Klaus-Dieter Bolz

INTRAVASCULAR ULTRASONOGRAPHY
Clinical and experimental studies with a new diagnostic tool

Norwegian University of Science and Technology
Department of Diagnostic Radiology
Trondheim – Norway

TAPIR

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LIST OF PAPERS

The papers will later be referred to by their Roman numerals.

I Bolz KD, Tveit K, Nordby A, Myhre HO, Gåserud K, Østrem G, Ommedal S, Angelsen BAJ. Intravascular ultrasonographic appearance of angiographically normal arteries related to age and the occurrence of vascular disease. Acta Radiol 1992;33:532-537.

II Bolz KD, Myhre HO, Angelsen BAJ, Nordby A. Intravascular ultrasonography: Normal and pathologic findings in the great veins. Acta Radiol 1993;34:329-334.

III Bolz KD, Aadahl P, Mangersnes J, Rødsjø JÅ, Jørstad S, Myhre HO, Angelsen BAJ, Nordby A. Intravascular ultrasonographic assessment of thrombus formation on central venous catheters. Acta Radiol 1993;34:162-167.

IV Bolz KD, Fjermeros G, Widerøe TE, Hatlinghus S. Catheter malfunction and thrombus formation on double-lumen hemodialysis catheters: an intravascular ultrasonographic study. Am J Kidney Dis 1995;25:597-602.

V Bolz KD, Hatlinghus S, Wiseth R, Myhre HO, Grønningsæter Å. Angiographic and intravascular ultrasonographic findings after endovascular stent implantation. Acta radiol 1994;35:590-596.

VI Gronningsaeter A, Lie T, Bolz KD, Heimdal A. Ultrasonographic stent-imaging artifacts. J Vascular Invest 1995;1:140-149.

VII Bolz KD, Nordby A. In vivo thrombogenicity of intravascular ultrasound imaging catheters. Acta radiol 1995; 36:280-283.

INTRODUCTION

History

Intravascular ultrasonography (IVUS) is a new imaging modality which provides high resolution cross sectional real-time images of the vessel lumen and vessel wall including its various layers.

The first intravascular real-time ultrasound (US) catheter was already constructed in 1972 by Bom et al. (9). This imaging catheter had still significant technological limitations. Not until the end of the 1980s miniaturization and refinements in transducer manufacturing and computerized image processing resulted in clinically suitable instruments.

The development of the new imaging technology accellerated as a result of new second-generation therapeutic catheters for peripheral and coronary plaque removal, including mechanical atherectomy and laser ablation devices. These new "debulking" devices have the risk of vessel perforation and have increased the need for more comprehensive and detailed information about the thickness and distribution of atheroma including its depth within the vessel wall.

Principles of intravascular cross-sectional imaging

Ultrasound imaging is achieved by transmitting a short pulse into the tissue and displaying the amplitude of the backscattered signal. To obtain a 360 degree cross sectional image, one must scan the ultrasound beam through a full circle and syncronize the beam direction and deflection on the display. This can be achieved by mechanically rotating the transducer (10,19) or by a stationary transducer which reflects the ultrasound beam on a rotating mirror (124). A third method uses electronically switched multi-element arrays (47). A schematic representation of the imaging methods is given in fig.1. Each of the methods has its advantages and limiting factors (4,16-17,31). The ultrasound frequency used is between 12.5 MHz and 30 MHz. The spatial resolution increases with increasing US-frequency at the expense of decreased penetration.

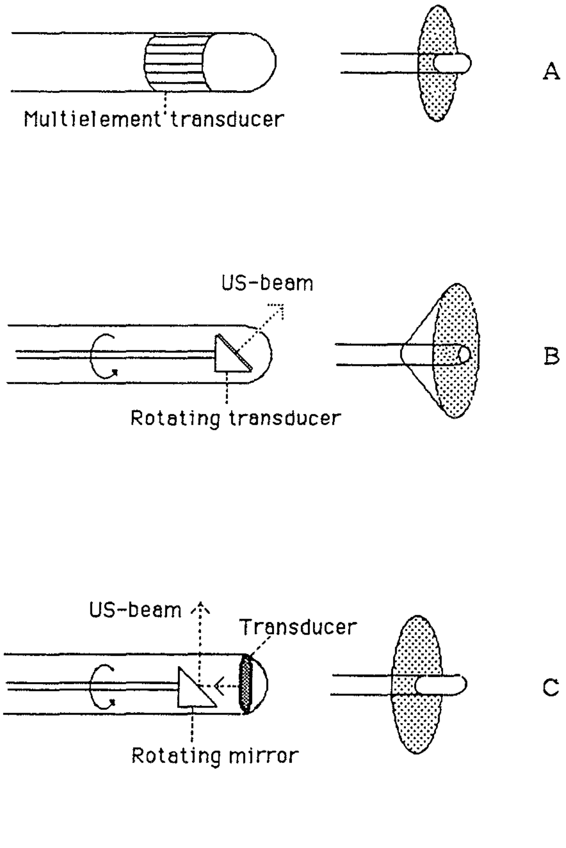

Figure 1 Schematic presentation of the 3 types of intravascular US-imaging catheters and their image plane. A) Multiple- element catheter: Individual transducer elements are arranged in a circumferential pattern around the catheter tip. Sequential switching of the elements cause a beam swept in 360-degree plane perpendicular to the catheter. B) Mechanically rotated transducer device: The transducer crystal is rotated along the axis of the shaft which contains the electrical transducer wires. C) Fixed transducer / rotating mirror device: The US-beam is directed toward an angled reflector rotated by the shaft. (Modified after Yock et al., ref.124)

Advantages of Intravascular Ultrasound Imagig

Conventional contrast angiography provides only a longitudinal image of the contrast filled vessel lumen, giving information about the anatomic site and extent of arterial occlusive disease, blood-flow, and collateral circulation. Unless there are gross calcifications, the vessel wall or the atheroma itself can not be seen.

An alternative imaging modality is optical fiber angioscopy. In fiber angioscopy the vessel has to be blocked with a balloon upstream and the blood removed by flushing with a physiological solution. The vessel lumen is depicted as a tunnel and the method can only visualize the endothelial surface of the vessel wall.

In intravascular ultrasound imaging the vessel does not have to be cleared of blood. The ultrasound beam penetrates into the vessel wall permitting imaging of structures past the surface. By showing the thickness of the plaque and the vessel wall in any direction, the method is a potential ideal guidance modality for new therapeutic catheter techniques (Fig.2).

Background for the present studies

At the time of our first studies a number of early in vitro and in vivo investigations had confirmed that this technique can be used to characterize and quantify arterial wall abnormities and disease. Furthermore, that lumen dimensions and wall thickness can be measured (21,25,44-45,47,55,65,69,74-77,122-123) and the effect of interventional procedures (20,27,51-52,82,98,106,108,125) as well as the effect of pharmacologic therapy (121) can be evaluated.

However, there was still a dispute about the normal ultrasound appearance of muscular and elastic arteries and the precise correlation between the ultrasound images and the microscopic anatomy of the vessel wall.

At this time only a few investigations concerning intravascular US in venous structures had been published (25,67,89) and there were no systematic studies about the normal US appearance of the venous wall.

Moreover, only preliminary reports concerning the value of intravascular ultrasound as an adjunct imaging method during and after the implantation of vascular stents had been published (51,98,114).

In addition there was a lack of information about the potential risks of intravascular ultrasound catheters in clinical use. Structural irregularities on the catheter surface and mechanical vibrations caused by the rotating wire could suggest that these devices had a higher thrombogenicity than conventional angiographic catheters.

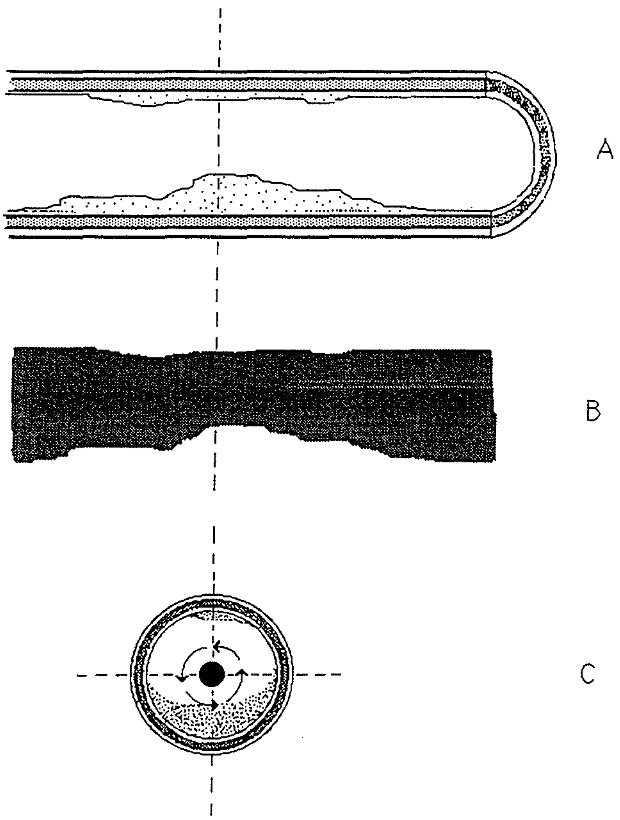

Figure 2 (A) Schematic drawing of an arterial segment with an atherosclerotic plaque. Angiography (B) shows only a longitudinal shadow of the contrast filled vessel lumen. Intravascular US imaging (C) provides cross-sectional image of vessel lumen, atheroma, and vessel wall structures.

AIMS OF THE STUDY

The aims of the study were:

1) To study the in vivo US-appearance of muscular and elastic arteries in young healthy persons and to compare the findings with the intravascular US-images of adult and elderly patients with and without arterial disease.

2) To investigate the possibility of whether one selected segment of the iliac arteries could give information about the possible presence and extent of pathologic changes in the rest of the arterial tree.

3) To study the US-findings in normal and diseased veins.

4) To assess the potential role of intravascular US in the diagnosis of thrombus formation on central venous indwelling catheters.

5) To evaluate the benefit of intravascular US imaging as a supplement to follow-up angiography after endovascular stent implantation.

6) To evaluate the frequency and significance of thrombus formation on the surface of intravascular US imaging catheters.

METHODS

Instruments

The clinical investigations were performed by two types of mono-element imaging catheters:

1) A fixed transducer / rotating mirror device (Cardiovascular Imaging Systems Inc., Sunnyvale, CA, USA) in combination with the artery scanner "CVIS Insight", which prototype had been developed by the Department of Biomedical Engineering and SINTEF UNIMED in Trondheim.

2) A rotating transducer device "Sonicath" (Boston Scientific Corporation, Watertown, MA, USA) in combination with the imaging system IVUS (Diasonics, Milpitas, CA, USA).

Both imaging systems were at this time approved by the Federal Food and Drug Administration (F.D.A.). For clinical use in Norway special permission was obtained by the national authorities ("KONTROLLEN FOR MEDISINSK ENGANGSUTSTYR" and "DET SÆRLIGE TILSYN MED ELEKTROMEDISINSK UTSTYR").

The dimensions of the catheters were 4.5 F (1.45 mm), 5.0 F (1.7 mm), 6 F (2.0 mm), and 8.0 F (2.7 mm). Most catheters were used in combination with a guidewire; where as some catheters had a fixed guide tip or rounded tip without guide. Depending on the type of the catheter, introducer sheaths from 6 to 9 F (2.0-3.0 mm) were used.

The US frequencies were 12.5 MHz, 20 MHz or 30 MHz respectively. At 20 MHz the CVIS catheter has an axial resolution (perpendicular to the long axis of the catheter) of 0.12 mm and a lateral resolution (perpendicular to the axis of the US-beam) of 0.23 mm. The focus depth is 3.8 mm. (Informations obtained from the manufacturer). The 20 MHz "Sonicath" catheter has an axial resolution of 0.2 mm and a lateral resolution of 0.4 mm (62). The number of frames per second is 15-25 for both systems, corresponding to 900 - 1500 rpm (rotations per minute).

All catheterizations were done under flouroscopic guidance and continuously recording the US image on a videotape. The position of the US catheter in the regions of interest was documented by radiographs or by annotating anatomical landmarks. The video records were analyzed off line in slow motion after completed catheterization. Measurements on US images were either done by a caliper on the monitor, using the included measurement program, or by a ruler on the hardcopies.

Patients

The clinical investigations include 70 individuals. All were patients referred for diagnostic arteriography or venography. In some patients who underwent catheter based interventional procedures the use of intravascular ultrasound imaging was considered to be indicated as adjunct to the therapeutic procedure. In all other cases, except individuals referred for angiographic documentation of abolished intracranial circulation, a written consent was given after proper information about the procedure had been given.The study was approved by the regional ethics committee.

The imaging catheter remained in the vessel from 3 to 20 min (mean 9 min). Patients undergoing intravascular therapeutic interventions were heparinized with 5.000 to 10.000 IU heparin intraoperatively. In addition they were given 500 mg acetylsalicylic acid (ASA) 24 hours before the procedure and 100 to 500 mg ASA the day of the procedure. In the remaining patients no anticoagulant medication was given. During all procedures the catheters and guidewires were flushed with heparinized saline (6.000 IU / 1.000 ml).

In order to get personal experience and training with the new US devices, the clinical studies were preceded by catheterization and intravascular US-imaging on an anesthesized pig. These experiments were approved by the national committee for animal experiments ("Utvalg for forsøk med dyr").

SUMMARY OF RESULTS

Paper I

The US images of angiographically normal external iliac arteries of 22 individuals were related to the age and medical history of the patients. A typical 3-layered appearance of the arterial wall was found in young healthy individuals as well as in adult and elderly subjects.

There was no difference in the ultrasonographic appearance of muscular and elastic arteries.

In patients with extensive obtructive atherosclerosis in other parts of the arterial tree, a segment of the iliac artery could have the same appearance as seen in young, healthy individuals.

Paper II

The US investigation of the great veins in 25 patients showed that normal veins have a homogeneous wall structure. In two patients with obstruction of the inferior vena cava above the imaging level, the venous wall had an "artery-like" stratified wall structure. In 4 cases valves or valve-like structures were observed. Anatomic variants such as spurs and webs were seen in 3 and mural thrombi or postthrombotic wall changes in 4 patients. In one case a sphincter-like ostium venae cavae was observed. In 2 patients thin filaments within the right atrium, most likely representing Chiari nets, were seen.

Paper III & IV

In vitro experiments were performed in order to assess the potential role of IVUS in the diagnosis of thrombus formation on central venous indwelling catheters. Various types of central venous catheters were studied. All thrombi protruding more than one mm from the catheter surface could be identified.

In a clinical study of 23 patients who had a central venous catheter, including 14 doubel-lumen hemodialysis catheters, in 5 cases a catheter / mural thrombus, occlusive vein thrombosis or superior caval vein stenosis was found. In all these five cases the central venous catheter either was obstructed or malpositioned, or the patients had clinical signs of catheter induced complications. In one case the hemodialysis catheter was obstructed by an intraluminal catheter thrombus but no thrombus formation in the venous system was found. The degree of thrombus formation was independent upon indwelling duration of the catheter.

Paper V & VI

In 14 consecutive patients who underwent follow-up angiography after intravascular stent implantation IVUS of the stent and the adjacent vessel segments was performed or attempted. In the peripheral arteries, IVUS did not reveal more information concerning vessel and stent diameter, stent stenosis and intraluminal surface contact than angiography alone. Stents in the coronary arteries were insufficiently visualized by conventional radiologic methods and only IVUS permitted an exact stent identification and differentiation between stent stenosis and stenosis of the native vessel.

Artifacts caused by the highly reflective metallic stent struts interfered with the native vessel wall and partly obscured its structural details. In an experimental study these artifacts were analyzed. Three wave propagation effects were described, denoted shadowing, transducer-stent reverberations and stent-filament reverberations. It was documented that small dissections or cavities which may exist between the stent and the vessel wall due to sub-optimal stent adaptation can be difficult or impossible to detect because of these artifacts.

Paper VII

The frequency and significance of thrombus formation on the surface of intravascular US imaging catheters was evaluated by means of the US imaging system itself. In 32 arterial and 38 venous procedures the US findings were observed during withdrawal of the catheter into the introducer sheath at the end of the catheterization. Thrombus formation was observed in 5 cases (7%). The largest thrombus fragments had a cross-sectional dimension of 2.2 x 1.0 mm. There was a significant correlation between the incidence of thrombus formation and the occurrence of malign neoplastic disease. No relationship was found between the frequency of thrombus formation and the duration of the procedure or the type of US catheter.

General Discussion

US-findings in normal arteries

At the time of our first studies there was a debate about the *in vivo* US appearance of normal muscular and elastic arteries and the precise correlation between the US images and the microscopic anatomy of the vessel wall.

In vitro studies had shown that smooth muscle in the media is echolucent, whereas collagen in the adventitia, and elastin in the intima are echodense (45,69). Several authors (81,124) concluded that the 3-layered appearance only characterizes muscular arteries: the echogenic inner layer representing the intima, the middel low-echogenic layer the muscular media, and the echogenic outer layer the adventitia as seen in gross histologic examination. Elastic arteries, such as the aorta and the supra-aortic vessels would have an homegeneous wall structure. Others (27,75) found a 3-layered US-image not only in muscular arteries, but also in the aorta. In one study (27) the 3-layered appearance of the iliac arteries could not be confirmed in several otherwise healthy kidney donors.

In our study (Paper I) we investigated the *in vivo* US-appearance of muscular and elastic arteries in young healthy persons and compared the findings with the intravascular US-images of adult and elderly patients with and without manifestations of atherosclerotic disease. Since the young, otherwise healthy individuals were patients with angiographically documented brain-death it was justified to catheterize not only the iliac arteries and the aorta, but also the supraaortic branches. In addition, we could prolong the catheterization-time without fear of thrombo-embolic complications. In cases where angulation of the catheter or unstabel catheter position caused inconsistent and asymmetric images, we could pass the catheter several times through the actual vessel segment until optimal image quality was obtained (Fig.2, Paper I). Some of these patients were children who had a small aortic diameter, allowing better visualization of the wall structures than in adults. In the adult aorta unstable catheter position due to pulsatory movements and the large vessel diameter decrease image quality.

Contrary to other investigators (27) we could confirm the typical 3-layered structure of the arterial wall in all patients, irrespective of age. Furthermore, we found no difference in the overall US appearance of the external iliac artery, the aorta, and the subclavian artery in young healthy persons. Thus, we could not confirm the statement of others (81,123) that arteries with a muscular media show an echolucent middel layer and that those with a media composed primarily of elastic tissue do not. In addition, our observations indicate that the high-echogenic inner ring cannot represent the tunica intima itself. The thickness of the human intima in an adult aorta is about 0.12 mm (8,102), in children even less. Nevertheless we found an echogenic inner ring in the aorta and supra-aortic arteries in children even using a transducer of 12.5 MHz which has a poorer axial resolution than the thickness of the tunica intima. Moreover, elastic arteries are characterized by the lack of a defined tunica media composed of smooth muscle. Consequently the echolucent middel ring in our studies of elastic arteries cannot represent a muscel layer.

Our observations reflect some of the difficulties in the interpretation of in vivo US-findings, which are caused by intrinsic limitations of the method. Obtaining a true cross-sectional image requires positioning of the transducer coaxially within the vessel so that the scanning plane is perpendicular to the axis of the vessel. Oblique scanning leads to false thickening of the vessel wall and loss of the layered structure (31). In larger vessels such as the adult aorta, rapid pulsatory movements and the limited imaging radius may preclude complete visualization of the vessel wall in one single image.

In addition, our observations demontrate difficulties in the interpretation of US-findings and the analysis and quantification of vessel wall structures, which are not restricted to intravascular investigations. They have also been discussed in connection with non-invasive US-measurements of the arterial wall (23,78,83,84).

In vitro analysis of artifacts in intravascular ultrasound imaging have demonstrated the impact of the radial point spread function (PSF) of the imaging system on measurements of structures of low thickness (31). The PSF causes a thickening of any distinct interface on US images and is also known as "blooming" effect. The thickness of any thin structures will be overestimated because the signal is convolved with the PSF of the imaging system. Thus, on US images obtained from a plexi-glass tube filled with water, the interface between water and the wall of the tube will be imaged not as an extremely thin interface but as an halo of considerable thickness.

In the arterial wall the bright internal ring on the US-image is probably caused by the interface between blood and the tunica intima with its highly reflectant lamina elastica interna. Since these structures are thin $(< 0{,}12 \text{ mm})$ it is the radial PSF of the imaging system which determines the thickness of the high-echogenic inner ring and not the intima itself. The thin echolucent middel ring is probably caused by an acoustic homogenous zone with little scattering which exists in both muscular and elastic arteries.

The description of this phenomenon corresponds not only with our own in vivo observations but also with the results of in vitro microdissection studies of others (78,95): It seems that the intima itself is of minor importance in generating the 3-layered image, but that the inner echogenic ring is caused by the *interface* between the blood and the highly reflective elastic elements in the arterial wall.

Thickening of the intima is supposed to be an early sign of atherosclerosis (102). Thus repeat intravascular US imaging of a segment of the distal pelvic arteries could be useful in the detection and monitoring of early atherosclerotic vessel wall changes. Our study has shown, however, that the ultrasound investigation of an angiographically normal arterial segment, selected by random, can show a normal appearance, even in patients with extensive atherosclerotic changes in other parts of the arterial tree.

Normal and pathologic findings in the great veins

As shown in Paper II, the normal venous wall has an homogeneous US appearance. This is in accordance with the fact that the main histologic difference between veins and arteries is the relative lack of elastic structures in the venous wall. In large and medium sized veins the tunica intima is frequently feebly developed and some authors consider the inner and middle coats as forming one layer (8).Thus there is no distinct acoustic interface between blood and a highly reflective elastic membrane.

In two patients with obstruction of the inferior vena cava above the imaging level, the venous wall had an "artery-like" stratified wall structure. No final explanation of these single observations can be given, but it seems most likely that this is a response to the chronically increased intraluminal venous pressure. A similar wall composition was found in the two saphenous vein coronary bypass grafts studied in Paper V. Similar changes in the US-apperance of veins used as autologous grafts in the arterial bed were also observed by others (18).

The venous system is characterized by a wide range of anatomic variants. Paper II demonstrates that IVUS provides in vivo visualization of the morphology and motility of small intraluminal venous structures which cannot be revealed by traditional diagnostic methods. The ultrasonographic appearance of ectopic valves, valve rudiments, anatomic variants and structures such as spurs and webs were demonstrated. Knowledge of the US-appearance of these structures is a prerequisite with regard to potential diagnostic applicabilities of IVUS in the venous system.

The demonstration of valve-like folds in the entrance of the azygos vein in two out of our patients may be of interest as an historic curiosity. According to the literature, the first observation of venous valves was made at this anatomical site by the Italian anatomist Gianbattista Canano. It seems certain that Vesalius, who gave the first complete anatomical description of the veins in 1555, was told about these valves by Canano ten years earlier. But he could not find them himself and subsequently denied their existence (33). Reviewing textbooks of anatomy and radiology, we found that most authors describe the superior vena cava as a valveless tube whereas typical valves occur in the azygos arch, but not in its orifice (6,12,60,63,97,99). We found only one author who describes the phlebographic presence of a valve at the entrance of the azygos vein into the superior vena cava (29). One anatomical textbook (97) describes two sagittal valves at the confluence between the internal jugular vein and subclavian vein. In contrast, in our series there were no valves at this site.

Thrombus formation on central venous catheters

At the time of our studies most investigators had used IVUS as an adjunct to catheter-based therapeutic procedures. Previous investigations had shown that the method was able to detect dissections and intimal flaps (82,106,108) and distinguish between fibrous, lipid-rich, and calcified plaques (44,85). Fibrous plaques were characterized by bright, relatively homogeneous echo signals. Lipid-rich plaque produced echolucent zones often located within fibrous plaque. Calcified plaque were characterized by bright echo signals beyond wich signal drop-out or acoustic shadowing occured.

