Intravascular Ultrasound Imaging
— In vitro and vivo validation —

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Intravascular ultrasound imaging is a new technique for visualizing arterial structures. The purpose of this study was twofold; first, to assess the ability of this intravascular ultrasound catheter to generate cross-sectional images of human artery segments in vitro and second, to determine the reliability of intravascular ultrasound technique in the evaluation of human arteries in vivo. For the in vitro study, ultrasound images of the arteries were presented as a two-dimensional, 360° display of vessel cross-section perpendicular to the long-axis of the probe. The ultrasound scanning provided an accurate description with high resolution of lumen structure and lumen-intima interface in all vessel specimens. There was a good correlation between the planimetric luminal area on the ultrasound images and the area obtained from histologic images (r=0.92). There was also a good correlation in the plaque thickness between ultrasound and histological examination (r=0.88). In the in vivo study, the ultrasound catheter was easily introduced, readily manipulated, and images were successfully obtained in all patients. No untoward effects were noted during manipulation of the catheter. There was a good correlation in the arterial dimension between ultrasound and angiographic measurements (r=0.93). Thus, intravascular ultrasound imaging appears to be useful for characterizing and quantitating arterial lesions.

(Ipn Circ J 1992; 56: 572—577)

An intravascular ultrasound imaging system has the unique ability to provide cross-sectional images of the arterial wall. The potential value of ultrasound to characterize the morphological features of cardiovascular tissue has been extensively studied in recent years!—11 Ultrasound tissue characterization can detect the presence and severity of atherosclerotic lesions as well as differentiate normal from fatty, fibrous and calcified regions within the vessel wall! Initial studies with intravascular ultrasound imaging systems have been reported and show great promise? The purpose of this study was to define the ability of a newly developed intravascular ultrasound imaging system to visualize cross-sectional images of human atherosclerotic artery in vitro and to determine the reliability of intravascular ultrasound technique in the evaluation of various human arteries in vivo.

METHODS

Ultrasound probe
A prototype ultrasound imaging catheter (Aloka Inc., Tokyo, Japan) was used in this

Key words:
Intravascular ultrasound
Atherosclerosis

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study. A single 20-MHz ultrasound transducer was mounted in the distal end of a 2.0 mm diameter catheter. Image resolution was approximately 0.15 mm axially along the ultrasonic beam. The slice thickness and the lateral resolution of the ultrasound beam varied directly with distance from the probe and was approximately 0.5 mm for the 4-6 mm diameter vessels.

Ultrasound and histological examination (in vitro study)

Common carotid and iliac arteries were removed at autopsy from humans within 4 to 12 h after death. Arterial specimens approximately 20 mm long were frozen and stored at \(-70^\circ\text{C}\). For in vitro studies, the specimens were thawed and embedded in a saline solution. Care was taken to select straight arteries to allow adequate access of the ultrasound catheter in the artery. The intravascular ultrasound imaging catheter was aligned coaxial to the arterial segment, and the entire arrangement was immersed in a saline bath, which was kept at room temperature. Images were taken at 2 mm intervals along the entire length of the artery. The gain and contrast were adjusted for each image to provide optimal image quality. The position of the ultrasound transducer was indicated by measuring the length of the inserted portion of the catheter and marking this position in ink on the specimen to ensure that histopathologic sections were obtained from the same location as the ultrasound images.

After the ultrasound examination, the arteries were fixed in 10% buffered formalin for 12 h, and subsequently decalcified in a standard Cal Ex solution (Fisher Inc.) for 5 h. The arteries were processed for routine
Fig. 3. Comparison between histologic cross section (right) and corresponding echographic section (left) from an iliac artery with an advanced atherosclerotic lesion. A distinct atherosclerotic lesion characterized by bright echoes is seen between the 2 and 6 o’clock positions. Because of ultrasound attenuation and reflection of the ultrasound caused by calcification in this lesion, no echoes were derived from the intima, media or adventitia.

Fig. 4. Comparison of plaque thickness evaluated by histology and intravascular ultrasound.

paraffin embedding. Transverse sections (5 μm thick) perpendicular to the longitudinal axis of the artery were cut at 2 mm intervals. The sections were arranged from proximal to distal. The histologic sections were stained with the Verhoeff’s elastin van Gieson stain technique. With the Verhoeff’s elastin stain, a highly selective black staining of elastin fiber is obtained. The van Gieson technique is used as counterstaining for muscle and connective tissue. In addition, sections were stained with the hematoxylin azophloxine technique to delineate connective tissue and calcium.

The analysis was performed on stop frame images taken from the real-time intravascular ultrasound images. The arterial wall and plaque characteristics as documented by histologic study were compared with the corresponding echographic cross sections. The absolute luminal area was determined by planimetry with previously validated software. After the area measurement, the thicknesses of the different layers that appeared on the ultrasound image were measured. The relative thickness of each layer was used for comparing the ultrasound structures with the histopathologic specimens. The histopathologic specimens were photographed and enlarged together with a calibrator. The absolute luminal area on the prints was then determined by planimetry. The planimetric luminal areas on the ultrasound images were compared with those of the histopathologic specimens. A simple linear regression analysis was used for this comparison.

