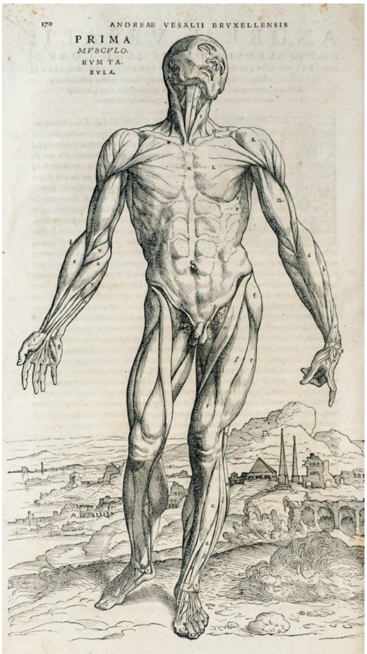
General introduction

“Primum non nocere”[1], “first, do no harm”. It is part of the Hippocratic oath that all physicians take. This serves as a reminder to all medical professionals to consider the consequences of their actions. 500 years later Ovidius, however in the book ‘Tristia’ stated: “nil prodest, quod non laedere possit idem”, “Nothing is useful which cannot at the same time be harmful.” In the medical profession we always deal with the double-edged sword; every cure has a potential for harm. Therefor our job is to minimize this harm by constantly improving our knowledge of anatomy and physiology. With the accent on the Anatomy where it concerns surgical approaches.

With the new insights in the anatomy of the forearm, as presented in this thesis and especially the new insights in the course of the various nerves in that proximity, the author tries to diminish the harmful side of an otherwise very helpful intervention. Thus, an attempt is made to prevent damage to these nerves during surgical intervention and consequently preventing neuropathic post-operative pain.

Hippocrates was the founder of modern medicine and the concept of evidence-based medicine. In the following centuries the anatomical knowledge was gathered by dissection of corpses of the deceased and evaluation of wounds. In the human, anatomy was mostly depicted in an artistic way. However, in 1543 Vesalius was the first to give a systematic description of the human body.



Surgery in the pre-anesthetic era was performed by barbers and barbers' apprentices and mostly consisted of amputations, wound management and fracture management. The need to study Anatomy was not very urgent, because the body was in fact never entered. Anatomy was studied by Medicinae Doctores who translated Arabic texts into Latin texts, mostly in a way botanists tried to categorize and inventory the (biological)world around them. Give every part of God's universe a name and place in the order which was created by the almighty.

Later, the history of surgery and anatomy became closely related; most surgeons where also anatomists. In between surgical interventions they studied the anatomy of corpses. Anatomical knowledge was key. A good surgeon in those days had to be fast, because of the lack of anesthesia. For example, a lower leg amputation in those days took twenty seconds instead of one hour[2]. In October of 1846 the first operation under general anesthesia was performed, a tumor was removed from Gilbert Abbot's jaw[3]. Since the invention of general anesthesia surgeons could take their time and develop new surgical techniques. The emphasis shifted from anatomical knowledge to finding new operating techniques.

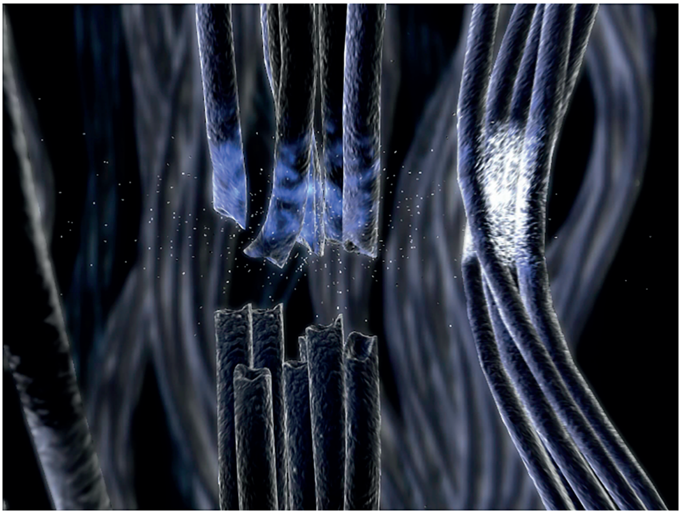
In the early days of surgery survival rates after surgery were very low. Finding new surgical techniques caused steep learning curves. The operations were tested on patients, often at the expense of these patients. At that time these high mortality rates were socially accepted because of the lack of alternatives. Nowadays post-operative fatalities of this magnitude are not accepted. These new social circumstances forces surgeons to return to the anatomy lab. Not only to try out new techniques on embalmed human specimens before implementing the technique in vivo, but also to improve existing techniques and to prevent per- and post-operative complications.

