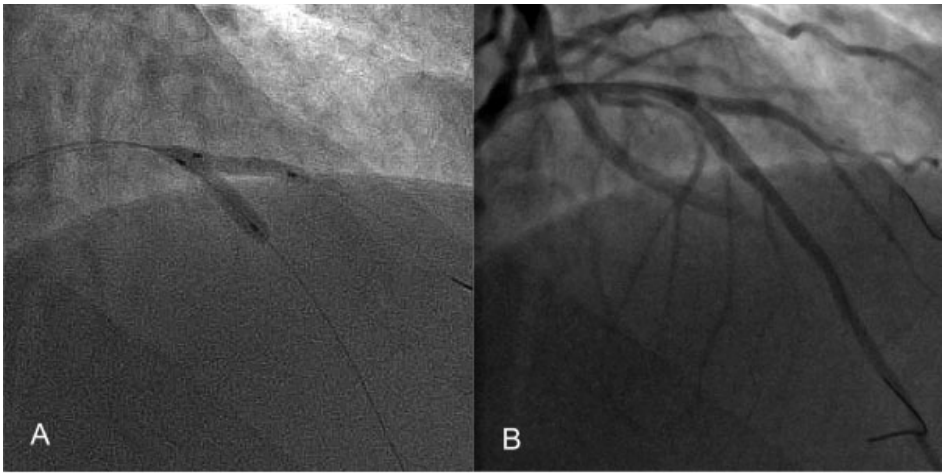

Figure 3. (A) The postdilatation with "kissing" balloons using a Maverick 2.5 x 15 mm in the diagonal and a Maverick 3.0 x 15 mm in the LAD at 16 atmospheres. (B) The final angiographic result of the crush.

DISCUSSION

Magnetic navigation is a novel technique that was successfully used to cross a crushed stent where traditional methods had failed. The tip of the steerable wire employed can rotate in three-dimensions depending on the programmable vector created by the magnetic field. This has the advantage that it can be performed within the coronary artery itself and is aided by a digitally reconstructed image of the coronary vessel. This technique was crucial to the success of this case as it was necessary to fully appose the crushed stent against the dissection using the "kissing" balloons technique.

CONCLUSION

This is the first report of the use of the MNS to successfully cross a crushed stent in the management of a bifurcation lesion. The advantage of this technology is that it produces a three-dimensional digitally constructed visual map and can precisely direct a guide wire along a chosen path. This can potentially reduce the time of the procedure, the amount of contrast needed, and radiation exposure.

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CHAPTER 18

Magnetically Supported PCI: Success after failed surgery and conventional PCI

INTRODUCTION

Magnetically supported PCI is starting to deliver on its potential to improve and extend on several aspects of percutaneous cardiac treatment. In particular, the ability to control tip direction more accurately and independently of bends or friction has allowed for increased utilization. We present a patient in whom both surgery and previous conventional PCI failed to produce a satisfactory long term result. The use of magnetic navigation allowed for successful revascularization of an extremely tortuous conduit, restoring blood supply to a large territory of myocardium.

The System

The Niobe® II magnetic navigation system (MNS: Stereotaxis, St Louis, Missouri) has two external magnets that produce a 15-cm uniform magnetic field. Through computer-controlled magnet movements, the magnetic field can be directed 360° in all planes. When the field is changed, the deflection of the magnet at the wire tip also changes, resulting in reproducibly precise steering. The system has an adjustable touch screen at the lab table that is the interface between the operator and the MNS (Figure 1). The current system has three main advantages with regards to tortuosity. First, it produces a 3-D, volume-rendered reconstruc-

Figure 1. System in position for PCI. M indicates magnets in tilt position for better lateral movement of the image intensifier. T indicates touch screen interface to give real-time instruction to the MNS. S indicates in-lab main screen monitor. *See this figue in color in the Appendix page 378.*

tion from angiographic images, providing better morphological information about the artery. Second, the spatial coordinates, or location, of the reconstruction within the patient are known. Third, the model gives real-time, online vectors, which direct the external magnetic field to navigate the wire through the 3-D reconstruction. As a result, operators have the ability to utilize real-time 3-D information in patient therapy.

System costs

The current list price for the Stereotaxis Magnetic Navigation System is $1.9 million. The size of a typical modern Stereotaxis cath lab room is 770 square feet (72 square meters). The cost of magnetic shielding generally ranges from $50,000–$100,000 and consists of minimal common steel shielding in the walls, ceiling and floor. There is a range of magnetically enabled Stereotaxis 0.014" guidewires that are priced at a marginal premium over conventional wires. All other PCI equipment is standard and compatible with the Stereotaxis guidewires and MNS. No additional consumable items are required. All third-party billing occurs as part of a standard PCI intervention; therefore, all current reimbursement applies and there is no effect on current billing practices.

Case Report

This report describes a 60-year-old man with multiple medical pathologies and a burdened cardiac history. Past medical history included severe airways disease (FEV1 of 1 litre), ulcerative colitis with chronic iron deficiency anemia despite iron therapy, previous GI bleeding, gout, hypertension and hypecholesterolaemia, and a family history of ischemic heart disease and peripheral vessel disease.

The patient had undergone an aortic valve replacement 8 months prior for significant calcific aortic stenosis. At that time, he received a jump saphenous vein graft (SVG) that anastomosed to the obtuse marginal branch (OM) and then the right posterior descending coronary artery (RDP). At the time of the operation, the cardiothoracic surgeon had noted that although the RCA had been grafted, it was heavily calcified, of poor quality and not suitable for further surgical treatment. The patient had a difficult recovery after the coronary artery bypass graft (CABG) operation with persistent hypotension, in part due to episodes of arrhythmia such as sinus bradycardia that was externally paced, and also atrial fibrillation (AF), for which he was later cardioverted. He had some generalized oedema and, once extubated, dyspnoea that resolved slowly.

Unfortunately, 2 months after surgery, the patient again began to suffer with chest pains (despite a satisfactory Hb) that could not be fully controlled with medication. Angiography showed the proximal end of the graft was occluded but with a patent section of graft between the OM and the RDP.

However, this remaining section of the SVG was compromised by severe lesions at both anastomoses with an adversely acute angle in the stenosis just before the OM anastomosis (Figure 2).

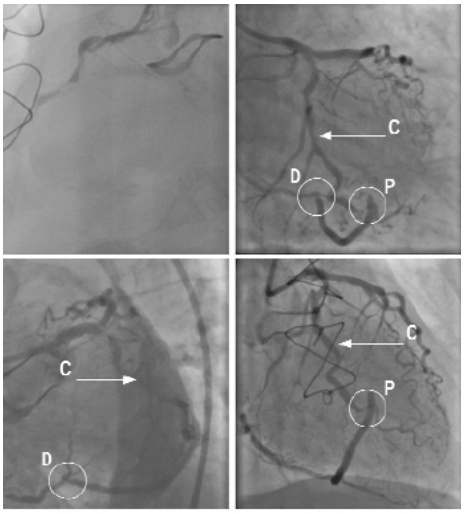

Figure 2. The top left panel shows the occluded RCA that could not be opened anterogradely. The other three panels are different views showing Cx tortuousity and severe lesions at proximal and distal anastomoses of the SVG. C indicates the Cx. P indicates the proximal anastomosis. D indicates the distal anastomosis.

Further surgery was refused and conventional PCI using biplane angiography was attempted, with a view to reopening the RCA or if unsuccessful, intervening on the tortuous Cx-OM-SVG-RDP (Cx: circumflex artery). The RCA was heavily calcified. Despite the use of stiff occlusion wires and a variety of balloons for support, a wire could not be passed and the attempt was stopped due to the presence of dissection. An attempt to pass the wire into the SVG via the left coronary artery (LCA) was unsuccessful due to tortuosity and despite the use of multiple catheters and wires. For the attempts on both vessels, a total of 5 guiding catheters and 7 angioplasty guide wires, including Asahi Miracle 3, Asahi Miracle 6 (Abbott Vascular Devices, Redwood City, CA) and Crosswire NT (Terumo Medical Corporation, Somerset, NJ), were used.

The Magnetic Procedure

Reconstruction.

A decision was made to attempt a further procedure with the MNS. A 3-D reconstruction (Figures 3–4) showed that the sum of all the angles from the LMS to the RCA was over 1180° (equivalent to over 3 complete turns of a corkscrew). Currently, an analysis of the reasons

for prolonged procedures (with respect to wire passage across a lesion) is ongoing. Both the number of bends and the degree of angulation seem to be strongly related to a prolonged crossing time. Each bend adds friction to conventional wire rotation and therefore steering, and this friction becomes greater as the angulation increases (as the wire is more deformed and may also be pushed more forcefully against the vessel wall). Thus the cumulative angulation may be extremely relevant to procedural duration and success.

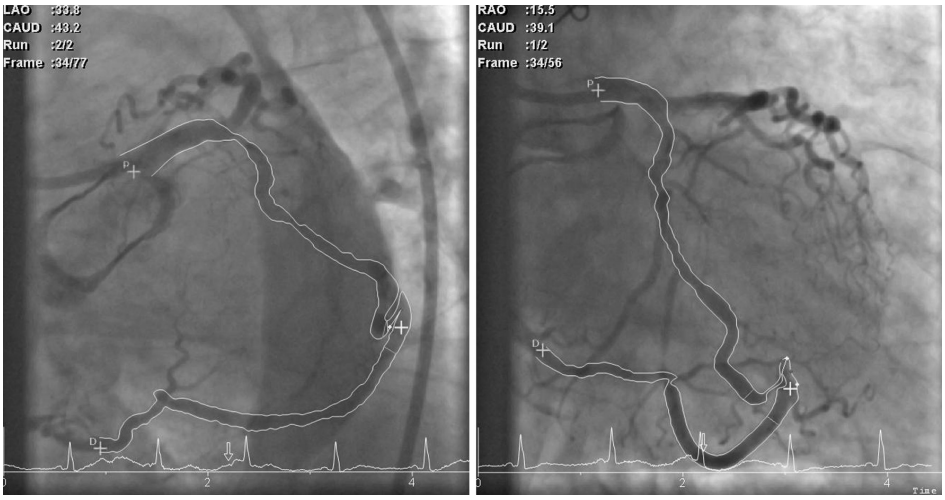

Figure 3. Panels showing different fluoroscopy views with vessel edges marked by edge detection software (CardiOp-B, Paieon Medical Inc., Rosh Ha'ayin, Israel) before reconstruction. P indicates proximal point. D indicates distal point. *See this figue in color in the Appendix page 397.*

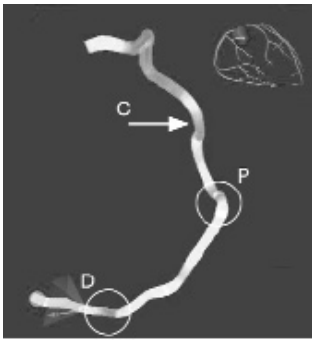

Figure 4. Three-dimensional reconstruction of target pathway. C indicates the tortuous Cx. P indicates the proximal anastomosis. D indicates the distal anastomosis. *See this figue in color in the Appendix page 397.*

Navigation.

One of the prime benefits of the MNS 3-D reconstruction is that it provides an endoluminal view with a computed 3-D center line (Figure 5). This view offers a tailored direction for the magnetic field vector at every point in the vessel. There is also a white-line overlay that is a

roadmap on the fluoroscopy screen. Tip advancement is shown on the white-line overlay in tandem with operator advancement of the wire. The 3-D vector changes simultaneously to keep the wire pointing down the chosen path. The Titan™ Soft Support 2 mm angled tip wire (Cordis Corp., Miami, FL) was navigated through the tortuous LMS, Cx and OM using the vectors as far as the stenosis before the first anastomosis (with the adverse angle). At this stage, finer navigation was required to reach the SVG. Careful interrogation, by changing the angulation using the endoluminal view (the vector can be changed in the endoluminal view by double-tapping the screen at any point), and increasing the magnetic field strength to 0.1 Tesla, managed to get the wire tip to angulate enough to pass into the body of the graft. At this point, a 1.5 mm Maverick over-the-wire balloon (Boston Scientific Corp., Natick, MA) was passed to the graft body and used for support. The wire was then advanced through the graft using vector control and then into the RDP. In order to maximize support, the balloon was advanced to the RDP and an Iron Man support wire (Abbott Vascular) exchanged.

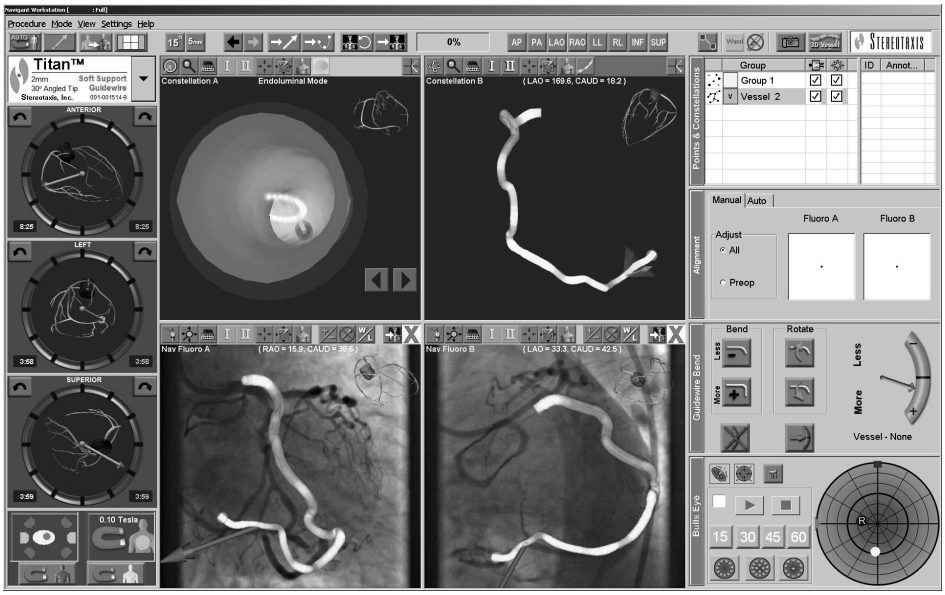

Figure 5. Screen of Stereotaxis Navigant program during procedure, showing top left panel with endoluminal view. The top right panel shows the reconstruction. The bottom 2 panels are static captured fluoroscopy images with the reconstruction for that angle superimposed. *See this figue in color in the Appendix page 398.*

Intervention.

Both anastomoses were predilated. However, on the first attempt to pass a stent, there was excess resistance in the Cx that nearly caused wire retraction. The Cx was predilated, and both the anastomoses and the Cx were then stented (Figure 6). There was a good result, with TIMI 3 flow at the conclusion of the procedure (Figure 7).

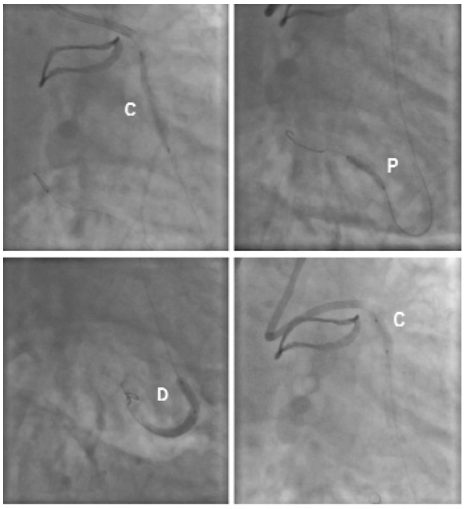

Figure 6. Interventions. The top left panel shows predilation of Cx. The top right panel shows stent placement in distal anastomosis. The bottom left panel shows stent deployment at the proximal anastomosis. The bottom right panel shows one of the stents being deployed in the Cx. C indicates the Cx. P indicates the proximal anastomosis. D indicates the distal anastomosis.

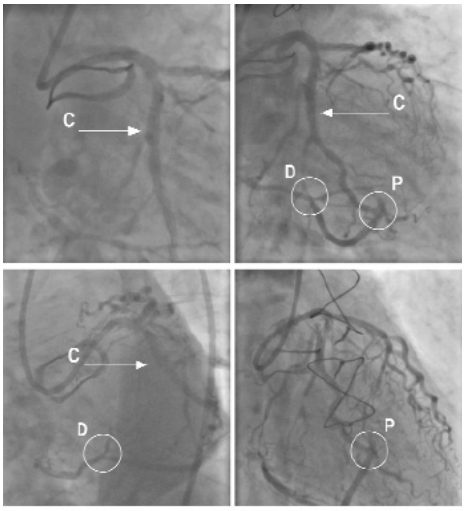

Figure 7. Results of stenting from different views. C indicates the Cx. P indicates the proximal anastomosis. D indicates the distal anastomosis.

DISCUSSION

The potential advantages of magnetic navigation are especially relevant to excessively tortuous vessels. It is in these cases where the advantages of magnetic steering are most obvious over conventional procedures:

1) A conventional procedure has to use the same tip shape throughout. While appropriate for some angles, it is not ideal for multiple bends of varying angulation.
2) Once inside the patient, the tip shape of a conventional wire cannot be changed without retrieving the wire and losing position or exchanging through a support catheter.
3) After a conventional wire has been passed distally, there may be resistance when trying to rotate the wire tip for manipulation.

In contrast, the tip of a magnetically-enabled wire can be directed at will in any direction. Therefore, the tip shape is variable at will, is adjustable in situ for a particular bend and is independent of rotation of the wire (and thus friction from the bends in the vessel). Such abilities may be of significant benefit in challenging cases.

While the system is relatively intuitive and usable after minimal experience, we are finding that further improvement continues steadily as the range of additional features is explored. The experience at our institutions is a little over 350 cases and rising. A variety of randomization studies and registries are currently ongoing or under analysis.

Future Directions

The MNS has other potentially valuable capabilities. For PCI, the integration of other 3-D, volume-rendered imaging such as multislice computed tomography (MSCT) (Figure 8), as well as the possibility of other useful functions such as magnetically navigable ablation or remote control navigation, may be advantageous. In addition, the integration of data such as the electromechanical maps from the Carto RMT™ system (Cordis, Figure 9) may enhance procedures such as stem cell therapy.

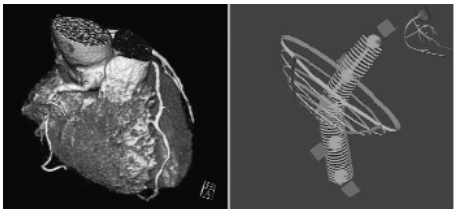

Figure 8. The left panel shows raw MSCT with the path of occluded RCA marked (purple diamonds). The right panel shows the reconstructed vessel from the scan. *See this figue in color in the Appendix page 398.*

Limitations

Software**.** While 3-D imaging represents improved appreciation of coronary anatomy compared to the 2-D black-and-white x-ray images that have been the standard manner of visualizing coronary arteries, the current reconstructions are static. Dynamic road-mapping is an area under development.

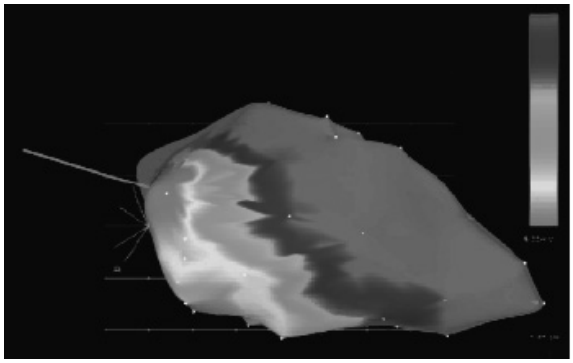

Figure 9. An electromechanical map which can be integrated into the Magnetic Navigation System. *See this figue in color in the Appendix page 398.*

Hardware**.** The internal guide wire magnets are currently rigid 3 mm wire tips, with a 2 mm option. While the rigidity can potentially restrict the movement of the magnet tip in a lesion of less than 3 mm diameter, to date, there has been only a mild clinical impact, mainly when attempting to enter side branches that may come off at right angles within a tight lesion. A flexible tip (with several magnets) is under development for enhanced navigation.

Strategies**.** The range of options within the system translates into a number of possible strategies that may develop in an evolutionary fashion. One example of a hybrid strategy is the manipulation of an angled wire without a magnetic field, bringing in the magnets as necessary. The use of presets and the 2-D clockface allow for relatively speedy use of the system, and may better suit procedures in simple lesions or where time plays a role, such as primary PCI. Performing a 3-D reconstruction may give a better idea of the anatomy and provide more individually tailored pre-calculated vectors for navigation.

Bringing together reconstructions from diagnostic images and using navigation with the white-line overlay and minimal contrast may be helpful when it is necessary to reduce contrast volume. Additionally, 3-D reconstruction may be especially useful in extremely long and tortuous segments.

CONCLUSIONS

MNS has been shown to aid PCI of complex and tortuous vessels. System capabilities, together with other current and forthcoming options, indicate that MNS could have a major impact on the performance of PCI. In our opinion, the finer wire tip control, the extended anatomical information, the potential for integration in using other 3-D sources such as MSCT in real time, together with forthcoming developments such as flexible wire-tips, ablative wire-tips and navigable injection catheters, may produce a formidable system.

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Patterson MS

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CHAPTER 19

3D reconstruction from contrast coronary angiography in Magnetic Percutaneous Coronary Intervention

ABSTRACT

The magnetic navigation system allows precision wire-tip control that is guided by computer generated 3D models based on fluoroscopic images. These images can be post-processed and the information used to facilitate steering of wires in difficult anatomy. This report illustrates two of these reconstruction software packages in a challenging saphenous vein graft case.

INTRODUCTION

Magnetic navigation in Interventional Cardiology makes use of on-table 3D reconstruction imaging to both enhance the visualization of coronary arteries as well as to supply individualized directional information to navigate tortuous vessels. These images can be post-processed and integrated to facilitate steering of wires and provide information on the course and anatomy of the vessel. The Niobe® II Magnetic Navigation System (MNS; Stereotaxis, St Louis, Missouri, USA) and it's use have been described in detail previously (1-5). Using computer-controlled movements of the magnets, a 15-20 cm uniform magnetic field volume centred on the heart of the patient can be reliably and reproducibly directed in 360° in all planes. This reproducibly deflects a magnetic wire tip to give precise steering.

The MNS is fully integrated at our center with the Integris Allura FD10 cardiovascular imaging system (Philips Medical Systems, Eindhoven, The Netherlands). Two of the reconstruction software packages currently available are the *3DCA* software on the stand-alone Interventional Tools workstation (Philips Medical Systems, Eindhoven, The Netherlands), and the *Cardi-Op B*™ software, (Paieon Medical Inc., Rosh Ha'ayin, Israel) that is integrated in the MNS Navigant software. Both systems reconstruct from 2 frames at different angles, the Paieon system uses 2 separate contrast injections at separate angles (see figures 1 and 2) while the Philips system uses 2 frames from a rotational acquisition using a single contrast injection (see figures 1 and 2). The new *3DCA* reconstruction software from Philips had recently been installed and it was decided to use this as well as make a second, 'back-up' 3D reconstruction from the diagnostic CD (therefore no extra contrast was used).

This report illustrates these 3D reconstruction techniques in a challenging case.

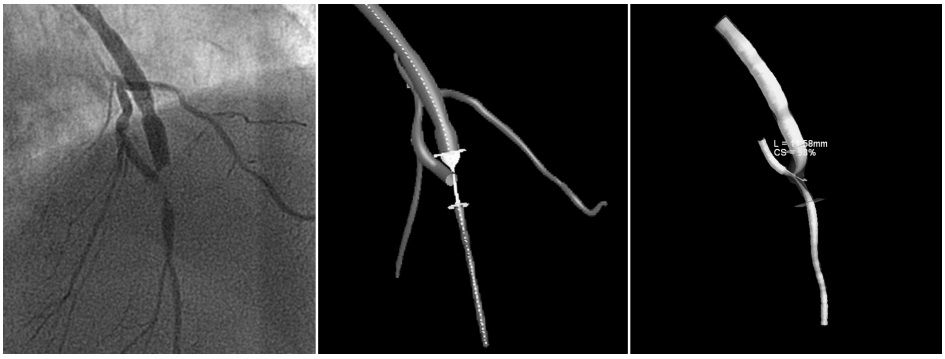

Figure 1. This shows the RAO view; the left panel shows the angiographic view of SVG-LAD showing the tandem lesion at and beyond the anastomosis, the middle panel shows 2 views of the 3DCA reconstruction and the right panel shows 2 views of the Cardi-Op B™ reconstruction. *See this figue in color in the Appendix page 379.*

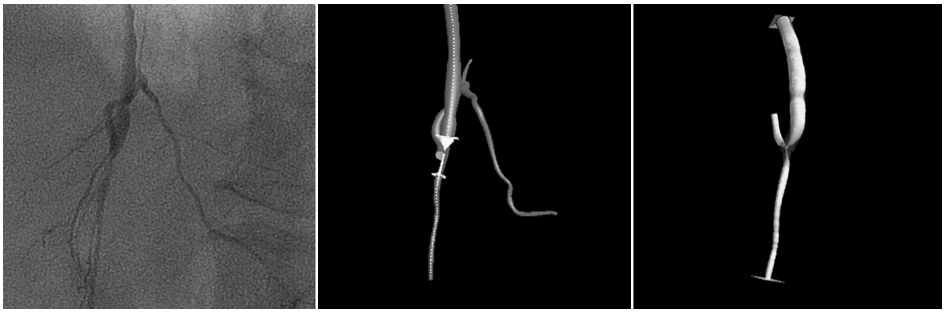

Figure 2. This shows the LAO view; the left panel show the angiographic view, the middle panel shows the reconstruction produced by the Philips software, the right panel shows the reconstruction produced by the Paieon software. *See this figue in color in the Appendix page 399.*

CASE REPORT

A 65 yr old man who had had CABG in 1999, with 4 single venous grafts to the LAD, OM1, OM3 and the RCA, presented with a recurrence of his stable angina (Canadian Cardiovascular Society grade II) on exertion. He had undergone angiography that showed that in the trajectory of the LIMA-LAD graft, there was a complex lesion with 2 subtotal stenoses, the first situated just proximal to the anastomosis and the second just distal to the anastomosis in the distal LAD, see figures 1-3. The territory of the retrogradely perfused proximal LAD was not insignificant as it supplied a number of septals and a large diagonal branch. However the proximal section of LAD was not severely stenosed, see figures 1 and 2. The majority of magnetic procedures at our institution are unselected and this was one such procedure.

Percutaneous Interventional strategy.

The radial approach is standard in our institution with a view to reduction of complications and convenience for patient and operator so the right radial technique was used with a Kimny catheter and weight-adjusted unfractionated heparin. It was decided to predilate the entire lesion, with a wire passed retrogradely into the proximal section of LAD for protection in case of mechanical pinching by plaque shift. This strategy was chosen for 2 reasons. First the lesion was located at the graft anastomosis that included surgically sutured tissue with a possible chance of incomplete balloon expansion. Second, if flow was well maintained after predilatation, the wire in the proximal section of the LAD would be removed to avoid trapping the magnetically tipped wire at an acute angle and risking the problem of magnetic wire lock (6).

Percutaneous Intervention.