The US image of *thrombus* was characterized by a granular or speckled appearance

with varying sonographic grey levels (82,118). In an in vitro study (118) the method permitted the detection of thrombus with 92% sensitivity and specificity.
In another investigation (67) the method had been used successfully for imaging intraluminal thrombus associated with the application of vena cava filters. To our knowledge there were no published studies concerning thrombus formation on central venous catheters.

Thrombus formation on central venous indwelling catheters, including double-lumen hemodialysis catheters, is a significant clinical problem. According to the Medical Device Reporting of the Federal Food and Drug Administration, in the USA central venous catheters were associated with 170 complications, including 52 deaths, during a 2-year period.Thrombosis and thromboembolic events were under-reported in this report compared with the medical literature (93). In one report including the autopsy material of one year, from one hospital, 10 cases of fatal thromboembolism after central venous catheterization were found (72). This discrepancy is probably due to the lack of reliable methods for in vivo documentation of thrombus formation on central venous catheters. Modified conventional phlebographic techniques has hitherto been the method of choice. But these methods have limitided diagnostic value. In phlebographic studies via the cubital veins, minor thrombi will "drown" in the contrast medium. Because of multiple side holes, the angiographic findings may be ambiguous in studies via a dialysis catheter. In patients with partly or completely obstructed catheters, injection of contrast medium into the catheter may be impossible. Moreover, it is desirable to visualize the catheter before withdrawal, since thrombi may loosen and embolize during this maneuvre and the vessel wall may be injured if the catheter is adherent to a parietal thrombus.

In addition to these technical disadvantages there are no published systematic phlebographic studies concerning the frequency of thrombus formation on central venous catheters in asymptomatic patients. We therefore applied IVUS to evaluate the frequency of thrombus formation on central venous catheters (Paper III & IV) and its significance for the function of hemodialysis catheters (Paper IV).The presented material demonstrates that IVUS overcomes the diagnostic limitations of conventional phlebography. Moreover, the method provides valuable information about catheter movement, catheter malposition and vessel wall injuries. Small thrombi with a size of only 2 mm could be recognized. Although the sensitivity of the method was not compared with phlebography in our study it seems unlikely that contrast phlebography could have visualized thrombi of this size. Other investigators have applied intravascular US to assess thrombus trapped in inferior vena cava filters and compared the method with contrast cavography (67). In their study IVUS was superior to cavography in 6 out of 12 cases in its ability to demonstrate the presence and extent of intraluminal thrombus.

The findings in Paper III & IV demonstrate that thrombus formation on central venous catheters is not related to the indwelling duration or the type of catheter. In most cases, even after an indwelling duration of several months, no thrombus could be found. On the other hand, catheter malposition seems to induce thrombosis for a certain degree already after few hours, probably because of vessel wall injuries (patient no.4, Paper III). It is also demonstrated that obstruction of an hemodialysis catheter may occur without any thrombus formation in the veins (patient no.11, Paper IV). This is an important information which may prevent the application of unneccessary systemic fibrinolytic therapy.

Imaging of intravascular stents & stent imaging artifacts

At present there is little information about the benefit of IVUS as a routine method during and after interventional procedures. In selected cases it may provide valuable information which can influence the outcome of the procedure. However, documentation whether routine application of the method can improve the long-term results in a larger series is difficult.

In Paper V we attempted to evaluate the benefit of IVUS as a routine supplement to follow-up angiography after endovascular stent implantation. The series is small and consists mainly of peripheral and a few coronary stents. In accordance with other and larger investigations (39) the coronary stents were insufficiently visualized by conventional radiologic methods and only IVUS permitted en exact identification of the stent position. In peripheral stents, which have a larger strut thickness, IVUS did not reveal more information concerning vessel and stent diameter, stent stenosis and intraluminal surface contact than angiography alone.

In addition, artifacts caused by the highly reflectant metallic stent struts, interfered with the native vessel wall and partly obscured its structural details.This is a serious drawback in the evaluation of intravascular stents since optimal stent adaption to the arterial wall is supposed to be a prerequisite for long term patency of the stented vessel.

As discussed in connection with US imaging of the normal arterial wall, various artifacts may lead to misinterpretation of intravascular US findings. Most of these are described in the literature (16-17,31-32,41-42,48). However, little attention was payed to artifacts caused by metallic stent filaments. In Paper VI the results of an experimental study are presented in which these artifacts were analyzed. It is important that the operator understands these wave propagation effects which in the paper are denoted shadowing, transducer-stent reverberations and stent-filament reverberations. These artifacts may lead to misinterpretation of the US-image and inhibit the detection of small cavities and dissections which may exist between the stent and the vessel wall.

Thrombogenicity of intravascular ultrasound imaging catheters

Little attention has been paid to the potential risks of thromboembolic complications related to the use of intravascular US imaging devices. Some of the 1st generation US imaging catheters had irregularities on the surface of its asymmetric tip to allow for the electric lead and there are side channels for the guidewire in the distal end of the catheter. Such irregularities on the catheter surface may produce turbulence of the blood stream, thereby contributing to an increased thrombogenicity. In addition it is possible that mechanical vibrations, caused by the rotating wire within the catheter lumen, may influence the clot-promoting properties of the imaging device.

In many therapeutic and diagnostic procedures these catheters pass through tortuous, atherosclerotic, stenosed or occluded vessel segments with reduced blood flow and are more or less in contact with thrombotic material and ulcerated or traumatized intima. In case of thromboembolic complications, it is difficult to decide whether the therapeutic procedure itself or the imaging catheter is responsible for the event. Patients who undergo interventional catheterizations are usually heparinized and medicated with acetylsalicylic acid. It was therefore of special interest to get information about whether the use of IVUS demands special precautions, such as anticoagulant treatment or limited duration of the imaging procedure in patients who undergo diagnostic catheterizations.

Since IVUS is a suitable method for the detection of intraluminal thrombus and catheter thrombus, it was natural to investigate possible thrombus formation on the surface of the catheter by means of the US imaging system itself. At the end of the procedure the US catheter was slowly pulled back into the introducer sheath. The US findings during withdrawal were observed in order to detect thrombi which were wiped off from the catheter surface or thrombus aggregation on the introducer sheath. The method has its limitations but is comparable with previous angiographic studies of “pull-out” thrombi by other investigators (53,96). Of special interest were the venous catheterizations. None of these patients had received any anticoagulant medication. Furthermore, because of the relatively low blood flow velocity in the venous system, it is likely that thrombus formation on the catheter surface is more frequent in venous than in arterial procedures.

The incidence of thrombus formation in this group was 13% and related to the occurrence of malignant neoplastic disease, which may indicate an increased coagulability in these patients. The detected “pull-out” thrombi were small and it is unlikely that they had any clinical consequence.

CONCLUSIONS

1) A typical intravascular US image of the arterial wall containing three layers is found in young, healthy individuals as well as in adult and elderly subjects.

2) At frequencies of 12.5 to 30 MHz there is no difference in the in vivo US appearance of muscular and elastic arteries in young individuals.

3) In patients with extensive clinical and arteriographic atherosclerosis in other parts of the arterial tree, a segment of the iliac arteries can have the same appearance as seen in young healthy individuals.

4) In the major veins IVUS provides cross-sectional in vivo visualization and the demonstration of the motility of small intraluminal structures which cannot be revealed by traditional diagnostic methods. Further investigation of these structures may add to the information about anatomy and function of various venous segments.

5) IVUS is a suitable method for the visualization of thrombus formation on central venous catheters. The method has several advantages compared to traditional phlebographic methods and may provide new information related to complications following application of central venous catheters in general. The method may be helpful in the decision whether a malfunctioning indwelling catheter should be removed or whether fibrinolytic treatment should be started and it permits repeat follow-up studies of such therapy.

6) The benefit of IVUS as a routine supplement to follow-up angiography after

peripheral endovascular stent implantation is limited since angiography alone reveals most of the information which is relevant in the clinical setting. The investigator should be aware that small dissections or cavities between the stent and the vessel wall can be difficult or impossible to detect with this method because of artifacts caused by the highly reflective stent filaments.

7) The thrombogenicity of intravascular US imaging devices is not higher than that of conventional angiographic catheters. The observed "pull-out" thrombi were small and it is unlikely that they have any clinical significance.

Future developments

This work was carried out at a time when intravascular ultrasonography still was in an early evolving phase. In the mean time further developments such as three-dimensional image reconstruction and "hybrid" catheters which allow simultaneous US- imaging, balloon-dilatation, pressure- and flow-measurements, have opened new perspectives.

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Paper I

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FROM THE DEPARTMENTS OF RADIOLOGY AND SURGERY, UNIVERSITY HOSPITAL OF TRONDHEIM, AND THE DEPARTMENT OF BIOMEDICAL ENGINEERING, UNIVERSITY OF TRONDHEIM, TRONDHEIM, NORWAY.

INTRAVASCULAR ULTRASONOGRAPHIC APPEARANCE OF ANGIOGRAPHICALLY NORMAL ARTERIES RELATED TO AGE AND THE OCCURRENCE OF VASCULAR DISEASE

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Abstract

In 22 individuals (mean age 52 years) the ultrasonographic images of arteries defined as normal by arteriography were studied and related to the age and medical history of the patients. The series was divided into 2 groups: patients with clinical manifestation of atherosclerosis and patients without a history of arterial disease. The study included 6 young patients (mean age 14 years) referred for angiographic documentation of abolished intracranial circulation. A typical 3-layered appearance of the arterial wall was found in young healthy individuals as well as in adult and elderly subjects. There was no difference in the ultrasonograhic appearance of muscular and elastic arteries. In patients with extensive obstructive atherosclerosis affecting other parts of the arterial tree, a segment of the iliac artery can have the same appearance as seen in young healthy individuals. There are indications that severe hypertension can result in a thickening of the middle low-echogenic layer of the arterial wall. In patients with chronic renal insufficiency, small calcifications in the middle layer were a typical finding.

Key words: Arteries, US; ultrasound (US), intravascular; atherosclerosis.

Intravascular ultrasound (US) imaging is a new, evolving modality in which a high frequency transducer placed on the tip of a catheter provides high resolution cross-sectional real-time images of the vessel wall including its various layers. Recent in vitro and in vivo studies have shown that this technique can be used to characterize and quantify arterial wall abnormalities and disease. Furthermore, lumen dimensions and wall thickness can be measured. Thus interventional procedures as well as the effect of pharmacologic therapy can be evaluated (2–16, 18, 19, 22, 23, 25–28, 31, 32).

A number of in vitro and in vivo investigations have demonstrated a typical 3-layered appearance on the US image of the arterial wall, suggested to represent the intima, the media, and the adventitia as observed at gross histologic examination. Most investigators conclude that this 3-layered appearance of the vessel wall is a normal US finding (4, 9, 15). Others could not confirm this finding in several otherwise healthy kidney donors without evidence of arterial disease (5).

Several in vitro studies have correlated the US findings to histologic examinations (6, 12–14, 24, 30). The results are partly contradictory, and there is still debate on the anatomic substrata for the US findings from in vivo imaging of muscular as well as elastic arteries. Results from in vitro observations cannot without reservations be transferred to in vivo findings. Most published clinical investigations have hitherto been performed in elderly patients referred to arteriographic investigation for atherosclerotic manifestation. No systematic investigations have been performed in vivo of normal arteries in younger persons without evidence of arterial disease.

The main purpose of our investigation was to study the US images of arteries defined as normal by arteriography. The findings were related to the age and medical history of the patients. Furthermore, the study was designed to investigate the possibility of whether one selected segment of the iliac arteries could give information about the possible presence and extent of pathologic changes in the rest of the arterial tree.

Material and Methods

The series includes 22 individuals (12 men, 10 women, mean age 52 years, range 6–87 years). All patients were

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Table 1

Indications for angiography

Patients without atherosclerotic manifestations	11
Documentation of abolished intracranial circulation	6
Pelvic angiography prior to replacement of hip prosthesis	2
Pancreatic angiography (insulinoma?)	1
Renal angiography (anomalous renal artery?)	1
Hepatic angiography (liver metastasis)	1
Patients with atherosclerotic manifestations	11
Intermittent claudication, arteriography prior to vascular surgery	5
Intermittent claudication, iliac PTA	3
Percutaneous transluminal renal angioplasty of known renal artery stenosis	2
Pelvic arteriography prior to kidney transplantation (renal tuberculosis, ischemic heart disease)	1
Total	22

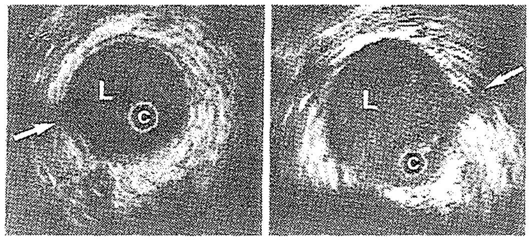


Fig. 1. Typical US appearance of the external iliac artery (a) and external iliac vein (b). The arterial wall shows 3 layers: an echogenic inner layer, a thin dark middle layer, and an echogenic outer layer. The vein has a homogeneous wall structure. L – vessel lumen, c – catheter. The shadowing phenomenon (→) is an artifact caused by the guide wire. Catheter diameter 2 mm.

referred for arteriography and divided into 2 separate groups: 1) patients without a history of arterial disease; 2) patients with a medical history and clinical signs of intermittent claudication or critical leg ischemia, angina, myocardial infarction, TIA, or renal artery stenosis. The indications for arteriography are shown in Table 1.

Concomitant diseases included severe hypertension (n = 3), diabetes (n = 3), chronic renal insufficiency (n = 3), and hypercholesterolemia (n = 1). In all patients transfemoral arteriography of the pelvic arteries was performed using the Seldinger technique. Following arteriography intravascular US imaging of a segment of the external iliac artery located over the iliosacral joint in the frontal projection was performed. The reason for choosing the iliosacral joint as a reference point was the need for an anatomic landmark that could easily be identified on fluoroscopy in case several subsequent investigations should become necessary during the same procedure. Furthermore, this segment of the artery has a relatively straight anatomic course through which the catheter can easily be passed. This part of the arterial system is characterized as a muscular artery. It was a prerequisite that this part of the artery had a normal angiographic appearance. In 2 patients the contralateral side of the iliac arteries was investigated after crossing the aortic bifurcation with the US catheter.

In 19 cases the common iliac artery and in 13 patients the abdominal aorta were also investigated. In 3 children the thoracic aorta and the subclavian artery were studied, and finally the common carotid and the vertebral arteries were investigated in 2 children.

In addition to the studies of arteries, the iliac veins were investigated in 4 patients, referred for either cavography or for catheterization of the renal veins.

Eleven of the arterial investigations were performed with an 8 F or 5 F (2.7 or 1.7 mm) CVIS ultrasound imaging catheter (Cardiovascular Imaging Systems Inc., Sunnyvale, CA) using 20 and 30 MHz transducers, respectively. In the other 11 cases a 6 F (2.0 mm) Sonicath imaging catheter (Boston Scientific, Waterstone, USA) with 20 or 12.5 MHz transducers were used. Imaging with the Sonicath catheters is based on a rotating US transducer, while the CVIS catheters contain a fixed transducer combined with a rotating mirror which reflects the US beam at the vessel wall. Image resolution and radius of penetration of the US beam varies depending on the frequency of the transducer. At 20 MHz axial resolution in depth, perpendicular to the long axis of the catheter, is 0.08 to 0.15 mm (5, 32). The catheters were used in combination with the US imaging systems IVUS (Diasonics, Milpitas, CA) and CVIS Insight.

Depending on the type of the catheter arterial introducer sheaths 6 to 8 F were used. In 13 cases the catheterization was performed over a guide wire. Patients undergoing angioplasty were anticoagulated with 5 000 IU Heparin. No anticoagulation was used in the other patients. The investigations lasted 3 to 20 min. No complications related to this examination were observed.

The measurements on the arteriograms were made by a ruler with the catheter as a reference. The US measurements were either done by a cursor on the monitor, using the included measurement program, or by a ruler on the hardcopies.

The investigation was approved by the regional ethical committee.

Six of the 7 young "healthy" individuals included were patients referred from our intensive care unit for arteriographic investigation of the intracranial circulation following severe traffic accidents. According to Norwegian law, arteriographic documentation of abolished intracranial circulation forms a basis for the criteria of brain death. In the rest of the series, including an 18-year-old boy suspected of having a renal vascular anomality, a written consent was given after proper information about the procedure was provided.

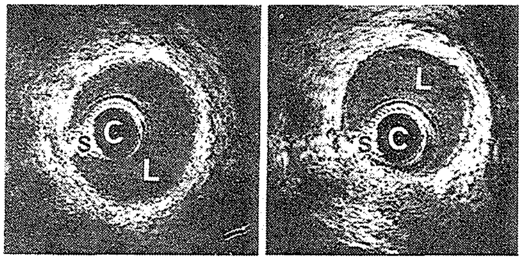
Results

In all cases US imaging of the external iliac artery revealed 3 layers of the arterial wall, irrespective of which transducer

Table 2

Intravascular US observations in angiographically normal segments of the external iliac artery

Category of patients	Mean age (range)	n	US observations	n
Young, healthy individuals	14 (6–27)	7	Regular 3-layered appearance	7
Adults and elderly subjects without atherosclerotic manifestations	64 (59–72)	4	Regular 3-layered appearance	4
Adults and elderly subjects with atherosclerotic manifestations	71 (63–87)	11	Regular 3-layered appearance	4
			Calcified plaque	1
associated with				
severe hypertension (n = 3)			Thickening of low-echogenic middle layer	2
chronic renal failure and diabetes (n = 2)			Calcifications in the low-echogenic middle layer	2
chronic renal failure, diabetes and rheumatoid arthritis (n = 1)			Thinning and disintegration of wall structures, small calcifications	1
high age (n = 1)			Thickening and increased echogenicity of middle layer, decreased echogenicity of outer layer	1
Total	52 (6–87)	22		22



a b

Fig. 2. US images of the external iliac artery in a 27-year-old woman with severe brain injury, both obtained from the same arterial segment. In a) there is no layering of the wall structure. After repeated catheter passage 70 s later the 3-layered wall structure is visualized (b). s – catheter-strut-signal. Distance between 2 calibration marks 1 mm.

frequency had been applied: One echogenic inner, a middle low-echogenic, and an echogenic outer layer (Table 2). A more homogeneous wall structure without the stratified arrangement was observed in pelvic veins (Fig. 1).

Young, healthy individuals. In young, healthy individuals it was sometimes difficult to identify the various layers of the arterial wall. Often the layers were only identified following repeated investigation of the actual arterial segment and sometimes the layers could only be observed in a part of the arterial circumference (Fig. 2).

No attempt was made to measure the thickness of the various layers, because the small dimensions were close to the limitation of the resolution of the imaging system. Furthermore, the thickness of the arterial wall changes due to pulsatory movements. From a rough visual estimation the inner high-echogenic layer and the middle low-echogenic layer had approximately the same thickness.

In most patients it was not possible to visualize the aortic wall structures sufficiently due to the large luminal diameter and the arterial pulsations. In 3 children with a small aortic diameter, however, good visualization of the abdominal aorta and the thoracic aorta was obtained. These images could not be differentiated from those obtained from the external iliac artery regarding the composition of the arterial wall. The same results were found at investigation of the subclavian artery in 3 young patients aged 13, 17, and 27 years, and from the common carotid artery and vertebral artery in 2 children aged 8 and 13 years, respectively (Fig. 3).

Adults and elderly patients without atherosclerosis. The US images of the external iliac artery in this group had the same overall appearance as in children and young patients. There was a high-echogenic inner layer appearing as a thin lamellated structure. The low-echogenic middle layer of the arterial wall in this group had approximately the same thickness as the inner one (Fig. 4 a).

Adults and elderly with atherosclerotic manifestations. In spite of the relatively high age and the fact that this group had clinical signs of obliterating atherosclerosis, in 4 of these patients the external iliac artery had the same US appearance as described in young, healthy individuals (Fig. 4 b).

In 7 patients, however, the US image was different from the rest of the series (Table 2). Two out of 3 patients with severe hypertension had a low-echogenic middle layer of the arterial wall which seemed to be thicker than the high-echogenic inner layer. This finding was especially pronounced in a patient with severe renovascular hypertension that had lasted for about one year. But it was impossible to obtain accurate measurements because of pulsatory movements (Fig. 5 a).

One out of 3 patients with chronic renal insufficiency had a thinner overall thickness of the arterial wall, almost disintegrated wall structures and small calcifications (Fig. 5 b). This pattern was demonstrated in one patient treated by hemodialysis having in addition diabetes and rheumatoid arthritis. In the 2 other patients with chronic renal insuffi-

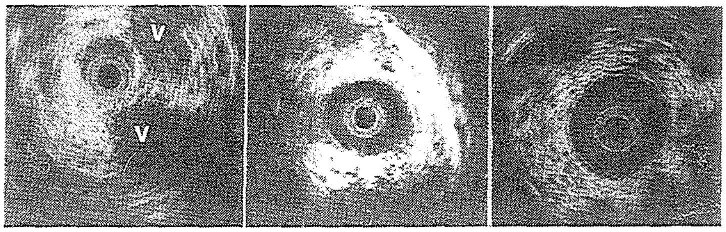


Fig. 3. Images obtained from the vertebral artery (a), subclavian artery (b), and abdominal aorta (c) of a child, 13 years of age. There is no difference in the overall US appearance of the vessel wall structure compared with images obtained from the external iliac artery. In a) the echogenic inner layer is visualized at 1 o'clock. v – neighbor vessels. Catheter diameter 2 mm.

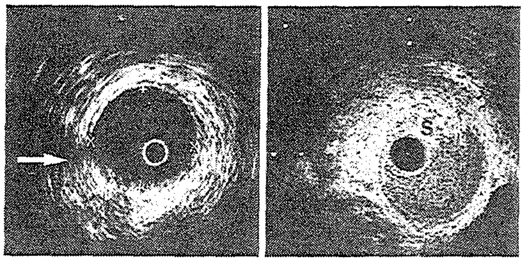


Fig. 4. US images of the external iliac artery of a 72-year-old woman without atherosclerotic manifestations (a) and a 63-year-old man with intermittent claudication and ischemic heart disease (b). There is no difference observed in the composition of the vessel wall. In a) there is a catheter with rotating transducer, in b) a fixed transducer/rotating mirror device. Therefore the overall appearance of the images is different. → – a guide wire artifact. s – catheter-strut-signal. The distance between the calipers (x, +) in a) is 10 mm, the distance between the closest calibration marks in b) is 2 mm.

ciency and diabetes, small calcifications in the middle layer of the arterial wall were observed (Fig. 5 c). One of these patients also had extensive mediasclerosis of the femoral arteries.

In the oldest patient (87 years of age), the middle layer of the arterial wall was thickened and had partly an abnormal high echogenicity while the echogenicity of the external ("adventitial") layer was lower than normal (Fig. 5 d). This patient, who was referred for PTA of the common iliac artery, had a normal blood pressure, and a normal kidney function.

Many patients in this group had extensive atherosclerotic changes angiographically with multiple, high-grade stenoses in other parts of the iliac arteries. There was, however, no obliterating process at the arterial segment of the iliac artery which was investigated by US. Only one patient had a small calcified plaque (Fig. 5 e).

Like others (3) we found a highly significant correlation ($r=0.91$, $p<0.0001$) between the arterial diameter as measured by arteriography and that measured by US (Fig. 6).