The doctor-patient relationship has changed significantly over the years[4]. Decades ago the patient came to the surgeon with a problem and dared not question his advice. Now the patient is much more informed and starts discussions with the doctor. They complain more about post-operative complications, such as pain, because they know it doesn't always have to be "just part of the surgery". The surgeon is forced to investigate why patients have pain after surgery.

But what is pain exactly? "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage."[5] The reason for pain is to make us think about the cause of the pain and prevent further damage. As such, pain can be seen as a protective mechanism. When a person is in pain after trauma this is called nociceptive pain. Nociceptors register pain and pass this on to the central nervous system and the brain, if there is no stimulus this pain fades. Another form of pain that can occur postoperatively is neuropathic pain. This is pain caused by damage or disease of the peripheral or central nervous system and causes pain and also hyperalgesia.[6]

The cause of neuropathic pain until now is not clearly identified. It remains unclear at which level the actual problem is located: distal segment, Dorsal Root Ganglion or even central parts of the nervous system[7]. It has been postulated that Nerve Growth Factor (NGF) plays a role in neuropathic pain[8-11], although the exact mechanisms remain unclear[12,13]. When a nerve is transected, Schwann cells, but also other cells, produce NGF's[14,15] in the entire distal segment of this transected nerve. This production is being initiated by the axonal degeneration and the Schwann cell up-regulation, also known as Wallerian degeneration.

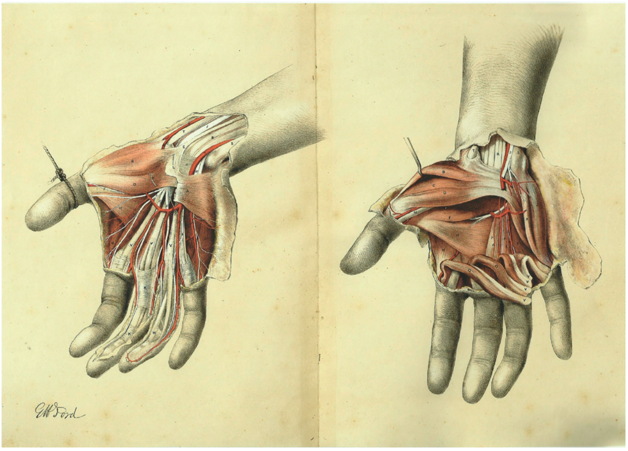
This suggests that if two nerves overlap anatomically the increase of secretion of NGF that is mediated by the injured nerve, results in binding to the high affinity NGF receptor, tyrosine kinase A (TrkA). This in turn leads to possible sprouting and morphological changes of uninjured fibers, that ultimately causes neuropathic pain. This pain causes severe socio-economic problems [16,17], such as partial or even full disability. Many studies have tried to find a treatment for neuropathic pain, but no definitive solution has been found. Neuropathic pain remains a hard to treat problem[18]. Many medicinal interventions have been tried but did not have the desired effect[19], also surgical interventions are not always successful.



One of the most frequent complications after wrist surgery is pain[20-23]. Following the above-mentioned theory this pain could be result of the close anatomical relation between the nerves of the forearm, such as the Lateral Antebrachial Cutaneous Nerve (LABCN) and the Superficial Branch of the Radial Nerve (SBRN). In order to prevent neuropathic pain two problems should be addressed. First the complex anatomy of the forearm should be better understood and second, as a consequence, surgical procedures should be adapted and improved accordingly to prevent damage in high risk areas.

Considering the infamous resistance of neuropathic pain to treatment, it is better to prevent nerve damage during surgical intervention than to treat the post-operative pain afterwards.

The wrist is one of the most complex anatomical regions in the human body. It starts out with the wrist joint. In the human body, based on the defining movement axes several kinds of joints are described: Hinge, pivot, ball and socket, saddle, condyloid and gliding joints. The wrist is the odd man out. Morphologically the wrist joint as a whole cannot be categorized other than a compiled joint. But functionally it closely resembles the range of motion as seen in a ball and socket joint[24-26]. The arrangement of the bones in the wrist makes it very unstable, therefore a complex configuration of ligaments stabilizes the joint. Another odd fact of the wrist is that there is no muscle group directly in the proximity of the wrist. All movement comes from muscle (bellies) situated in the forearm. Finally, the anatomy of the nerves in the distal forearm is very complex. The nerves are closely interrelated. Due to the embryological (segmental) development, the distribution area's show overlap and the branches of the nerves sometimes physically touch and cross each other. This makes the wrist susceptible to neuropathic pain.