3D reconstructions were made, see videos 1 and 2. Using these it proved easy to pass Titan™ 3mm angled Soft Support wires anterogradely into the distal LAD and a second wire retrogradely into the proximal LAD. Predilation produced a good result with no deterioration of the proximal section of the LAD, see figure 3, so the second wire was retracted into the graft. A 3.0 x 12mm Taxus (Boston Scientific) was deployed across the anastomosis, see figure 3. At this point the patient experienced chest discomfort with associated anterolateral ST depression. In addition to the injection of nitrates, the wire in the graft was advanced with the vector adjusted for the proximal section of the LAD in case a dilation to fenestrate the stent was needed. This passed easily, however by this time the symptoms had resolved and the ST changes returned to baseline. Contrast injection showed a good result with TIMI 3 flow throughout the territory, see figure 3. There was a total of 200ml of contrast media used, the fluoroscopy time was 17.4 minutes and the total procedure time was 64 minutes. The patient had had no further symptoms at 6 months follow-up.

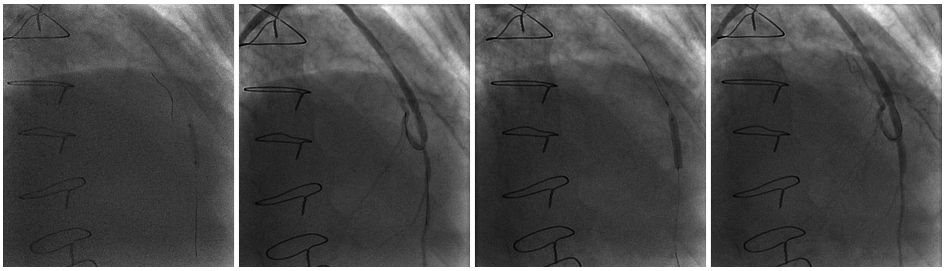

Figure 3. The 2 left panels show the predilatation of anastomosis (wire withdrawn) with and without contrast with the LAD retrogradely recannulated, the right 2 panels show the stent deployment and final angiographic result showing TIMI 3 flow in all territories.

DISCUSSION

This case report demonstrates the 3D reconstruction of difficult coronary anatomy that was used to allow easy vessel cannulation of an extreme angulation that could have proved challenging for a conventional wire. Conventional wire steering in the coronary tree is achieved by rotation of the wire that inexactly points the fixed-angle tip, a process that is affected by factors such as the angle of the viewed 2D image, the manual dexterity of the operator, and the friction or resistance on the wire shaft.

Magnetic navigation acts directly on the distal, deflectable wire tip to give precisely guided 3D wire-tip direction that is independent of wire rotation and resistance on the wire-shaft. This report demonstrates the production of a real-time 3D reconstruction with the patient on the table.

These 3D models of complex lesions give precalculated directions for navigation that may be useful in difficult and angulated anatomy. This technology has been shown to be able to succeed in angulations that could not be successfully cannulated with a conventional wire (7). As the challenge of complex PCI increases (8), magnetic navigation may facilitate such procedures. However, the use of such technology will depend on the ease of use together with the speed and accuracy of the reconstruction.

CONCLUSION

This software allows the production of individualized 3D models during the procedure that can be used for patient treatment. These images give better representations of the anatomy and also supply the computer-calculated vectors that allow magnetic navigation. Potentially this software, and the improvements in image acquisition and image processing, may improve wire passage and cannulation of vessels to result in reductions of complications, procedural time, irradiation and contrast media use.

ACKNOWLEDGEMENT

The authors are grateful to Joep Maeijer for help with preparation of the images.

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CHAPTER 20

Magnetic Navigation System Assisted Stenting of Coronary Bifurcation Lesions

ABSTRACT

Background: Magnetic guidewire navigation assisted percutaneous coronary interventions (MPCI) could have certain advantages in the treatment of coronary bifurcation lesions.

Objective: We aimed to report the angiographic characteristics of the bifurcation lesions, as well as the procedural- and clinical outcome of the MPCI-patients treated in our center during 2005-2009.

Methods: In the study period, a total of 76 patients were assigned to undergo MPCI for bifurcation lesions. The lesion characteristics and the effect of the treatment were assessed by performing pre- and post-procedural diagnostic angiography and quantitative coronary angiography.

Results: Stable coronary artery disease was the most common reason for revascularization (75%). Two-thirds of the patients (age 65 years, 78% male) had a bifurcation lesion located in LAD/D1. Fifty-seven out of 78 lesions (73%) had a diseased side branch and most bifurcation angles were ≥45° (65%). Complex stenting techniques were used in the majority of the lesions (64%) and only 13 dedicated bifurcation stents were implanted. All 59/78 (76%) fenestration attempts were successfully performed. The average acute gain in minimal luminal diameter was 1.08±0.81mm, 0.80±0.70mm and 0.59±0.56mm for the proximal-, distal- and the side branch, respectively. The procedural success rate was 85% with a procedure time of 107±43 minutes, fluoroscopy time of 34±24 minutes and contrast use of 338±136 ml. At a mean of 1.8-years follow-up, 15 patients (20%) had a major adverse cardiac event, of which 8 were post-procedural myocardial infarctions.

Conclusion: MPCI is associated with good procedural-, fenestration and clinical success rates in the treatment of coronary bifurcation lesions.

INTRODUCTION

Nearly 20% of all percutaneous coronary interventions (PCI) performed worldwide are because of coronary artery bifurcation lesions (1). Throughout the years, several single stenting- and double stenting strategies have been explored to overcome the worse procedural- and clinical success rates of the treatment of bifurcation lesions compared to non-bifurcation lesions (2,3). Although some bifurcation treatment strategies such as the "crush" technique were developed to ensure scaffolding of the side branch ostium, it proved to be technically demanding, in certain cases, to enter the side branch for the desired kissing balloon dilatation post-stent implantation (4,5). The complexity of these techniques could result in a longer fluoroscopy time and more contrast use, eventually to the detriment of both patient and operator. Additionally, some coronary bifurcation lesions are difficult to reach due to the associated angulations. Because of these shortcomings, there has been a lot of interest in developing dedicated bifurcation stents and implementing novel systems in daily PCI-practice (6-9).

Magnetic navigation system assisted percutaneous coronary intervention (MPCI) appeared to be not only safe and applicable in chronic total occlusions and tortuous vessels, but also significantly reduced procedural time, contrast use and fluoroscopy time in distal and/or complex coronary lesions compared to conventional PCI (10-12). Even in the treatment of a coronary bifurcation lesion that could not be completed conventionally, MPCI showed to be successful (13).

Until this date there are no studies reporting the treatment of coronary bifurcations lesions with MPCI. The aim of the present study was to describe the angiographic characteristics of the coronary bifurcation lesions, as well as to assess the acute procedural and clinical outcome of MPCI in the treatment of coronary bifurcation lesions.

METHODS

Patient population

From August 2005 until April 2009, a total of 76 patients with coronary bifurcation lesions were treated in our center due to stable angina, unstable angina or acute myocardial infarction with the magnetic navigation system (MNS) (14). Hemodynamic unstability or any contra-indication for the MNS, such as having a pacemaker, resulted in a conventional PCI. Every patient was pre-treated with aspirin and ≥300mg clopidogrel and all procedures were performed according to standard clinical guidelines by MNS trained interventional cardiologists, who had unrestricted access to both magnetic tipped and conventional guidewires. The utilized stenting technique depended on the strategy of the operating interventional cardiologist.

Between March 2007 and October 2007 patients were treated exclusively with Everolimus-eluting stents because of the Xience-Stent Evaluated At Rotterdam Cardiology Hospital (X-

SEARCH). Outside this timeframe, the implantation of type stent, drug-eluting-/non-eluting stent and dedicated-/non-dedicated bifurcation stent, was the choice of the operator.

The post-PCI antiplatelet regimen consisted of ≥80mg aspirin lifelong and ≥75mg clopidogrel for one month if bare-metal stents were used and ≥3 months if drug-eluting stents were used. During this time period, the policy changed into the usage of clopidogrel for at least 12 months if drug-eluting stents were used.

The procedural flow sheets were used to collect angiographic and procedural data including the materials used, contrast media (ml) and procedure time (min.).

Definitions

Clinical data were collected with the use of our electronic database. All patients using antidiabetic medication were categorized as having diabetes. A blood pressure of ≥140/90mHg or the usage of antihypertensive medication was defined as hypertension, regardless of the prevalence of diabetes. Hypercholesterolemia was defined as the usage of lipid lowering drugs or a fasting total cholesterol ≥6.2mmol/l.

Procedural success was defined as the successful deployment of the stent and a residual stenosis <50% by QCA in the presence of Thrombolysis in Myocardial Infarction (TIMI) 3 flow grade without the occurrence of events (death, acute stent thrombosis, myocardial infarction (MI), emergent coronary artery bypass grafting and stroke) during or within 2 days post-intervention. Procedural time (min.) was measured by calculating the elapsed time between the femoral sheath being inserted and the patient leaving the operating room. The contrast media (ml) used during the whole procedure was measured. The fluoroscopy time (min.) during the whole MPCI-procedure was automatically recorded by the digital angiography system (AXIOM Artis dCF, Siemens, Forchheim, Germany).

Major adverse cardiac event (MACE) was defined as a composite of death, myocardial infarction (MI) or a target-vessel revascularization (TVR) during follow-up. MI was diagnosed by recurrent symptoms, the development of ST-segment elevation or left bundle branch block on electrocardiography with a CK-MB rise of three times the upper limit of normal (>22.5ug/l) and positive troponin levels (>0.02ug/l) in the laboratory values. TVR was defined as a repeat PCI procedure in the same index vessel.

Magnetic Navigation System and guidewires

The MNS (Niobe® II MNS, Stereotaxis, St Louis, Missouri) is a fully independent operating system that cooperates with the C-arm single-planar digital angiography system (AXIOM Artis dFC, Siemens, Forchheim, Germany). By using two computer-controlled neodymium-iron-boron magnets located on either side of the fluoroscopy table, a 15-20 cm spherical magnetic field of 0.08 Tesla is created within the patient. The generated magnetic vector can

either be controlled by selecting a certain direction on the touch screen of the Navigant™ Work Station (NWS, Stereotaxis, Inc., St. Louis, Missouri), which in turn redirects the external magnets in all possible positions (rotation, translation, tilt), or by constantly calculating the course of the coronary artery in three real space coordinates using dedicated software and accordingly adjusting the tip (CardiOp-B, Paieon Medical Inc., Rosh Ha'ayin, Isreal).

The following magnetic tipped guidewires, which were available in variable sizes and stiffness, were used in the coronary interventions: (1) Titan™ (Stereotaxis, St. Louis, M. USA) and (2) Cronus™ (Stereotaxis, St Louis, Missouri, USA). Damaged guidewires could be exchanged for a similar or a different magnetic tipped wire.

Coronary bifurcations

The lesion was classified as a bifurcation lesion if the parent vessel (≥2.5mm) had a significant diameter stenosis of >50%, with or without involvement of the origin of the side branch (≥2mm) by visual estimate. The coronary bifurcation lesions included lesions in the left anterior descending coronary artery (LAD) and a diagonal, the left circumflex artery (LCx) and an obtuse marginal (OM), the left main stem and the LAD or LCx and the right coronary artery (RCA) with the posterior descending artery (PDA) or ramus posterolateralis (RPL). The coronary bifurcation lesions were classified according to the Medina numeric classification and American College of Cardiology/American Heart Association ACC/AHA classifications (15,16). The bifurcation lesions were treated with one or two stent techniques such as "provisional", "culotte", "crush", "T-stent" and bifurcation lesion dedicated stents (Stentys™, Tryton™ and Nile® Croco).

Quantitative coronary angiography

All coronary angiograms were analysed online by two independent researchers. Pre-procedural and post-procedural quantitative coronary angiography (QCA) was performed by using CAAS 5.5 (PIE medical software, Maastricht, the Netherlands). These measurements were performed for reference diameter, minimal luminal diameter and percentage diameter stenosis in three different segments of the coronary bifurcation. An independent interventional cardiologist was asked for advice in case of a disagreement.

Statistical analysis

Continuous and categorical data were expressed as mean and percentages (± standard deviation), respectively. The Mann-Whitney U test was used to compare between two different groups consisting of continuous variables. All statistical tests were two-tailed ($p<0.05$ regarded as significant) and performed with SPSS for Windows version 15 (SPSS inc., Chicago, Illinois, USA).

RESULTS

Sample characteristics

The baseline characteristics of the MPCI-patients are shown in Table 1.

Table 1: Baseline characteristics of 76 patients with 78 coronary bifurcation lesions undergoing MPCI.

	MPCI (n=76)	
	Coronary bifurcation lesions (n=78)	
Demographic characteristics		
Age, years (SD)	65.4	(9)
Male, %	77.6	(59/76)
Cardiac history (%)		
Prior MI	36.8	(28/76)
Prior PCI	31.6	(24/76)
Prior CABG	11.8	(9/76)
Risk factors (%)		
Current smoking	7.9	(6/76)
Hypertension	51.3	(39/76)
Hypercholesterolemia	67.1	(51/76)
Diabetes	21.1	(16/76)
Familiy history	51.3	(39/76)
Indication (%)		
Stable angina	75.0	(57/76)
Unstable angina	23.7	(18/76)
Acute MI	1.3	(1/76)
AHA Lesion class (%)		
Type A	0.0	(0/78)
Type B1	37.2	(29/78)
Type B2	50.0	(39/78)
Type C	12.8	(10/78)
Treated vessel (%)		
RCA	6.4	(5/78)
LAD	69.2	(54/78)
LCX	20.5	(16/78)
LM	3.8	(3/78)
Medication (%)		
Aspirin	100	(76/76)
Clopidogrel	100	(76/76)

Data are presented as percentages or means (±SD). AHA=American Heart Association; CABG=Coronary artery bypass graft; MI=Myocardial Infarction; PCI=Percutaneous coronary intervention; MPCI=Magnetic guidewire navigation percutaneous coronary intervention; RCA=Right coronary artery; LAD=Left anterior descending coronary artery; LCx=Left circumflex coronary artery; LM=Left main; SD=Standard deviation.

Seventy-six patients had MPCI for the treatment of total 78 coronary artery bifurcation lesions. The median follow-up period was 1.8 years (interquartile range, 1.2 to 2.5 years).

The MPCI-patients were on an average 65 (±SD 9.5) years old and 78% of the population consisted of men. Fifty-seven patients (75%) were treated due to stable angina, 18 patients (24%) due to unstable angina and 1 patient (1%) was treated due to an acute myocardial infarction.

The majority of the lesions involved the LAD/Diagonal bifurcation (n=54 lesions, 69%), followed by the LCx/OM bifurcation (n=16 lesions, 21%), RCA/PDA or RPL (n=5 lesions, 6%) and left main stem/LAD or LCx (n=3 lesions, 4%).

Procedural and clinical outcome

The procedural characteristics of the coronary bifurcation lesions are showed in Table 2.

Table 2: Procedural characteristics of the 78 coronary bifurcation lesions treated by MPCI.

Pre-intervention		
Proximal main branch RD, mm (SD)	2.6	(0.7)
Distal main branch RD, mm (SD)	2.3	(0.7)
Side branch RD, mm (SD)	1.9	(0.5)
Proximal main branch MLD, mm (SD)	1.8	(0.8)
Distal main branch MLD, mm (SD)	1.6	(0.6)
Side branch MLD, mm (SD)	1.3	(0.5)
Proximal main branch DS, % (SD)	29.9	(21.2)
Distal main branch DS, % (SD)	28.4	(20.3)
Side branch DS, % (SD)	32.3	(21.5)
Post-intervention		
Proximal main branch RD, mm (SD)	3.2	(0.6)
Distal main branch RD, mm (SD)	2.7	(0.6)
Side branch RD, mm (SD)	2.2	(0.5)
Proximal main branch MLD, mm (SD)	2.9	(0.6)
Distal main branch MLD, mm (SD)	2.4	(0.5)
Side branch MLD, mm (SD)	1.9	(0.5)
Proximal main branch DS, % (SD)	8.9	(10.6)
Distal main branch DS, % (SD)	11.6	(11.9)
Side branch DS, % (SD)	17.5	(17.2)
Acute luminal gain		
Proximal main branch, mm (SD)	1.1	(0.8)
Distal main branch, mm (SD)	0.8	(0.7)
Side branch, mm (SD)	0.6	(0.6)

Stenting technique		
Provisional, % (SD)	36.4	(0.5)
Crush, % (SD)	33.8	(0.5)
Culotte, % (SD)	22.1	(0.4)
T-stenting, % (SD)	7.8	(0.3)
Stent characteristics		
Number of implanted stents (SD)	1.7	(0.5)
Average stent diameter, mm (SD)	3.0	(0.9)
Total stented length, mm (SD)	31.8	(13.4)
Dedicated stents used, % (SD)	16.7	(0.4)
Tryton™, % (SD)	11.5	(0.3)
Stentys™, % (SD)	3.9	(0.2)
Nile Croco™, % (SD)	1.3	(0.1)
Main vessel stented, % (SD)	89.7	(0.3)
Side branch stented, % (SD)	76.9	(0.4)
Other vessel stented, % (SD)	25.6	(0.4)
Fenestration, % (SD)	75.6	(0.4)
Final kissing balloon, % (SD)	68.0	(0.5)
Bifurcation angle <45°, % (SD)	32.0	(0.5)
Bifurcation angle 45°-90°, % (SD)	53.3	(0.5)
Bifurcation angle 90°-135°, % (SD)	13.3	(0.3)
Bifurcation angle 135°-180°, % (SD)	1.3	(0.1)
Procedure time, min (SD)	108.8	(44.1)
Fluoroscopy time, min (SD)	34.3	(24.1)
Contrast use, ml (SD)	340.8	(135.7)

MPCI=Magnetic guidewire navigation percutaneous coronary intervention; RD=Reference diameter; MLD=Minimal luminal diameter; DS= Diameter stenosis; SD=Standard deviation; DES=Drug-eluting stents

An average of 1.7±0.5 stents were implanted per patient with a total stented length of 31.8±13.4 mm. A Medina class of (1,1,1) was present in 30 bifurcation lesions (38.5%), (1,0,1) in 15 lesions (19.2%), (1,0,0) in 9 lesions (11.5%), (1,1,0) in 10 lesions (13.0%), (0,0,1) in 6 lesions (7.7%), (0,1,0) in 2 lesions (2.6%) and (0,1,1) in 6 lesions (7.7%) (Figure 1). This resulted in 64 (82%) diseased proximal main vessels, 48 (62%) diseased distal main vessels and 57 (73%) diseased side branches. The XIENCE™ V Everolimus-eluting stent (Abbott Vascular, Santa Clara, California) was the most implanted stent (42%), followed by the Paclitaxel-eluting stent (35%) (TAXUS™, Express2™ or Liberté™, Boston Scientific, Natick, MA, USA). Dedicated stents were used in 13 lesions (16.7%), of which 9 Tryton™ side-branch stents (Tryton Medical, Inc., Newton, MA, USA), 3 Stentys™ stents (Stentys SAS, France) and 1 Minvasys Nile™ Croco stent (Minvasys, Genevilliers, France)). Pre-dilatation and post-dilatation was performed in 45/78 (58%) and 59/78 (76%) lesions, respectively. All 59 fenestration attempts were successfully performed. TIMI 3 flow was obtained in all patients except one, in which the magnetic wire could not successfully cross the lesion. The guidewire was entangled in an aneurysm in the LAD, which was located proximal to the bifurcation lesion. This patient was referred for an urgent coronary artery bypass because of a dissection.

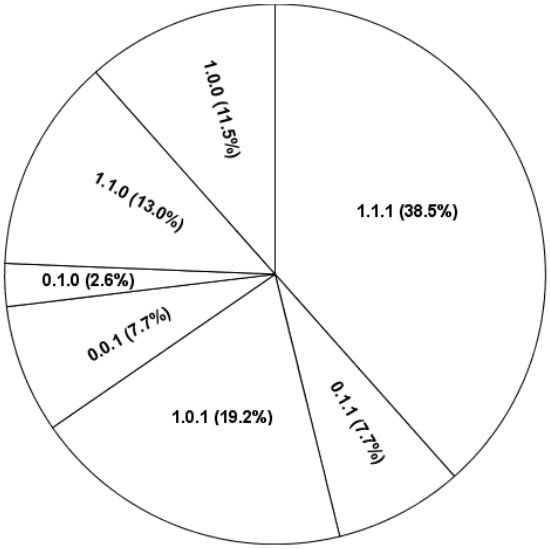

Figure 1: The Medina class of the coronary bifurcation lesions.

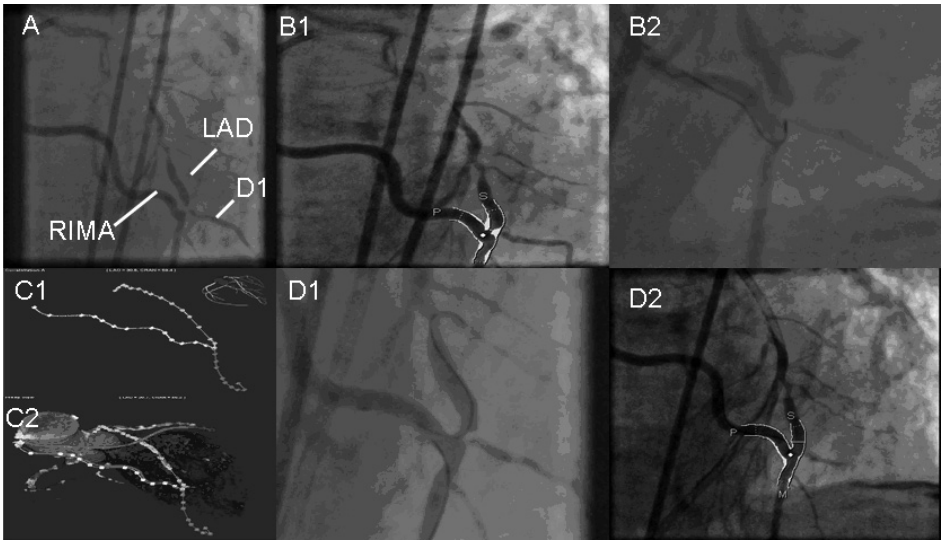

Figure 2: Case example. (A) The LAD showed a significant lesion just proximal to the anastomosis of the LIMA graft (bifurcation lesion (0,0,1) with the ramus diagonalis). (B1) The QCA pre-stent implantation revealed a diameter stenosis of 64% in the side branch (minimal luminal diameter 0.89mm; reference diameter 2.48mm). (B2) Magnetic vectors are used to steer guidewire. (C1) Multislice CT can be utilized to create a vessel road map. (C2) Three-dimensional reconstruction. (D1) Guidewire through ostial lesion (provisional stenting technique). (D2) The QCA post-stent implantation (Xience V 3x8mm), showed a 9% diameter stenosis in the side branch (minimal luminal diameter 2.09mm; reference diameter 2.30mm). *See this figue in color in the Appendix page 399.*

The QCA-analysis showed that the acute luminal gain in the proximal main branch, distal main branch and side branch were 1.1±0.8mm, 0.8±0.7mm and 0.6±0.6mm, respectively. The median contrast use was 341±136 ml and the procedural- and fluoroscopy times were 109±44 minutes and 34±24 minutes, respectively.

At a median of 1.8-years of follow-up, 15 patients (20%) had a MACE, of which 8 post-procedural myocardial infarctions within the first 48 hours (Figure 3). These patients had a mean CK-MB value of 33±11 ugram/liter and a troponin level of 0.92±0.59 ugram/liter. There were 4 target-vessel revascularizations and 3 deaths, of which 1 cardiac death, during the follow-up period. None of the 76 patients had a stent thrombosis. The procedural time, fluoroscopy time and contrast use of the MPCI-procedures in which fenestration was performed, did not significantly differ from MPCI-procedures without fenestration (113±43 min. versus 95±46 min., p=0.25; 34±25 min. versus 34±24 min, p=0.95; 341±141 ml versus 341±121 ml, p=0.89, respectively).

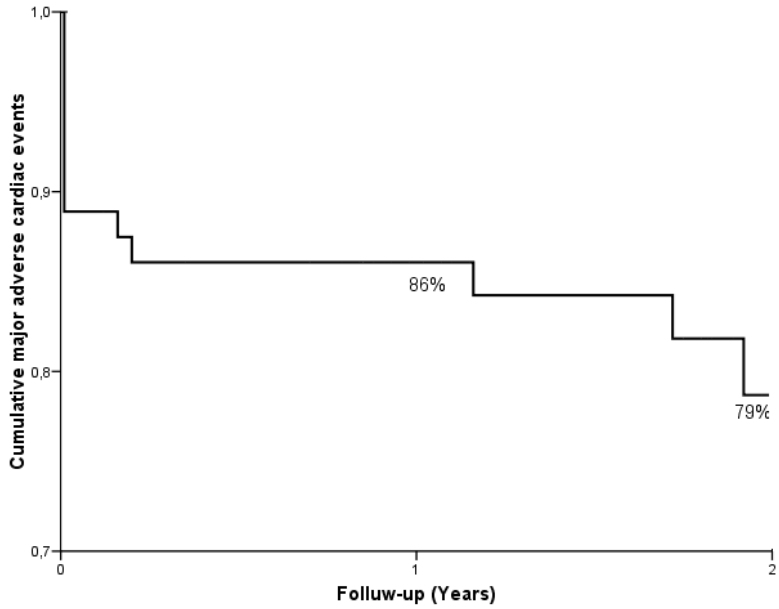

Figure 3: Cumulative major adverse cardiac events curve of the 76 patients treated with MPCI.

DISCUSSION

This study describes the angiographic characteristics of coronary bifurcation lesions and the associated procedural- and clinical outcome after MPCI. The main finding of this study is that MPCI was shown to be feasible in the treatment of coronary bifurcation lesions with good clinical- and procedural success rates. All fenestration attempts were successfully performed

and only one patient could not be treated due to wire entanglement in a coronary aneurysm. Fenestration was not associated with a longer procedural time, fluoroscopy time or more contrast use than procedures without fenestration.

The optimal treatment of bifurcation lesions remains a delicate issue in the interventional cardiology. Stenting of bifurcation lesions are still associated with increased risk of stent thrombosis (acute, subacute and late) and higher MACE rates compared to non-bifurcation lesions (17,18). Although the implantation of drug-eluting stents in bifurcation lesions have been shown to be more effective in reducing restenosis, bifurcation stenting still has moderate results (19-21). We previously described that the implantation of drug-eluting stents in 241 de novo bifurcation lesions with the crush-technique (n=231 patients) resulted in a MACE-free survival of 83.5% at 9-months follow-up (3). In a more recent study, the crush-technique could not show superiority to provisional stenting in terms of MACE at 6-months (15.8% vs. 15%; p=NS) (22). It is noteworthy that these event rates are already comparable to our study, however both studies have a follow-up period of less than one year. The main factor that ensures a good short- and long term outcome is the performance of a final kissing balloon dilatation regardless of the utilized stenting technique (3,5,23,24). The procedural duration, fluoroscopy time and contrast consumption of primary PCI patients, patients with a single discrete stenosis and patients with distal and/or complex lesions treated with MPCI were all considerably lower than the findings of our study. An explanation for the less procedure time, fluoroscopy time and the amount of contrast used compared to our study could be due to the fact that 25% of our patient population had another coronary vessel treated in the same procedure. Moreover, some patients had multiple bifurcation lesions treated during the same catheterization.

We believe that the relatively low MACE rate found in our study could be mainly attributed to primarily using drug-eluting stents, the good post-procedural QCA results and the high degree of kissing balloon dilatation post-stent implantation.