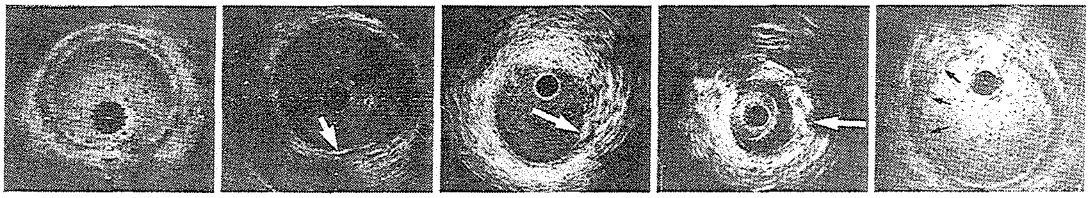
Discussion

To our knowledge there are hitherto no published clinical investigations of the US appearance of normal human arteries which include healthy young individuals and children. Since cerebral arteriography in our country is necessary to confirm the diagnosis of brain death, it was found justified to introduce the US imaging catheter to study the arterial tree in some of these patients after the diagnosis of completely abolished cerebral circulation had been made. This also gave us the opportunity to visualize the subclavian artery and neck arteries in some patients. Furthermore, we could take the time necessary to get repeated visualization of a certain arterial segment for proper documentation.

Contrary to other investigators (5), we could confirm the typical 3-layered structure of the arterial wall in all individuals irrespective of age. However, for proper visualization it may be necessary to pass the catheter several times through the actual vessel segment. Angulation of the catheter and unstable catheter position due to pulsatory movements may cause inconsistent and asymmetric imaging of the inner high-echogenic ring. These findings should not be interpreted as fatty streaks or asymmetric echogenic atheromatous thickening of the intima.

Furthermore, we found no difference in the overall US appearance of the external iliac artery, the aorta, and the subclavian artery in young healthy persons. Thus we cannot confirm the statement (19) that arteries with a muscular media depict a 3-layered appearance and that those with a media composed primarily of elastic tissue do not.

In spite of a series of in vitro studies, the anatomic substrata of the 3-layered US appearance of normal and minimally atherosclerotic human arteries are still controversial. Thus MEYER et al. (12) concluded that the intima and adventitia are high-echogenic because of their large collagen content, and the muscular media is hypoechoic due to the relative lack of collagen, while GUSSENHOVEN et al. (6, 7) suggested that the middle ring is hypoechoic due to the scarcity of elastin in the muscular media while the bright reflections are caused by the internal and external elastic lamina. NISHIMURA et al. (14) observed different US charac-



a b c d e

Fig. 5. US images with pathologic changes obtained from the external iliac artery of 5 patients. a) Thickening of the low-echogenic middle layer in a patient with severe renal hypertension. Distance between closest calibration marks 2 mm. b) Thinner overall thickness of the arterial wall, disintegration of wall layers and faint calcification (→) of the inner layer at 6 o'clock with signal drop-out. Distance betweeen closest calibration marks 1 mm. This patient had renal insufficiency and in addition diabetes and rheumatoid arthritis. c) Small calcification (→) in the middle wall layer at 4 o'clock with signal drop-out in another patient with chronic renal insufficiency and diabetes. d) Prominent calcified plaque at 3 o'clock (→) in a patient with intermittent claudication. e) Thickening of the middle wall layer with anomalous high echogenicity from 8 to 12 o'clock (→) and unusual low echogenicity of the outer layer in an 87-year-old patient. Distance between closest calibration marks 1 mm.

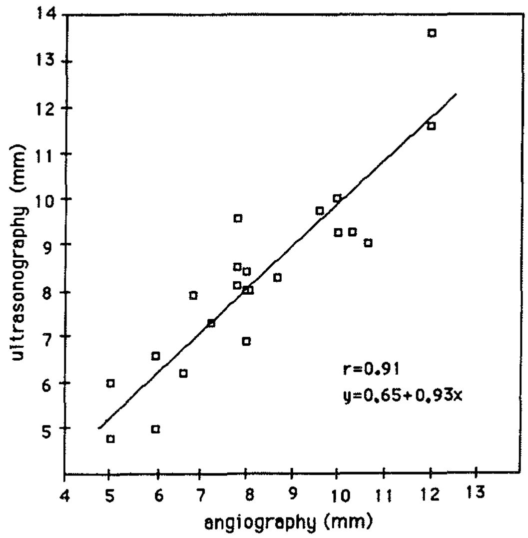


Fig. 6. Regression plots and regression line of maximal lumen diameter as measured by angiography and US. There is a highly significant correlation ($r=0.91$, $p<0.0001$).

teristics depending on the relative amount of smooth muscle cells and elastic fibers in the media of the arteries found at histologic examination. WEBB et al. (30) in microsurgery investigations and perfusing bovine coronary artery segments over a graded range of pressures found that the echogenic inner layer mainly represents the internal elastic lamina. This layer became more prominent in nonpressure-fixed in vitro specimens.

Other groups who have used microdissection techniques to determine the histologic origin of the 3-layered appearance of normal muscular arteries (24) found that the bright inner echo signals were due to the interface of blood with the intima or internal elastic lamina, or both. The bright outer ring was thought to be due to the acoustic interface between media, adventitia, or external elastic lamina, respectively. Similar conclusions were reached by NOLSØE et al. (17) who investigated the US appearance of the normal aortic wall by in vitro dissection studies and needle experiments. They concluded that the intima itself is of no importance in generating the image but that the inner echogenic ring is rather the interface between the blood in the lumen and the tissue itself.

These microdissection studies correspond with our observations of an echogenic inner ring in the aorta and subclavian artery even in young patients. According to histology textbooks (1) the intima of a normal aorta in adult humans is approximately 0.12 mm and in the supraaortic arteries even less. The axial resolution of a 20 MHz transducer is 0.08 to 0.15 mm. We found an echogenic inner ring in the aorta and subclavian artery in children using a transducer of 12.5 MHz which has a poorer axial image resolution than the 20 MHz transducer.

Recent research seems to indicate that the early sign of atherosclerosis is thickening of the intimal and medial layers (20, 21, 29). Consequently, intravascular US imaging could be useful in the detection and monitoring of early atherosclerosis. Our study has shown, however, that the US investigation of an arteriographically normal arterial segment selected by random can show a normal appearance, even in patients with extensive atherosclerotic changes in other parts of the arterial tree.

Conclusions. 1) The typical US image of the arterial wall containing 3 layers is found in young, healthy individuals as well as in adult and elderly subjects; 2) At frequencies of 12.5 to 30 MHz there is no difference in the in vivo US appearance of muscular and elastic arteries in young individuals; 3) In patients with extensive clinical and arteriographic atherosclerosis in other parts of the arterial tree, a segment of the iliac arteries can have the same appearance as that seen in young, healthy individuals; 4) Single observations from our patients indicate that severe hypertension can result in a thickening of the middle low-echogenic layer of the arterial wall. In patients with chronic renal insufficiency small calcifications in the middle layer were a typical finding. In very old patients the US image of the arterial wall was characterized by increased echogenicity and thickening of the middle layer and decrease of echogenicity in the outer layer, probably due to degeneration of the media and loss of elastic components of the external elastic lamina.

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Paper II

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INTRAVASCULAR ULTRASONOGRAPHY

Normal and pathologic findings in the great veins

K.-D. BOLZ, H. O. MYHRE, B. A. J. ANGELSEN and A. NORDBY

Abstract

The intravascular ultrasonographic findings in normal and diseased veins after transfemoral catheterization of 25 patients are presented. The iliac veins, the inferior and superior vena cava, the renal veins, the right atrium, both brachiocephalic veins, and the right internal jugular vein were studied. In 4 cases valves or valve-like structures were observed. Anatomic variants such as spurs and webs were seen in 3 and mural thrombi or postthrombotic wall changes in 4 patients. In one case a sphincter-like ostium venae cavae was observed. In 2 patients thin filaments within the right atrium, most likely a Chiari net, were seen. Two patients had an abnormal, stratified "artery-like" vessel wall structure. This new imaging modality has several potential applicabilities in the veins and may contribute new information about anatomy and function of the venous system. It provides cross-sectional in vivo visualization and the demonstration of motility of small intraluminal structures which cannot be revealed by traditional diagnostic methods. Because of the wide range of anatomic variation in the venous system, knowledge of its normal intravascular ultrasonographic appearance is a prerequisite for further clinical investigations.

Key words: Veins, pathology; —, anatomy; ultrasonography, intravascular.

Intravascular ultrasound imaging is a new method which provides cross-sectional in vivo real-time visualization of vascular morphology with hitherto unknown image resolution. Most investigators have used this method as an adjunct to catheter-based therapeutic procedures in the peripheral and coronary arteries (6, 8, 14, 15, 26–28). There are, however, several potential diagnostic applicabilities of this method in the venous system. We have recently shown that intravasal ultrasonography is a suitable method for the visualization of thrombus formation on central venous catheters (3). Others have used the method in the assessment of chronic thromboembolic pulmonary disease (6, 23) or tumor infiltration into venous structures (18).

Because of the wide range of anatomic variations, knowledge of the normal intravasal ultrasound appearance is a prerequisite for further clinical studies in the venous system. We therefore present the ultrasonographic findings in normal and diseased veins after transfemoral ultrasound imaging of 25 patients.

Material and Methods

The series of 25 individuals includes 12 men and 13 women, with a mean age of 48 years (range 23–87 years). In 6 of these patients the ultrasound investigation was carried out after arteriographic documentation of abolished intracranial circulation. The indications for central venous catheterization in the other patients are shown in Table 1. The study was approved by the regional ethics committee. Except in patients with abolished intracranial circulation, a written consent was given after proper information about the procedure.

Most of the ultrasound investigations were performed via the right femoral vein. In patients undergoing cavography or renal vein catheterization the ultrasound catheter was inserted on both sides, one side at a time. The renal veins were imaged after insertion of a preformed angiographic catheter and shifting this catheter with the imaging catheter over a long guidewire.

In 19 patients a 6.2 F (2.0 mm) Sonicath Sidesaddle catheter (Boston Scientific, Waterstone, USA) with a 20 MHz transducer in combination with a 0.6-mm guidewire was used. In 2 patients we used the same catheter type, but with a 12.5 MHz transducer. Four patients were investigated

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Table 1

Indications for central venous catheterization in 25 patients studied by intravascular ultrasound

Diagnosis	n
Chronic venous insufficiency	7
Suspected pulmonary embolism	2
Renal hypertension	1
Renal carcinoma	2
Liver metastasis	1
Suspected thrombus formation on central venous indwelling catheters	6
Abolished intracranial circulation	6

without the use of a guidewire, 2 of them with a CVIS 8 F (2.7 mm), 20 MHz catheter (Cardiovascular Imaging Systems Inc., Sunnyvale, CA) and 2 with a Sonicath 6 F (2.0 mm) catheter with rounded tip. The axial resolution of the imaging system – the resolution perpendicular to the long axis of the catheter – is in the range of 0.08 to 0.15 mm, at 12.5 MHz somewhat poorer. The radial field of view is about 20 mm.

In all cases 8 F (2.7 mm) introducer sheaths were used. Under fluoroscopic guidance and continuously recording the ultrasound image on a videotape, the ultrasound catheter was passed through the venous system. The position of the ultrasound catheter in the regions of interest was documented by radiographs. The video recordings were analyzed off-line in slow motion after completed catheterization. The number of the various vein segments studied by ultrasound is shown in Fig. 1. Mean catheterization time after insertion of the introducer sheath was 7.5 min (range 3–20 min). There were no complications following the ultrasound investigations.

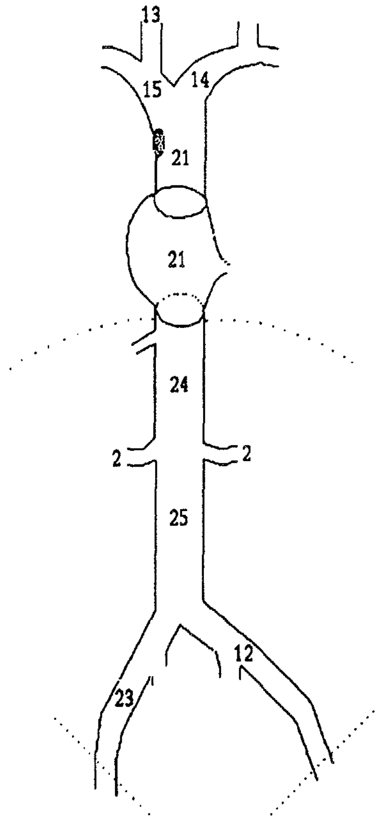


Fig. 1. Number of various vein segments imaged by intravascular ultrasonography after transfemoral catheterization of 25 patients.

Results

Ultrasound images of one or both iliac veins were obtained in all patients (Fig. 2). It was sometimes difficult to pass the left common iliac vein with the imaging catheter, but by use of a guidewire the caudal part of the inferior vena cava could be catheterized in all patients. One patient had a tumor obstruction of the infrarenal vena cava. In the other 24 cases the entire inferior vena cava was investigated. Catheterization of the superior vena cava and its central branches could easily be performed in all cases where it was attempted (Fig. 1). Because of its large luminal diameter only a partial view of the inferior vena cava was obtained in most cases. In addition, pulsatory movements and marked respiratory changes of vessel circumference made interpretation of the images difficult. The orifice of the renal and hepatic veins could be visualized in all cases. There was a better visualization of the superior vena cava and its tributaries due to less respiratory caliber variation (Fig. 2). A major problem in all investigated vessel segments was the lack of a reliable spatial orientation – left/right, anterior/posterior – when the catheter was in a position without typical anatomic landmarks.

Specific ultrasonographic findings which cannot be revealed by traditional diagnostic methods are shown in Table 2.

Wall structure. Most of the veins had a homogeneous wall structure. In 2 cases, however, the caudal inferior vena cava had an "artery-like" stratified wall composition (Fig. 3). In both these patients there was a partial or complete obstruction of the inferior vena cava above the investigated level.

Vessel shape. Respiratory changes of vessel shape and lumen could easily be differentiated from constant compressions by "normal" external structures, such as bones or crossing arteries. Fig. 4 shows an impression from the spine on the inferior vena cava in a slim patient. In another case there was a constant deformity of the left common iliac vein, caused by a crossing, tortuous artery (Fig. 5). In one case a "sphincter-like" appearance of the foramen venae cavae could be observed (Fig. 6). This image was caused by pulse synchronous caliber changes and was not related to

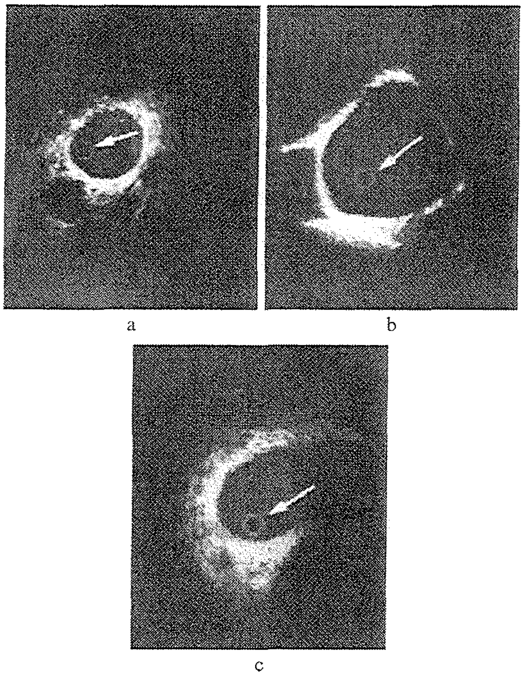


Fig. 2. Typical ultrasonographic appearance of the external iliac vein (a), the superior vena cava at the level of the pulmonary artery (b), and the left brachiocephalic vein at its entrance into the vena cava (c). The imaging catheter appears as a black circle, surrounded by a bright halo, and has a diameter of 2 mm (→). The guidewire is withdrawn.

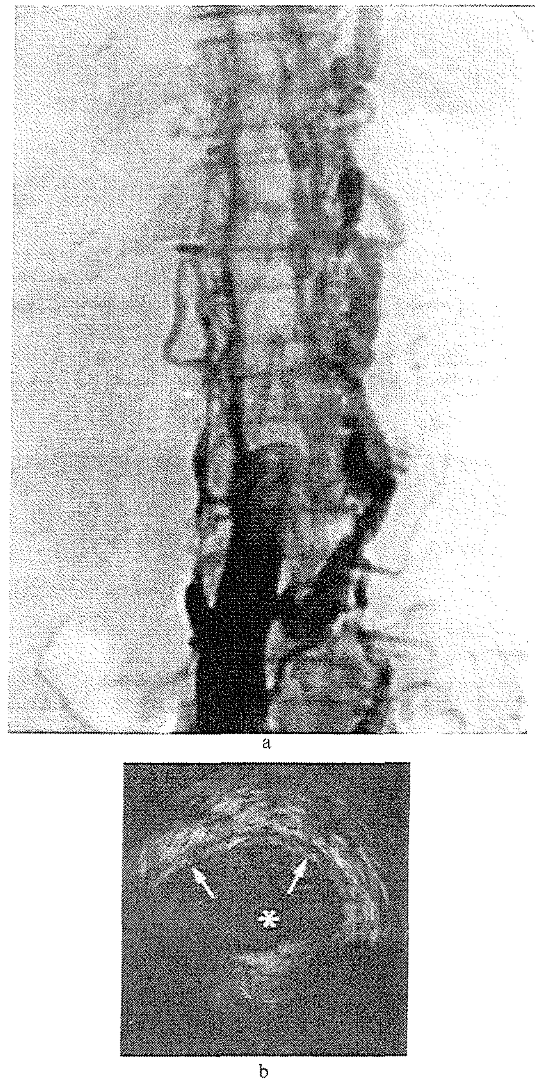


Fig. 3. Cavography in a 71-year-old patient with occluded inferior vena cava (a). Intravasal ultrasonography below the obstruction (b) shows a stratified "artery-like" wall structure (→). * imaging catheter.

Table 2

Intravascular ultrasonographic findings in the great veins after catheterization of 25 patients

Observation	n
Abnormal, "artery-like" wall structure	2
Valves/valve-like structures	4
Spurs/webs	3
Chiari net	2
Sphincter-like ostium venae cavae	1
Mural thrombus/postthrombotic wall changes	3

respiratory movements of the diaphragm. We could not reproduce this finding in other patients.

Valves. A typical, but incompetent, bicuspid parietal valve in the right external iliac artery was observed in one patient (Fig. 7 a). In the same patient a spur-like high-echogenic irregularity of the vessel wall was found in the right common iliac artery (Fig. 7 b). This finding was interpreted as a valve rudiment. In 2 cases there were valve-like sagittal folds at the orifice of the azygos vein, in all other patients there was a smooth junction between the azygos vein and the superior vena cava (Fig. 8). No valves were found at the confluence between the brachiocephalic and the jugular vein, or in the 4 renal veins which were investigated.

Spurs and webs. In one case a membraneous intraluminal structure, partly dividing the vessel lumen in 2, was found at the confluence of the left common iliac vein with the vena cava (Fig. 9). Another patient had a thickened vessel wall with an intraluminal ridge at the same location. In 2 patients gossamer-like floating filaments suspended in the right atrium were observed (Fig. 10). These probably represented a Chiari net or filaments from a fenestrated

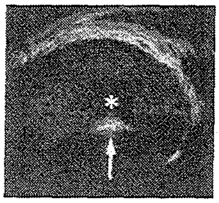
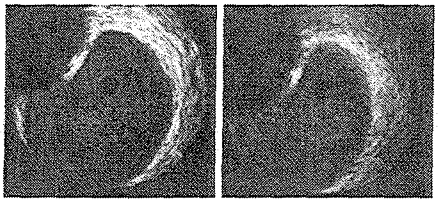
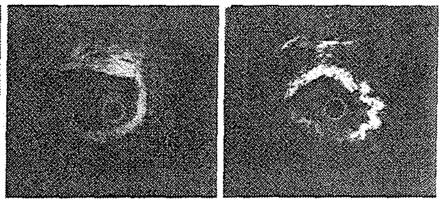
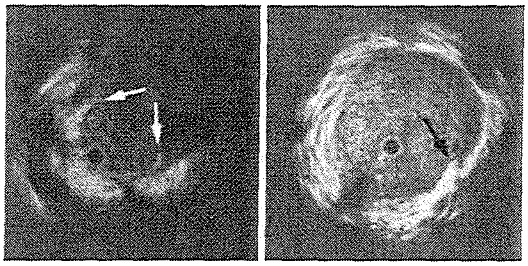




Fig. 4 5a 5b 6a 6b

Fig. 4. Impression by the spine of the inferior vena cava in a slim patient. → the bone reflex. The imaging catheter (*) is close to the osseous structure. Note the broad shadowing phenomenon that obscures a 140° sector of the vessel wall.

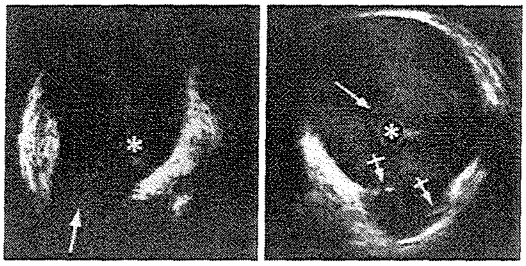
Fig. 5. Constant impression in the wall of the common iliac vein from 9 to 12 o'clock, caused by a tortuous crossing artery. a) Diastole, b) systole.

Fig. 6. Cross-sectional images obtained in the diaphragmatic portion of the inferior vena cava. a) Diastole, b) systole. Pulsatory changes induce a sphincter-like appearance of the vena cava in the systole.



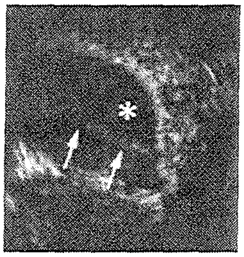
a b

Fig. 7. a) Typical bicuspid valve (→) in the right external iliac vein. b) The same patient. High echogenic vessel wall irregularity (→), probably a valve rudiment, in the right common iliac vein.



a b

Fig. 8. Regular entrance of the azygos vein (→) into the superior vena cava (a). In (b) there are valve-like sagittal folds in the orifice of the azygos vein (+→). (→) – a 5 F (1.7 mm) central venous catheter. (*) Imaging catheter with guidewire reflex.



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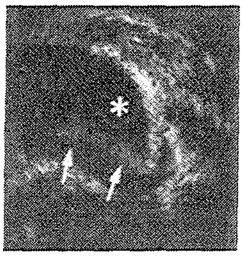

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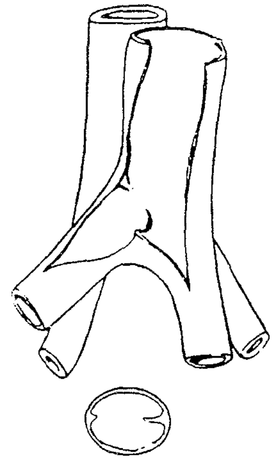

c

Fig. 9. a, b) A membraneous intraluminal structure (→) at the confluence between the left common iliac vein and the vena cava. c) Reproduction of an original anatomic drawing, posterior view. (Reference 20: with permission of Steinkopff Verlag, Darmstadt.)

ostium venae cavae. In another patient a similar structure was found just below the diaphragm close to the entrance of an hepatic vein.

Thrombus formation/postthrombotic changes. In 3 patients who had a central venous catheter, thrombus formation on the catheter wall, parietal thrombi, occlusive vein thrombosis or postthrombotic vessel wall changes were found (Fig. 11). A more detailed description of these findings is given elsewhere (3).

Tumor infiltration. In one of the patients abdominal CT showed an infiltration of the ventral wall of the inferior vena cava by a liver metastasis from a colon cancer. This finding was confirmed by intravasal ultrasonography, but was better visualized at CT. A condition diagnosed as renal vein thrombosis by intravasal ultrasound was shown to represent invasive tumor growth during surgery.

Discussion

Intravascular ultrasonography provides in vivo visualization of the morphology and motility of small intraluminal

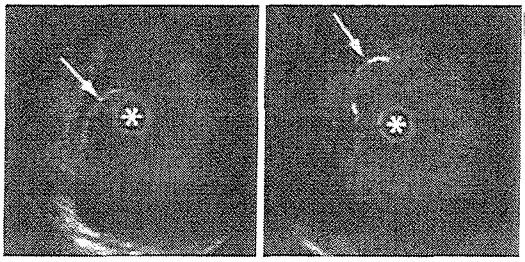

Fig. 10. a, b) Gossamer-like floating filaments (→) suspended within the right atrium, most likely representing a Chiari net. (Both images from the same patient.)

