Title

Experience With Intravascular Ultrasound Imaging Of Human Atherosclerotic Arteries

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Experience with intravascular ultrasound imaging of human atherosclerotic arteries

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ABSTRACT

Normal human arteries have a well-defined structure on intravascular images. The intima appears very thin and is most likely represented by a bright reflection arising from the internal elastic lamina. The smooth muscle tunica media is echo-lucent on the ultrasound image and appears as a dark band separating the intima from the adventitia. The adventitia is a brightly reflective layer of variable thickness. The thickness of the intima, and therefore of the atherosclerotic plaque can be accurately measured from the ultrasound images and correlates well with histology. Calcification within the wall of arteries is seen as bright echo reflection with shadowing of the peripheral wall. Fibrotic regions are highly reflective but do not shadow. Necrotic liquid regions within advanced atherosclerotic plaques are seen on ultrasound images as large lucent zones surrounded by echogenic tissue. Imaging can be performed before and after interventional procedures, such as laser angioplasty, balloon angioplasty and atherectomy. Intravascular ultrasound appears to provide an imaging modality for identifying the histologic characteristics of diseased arteries and for quantifying plaque thickness. It might be possible to perform such quantification to evaluate the results of interventional procedures.

1. INTRODUCTION

Atherosclerosis is an important disease process that produces variable thickening from cellular infiltration and proliferation, fibrosis, calcification and necrosis of the arterial wall. No presently available diagnostic method allows this process to be completely characterized in human coronary arteries in vivo. External 2-dimensional ultrasound imaging during direct exposure of the heart at the time of surgery [1] allows measurement of arterial wall thickness. Contrast coronary angiography provides an image of lumen contour, but gives no information about either the volume or composition of the atheroma present.[7] A mild degree of lumen narrowing on angiography may, in reality, represent a large atheroma volume [6]. Chest fluoroscopy provides a crude estimate of the degree of calcification present in an artery, but is difficult to quantify and the specific location of the calcification within the artery wall cannot be discerned. If one could know the histologic contents of human atheromata it might be possible to "type" atherosclerotic plaques, that is to characterize plaques in vivo according to their contents. This would facilitate the study of how atheromatous plaques change over time, and possibly to provide information useful for interventional cardiologic

procedures, such as laser, mechanical atherectomy and balloon dilatation.

It is known that ultrasound imaging offers the potential for evaluation of arterial wall thickness [1,3,10,13]. Intravascular ultrasound transducers on the ends of catheters have been used in vitro (Mallery,) and in vivo [11,13,14,17] to image human arteries. This approach allows the arterial wall to be imaged from inside the artery opening the possibility of imaging human coronary arteries in the catheterization laboratory as a routine complement to diagnostic angiography as well as before, during, and after PTCA, laser and atherectomy intervention.

The purpose of this study is to document our experience in identifying normal and atherosclerotic human arterial wall structures using a miniature intravascular ultrasound imaging catheter.

2. METHODS

This study employed an imaging catheter with a single 20 mHz ultrasound transducer oriented so that the ultrasound beam was aimed parallel to the long axis of the catheter. The ultrasound beam was reflected from a metal mirror so that the beam exited the catheter perpendicular to the long axis of the catheter. This design, which permitted imaging up to the surface of the catheter since the initial transducer oscillations occurred in the space between the transducer and the mirror, was developed by Intertherapy Inc, Costa Mesa, CA. The diameter of the catheter was 1.2 mm. In order to construct an image, the catheter was hand-rotated through 360 degrees inside an artery. During rotation the B mode ultrasound representation was painted as a circle on the screen using position information provided by an angular potentiometer attached to the proximal end of the catheter. The resulting image was a cross-section of the artery.

In the present study the catheter was mounted in a precision positioning device which was used during imaging, to control the height, angle, and rotation of the catheter. Artery segments were positioned vertically in a beaker filled with physiologic saline. Using the positioning device the catheter was advanced along the course of the artery. At each one millimeter increment the catheter was rotated 360 degrees to construct a separate cross-sectional image. Thus, a series of cross-sectional images along the course of the artery segment were obtained.

Fresh (less than 4 days old) refrigerated arterial segments from human coronary, carotid and femoral arteries were imaged at room temperature in a saline bath. Measurements were made of intimal, medial and total arterial wall thickness from ultrasound images in four orthogonal quadrants, and the corresponding quadrants from hematoxylin and eosin stained histologic sections of the same arteries. To facilitate measurement of the histology, all histologic specimens were photographed at known magnification such that the resultant photograph was similar in size to the ultrasound image. To maintain proper radial alignment of ultrasound and histologic images, the thickest part of the arterial wall from the ultrasound image was rotated to align with the thickest wall of the histology images. In the several cases where was fairly uniform arterial wall thickness an eccentric piece of calcium in the arterial wall was used to ensure proper radial alignment of images. Arterial specimens were imaged from one end to the other in 1 mm increments with the ultrasound device; histologic sections were likewise made in 1 mm increments from the specimen. Thus, a given ultrasound image corresponds within 0.5 mm to the

histologic section. In addition, internal markers, such as pieces of calcium, were used to check that ultrasound images and histologic sections were aligned. More than 100 arteries were imaged altogether.

