



Feature Topic: Stents in Clinical Practice

Morphologic Change in Coronary Artery Stenosis With the Medtronic WiktorTM Stent: Initial Results From the Core Laboratory for Quantitative Angiography

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The purpose of this study was to assess the early changes in stenosis geometry after implantation of the Medtronic WiktorTM stent in human coronary arteries. Morphologic changes were evaluated by quantitative coronary angiography using automated edge detection. The hemodynamic significance of the morphologic changes were assessed by the calculation of the theoretical pressure drop across the dilated and stented stenosis derived from the Poiseuille and turbulent resistances assuming a coronary blood flow of either 0.5, 1, or 3 ml/sec. Fifty patients were studied before and immediately after stent implantation. The stented coronary artery was the left anterior descending artery in 26 patients, the circumflex artery in eight patients, and the right coronary artery in 16 patients. Stent implantation resulted in an additional increase in the minimal luminal cross-sectional area and minimal luminal diameter of the dilated vessel without changing the curvature of the stenosis. Furthermore, there was a significant reduction of the "plaque area." This was associated with a normalization of the calculated resistances to flow and pressure drop across the stenosis. To a minimal extent, recoil (0.1 ± 0.36 mm) was observed after stent implantation.

Key words: coronary stent, quantitative analysis, stenosis geometry

INTRODUCTION

Percutaneous Transluminal Coronary Angioplasty (PTCA) is now accepted as a safe and effective therapy for obstructive coronary artery disease. Gained experience and improved catheter technology have resulted in a high initial success rate [1-3]. These favorable initial results are offset by a restenosis rate of 30% to 40% during the first 6 months after the procedure [4-5]. Stenting of the dilated vessel may offer an alternative approach for the prevention of restenosis [6]. Different prostheses have been developed and tested in animal experiments and implanted in humans [7-11]. The WiktorTM stent (Medtronic Inc., Minneapolis, Minn. USA) is a new intravascular prosthesis which, in contrast to the Wallstent[®] (Schneider, Zürich, Switzerland) and Palmaz-Schatz[®] stent (Johnson & Johnson, Warren, USA), is not a mesh made of stainless steel, but a radiopaque single loose interdigitating tantalum wire which undergoes oxidation after implantation. The resultant oxide (TaO₅) is not only very stable, implying less changes in surface charge, but also corrosion resis-

tant [12]. Potentially, the smaller amount of endothelial surface covered by the stent (less than 10% of the vascular endothelium is covered by a full expanded stent) in conjunction with the electrochemical characteristics of this stent protect against thrombus formation. As a result

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of the loose configuration, it has been hypothesized that the WiktorTM stent accommodates more adequately to the natural bending of the coronary artery in contrast to the stents with a more rigid and stiff mesh architecture such as the Palmaz-Schatz[®] stent. The WiktorTM stent, like the Palmaz-Schatz[®] stent, is a balloon expandable endoluminal prosthesis and does not exert an active radial force on the vascular wall after deployment as occurs with the Wallstent[®] [13]. However, the loose configuration of the WiktorTM stent may have less scaffolding properties compared to the other two intravascular prostheses.

The purpose of this study was to assess the early morphologic changes in stenosis geometry, including the occurrence of recoil, by quantitative coronary angiography and to assess the physiological significance of these changes by calculating the pressure drop across the stenosis for a theoretical blood flow of 0.5 to 3 ml/sec after WiktorTM stent implantation in human coronary arteries.

MATERIALS AND METHODS

Patients

Fifty patients (45 male, five female, median age 57 years—range 30–77) were studied. The patients were treated and investigated in the following centers: Department of Cardiology, Hôpital Cardiologique Lille, France, Department of Cardiology, Klinikum der J.W. Goethe Universität Frankfurt, Germany, Department of Cardiology, Ottawa, Ontario, Canada, Department of Cardiology, University Hospital Gasthuisberg, Leuven, Belgium, Department of Cardiology, Medical Clinic I RWTH Aachen, Germany, Department of Cardiology, Georg August Universität, Göttingen, Germany, and the Catheterization Laboratory, Thoraxcenter, Rotterdam, Netherlands. Written informed consent was obtained from every patient. WiktorTM stent (Medtronic Inc., Minneapolis, Minn., USA) was implanted because of a first restenosis of a native coronary artery in 33 patients, a second restenosis in 12 patients, and a third restenosis in five patients. In all patients objective evidence of ischemia was documented. The dilated and stented coronary artery was the left anterior descending artery in 26 patients (62%), the circumflex artery in eight patients (16%), and the right coronary artery in 16 patients (32%). The nominal diameter of the balloon on which the stent was mounted was 3.0 mm in 23 patients, 3.5 mm in 20 patients, and 4.0 mm in seven patients (14%). The nominal diameter of the balloon for the total study group (mean \pm SD) was 3.35 ± 0.36 mm.

Description of the Stent

The endoprosthesis used in this study is a balloon-expandable stent (WiktorTM, Medtronic Inc., Minneapolis, Minn., USA) constructed of a single tantalum wire

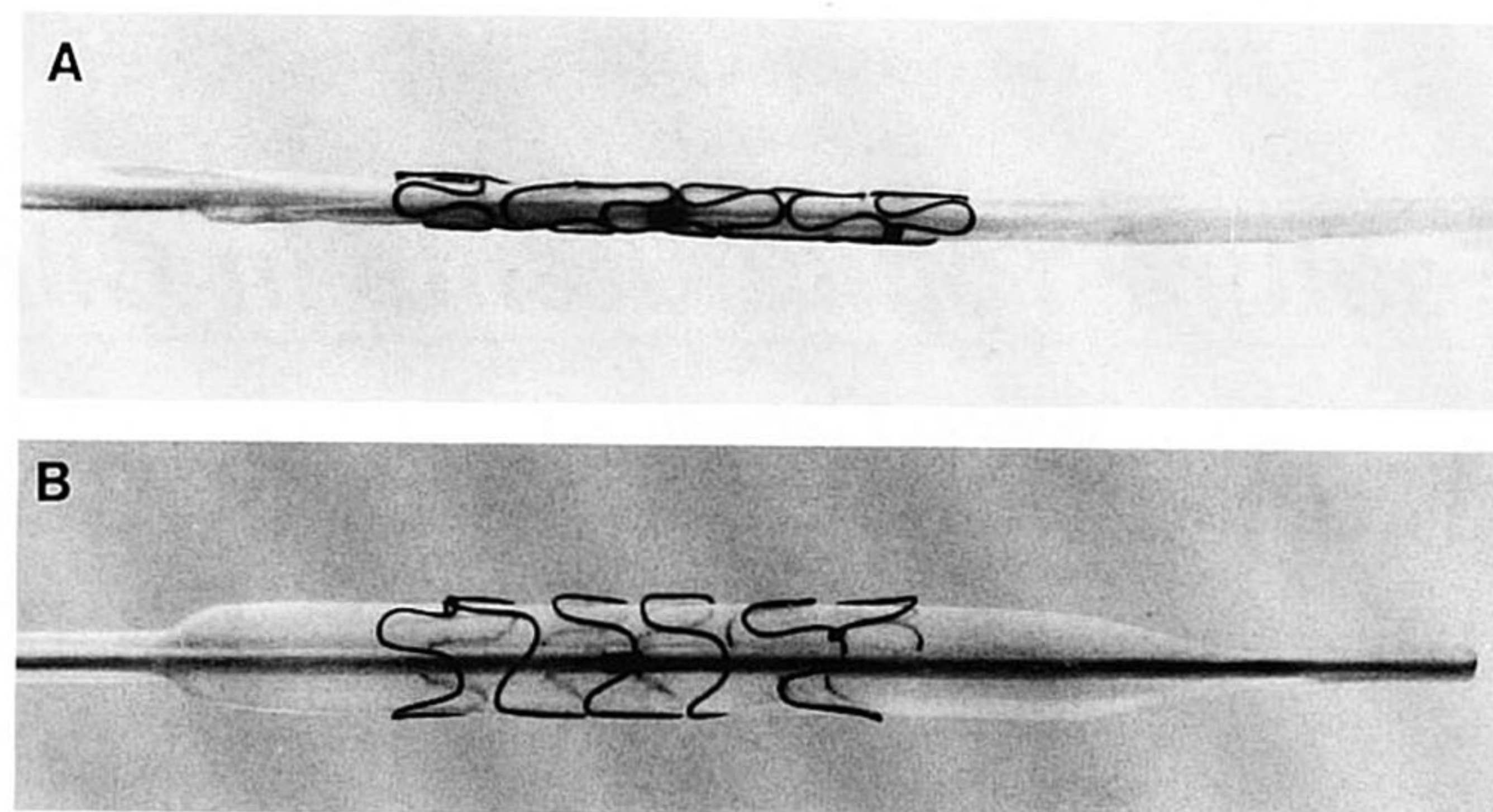


Fig. 1. a: WiktorTM stent crimped onto an polyethylene angioplasty balloon before inflation. b: WiktorTM stent on fully inflated angioplasty balloon.