The MNS is already successfully being used in cardiac electrophysiological procedures and has shown to be feasible in a variety of coronary lesions (6,25-29). The ability of precisely steering a guidewire through the coronary arteries and (crushed) stents is an innovative approach in the treatment of coronary lesions. The actively three dimensional controllable magnetic tipped guidewire can especially be useful in difficult vessel angles or in entering the side branch. We already described the value of the MNS in gaining entry to the side branch through a crushed stent after unsuccessful conventional PCI (13). The conventional PCI could not be completed because it was impossible to cross the stent struts of the crushed stent in spite of several different wires and techniques. The patient was treated the next morning with MPCI. After three-dimensional vessel reconstruction, the magnetic tipped guidewire could easily cross the crushed stent. Even in secondary revascularization procedures of

bypass grafts which could not be completed with conventional wires due to the associated difficult angles, it has proven its value (29). When used for the treatment of distal complex lesions, MPCI have been shown to reduce procedural time, fluoroscopy time and amount of contrast use compared to conventional PCI (29.9±17.6 versus 41.1±21 min, p=0.007; 7.5±7.3 versus 16.1±22.4 min, p=0.02; 122±82 versus 180±147 ml, p=0.02, respectively (27).

There remain several shortcomings of the MNS, which limits the widespread use. First of all, the time it takes to get familiar with the MNS combined with the preparation time of the system makes it doubtful whether such a system is profitable for the treatment of bifurcation lesions. Secondly, (crucial) time can be lost in redirecting the external magnet in the desired positions, in comparison with the fast eye-hand coordination during conventional PCI. Third, novel conventional wires have a more even transition of the tip with the shaft in contrast to magnetic tipped wires, which therefore are limited in the flexibility. Finally, the high initial costs for the hardware and software of the MNS make it difficult to determine whether such systems are profitable to use for just only specific subsets of coronary lesions.

In conclusion, the MNS showed itself to be feasible in coronary bifurcation lesions. The main benefit of this novel system is the easier crossing of stent struts, resulting in a high likelihood of crossing success. Due to the fact that wire crossing through the stent struts was successful in the first attempt, the fenestration process did not prolong procedure time, fluoroscopy time or contrast use. However, it remains debatable whether the pros of the MNS outweigh the cons in the treatment of bifurcation lesions. Nevertheless, a randomized controlled trial is necessary to reach conclusive results on this subject.

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CHAPTER 21

Primary percutaneous coronary intervention using magnetic navigation

INTRODUCTION

The rapid restoration of full TIMI 3 flow is crucial in primary percutaneous coronary intervention (PCI) (1). However, angiographic success is not always obtained (2-6). Magnetic navigation might facilitate primary PCI by allowing more accurate manipulation. However, there has been concern that the use of this procedure could delay reperfusion.

The magnetic navigation system (MNS: Stereotaxis, St Louis, Missouri, USA) can be used immediately by using the preset vector control or freestyle navigation with the 2D clockface view, see figure 1. The system allows for precise navigation without the need for excessive wire rotation. In case of more complex anatomy, a 3D reconstruction can be used (Software: CardiOp-B: Paieon Medical Inc., Rosh Ha'ayin, Israel) for individualised navigation (7).

This report describes the feasibility of the MNS to quickly and successfully complete a complex primary PCI that involved aspiration thrombectomy and a bifurcation procedure.

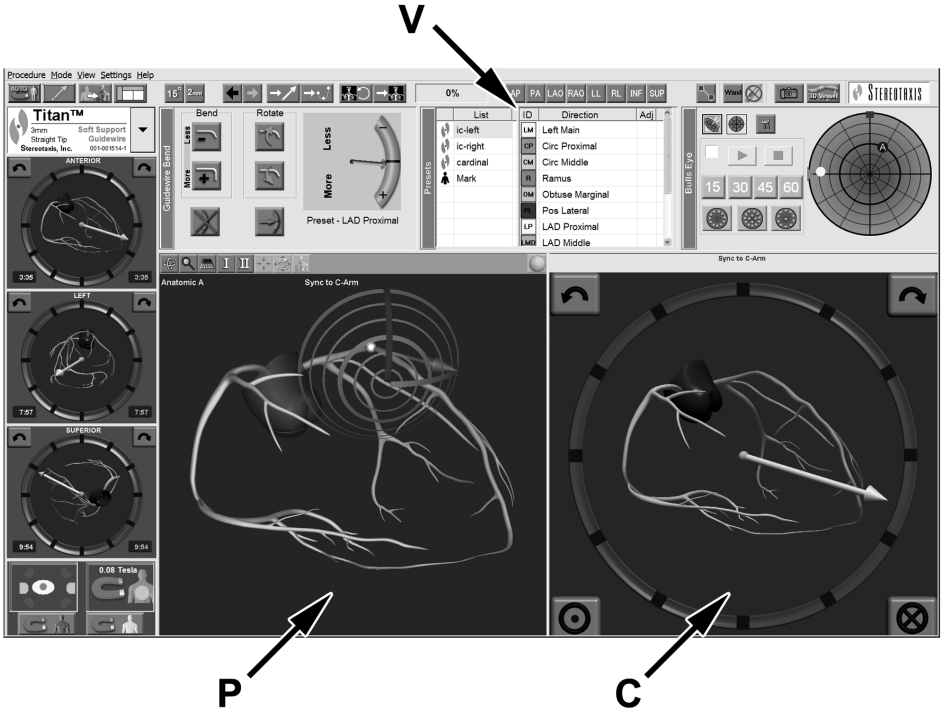

Figure 1. The screen of the Navigant workstation, the panel (P) shows virtual coronary tree of the preset navigation with the list of preset vectors (V) seen above. The panel (C) shows the 2D clock face. *See this figue in color in the Appendix page 395.*

Case report

A 48 year old man presented to the emergency department with an evolving STEMI requiring immediate reperfusion. Angiography showed a proximal occlusion of the left circumflex (LCx) with an obvious filling defect and TIMI 0 distal flow, see figure 2.A Titan™ 3mm angled Soft Support wire was chosen. While the wire and an aspiration catheter were brought and prepared, the patient was put in the magnetic isocenter position by visualising the catheter tip and cardiac silhouette on X-ray in two orthogonal views. Navigation was performed using preset vectors through the left main stem (LMS) and proximal LCx to reach the lesion. The lesion was eccentric and more irregular on the superior aspect, see figure 2. An inferior vector was selected on the 2D clock freestyle navigation to cross this section in order to reduce contact and possible dislodgement of material. The crossing time from the tip of the catheter was 28 seconds and 2 ml of contrast was given. Contrast injection confirmed TIMI 1 flow and an aspiration catheter removed a large portion of the thrombus to produce TIMI 3 flow in two branches, but with obvious residual stenoses, see figure 2.

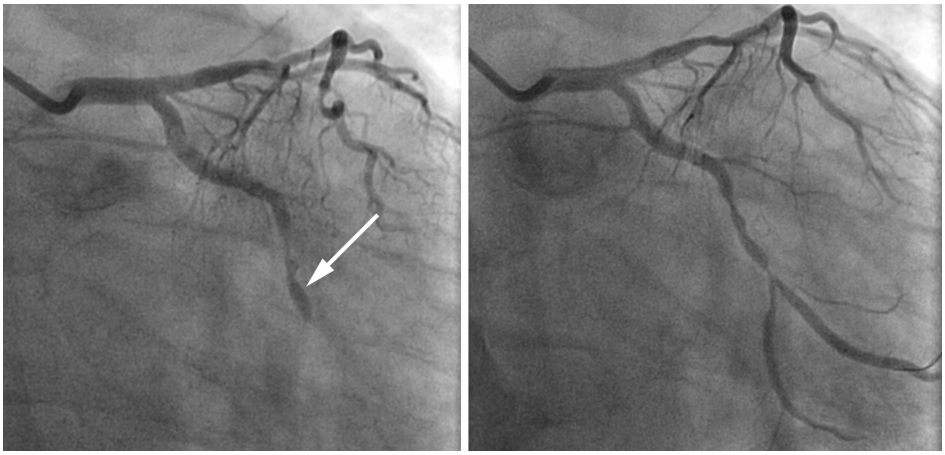

Figure 2. The left panel shows the occluded OM branch with an eccentric lesion, more irregular on the superior aspect, before the occlusion, the right panel shows the restoration of flow to two distal branches after aspiration thrombectomy.

A 3.0 x 25mm Skylor™ produced a good result in the main branch, but there was pinching of the ostium of the side branch, see figure 3.

It was decided to fenestrate the stent into the side branch. The passage of a second Titan™ 3mm angled Soft Support wire into the side branch took eight seconds with no contrast used. Kissing balloons produced a good result with TIMI 3 flow in both vessels, see figure 4.

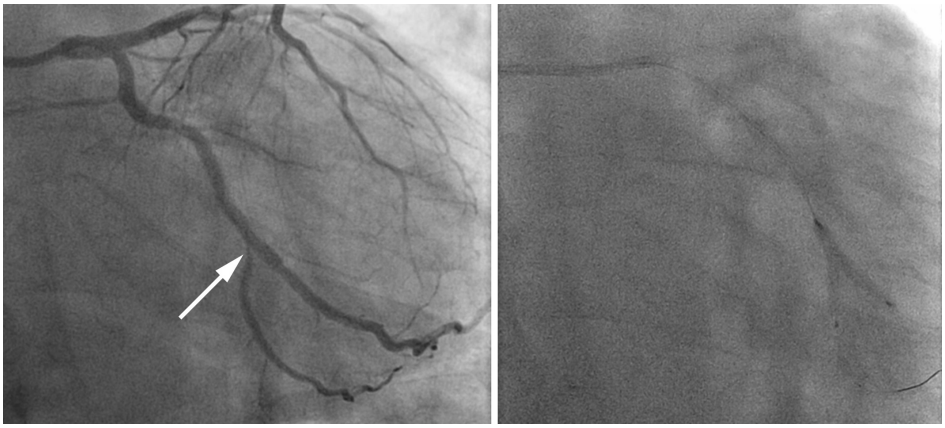

Figure 3. The left panel shows the result of the stent with pinching of the ostium (arrowed) to the inferior branch, the right panel shows the deployment of kissing balloons.

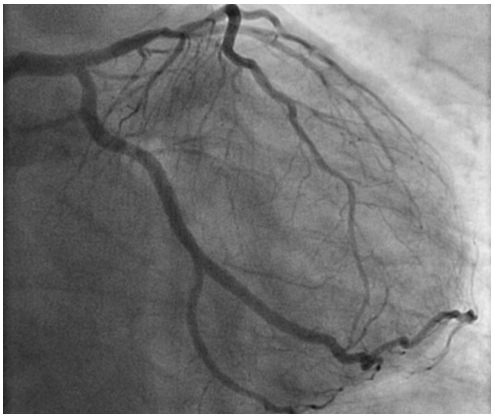

Figure 4. The final result showing TIMI 3 flow in both distal branches.

Further diagnostic angiography showed a moderate lesion in the LAD and a normal, dominant RCA. The total time for the procedure was 23 minutes. The subsequent clinical course was uneventful and the patient was discharged three days after admission.

DISCUSSION

There is strong evidence that swift restoration of flow in the obstructed infarct artery after the onset of symptoms of a STEMI is key determinant of short – and long term outcome (3-7) - therefore, current guidelines advocate rapid evaluation for reperfusion therapy and the prompt implementation of a reperfusion therapy at presentation (1). PCI is a very effective method for re-establishing coronary perfusion and is suitable for approximately 90% of

patients (2-6). In cases with more complex anatomy the magnetic navigation system may provide extra benefits such as 3D reconstruction (7).

The magnetic navigation system uses two permanent magnets, mounted on mechanical positioners, on either side of the fluoroscopy table (7). These magnets create an interacting magnetic field to produce an approximately spherical 15 cm uniform magnetic field of 0.08 T. The movement of the magnets allows the direction of the applied magnetic field vector to be orientated in 360° on all planes. The result is control of direction of the wire tip, in vivo, without the need for a pre-shaped wire tip angle.

The current case demonstrates that the procedure can be performed rapidly during primary PCI with the use of 2D controls such as the use of preset vectors or the 2D clock face. However, should more complex anatomy be uncovered, then an interactive 3D coronary model can be created from two views allowing accurate individualised navigation, see figure 5.

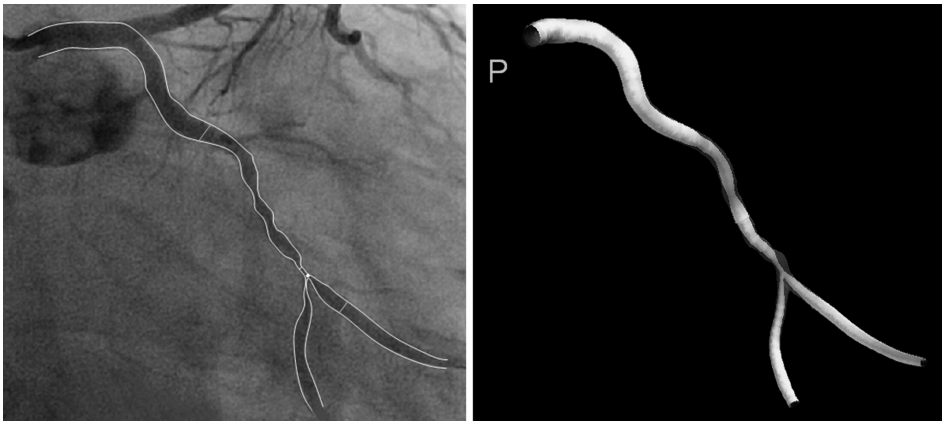

Figure 5. The left panel shows the edges detected on the fluoroscopy image (two views required), the right panel shows the 3-dimensional reconstruction of the infarct related coronary artery. *See this figue in color in the Appendix page 399.*

Theoretically, the MNS may have two particular benefits in primary PCI. First, precise control of the magnetic tip needs less movement when compared with conventional wires that must be rotated to steer. This improves not only the navigation to, but also past an eccentric thrombus-laden lesion. Possibly this may help to reduce thrombus dislodgement and subsequent distal embolisation (8). Second, the lack of rotation of a second wire reduces the risk of wire entwinement that could both impair both steering as well as smooth balloon delivery.

CONCLUSION

Primary PCI is not only feasible with the MNS but may give procedural advantages. Furthermore, the option of 3D reconstruction is available when complex anatomy is uncovered. This case demonstrates the feasibility of the MNS to rapidly perform primary PCI and support complex procedures that sometimes occur in this emergent situation.

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CHAPTER 22

Primary percutaneous coronary intervention by magnetic navigation compared with conventional wire technique

ABSTRACT

Aims: Comparison of magnetic guidewire navigation in percutaneous coronary intervention (MPCI) vs. conventional percutaneous coronary intervention (CPCI) for the treatment of acute myocardial infarction.

Methods and results: We compared 65 sequential patients (mean age 61+15 years) undergoing primary MPCI with those of 405 patients undergoing CPCI (mean age 61+13 years). The major endpoint was contrast media use. Technical success and procedural outcomes were evaluated. Clinical demographics and angiographic characteristics of the two groups were similar, except for fewer patients with previous coronary artery bypass grafting (CABG) and hypertension in the CPCI group and fewer patients with diabetes in the MPCI group. The technical success rate was high in both the MPCI and CPCI groups (95.4 vs. 98%). There was significantly less contrast media usage in the MPCI compared with the CPCI group, median reduction of contrast media of 30 ml with an OR = 0.41 (0.21–0.81). Fluoroscopy times were significantly reduced for MPCI compared with CPCI, median reduction of 7.2 min with an OR = 0.42 (0.20–0.79).

Conclusion: This comparison indicates the feasibility and non-inferiority of magnetic navigation in performing primary PCI and suggests the possibility of reductions in contrast media use and fluoroscopy time compared with CPCI.

INTRODUCTION

Magnetic navigation uses two computer-controlled magnets to produce an adjustable magnetic field to precisely and actively deflect a tip-mounted magnet on an angioplasty wire. This gives the fundamentally new ability of active control of the angle of approach of the 'front-end' of the wire. The precise steering of a wire has a number of potential advantages in percutaneous coronary intervention (PCI). It could enhance wire passage by maintaining a coaxial vessel orientation, by steering away from eccentric lesions or thrombus, by enabling more accurate sidebranch cannulation, or by reducing problems inherent with conventional wires such as wire entanglement in two wire procedures. Percutaneous coronary intervention using magnetic navigation is feasible in a variety of lesion types (1-8) and shows an advantage in distal lesions (7). However, although use in primary PCI has been described, (8) the potential benefit remains unknown. It is conceivable that magnetic navigation may give an advantage in both the straightforward cases (6) and particularly in complex cases (7). Timely reperfusion of patients undergoing primary PCI is a priority (9-13). However, magnetic guidewire navigation PCI (MPCI) requires both preparation and familiarity for efficient use and therefore it remains unclear as to whether the burden of the additional preparation and performance of this wire technique is detrimental.

We examined the feasibility of MPCI vs. conventional guidewire navigation PCI (CPCI) by comparing patients having MPCI for acute myocardial infarction with historical control patients who had undergone CPCI as part of a previous trial in primary PCI, the PASSION trial (14,15).

METHODS

Selection of patients and age-matched controls

Between November 2006 and July 2007, 240 consecutive patients underwent primary PCI in our centre. From this patient group, 65 sequential patients presenting to MPCI operators underwent primary MPCI. The patients who underwent MPCI were all within the age of 18–80 and had not had thrombolysis. There were no patients with a contraindication to aspirin or clopidogrel, cardiogenic shock requiring support, known intracranial disease or life expectancy less than 6 months. Patients who were intubated and ventilated did not have their procedure in the magnetic navigation room due to restricted space. There were no specific contraindications to MPCI in this series, but care was taken to check that there were no previously implanted ferrous devices. None of the patients in the MPCI group had pacemakers or implantable cardiac defibrillators. Other non-primary PCI patients with implanted electronic devices have undergone MPCI procedures and should be monitored during the procedure

and the devices checked afterwards. The baseline characteristics, angiographic characteristics, and procedural outcomes of these patients were compared with a historical control group, which consisted of the cohort of patients that had been treated by primary CPCI for acute myocardial infarction as part of the PASSION trial (14,15). Exclusion criteria for the PASSION group have been previously described (14). Patients were excluded if they had received thrombolytic therapy, the infarction was caused by in-stent thrombosis or restenosis, there was a contraindication to aspirin, clopidogrel, or both, patients were participating in another clinical trial, cardiogenic shock was evident before randomization, the neurological outcome after resuscitation was uncertain, they had undergone intubation, ventilation, or both, there was known intracranial disease, or the estimated life expectancy was less than 6 months.

In summary, differences between the two groups were that MPCI procedures were only performed if one of the two trained operators were present or had on-call duty and the magnetic room was available. In addition, patients in the PASSION trial were only randomized after successful wire passage (and therefore with enough flow to assess vessel size) and that complex anatomy such as in-stent restenosis or stent thrombosis were contraindicated, while the magnetic procedure registry includes all patients who had their procedure in the MPCI room and complex anatomy was not excluded.

All patients gave informed consent to the proposed procedure. Thrombectomy was performed at the discretion of the operator. Angiography of the other coronary vessels was performed routinely in all cases in both groups.

The magnetic navigation system

The Niobe® II magnetic navigation system (MNS; Stereotaxis, St Louis, MO, USA) has been described in detail previously (1-3). The system comprises two external magnets with the controls and software for applying and changing the magnetic field (Figure 1). A 15–20 cm spherical volume with a uniform magnetic field is produced that is centred on the heart of the patient and can be reliably and reproducibly directed in 360° in all planes. A number of methods are available to alter the direction of the magnetic field. The 2D clockface is displayed in the plane of the fluoroscopy screen and so 360° can be selected in this plane, and two icons at the bottom corners of this window direct the field into (denoted by a circled 'X'), and out of (denoted by a circled '.'), the plane of fluoroscopy giving the operator 3D control (Figure 2). Selection by presets uses the average directions of vessel segments taken from 50 MSCT scans and thus automatically incorporates 3D directions. The use of a 3D reconstruction from patient images is essentially an individualized set of presets. The selection of a direction by the operator leads to movement of the two external magnets to change the magnetic field vector in three dimensions that will actively deflect the magnetic wire tip and result in reproducible steering. The operator interfaces with the system via the Navigant™ Work Station software. Navigation in MPCI cases was performed using preset and clockface

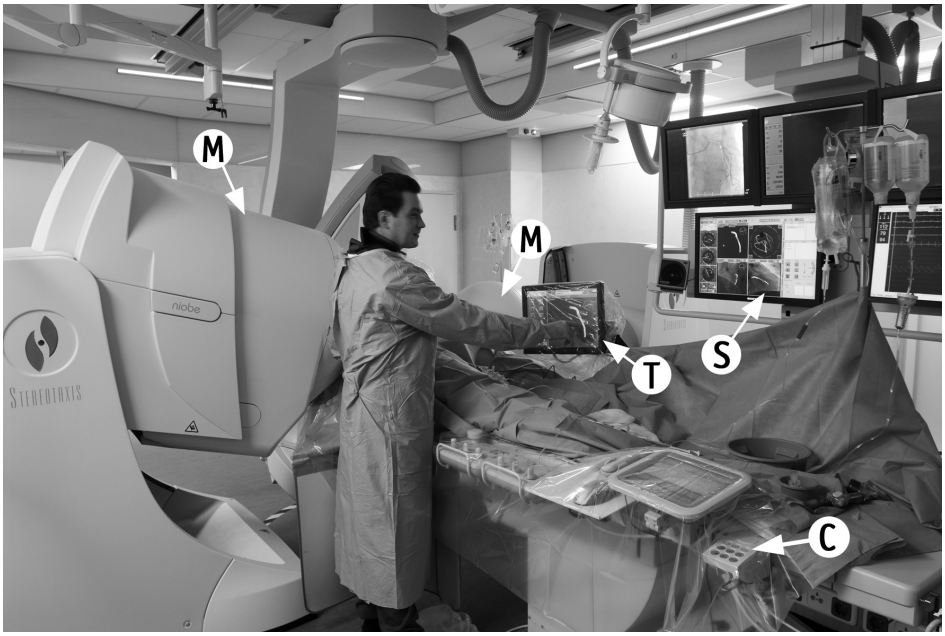

Figure 1 The Niobe® Magnetic Navigation System in position for PCI. M indicates magnets in tilt position for better lateral movement of the image intensifier. T indicates touch screen interface to give real-time instruction to the MNS. S indicates in-lab main screen monitor, C indicates the controls for magnet deployment. *See this figue in color in the Appendix page 394.*

navigation for two reasons. First, it was felt to be suitable in terms of practicality and feasibility in order to reach and cross most/all lesions as it can be used as soon as the magnets are in position rather than waiting for the production of a reconstruction that can be time consuming. Secondly, the 3D reconstruction can only be made properly with a patent vessel so this excluded a significant proportion of cases.

The use of the system requires the patient to be placed at the fluoroscopic and magnetic isocentre. This is performed directly on engagement of the coronary artery by fluoroscopy in a lateral position for the correct vertical table height and then a further angulation such as LAO 45° to obtain a suitable horizontal position. Angiographic films can then be taken to identify the site and anatomy of the occlusion. The magnets are then brought in. These manoeuvres were routinely performed as the wire, thrombectomy device, indeflator, and other equipment were being unpacked and prepared. The procedural time for MPCI includes all the time needed for system preparation such as isocentering and adjusting patient position (see Discussion). The angioplasty wires for magnetic procedures were the standard magnetically enabled wires supplied by the company.

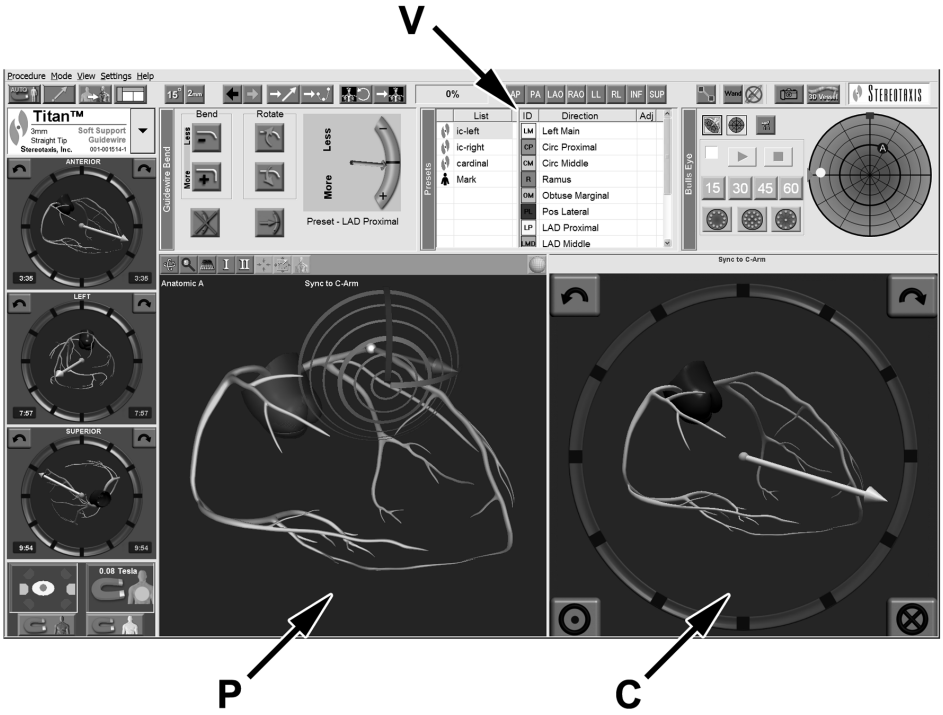

Figure 2 The screen of the Navigant™ workstation (2.11 version), the panel (P) shows virtual coronary tree of the preset navigation with the list of preset vectors (V) seen above. The panel (C) shows the 2D clockface with two icons in the bottom corner that allow direction of the vector into (denoted by circled 'X'), or out of (denoted by circled '.'), the plane of fluoroscopy. *See this figue in color in the Appendix page 395.*

Magnetically enabled wires

A series of magnetically enabled disposable guide wires, which are custom designed for use with the MNS, are available in a variety of sizes and a range of stiffness. For this comparison, the Titan™ guidewires were used (Figure 3). They are specifically designed to be more flexible and steerable for magnetic navigation. They are 180 cm moderate support, hydrophilic coated wires with a diameter of 0.014 in/0.36 mm having a flexible 2 cm distal coiled tip at the end of which is a gold cup attached to a 2 or 3 mm neodymium-iron-boron magnet.

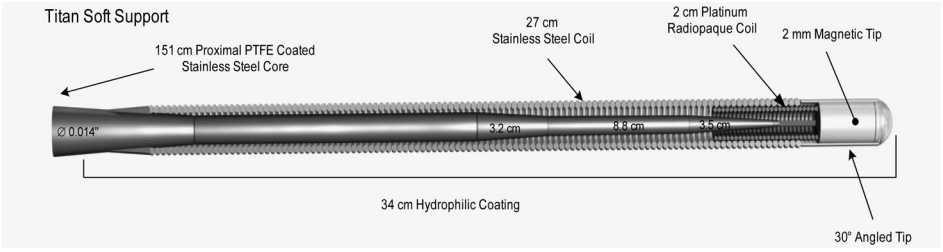

Figure 3 The structure of Titan™ Soft Support magnet wire tip. *See this figue in color in the Appendix page 400.*

Percutaneous coronary intervention procedure

The inner diameter of all 6 F guides was 0.70 in. The choice of guiding catheter and equipment was left entirely to the discretion of the operator and followed routine practice as did the use of drug-eluting stents, bare metal stents, and the use of glycoprotein IIb/IIIa receptor antagonists. There were no restrictions on the operators' choice of conventional wire or routine practice. Routine procedure in our institution is to take at least two orthogonal planes after the intracoronary administration of 100–200 mg of nitroglycerine and to repeat these at the end of the procedure. There were no additional views in the PASSION trial patients that were only for study purposes. Thrombectomy was performed at the discretion of the operator. Angiography of the other coronary vessels was performed routinely in all cases in both groups.