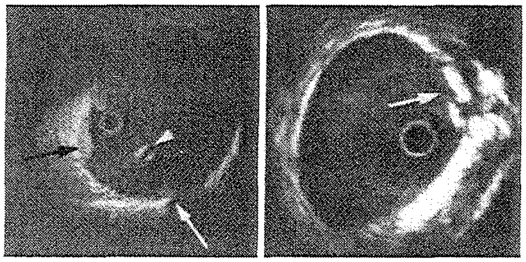

Fig. 11. a) Small mural thrombi (→) in the superior vena cava in a patient with a double-lumen central venous catheter (▶). b) High echogenic vessel wall irregularities (→) in the right internal jugular vein in another patient, probably representing postthrombotic changes after previous cannulation at this site.

structures which cannot be revealed by traditional diagnostic methods. With regard to potential diagnostic applicabilities in the venous system the presented material provides a basis for understanding some of the normal variations in the great veins.

Previous anatomy studies have shown the presence of more or less competent valves and valve-rudiments in the external iliac vein in 22 to 33% of cases and occasionally also in the common iliac vein (1, 10, 22). At pelvic phlebography these structures are rarely observed because of their small dimensions. The demonstration of valve-like folds in the entrance of the azygos vein in 2 of our patients is of special interest. Reviewing textbooks of anatomy and radiology we found only one author who describes the phlebographic presence of a valve at the entrance of the azygos vein into the superior vena cava (9). Most authors describe the superior vena cava as a valveless tube whereas typical valves occur in the azygos arch, but not in its orifice (2, 4, 16, 19, 24, 25).

The frequent presence of intraluminal spurs and webs at the confluence of the left common iliac vein and inferior vena cava is well known (7, 20, 21). The ultrasonographic observations (Fig. 9) have a striking similarity with anatomic studies of these structures (20). However, the interpretation of our findings must be taken with some reservations, since they are not verified by autopsy.

In the past, sphincter-like structures at the orifices of the vena cava have been suggested by several investigators (5, 11, 17). In certain diving mammals the function of such a caval sphincter, connected with the diving reflex, is documented by angiographic techniques (13). Angiography, however, provides only longitudinal views of the vessel, which is not optimal for the demonstration of constricting, circular structures. Thus our observation in Fig. 6 is of special interest as it could indicate the existence of a caval sphincter in man, perhaps as a phylogenetic reminiscence. We could not reproduce this finding in other patients, probably due to the more or less angulated course of the vena cava in its diaphragmatic portion.

The demonstration of a stratified, "artery-like" wall composition observed in 2 patients with completely or partly obstructed inferior vena cava may represent a functional adaptation to increased intravascular pressure, similar to autologous vein grafts used as arterial substitutes. It is known that chronic elevated venous pressure may cause "phlebosclerotic" thickening of the vessel wall structures (12). It could also be, that increased wall tension alone is inducing artery-like acoustic properties in the vessel wall, without morphologic changes.

Conclusions. Intravascular ultrasonography has several potential applicabilities as a diagnostic tool in the venous system. The method provides cross-sectional in vivo visualization and demonstration of mobility of small intraluminal structures with high image resolution. The knowledge of the ultrasonographic appearance of normal intraluminal structures and anatomic variations which are described in this investigation is a prerequisite for further clinical studies. Further investigation of these structures may add to the information about anatomy and function of various venous segments.

ACKNOWLEDGMENT

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Paper III

FROM THE DEPARTMENTS OF RADIOLOGY, ANESTHESIOLOGY, ONCOLOGY, INTERNAL MEDICINE, AND SURGERY, UNIVERSITY HOSPITAL, AND THE DEPARTMENT OF BIOMEDICAL ENGINEERING, UNIVERSITY OF TRONDHEIM, TRONDHEIM, NORWAY.

INTRAVASCULAR ULTRASONOGRAPHIC ASSESSMENT OF THROMBUS FORMATION ON CENTRAL VENOUS CATHETERS

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Abstract

In vitro experiments were performed in order to investigate the appearance of different types of central venous catheters at intravascular ultrasonography. The experiments were repeated with artificially produced thrombi which were made adherent to the catheter wall. All thrombi larger than 1 mm could be identified. In a clinical study including 12 patients who had a central venous catheter, transfemoral intravascular ultrasonography was performed. The catheters had been in place for an average period of 54 days (range 1–360 days). In 3 patients a catheter thrombus, mural thrombus, or occlusive vein thrombosis was found. In 2 of these patients the catheter was occluded, in the 3rd patient it was malpositioned into the contralateral brachiocephalic vein. There were no complications following the ultrasonographic procedures. Mean catheterization time was 7.5 min (range 3–20 min). The advantages of this new method compared with conventional phlebographic studies and its impact on further clinical investigations are discussed.

Key words: Ultrasound (US), experimental; —, intravascular; catheters and catheterization, complications; veins, thrombosis; —, US.

Central venous catheters for monitoring of pressure balances, administration of drugs, fluids, parenteral nutrition, or hemodialysis have been used worldwide for about 30 years. It is well known that thrombus formation on these catheters may occur (1, 3, 6, 8, 11, 14, 17), but there is little information about the frequency and clinical relevance of this complication. The results of conventional phlebographic studies (1, 3, 6, 14) are equivocal, reflecting the fact that there is no reliable method for identification of thrombus formation in vivo. Intravascular ultrasound imaging is a new, evolving modality in which a high frequency transducer placed on the tip of a catheter provides high resolution cross-sectional real-time images of the vessel wall including its various layers. Recent in vitro and in vivo studies have shown that this technique can be used to characterize and quantify arterial wall abnormalities and disease (2, 4, 5, 7, 9, 10, 15, 16). The purpose of this study was therefore to evaluate intravascular ultrasonography as a new method for assessment of thrombus formation on central venous catheters.

Material and Methods

In vitro experiments. In a plastic tube of 2 cm diameter, filled with water and illuding the superior vena cava, different types of central venous and angiographic catheters and one pacemaker-lead were studied by means of a 6.2 F (2.0 mm), 20 MHz and 12.5 MHz intravascular ultrasound catheter (Boston Scientific, Waterstone, USA). At 20 MHz axial resolution of these imaging catheters – the resolution perpendicular to the long axis of the catheter – is in the range of 0.08 to 0.15 mm, at 12.5 MHz somewhat poorer. The radial field of view is about 20 mm. A list of the studied objects is shown in Table 1.

The experiments were repeated with artificially produced thrombi which had been made adherent to the catheter wall and then photographed before ultrasound imaging. The catheter surface was made adhesive by means of a thin film of cyanoacrylate glue (Hermetite, Hunting Specialised Products Ltd., Leeds, UK). The thrombi were produced by adding thrombin powder (Thrombostat, Parke Davis) to human blood and rotating the catheters in the clots. Before imaging, the catheters were flushed with isotonic saline to avoid air in the lumen, which would interfere with the ultrasound image.

The experiments were then repeated in the same manner,

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Table 1

Objects studied by intravascular ultrasonography

Object, manufacturer	Dimensions		Material
	F	mm	
Angiographic guidewire	<3	0.9	Stainless steel
CVC Secalon, Viggo, Swindon, UK	5	1.7	Polyurethane
Pacemaker lead, Vygon Med. Chir. Werke, Aachen, Germany	6	2.0	Polyethylene+metallic lead
Angiographic catheter, Cook	6	2.0	Polyethylene
Angiographic catheter, Cook	7	2.3	Polyurethane, braided steel core
CVC Certofix Trio, Braun-Melsungen, Germany	7	2.3	Polyurethane
Hickman, Quinton Instr. Co., Seattle, WA, USA	10	3.3	Silicone-rubber
Dialysis catheter Permcath, Quinton	13	4.3	Silicone-rubber
Dialysis catheter Hemocath, Med. Co. Inc., Harleysville, PA, USA	13	4.3	Silicone-rubber

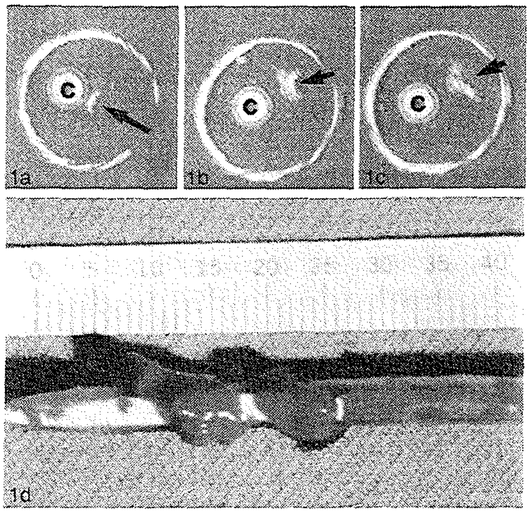

Fig. 1. In vitro ultrasonographic appearance of an hemodialysis catheter imaged in water: a) without thrombus but with an acoustic interface (→); b) and c) with thrombus (→). d) Catheter with adherent thrombus photographed prior to imaging. C – imaging catheter. Scale in mm.

but the plastic tube was filled with heparinized blood instead of water.

Clinical study. In 12 patients having a central venous catheter, intravascular ultrasonography of the right atrium, the superior vena cava, both brachiocephalic veins, and the central part of the right internal jugular vein was carried out. The catheterization was performed via the right femoral vein after local anesthesia (Xylocain, Astra, 5 mg/ml). 6.2 F (2.0 mm) 20 MHz imaging catheters (Sonicath Sidesaddle, Boston Scientific) were used in combination with a 0.64 mm guidewire and 8 F (2.7 mm) introducer sheaths. Under fluoroscopic guidance and continuously recording the ultrasound image on a videotape, the imaging catheter was passed along the central venous catheter and in addition placed selectively into the contralateral brachiocephalic vein. The position of the ultrasound catheter in the regions of interest was documented by radiographs. Mean catheterization time after insertion of the introducer sheath was 7.5 min (range 3–20 min). There were no complications following the ultrasonographic investigations.

The video records were analyzed off line in slow motion after completed catheterization.

The investigation had been approved by the regional ethical committee.

Six patients with a central venous catheter in place had been referred from the intensive care unit for arteriographic investigation of the intracranial circulation. According to Norwegian law, arteriographic documentation of abolished intracranial circulation forms a basis for meeting the criteria of brain death. In the rest of the series a written consent was given following proper information about the procedure. The catheters had been in place for a mean of 54 days (range 1–360 days). The indications for central venous cannulation, catheter types and indwelling time are shown in Table 2.

Results

In vitro experiments. The ultrasonographic appearance of the imaged catheters was characterized by a bright echo according to the interface between the catheter surface and the fluid. The pacemaker lead and the angiographic catheter with braided steel core gave the brightest echoes. In the other catheters the echogenicity was proportional to the catheter dimension and was not influenced by the catheter material. When studied in blood all catheters caused a marked shadowing phenomenon. All thrombi protruding more than 1 mm prominent from the catheter surface could be identified, both with 20 MHz and with 12.5 MHz transducers (Fig. 1). Surrounded by blood, the thrombi appeared as inhomogeneous granular or speckled echo signals with gray level shades markedly higher than those of blood. This finding is in accordance with in vivo ultrasonographic observations of intraarterial thrombi described by others (10, 16, 18). Identification of the thrombi was possible irre-

Table 2

Indications for central venous cannulation, catheter types, indwelling duration and ultrasonographic findings in 12 patients studied by intravascular ultrasound

Patient	Indication for CVC	Catheter type	Indwelling duration, days	Thrombus formation +/−	Remarks
1	Intensive care/brain damage	Secalon	1	−	
2	Histiocytosis X	Vascuport	360	+	CVC obstructed
3	Hemodialysis	Permcath, Quinton	49	+	CVC obstructed
4	Intensive care/brain damage	Secalon, Viggo	1	+	CVC malposition
5	Intensive care/brain damage	Certofix Trio, B-M	5	−	
6	Intensive care/brain damage	Secalon, Viggo	5	−	
7	Renal carcinoma	Hickman, Quinton	7	−	
8	Hemodialysis	Permcath, Quinton	53	−	
9	Intensive care/brain damage	Certofix Trio, B-M	8	−	
10	Hemodialysis	VasCath, Med. Co. Inc.	63	−	
11	Bladder carcinoma	Hickman, Quinton	90	−	
12	Intensive care/brain damage	Certofix Trio, B-M	2	−	

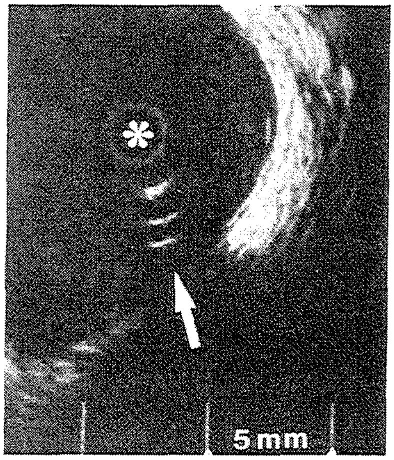

Fig. 2. In vivo ultrasonographic appearance of a 7-F (2.3 mm) triple-lumen catheter (Certofix Trio). There are 3 echoes (→) reflecting the 3 lumina in the proximal segment of this catheter. Note the marked shadowing phenomenon behind the catheter which obscures the vessel wall. * imaging catheter.

spective of their position in relation to the imaging catheter. The thin fibrin sleeves on the catheter surface could not be identified. Double lumen and triple lumen catheters may cause complex echoes according to their multiluminal construction (Fig. 2).

Clinical study. Nine out of the investigated 12 patients did not show any kind of thrombus formation. There were free movements of the catheters within the vessel lumen and no vessel wall abnormalities could be observed. Three out of these patients had indwelling catheters which had been in place for 7 to 12 weeks.

In 3 patients a catheter thrombus, mural thrombus, or occlusive venous thrombosis were found. In one of these 3 cases the patient had a partly obstructed hemodialysis catheter which had been in place for 49 days. A 4 × 3-mm-large thrombus was observed (Fig. 3). The thrombus started at the proximal endhole of the catheter and was adherent to the wall of the superior vena cava for about 2 cm, restricting the movement of the catheter. This patient, who previously had a hemodialysis catheter inserted via the right jugular vein, now had the catheter inserted from the left side. Intravascular ultrasound imaging of the left brachiocephalic vein identified an obstructing thrombus of the lumen. Subsequent imaging of the right brachiocephalic vein and central part of the right jugular vein disclosed high-echogenic wall irregularities, probably representing postthrombotic changes after previous cannulation at this site.

In the 2nd case a 5 F (1.7 mm) indwelling catheter for drug administration had been in place for 360 days. The catheter was obstructed and the patient was investigated for possible catheter infection because of increased body temperature. Intravasal ultrasound imaging showed a 2 × 3-mm-large catheter thrombus and in addition a parietal thrombus of about the same size at the wall of the superior vena cava.

In both these cases the indwelling catheter was removed following the examination without any clinical signs of pulmonary embolism. Microbiologic examination of the withdrawn catheters disclosed no bacterial growth.

A thrombus formation was also observed in a 3rd case. The patient had abolished intracranial circulation and a 5 F (1.7 mm) catheter which had been in place for only one day. This catheter was malpositioned with its distal end located in the contralateral brachiocephalic vein, probably restricting free movement of the catheter tip. A thrombus of about 2 mm at the distal end of the catheter was observed. In addition, a 2 × 2-mm-large embolus was identified within the bloodstream by slow motion analysis of the video records (Fig. 4).

Discussion

Complications associated with central venous catheters represent a significant clinical problem. According to the

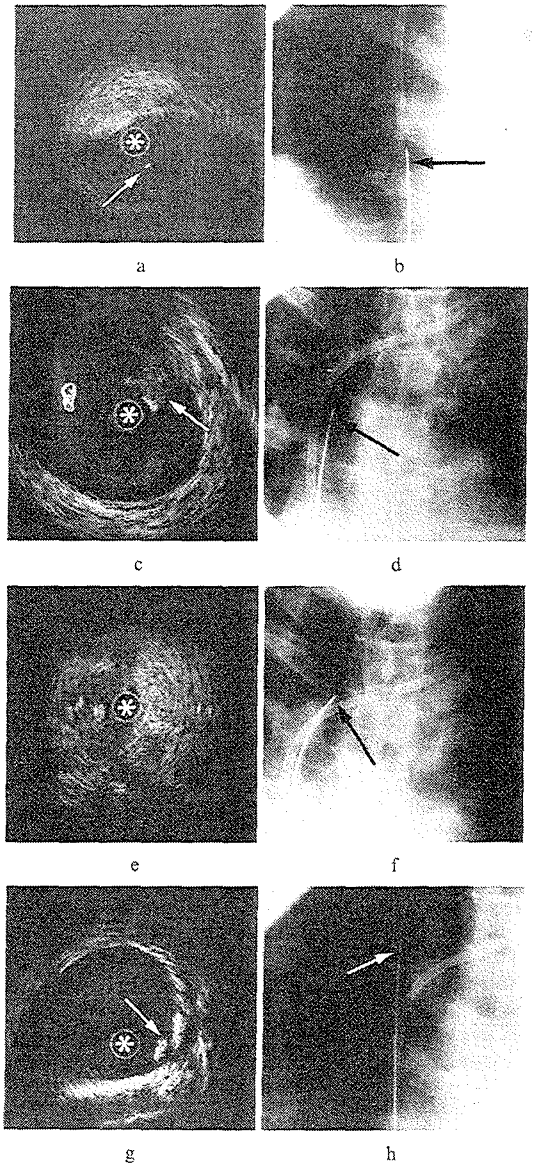

Fig. 3. Intravascular ultrasonographic findings (a, c, e, g) and radiographs (b, d, f, h) showing the site of recording in patient No. 3, who had a partly obstructed hemodialysis catheter inserted from the left side. a) Regular ultrasonographic appearence of catheter tip (→) within right atrium and b) radiograph showing the imaging catheter tip (→) and the catheter. c) Combined catheter/mural thrombus (→) in the superior vena cava and d) imaging catheter tip (→) at the recording level. e) Thrombotic occlusion of the left brachiocephalic vein. g) High-echogenic vessel wall irregularities (→) in the right brachiocephalic vein, probably representing post-thrombotic changes after previous cannulation at this site. * imaging catheter.

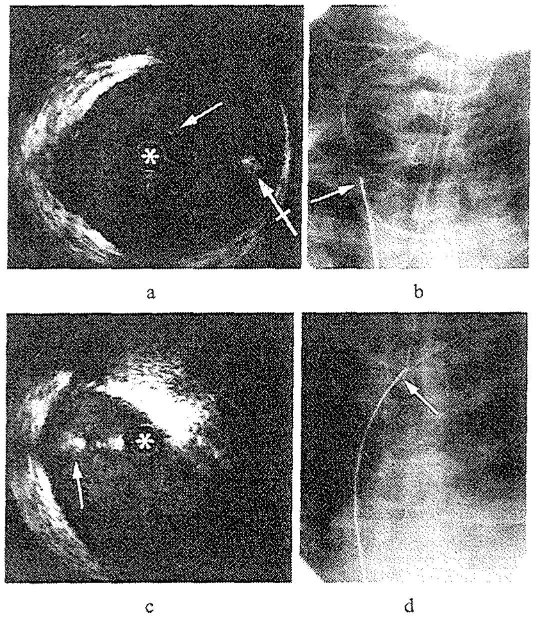

Fig. 4. Findings in patient No. 4 who had a 5 F central venous catheter malpositioned into the contralateral brachiocephalic vein. Ultrasonographs (a, c) and radiographs (b, d) showing the site of ultrasound recording (→). a) Regular ultrasonographic appearance of the central venous catheter in the right internal jugular vein (↔). A small embolus (↔) within the bloodstream could be identified with the imaging catheter in this position. c) Thrombus formation on the distal part of the central venous catheter. * imaging catheter with guide wire reflex.

Medical Device Reporting of the Federal Food and Drug Administration, in the US central venous catheters were associated with 170 complications, including 52 deaths, during a 2-year period (12). Infection and infection-related complications, thrombosis and thromboembolic events were under-reported in this report compared with the medical literature. This discrepancy requires further investigation and is probably due to the lack of reliable methods for documentation of these complications.

Previous studies of thrombus formation on central venous catheters are based on modified conventional phlebographic techniques: contrast injection into the cubital veins, and/or cineangiography during continuous contrast medium injection into the central venous catheter while this is being withdrawn (1, 3, 6, 14).

These methods have limited diagnostic value. In phlebographic studies via the cubital veins, minor thrombi will "drown" in the contrast medium. Injection of contrast medium into a central venous catheter during its withdrawal has several major disadvantages: In patients with partly or completely obstructed catheters this method may be impossible and any attempt at injection should be avoided. Forced injection into a partly obstructed indwelling catheter may

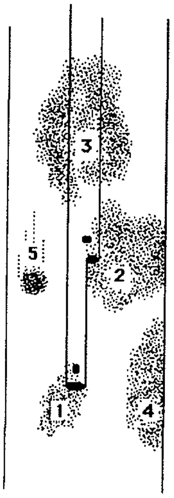

Fig. 5. Schematic drawing of a typical hemodialysis catheter showing various forms of thrombus formation which can be differentiated by intravascular ultrasonography. 1 – catheter tip thrombus on the distal end/side hole, 2 – combined catheter/mural thrombus on the proximal end/side hole, 3 – thrombus completely surrounding the catheter, 4 – mural thrombus, 5 – embolus.

cause disruption and separation of the catheter (13). In studying double or triple lumen catheters having multiple sideholes with this method, the results will be ambiguous. Finally it is desirable to visualize the catheter before withdrawal since thrombi may loosen and embolize during this maneuver. Furthermore the vessel wall may be injured if the catheter had been adherent to a parietal thrombus.

Echocardiography is a suitable method for identification of catheter tip thrombi within the right atrium. A recent echocardiographic study (11) of infants and children who had silicone central catheters placed for long-term access, showed that the incidence of right atrial thrombus was higher than suspected in patients who had catheter malfunction, sepsis, or cardiopulmonary dysfunction. The echocardiograms could also identify the extension of the clot into the central veins. But the method has a poor resolution compared with intravasal imaging.

Intravascular ultrasound imaging seems to overcome these problems. This new method permits in vivo real-time visualization of central venous catheters with hitherto unknown image resolution and provides important information not only about thrombus formation, but also about catheter movement, catheter malposition, and vessel wall injuries. Catheter thrombi, mural thrombi or a combination of both and their relation to the different catheter segments and sideholes can be differentiated (Fig. 5). The method may be helpful in the decision whether a malfunctioning catheter should be removed or not. In the case of fibrinolytic treatment of thrombus formation the effect of this therapy can be documented.

Mechanical loosening of an embolus could be a potential hazard of this method but seems to be negligible since the alternative, withdrawal of the catheter, most likely represents a greater risk.

Previous phlebographic investigations during withdrawal of the catheter as well as autopsy studies in many cases have shown thin fibrin sleeves surrounding the catheter surface (1, 3, 6). These fibrin sleeves cannot be visualized by intravascular ultrasound with the catheter in place. The incidence of this phenomenon is high and it is unlikely that it has any clinical significance.

Conclusions. Intravascular ultrasonography is a suitable method for the visualization of thrombus formation on central venous catheters. It has several important advantages compared with traditional phlebographic methods and may provide new information related to complications following application of central venous catheters in general. The method may be helpful in the decision whether a malfunctioning indwelling catheter should be removed or whether fibrinolytic treatment should be started and it permits repeated follow-up studies of this therapy.