(0.125 mm in diameter) which is formed into a sinusoidal wave and wrapped into a helical coil structure. This prosthesis is crimped onto the deflated polyethylene balloon of a standard angioplasty catheter (Fig. 1a). The features of this prosthesis design are such that by inflating the balloon the diameter of the stent increases without any alteration in length (14–16 mm, Fig. 1b). The crimped stent profile is approximately 1.5 mm. The maximal diameter of the balloon during inflation determines the ultimate size of the prosthesis on implantation. One inflation at 6–8 atm is sufficient to open the stent and allows the safe withdrawal of the deflated balloon.

Stent Implantation

One day prior to stent implantation acetylsalicylic acid 300 mg/day was started. Dextran (100 cc/hr) was administered 2 hr before the implant and continued throughout the procedure. A minimum of 500 cc was infused. A total of 20,000 units of heparin was injected intravenously. Full heparinization was maintained until therapeutic levels of coumadin therapy were achieved. Conventional balloon angioplasty was performed and repeated until the desired angiographic result was obtained. After control coronary angiography for subsequent quantitative analysis, the balloon/stent system was advanced over a 0.014-in steerable guidewire under fluoroscopic control to the treated lesion site. The balloon was inflated until the desired expansion of the stent was achieved. Subsequently the balloon was deflated and the catheter was removed under negative pressure while leaving the stent in place. In case of incomplete expansion of the stent, a repeat balloon dilatation within the stent was performed. After repeat coronary angiography, the guiding catheter was removed. The post-procedure drug therapy consisted of coumadin for a minimum of 3 mon and acetylsalicylic acid (300 mg/day) for 6 mon.

Quantitative Coronary Angiography

The coronary cineangiograms were analyzed by a computer-assisted Cardiovascular Angiography Analysis System (CAAS), described in detail elsewhere [14,15]. Briefly, this system allows an objective and reproducible quantification of a coronary artery stenosis. A 35-mm cineframe was selected and digitized with a CCD-camera at very high resolution (1330×1770 pixels) and electronically a region of interest (512×512 pixels) encompassing the arterial segment to be analyzed was selected for subsequent analysis by the computer.

Contours of the arterial segment were detected automatically on the basis of the first and second derivative functions of the brightness profile, and corrected for pin-cushion distortion from the image intensifiers. A calibration factor was derived from a computer processed segment of the angio-catheter. From the arterial contour data, a diameter function was computed. The minimal luminal diameter and a reference diameter, computer-estimated by the interpolated diameter technique, were expressed in millimeters. On the basis of the proximal and distal centerline segments and the computed reference diameter function, the reference contours over the obstructed region were reconstructed. The extent of the obstruction was determined from the diameter function on the basis of curvature analysis and expressed in millimeters. The curvature is computed as the average value of all the individual curvature values along the centerline of the coronary segment, with the curvature defined as the first derivative of the tangent as it moves along the centerline which for a circle is equal to the reciprocal of the radius. The difference in area between the reference and the detected contours over the lesions ("plaque area," in mm^2) is a measure for the atherosclerotic plaque [16]. The inflow angle is the average slope of the diameter function between the position of the minimal obstruction diameter and the position of the proximal boundary of the stenotic lesion. The outflow angle is the average slope of the diameter function of the minimal obstruction diameter and the position of the distal boundary of the stenotic segment.

The severity of the stenosis can also be expressed as a percentage area stenosis: assuming circular cross-sections at the obstruction and reference position, corresponding luminal areas (mm^2) were calculated by comparing the minimal area value at the obstruction with the reference value obtained following the interpolated diameter technique. An illustration of such a quantitative analysis of a coronary artery is shown in Figure 2.

Elastic recoil was calculated as the difference between the mean diameter of the balloon when fully inflated and the mean diameter of the stented segment immediately after stent delivery and withdrawal of the balloon. Single

identical views during complete expansion of the balloon and immediately after stent implantation were chosen for automated edge detection.

Hemodynamic Assessment

To assess the physiological significance of the obstruction and its changes after angioplasty and stenting, the theoretic pressure drop was calculated using the arteriogram and digital computation, according to the formulae described in the literature: $P_{\text{grad}} = Q \cdot (R_p + R_t)$, where P_{grad} is the theoretic transtenotic pressure decrease (mm Hg) over the stenosis, Q is the mean coronary blood flow (ml/sec), R_p is the Poiseuille resistance, and R_t is the turbulent resistance [17,18].

These resistances have been defined as follows:

$$R_p = C1 \cdot (\text{length obstruction}) / (\text{minimal cross-sectional area})^2,$$

where $C1 = 8 \cdot \pi \cdot (\text{blood viscosity})$ with blood viscosity = $0.03 \text{ g/cm} \cdot \text{sec}$;
and

$$R_t = C2 \cdot (1/\text{minimal cross-sectional area} - 1/\text{normal distal area})^2,$$

where $C2 = (\text{blood density})/0.266$ with blood density = 1.0 g/cm^3 .

The theoretic transstenotic pressure drop was calculated for theoretic coronary blood flow of 0.5, 1, and 3 ml/sec. The Poiseuille and turbulent contributions to the flow resistance were determined from stenotic geometry assessed by quantitative coronary angiography.

Statistical Analysis

All values are expressed as mean with the standard deviation of the mean. Comparisons between measurements obtained after PTCA and stenting were made after variance analysis with the Student's *t*-test for paired observations. A statistical level <0.05 was considered as significant.

RESULTS

The morphologic and hemodynamic data (mean \pm SD) are presented in Tables I, II, and III.

Stent implantation after balloon angioplasty resulted in an additional increase in minimal luminal cross-sectional area and minimal luminal diameter with a concomitant decrease in percentage area and percentage diameter stenosis compared with the postangioplasty state (Table I). Moreover, there was a significant decrease in plaque area and inflow and outflow angles while the curvature of the lesion was respected (Table II).

This morphologic improvement was associated with a decrease in both the calculated turbulent and Poiseuille resistance, as well as the virtual disappearance of the theoretical transstenotic pressure drop for a theoretical flow of 0.5, and 3 ml/sec (Table III).