The interventional staff includes five senior operators; CPCI procedures were performed by all five operators, whereas MPCI procedures were performed by two of the five operators. Aspirin, 500 mg i.v. and clopidogrel, 600 mg p.o. were given to all patients. Unfractionated heparin, 10 000 IU/kg, was given as an intravenous bolus at the beginning of the procedure. Routine access was via the radial approach.

Angiographic variables

All angiograms were stored in a computer database and analysed off-line by an independent observer, using CAAS 2003 Camtronics (Philips Medical Systems, Eindhoven, The Netherlands).

Definition of endpoints

The major endpoint was the amount of contrast media used to complete the procedure. Secondary endpoints were fluoroscopy time, total procedural time, number of wires, number of balloons and stents, and major adverse cardiac events. The aim was to evaluate procedural outcome in both groups in terms of contrast media use, technical success, procedural and fluoroscopy duration, and material consumption. Technical success was defined as an intraluminal wire position distal to the stenoses. Procedural success was defined as (i) TIMI Grade III flow (16), (ii) 30% residual stenosis, and (iii) absence of clinical events during the admission (death, acute stent thrombosis, re-infarction before discharge, emergency coronary artery bypass grafting, and stroke). Procedural duration was measured from the time of sheath insertion until the removal of the guiding catheter at the end of the procedure (and included all the time needed for system preparation such as isocentring and adjusting patient position, see Discussion). Fluoroscopy times were automatically recorded by the Poly Diagnost (C2) Digital Cardiac Imaging System (Philips). Additional endpoints were the length and diameter of stents per patient. Distal embolization was specifically noted in the MPCI patients.

Statistical analysis

For comparison of continuous variables between the two groups, the unpaired two-tailed Student's t-test was used or, for skewed data, such as contrast media, the Wilcoxon's rank sum test, and these were expressed as the median and inter-quartile range. Comparison of categorical variables between the two groups was performed using the Chi-squared test, or in cases of a minimum expected count less than 5, the Fisher exact test, and these were expressed as the number and/or percentage.

A two-sided P-value less than 0.05 was considered statistically significant. Statistical tests were carried out with the SPSS 14.0 statistical software package (Chicago, IL, USA). All continuous endpoints were dichotomized according to the worst tertile vs. the other two tertiles. As the number of MPCI patients was restricted, a propensity score was used and included in a logistic model to adjust MPCI vs. CPCI for contrast media consumption, fluoroscopy, etc.

RESULTS

Baseline demographics

Primary MPCI in 65 consecutive patients was compared with primary CPCI of 405 historical control patients. Baseline clinical characteristics were similar in both groups, although there were fewer patients with previous coronary artery bypass grafting (CABG) and hypertension in the CPCI group compared with the MPCI group.

Table 1. Clinical characteristics.

Characteristics	Magnetic PCI (N=65)	Conventional PCI (N=405)	P Value
Age-yr	61±15	61±13	0.97
Male sex	75.4	75.3	1.00
Diabetes mellitus	4.6	13.3	0.22
Hypertension	40.2	32.3	0.05
Hypercholesterolemia	15.4	25.7	0.07
Family history of CAD	46.2	35.8	0.11
History of smoking cigarettes	44.6	51.4	0.31
Previous PCI	7.7	3.7	0.14
Previous CABG	4.6	0.9	0.03
Previous myocardial infarction	4.6	7.4	0.41

Presented as percentages (within parentheses) or in other cases means ±SD. N= number.

There were fewer patents with diabetes in the MPCI group. Baseline angiographic variables showed that the reference vessel diameter in the MPCI group was marginally, but statistically,

smaller than the CPCI group and that there was a statistically significant predominance of ACC/AHA type C lesions in the MPCI group.

Table 2. Angiographic characteristics.

Variable	Magnetic PCI (N=65)	Conventional PCI (N=405)	P value
Vessel disease %			0.23
1VD	47.7	55.1	
2VD	38.5	28.0	
3VD	13.8	16.9	
Target lesion mm (SD)			
Reference diameter	2.88±0.51	3.13±0.48	<0.001
MLD	0.12±0.35	0.18±0.39	0.21
DS	95.6±13.19	92.5±16.4	0.16
TIMI flow %			
0	70.8	64.4	
1	4.6	8.1	
2	15.4	14.1	
3	7.7	13.3	
ACC/AHA lesion class			<0.001
A	0.0	2.8	
B1	3.1	23.0	
B2	7.7	10.6	
C	89.2	67.2	

Presented are the percentages of patients or in other cases means ±SD. N= number.

Lesions had a similar distribution in the three coronary arteries

Table 3. Target vessel location.

Target vessel	Magnetic PCI N (%)	Conventional PCI (N=405)
RCA	20 (30.7)	169 (41.7)
RCA1	3 (4.6)	73 (18)
RCA2	13 (20)	56 (13.8)
RCA3	3 (4.6)	35 (8.6)
RCA4	0 (0)	2 (0.5)
RCA16	1 (1.5)	3 (0.7)
LCA	32 (49.2)	209 (51.6)
LMS	0 (0)	9 (2.2)
LAD		
LAD6	26 (40)	116 (28.6)
LAD7	5 (7.7)	75 (18.5)
LAD8	0 (0)	6 (1.5)
LAD9	1 (1.5)	3 (0.7)
LAD10	0 (0)	0 (0)

Cx	11 (16.9)	23 (5.6)
Cx11	6 (9.2)	11 (2.7)
OM12b	5 (7.7)	13 (3.2)
Cx13	0 (0)	3 (0.7)
Cx14	0 (0)	6 (1.5)
Cx15	0 (0)	0 (0)
SVG	2 (3.1)	3 (0.7)

Presented are the absolute numbers of lesions with percentages (within parentheses).

Overall technical and procedural success was high (95.4% MPCI vs. 98.0% CPCI) in both groups.

Table 4. Procedural outcome.

Variable	Magnetic PCI (N=65)	Conventional PCI (N=405)	P value
Procedural success %	95.4	98.0	0.19
No. of wires per patient	1,48±0.85	1,3±0.60	0.04
No. of balloons used per patient	0.71±1.04	0.51±0.73	0.059
No. of stents implanted per patient	1.42±0.90	1.32±0.63	0.30
Procedural duration-min	29 (19-36)	31 (23-41)	0.20
Fluoroscopy time-min	7.4 (3.58)	9 (6-31)	<0.05
Contrast consumption (Mean)-ml	170 (100-200)	200 (150-250)	0.001
Sidebranch involvement			
Sidebranch present	40.0	11.6	<0.0001
Sidebranch protected	12.3	4.2	0.6
Sidebranch deteriorated	18.5	5.7	<0.0001
Sidebranch treated	13.8	3.7	0.1
Complex lesions			
SVG	3.1	0.7	0.02
In-stent thrombosis	6.2	0	0.01
Calcification	10.7	11.1	0.9
Tortuosity	12.3	8.2	0.01

Presented are the means ±SD or otherwise percentages. N= number.

There was significantly less contrast media use in the MPCI compared with the CPCI group [170 mL (100–200) vs. 200 mL (150–250); $P < 0.001$]. Procedural times were not significantly different for MPCI compared with CPCI [29 min (18–35) vs. 31 min (23–41), $P = 0.20$], whereas the reduction of fluoroscopy times reached statistical significance [7.4 min (3.58–11) vs. 9 min (6–13.1), $P < 0.05$].

Multivariate analysis showed that there was significantly less contrast media use in the MPCI compared with the CPCI group, OR = 0.41 (0.21–0.81) (Table 5). Fluoroscopy times were significantly reduced for MPCI compared with CPCI, OR = 0.42 (0.20–0.79).

Table 5. Results of logistic regression.

End point	OR	95%CI
Contrast consumption		
MPCI vs CPCI	0.35	0.16-0.75
Fluoroscopy time-min		
MPCI vs CPCI	0.36	0.17-0.77
Procedural duration-min		
MPCI vs CPCI	0.35	0.16-0.76
No. of balloons used per patient		
MPCI vs CPCI	0.66	0.33-1.31
No. of wires per patient		
MPCI vs CPCI	1.57	0.78-3.18

Distal embolization was seen in 7.7% (5/65) of patients in the MPCI, unfortunately that data was not available from the PASSION trial, but this figure is below the 15.2% incidence quoted in the literature (17).

DISCUSSION

This comparison of magnetic navigation with conventional wire technique in patients undergoing primary PCI suggests that MPCI procedures can be performed as effectively, as defined by contrast media use, procedural time, fluoroscopy time, and success rate, as CPCI. Indeed, the results show equivalent procedural performance with significant reductions in the contrast media use and fluoroscopy time. Previously published data from this registry showed that magnetic navigation in simple lesions significantly benefited only one of these three parameters (with a small reduction in median contrast media use and non-significant trends in fluoroscopy and procedural times in simple lesions) (6), whereas all three were significantly improved in complex lesions (7). In this comparison, two of the three parameters were significantly improved and one was not significantly improved, suggesting an intermediate position for this subgroup However, these comparisons are hypothesis-generating and there may be other confounding factors, thus to reach a definitive conclusion, randomized studies are required.

The rapid restoration of full TIMI 3 flow is crucial in primary PCI (9) with strong evidence that swift restoration of flow in the obstructed infarct artery is a key determinant of short- and longterm outcome (10-14). However, reported rates of achieving TIMI 3 flow, range from only 70 to 90% (10-14) and this leaves a proportion of procedures where improvement is possible. Potentially this lack of success could be due to the more complex anatomy where the MNS would help.

This new technique gives the operator new and definable capabilities. Active tip adjustment can change the angle of approach of the tip as required, in order to maintain the tip coaxially through normal vessel, or in order to steer around bends or into sidebranches.

Three dimensional directability is obtained by using the clockface (automatically displayed in the plane of the 2D image), by using presets (average directions of vessel segments), or, in cases with more complex anatomy, by using a 3D reconstruction from patient images. Furthermore, primary PCI using the MNS could conceivably give benefits such as minimizing wire-tip rotation thus reducing wire entwinement, or allowing circumnavigation around friable thrombotic lesions, a known predictor of distal embolization and no-reflow phenomena (18). In this comparison, embolization was recorded only in the MPCI group (and not in the PASSION group), but the rate seen was lower than reported in the literature (19). In this comparison, an increased use of wires was seen. The cases where multiple wires were used have been reviewed and a number of reasons appear to be related to this. First, there were more bifurcational lesions in the MPCI group and a greater tendency to choose a second wire (Table 4). Second, there was a more complex case mix in the MPCI group that included, for example, in stent thrombosis. In two of the five in-stent thrombosis cases, multiple wires were used. Third, the stainless steel core of the Titan wire has a poorer memory (or the tendency to return to its previous shape), than conventional wires and a replacement was needed in three bifurcation lesions. Fourth, the use of conventional wires was not prohibited. This occurred in two cases. In one case, a Filterwire Ex wire (Boston Scientific, Natick, MA, USA) was deployed in one saphenous vein graft (SVG) case after the magnetic wire had been successfully passed and the restored flow showed a lesion in which distal protection was felt to be necessary. In a second case, the magnetic wire failed to enter a sidebranch so a conventional wire was tried but also failed to cross. However, flow improved and the result was accepted.

With regard to the performance of the rigid magnetic wire tip, no traumatic problems were seen with forward passage as the shaft behind the magnetic tip buckles similar to a conventional wire. However, in principle this rigidity could be an issue in sharply angulated turns that are narrow and constrained, and it is known that MPCI requires extra attention in order to avoid such problems as magnetic wire lock (19). This comparison included procedures performed from approximately 3 months after system acquisition (as a previous publication (5) suggested a learning curve) and was performed with the normal emergency team (that is two nursing staff in addition to the attending physician). The data in this comparison support the premise that, when the procedure is performed by experienced staff, there is no additional time delay but rather could lead to an advantage.

In this study, even at this early stage in its development, the use of MPCI appears as safe, feasible, and successful as CPCI.

Study limitations

This comparison has the limitations associated with comparing a registry with historical controls and the lack of randomization. There were differences in the performance of the procedures. Only two of five CPCI operators performed MPCI and, although all five opera-

tors are experienced operators, and there was proportionately more experience in the CPCI group, operator bias cannot be excluded. The patients and the performing physicians were not blinded to the type of procedure. The inclusion of the two groups was slightly different as inclusion in the magnetic procedure group depended on the presence of an operator and the availability of the magnetic room, whereas the PASSION study patients were performed by all operators. The target lesion characteristics were also slightly different. The PASSION study included those patients in whom the wire had successfully crossed the lesion and may have led to exclusion of more complex anatomy such as SVGs, stent thrombosis, or in-stent restenosis, whereas the MPCI group included all patients irrespective of stent thrombosis (five patients) or the presence of SVGs. In addition, MPCI was generally performed in smaller vessels (reference diameter 2.8 vs. 3.1 mm, $P < 0.0001$), the occurrence of hypertension was higher (40.2 vs. 32.3%, $P = 0.05$) and the occurrence of previous CABG was higher (4.6 vs. 0.9%, $P = 0.03$) compared with CPCI. However, these data suggest that more favourable patients were in the CPCI group, and had there been an equal distribution of these variables the results might have been further in favour of MPCI.

CONCLUSION

Primary PCI using the MNS appears feasible and does not negatively influence use of contrast media or irradiation. This is coupled with potential advantages such as reduction of wire entwinement. In addition, the option of 3D reconstruction remains available if complex anatomy is uncovered. This comparison suggests the feasibility and non-inferiority of the MNS in performing primary PCI and could aid the complex procedures sometimes needed in this emergent situation. Randomized controlled trials are warranted in order to further investigate the use of MPCI in this population.

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CHAPTER 23

Magnetic Percutaneous Coronary Intervention – the Dutch multi-center experience

ABSTRACT

Background: Magnetic navigation is a novel technology that actively steers an angioplasty wire-tip and may improve PCI procedures. There are no large multicenter reports of long term MACE and survival. The systems in the Netherlands represent some of the most intensively used systems for percutaneous coronary intervention and this report describes the results of nearly 1500 patients to 3 years.

Methods and Results: We compared 1441 sequential patients (mean age 65±11yr) undergoing magnetically navigated percutaneous coronary intervention (MPCI) with those of 1441 patients (mean age 64±12yr) undergoing conventional percutaneous coronary intervention (CPCI) who were matched by the propensity score. The major endpoint was mortality at an average of 2 years with secondary endpoints of MACE, procedural duration and fluoroscopy time, and contrast media use. Technical success and procedural outcomes were evaluated. Clinical demographics and angiographic characteristics of the two groups were similar, except for fewer patients with hypercholesterolaemia in the CPCI group and fewer patients with previous myocardial infarction in the MPCI group.

Overall technical and procedural success was high (95.4% MPCI versus 98.0% CPCI) in both groups. There was significantly less contrast media use in the MPCI compared to the CPCI group (130.5ml ± 89.9 versus 288.7ml ± 148.3; P<0.0001). Fluoroscopy times were not significantly different for MPCI compared to CPCI while the reduction of procedural times reached statistical significance (34.15min ± 22.5 versus 84.3min ± 46.3; p<0.0001).

Cumulative mortality was better in the magnetic navigation group at 1, 2 and 3 years compared to the conventional PCI.

Logistic regression showed that there were a number of factors influencing outcome with older patients multi-vessel disease (1.44 [1.15-1.81]) and had a greater incidence of diabetes (1.41 [1.10-1.81]) benefiting the most.

Conclusion: This comparison, that is the largest series reported to date, suggests a reduction in mortality and MACE at 3 years.

Abbreviations and acronyms

PCI - percutaneous coronary intervention

MPCI - magnetic guidewire navigation PCI

CPCI - conventional guidewire navigation PCI

MNS - magnetic navigation system

ACC - American College of Cardiology

AHA - American Heart Association

INTRODUCTION

Magnetic navigation gives the operator new capabilities for approaching percutaneous coronary intervention (PCI) such as precise tip adjustability, computer-enhanced, image-guided tip orientation and computer-enhanced image processing.(1,2) The Stereotaxis magnetic navigation system has been shown to be feasible in general populations for PCI. (3-8) Subgroup analysis of registry data has suggested that benefit increases with increasingly complex anatomy (6-8). The use of the system suggests that increasingly complex lesions benefit proportionately more. In addition, case reports describe the successful completion of procedures that have failed conventionally (9,10).

The systems in the Netherlands are some of the most intensively used systems for percutaneous coronary intervention world-wide in centres with an interest in innovation. This article describes the experience of the systems in the Netherlands and the series represents the largest with the longest follow-up to date.

METHODS

Patients

A total of 1523 patients underwent magnetically navigated percutaneous coronary intervention (MPCI) in the 2 centres with one centre performing 489 procedures from June 2005 to April 2009 and the other performing 952 procedures between September 2006 and May 2009. All patients were included irrespective of their clinical presentation and lesion characteristics.

These patients were matched by propensity score with 3855 concurrent patients from 2 consecutive registries. Control patients were selected from the T-SEARCH and X-SEARCH registries. The methods and design of T-SEARCH (11) and the X-SEARCH (12) have been described previously. Control patients for matching in this analysis were eligible if their procedure had been performed in the same time period as the magnetic procedures (from June 1, 2005 until Feb 28, 2007 patients were taken from the T-SEARCH registry and from March 2007 until April 30, 2009 patients were taken from the X-SEARCH registry).

The magnetic navigation system

The Niobe® II magnetic navigation system (MNS; Stereotaxis, St Louis, Missouri, USA) has been described in detail previously (1-10). The cost of the system is $1.9 million. The size of a typical modern Stereotaxis cath lab room is 770 square feet (72 square meters). The cost of magnetic shielding generally ranges from $50,000–$100,000 and consists of minimal common steel shielding in the walls, ceiling and floor. The cost may be a reason why the system

has relatively limited market penetration and the institutions that use it have had a pioneer role. Training of operators and nurses/technicians is needed before efficient use, a learning curve of approximately 150 procedures has been suggested (4). In one center the MNS is fully integrated with the Integris Allura FD10 cardiovascular imaging system (Philips Medical Systems, Eindhoven, The Netherlands) while at the other center the MNS is fully integrated with the C-arm digital angiography system (AXIOM Artis dFC;Siemens, Forchheim, Germany). The operator interfaces with the system using a touchscreen to the Navigant™ Work Station software (NWS, Stereotaxis, Inc., St. Louis, MO).

A 15-20 cm spherical uniform magnetic field volume is produced that is centered on the heart of the patient and can be reliably and reproducibly directed in 360º in all planes. Selecting a 3D direction on the computer screen, leads to movement of the 2 external magnets to give a precisely directed magnetic field vector that will actively deflect the magnetic wire tip resulting in reproducibly precise steering.

Magnetically Enabled Wires

A series of magnetically enabled disposable guide wires, that are custom designed for use with the MNS, are available in a variety of sizes and a range of stiffness. In this comparison, all three generations of magnetic guidewires, Cronus™, Titan™ and Pegasus™ guidewires were used, see figure 1. These are specifically designed to be more flexible and steerable for magnetic navigation. These are 180cm moderate support, hydrophilic coated wires with a diameter of 0.014 in / 0.36 mm having a flexible 2 cm distal coiled tip with a 2 or 3mm neodymium-iron-boron magnet attached at the end.

PCI procedure

All patients gave informed consent to the proposed procedure. The choice of guiding catheter and equipment was left entirely to the discretion of the operator and followed routine practice as did the use of drug-eluting stents, bare metal stents and the use of glycoprotein IIb/IIIa receptor antagonists. There were no restrictions on the operators' choice of conventional wire. The angioplasty wires for magnetic procedures were the standard magnetically enabled wires supplied by the company, see previous paragraph.

Standard procedural medication was aspirin, 500 mg i.v. and clopidogrel, 600mg p.o. for all patients. Weight adjusted unfractionated heparin, 100 IU/ kg, was given as an intravenous bolus at the beginning of the procedure. The standard approaches were those routinely used, the radial artery or the femoral artery, at each respective center.

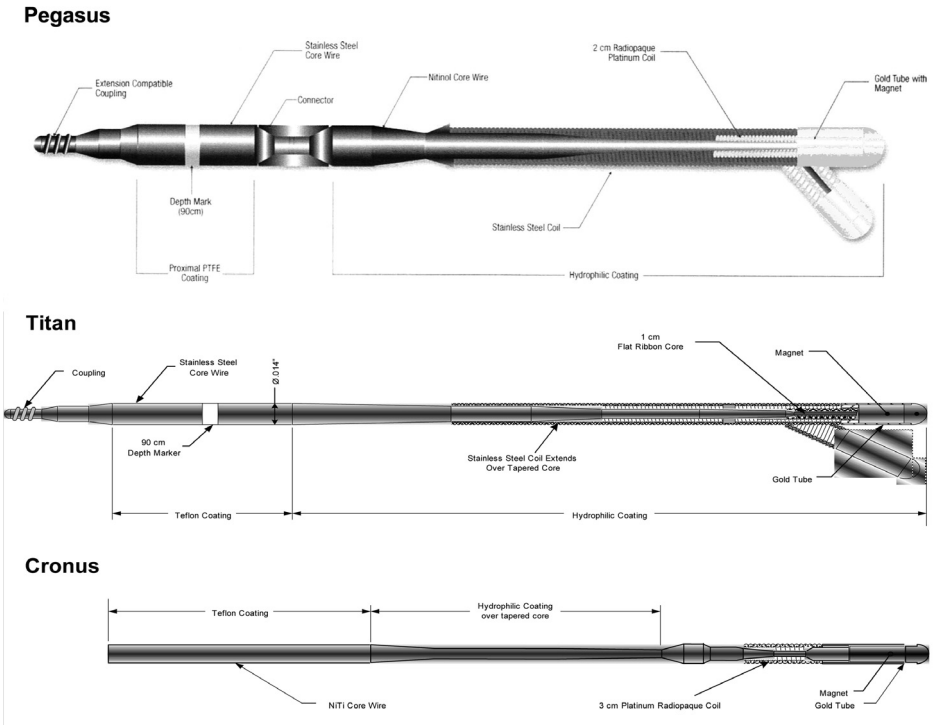

Figure 1. The three generations of magnetic guidewires used in the procedures, the Cronus™, the Titan™ and the Pegasus™ wires. *See this figue in color in the Appendix page 375.*

Angiographic variables

All angiograms were stored in a computer database and analyzed off-line by an independent observer, using CAAS 2003 Camtronics (Phillips Medical Systems). Lesion types were graded according to the ACC/AHA lesion classification (13).

Follow-up

At the time of the follow-up, June 1 2009, vital status was obtained retrospectively by review of the hospital records and checked against the civil registries. A postal questionnaire was sent to patients. A distinction was made between cardiac death (sudden death within 1 h of complaints, fatal acute myocardial infarction, congestive heart failure) and non-cardiac death (all other causes). Follow-up was complete in over 90% of patients at 2 years and median follow-up was 1.9 years.

Statistical analysis

Methods for Propensity Scoring Matching

In order to correct for differences in baseline characteristics between the treatment groups, the propensity score methodology was used to identify comparable patients treated with different strategies. The propensity score was initially proposed by Rosenbaum and Rubin and has been used in prior observational studies to help adjust for treatment selection bias (14–16) .

A propensity score for each patient was constructed, providing an estimate of the propensity for belonging to one treatment group rather than the other by performing multiple logistic regression with the endpoint the type of intervention (CPCI coded as 0, MPCI as 1). All factors that might be predictive of receiving either intervention were evaluated. These included age, sex, prior myocardial infarction, prior angioplasty, unstable versus stable angina, diabetes, dyslipidemia, hypertension, and ejection fraction (normal, moderate or poor). The patient characteristics before the matching according to 1523 MPCI patients and conventional patients from the T-SEARCH and X-SEARCH registries are shown in Table 1.

Table 1. Baseline Characteristics before matching. For age means ±SD are given, and in all other cases percentages of patients. CAD denotes coronary artery disease.

Characteristics	Magnetic PCI (N= 1523)	Conventional PCI (N= 3855)
Age-yr	64.6±11.4	63,5±11.8
Male sex	73.7	72.8
Diabetes mellitus	19.6	21.0
Hypertension	43.2	46.3
Hypercholesterolemia	40.7	55.6
Family history of CAD	41.0	39.9
History of smoking cigarettes	20.9	29.0
Previous PCI	32.9	25.0
Previous CABG	11.0	8.1
Previous myocardial infarction	25.4	28.1

Presented as percentages (within parentheses) or in other cases means ±SD. N= number.

The two study populations were far from similar. To obtain improved insight in the differences, patients were divided into four quartiles according to their propensity score.

Second, each MPCI patient was matched with 1 CPCI patient with the same or nearest propensity score. As a result, the matched CPCI population resembled the MPCI cohort after the matching, see Table 2.

Table 2. Baseline Characteristics after matching. For age means ±SD are given, and in all other cases percentages of patients. CAD denotes coronary artery disease.

Characteristics	Magnetic PCI (N= 1441)	Conventional PCI (N= 1441)
Age-yr	63.8±11.4	63.8±11.4
Male sex	73.7	73.4
Diabetes mellitus	19.6	20.5
Hypertension	43.2	46.0
Hypercholesterolemia	40.7	54.8
Family history of CAD	41.0	43.9
History of smoking cigarettes	20.9	20.3
Previous PCI	32.9	32.9
Previous CABG	11.0	10.1
Previous myocardial infarction	25.4	30.8

Presented as percentages (within parentheses) or in other cases means ±SD. N= number.

For comparison of continuous variables between the two groups, the unpaired two-tailed Student`s t-test was used or, for the skewed data (as for median of the contrast use), the Mann-Whitney U-test. Comparison of categorical variables between the 2 groups was performed using the Chi-square test, or in case of a minimum expected count less than 5, the Fisher exact test. Continuous variables were expressed as mean ± SD for non-skewed data, medians were expressed as 95% CI for skewed data. Categorical data were expressed as numbers of patients and percentage of patients. A P value less than 0.05 was considered statistically significant. Statistical tests were carried out with the SPSS 14.0 statistical software package (Chicago, IL).

Cumulative survival curves were constructed using the Kaplan–Meier method. Among patient subgroups the log-rank test was used to compare survival curves. A logistic multivariable regression, stratified by the procedure type CPCI or MPCI, was used to adjust for the baseline differences to determine the impact on in-hospital mortality and hospital complications. Odds ratios and 95% confidence intervals were calculated to test for significant differences.

RESULTS

1441 patients who had undergone MPCI were successfully matched. 1412 (98.0%) were followed up by interrogating the civil registry, and by postal questionnaire. The median follow-up was 1.9 years with a low overall mortality was 3,5%.