Ultrasound and angiographic examination (in vivo study)

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Seven patients undergoing cardiac catheterization for symptomatic angina were asked to participate, and they signed the Human Subjects Review Committee Consent Form. A 7F sheath was placed in the femoral artery. The ultrasound catheter was then inserted via the arterial sheath under fluoroscopic guidance. Movement of the ultrasound catheter to a portion as near as possible to the center of the vessel was frequently required to obtain a high quality 360° image. When an acceptable image was obtained, it was recorded on 1/2-inch videotape for subsequent review. The vessel diameter was measured in three separate planes that bisected the vessel by visually placing a cursor on the opposite side of the artery. These three measurements were averaged to obtain a mean vessel diameter. Measurements of diameter were evaluated by two different observers who did not know other patient's findings.

A contrast angiogram was obtained for each vessel site imaged with the intravascular ultrasound catheter. Biplane cineangiography was performed during hand injection of 2–6 ml contrast medium (iopamiron) via either the arterial sheath or an angiographic catheter placed proximal to the imaging site. The radiographic system consisted of an image intensifier with a 5 inch field of view and a 35 mm camera operating at 30 frame/sec. A standard radiographic grid was filmed to correct for radiographic magnification. For each vascular site, the cineangiograms were projected on a ground glass screen using a back projection method without rotating mirrors or other potentially distorting optical devices. Vessel diameter was measured using calipers to the nearest 0.5 mm. Because the ultrasound catheter was radiopaque, it was possible to make ultrasonic and angiographic measurements at the indentical site. Vessel diameter by ultrasound and cineangiography was compared by linear regression analysis.

RESULTS

In vitro study

Ultrasound images of the arteries were presented as a two-dimensional, 360° display of cross-section perpendicular to the long-axis of the probe (Fig. 1). The ultrasound scanning provided an accurate description with high resolution of lumen structure and lumen-intima interface in all vessel specimens. A characteristic three-layered appearance of vessels was clearly identified. The tunica media was seen as an echo-luent zone between the more intense echoes of the intima and adventitia laminae. The correlation between the planimetric luminal area on the ultrasound images and the area obtained from histologic images is shown in Fig. 2. The correlation coefficient was 0.92.

From comparative analysis between ultrasound images and corresponding histological sections, plaque morphological subtypes were characterized. Plaques with calcified deposits were clearly observed by the presence of bright echoes casting echo-free shadows onto deeper tissue zones (Fig. 3). Fibrous lesions yielded dense, homogeneous echo reflections without echo-free shadowing, whereas extracellular lipid components were much less echogenic.

Among the seven arteries studied, a total of 60 positions were analyzed to calculate the plaque thickness from both the histological and the corresponding echocardiographic section. The site and extent of the lesion were accurately determined from the echocardiographic images. There was a good correlation in the plaque thickness between ultrasound and histological examination (Fig. 4).
In vivo study

The ultrasound catheter was easily introduced, readily manipulated, and images were successfully obtained in all patients. No untoward effects were noted during manipulation of the catheter. The image quality was variable and dependent on catheter orientation in the vessel. The best images were obtained with the catheter centrally located in the vessel and orthogonally positioned with reference to the vessel long axis. Vessel diameter ranged from 7.3 mm to 11.7 mm (mean 9.4 mm) by intravascular ultrasound, and ranged from 36.3 mm to 13.2 mm (mean 9.6 mm) by cineangiography. There was a good correlation in the arterial dimension between ultrasound and angiographic measurements (r=0.93, Fig. 5).

DISCUSSION

This study demonstrates the ability of intravascular ultrasound imaging to provide real-time cross-sectional images of arterial lumen and wall characteristics both in vitro and in vivo. Significant correlations were found between the ultrasound and histological measurements of arterial cross-sectional area and plaque diameter. A significant correlation was also observed in the arterial diameter between ultrasound and angiographic measurements in vivo. In addition to these significant morphometric correlations, ultrasound images accurately predicted the plaque distribution and its histological composition in most of the examined sites. The correlation of the luminal area between the ultrasound images and histologic sections was close. However, there area several sources of error in trying to compare the area by ultrasound with histologic sections. The histologic preparation may produce artificial compression and distortion. In addition, fixation in formalin may produce shrinkage of the tissue. For these reasons, it is possible to speculate that ultrasound calculations in vivo may be a more accurate determination of the true size of anatomic structures than are measurements derived after histologic preparation.

The ability to assess vessel wall morphology and luminal characteristics of diseased arteries may potentially have valuable applications in the field of cardiovascular medicine. It is important to be able to determine the severity of atherosclerotic lesion, for which the current method of angiography has many limitations. Because angiography records only a silhouette of the vessel lumen, radiography will often misrepresent the extent of luminal narrowing. Not surprisingly, several studies have shown considerable intraobserver and interobserver variability in the interpretation of cineangiography and discrepancy between coronary angiogram and postmortem examination. The nature of an atherosclerotic obstruction may provide important prognostic implications about whether an interventional procedure, such as angioplasty or athectomy, might be successful. In addition, certain characteristics of an atherosclerotic lesion, such as the presence of ulcerated plaque or a thrombus, may have important implications for immediate prognosis of a patient.

The clinical significance of these observations remains to be determined by large clinical studies that will follow patients for clinical correlations. Our study demonstrates that intravascular ultrasound imaging appears feasible and promising method for identifying normal and diseased arterial structures. Ultrasound characterization of plaque composition is feasible and may provide important new perspective on anatomic features. These high quality ultrasound images allow quantitative assessment of the extent of athelomatous involvement of the artery as well as the morphology and character of the atheloma tissue. A variety of improvements in image quality and reduction of the catheter size will likely occur in the future. The ultimate clinical role of intravascular ultrasound in the evaluation of coronary artery disease will be dependent on the technological refinements that can be achieved in the near future.

REFERENCES

Japanese Circulation Journal Vol.36, June 1992