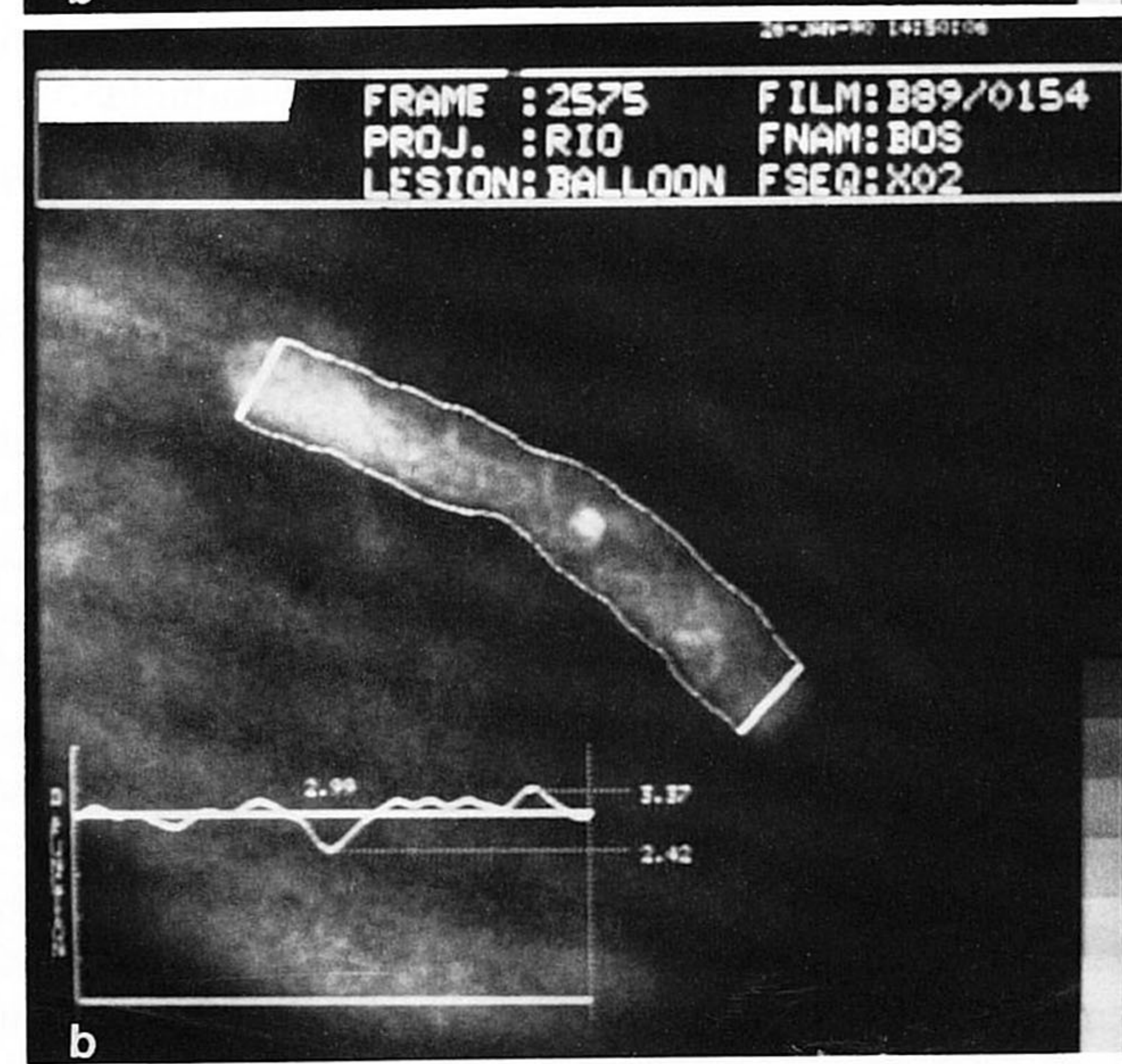
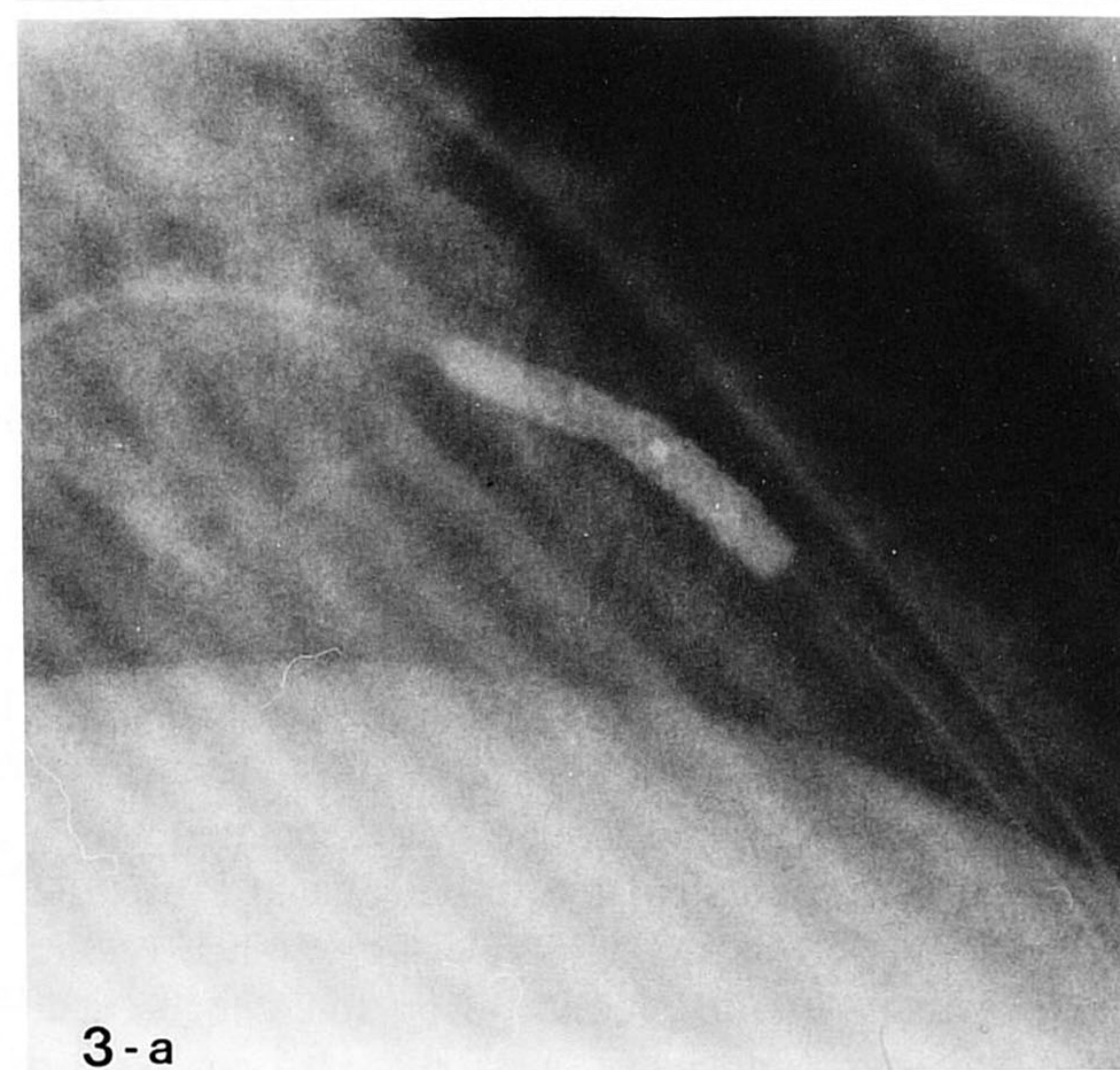