3. OBSERVATIONS FROM NORMAL HUMAN ARTERIES

Normal human muscular arteries had a characteristic three layer appearance on intravascular ultrasound images (Figure 1). The muscular medial layer of the artery, the tunica media, was relatively echo-lucent, and provided a reference point in the arterial cross-section separating intima from adventitia. The intima was seen extending from the lumen-tissue interface to the echo-lucent media. This corresponds with the lumen surface to the internal elastic lamina on histology.

4. OBSERVATIONS FROM ATHEROSCLEROTIC HUMAN ARTERIES

Atherosclerotically diseased human arteries had walls which were variably thickened (Figure 2). Calcification of arteries was seen in most of the diseased specimens studied. Shadowing of the distal wall caused by the tremendous reflective capability of calcium, preventing insonation of tissue beyond the calcium, is the ultrasonic hallmark of calcification (Figure 3). When present, shadowing prevented wall thickness measurements in the region of the artery containing the calcium. Liquid necrotic regions within plaques ("lakes") were seen large echo-lucent regions surrounded by echogenic tissue on the ultrasound images (Figure 4).

By ultrasound intimal thickness varied from 0.5 mm to 2.3 mm. In regions of normal intimal thickness by histology, where the intima consists only of the endothelium, the ultrasound images show a band of echoes 0.5 mm thick. The correlation by linear regression of ultrasound imaging intimal thickness compared to direct measurement of intimal thickness using micro-calipers to measure the artery wall thickness from histologic sections was very good (R value = 0.91).

Of note, echo measurements appear to overestimate slightly intimal and total wall thickness.

5. IMAGING AFTER INTERVENTIONAL PROCEDURES

Arteries have been imaged before and after interventional cardiologic procedures in vitro. Laser ablation of intimal plaque was clearly seen on ultrasound images (Figure 5). Arteries imaged before and after balloon dilatation showed obvious lumen enlargement and intimal rupture (Figure 6). Atherectomy catheter removal of plaque was plainly visualized on the ultrasound images (Figure 7), where a single cut with a Simpson atherectomy catheter is shown.

6. CONCLUSIONS

The results of these studies support the hypothesis that intravascular imaging with ultrasound is an accurate and reproducible method for measuring arterial intimal thickness. In order to accomplish this measurement accurately, however, it is necessary to visualize clearly the medial layer of the artery. We observed during the course of these studies that the medial muscular layer of arteries could be differentiated from adjacent tissues by its relative echo lucency in 61% of specimens. This lucency has been attributed to the muscular layer having less collagen than the fibrous adventitia or the elastic and fibrous internal elastic lamina (Picano).

Several factors were identified during the study which limit the ability to measure the thickness of some of the artery layers. For example, the media was seen to thin noticeable or disappear on ultrasound images as it passed behind atheromata. This was especially noticeable behind moderate eccentric atheromas and might be caused by attenuation of the ultrasound signal passing through the thickest portion of the atheroma. An alternate and more likely be explanation is that there is actual thinning of the media behind thick, eccentric plaques. Support for this latter hypothesis is the observation that thinning of the media was seen on the histologic sections behind thick atheroma. In addition, the presence of extensive calcification prevents wall thickness measurements because of ultrasound shadowing.

It should be noted that the present study was limited to evaluating arteries in vitro at room temperature in saline in an apparatus with carefully controlled and restricted motion of the catheter. Imaging in pulsatile, mobile, living, blood-filled arteries provides several potential technical obstacles which may degrade image quality.

We conclude that intraarterial ultrasound imaging appears feasible and shows promise as a method for accurately measuring normal and diseased arterial plaque thickness, thereby allowing an assessment of the extent of atheromatous involvement of artery walls. Various histologic characteristics of diseased arteries can be identified. Ultrasound imaging also permits visualization of diseased arteries before and after vascular interventional procedures.