History teaches us that new theories can give new insights into well-established facts. Many researchers have studied the anatomy of the nerves of the forearm [20,27-32], however none have studied the course of the nerves with attention to the above-mentioned theory. In general, Anatomy is seen as a static science. Since Vesalius wrote his major work on the human anatomy, it is sometimes thought that there cannot be any 'new anatomy'. However, the opposite is true. Each time the human body is asked a new question, the body gives a new answer and 'new' anatomy emerges. That's to say, the structure has been there forever, but the context and the relevance are new. In addition, new computer techniques made it possible to have a new perspective on anatomy. Computer Assisted Surgical Anatomy Mapping (CASAM) is a novel computer program in which photos of multiple objects of different size but overall same shape can be warped in such a way that they will have the same dimensions and therefore can be compared directly. In short: out of about 20 specimen, an average specimen can be construed and so for instance, the arm of a 40-year-old, muscular female specimen can be compared to a small, cachectic, 80-year-old male specimen. Using this visual tool, it was possible to identify safe zones and possible danger areas with regard to overlap of the nerves. These images in turn were used to consider other incision techniques to possibly prevent neuropathic pain.

By dissecting specimens and uploading the photos in the CASAM system, the images of the dissected specimens can be warped and can then be analyzed. CASAM can be used for purely anatomical purposes, such as the course of a nerve in the forearm. But besides the anatomical purpose, CASAM can also be used to improve the way we learn surgical techniques. By testing surgeons' technique against the database of nerves, a direct feedback loop can be established to improve learning and diminish the learning curve.

To acquire new information not every person would benefit from the same method. It has been known that some people are best served by reading a book and others rather see pictures or moving images[33]. Up until now surgical research has been presented in the form of texts and tables. The use of CASAM creates a new dimension in learning and should be added to other teaching tools. By creating a picture, the instruction is optimized as the warped average structure tells us the same as a text and a table combined. For surgeons who are visually oriented this tool could help them to optimize their operation strategy pre-operatively.

THESIS OUTLINE.

For this study a surgical complex region was chosen: the dorsolateral side of the forearm. Complex in several ways. The anatomy of the wrist comprises of lots of anatomical structures in close relationship to each other. There is a wide range of described injuries in the wrist and consequently, a lot of different surgical procedures are performed in this region.

In this thesis the anatomy forms the starting point. Forearms were extensively dissected and three nerves were studied. The Superficial Branch of the Radial Nerve (SBRN), the Lateral Antebrachial Cutaneous Nerve (LABCN) and the Dorsal Branch of the Ulnar Nerve (DBUN). During the dissection process recurring patterns in the course of the SBRN were discovered and in **Chapter 2** newly identified patterns of the SBRN were explained which could help prevent iatrogenic damage to the nerve.

The DBUN was also investigated for recurring patterns in the course of the nerve. In **Chapter 3** the course of the DBUN is described in detail using new techniques that were not used previously for the mapping of the nerves in the forearm.

Using this new technique, the course of various nerves in different specimen could be visually compared. In **Chapter 4** we show the correlation between the LABCN and the

SBRN. The close proximity of the two nerves could explain why neuropathic pain of the forearm is such a big and hard to treat problem.

In **Chapter 5** anatomical variation in the anatomy of the carpal bones of the wrist is demonstrated. The fusion of the trapezoid and scaphoid bone caused an alteration in the complex movement of the carpalia causing pain in the scapho-lunate ligament area.

Using the database of nerve patterns, we compare existing incision lines in the wrist against the course of the nerves of the forearm. In **Chapters 6&7** we try to use the knowledge learned in the earlier studies to improve the surgical techniques in order to prevent neuropathic pain.

In **Chapter 6** the 'golden standard' locations of Schanz pins for external fixation of distal radius fractures is evaluated with regard to the course of the nerves in the forearm. When using the 'golden standard' there is risk for damage to neurological structures. A new proposed insertion site is contemplated and tested in relation to the mapped neural anatomy and on cadaver arms.

The surgical techniques for the release of the first extensor compartment as a treatment of Quervain's Disease are studied and covered in **Chapter 7**. Four widely used techniques are compared to the course of the SBRN and the LABCN from our database and recommendations are given accordingly.

The upcoming technique of wrist arthroscopy was also examined. Although wrist arthroscopy has been around since the early 70's it was initially meant as a diagnostic tool. In the last decade it is used more and more as a therapeutic tool, increasing the chance of iatrogenic damage. Younger, less experienced surgeons are also adopting this technique. In **Chapter 8** we analyzed the arms of embalmed human anatomic specimen, used in a wrist arthroscopy workshop and assessed the anatomical damage that had occurred.

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