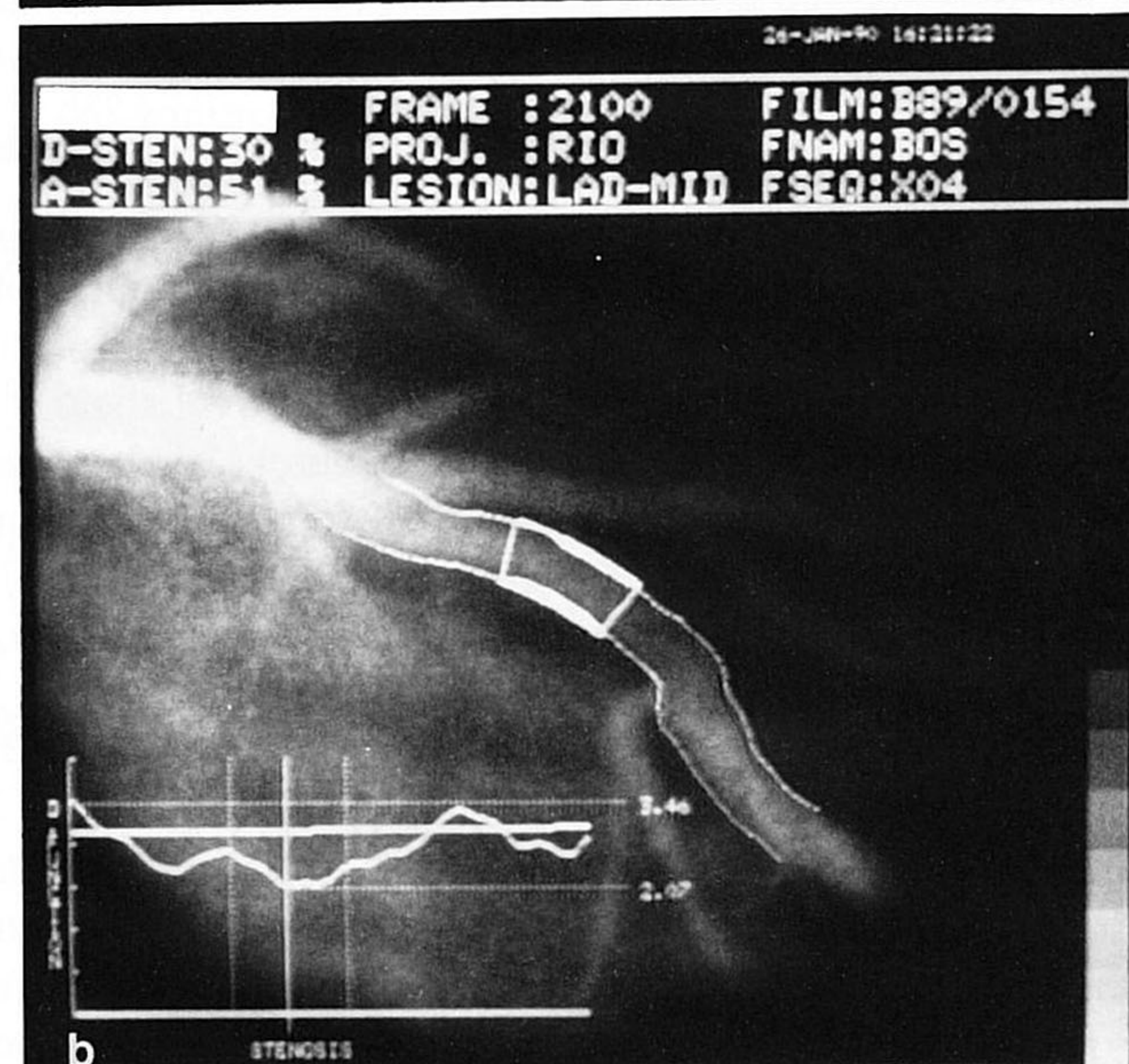
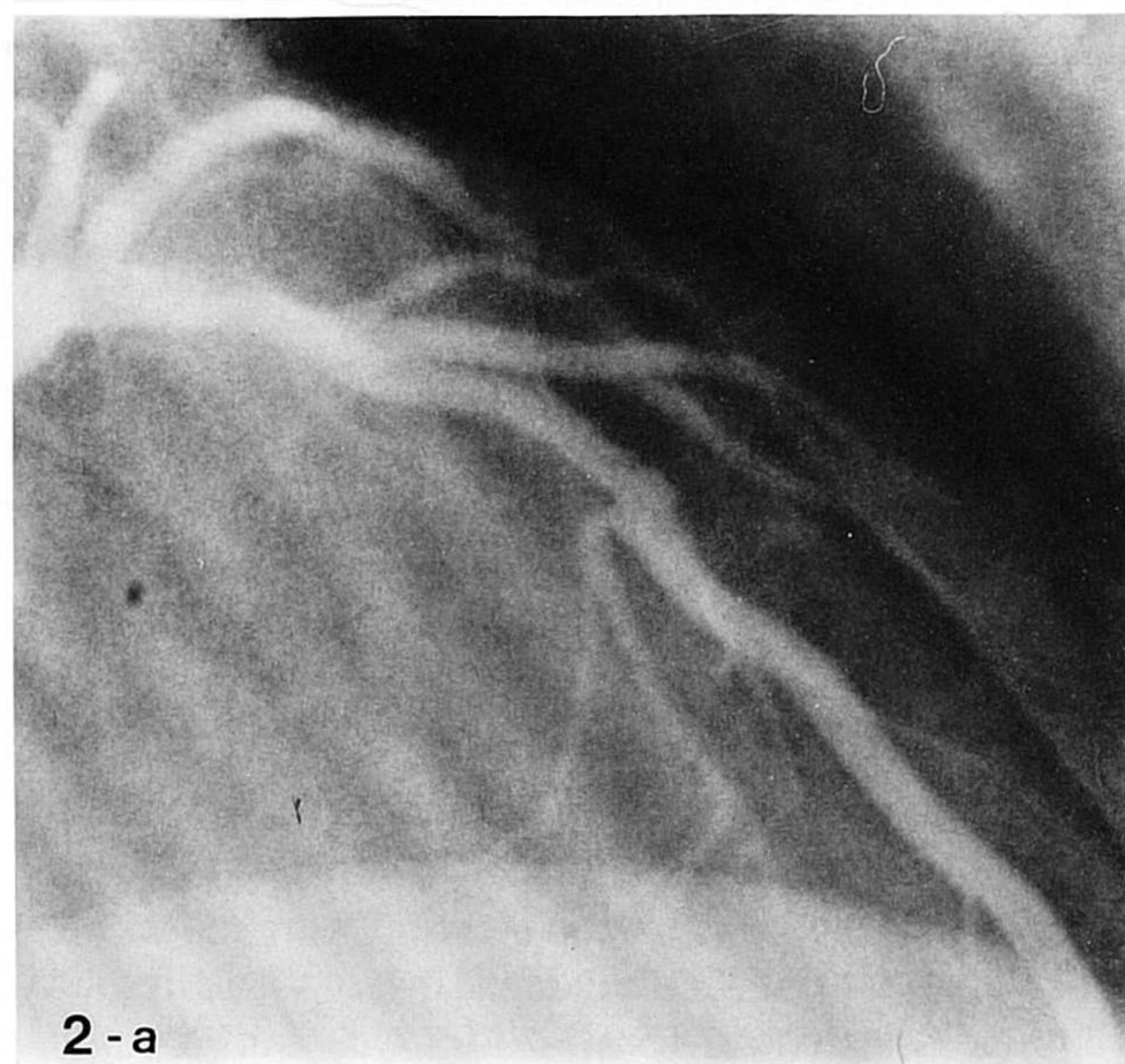