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Paper IV

Catheter Malfunction and Thrombus Formation on Double-Lumen Hemodialysis Catheters: An Intravascular Ultrasonographic Study

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● Intravascular ultrasound imaging (IVUS) is a new method that permits in vivo visualization of central venous catheters with hitherto unknown image resolution. It provides information not only about thrombus formation, but also about catheter movement, catheter malposition, and vessel wall injuries. In the present investigation the method was applied to evaluate the frequency of thrombus formation on double-lumen hemodialysis catheters and its significance for catheter malfunction. In 14 patients who had a double-lumen hemodialysis catheter for temporary or long-term vascular access, IVUS of the catheter and the mediastinal vein stems was performed. Mean indwelling duration at the time of the ultrasound investigation was 101 days (range. 3 to 730 days; median, 58 days). Four patients had catheter-related thrombotic complications: IVUS failed to detect an intracatheter thrombus in one case; a catheter thrombus and superior vena cava stenosis were found in a catheter with normal function in one case; in one case with catheter malfunction, a combined catheter-mural thrombus was found; and in the remaining case, a catheter thrombus and a mural superior vena cava thrombus were found in a patient with normal catheter function and pulmonary emboli. Thus, two of 12 patients with well-functioning catheters (16%) had thrombotic complications demonstrated by IVUS, and one of two patients with catheter malfunction had thrombus identified by IVUS. It is concluded that thrombus formation is less likely in patients without signs of catheter malfunction. At present the main value of IVUS is as a research tool, but with more experience and a larger patient population it may become a valuable alternative or supplemental method in the diagnosis of catheter malfunction.

INDEX WORDS: Intravascular ultrasound; hemodialysis catheter; complication; thrombosis; superior vena cava stenosis.

COMPLICATIONS related to hemodialysis catheters for temporary or long-term vascular access are a significant clinical problem.[1-7] The use of felt-cuffed tunneled jugular double-lumen catheters has reduced the infection rate.[8-10] However, malfunction because of clotting of one or both catheter lumina, catheter-induced venous thrombosis, and subsequent venous stenosis remain a problem.[8-16] Conventional venography has proven to be useful in the diagnosis of catheter thrombus formation and venous stenosis.[7,9,12,15,17] However, to our knowledge there have been no systematic venographic studies of asymptomatic patients. Therefore, the exact frequency of these complications that may be asymptomatic is unknown.

Intravascular ultrasound imaging (IVUS) is a new imaging modality in which a high-frequency transducer placed on the tip of a catheter provides high-resolution, cross-sectional, real-time images of the vessel wall, including its various layers. In previous studies[18,19] we have shown that this new method permits in vivo visualization of central venous catheters with hitherto unknown image resolution. It provides important information not only about thrombus formation, but also about catheter movement, catheter malposition, and vessel wall injuries. Catheter thrombi, mural thrombi, or a combination of both and their relationship to the different catheter segments and side holes can be differentiated.

The method was applied in the present investigation to evaluate the frequency of thrombus formation on double-lumen hemodialysis catheters and its significance in the occurrence of catheter malfunction.

MATERIALS AND METHODS

Patients

During a 24-months period 30 patients in our department underwent hemodialysis via a tunneled, Dacron-cuffed, jugular double-lumen catheter. VasCath (Medical Components, Harleysville, PA) and PermCath (Quinton Instrument Company, Seattle, WA) catheters were used in 28 and two cases, respectively. Four of the patients (13%) had manifestations of catheter-induced complications, such as catheter malfunction (blood flow rate <200 mL/min), catheter infection, and/or pulmonary embolism. These four patients were suspected to have thrombotic complications and were examined by IVUS.

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Table 1. Indwelling Duration, Catheter Function, and Clinical Signs of Catheter-Induced Complications in 14 Patients Studied by Intravascular Ultrasound

Patient No.	Indwelling Duration (d)	Catheter Malfunction	Catheter-Induced Complications
1	90	—	—
2	49	Obstruction	—
3	53	—	—
4	63	—	—
5	69	—	Dyspnea/ pulmonary embolism
6	6	—	—
7	6	—	—
8	81	—	—
9	3	—	—
10	3	—	—
11	174	Obstruction	—
12	5	—	—
13	80	—	—
14	730	—	Exit site infection

In addition, 10 asymptomatic volunteers with normal catheter function were examined in the same manner. After proper information about the procedure the patients gave their written consent. The study was approved by the regional ethical committee. Catheter type, indwelling duration at the time of the ultrasound investigation, manifestations of catheter-related complications, and catheter function are summarized in Table 1.

Ultrasound Procedure

The ultrasound imaging was performed via the right femoral vein after local anaesthesia (5 mg/mL Xylocaine; Astra, Södertälje, Sweden). In combination with a 0.025-inch guidewire and 8- or 9-french introducer sheaths, 6.2-french 20-MHz Sonicath Sidesaddle (Boston Scientific, Watertown, MA) or CVIS 8-french 20-MHz (Cardiovascular Imaging Systems Inc, Sunnyvale, CA) imaging catheters were used.

Under fluoroscopic guidance and continuously recording the ultrasound images on a videotape, IVUS of the right atrium, the superior vena cava, and both brachiocephalic veins and their confluence with the internal jugular vein was carried out. The position of the ultrasound catheter in the regions of interest was documented by radiographs. The video records were analyzed off line in slow motion after catheterization was complete. The mean catheterization time after insertion of the introducer sheath was 7.5 minutes (range, 3 to 20 minutes). There were no complications following the ultrasonographic investigations.

The hemodialysis catheter normally appears as a bright, distinct echo according to the acoustic interface between the catheter surface and blood. Behind this acoustic interface there is a marked shadowing phenomenon. Thrombus appears as a granular or speckled mass with an echogenicity markedly higher than blood. In some cases artifacts from the ultrasound catheter strut signal may cause ambiguous findings. This problem can be avoided by rotating the imaging catheter within the vessel. Further details concerning the imaging procedure are described elsewhere.[18,19]

RESULTS

The results of the ultrasonographic investigations are provided in Table 2.

None of the 10 asymptomatic patients with normal catheter function showed any kind of thrombus formation. There was free movement of the catheters within the vessel lumen and no vessel wall abnormalities could be observed (Fig 1).

The ultrasonographic findings were completely normal in patient no. 11, who had a partly obstructed catheter. After removal and dissection of the catheter, a small ball-like intraluminal thrombus within the catheter tip was found. The thrombus worked like a ball valve, allowing injection into the catheter lumen, but preventing aspiration.

In another case of catheter malfunction without other manifestations of catheter-induced complications (patient no. 2), a 4 × 3 mm large combined catheter/mural thrombus was observed (Fig 2B). The thrombus started at the proximal end hole of the catheter and was adherent to the wall of the superior vena cava for approximately 2 cm, restricting the movement of the catheter. This patient, who previously had a hemodialysis catheter inserted via the right jugular vein, now had the catheter inserted from the left side. Intravascular ultrasound imaging of the left brachiocephalic vein identified an obstructing thrombus of the lumen (Fig 2C). Subsequent imaging of the right brachiocephalic vein and central part of the right jugular vein disclosed high-echogenic wall irregularities (Fig 2D), probably representing postthrombotic changes after previous cannulation at this site. Since the mass of the documented thrombus was small, the catheter was removed without previous thrombolytic therapy. A new catheter was inserted and has functioned well since replacement.

Patient no. 14 had an exit site infection but normal catheter function. Intravascular ultrasound imaging revealed that the distal portion of the catheter was surrounded by an approximately 1 mm-thick thrombus layer (Fig 3B). In addition, an asymptomatic high-grade stenosis of the superior caval vein at the confluence of the brachiocephalic veins was found. The caval lumen diameter at this level was reduced to approx-

Table 2. Intravascular Ultrasound Findings and Indwelling Duration in Four Patients With Catheter Malfunction or Clinical Signs of Catheter-Induced Complications

Ultrasound Findings	Catheter Function	Signs of Catheter-Induced Complications	Indwelling Duration	Patient No.
Normal	Obstruction	None	174	11
Combined catheter/mural thrombus, thrombotic occlusion of brachiocephalic vein, postthrombotic changes of contralateral venous wall	Obstruction	None	49	2
Catheter thrombus, superior caval vein stenosis	Normal	Exit site infection	730	14
Catheter thrombus, mural superior vena cava thrombus	Normal	Pulmonary embolism	69	5

imately 8 mm and there were small calcifications within the vessel wall that were not visible on the plain radiographs (Fig 3A). The infection was successfully treated by antibiotics. Since the catheter was well functioning and the patient had no symptoms from the caval vein stenosis, it was preferred to leave the catheter in place. The thrombus sheath surrounding this catheter was not regarded to be a risk to the patient.

Patient no. 5 had normal catheter function, but suffered from dyspnoea and had scintigraphic signs of recurrent pulmonary embolism. In this case the dialysis catheter was malpositioned, with the catheter tip just above the level of the right atrium. Intravascular ultrasound imaging showed a 10 × 8 mm mural thrombus fixed to the superior caval wall just below the distal end of the dialysis catheter that was coated with an approximately 1 mm-thick layer of thrombus. This patient was anticoagulated before removal of the catheter. This treatment was continued for 8 weeks after removal of the catheter; there were no further symptoms of pulmonary embolism.

DISCUSSION

Previous in vivo studies of thrombus formation on central venous catheters are based on modified conventional phlebographic techniques: contrast injection into the cubital veins and/or cineangiography during continuous contrast injection into the central venous catheter while this is withdrawn.[20-23] These conventional radiologic methods have limited diagnostic value. In phlebographic studies via the central venous catheter or cubital veins, minor thrombi will "drown" in the contrast medium. Because of multiple side holes, the angiographic findings may be ambiguous in studies via the dialysis catheter. Injection of contrast medium into a central venous catheter during its withdrawal has several major disad-

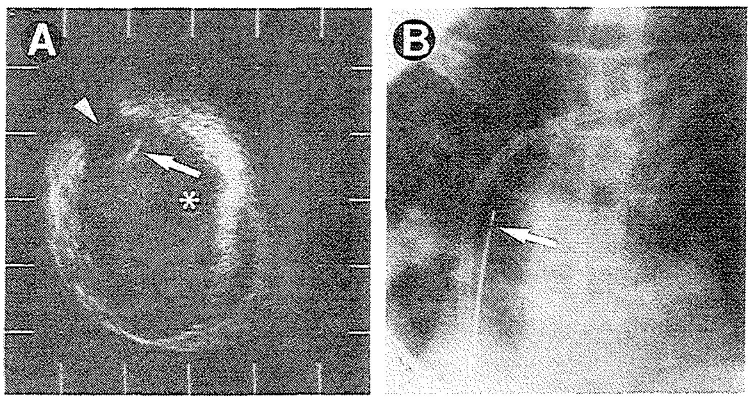

Fig 1. (A) Normal ultrasonographic appearance of hemodialysis catheter imaged within the superior caval vein. There is a distinct acoustic interface between the blood and catheter surface (arrow) with a marked shadowing phenomenon behind the catheter that obscures the vessel wall (arrowhead). Asterisk indicates the imaging catheter. Distance between two calibration marks = 5 mm. (B) Radiograph showing the site of recording. Arrow indicates the imaging catheter.

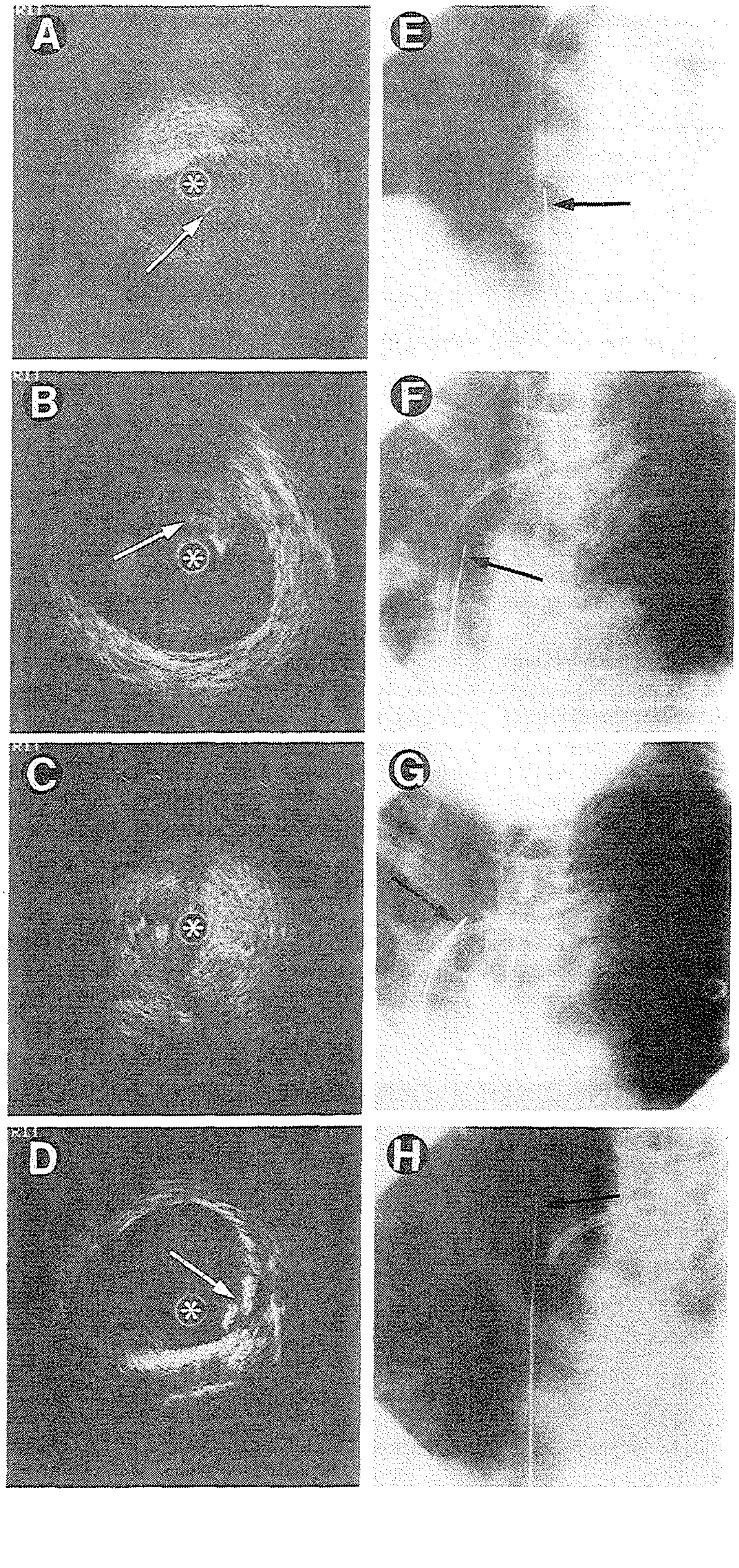

Fig 2. Intravascular ultrasonographic findings (A, B, C, and D) in patient no. 2. (A) Regular ultrasonographic appearance of the catheter tip (arrow) within the right atrium. (B) Combined catheter/mural thrombus (arrow) in the superior vena cava. (C) Thrombotic occlusion of the left brachiocephalic vein. (D) High echogenic vessel wall irregularities (arrow) in the right brachiocephalic vein, probably representing postthrombotic changes after previous cannulation at this site. The radiographs shown in E, F, G, and H demonstrate the site of the ultrasonographic probe corresponding with A, B, C, and D, respectively. The asterisks indicate the imaging catheter, which has a diameter of 2 mm. (Reprinted with permission.[18])

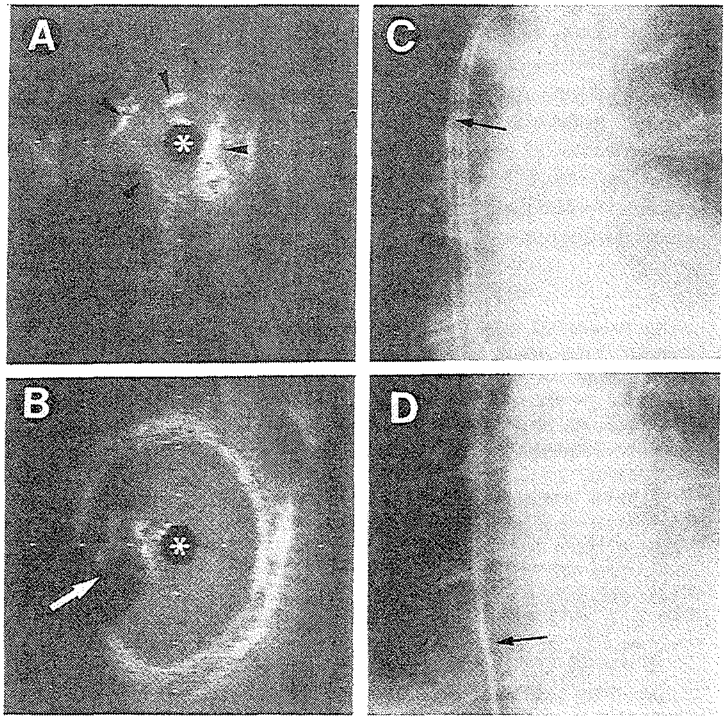

Fig 3. (A) Ultrasound image at the level of the brachycephalic vein confluence in patient no. 14. There is an irregular stenosis of the caval lumen. There are multiple high echogenic structures with shadowing phenomenon (arrowhead), representing small calcifications in the vessel wall. (B) Intravascular ultrasound image of the distal portion of the hemodialysis catheter in the same patient. The catheter appears as a speckled echogenic structure (arrow), indicating that its surface is coated with thrombus. (C and D) Radiographs showing the site of recording in A and B, respectively. The asterisks in A and B and the arrows in C and D indicate the imaging catheter. The distance between two calibration marks in A and B = 4 mm.

vantages. In patients with partly or completely obstructed catheters, injection of contrast medium into the catheter may be impossible. In addition, it is desirable to visualize the catheter before withdrawal, since thrombi may loosen and embolize during this maneuver and the vessel wall may be injured if the catheter is adherent to a parietal thrombus.

In spite of the small patient population in the present investigation, the study showed that IVUS is a suitable imaging method that overcomes the disadvantages of conventional radiologic methods.

Transthoracic echocardiography is an alternative imaging method. It has proven to be useful for identification of catheter tip thrombi within the right atrium,[14,24,25] but the method has a poor resolution compared with intravascular imaging. Thrombi within the mediastinal veins can only be demonstrated in exceptional cases.

Biplane transesophageal echocardiography reveals thrombus formation not only within the right atrium but also within the superior vena cava.[25] However, this method also is of limited value. Intravascular ultrasound imaging not only has a higher resolution but also permits selective imaging of the peripheral mediastinal veins. In addition, transesophageal echocardiography is unpleasant for most patients and may have harmful side effects. Our patient no. 5 underwent transesophageal echocardiography subsequent to the IVUS investigation. Neither the 10×8 mm mural thrombus in the superior vena cava nor the sheath of catheter thrombus could be revealed by transesophageal echocardiography.

Since catheter thrombus obstruction can be treated effectively by systemic thrombolysis without knowing the exact extent and size of the thrombus,[9,17,26] at present the main value of the method is as a research tool. It permits repeated follow-up studies after thrombolytic treatment and may be helpful in the decision regarding whether a malfunctioning catheter should be replaced. In caval vein stenosis, angioplasty with subsequent stent implantation may be indicated.[11] In these cases the cross-sectional ultrasound findings will provide important information that may facilitate the interventional procedures.

The value of the present study is limited because of its small sample size. In addition, the equipment necessary to use this new technique is expensive and it is not readily available in many hospitals. More extensive studies in a larger series of patients will be necessary to define the role of IVUS as an alternative or supplemental method in the diagnosis and treatment of catheter malfunction.

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Paper V

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ANGIOGRAPHIC AND INTRAVASCULAR ULTRASONOGRAPHIC FINDINGS AFTER ENDOVASCULAR STENT IMPLANTATION

K.-D. BOLZ, S. HATLINGHUS, R. WISETH, H. O. MYHRE and A. GRONNINGSÆTER

Abstract

The study was an attempt to evaluate the benefit of intravascular ultrasound imaging (IVUS) as a supplement to follow-up angiography after endovascular stent implantation. A consecutive series of 15 patients underwent stent implantation in the peripheral or coronary arteries. Ten Palmaz stents, 3 Palmaz-Schatz stents and 2 Wallstents were used. After a period from 1 to 6 months (mean 3.2 months) follow-up angiography was performed. In 12 cases the angiography was combined with IVUS of the stent and the adjacent vessel segments. In one case IVUS failed due to the tortuous course of the vessel, in another case the stent was occluded, and in one case IVUS was considered too hazardous. In stents of diameter ≥ 5 mm, ultrasound (US) did not reveal more information concerning vessel and stent diameter, stent stenosis and intraluminal surface contact than angiography alone. Smaller stents were insufficiently visualized by conventional radiologic methods. In small stents only IVUS permitted an exact stent identification and differentiation between stent stenosis and stenosis of the native vessel. At US imaging artifacts, caused by the highly reflectant metallic stent struts, interfered with the native vessel wall and partly obscured its structural details.

Key words: Stents, interventional procedures; —, technology; —, vascular; ultrasonography, intravascular.

The role of intravascular ultrasound imaging (IVUS) in clinical routine has not been clearly defined. The method may extend our understanding of the nature of atherosclerotic lesions and the mechanisms of therapeutic interventions. At present there is little information about the value of the method in a clinical setting. A number of investigations have shown that IVUS provides information about cross-sectional size and shape of the vessel lumen, composition of atheroma – calcified or not calcified –, presence of ulcerations, dissections or intimal flaps. Thus, US imaging before and during angioplasty or atherectomy may be of value to choose the optimal therapeutic procedure (3, 5, 6, 8, 10, 11, 14, 15, 17).

An attempt was made to evaluate the possible benefit of IVUS, applied as a supplement to the angiographic follow-up after implantation of endovascular stents.

Material and Methods

The material consists of a consecutive series of 15 patients who underwent peripheral or coronary stent implantation. Indications for stent application were a) long-segment iliac stenoses; b) iliac lesions extending to the aortic bifurcation; c) eccentric stenoses with irregular surface or ulcerated plaques; d) chronic iliac occlusions; e) inadequate immediate post-PTA/PTCA response; or f) recurrent restenosis after PTA/PTCA.

Stenting procedure. The indication for stenting, choice of stent and stent diameter, and the stenting procedure were performed without the use of IVUS. The pre- and intraoperative angiograms included at least 2 orthogonal views. A stent/artery ratio of 1:1 or more was aimed for. Vessel diameters were measured by a caliper on the fluoroscopy screen by means of a ruler taped to the patient and by means of a Lunderquist vessel measure guide (William Cook Europe). Indications for stenting, stent localization, type of stent and stent diameter are shown in the Table.

Primary technical success of stent placement with initial relief or improvement of symptoms was achieved in all

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Table

Fifteen consecutive patients who underwent follow-up angiography after intravascular stent implantation. IVUS of stent was performed or attempted in 14 cases

Pat/ Sex/Age	Lesion localization	Stent indication	Stent type/manufacturer	Stent diameter, mm
1/M/63	Saphenous vein coronary bypass graft	Restenosis after previous PTCA	Palmaz-Schatz (Johnson & Johnson)	3.50
2/M/69[1]	Saphenous vein coronary bypass graft	Stenosing flap	Palmaz-Schatz (Johnson & Johnson)	3.25
3/F/78[2]	Left coronary LAD	Occluding dissection after PTCA	Palmaz-Schatz (Johnson & Johnson)	2.50
4/M/69	Common iliac artery	Eccentric restenosis after previous PTCA	Palmaz, large (Johnson & Johnson)	9.00
5/F/65[3]	Left subclavian artery	Eccentric stenosis Recurrent peripheral embolization	Palmaz, medium (Johnson & Johnson)	7.00
6/M/66	External iliac artery	Complex long-segment stenosis	Wallstent (Pfizer-Schneider)	9.00
7/M/49	External iliac artery	Irregular eccentric stenosis	Palmaz, medium (Johnson & Johnson)	8.00
8/M/59	Common iliac artery	Complex long-segment stenosis	Palmaz, large (Johnson & Johnson)	10.00
9/M/73	Common iliac artery	Complex long-segment stenosis	Palmaz, large (Johnson & Johnson)	10.00
10/M/43	Common/external iliac artery	Complex long-segment stenosis	Palmaz, large (Johnson & Johnson)	9.00
11/M/58	Common/external iliac artery	Complex long-segment stenosis	Wallstent (Pfizer-Schneider)	9.00
12/F/77	External iliac artery	Irregular eccentric stenosis	Palmaz, medium (Johnson & Johnson)	7.00
13/M/80	Common iliac artery	Complex long-segment stenosis	Palmaz, large (Johnson & Johnson)	10.00
14/M/49	External iliac artery	Irregular eccentric stenosis	Palmaz, large (Johnson & Johnson)	9.00
15/M/63	Common iliac artery	Complex long-segment stenosis	Palmaz, large (Johnson & Johnson)	10.00

1) IVUS failed. 2) Occluded stent. 3) IVUS not attempted because of high risk.