Propensity matched demographics

The mean age was 64 years, and approximately 73% of patients were men in both groups. After matching, the baseline characteristics were similar in both groups although there were

fewer patients with hypercholesterolemia (40.4% MPCI versus 53.6% CPCI; P = <0.001) and more patients with previous MI in the CPCI group compared with the MPCI group (25.0% MPCI versus 29.5% CPCI; P = 0.006), see Table 2. There were equal numbers of patients with diabetes (19.4% MPCI versus 21.3% CPCI; P = NS), a family history of coronary artery disease, a history of smoking within 1 year and previous percutaneous intervention (32.5% MPCI versus 31.3% CPCI; P = NS) and CABG (10.8% MPCI versus 10.6% CPCI; P = NS) in both groups. Lesions had a similar distribution in the 3 coronary arteries, see Table 4.

Table 3. Angiographic characteristics. Presented are the percentages of patients with percentages (within parentheses) or in other cases means ±SD.

Variable	Magnetic PCI (N= 1441)	Conventional PCI (N= 1441)
Vessel disease %		
1VD	55.0	54.5
2VD	30.5	27.6
3VD	14.4	17.9
0	224(18.1%)	224(18.1%)
1	45(3.6%)	45(3.6%)
2	65(5.2%)	65(5.2%)
3	905(73.0%)	905(73.0%)
ACC/AHA lesion class		
A	6.6%	9.9
B1	24.7%	33.0
B2	18.3%	28.5
C	50.3%	28.5
Stable angina	65.3	69.4
Unstable angina	25.8	23.4
Acute MI	8.9	7.2

Presented are the percentages of patients or in other cases means ±SD. N= number.

Procedural parameters

Overall technical and procedural success was high (95.4% MPCI versus 98.0% CPCI) in both groups. There was significantly less contrast media use in the MPCI compared to the CPCI group (130.5ml ± 89.9 versus 288.7ml ± 148.3; P<0.0001). Fluoroscopy times were not significantly different for MPCI compared to CPCI (19.6min ± 129.0 versus 21.7min ± 18.5; p=0.56) while the reduction of procedural times reached statistical significance (34.15min ± 22.5 versus 84.3min ± 46.3; p<0.0001), see Table 5.

Multivariate analysis showed that there was significantly less contrast media use in the MPCI compared to the CPCI group, OR = 0.41 [0.21-0.81] see Table 5. Fluoroscopy times were significantly reduced for MPCI compared to CPCI OR = 0.42 [0.20-0.79], see Table 5.

Table 4. Target vessel location.

Target vessel	Magnetic PCI (N = 1523)	Conventional PCI (N= 1441)
RCA		
RCA1	130(9.2%)	129(10.4%)
RCA2	177(12.5%)	141(11.4%)
RCA3	69(4.9%)	54(4.4%)
RCA4	23(1.6%)	22(1.8%)
RCA16	19(1.3%)	3(0.2%)
LCA		
LMS	19(1.3%)	38(3.2%)
LAD		
LAD6	290(20.5%)	195(15.8%)
LAD7	194(13.7%)	238(19.2%)
LAD8	25(1.8%)	51(4.1%)
LAD9	69(4.9%)	64(5.2%)
LAD10	12(0.8%)	10(0.8%)
Cx		
Cx11	119(8.4%)	79(6.4%)
OM12b	144(10.2%)	74(6.0%)
Cx13	66(4.7%)	96(7.8%)
Cx14	32(2.3%)	32(2.6%)
Cx15	4(0.3%)	3(0.9%)
SVG	23(1.6%)	

Presented are the absolute numbers of lesions with percentages (within parentheses).

Table 5. Procedural parameters.

Variable	Magnetic PCI (N= 1523)	Conventional PCI (N= 1523)	P value
Procedural duration-min	34.15±22.5	84.3±46.3	P < 0.0001
Fluoroscopy time-min	19.6±129.0	21.7±18.5	P = 0.56
Contrast consumption (Mean)-ml	130.5±89.9	288.7±148.3	P < 0.0001

Presented are the means ±SD or otherwise percentages. N= number

Table 6. Cumulative survival, (see also Kaplan-Meier Curves (figure 3.)

	1 year	2 year	3 year
Magnetic PCI	97.4%	95.7%	91.7%
Conventional PCI	93.5%	91.3%	88.9%

Cumulative mortality was better in the magnetic navigation group at 1, 2 and 3 years compared to the conventional PCI group (97.4, 95.7 and 91.7% versus 93.5, 91.3 and 88.9% respectively), see table 7 and figure 3.

Table 7: Results of logistic regression.

End point	OR	95%CI
Age		
MPCI vs CPCI	1.03	1.02-1.04
Unstable angina		
MPCI vs CPCI	0.71	0.54-0.93
Previous CABG		
MPCI vs CPCI	1.36	1.01-1.85
Multi-vessel disease		
MPCI vs CPCI	1.44	1.15-1.81
Diabetes		
MPCI vs CPCI	1.41	1.10-1.81
AHA/ACC Type B2/C		
MPCI vs CPCI	1.48	1.18-1.86
Bifurcation		
MPCI vs CPCI	0.73	0.64-0.84

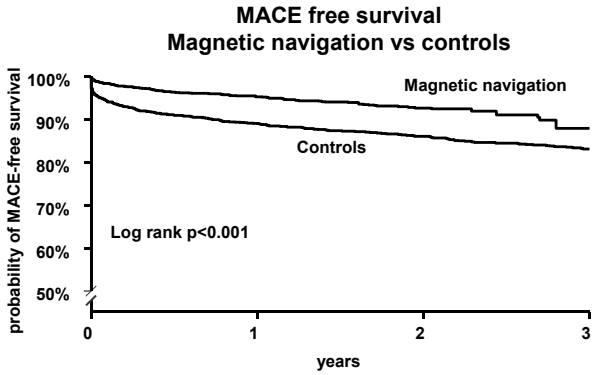

Figure 2. Kaplan-Meier curve for MACE free survival.

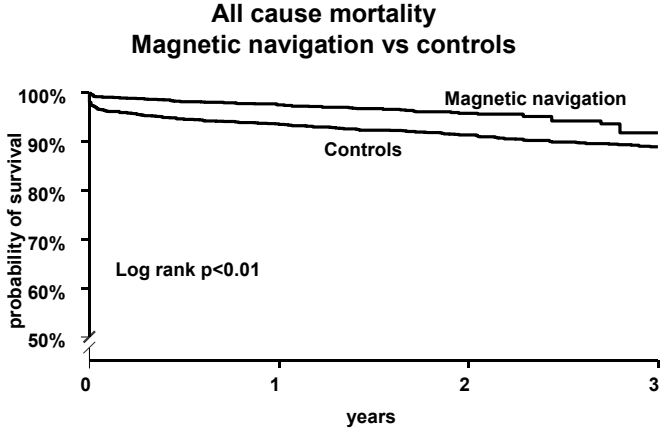

Figure 3. Kaplan-Meier curve for all cause mortality.

Logistic regression

Logistic regression showed that there were a number of factors influencing outcome, see table 7. Patients who benefited more from a magnetic procedure were older (1.03 [1.02-1.04]) with more multi-vessel disease (1.44 [1.15-1.81]) and had a greater incidence of diabetes (1.41 [1.10-1.81]) and AHA/ACC type B2/C lesions (1.48 [1.18-1.86]). Patients with unstable angina (0.71 [0.54-0.93]) and bifurcation lesions (0.73 [0.64-0.84]) benefited less.

DISCUSSION

This is the first multi-center study examining the real-world experience MACE and long-term survival of using the Niobe Stereotaxis MNS for describing the total Dutch experience of magnetic navigation PCI. The cases have been matched with patients from concurrent CPCI registries as a control, the T-SEARCH registry (11) and X-SEARCH (12) registries. The results suggest that procedures can be performed with a use of time and contrast media use that is at least as short as conventional and is in line with previous studies that indicate a reduction in procedural time and contrast use (6,7).

Furthermore in this follow-up, mortality is not adversely affected and again suggests that there could be a survival advantage. Logistic regression identifies markers for more complex procedures such as the clinical factors of increasing age and diabetes as well as the anatomical/angiographic factors of previous CABG and AHA/ACC grade of B2 or C as benefiting. However, in contrast to these, the presence of unstable angina or a bifurcation does not benefit from magnetic navigation.

PCI by magnetic navigation in this study appears to be at least as safe as conventional PCI. In this study the Kaplan-Meier curves suggest a mortality benefit. However such non-randomized data must be interpreted with care as bias could be caused by anything ranging from pure coincidence to striving for a more complete revascularization.

Challenges for the future include improving identification of patients who might benefit, the further development of wires, and the investigation and development of integrated information procedures.

Study Limitations

This comparison has the limitations associated with retrospective cohort studies in that procedures were not randomized. This limitation was addressed by using propensity matching, however as shown in table 2, matching did not remove all differences in patient demographics.

This article describes the results over nearly 4 years, and the system and the wires have undergone a transition in this time. It has been shown that there is an improvement in the wires that is reflected in success and decreased fluoroscopy times (5). This suggests that there may have been a heterogeneity in attempted and/or completed procedures

In addition, a combined database for the magnetic patients from 2 hospitals was used but matched with conventional patients from one center. This could lead to bias due to different practices between hospitals.

The CPCI patients were taken from the T-SEARCH and X-SEARCH registries where the patients all received Taxus or Xience V stents while the magnetic procedures used unselected stents i.e. both bare metal stents and other DES. As the results for the Xience V have been superior to BMS or other DES, this would have been a factor in favour of the conventional group.

In one center, procedures are often performed by supervised trainees who might have more of a tendency to more frequent checks that could affect contrast media use and fluoroscopy use. This may be compounded by a frequent use of invasive diagnostics such as IVUS or novel technologies such as optical coherence technology.

The system and it's consumables are under continuing development and this article describes all cases using different software system (2.7, 2.10, 2.11 and 3.0) and different wires (Cronus™, the Titan™ and the Pegasus™ wires). This will lead to heterogeneity.

CONCLUSION

This article describes the real-world use of the Stereotaxis Magnetic Navigation system and describes the initial results and suggests the possibility of a survival benefit that is maintained at 3 years. More complex procedures appear to derive more benefit as reflected by the benefit in older patients with more diabetes, multivessel disease and a higher incidence of AHA/ACC type B2/C lesions.

ACKNOWLEDGEMENT

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CONFLICT OF INTERESTS

The authors have no conflicts of interest to disclose.

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PART V

Summary and conclusions

CHAPTER 24

Summary and Conclusions

The treatment of ischemic heart disease has both medical treatment with a range of drugs coupled with invasive, mechanical treatments such as percutaneous coronary intervention and coronary artery bypass grafting. This PhD examines the use of a new technology, the magnetically controllable direction of a wire tip that is to be used to deliver the balloons and stents used in percutaneous coronary intervention.

SUMMARY OF POINTS FROM THE LITERATURE

The current thesis has examined the development of magnetic navigation from early feasibility testing through early clinical development and use.

Feasibility

Magnetic navigation for percutaneous coronary intervention has been illustrated in the wide range of coronary lesions, from simple lesions to complex, from acute occlusion to chronic occlusions.

In addition, the system can be used in a wide range of cardiac procedures that not only includes percutaneous coronary interventions but also other procedures such as stem cell delivery or coronary sinus lead placement.

There appears to be a learning curve that may be optimised by the use of an defined, small group of users that regularly perform procedures. In addition early experience should not concentrate solely on difficult cases.

Lesion type

The use of magnetic navigation appears safe and feasible in percutaneous coronary intervention of all lesion types. There is a gradation in the benefit derived from the use of the system with lesions that are considered more complex deriving more benefit. While there is a potential benefit in the use of this system in reduction of contrast media use, irradiation and procedure times, difficult lesions appear to be more or less amenable to benefit from this technique.

Angiographically simple elective lesions benefit the least. In these cases the anatomy is already known from before and the patient is normally clinically stable. Here thought and preparation can be thorough from decisions regarding angiographic angle and material use.

A method to select patients based on the 3D morphology of the target vessel and lesion that could benefit from the use of the system has been developed.

The system is designed to facilitate navigation by accurate and 3D guided wire-tip navigation and this appears to have the most benefit when the anatomy is complex such as extreme tortuosity or chronic occlusion, the information from angiography is supplemented by integration of non-invasive diagnostic investigations such as MSCT.

The system also appears to be feasible and produce benefit in acute situations such as myocardial infarction. This benefit appears to be intermediate between the minimal or lack of benefit in simple lesions and the benefit in complex lesions. While it is possible to postulate that this is because these procedures are a mixture of these 2 types, other explanations cannot presently be ruled out.

FUTURE DEVELOPMENT

Software developments include newer versions of the Navigant software. In particular, ease of use of current functions and improvements in integration are planned.

Hardware projects in development include;

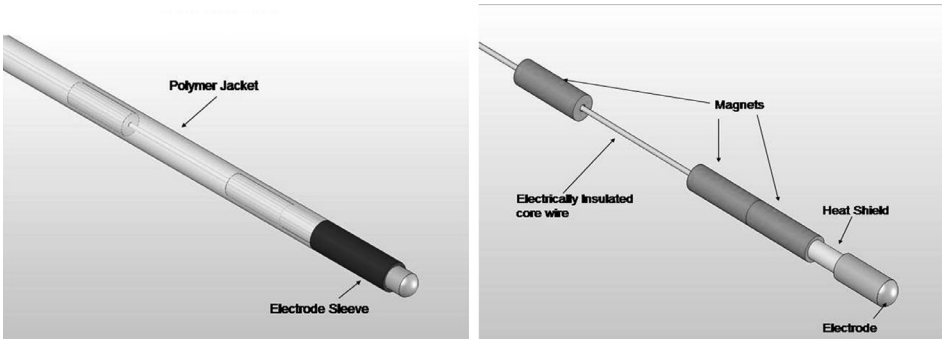

Figure 1. Magnetically controllable RF wire for hard and tough lesions. *See this figue in color in the Appendix page 380.*

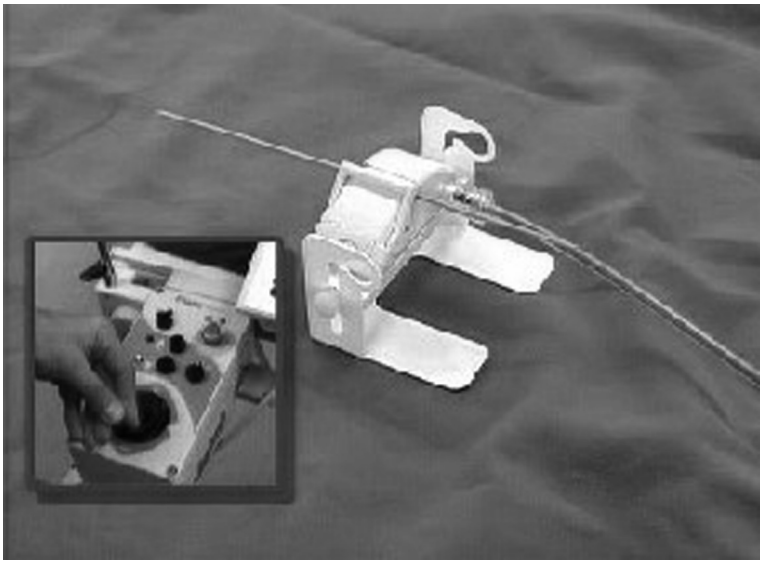

Figure 2. Remote control system. *See this figue in color in the Appendix page 380.*

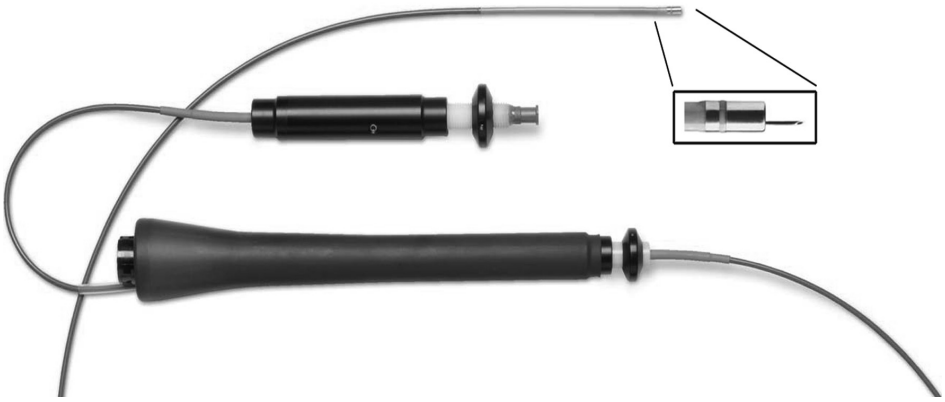

Figure 3. Stem cell delivery catheter combined with better electromechanical measurements. *See this figue in color in the Appendix page 379.*

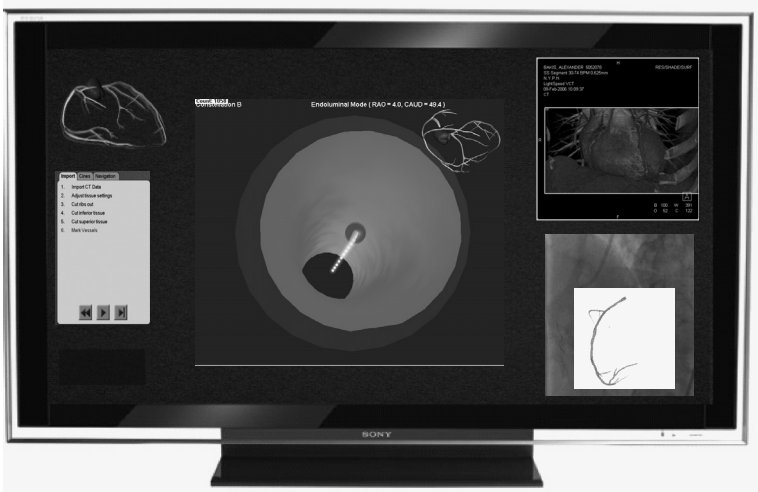

Figure 4. Odyssey screen. *See this figue in color in the Appendix page 380.*

Concluding remarks

The system has a number of new capabilities that are potentially advantageous to a PCI procedure. Individually a specific advantage may not play a crucial role in each and every procedure but together may allow for smoother and less troubled wire passage. Ultimately magnetic navigation could potentially increase efficiency, reduce procedure time, facilitate the application of advanced technologies, decrease irradiation of the operators and thus better use hospital resources to lower overall hospital costs.

The current advantages of this system in PCI include precise tip orientation, computer control and computer processing.

This new technology allows 3D reconstruction of a virtual coronary artery to be performed while the patient is on the table during an interventional procedure. These images may not only give a better appreciation of the anatomy with regards to tortuosity but also give a volume-rendered model with the computer-calculated vectors that allow magnetic navigation. These individualized, scale models supply the directions for deflecting the wire as it passes through the vessel. Potentially this software, and the improvements in image acquisition and image processing, may improve wire passage and cannulation of vessels to result in reductions of complications, procedural time, irradiation and contrast usage. This new technology could transform the practice of interventional procedures with the introduction of computer enhanced imaging that revolves particularly around the production of 3D models.

Samenvatting en conclusies

Samenvatting van punten uit de literatuur

De behandeling van ischemische hartziekte bestaat uit zowel de medische behandeling van een reeks van medicijnen in combinatie met invasieve, mechanische behandelingen, zoals percutane coronaire interventie en een coronaire bypassoperatie. Dit doctoraat heeft de ontwikkeling van magneet navigatie doorgemaakt vanaf onderzoek in toepasbaarheid tot analyse van klinische resultaten in patientengebruik.

Toepasbaarheid

Magneet navigatie is toepasbaar in percutane coronaire interventie van verschillende type laesies, van simpele laesies tot complexe, van acute laesies tot chronische.

Het systeem kan gebruikt worden voor verschillende procedures. Dit includeerd niet alleen percutane coronaire interventie, maar tevens ook andere procedures zoals stamcel toediening of het plaatsen van een lead in de Sinus Coronarius.

Een onderzoek laat zien dat er een leercurve nodig is om met het magneetsysteem te leren werken. Deze leercurve kan geoptimaliseerd worden door een kleine groep van gebruikers die frequent met het systeem werken, en de procedures te laten uitvoeren.

Tevens moeten beginnende gebruikers van het systeem zich niet alleen focussen op de moeilijk te behandelen laesies.

Type laesie

Het gebruik van magneet navigatie blijkt veilig en toepasbaar te zijn in alle type laesies bij percutane coronaire interventies.

Er is een gradatie in het voordeel van het systeem. Dit voordeel wordt meer gezien bij complexe coronaire anatomie.

Er is tevens een potentieel voordeel in het gebruik van dit systeem, namelijk vermindering van het gebruik van contrastvloeistof, vermindering van doorlichtingstijd tijdens de procedure, en vermindering van de proceduretijd.

Verschillen in anatomie kunnen verschillende voordelen geven bij het gebruik van deze techniek.

Angiografisch simpele laesies geven het minste voordeel met dit systeem. In deze omstandigheden is de anatomie reeds bekend, en is de patient meestal klinisch stabiel.
Voorbereiding en planning bij deze procedures kan vaak vooraf al gedaan worden.
Er is een methode, gebasseerd op de 3-D anatomie, ontwikkeld om patienten te selecteren die het meeste voordeel krijgen van het gebruik van het systeem.

Het systeem is ontworpen om een precieze 3-D richting van de draad te bewerkstelligen. Dit blijkt het meeste voordeel te geven in complexe anatomie. Tevens als de anatomie complex is, bijvoorbeeld bij extreem tortueuse vaten of chronische totale occlusies, kan de informatie van angiografie aangevuld worden door middel van de integratie van andere onderzoeken, zoals CT-scan.

Het systeem blijkt ook toepasbaar en voordelig te zijn bij acute situaties, zoals bij een myocard infarct.

Dit voordeel lijkt te liggen tussen het ontbreken van het voordeel in eenvoudige laesies en het voordeel bij complexe laesies. Het is mogelijk dat dit komt doordat deze procedures een mengeling is van twee soorten.

Anderen verklaringen kunnen momenteel niet worden uitgesloten.

TOEKOMSTIGE ONTWIKKELINGEN

Softwareontwikkelingen, inclusief nieuwe versies van de Navigant software.

Met name, het vergemakkelijken van voorlopige functies en verbetering in integratie zijn gepland**.**

Hardware projecten in ontwikkeling zijn:
1- Magneet bestuurbare RF draad voor harde laesies
2- Op afstand bedienbaar systeem
3- Stamcel delivery catheter, verbeterd met betere elektromechanische metingen
4- Odyssey scherm

Slotopmerkingen

Het systeem heeft een aantal nieuwe mogelijkheden die potentieel voordelig zijn voor een PCI-procedure.

Een individueel of specifiek voordeel kan geen cruciale rol spelen in elke procedure, maar samen kunnen zij zorgen voor soepelere passage van de draad met minder problemen.

Uiteindelijk kan het magnetisch navigatiesysteem de efficiëntie verhogen, de proceduretijd verlagen, het toepassen van geavanceerde technologieën vergemakkelijken, het verminderen van de doorlichtingstijd en dus leiden tot het beter gebruik van ziekenhuismiddelen m.a.g. lagere algemene kosten voor het ziekenhuis.

Het magnetisch navigatiesysteem(Niobe ®, Stereotaxis Inc, USA) is ontwikkeld voor het navigeren met magnetische producten (draden, catheters) in het menselijk lichaam door het regelen van een magnetisch veld.

De huidige voordelen van dit systeem bij percutane coronaire interventies zijn: precieze orientatie van de tip van de draad, controle van een computer en de computer verwerking.

Deze nieuwe technologie maakt het mogelijk om een 3D-reconstructie van een virtuele kransslagader te maken terwijl de patiënt op de tafel ligt tijdens een ingreep. Deze beelden geven niet alleen een betere beoordeling van de anatomie met betrekking tot kronkeligheid, maar geven ook een volume-gereguleerd model met daarin de computer berekende vectoren die magnetische navigatie mogelijk maken. Deze geïndividualiseerde modellen geven de richting weer voor het buigen van de draad bij het passeren door het vat.

Deze software, en de verbeteringen in beeld verwerving en beeldverwerking, kunnen bijdragen aan het beter passeren van de draad, canulatie van de vaten, wat leidt tot een vermindering van complicaties, procedurele tijd, doorlichtingstijd en het contrast gebruik. Deze nieuwe technologie kan in de praktijk transformeren tot interventionele procedures met de introductie van de computer Enhanced Imaging die vooral draait rond de productie van 3D-modellen.

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My copromoter Dr. Ron van Domburg has been a great support, not only for his expertise in statistics and analysis, but also in many other aspects related to the entire process from how to chase data, who to talk to, to suggestions on how to organise the defence.

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Other fellows and co-authors include Gert Jan Laarman, Emerson Perin, Kwame van der Hilst, Jeroen Braat, Sanne Hoeks, Saskia Rijkenberg, Guilherme Silva, Maurits Dirksen, Marlos Fernandes, Torrey Munger, Ashwini Pandey, Ruchir Sehra, Michael Talcott, Christopher Bichard, Jerett Creed, Jonathan Wong, Edie Oliveira, Yi Zheng, John Canales, Cristiano Cardoso, Keiichi Tsuchida, Shuzou Tanimoto, Jolanta Wentzel, Emanuelle Meliga, Steve Ramcharitar, Ferdinand van Nooijen, Geert-Jan Tangelder, Cihan Simsek, Michael Magro, Isabella Ciampichetti, Yoshinobu Onuma, Jin Ming Chen, Lisanne Schenkeveld and Joost Daeman

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Curriculum vitae

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Professional Qualifications

2004	**CCST** (Certificate of Completion of Specialist Training) Dual accreditation in Cardiology and General (Internal) Medicine.
1998	**MSc in Cardiology** University of Sussex.
1996	**MRCP (UK)** Royal College of Physicians, London.
1991	**MBBS** Kings College School of Medicine, London University.
1987	**BSc (Hons) in Psychology** (Intercalated) University College London, London University.

Current position

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Previous Consultant Appointments

Feb '04 to present	**Chef de clinic - Interventional Cardiology** Onze Lieve Vrouwe Gasthuis, Amsterdam.

Higher Specialist Training

Oct '96 to Feb '04	**SPECIALIST REGISTRAR TRAINING SCHEME IN CARDIOLOGY & GENERAL INTERNAL MEDICINE - SOUTH EAST THAMES WITH OVERSEAS EXPERIENCE AND RESEARCH**
Oct '03 to Feb '04	**Specialist Registrar in Cardiology & General Medicine,** Princess Royal University Hospital, Bromley.
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Aug '95 to Feb '96	**Senior House Officer in Cardiology,**London Chest Hospital, London.
Feb '95 to Jul '95	**Senior House Officer in Renal Medicine & Transplantation,** Kings College Hospital, London.
Aug '93 to Jan '95	**Senior House Officer Rotation,** Joyce Green Hospital, Dartford.
Feb '93 to Jul '93	**Senior House Officer in Accident & Emergency,** Kings College Hospital, London.
Sept '92 to Jan '93	**Senior House Officer & House Officer floating locum**, Joyce Green Hospital, Dartford.Feb '92 to Jul '92 Medical House Officer in Gastroenterology, Kings Liver Unit, Kings College Hospital, London.
Aug '91 to Jan '92	**Surgical House Officer,** Brook General Hospital, London.