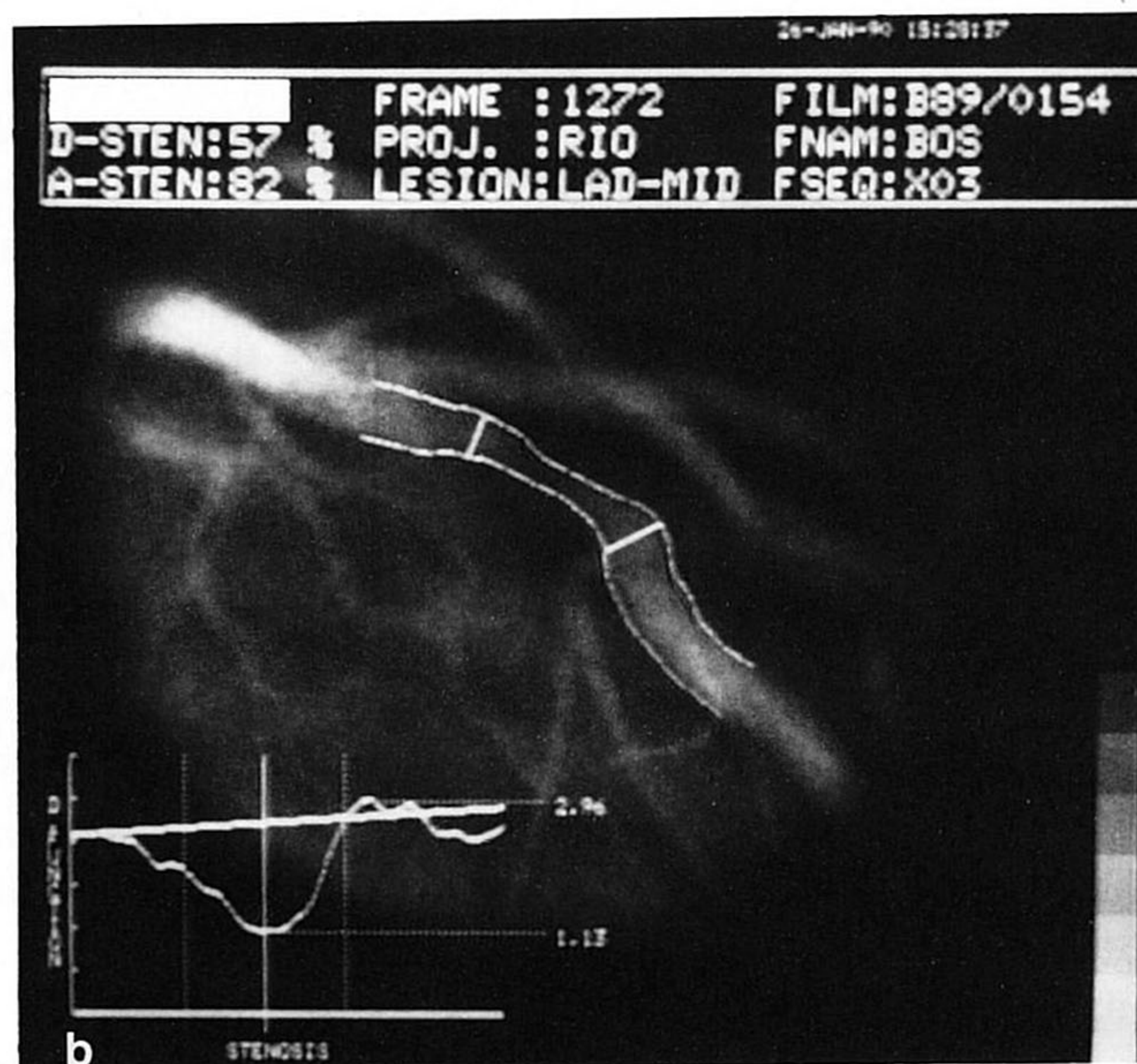
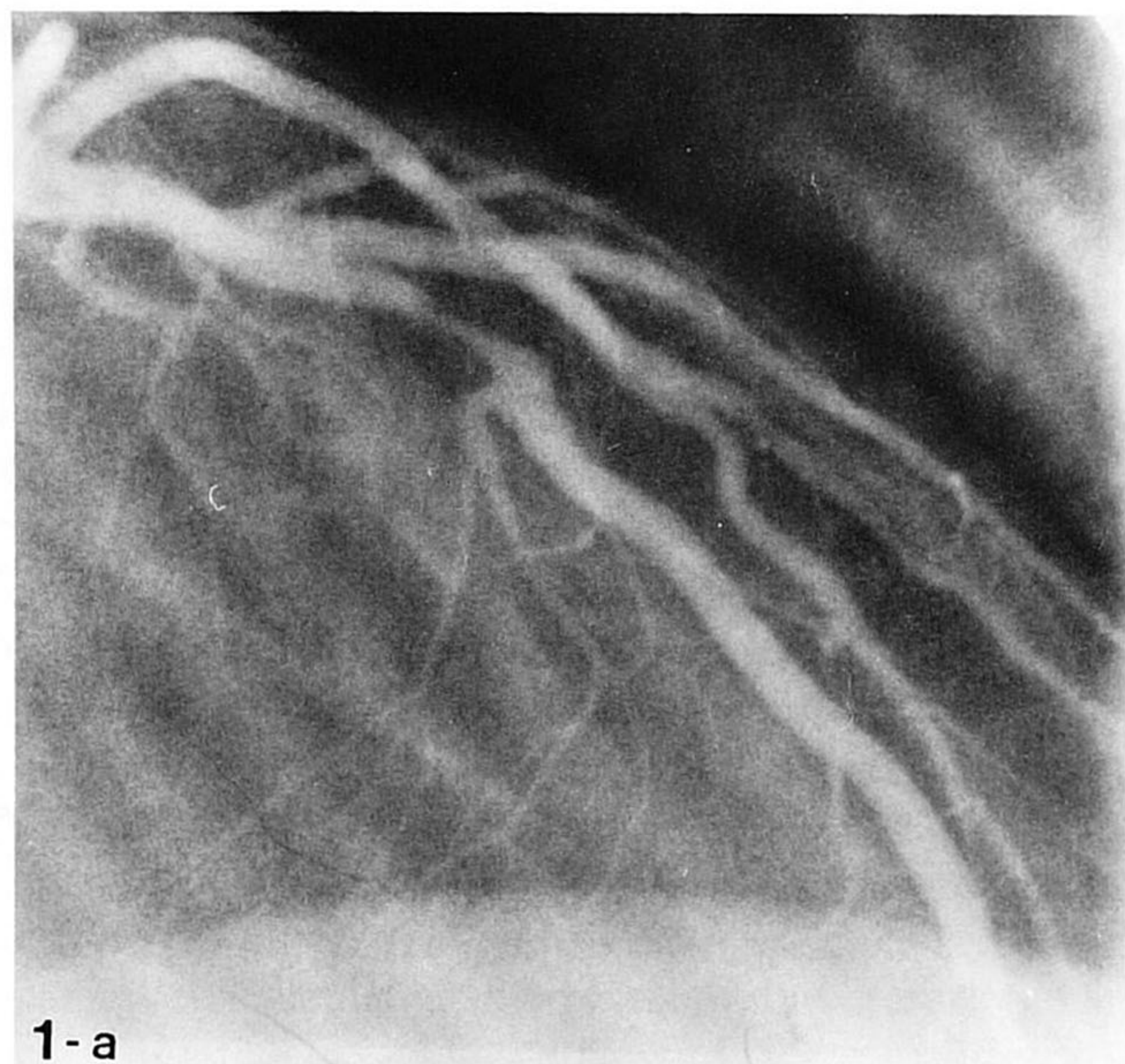