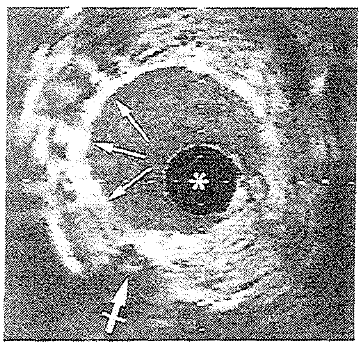

Fig. 1. Completely expanded Palmaz stent in the external iliac artery. Vessel wall calcification with signal drop-out at 7 o'clock (+→). Note the corona-like stent struts artifacts (→) which interfere with the structural details of the native vessel wall. * imaging catheter. Distance between calibration marks 1 mm.

patients, but in 2 cases of iliac stenoses stent deployment was suboptimal. The patient with subclavian artery stenosis stent experienced a minor transient ischemic attack during the stenting procedure. In the remaining cases there were no complications.

Adjuvant medical treatment. Preoperative medication with 500 mg acetylsalicylic acid (ASA) was given 24 hours before the procedure and 100 to 500 mg ASA on the day of the procedure. Intraoperatively a dose of 5 000 to 10 000 IU heparin was administered intraarterially. In patients with peripheral stents, medication with ASA continued for 3 months. In patients with coronary stents, postoperative heparinization continued for 24 hours i.v. at a rate of 1 000 U/h. Medication of ASA continued indefinitely. In addition, the patients with coronary stents were medicated with 75 mg dipyridamole 3 times/day and coumarin pre- and postoperatively.

Angiographic/US follow-up procedure. All patients, regardless of whether they had recurrent symptoms or were asymptomatic, underwent an angiographic investigation after a period of 1 to 6 months (mean 3.2 months). The

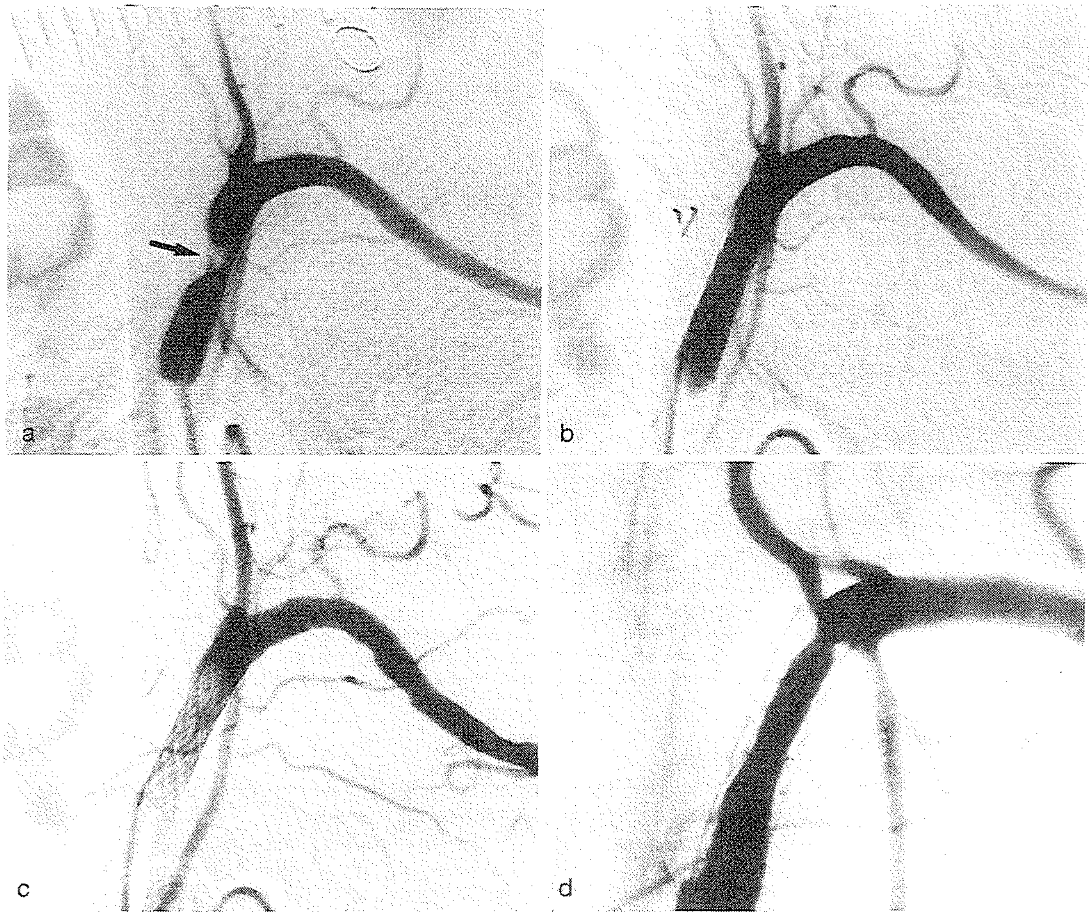

Fig. 2. Eccentric stenosis (→) of the left subclavian artery before (a) and after (b, c) stenting with a Palmaz medium stent expanded to 7 mm diameter. Significant intraluminal stent stenosis 4 months after treatment, probably representing neointimal hyperplasia (d). Excellent angiographic visualization of stent and vessel wall in multiple orthogonal views.

angiograms included at least 2 orthogonal views. Subsequent to the follow-up angiography, US imaging of the stent and the neighboring vessel segments was performed by means of CVIS 1006, 1000 or 1007 imaging catheters (Cardiovascular Imaging Systems Incorp., Sunnyvale, CA) having a 30 MHz or 20 MHz transducer and a dimension of 1.45 mm, 1.7 mm, or 2.7 mm, respectively. In all cases 0.36 mm or 0.64 mm guidewires were used. The IVUS findings were recorded on video tape. After completed catheterization the video recordings were analyzed and compared with the angiographic findings. The analysis of the video recordings was done by the same 2 investigators who had performed the angiography/US investigation. Special attention was paid to the details: a) visualization of the stent and the stent/vessel wall transition; b) angiographic versus US measured vessel diameter; c) intraluminal surface contact; d) differentiation between stent stenosis and intrastent neointimal hyperplasia/intraluminal thrombus formation; e) vessel wall composition.

Results

Early clinical results (Table). After initial improvement case no. 3 had recurrent unstable angina 3 months after endovascular treatment. At angiography the LAD stent was occluded. An attempt to recanalize the stent lumen with repeat angioplasty failed. Patient no. 12, who was asymptomatic after stenting of the external iliac artery, experienced recurrent claudication after 3 months. The 13 other patients were either asymptomatic or demonstrated significant clinical improvement at follow-up. Because patient no. 5 had experienced a transient ischemic attack during stenting, follow-up IVUS was considered contraindicated and only angiography was performed.

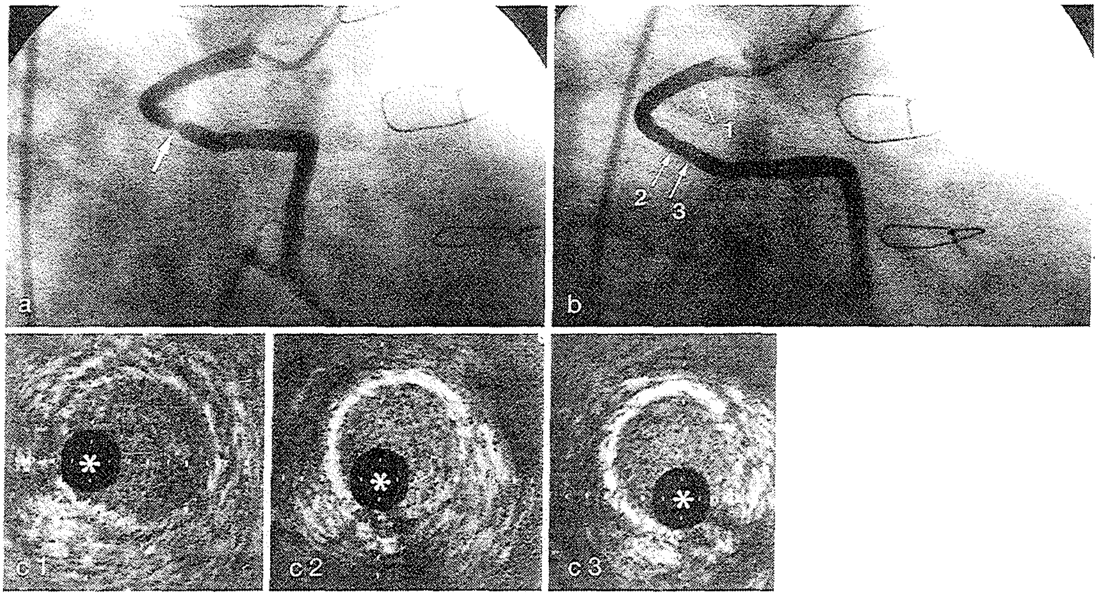

Fig. 3. Aortocoronary saphenous vein bypass graft which had been inserted 13 years previously showing restenosis (→) after previous PTCA before (a) and 3 months after stenting with a Palmaz-Schatz stent expanded to 3.5 mm (b). The stent is not visible at cineangiography but well visualized by US (c). 1, 2, 3 – vessel segments corresponding with the cross-sectional US images. Note the artery-like layered structure of the vessel wall (1). The closest distance between the calibration marks is 0.5 mm. * imaging catheter.

Stent visualization. The US images of the expanded stents, slotted tube stents (Palmaz, Palmaz-Schatz) as well as woven mesh stents (Wallstent), showed a characteristic echogenic pattern, caused by the highly reflectant metallic struts (Fig. 1). The reflected corona-like "rays" partially obscured the underlying structural details of the vessel wall.

Large- and medium-sized stents, expanded to a diameter ≥5 mm, were identified by fluoroscopy and radiography (Fig. 2). Visualization of the coronary stents was insufficient by fluoroscopy and conventional cineangiography or DSA and they could only be identified by IVUS (Figs 3, 4). However, the stiffness of the US-catheter tip restricted imaging to vascular segments without marked bends, which prohibited passage of the catheter (Fig. 4 c).

Vessel diameter. There was a highly significant correlation between the vessel diameter measured by US and conventional angiography, based upon multiple orthogonal views of angiographically normal vessel segments adjacent to the stented lesion ($r = 0.97$, $y = 1.07\,x - 0.09$).

Intraluminal surface contact. In one of the stented iliac arteries there was a gap between the distal end of the stent and the vessel wall which could be demonstrated by angiography (Fig. 5 b) as well as by US (Fig. 5 c). This had been recorded already during the stenting procedure but complete expansion of the stent failed because of heavily calcified eccentric plaque resisting balloon dilation. During stent application this patient experienced intensive pain in the back, and no further attempt was made to expand the stent completely.

Stent stenosis/native vessel stenosis. One patient receiving an iliac stent with an initial diameter of 8 mm showed an angiographic and US narrowing of the lumen diameter to 5.0 mm. The ratio between maximal stent length and diameter measured on the initial and follow-up angiograms demonstrated that the stent stenosis was due to elastic recoil of the vessel wall. There were no intraluminal filling defects at angiography or US.

In patient no. 12, who had recurrent claudication after 3 months, arteriography and IVUS revealed a high-grade stenosis about 2 cm distally to the open, completely expanded stent. This stenosis was successfully dilated with a 7.0-mm balloon.

In patient no. 5, angiography performed 4 months after stenting demonstrated a significant intraluminal stent stenosis while the original stent diameter was unchanged (Fig. 2 d). This finding was supposed to represent neointimal hyperplasia. Since the patient was relieved of her peripheral thromboembolic symptoms and had normal blood pressure in both arms, it was decided to follow her with clinical investigations.

Vessel wall composition. In several cases US imaging visualized more or less pronounced vessel wall calcifications which could not be seen at angiography. However, the reflecting rays of the metallic stent struts partly obscured and

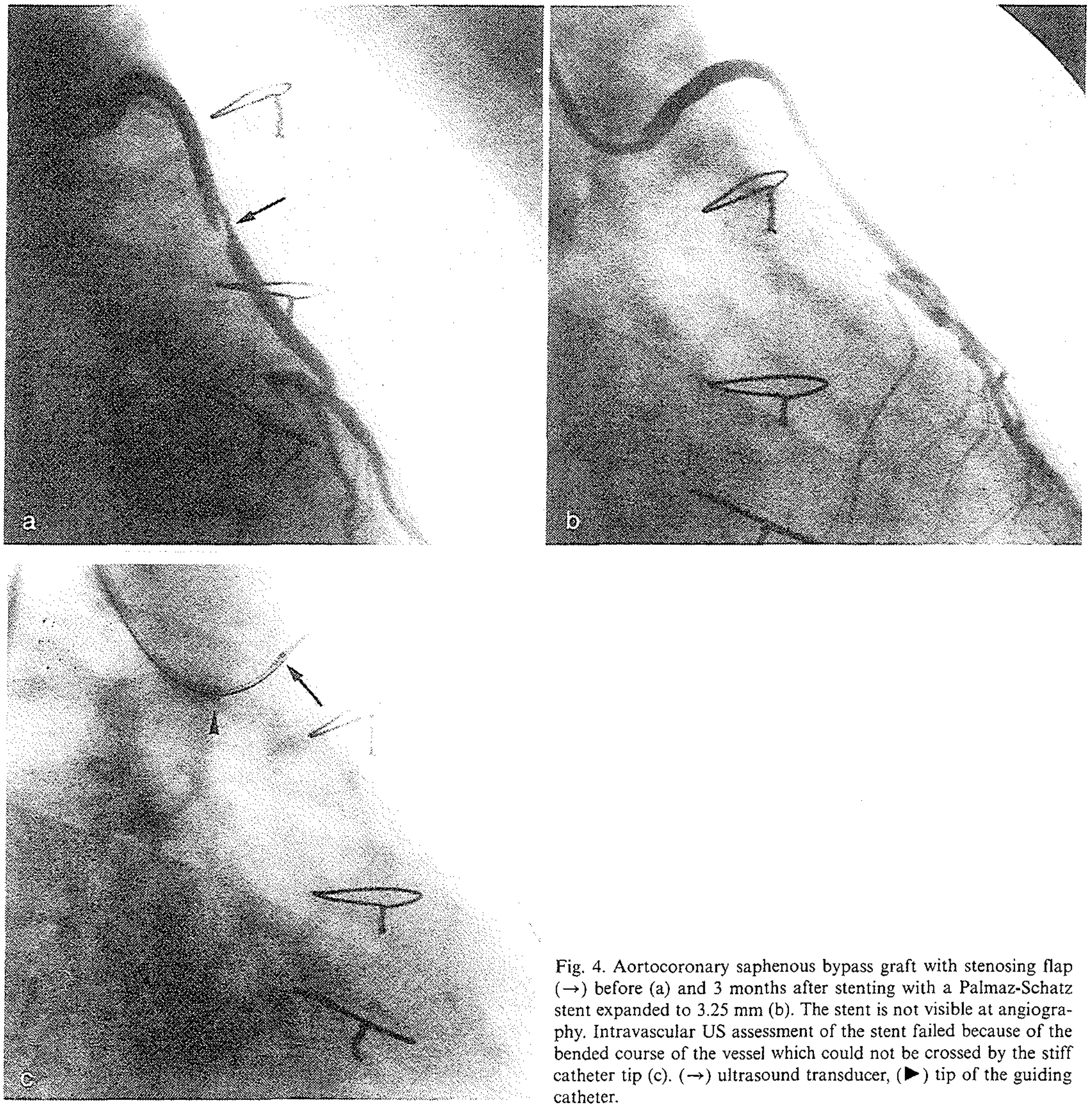

Fig. 4. Aortocoronary saphenous bypass graft with stenosing flap (→) before (a) and 3 months after stenting with a Palmaz-Schatz stent expanded to 3.25 mm (b). The stent is not visible at angiography. Intravascular US assessment of the stent failed because of the bended course of the vessel which could not be crossed by the stiff catheter tip (c). (→) ultrasound transducer, (▶) tip of the guiding catheter.

interfered with the underlying vessel wall structures (Figs 1, 5 c).

In cases where calcified plaques caused suboptimal stent deployment, this problem was already realized during the stenting procedure by angiography alone.

An interesting finding was the ultrasonographic wall architecture of the saphenous vein graft (Fig. 3) which had been inserted 13 years previously. In contrast to the US appearance of a normal vein, this vessel had an "artery-like", layered wall structure (Fig. 3 c).

Discussion

A number of investigations have shown that IVUS is a valuable research tool which may extend our understanding of the nature of atherosclerotic lesions and the mechanisms of therapeutic interventions. The US appearance of the vein graft (Fig. 3) demonstrates how IVUS can visualize structural changes in the vessel wall of autologous vein grafts used as arterial substitutes. A similar abnormal US appearance of the venous wall has also been observed in

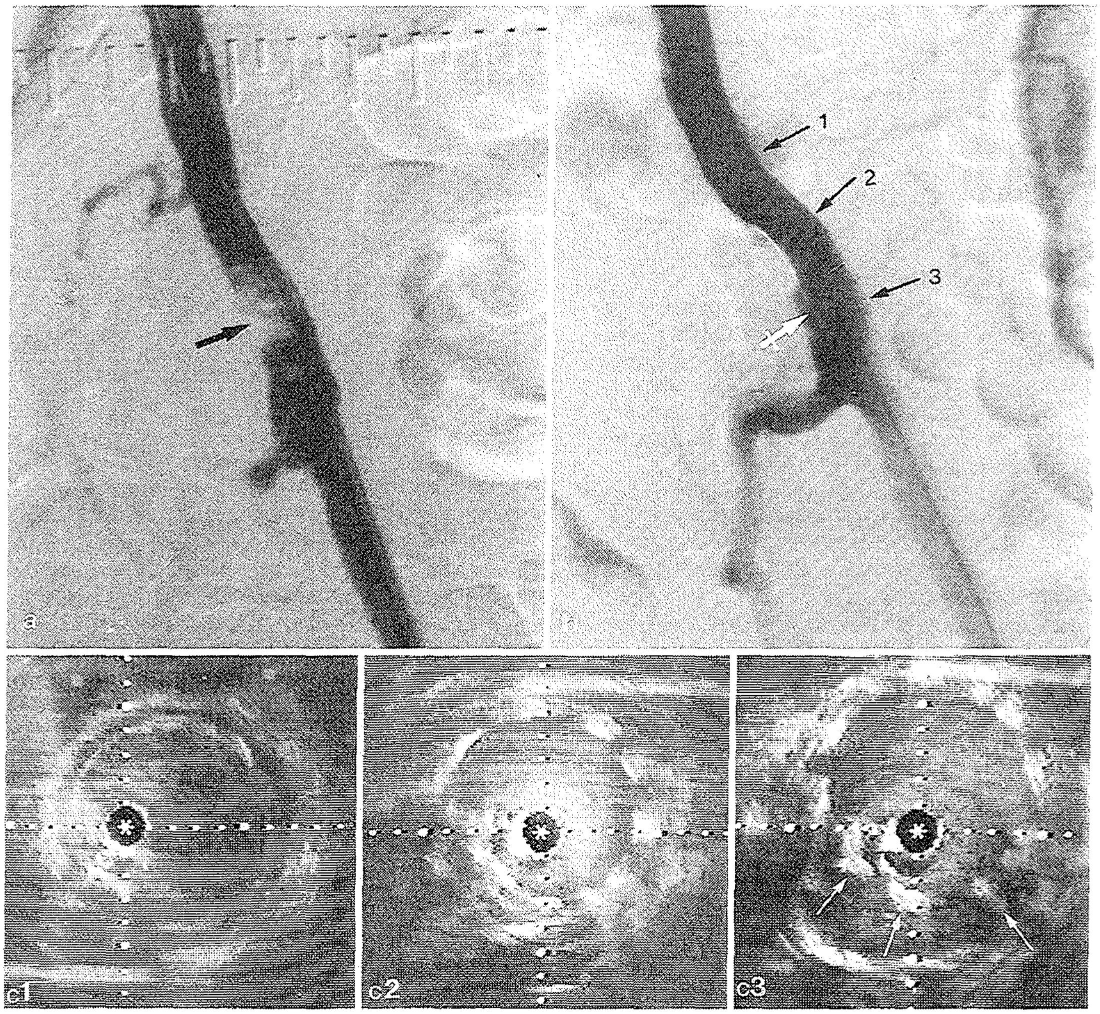

Fig. 5. Eccentric, calcified common iliac artery stenosis (→) before stenting (a) and after suboptimal placement of a Palmaz stent (b). There is a gap between the distal end of the stent and the vessel wall (↔). An eccentric residual stenosis caused by a heavily calcified plaque is visualized by DSA as well as by US (c). 1, 2, 3 – artery segments corresponding with the cross-sectional US images. There is a vessel wall calcification at 7 o'clock (c1). Note that the stent struts artifacts interfere with the eccentric calcified lesion from 6 to 9 o'clock (c2). Gap between vessel wall and expanded stent from 3 to 9 o'clock (c3). (→) stent struts protruding into the vessel lumen. The distance between the calibration marks is 1 mm. * imaging catheter.

chronic obstructed caval veins (1). Most likely these findings represent circumferential intimal fibrous hyperplasia which is the histologic response to high intraluminal pressure (7, 9, 12).

With regard to structural changes of the vessel wall after stenting, IVUS seems to be of limited value. Once the stent is delivered, the US artifacts caused by the highly reflectant metallic struts will interfere with the native vessel wall and partly obscure its structural details.

These artifacts occur in slotted tube stents (Palmaz, Palmaz-Schatz) as well as in woven mesh stents (Wallstent). An *in vitro* study in progress indicates (Gronningsæter, unpublished data) that these artifacts probably can be explained by the following effects: the transmitted pulse hits the metal wire, energy is reflected back to the transducer generating the bright echo from the metal, while some energy creeps multiple times around the wire at its surface. Some energy is emitted back to the transducer at each round trip generating the characteristic "tail" on the stent echo.

The findings concerning vessel and stent diameter measured by US and conventional angiography were in accordance with previous investigations (2, 4), which have shown a highly significant correlation when comparing these 2 techniques in angiographically normal arteries.

With regard to intraluminal stent stenosis it would have been of interest to know whether the stenosis was caused by neointimal hyperplasia or thrombus formation. However, previous studies have shown that both thrombus and fibromuscular intimal hyperplasia produce similar soft echoes and therefore cannot be identified by their US appearance alone (13, 15). Another study concluded that IVUS wasn't able to discriminate fresh from old thrombus either (16). Based on the results of these investigations, IVUS seems to be of little value in the decision about whether to treat a stent stenosis by balloon angioplasty or thrombolysis.

In small stents, insufficiently visualized by fluoroscopy, IVUS seems to be of benefit for the differentiation between stent stenosis and stenosed segments in the native vessel. It may also be useful for identifying the stent localization prior to subsequent aortocoronary bypass surgery.

In the future, the use of radiolucent nonmetallic stents may increase the importance of US imaging.