Teaching

I have been involved in organising and teaching in training sessions throughout my professional career. I have also attended and presented at National and International Cardiology meetings, and regularly present and contribute to Research Meetings within the College and the University. Specific experience has included:

Management & Administrative Experience

- Co-ordinated and organised staff duty rotas.
- I have organised patients and medical students for the practical issues affecting the Examinations for the Membership of the Royal College of Physicians.
- I have organised and conducted Outpatient Clinics in the institution of beta-blockers and DC cardioversion.
- I have helped with organisation and administration of the International Trans Radial Coronary Intervention Course held in Amsterdam. I was a faculty member in 2004.
- I regularly helped arrange and organise catheterisation and Intervention lists for efficient throughput and consideration for staff morale.
- Maintained high standards in report writing and progress notes.
- Discussed with colleagues current procedures and assisted in laying out policies of department.
- Experienced in supervising, guiding and encouraging junior colleagues.

List of publications

Symbiot™ Stent delivery via 8F guiding catheter from the right radial artery in an acute coronary syndrome due to a degenerating saphenous vein graft: A strategy for reducing access site complications. Banks M, **Patterson M**, Kiemeneij F. **Journal of Invasive Cardiology**. 2005 Feb;17(2):96-7.

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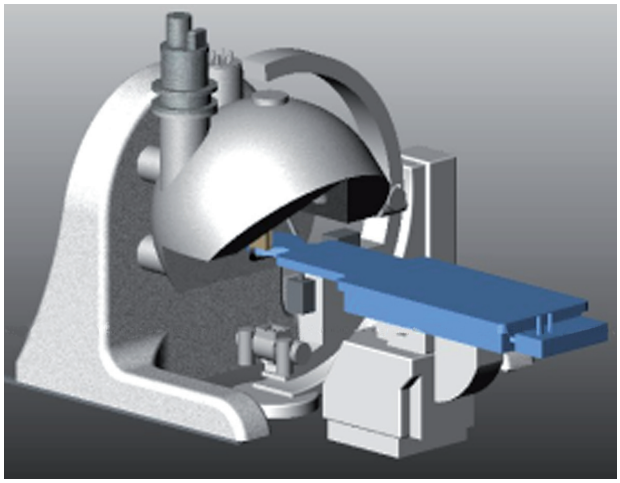
APPENDIX

Color Figures



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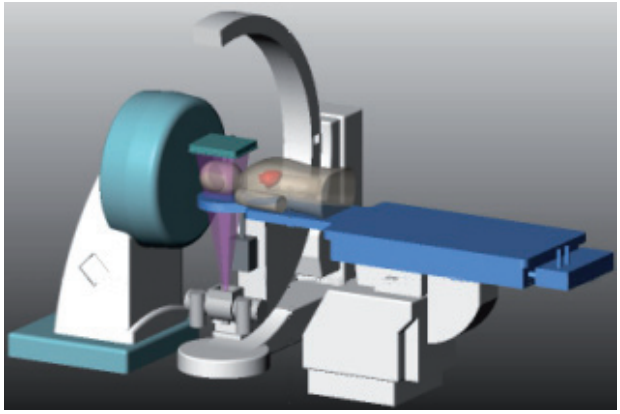

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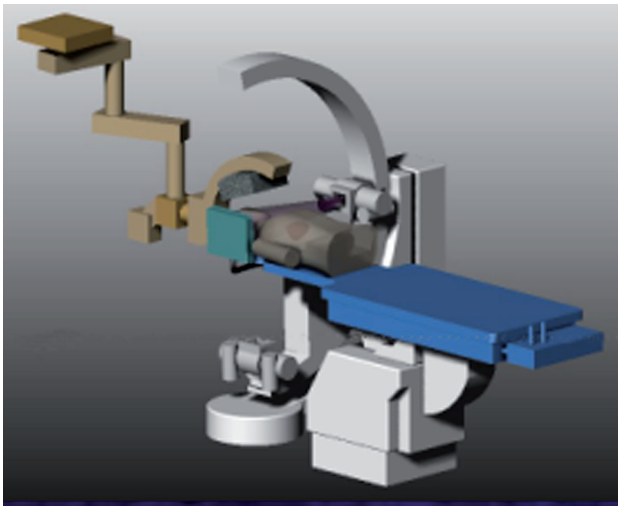

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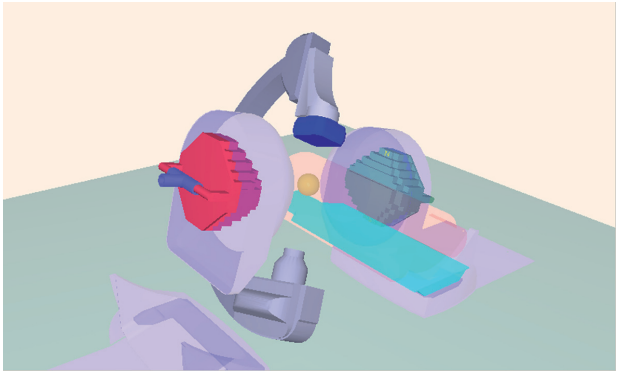

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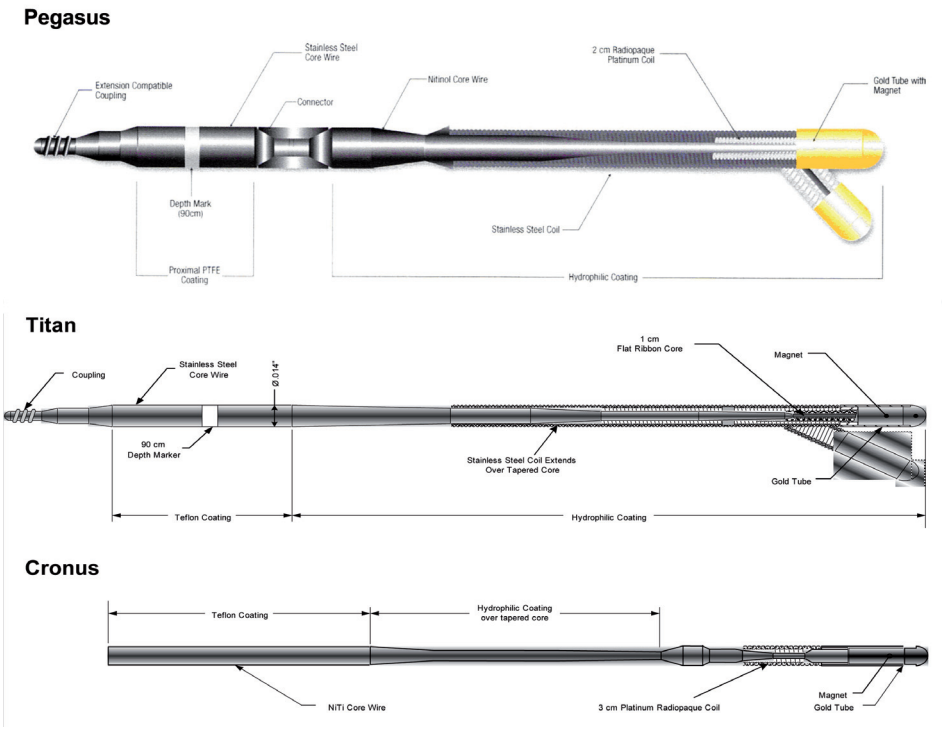

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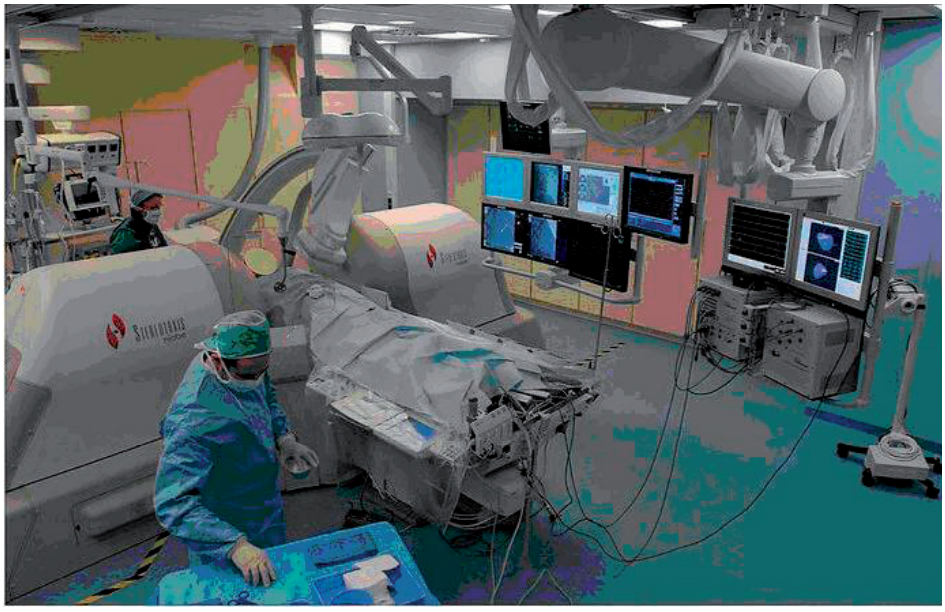

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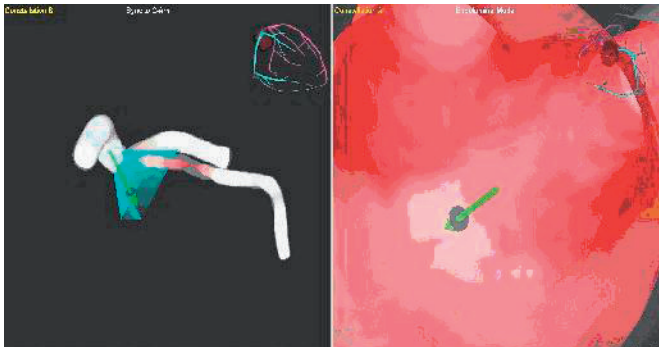

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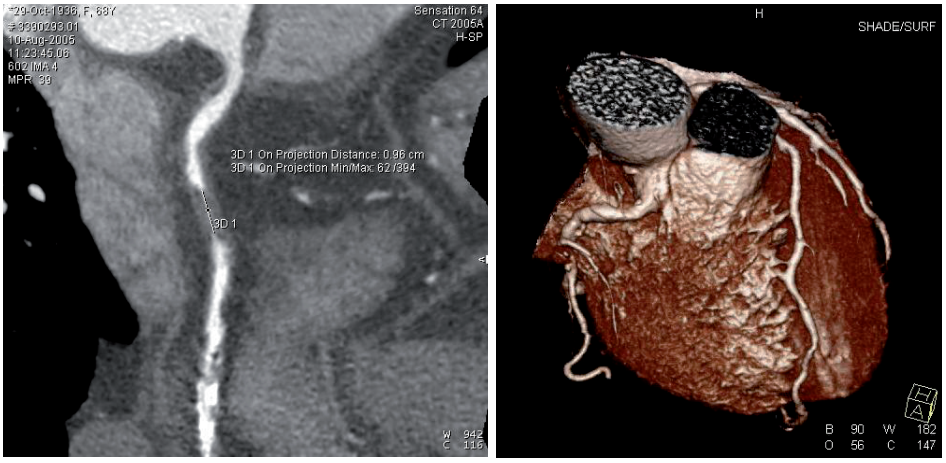

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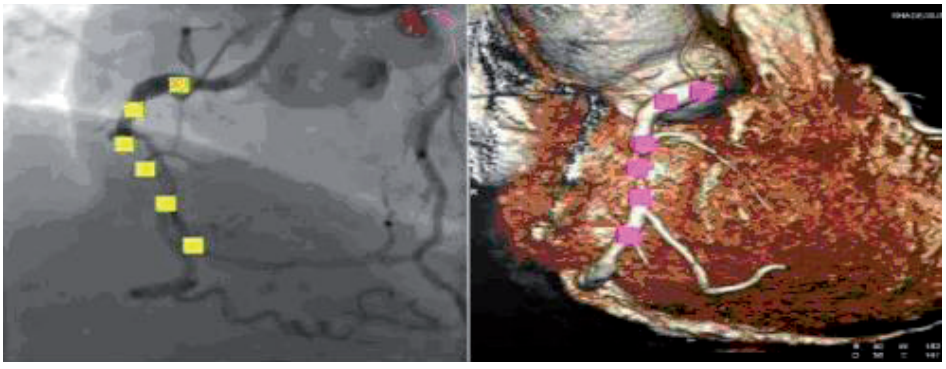

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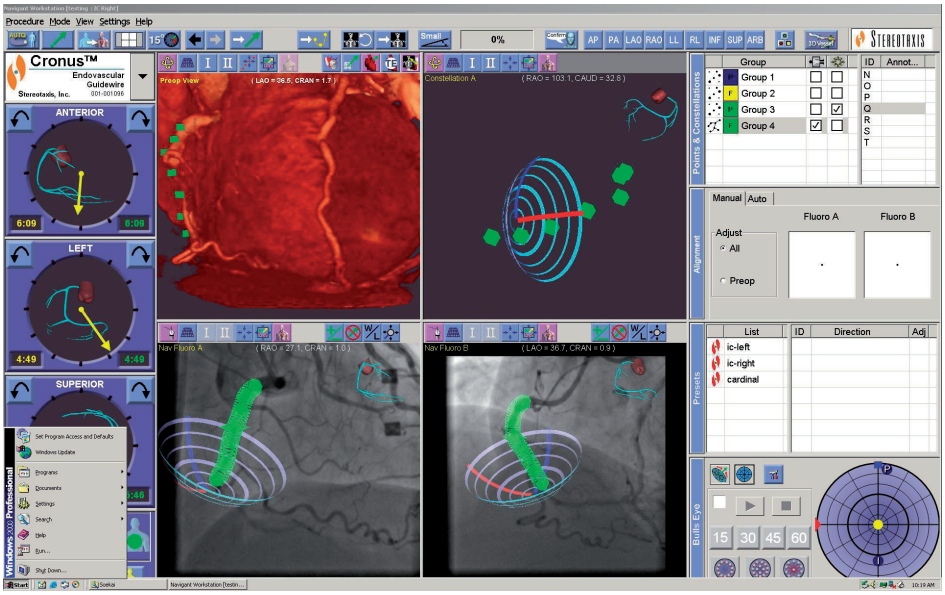

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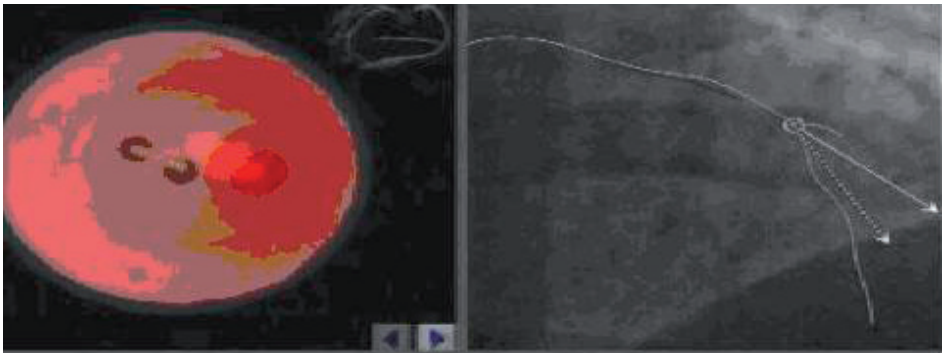

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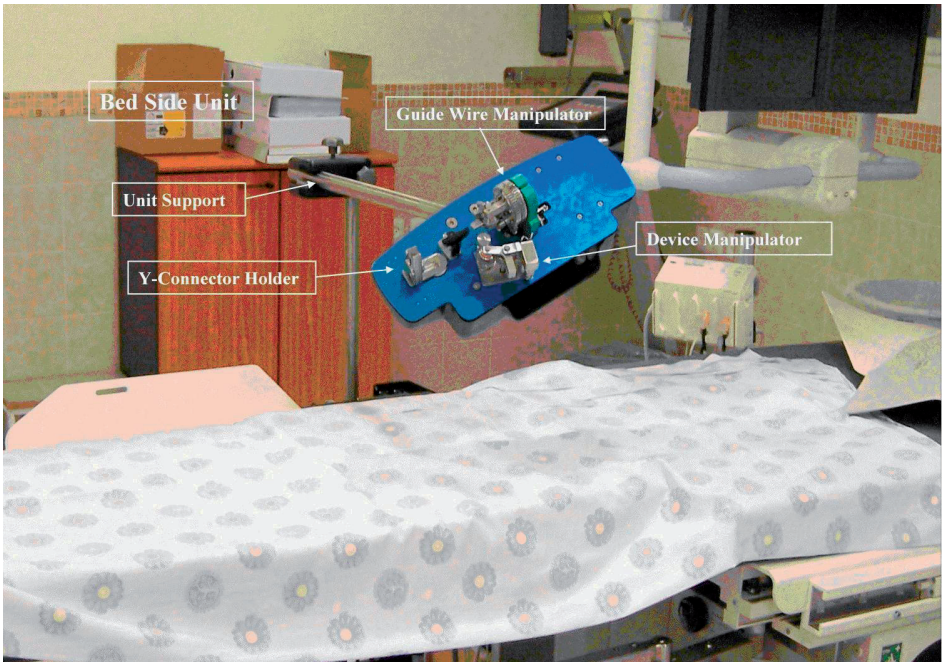

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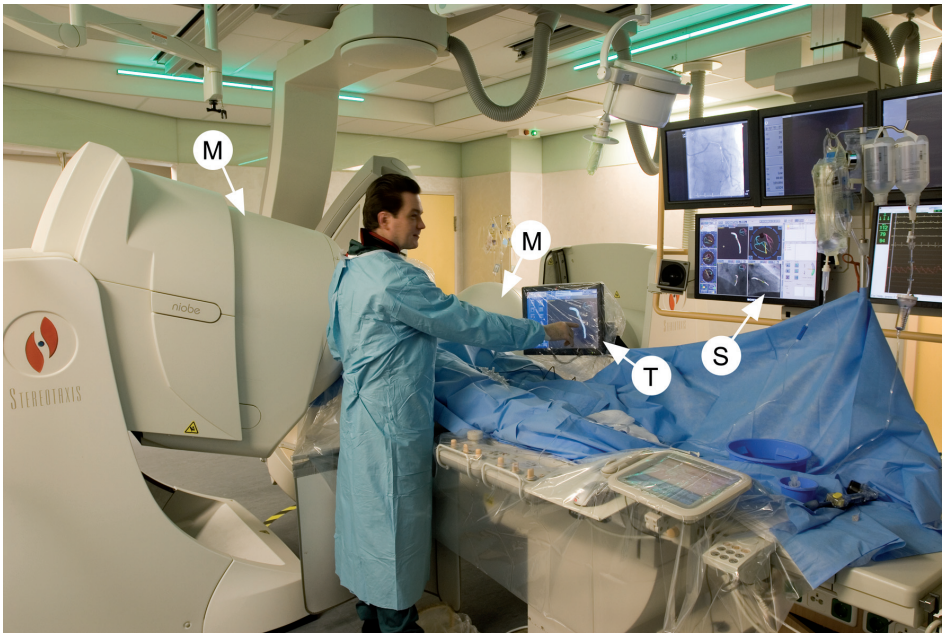

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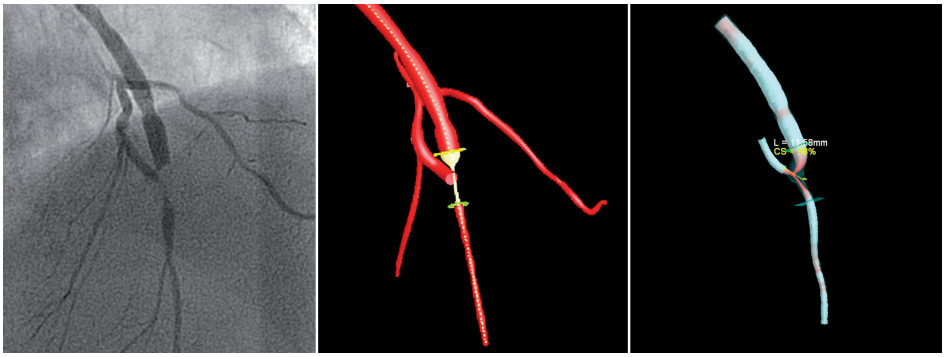

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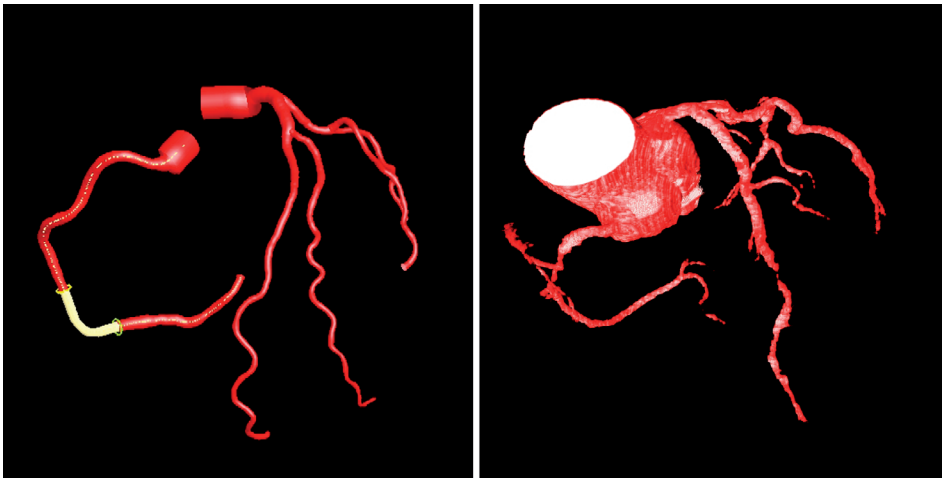

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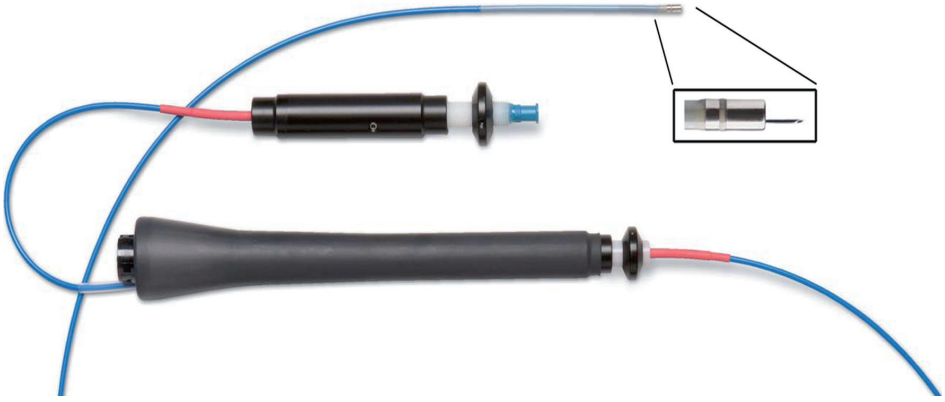

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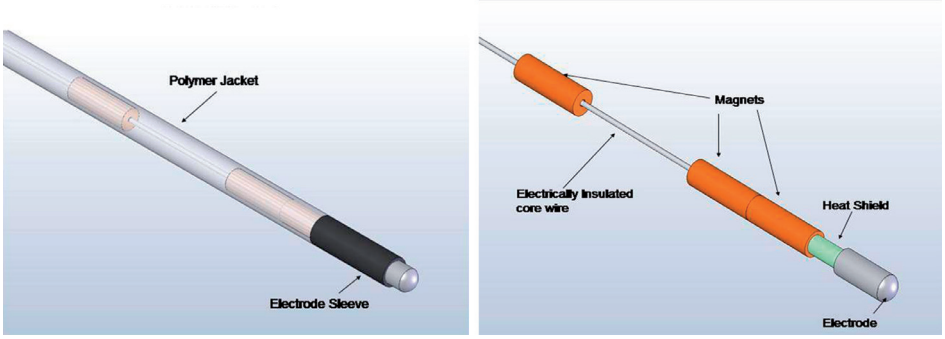

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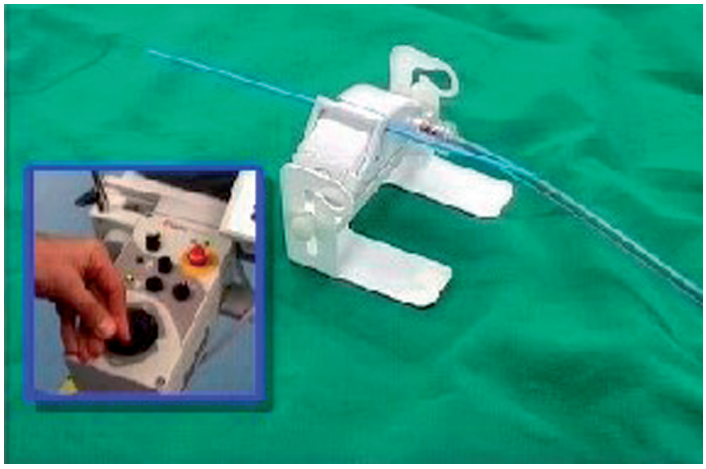

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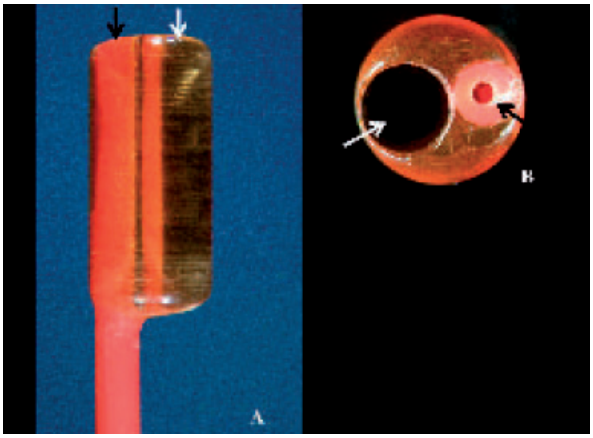

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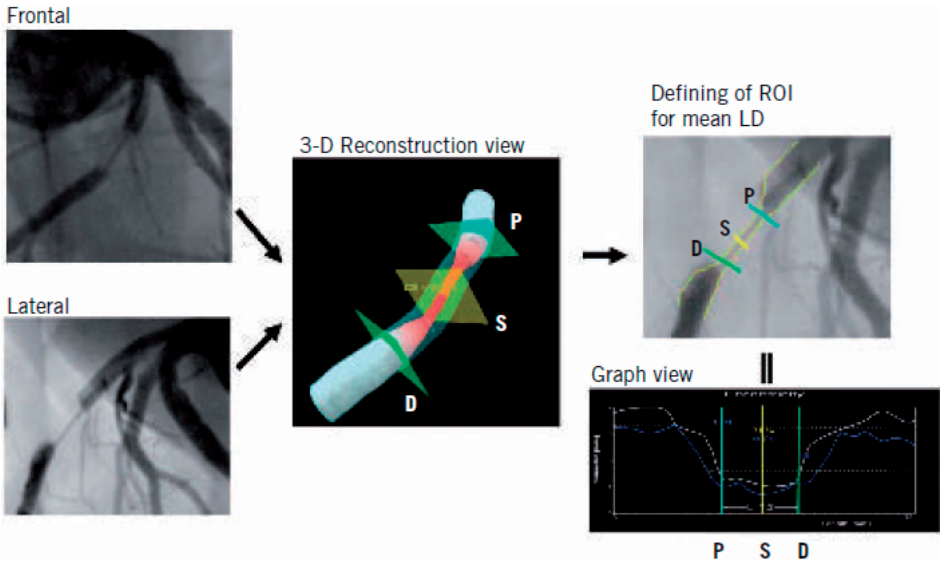