Fig. 2, 1a-3b.

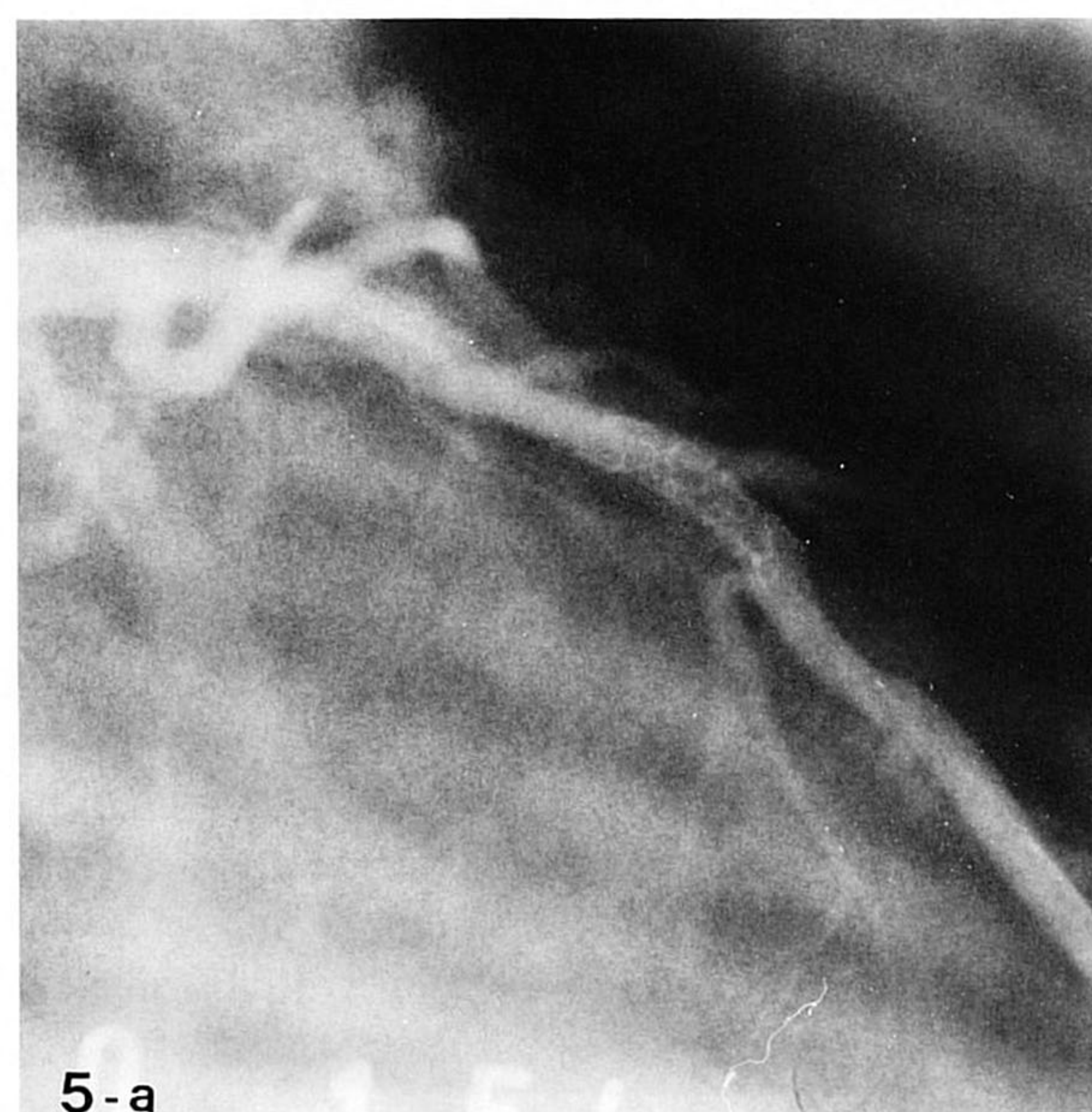
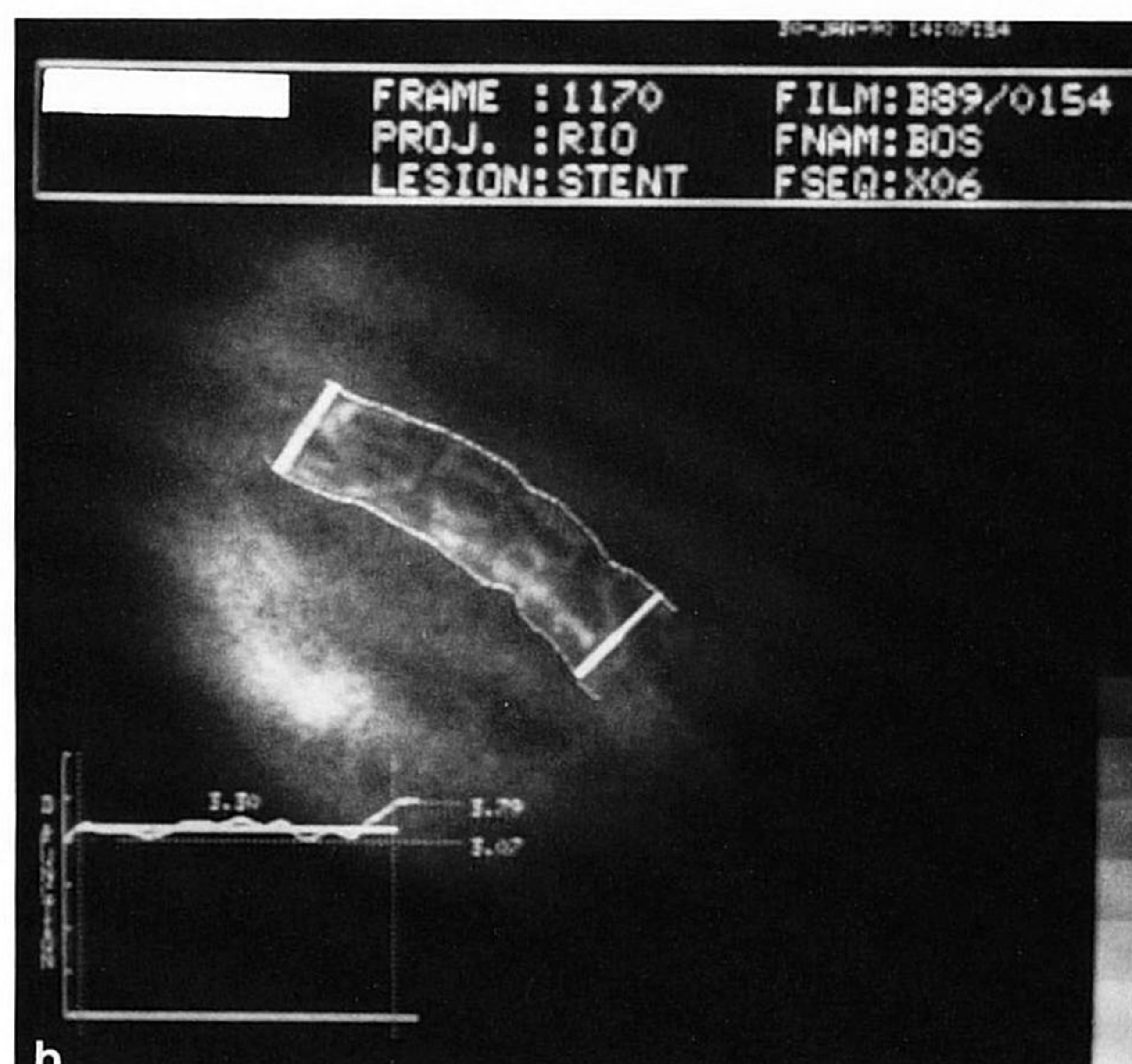
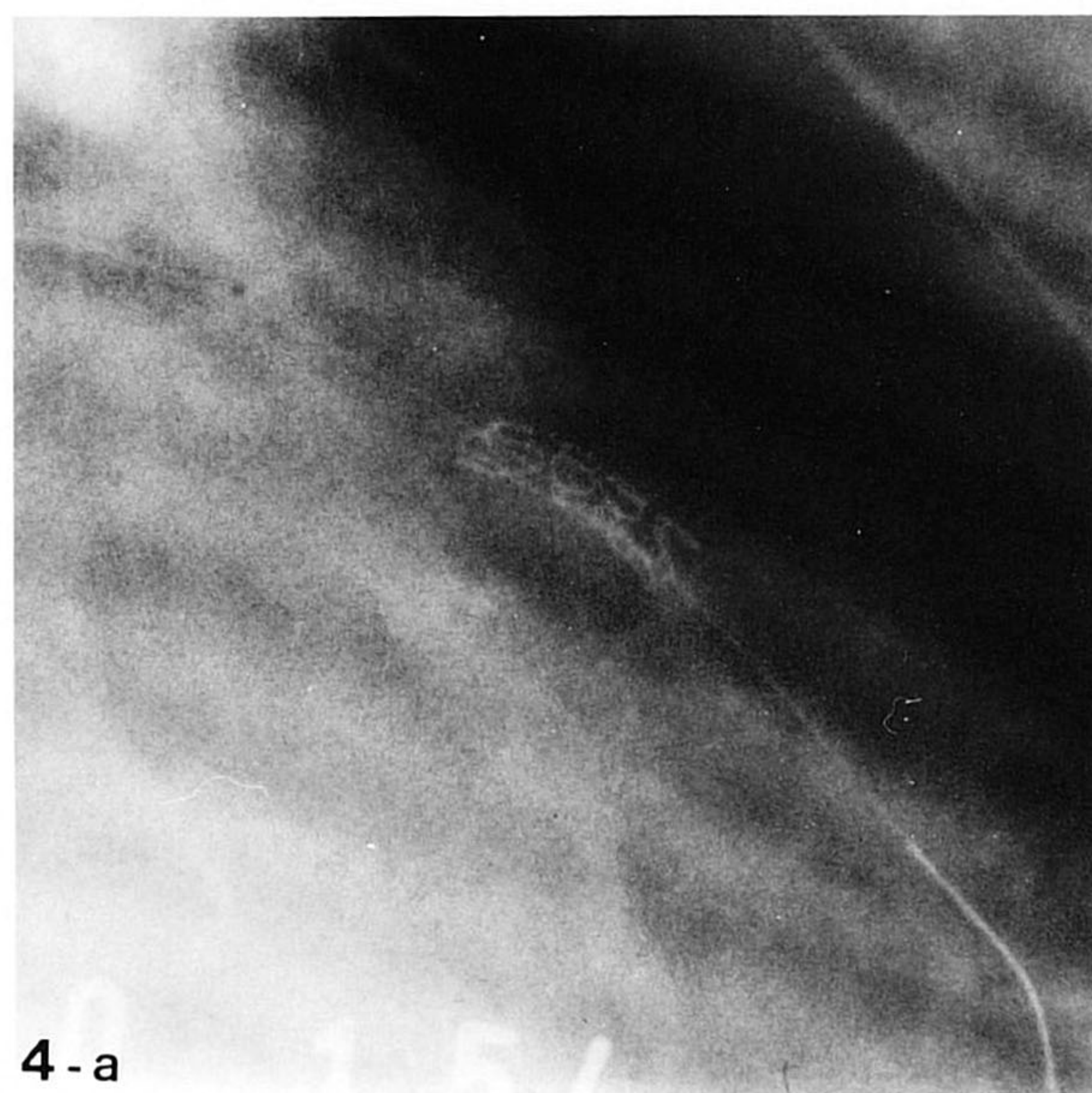