Case no. 2 demonstrates that imaging with current US devices is still limited by the stiffness of the catheter tip which in some cases prohibits the crossing of tortuous vessels. Smaller catheter dimensions probably will overcome this problem in the future.

Conclusions. In the follow-up of slotted tube stents and woven mesh stents with diameter ≥ 5 mm, IVUS is of little value since angiography alone reveals most of the information relevant in a clinical setting. In small stents, insufficiently visualized by radiography, IVUS permits an exact stent localization and differentiation between stent–stenosis and stenosis of the native vessel wall. Because of artifacts, caused by the metallic stent struts, structural changes of the vessel wall after stenting cannot be assessed by US.

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Request for reprints: Dr. Klaus-Dieter Bolz, Diagnostic Radiology, University Hospital, N-7006 Trondheim, Norway.

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Paper VI

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ORIGINAL ARTICLE

Ultrasonographic stent-imaging artifacts

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SUMMARY

Optimal stent adaptation to the arterial wall is supposed to be a prerequisite for long-term patency of the stented vessel. Intravascular ultrasonography (IVUS) provides cross-sectional images of the vessel and the stent that may offer important information about stent placement during the procedure. However, the presence of metal structures in biological media results in wave-propagating effects that should be recognized by the operator in order to avoid misinterpretation.

The most important effects are shadowing, transducer-stent reverberations and stent-filament reverberations. The impact these wave-propagation effects have on the stent image are described and illustrated by in vitro examples. A stent-filament reverberation is defined as the echo tail that follows the primary echo from the stent due to multiple reflections within the metal filament. This signal, which obscures the echo from the immediate vicinity of the stent, is modeled by an acoustic pulse bouncing back and forth between the two surfaces of a thin metal plate which is immersed in water. Some energy is emitted into the water at each internal reflection, thus generating the tail. In vitro experiments verifies the model.

The conclusion is that stent artifacts may inhibit the investigation of structural changes in the stented vessel segment as well as the detection of small dissections or cavities which may exist between the stent and the vessel wall due to sub-optimal stent placement.

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INTRODUCTION

Intravascular ultrasonography (IVUS) is now widely used as an adjunct to angiography during and after intravascular stent implantation.[1–6] It provides cross-sectional images of the stent, the vessel wall and the composition of the atherosclerotic lesion. Thus the method offers information which is important to evaluate whether proper placement of the stent has been obtained.

However, the IVUS technique is subject to different kind of artifacts and noise sources. Some of these are described in the literature,[7–13] but the description is incomplete. This paper addresses artifacts related to ultrasound imaging of metallic stents. The presence of metal structures in biological media results in wave-propagation effects that causes the image of a stent to deviate from the true physical shape of the stent. This is illustrated in Figure 1 with an in vitro and an in vivo stent image. A stent which is imaged in water appear on the monitor as a large spoke-pattern, its size is more than 5 times the size of the stent. This effect is less pronounced in vivo, but note that the thickness of the stent filaments appear to be more than 1mm while the actual thickness is less than 0.2 mm.

The aim of this study is to describe the most important wave-propagating effects related to IVUS imaging of stents and to illustrate these stent imaging artifacts by in vitro experiments. The artifacts obscure the IVUS image and may inhibit the investigation of structural changes in the stented vessel segment as well as the detection of small cavities which may exist between the stent and the vessel wall due to sub-optimal stent placement. It is important that the operator under-

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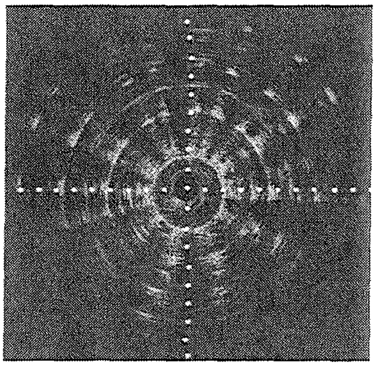

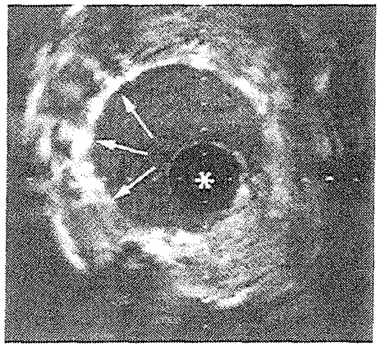

Fig. 1 (A) In vitro IVUS image of a Palmaz stent, extended to a diameter of 7mm. The reflection pattern deviates from the true physical shape of the stent. (B) In vivo image of same kind of stent extended to the same diameter. The arrows indicate echo from individual stent filaments which appear to be thicker than the actual thickness of the metal.

stands these effects in order to avoid misinterpretation.

MATERIALS AND METHODS

Stents

Four different stents were included in the study and noted Stent1–Stent4. The types and dimensions are listed in Table 1. Stent1 and Stent2 are balloon-expandable stents, manufactured by cutting slots in a stainless steel (316L) tube by laser technique. These stents keep their shape after the balloon pressure has been released. Stent3 and Stent4 are made of biocompatible stainless steel monofilaments, braided in a tubular mesh configuration. The stent is constrained and covered by a protecting membrane in the delivery system. When the stent is located in its final position, the membrane is pulled back and the stent expands. The various stents are shown in Figure 2.

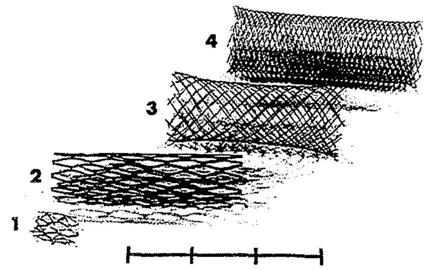

Fig. 2 Photograph of the four stents that were used in the experiments. From left to right: Stent 1–Stent4.

Instrumentation

An intravascular scanner (CVIS Insight, Cardiovascular Imaging Systems, Inc. CA, USA) with a 20 MHz (8F) rotating mirror catheter was used to obtain in vitro experimental data. The catheters are equipped with a so-called *strut*, which consists of a

Table 1 The four stent types used in the experiments are denoted Stent1–Stent4. The symbols D, L and T are refering to stent diameter (expanded), stent length (expanded) and filament thickness respectively

#	*Type*	*D‡*	*L‡*	*T*	*Application*
Stent1	Palmaz-Schatz (PS153)*	5 mm	6.5 mm	64 µm	Coronary
Stent2	Palmaz (PS30)*	7 mm	30 mm	127 µm	Peripheral
Stent3	Wallstent†	10 mm	33 mm	152 ± 4 µm‡	Peripheral
Stent4	Wallstent†	9 mm	30 mm	131 ± 4 µm‡	Biliary

*Johnson & Johnson, Interventional Systems Co, Warren, New Jersey, USA.
†Schneider (Europe) AG, Pfizer Hospital Products Group, Zürich, Switzerland.
‡Measured quantities.

metal pin holding the transducer thereby causing a shadow limiting the field of view to slightly less than 360°. The distance from the catheter axis to the focus of the beam is 3.8 mm.

A numerical calculation was performed in which a *measured* transmit pulse was used in order to obtain a realistic result. This waveform was measured by immersing the catheter in water and by aligning a hydrophone (Type: NT28-4, Force Institutes, Copenhagen, Denmark) towards the ultrasound beam. The signal was digitized by a storage oscilloscope (Philips PM3323) and transferred to a computer. The pulse duration was approximately 8 cycles at 20 MHz.

Phantom

A vessel-wall phantom was made in order to illustrate the situation where a stent is improperly adapted to the vessel wall. A 1mm thick membrane was made of silicon (RTV-E 602 Wacker Silicone, Wacker-Chemie GmbH, München, Germany) and folded to form a tube of diameter approximately 9 mm and with slightly irregular shape. The IVUS speckle pattern from this material is very similar to that from a vessel wall, however the penetration at 20 MHz is less, typically 2 mm.

Experiments

Three kind of experiments were performed in the study (one experiment of each kind):

1. Stents 1–4 were imaged in a water tank for illustration purposes. A catheter was fixed in a water tank containing approximately one litre of degassed water. The stent was placed over the catheter by hand and aligned during imaging in order to obtain the desired cross sectional image.
2. The silicon vessel-wall phantom was imaged with no stent present in the lumen as well as with Stent2 in-between the catheter and the phantom. The purpose was to demonstrate the effect of imaging a blood vessel through a stent. This was obtained by fixing the phantom to the catheter and insert/remove the stent by hand.
3. The primary echo with its echo tail was measured from three stainless steel plates for the purpose of model verification. Again the catheter was fixed in the water tank and the actual plate was located by hand in the beam focus during imaging. Angular alignment of the plate caused variable length of the echo tail, and the scanner was frozen at maximum possible length. The digitized image was transferred to a computer, and the beam containing the longest tail was used for comparison with the model data.

THEORY

This section describes the most important wave propagation effects related to IVUS-imaging of intravascular stents. There are three main effects to be described in the following:

Shadowing

Since the acoustic impedance in biological media and metal differ significantly, almost no acoustic power penetrates through a metal structure. A shadow region occurs behind the metal, the characteristics of the shadow depends on the size and the shape of the metal relative to the angular distribution of the ultrasound beam. The angular resolution of an intravascular catheter is specified by the manufacturer, usually varying between 0.15–0.3 mm. This is the width of the beam in the focus according to the manufacturers definition. However, there is acoustic energy in an even wider area.

The following situations may occur in stent imaging: 1) The ultrasound beam may pass between stent filaments entirely, i.e. no shadowing. 2) The beam may be partially reflected from one or more filaments, i.e. partially shadowing. 3) All energy may be reflected from one or more stent filaments, i.e. totally shadowing.

Transducer-stent reverberations

As the transmitted acoustic pulse hits a stent, a strong echo is reflected back to the transducer. This is the primary echo from the stent. However, this echo is reflected at the transducer surface causing a secondary pulse which propagates into the medium generating a secondary image of the stent and the surrounding tissue structures. This second representation of the stent is denoted a first order transducer-stent reverberation. Due to two times longer propagation path, this echo will be superimposed on the primary echo from tissue structures at twice the depth of the stent. A schematic illustration is given in Figure 3. In situations with low signal attenuation, for example in water, higher order reverberations may occur. The image in Figure 1(a) demonstrates primary echoes plus first, second and third order transducer-stent reverberations.

Stent-filament reverberations

When the ultrasound pulse hits a stent filament which is surrounded by soft material like water, blood or tissue, several possible wave-propagation effects may occur in the vicinity of the hitting point:

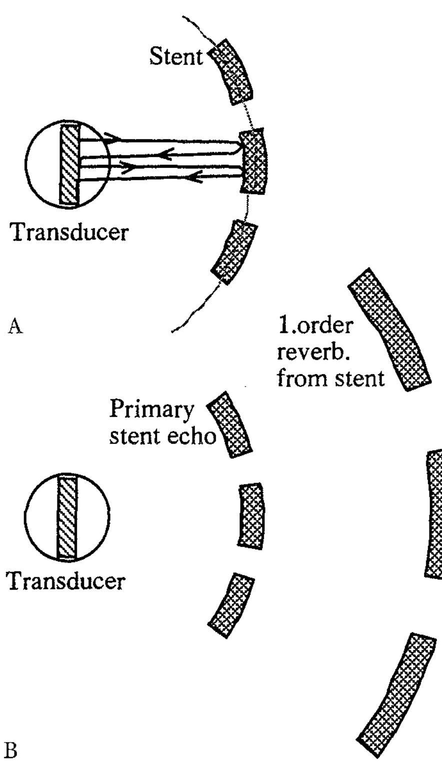

Fig. 3 (A) First order transducer-stent reverberations are illustrated by two times reflection between the transducer (left) and the stent filaments (right). (B) The resulting appearance on the screen is a double echo from the stent.

1) energy will be transmitted into the metal and undergo multiple internal reflections. 2) The metal filament may be excited and vibrate. 3) Energy may be converted to surface waves along the stent surface. These wave-propagation effects may result in re-emitted signals which return back to the transducer after a certain delay, thus resulting in a tail on the primary (and multiple) echo(s). A complete theoretical description of the above mentioned effects is very complex and beyond the scope of this work.

We postulate that the dominating effect in intravascular stent imaging is the first one: internal reflections in the metal. This is motivated from theoretical and experimental findings: the transducer/blood/metal/tissue-configuration in Figure 4 was modelled theoretically and arranged experimentally. There was a close correspondence between the numerical calculations and the measured results, i.e. the echo tails were comparable with the tails one observes in practical stent imaging. However, variations occur due to the fact that none of the stents consist of plane metal filaments. Stent1

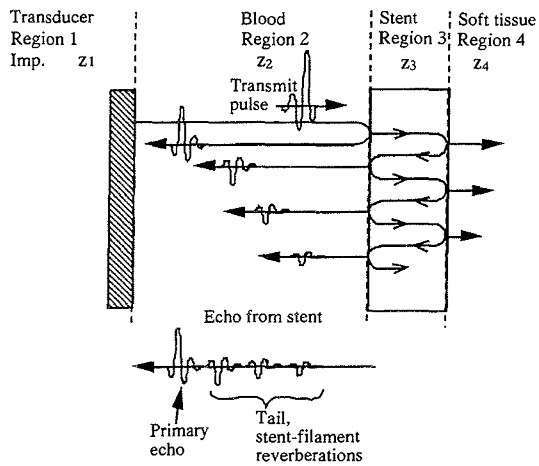

Fig. 4 The primary reason for stent-filament reverberations is supposed to be the sum of emitted power at each multiple reflection between the proximal and distal surface of the stent filament.

and 2 consist of curved metal filaments while Stent3 and 4 consists of cylindrical metal wires.

Reflection properties

The reflection pattern in a metal plate is described with reference to Figure 5. An incident pulse u_a propagates in region 2 (which is representing blood) and hits the surface of region 3 (steel). A major part of the signal is reflected back, here symbolized by u_b, while the remaining part of the energy propagates into region 3 and undergoes multiple reflections between the two surfaces. A small amount of energy is transmitted through the metal at each site of reflection.

The fraction of the incident pressure amplitude that is reflected and transmitted at the border between a region x and a region y is given by the reflection coefficient r_{xy} and the transmission coefficient τ_{xy} respectively:

$$r_{xy}=\frac{z_y-z_x}{z_x+z_y} \quad (1)$$

$$\tau_{xy}=\frac{2z_y}{z_x+z_y} \quad (2)$$

where z_i is the acoustic impedance of the material in region i, defined as the product of the mass density ρ_i and the wave velocity c_i:

$$z_i=\rho_i c_i \quad (3)$$

A list of material properties is provided in Table 2 from which the following coefficients can be

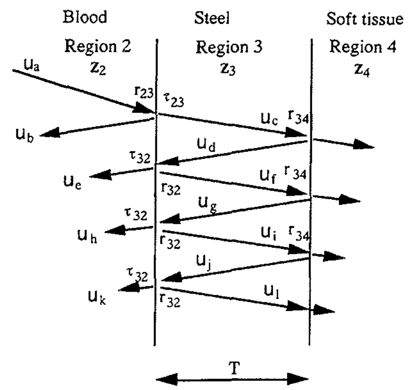

Fig. 5 Schematic illustration of reflections and transmissions associated with an incident pulse u_a that hits a metal plate (region 3) which is located between to other medias (region 2 and 4). The primary echo u_b is followed by an echo tail consisting of the contribution from multiple internal reflections (u_e, u_h, u_k, ...).

Table 2 Mass density ρ, wave velocity c and acoustic impedance z of a typical PZT5A-transducer, whole blood, stent (stainless steel) and soft tissue (aorta)[14–16]

Region	*Material*	ρ_i *(kg/m³)*	c_i *(m/s)*	z_i *(10⁶ kg/(m²s))*
1	Transducer	7.75	4350	33.7
2	Blood	1.048	1570	1.65
3	Stent	7.97	5690	45.3
4	Soft tissue	1.039	1501	1.56

calculated:

$r_{23}=\ 0.930$ (blood–steel)
$r_{34}=-0.933$ (steel–soft tissue)
$r_{32}=-0.931$ (steel–blood)
$\tau_{23}=\ 1.930$ (blood–steel)
$\tau_{32}=\ 0.070$ (steel–blood)

The primary echo from the stent can then be written:

$$u_b=u_a r_{23} \quad (4)$$

The echo tail u_t consists of the sum of all pulses transmitted out of region 3 and into region 2:

$$u_t=u_e+u_h+u_k+\ldots \quad (5)$$

The signal u_k is defined specifically as an example:

$$u_k=u_a\,\tau_{23}\,r_{34}\,r_{32}\,r_{34}\,r_{32}\,r_{34}\,\tau_{32} \quad (6)$$

Note that the primary echo from the stent is determined by the reflection coefficient r_{23} which is positive, i.e. the reflected pressure wave has the same polarity as the incident wave. However, echoes having undergone multiple reflections within region 3 are subject to an odd number of negative reflection coefficients which means that these echoes have opposite polarity relative to the primary echo.

The pulses that interfere after multiple reflections have the same shape as the incident wave (except the phase shift), i.e. they consist of N cycles at the transmit center frequency f_o. This means that the pulse length in the actual material is given by:

$$L_{Pi}=Nc_i/f_o=N\lambda_i \quad (7)$$

where λ_i is the wavelength in the material. The pattern of the resulting echo tail will depend on the metal thickness T, the pulse length L_{Pi} and the wavelength λ_i. A detailed description is given together with a graphic illustration in the next section.

RESULTS

Echo from thin metal plate

Numerical calculation

A theoretical description of the primary echo and its corresponding tail is given in this section. A numerical calculation was performed by inserting a realistic acoustic pulse (hydrophone measurement) as the incident wave u_a in Figure 5. The primary echo and the echo tail was calculated according to Equation 4 and 5 using a velocity of sound in the metal equal to $c = 5690\ s^{-1}$ which is the tabulated longitudenal velocity of sound in stainless steel (316).[16] The pulse length in this metal is then: $LP_3 = 2.27$ mm (Equation 7). The resulting signal was quadrature demodulated, low-pass filtered and the absolute value was displayed as a gray-level image versus metal plate thickness T. The result is shown in Figure 6 where the horizontal axis is range (primary echo to the left, the tail aims to the right) and the vertical axis is metal thickness.

Figure 6 illustrates that the echo tail depends on the plate thickness. The following observations can be made with reference to the Figure:

1. Constructive interference occur between pulses when $2T = \lambda_3 M$ (M = 1, 2, 3, ... and λ_3 is the wavelength in steel). Constructive interference means that the pulses that bounce back and forth between the two metal surfaces overlap in phase and sum up to a strong signal. This results in a bright and long tail occuring for the first time at thickness $T=$ 142 μm. Destructive interference means that pulses cancel each other, the result is a weaker and shorter tail. Maximum cancellation occur when $2T = 2K + 1)/2$ and $K = 0, 1, 2, \ldots$, for the second time at thickness $T = 213$ μm ($K = 1$).
2. Energy loss causes the signal (tail) to diminish as a function of range. Our model accounts for no other energy drop than power transmitted out of region 3 at each plate surface. This means that the intensity will drop a certain fraction at each point of reflection. Thus, the tail diminish more rapidly in a thin plate (due to many reflections in a short time interval) than in a thick plate.
3. When the plate thickness equals half the pulse length, $T = LP_3/2$, then multiple pulses will touch each other without overlapping. The result is a periodic pattern of resolvable pulses. This occurs at $T=$ 1.138 mm. A periodic pattern also occurs when $T < LP_3/2$, i.e. the pulses overlap. The reason is constructive and destructive interference between the overlapping fractions of the pulses.
4. The primary echo u_b will interfere with the first internal reflection u_e (and possibly others) and cause constructive or destructive interference depending on T. This is shown as a periodic intensity variation along the vertical line in range 0.4 mm.

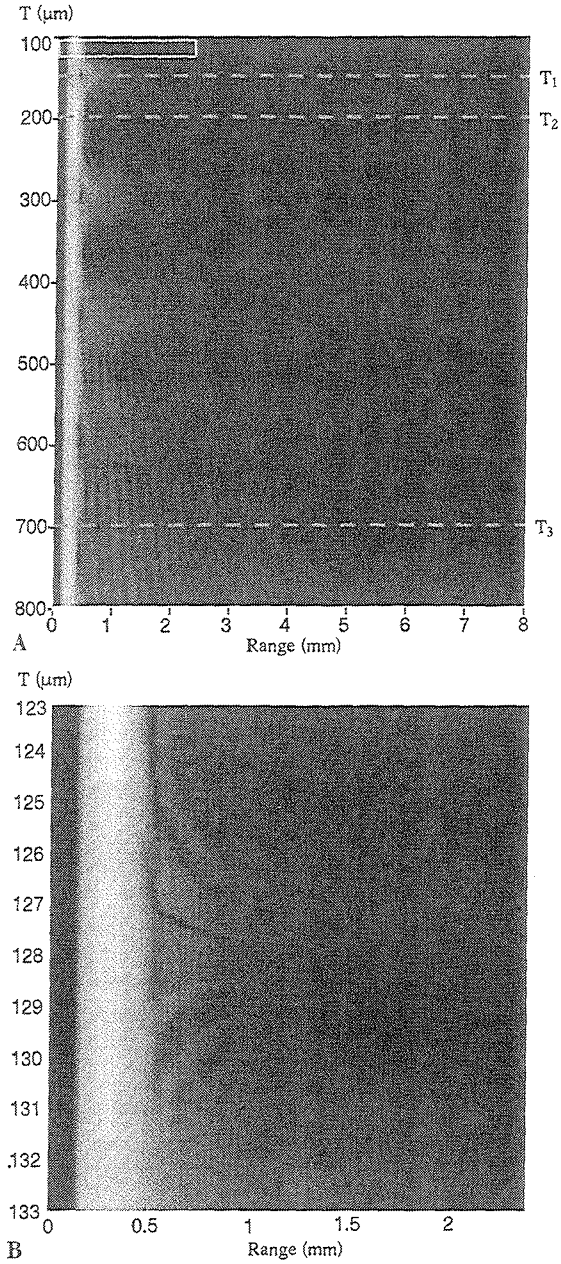

Fig. 6 (A) Calculated echo tail from the steel plate in Figure 5 versus metal thickness T. The primary echo is located left while the tail aims towards right. The length of the tail varies with T due to constructive and destructive interference. (B) Magnified view of the rectangle area in (A).

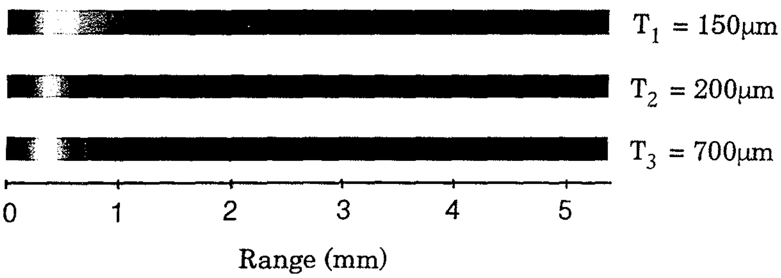

Fig. 7 Measured primary echo and tail from three stainless steel plates of different thicknesses corresponds well with theoretical result in Fig. 6.

Experiments

The theoretical results presented in Figure 6 were verified experimentally for three different stainless steel plates of dimension (10 mm × 100 mm) and thicknesses $T_1 = 150$ μm, $T_2 = 200$ μm and $T_3 =$ 700 μm. The ultrasound beam of a 20 MHz catheter was aligned perpendicular to the plate surface and the measured amplitude echoes were plotted from left to right (primary echo to the left). The range scale in Figure 7 is based on a measured velocity of sound in the metal ($c_3 = 6000$ m s^{-1}).