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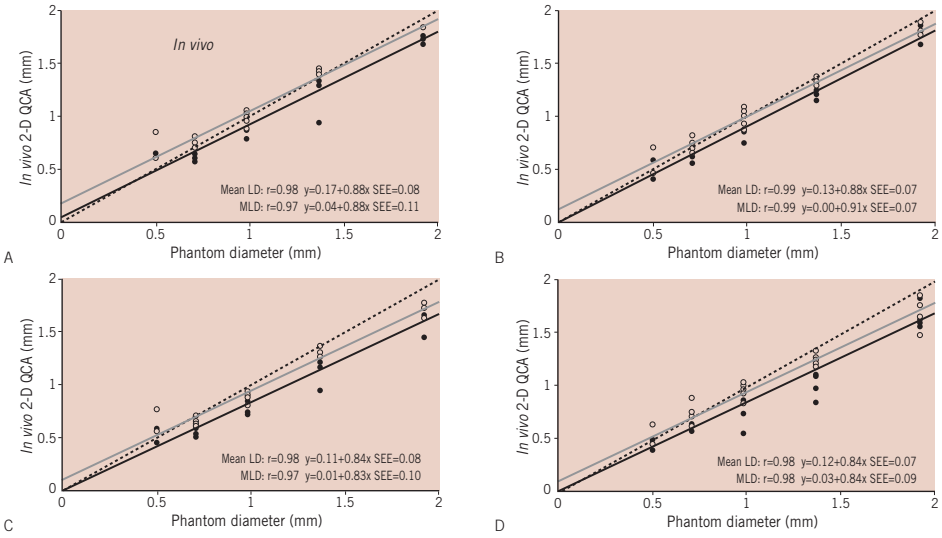

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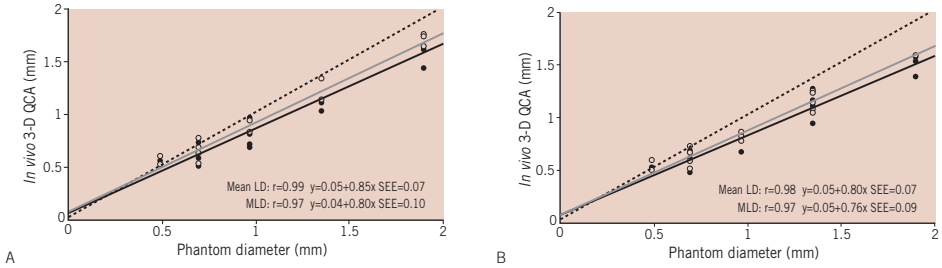

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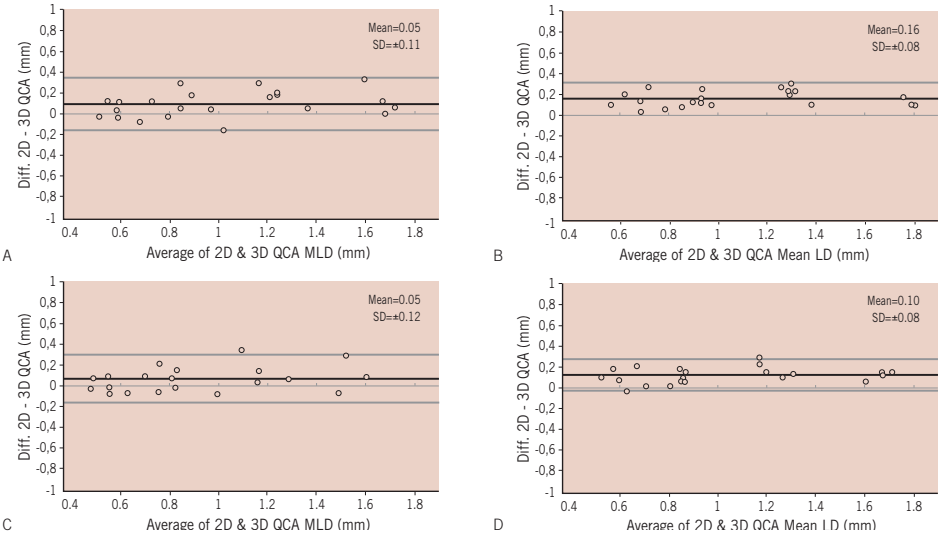

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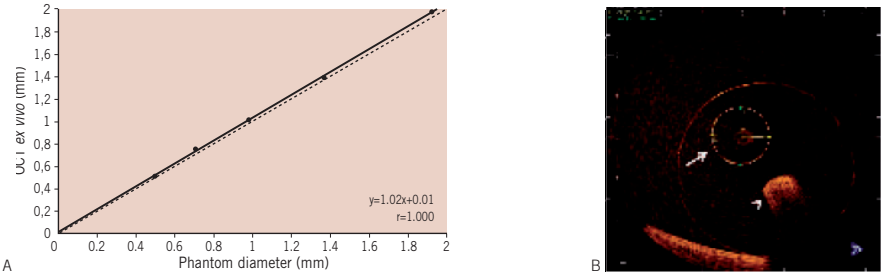

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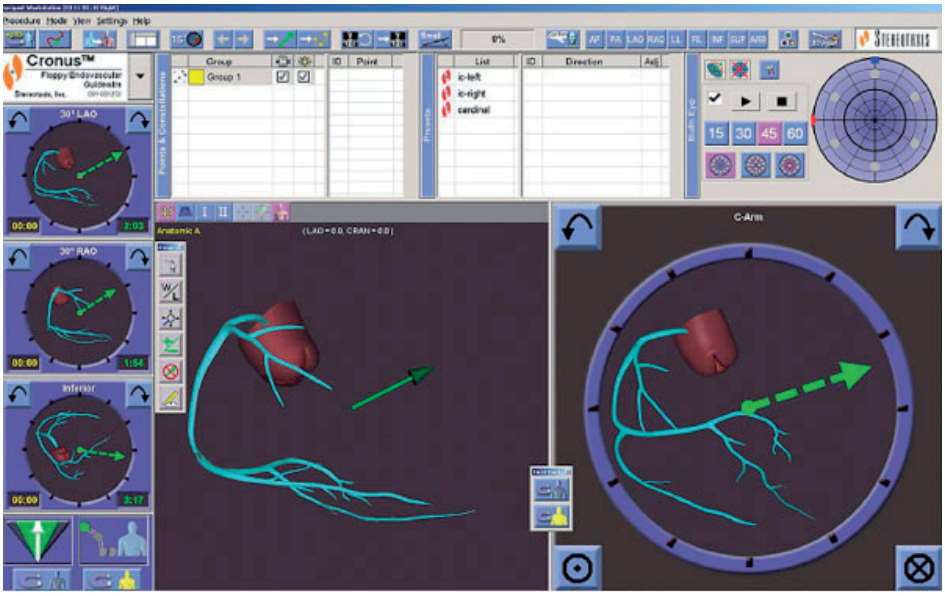

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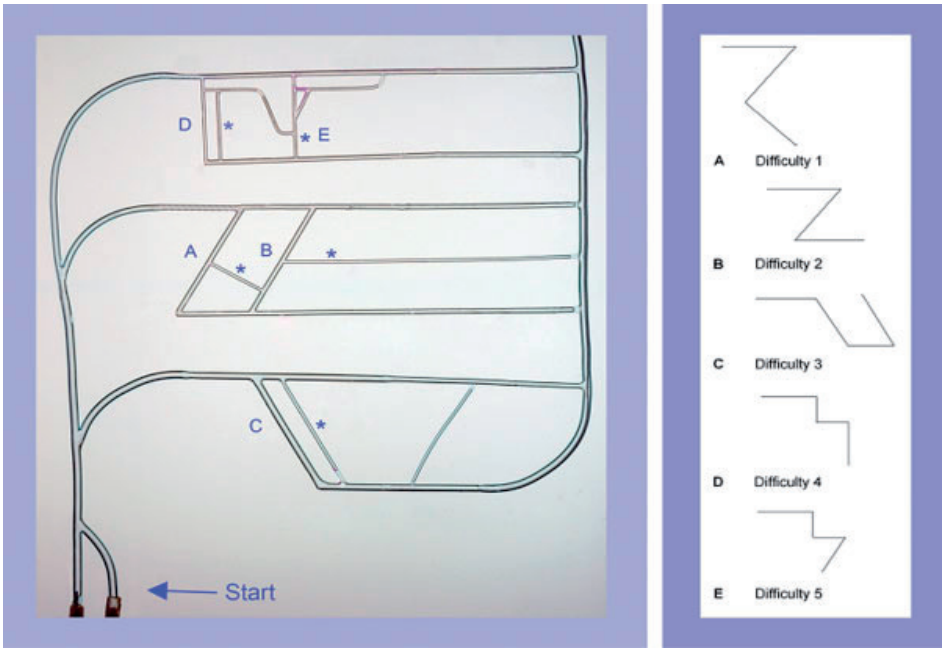

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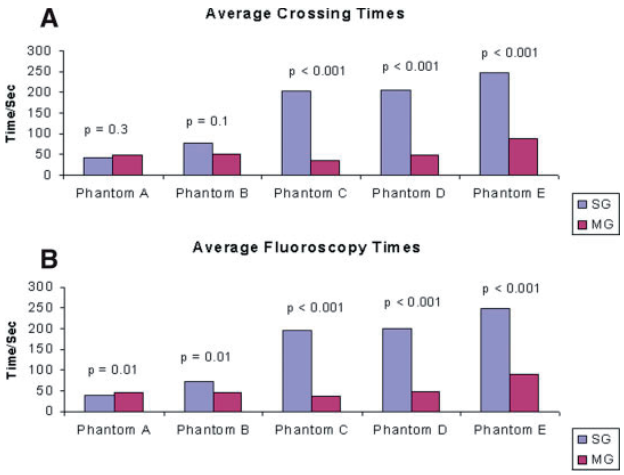

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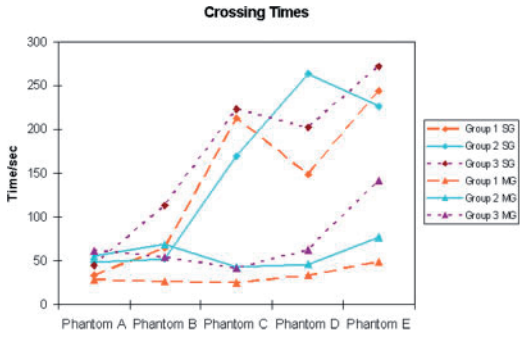

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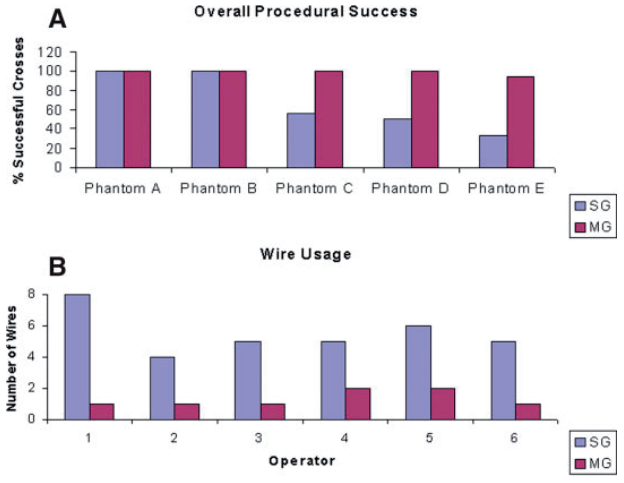

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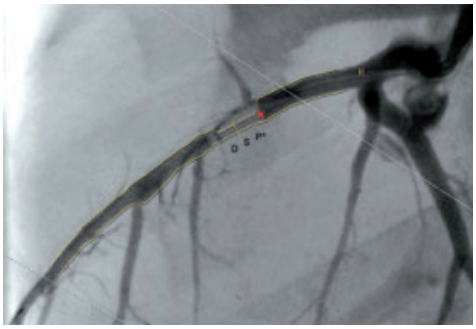

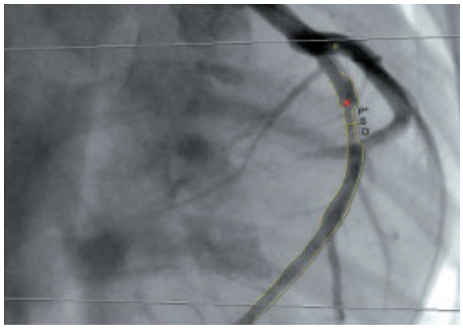

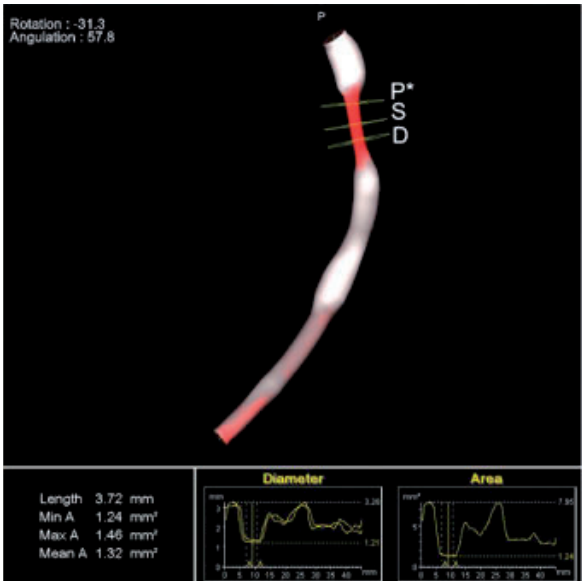

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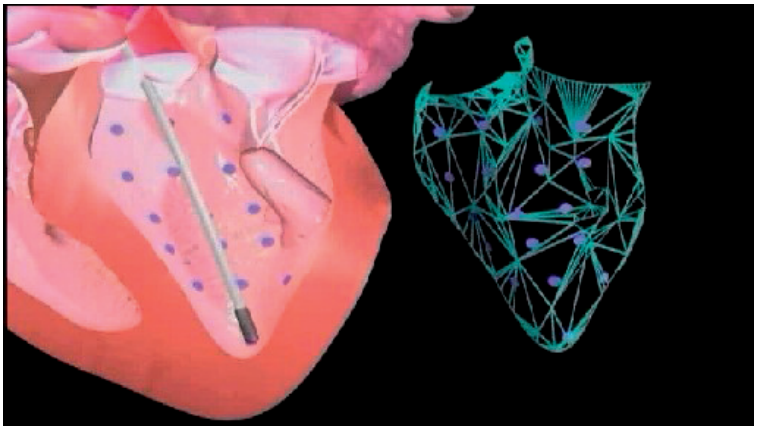

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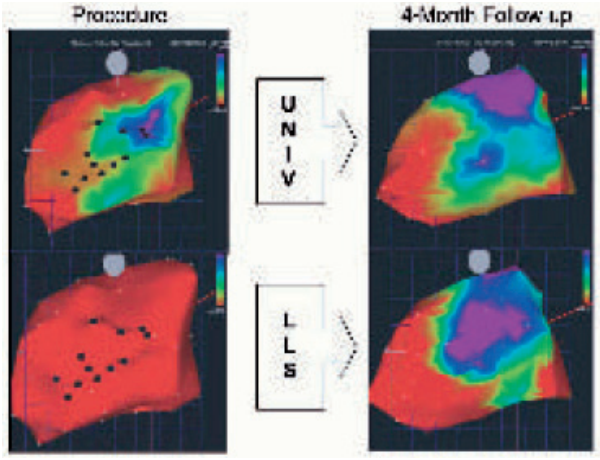

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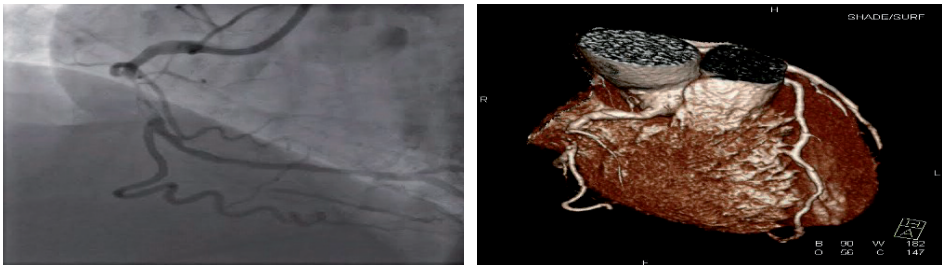

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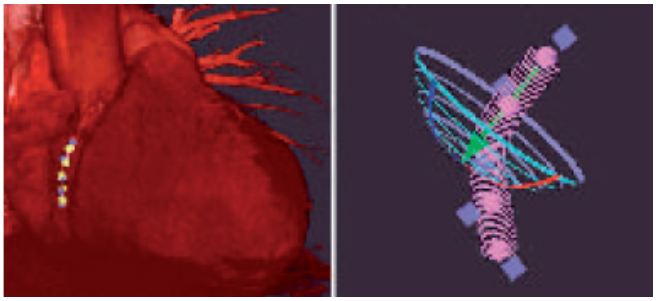

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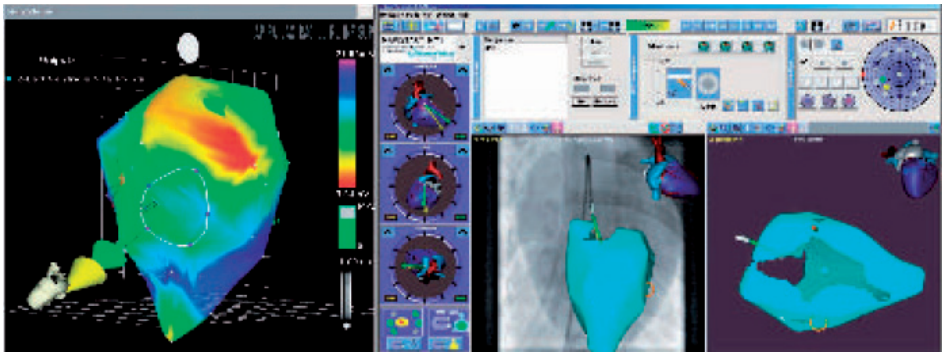

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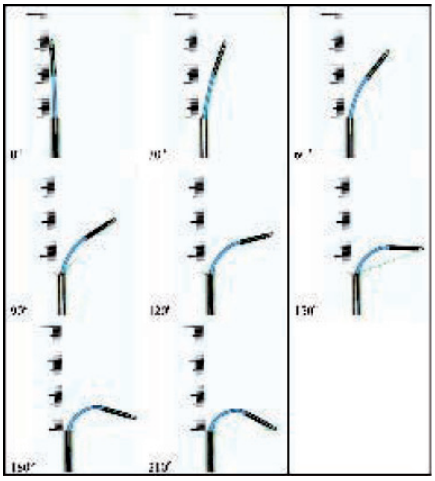

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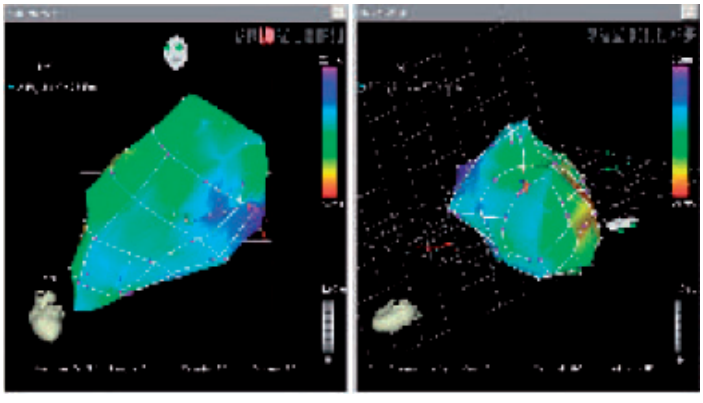

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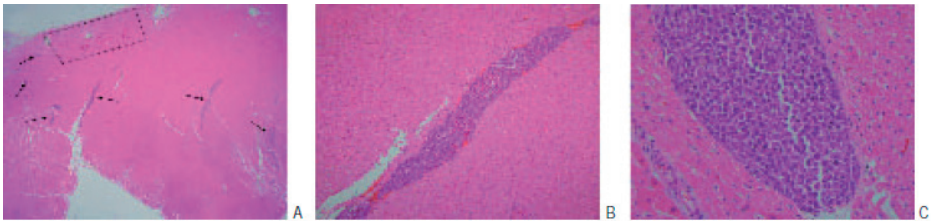

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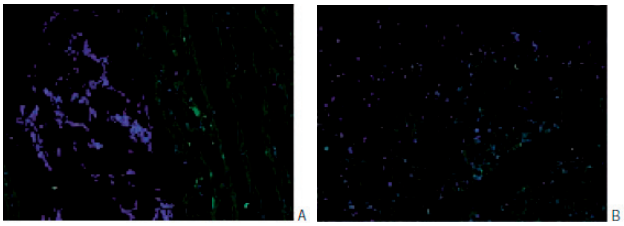

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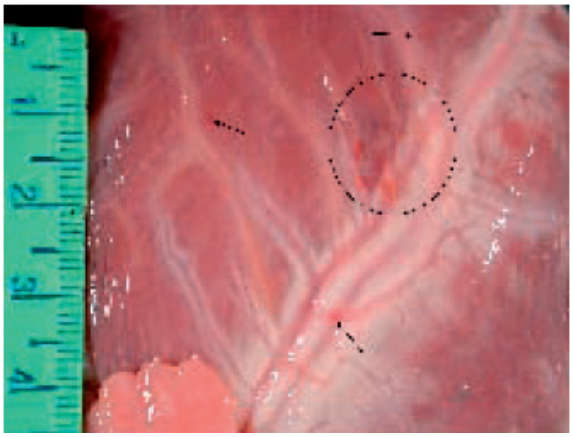

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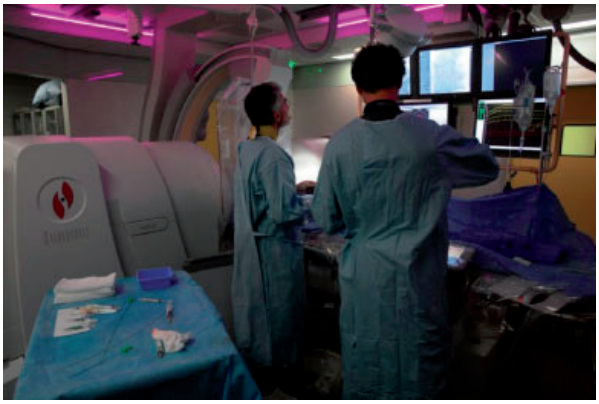

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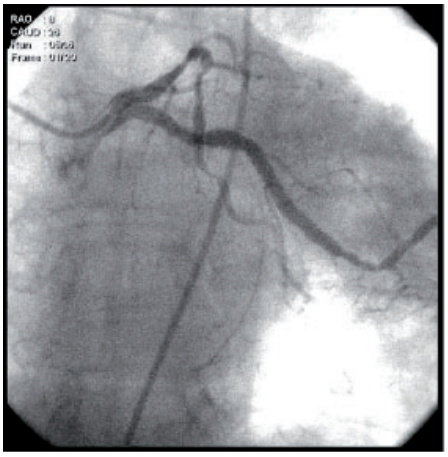

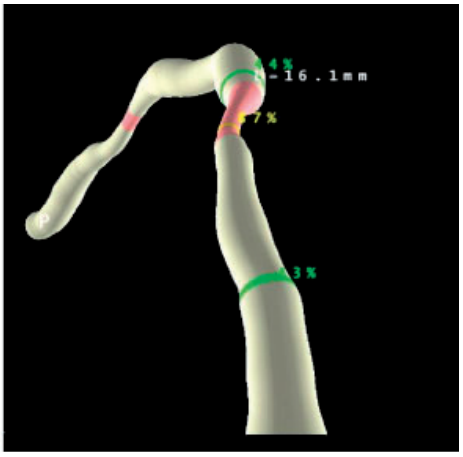

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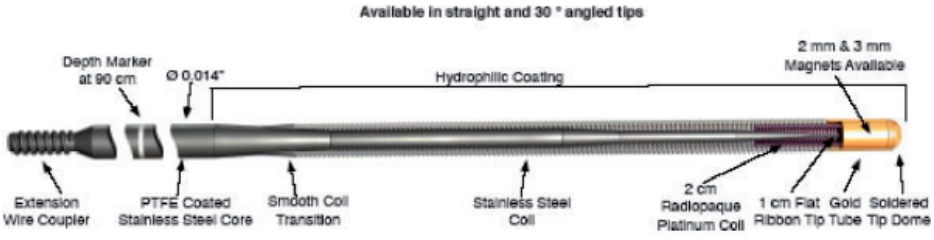

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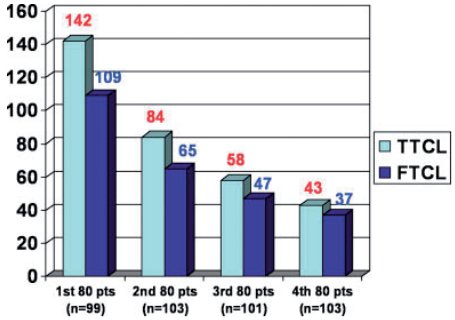

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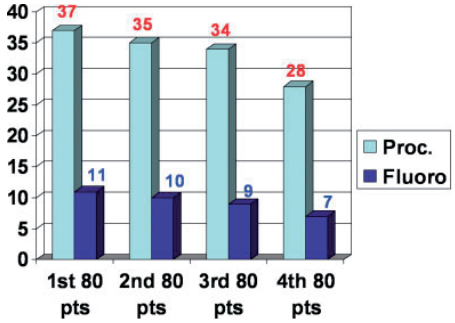

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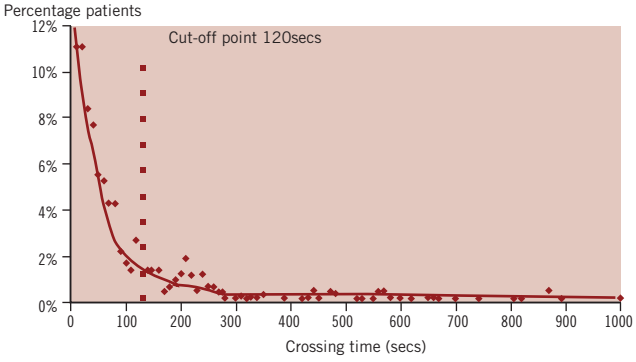