Fig. 2. Illustration of a quantitative analysis of a coronary artery. Single plane angiograms of the proximal left anterior descending before and after balloon angioplasty and immediately after stent implantation with superimposition of the automated contours of the region of interest. Below each angiogram is shown the diameter function of the detected contours of the artery. The minimal luminal diameter (vertical line) and the interpolated diameter function (horizontal line) from which the reference diameter is derived are shown. For further explanation, see text.

In most patients, the measured diameter of the balloon when fully inflated exceeded the measured diameter of the stent (Fig. 3). During maximum inflation the mean diameter of the balloon for the total study group was 2.98 ± 0.44 and the mean diameter of the stented segment immediately following implantation was 2.88 ± 0.43 mm (Table IV). This implies a recoil of 0.10 ± 0.36 mm or 3% ($P < 0.03$).

DISCUSSION

Coronary artery stenting has been introduced as an adjunct to PTCA in obstructive coronary artery disease [6-10,19,32]. The implantation of vascular endoprostheses may provide a useful approach to prevent occlusion and restenosis [6]. As for every therapeutic procedure, an objective and reproducible technique evaluating efficacy is needed. Computer based automated

TABLE I. Morphologic Changes Immediately After Balloon Angioplasty and Subsequent Stent Implantation

	Pre-PTCA	Post-PTCA	Post-stent	P_1	P_2
Extent obstruction (mm)	7.24 ± 2.48	6.63 ± 2.63	5.35 ± 1.86	NS	0.001
Reference diameter (mm)	2.81 ± 0.47	2.78 ± 0.48	2.91 ± 0.43	NS	0.001
MLD (mm)	1.09 ± 0.26	1.80 ± 0.32	2.45 ± 0.36	0.00001	0.00001
Diameter stenosis (%)	61.00 ± 9.19	34.00 ± 10.76	17.00 ± 7.18	0.00001	0.00001
Reference area (mm ²)	6.38 ± 2.15	6.26 ± 2.18	6.83 ± 2.07	NS	0.003
MLCA (mm ²)	0.99 ± 0.44	2.63 ± 0.92	4.83 ± 1.42	0.00001	0.00001
Area stenosis (%)	84.00 ± 7.58	56.00 ± 13.94	31.00 ± 11.57	0.00001	0.00001
	_____ P_1 _____		_____ P_2 _____		

MLCA, minimal luminal cross-sectional area; MLD, minimal luminal diameter. All parameters are expressed in mean ± SD.

TABLE II. Morphologic Changes Immediately After Balloon Angioplasty and Subsequent Stent Implantation

	Pre-PTCA	Post-PTCA	Post-stent	P_1	P_2
Curvature	21.00 ± 8.90	21.00 ± 8.65	20.00 ± 9.49	NS	NS
Plaque area (mm ²)	8.53 ± 4.33	5.13 ± 3.48	3.33 ± 2.29	0.00001	0.0004
Inflow angle	23.00 ± 6.28	15.00 ± 5.25	7.00 ± 15.64	NS	0.00001
Outflow angle	23.00 ± 10.39	19.00 ± 19.74	5.00 ± 15.17	NS	0.00001
	_____ P_1 _____		_____ P_2 _____		

All parameters are expressed in mean ± SD.

TABLE III. Hemodynamic Results Immediately After Balloon Angioplasty and Subsequent Stent Implantation

	Pre-PTCA	Post-PTCA	Post-stent	P_1	P_2
Rpois	18.00 ± 38.44	1.22 ± 1.72	0.47 ± 0.28	0.002	0.003
Rturb	11.00 ± 28.91	0.32 ± 0.72	0.02 ± 0.02	0.01	0.005
Pgrad (0.5 ml/sec)	29.00 ± 67.00	1.52 ± 2.42	0.49 ± 0.29	0.004	0.004
Pgrad (1 ml/sec)	48.00 ± 65.57	3.66 ± 6.26	1.00 ± 0.61	0.00001	0.004
Pgrad (3 ml/sec)	92.00 ± 126.75	6.45 ± 11.53	1.53 ± 0.99	0.00001	0.004
	_____ P_1 _____		_____ P_2 _____		

Rpois, Poiseuille resistance; Rturb, turbulent resistance; Pgrad, pressure drop. All parameters are expressed in mean ± SD.

edge detection angiographic analysis systems have reduced the variability resulting from visual and caliper-determined contour detection of coronary cineangiograms [20–22].

The optimal method to quantitatively analyze the immediate angiographic results of coronary stenting in native coronary arteries is still a matter of debate. At present, two techniques are available: automated edge detection and videodensitometry. The technique of automated edge detection is limited in eccentric lesions and in particular following balloon angioplasty when acute tears and dissections distort the anatomy. Videodensitometric measurements of cross-sectional area are independent of geometric assumptions regarding the shape of the stenosis and should, in theory, be more reliable than edge detection, especially after the disruptive action of balloon angioplasty, which is known to cause asymmetric enlargement of the lumen [23,24]. However, a recent

study has shown that edge detection and videodensitometry are equally acceptable methods of analysis after coronary stenting [25]. This may be explained by the more regular and smooth vessel contours after stenting, with tacking back of the intimal flaps by the scaffolding property of the stent in some cases and by the remodeling of the stented segment into a more circular geometry. Moreover, it has been shown that videodensitometry overestimates the minimal luminal cross-sectional area, particularly in smaller vessels with the WiktorTM stent [26]. This may be due to the radiographic characteristics of the stent itself.