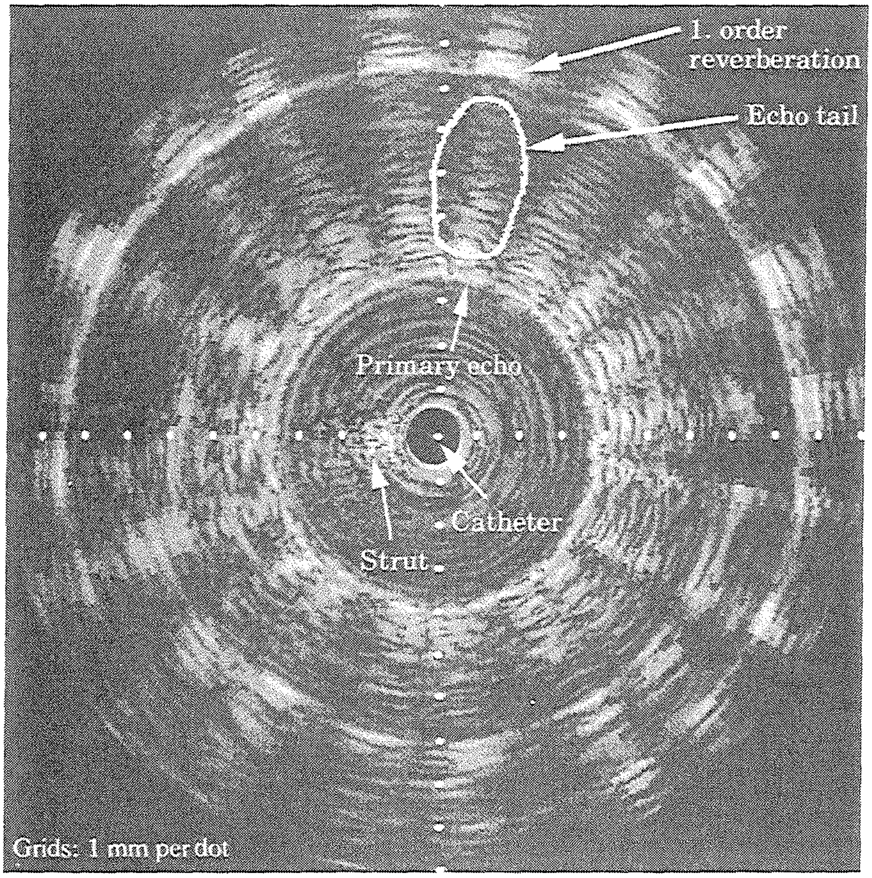

Fig. 8 Concentric in vitro 20 MHz image of Stent2 (Palmaz).

There is a close fit between the experimental results presented in Figure 7 and the theoretical result in Figure 6.

In vitro stent images

This section provides two images illustrating the transducer-stent and stent-filament reverberations. Both images were acquired by aligning a stent coaxial and concentric around the 20 MHz 8F catheter in a water bath.

The first image is shown in Figure 8 where Stent2 (a Palmaz stent with filament thickness $T_{\mathrm{Stent2}} = 127$ μm) is scanned in a plane that intersects the 20 individual filaments (see Fig. 2). The primary echo, the echo tail or stent-filament reverberation and the first order transducer-stent reverberation are clearly shown. Note that the individual stent filaments can not be resolved by observing the primary echo, probably due to side lobe energy from adjacent filaments. However, individual filaments are easily resolved in the echo tails and the first order reverberations.

Furthermore, the length of the tails is approximately 4–5 mm, but a stent with 127 μm wall thickness is supposed to induce a tail of approximately 1.5 mm's length according to Figure 6(b). This may indicate that other effects than multiple reflections between the filaments surfaces account for the stent-filament reverberations as well.

Figure 9 shows a 20 MHz image of Stent4, a fine-meshed Wallstent consisting of 12 filaments twisted clockwise and 12 which are twisted counter clockwise. The ultrasound beam is wide compared to the mesh-size, thus several filaments contribute to the echo in each beam direction. The result is a quite random speckle pattern, not very different from images obtained from vessel walls. Thus the individual stent filaments are not well resolved.

This stent type is also subject to stent-filament reverberations. However, the tails are less pro-

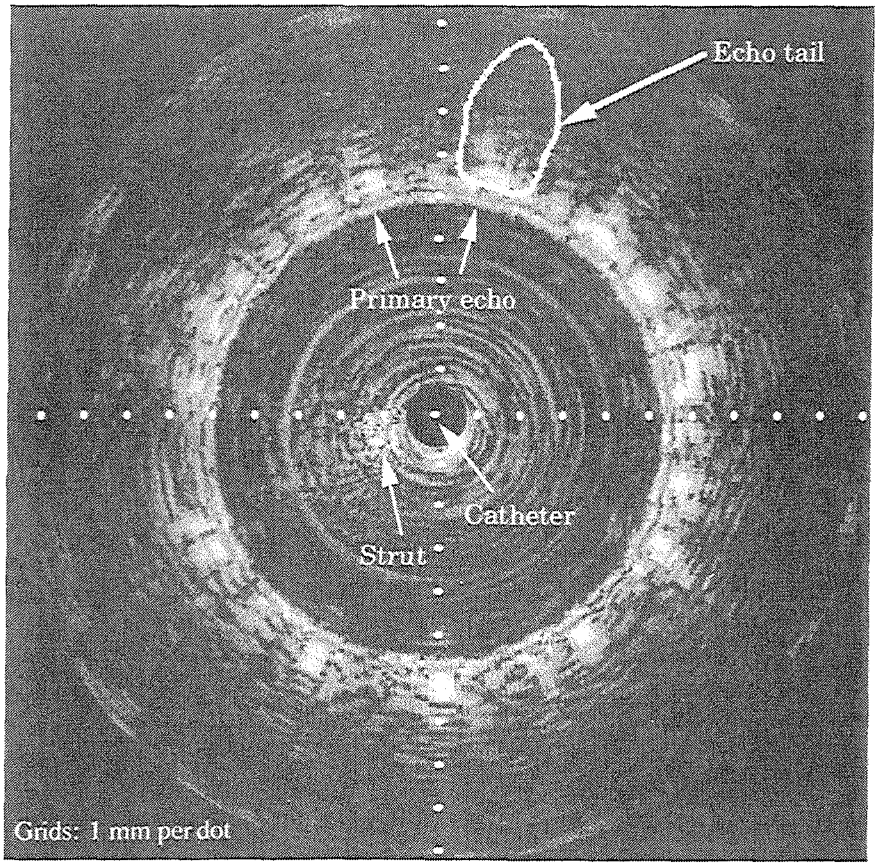

Fig. 9 Concentric in vitro 20 MHz image of Stent4 (Fine meshed Wallstent). The image from this stent is quite similar to that of a normal vessel wall due to a wide beam relative to the mesh size.

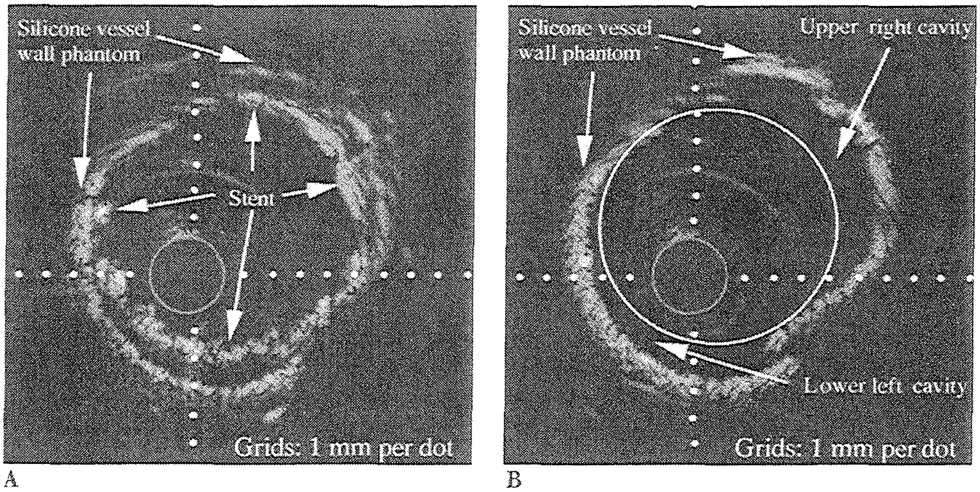

Fig. 10 (A) Silicone vessel-wall phantom imaged through Stent2 in a water tank. Shadowing and stent-filament reverberations make it difficult to discriminate the stent from the phantom as well as determining the water filled cavities. (B) Same image without the stent. The white circle indicates the location of the stent in (A).

nounced since several filaments contribute to the echo simultaneously. The filament consists of a cylindrical wire which means that the wave propagation within the metal is more complex than is the case with more flat and rectangular shaped filament cross sections (like Stent 1 and 2).

In vitro examples of Stent1 and Stent3 are not shown since they do not differ significantly from those presented.

In vitro image of stent in vessel-wall phantom

An experiment was conducted in order to illustrate that filament shadowing and stent-filament reverberations can make interpretation of ultrasound-guided stent-adaptation difficult. The silicone vessel-wall phantom was fixed over a 20 MHz catheter in a water tank, and Stent2 was inserted between the catheter and the phantom. The phantom was slightly larger than the stent yielding two water-filled cavities at either side of the phantom. The result is shown in Figure 10(a) where the stent is easily recognized between 4 and 10 o'clock, but difficult to distinguish from the phantom in other locations. The lower left cavity is recognized from 5 to 9 o'clock, but the upper right is hard to locate precisely. A reference image is shown in Figure 10(b) where the stent has been removed, and the white circle indicates the location of the stent in Figure 10(a).

CONCLUSION

Early endothelialization of the stent filaments seems advantageous to obtain long-term patency of a stented artery. Re-endothelialization is supposed to occur by lateral growth of endothelial patches between the struts.[17] Therefore documentation of optimal stent adaptation to the arterial wall is of special interest. Proper stent adaptation is also of utmost importance for endovascular treatment of aortic aneurysms. Intravascular ultrasonography can provide such information during the procedure, but our findings demonstrate that mis-interpretation is possible due to wave-propagation artifacts. One should be aware of the most important effects which can be summarized as follows

1. *Shadowing effect* and geometric distortion. The metallic stent filaments could be an obstacle for the entire beam or fractions of the beam to propagate behind the stent. The result is a total of fractional shadow behind the filament. This shadow is difficult to recognize since it is superimposed by echos from structures behind the stent and from stent-filament reverberations. This situation differ from the characteristic shadow often seen behind calcified plaques which are not influenced by artifacts.
2. *Transducer-stent reverberations* appear as multiple representations of the primary echo which can significantly obscure echo-information from biological structures in the corresponding depths. This is

a minor problem when the stent is located far from the catheter since the reverberations then occur beyond the most interesting field of view. However, this effect is of importance for the interpretation of the image when the stent is located close to the catheter.

3. *Stent-filament reverberations* appear as a tail on the primary echo which overwrites and obscure the image of biological structures in the immediate vicinity of the stent. These reverberations fill in the shadow which is caused by the stent filaments.

The shadowing effect as well as the reverberations inhibit investigation of structural changes in the vessel wall after stent implantation. In addition, small dissections or cavities which may exist between the stent and the vessel wall due to sub-optimal stent adaptation can be difficult or impossible to detect with this method.

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Paper VII

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IN VIVO THROMBOGENICITY OF INTRAVASCULAR ULTRASOUND IMAGING CATHETERS

K.-D. BOLZ and A. NORDBY

Abstract

This study evaluates the frequency and significance of thrombus formation on the surface of intravascular ultrasound (US) imaging catheters. The investigation includes 63 consecutive patients who underwent 32 arterial and 38 venous intravascular procedures. At the end of the imaging procedure the US findings were observed during withdrawal of the catheter into the introducer sheath. Thrombus formation was demonstrated in 5 (7%). The largest thrombus fragments had a cross-sectional dimension of 2.2×1.0 mm. There was a significant correlation between the incidence of thrombus formation and the occurrence of malign neoplastic disease. No relation was found between the frequency of thrombus formation and the duration of the imaging procedure or the type of US catheter. It is concluded that the thrombogenicity of intravascular US imaging devices is not higher than that of conventional angiographic catheters. The observed "pull-out" thrombi were small and it is unlikely that they could have any clinical significance.

Key words: Ultrasonography (US); —, intravascular; catheters and catheterization, complications; —, thromboembolism.

The frequency of thromboembolic complications during angiographic procedures ranges from 0.3% to 14% (5, 14). The thrombogenicity of the catheter is related to its chemical composition and structural characteristics (1, 2, 9, 10). The length and width of the catheter are also related to thrombus formation (8), as well as to the duration of the procedure (8, 12).

Intravascular ultrasound (US) imaging is a valuable method for the detection of intraluminal thrombi and thrombus formation on angiographic catheters (3, 4, 11). However, the US procedure may itself add to the risk of thrombus formation, a risk which has hitherto not been fully assessed. Some US catheters have an asymmetric tip to allow for the electric lead and side channels for the guidewire in the distal end. Such irregularities on the catheter surface may produce turbulence of the bloodstream, contributing to an increased thrombogenicity. In addition, it is possible that mechanical vibrations of the imaging system, caused by the rotating wire within the catheter lumen, may influence the thrombogenic properties of the imaging device.

The present investigation was performed to evaluate the frequency and significance of thrombus formation on the surface of intravascular US devices by means of the US imaging system itself.

Material and Methods

The study includes a series of 70 US procedures in 63 consecutive patients who underwent transfemoral intravascular US imaging. In 32 procedures the catheter was introduced into the femoral artery, whereas the remaining 38 investigations were venous catheterizations (Table 1). The series includes 12 individuals who were examined after angiographically documented arrest of the intracranial circulation. Like several other patients in the series they were part of a study of the normal US appearance of the arterial or venous vessel wall. Fifteen patients underwent intraarterial therapeutic procedures such as PTA and/or stent implantation. Fifteen other patients were investigated because of suspected thrombus formation on central venous indwelling catheters. Six patients in the group of venous and one patient in the group of arterial procedures had a known neoplastic disease with possibly increased coagulability.

Adjuvant medical treatment. The fifteen patients who underwent intraarterial therapeutic interventions were hepa-

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Table 1

Indications for catheterization/intravascular US imaging in 63 patients

Arterial procedures, 28 patients	n
Documentation of abolished intracranial circulation, US study of normal arteries	6
PTA and/or stent implantation in pelvic, renal or femoral arteries	15
Intermittent claudication, arteriography prior to vascular surgery	8
Renal angiography (anomalous renal artery?)	1
Pancreatic angiography (insulinoma?)	1
Hepatic angiography (liver metastasis?)	1
Venous procedures, 35 patients	
Abolished intracranial circulation, US study of the venous system	6
Suspected thrombus formation on central venous indwelling catheters	15
Cavography (chronic venous insufficiency)	9
Pulmonary angiography (suspected embolism)	2
Cavography (liver metastasis)	1
Cavography (renal carcinoma)	1
Selective renal vein catheterization (renal hypertension)	1

Table 2

Types and dimensions of US imaging catheters used in 70 imaging procedures in 63 patients

Catheter	Dimension	n
Sonicath side-saddle*	6.2 F (2.1 mm)	28
Sonicath rounded tip*	6.2 F (2.1 mm)	6
Cvis P 8065 fixed guide tip**	8.0 F (2.7 mm)	6
Cvis C 1007 over-the-wire**	8.0 F (2.7 mm)	6
Cvis C 1000 over-the-wire**	8.0 F (2.7 mm)	3
Cvis C 1000 over-the-wire**	5.0 F (1.7 mm)	14

Manufactured by *Boston Scientific, Watertown, MA, and ** Cardiovascular Imaging Systems Inc., Sunnyvale, CA.

rinized with 5 000 to 10 000 IU heparin intraoperatively. In addition they were given 500 mg acetylsalicylic acid (ASA) 24 hours before the procedure and 100 to 500 mg ASA the day of the procedure. In the remaining patients no anticoagulant medication was given. During all procedures the catheters and guidewires were flushed with heparinized saline (6 000 IU/1 000 ml).

US examination. Various types and dimensions of US imaging devices were used (Table 2). The diameters of the introducer sheaths were 2.0 mm, 2.7 mm and 3.0 mm, respectively.

In the arterial procedures the mean ratio between sheath diameter and vessel diameter measured by US was 0.36 (range 0.20–0.40; median 0.30). In the venous procedures it was 0.23 (range 0.10–0.20; median 0.2). Mean indwelling time of the introducer sheaths was 49 min (range 10–75 min) and 25 min (range 10–85 min), respectively, whereas the US catheter remained in the vessel for 3 to 15 min (mean 7 min) and 3 to 20 min (mean 9 min), respectively.

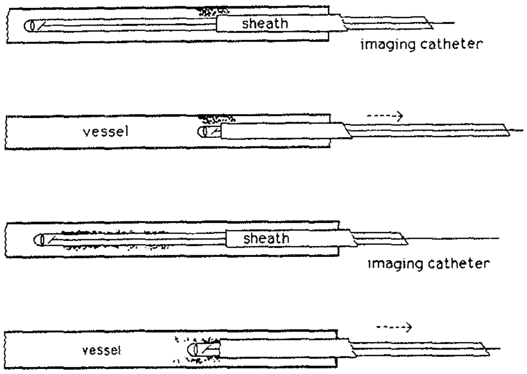

Fig. 1. Schematic drawings demonstrating 2 types of thrombus formation during US imaging, which can be observed when the imaging catheter is withdrawn. top) A thrombus fixed to the distal end of the introducer sheath and vessel wall will be seen just before the catheter tip is pulled back into the introducer. bottom) Thrombi surrounding the surface of the imaging catheter will be wiped off by the sheath when the catheter is drawn back. In the iliac vein they will be seen in the centripetal bloodstream when passing the US transducer. In the artery the thrombus will embolize to the periphery without passing the transducer, provided there is no obstruction of the bloodstream by the introducer sheath.

At the end of the procedure the US catheter was slowly pulled back into the introducer sheath. The US findings during withdrawal of the catheter were observed and recorded on a videotape in order to demonstrate possible thrombi which were wiped off from the catheter surface, or thrombus formation on the distal end of the introducer sheath.

Statistics. Fisher's exact probability test was used and p-values <0.05 were considered significant.

Results

Fig. 1 demonstrates types of thrombus which can be observed when the US imaging catheter is withdrawn: a) A thrombus fixed to the distal end of the introducer sheath just before the catheter tip is pulled back into the introducer; b) Thrombi surrounding the surface of the imaging catheter are wiped off by the sheath when the catheter is drawn back. In the iliac vein this is seen when it in the centripetal bloodstream passes the US transducer. In an artery the thrombus will embolize to the periphery without passing the transducer provided that there is no obstruction of the bloodstream by the introducer sheath.

Venous procedures. In 5 cases (13%) highly echogenic, intraluminal structures were observed just before the tip of the imaging catheter was withdrawn into the introducer sheath. These echoes were located close to the imaging catheter, were bright and homogeneous and were distinctly demarcated from the surrounding blood. The phenomenon

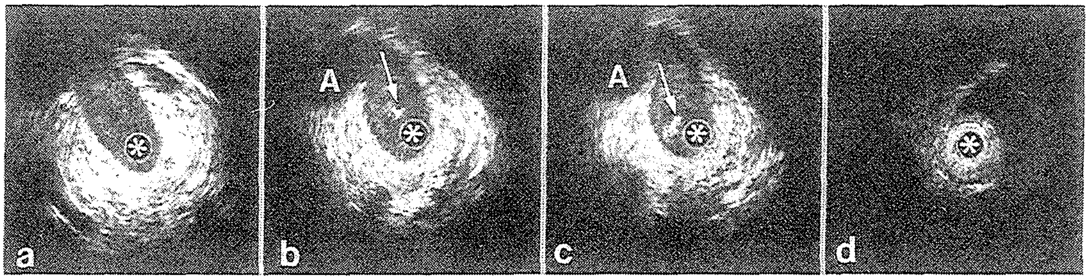

Fig. 2. "Pull-out" thrombus at the termination of a venous US imaging procedure. (The last 3 seconds of withdrawal of the imaging catheter.) a) Catheter tip within the external iliac vein; b) and c) thrombus fragments (→) within the venous lumen just before the catheter tip is completely drawn back; d) catheter tip within the introducer sheath. * imaging catheter, A – femoral artery. Catheter diameter 2.1 mm.

could only be observed for a short period of time, in most cases lasting less than 1 second, indicating that the finding represented particles floating in the bloodstream. The echoes had various shapes and dimensions; the largest measuring 2.2×1 mm (Fig. 2). Since the particles had the appearance of fresh thrombotic material (4, 11, 13), they were interpreted as thrombi, wiped off from the catheter surface. In none of the venous procedures was thrombus formation on the tip of the introducer sheath or vessel wall observed.

Arterial procedures. In none of the arterial procedures was any thrombus formation observed, either "pull-out" thrombi or thrombus formation on the tip of the sheath or vessel wall.

Intraobserver and interobserver variability. Several weeks after completion of the series the video recordings of all patients were restudied by the original examiner and by a different observer who was familiar with the interpretation of intravascular US images. All 5 patients with the primary diagnosis "pull-out" thrombus were identified by both observers independently.

Statistical analysis. In 4 of the 5 procedures in which "pull-out" thrombi were observed, the catheterization was performed with a Sonicath Sidesaddle 2.1 mm imaging catheter. This may indicate a causal relation between the use of this catheter type (e.g. the "sidesaddle" construction) and thrombus formation. However, most of the venous procedures were performed with this catheter type (24 of 38 procedures) and there was no significant difference between the catheter types ($p=0.4$).

Three of the 5 patients with thrombus formation had a known malign neoplastic disease. Only 3 of the remaining 30 patients in the series of venous catheterizations had known malignancy. Statistical analysis showed a significant correlation ($p=0.02$).

There was no relation between the duration of the imaging procedure and thrombus formation. The mean indwelling time of the imaging catheter in all venous procedures was about the same as in the procedures with demonstrated thrombi (9.0 and 9.6 min, respectively).

Discussion

It has been demonstrated by a variety of techniques that there is a high incidence of fibrinous sheaths around angiographic catheters at completion of the catheterization procedure (5–8, 12, 14). In the present investigation, thrombus formation was demonstrated in 7%. All of them were found in venous catheterizations. This is a rather low incidence compared with a previous oscillometric and arteriographic investigation, in which "pull-out" thrombi were found in 33% (12). The low incidence may be due to the fact that "pull-out" thrombi in arterial procedures may be carried with the bloodstream in the peripheral direction and not pass the US transducer. In addition, many of the patients with arterial procedures were heparinized and treated with ASA.

The aim of the present study was to get information about whether the use of US imaging catheters demands special precautions, such as anticoagulant treatment or limited duration of the imaging procedure. Therefore the group of venous catheterizations is of special interest. None of these patients had received any anticoagulant medication. Furthermore, because of the relatively low blood flow velocity in the venous system, it is likely that thrombus formation on the catheter surface is more frequent in venous than in arterial procedures. The incidence of thrombus formation in this group was 13% and related to the occurrence of malign and neoplastic disease, which may indicate an increased hemocoagulability in these patients.

Previous *in vitro* and *in vivo* studies have shown a high sensitivity and specificity in the detection of intraluminal thrombi by intravascular US imaging (3, 11, 13). In the present investigation some thrombotic material may have passed unnoticed, since we could only detect thrombus fragments which were wiped off during pull-out at termination of the procedure. However, the mass of thrombus material wiped off would be largest when the catheter is fully withdrawn. Thus, any thrombus fragments which could not be observed by the method used in the present study, would probably be of minor size. The largest thrombus fragments demonstrated had cross-sectional dimensions of about 2.2×1.0 mm. According to previous oscillometric and arteriographic investigations (7, 12) only thrombi larger than 2.5 mm seem to cause physical symptoms and signs of thromboembolism in peripheral arteries.

Conclusions. The present investigation demonstrated that thrombus formation on the surface of intravascular US imaging devices is not more frequent than in conventional angiographic procedures. Neither the duration of the procedure nor the type of imaging catheter had any influence on the risk of thrombus formation. The "pull-out" thrombi were small and it is unlikely that they could have any clinical consequence.

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