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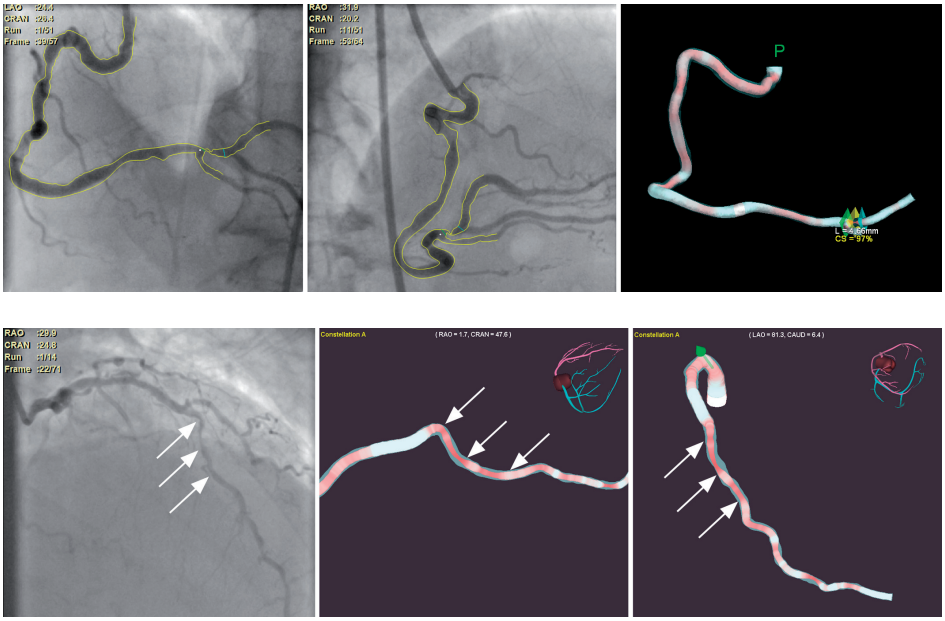

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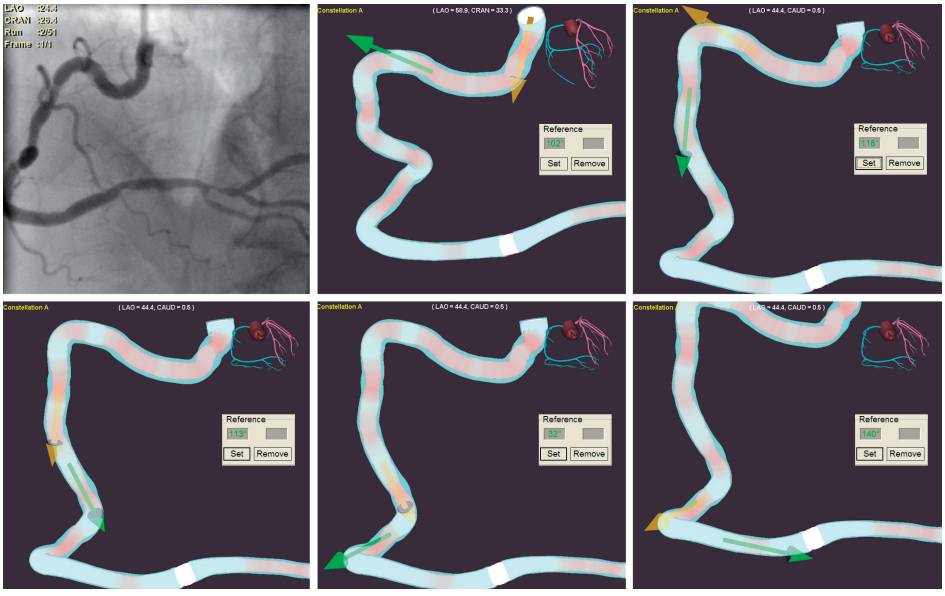

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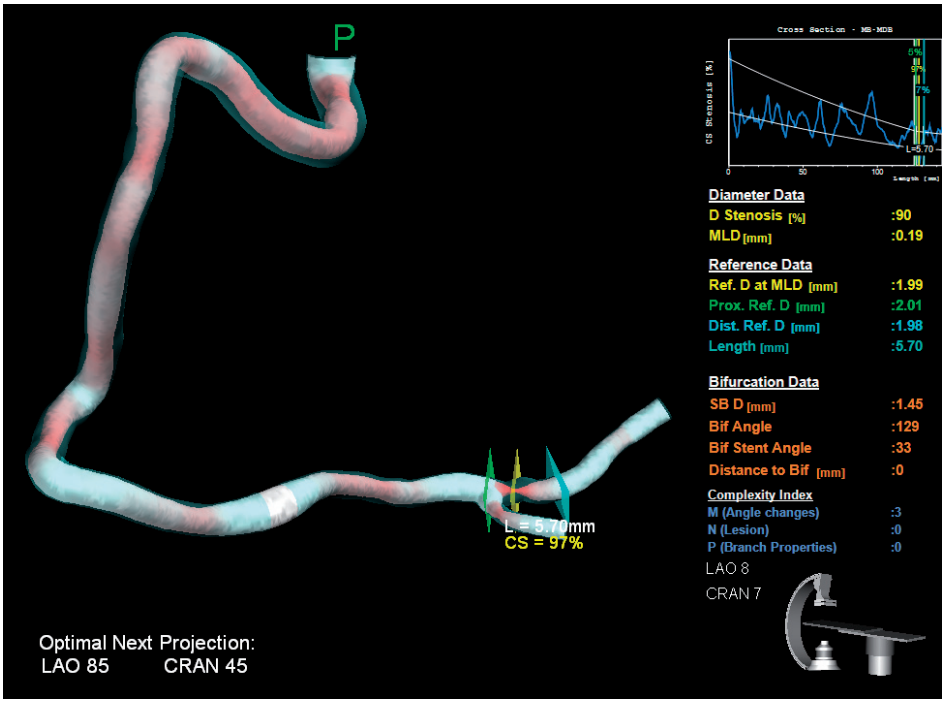

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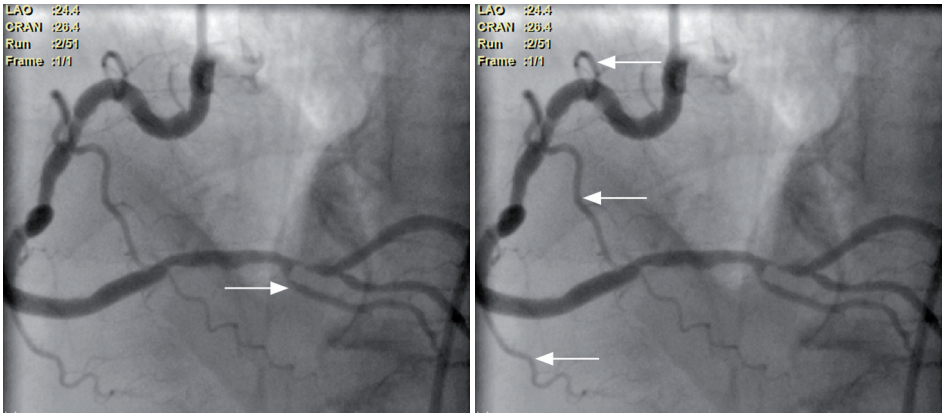

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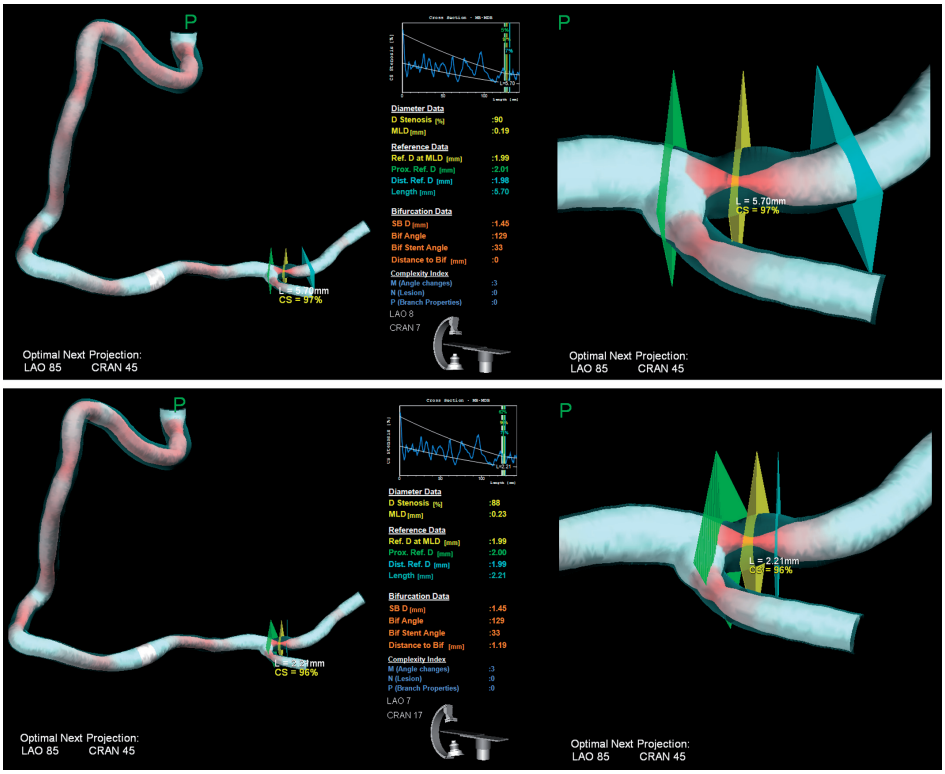

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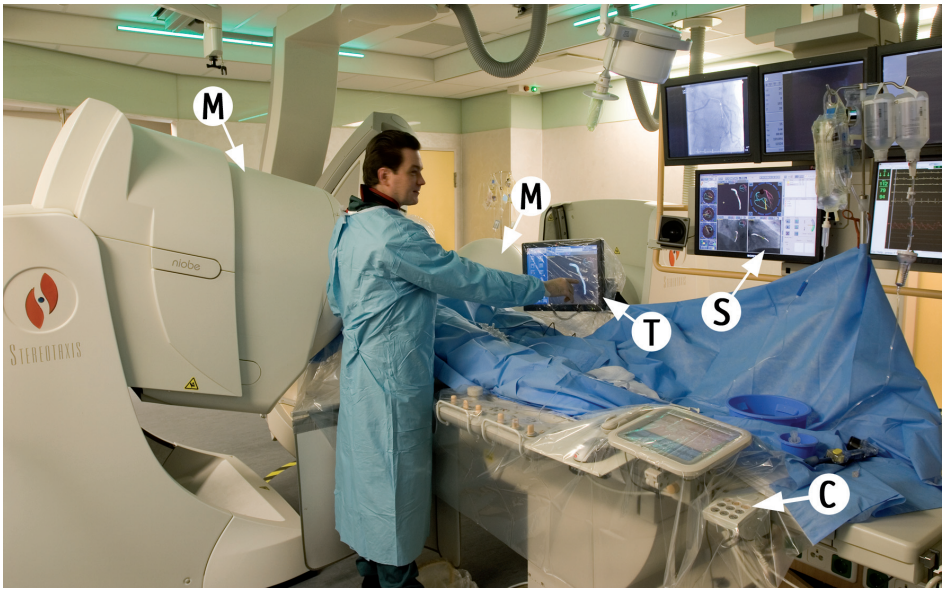

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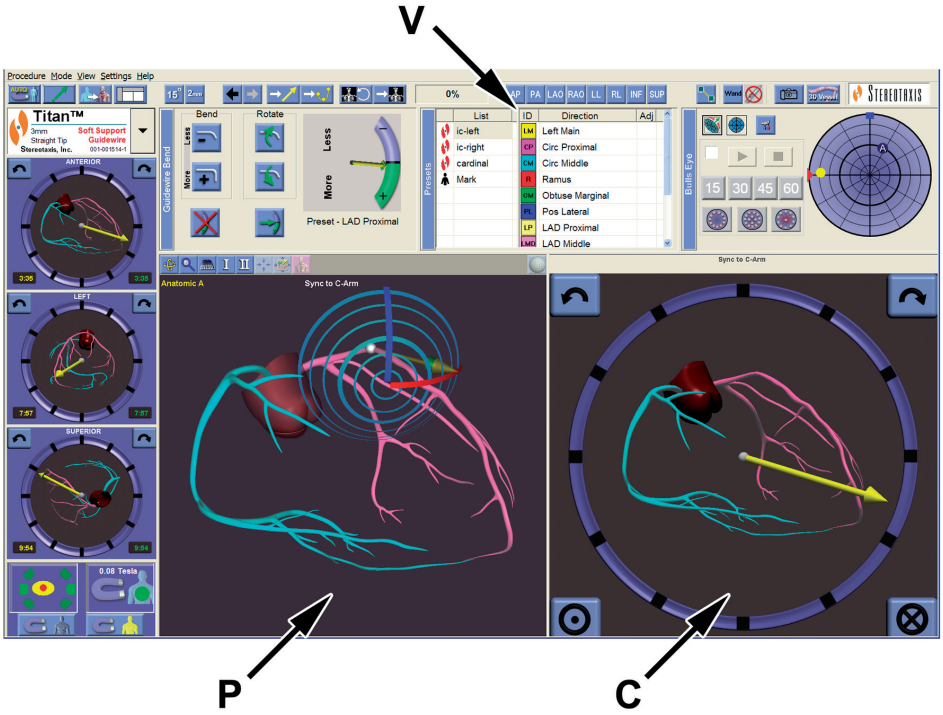

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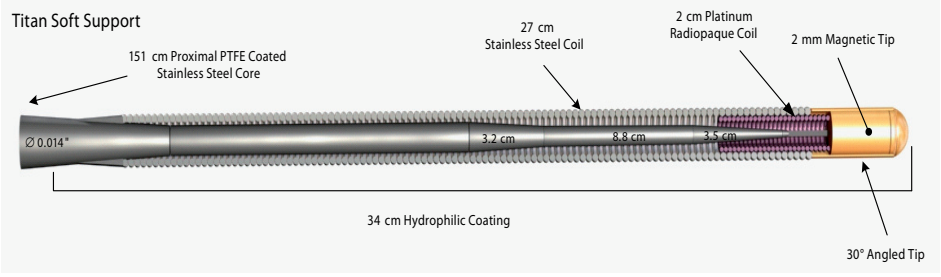

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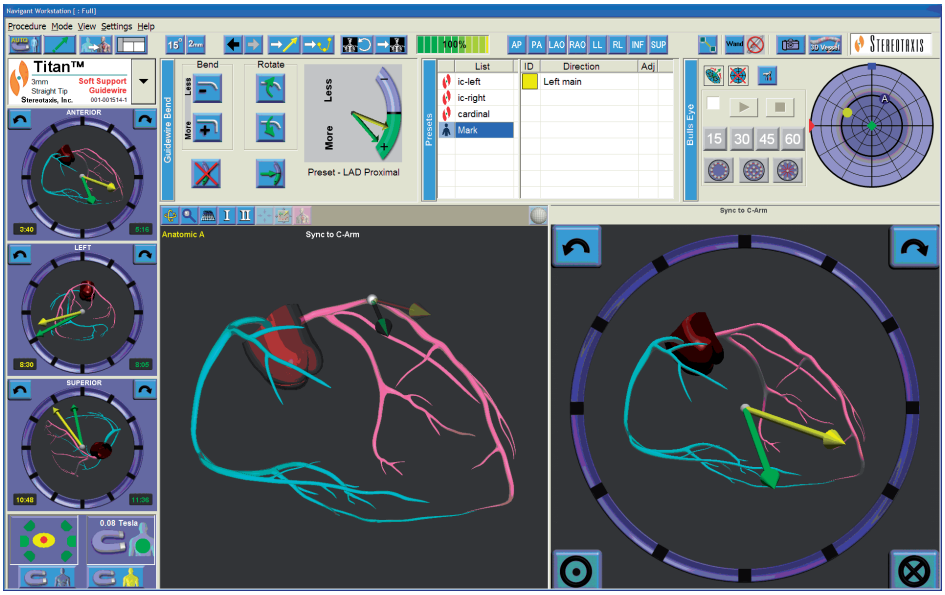

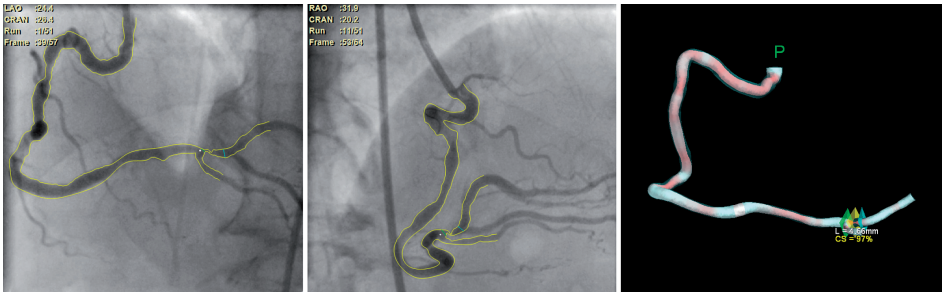

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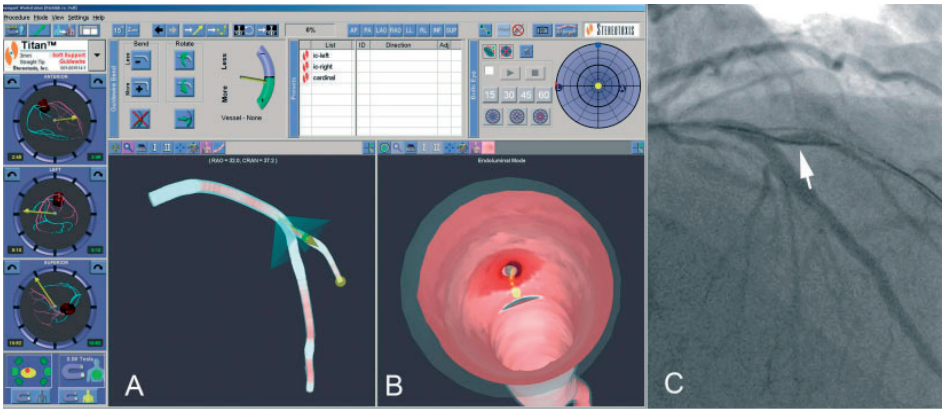
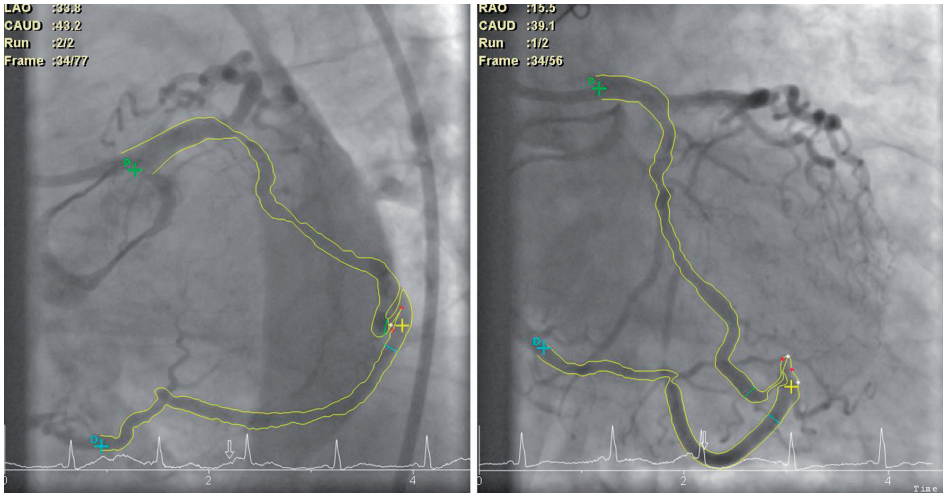
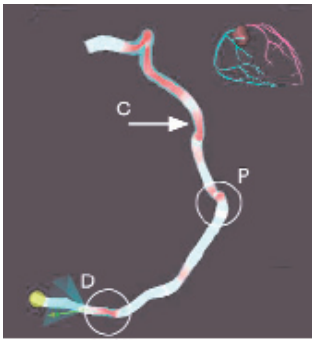


Chapter 17 Figure 2.



Chapter 18 Figure 3.



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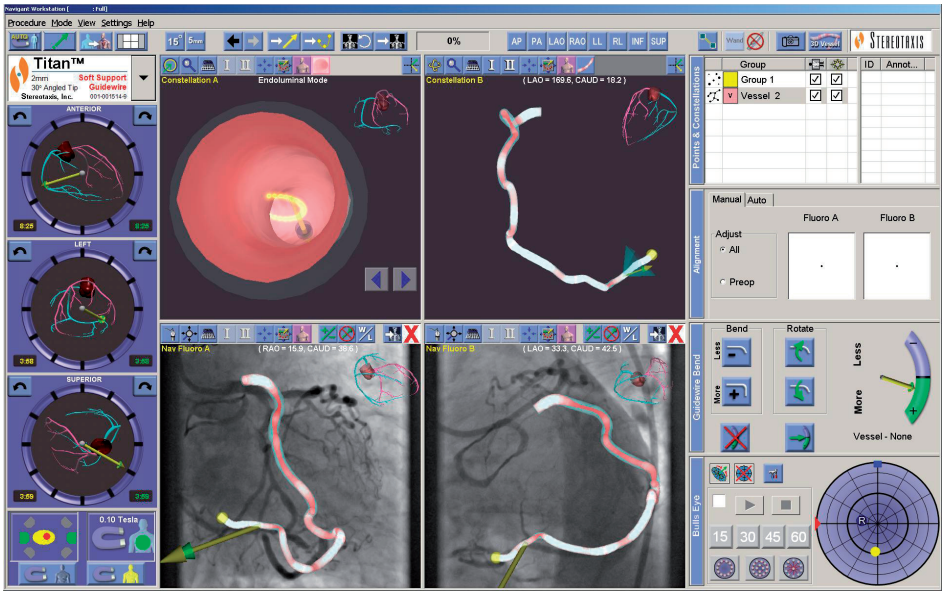

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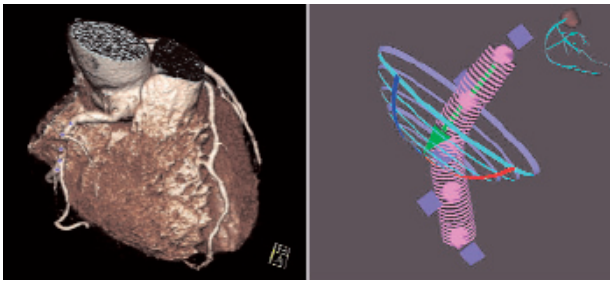

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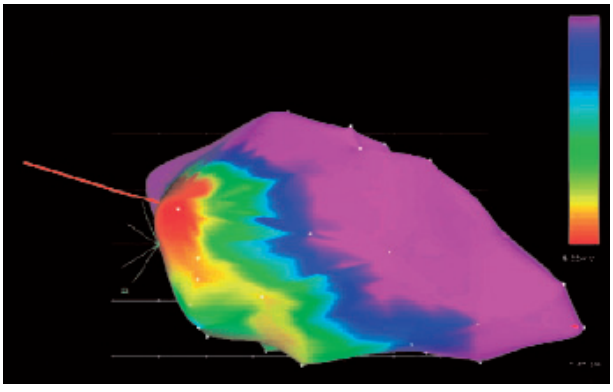

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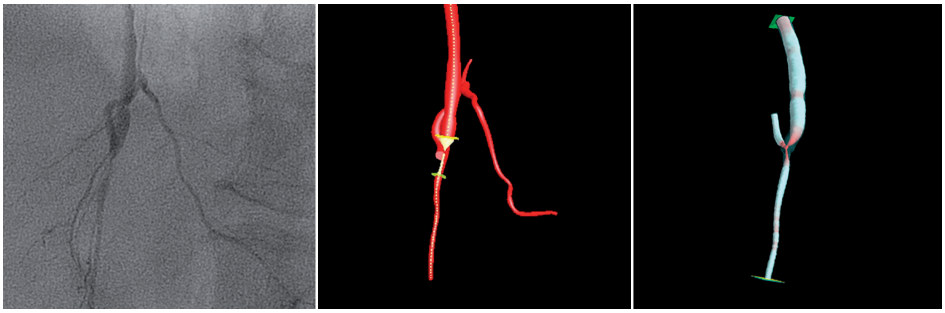
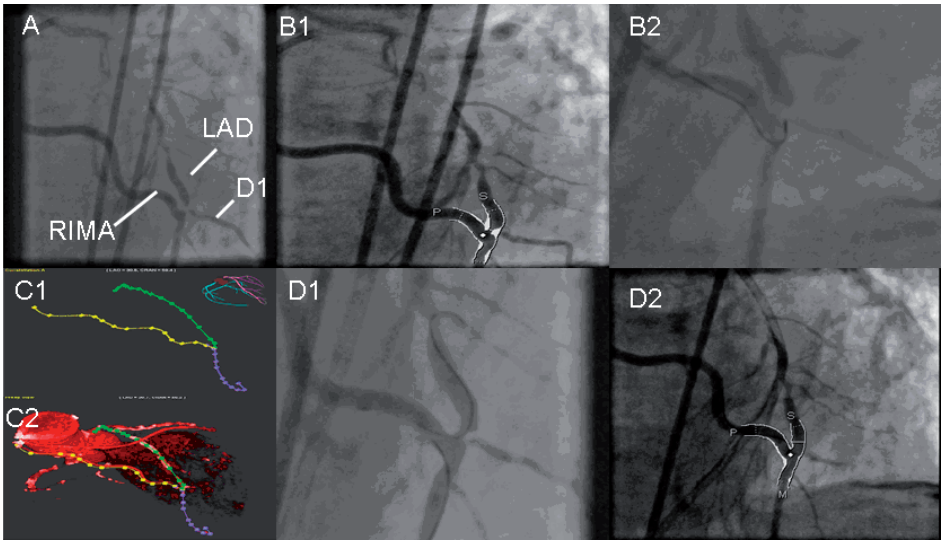
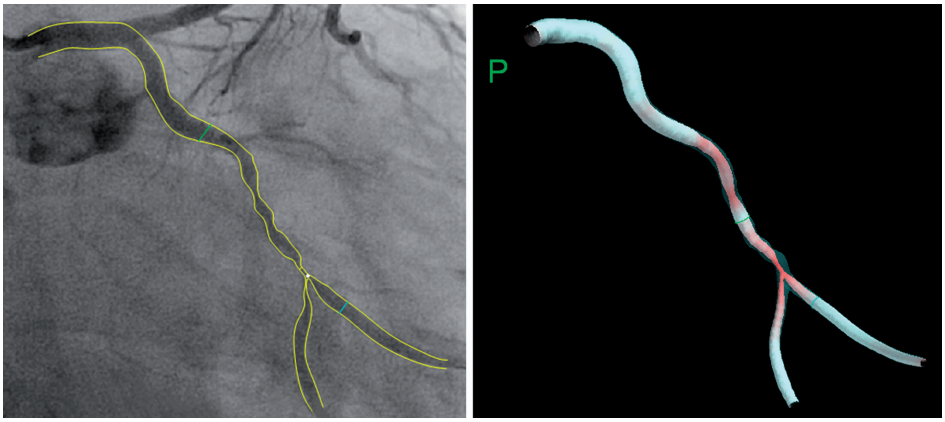


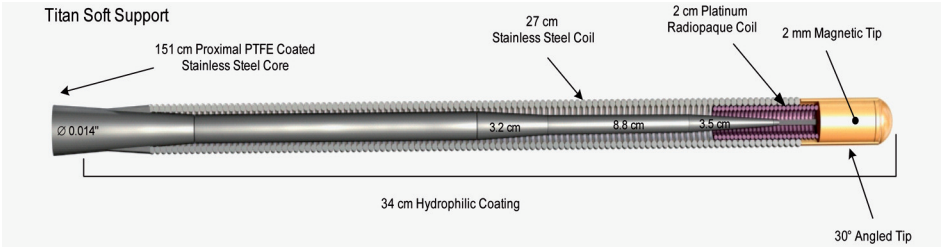
Chapter 19 Figure 2.



Chapter 20 Figure 2.



Chapter 21 Figure 5.



Chapter 22 Figure 3.