X-ray energy dispersion spectrometry studies from our laboratory have shown that the structure of the WiktorTM stent has only one element, tantalum, which has a higher atomic number than the elements contained in the Palmaz-Schatz[®] stent and the Wallstent[®]. Consequently, more X-ray energy is absorbed by the WiktorTM stent

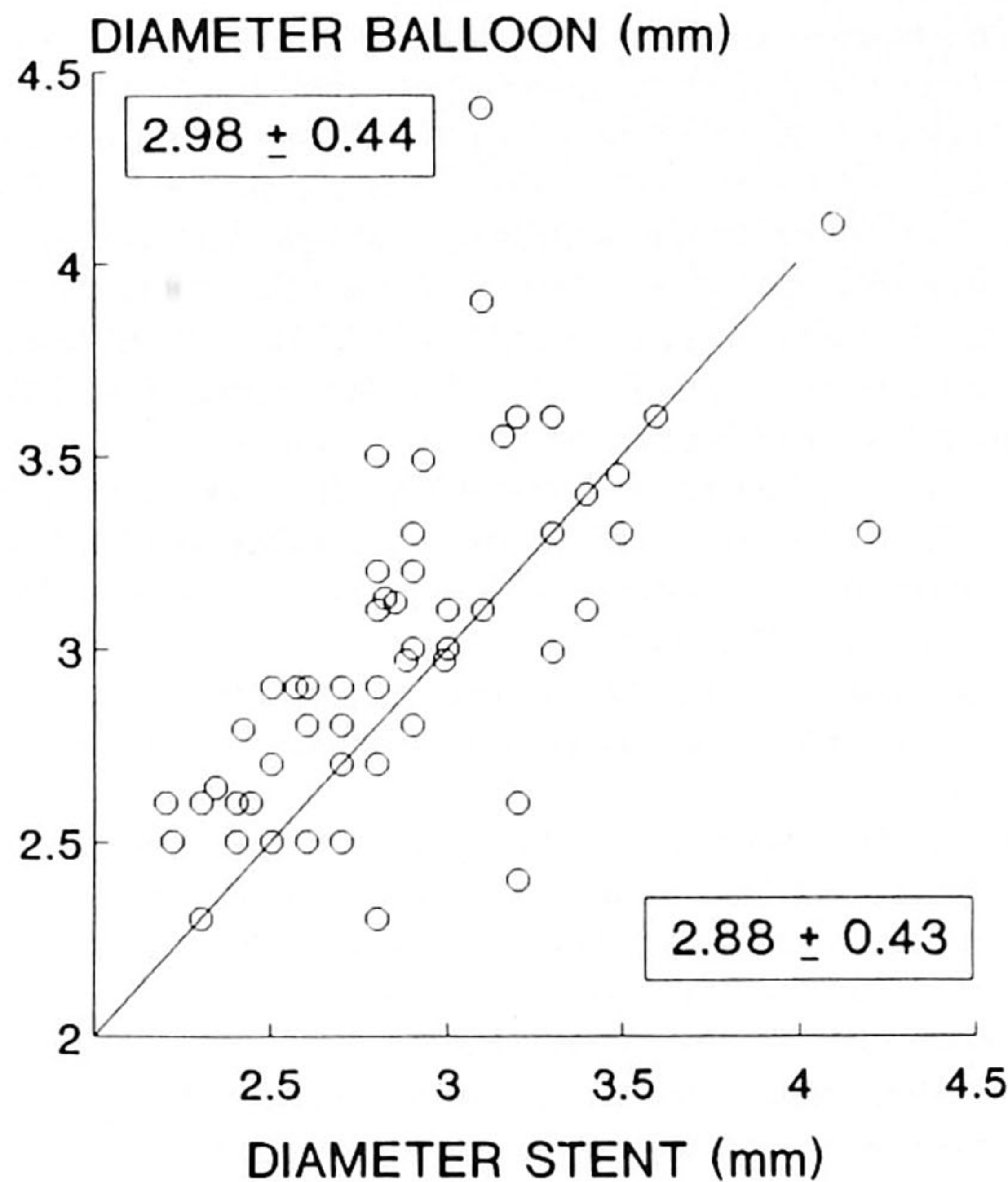


Fig. 3. Correlation between the measured diameter of the balloon when fully inflated and of the stent immediately after implantation.

wire. Furthermore, the WiktorTM stent has a greater wire cross-sectional area than the other two stents. These physical characteristics result in a higher radiopacity in comparison with the stainless steel stents. As a result, the intraluminal brightness profile generated by the WiktorTM stent makes automated edge detection the appropriate technique for quantification of the stented segment. Conversely, videodensitometry may be the technique of choice for the assessment of restenosis. Intimal hyperplasia developing within the stent may not be detected by edge detection technique, which is unable to distinguish between the radiopaque structure of the wire embedded in the vessel wall and the actual boundaries of the lumen radiopacified by the contrast medium. For these reasons, automated edge detection was used for the immediate angiographic assessment in this study.

The increase in minimal luminal diameter after balloon angioplasty (1.09 ± 0.26 mm to 1.80 ± 0.32 mm), is what has been observed in other series [27,28]. This emphasizes that prior to stenting the stenotic lesion has been dilated to the extent normally expected. The additional improvement after the implantation of the WiktorTM stent is comparable to what has been observed with either self expanding or balloon expandable stents [7,28,29]. The same holds for the minimal luminal cross-sectional area. There is a fivefold increase in the minimal luminal cross-sectional area after stenting (0.99 ± 0.44 mm² to 4.83 ± 1.42 mm²). As previously demonstrated, a normalization of the coronary flow reserve

TABLE IV. Nominal Diameter of the Balloon, Measured Diameter of Balloon at Maximal Inflation Pressure, and of Stented Segment by Edge Detection

Nominal diameter balloon	Measured diameter balloon	Measured diameter stented segment	P_1	P_2
3.35 ± 0.36 mm	2.98 ± 0.44 mm	2.88 ± 0.43 mm	0.0001	0.03
----- P_1 -----		----- P_2 -----		

All parameters are expressed in mean \pm SD.

may be expected with such an increase [30]. As indirect confirmation of the above findings, the pressure drop across the stenosis remains virtually zero even with a theoretical flow of 3 ml/sec and a normalization of the calculated resistances. In addition to the increase in the minimal luminal cross-sectional area, there is a significant change in plaque area, in the inflow and outflow angles, and in the extent of obstruction, while the natural curvature of the artery is respected.

However, the smaller mean diameter of the stented segment (2.88 ± 0.43 mm) in comparison with the measured diameter of the fully expanded balloon (2.98 ± 0.44 mm) suggests some recoil of the stented segment. This minimal recoil appears to be a true phenomenon since the accuracy and the precision of the CAAS system is -30μ and 90μ , respectively [13–15]. Furthermore, the recoil phenomenon has also been observed, although to a larger extent, after WiktorTM stent implantation in Yorkshire pigs [11]. The more pronounced recoil (10%) in the animal model compared to the 3% recoil in this study may be explained by the fact that in the former study the stent was implanted in normal animal coronary arteries. These angiographic data indicate that in contrast to balloon angioplasty, where recoil amounting to 50% has been documented [31], the WiktorTM stent appropriately scaffolds the vessel.

The measured diameter of the inflated balloon at an average inflation pressure of 6–8 atm (2.98 ± 0.44 mm) did not achieve the nominal size of the balloon (3.35 ± 0.36 mm) as specified by the manufacturer. The inflation pressure needed to obtain the nominal size of the balloon has been tested in air. It may be that a higher inflation pressure should be applied to achieve full expansion of the balloon to overcome the opposing forces exerted by the arterial wall and possibly by the stent itself.

CONCLUSIONS

Implantation of the WiktorTM stent results in a further improvement in stenosis geometry after balloon angioplasty. A fivefold increase in the minimal luminal cross-sectional area with a significant reduction of the inflow and outflow angles is observed without changing the curvature of the stenosis. This is associated with a nor-

malization of the resistances to flow. With the recommended inflation pressure of 6–8 atm, there is no full expansion of the balloon on which the stent is mounted. Furthermore, some recoil (0.10 ± 0.36 mm) is observed after stent implantation. This may be explained by the rather loose interdigitating coil structure of this particular stent.

Whether these observations will result in a reduced restenosis rate in comparison with balloon angioplasty and to an improved long-term clinical success rate remains to be determined.

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