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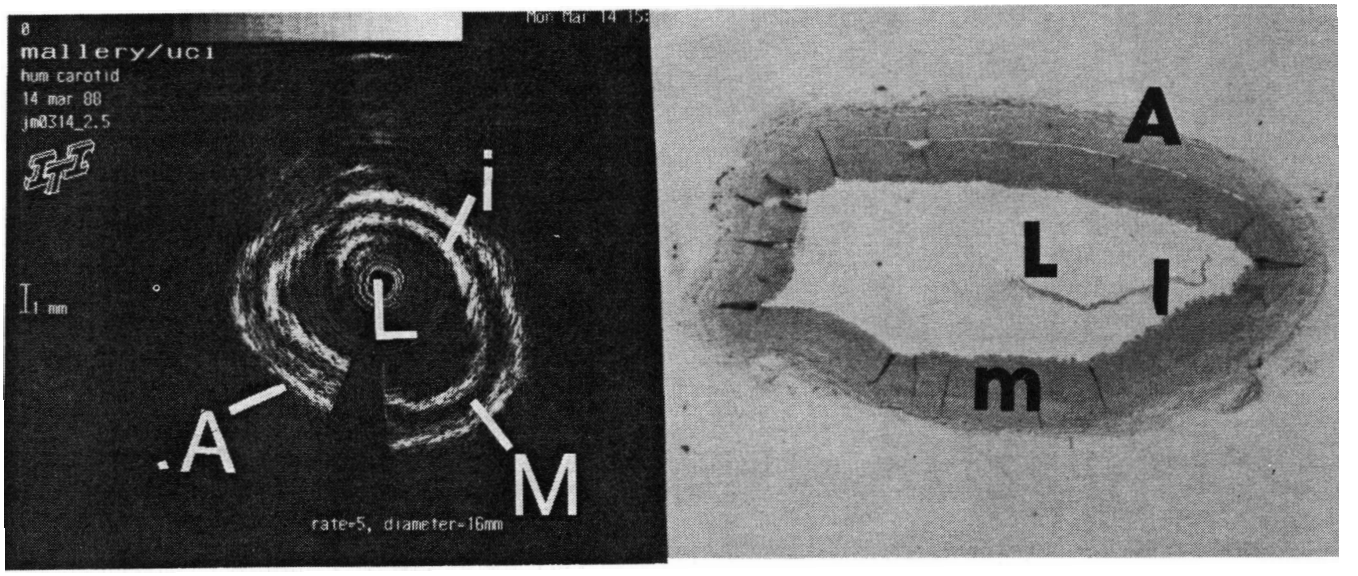

Figure 1. Ultrasound image (Left) and histology cross-section right showing intima (I), media (M), and adventitia (A) and lumen (L).

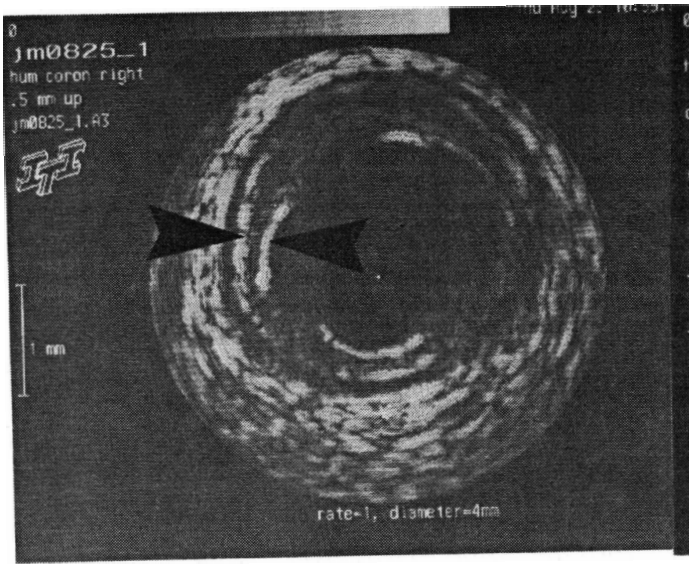

Figure 2. Intimal plaque is indicated by arrows.

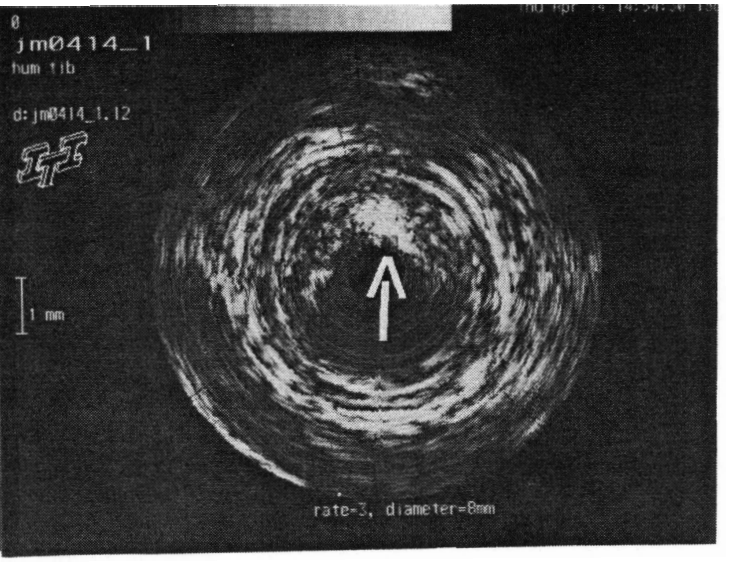

Figure 3. Bright reflection from calcium with peripheral shadowing (arrows).

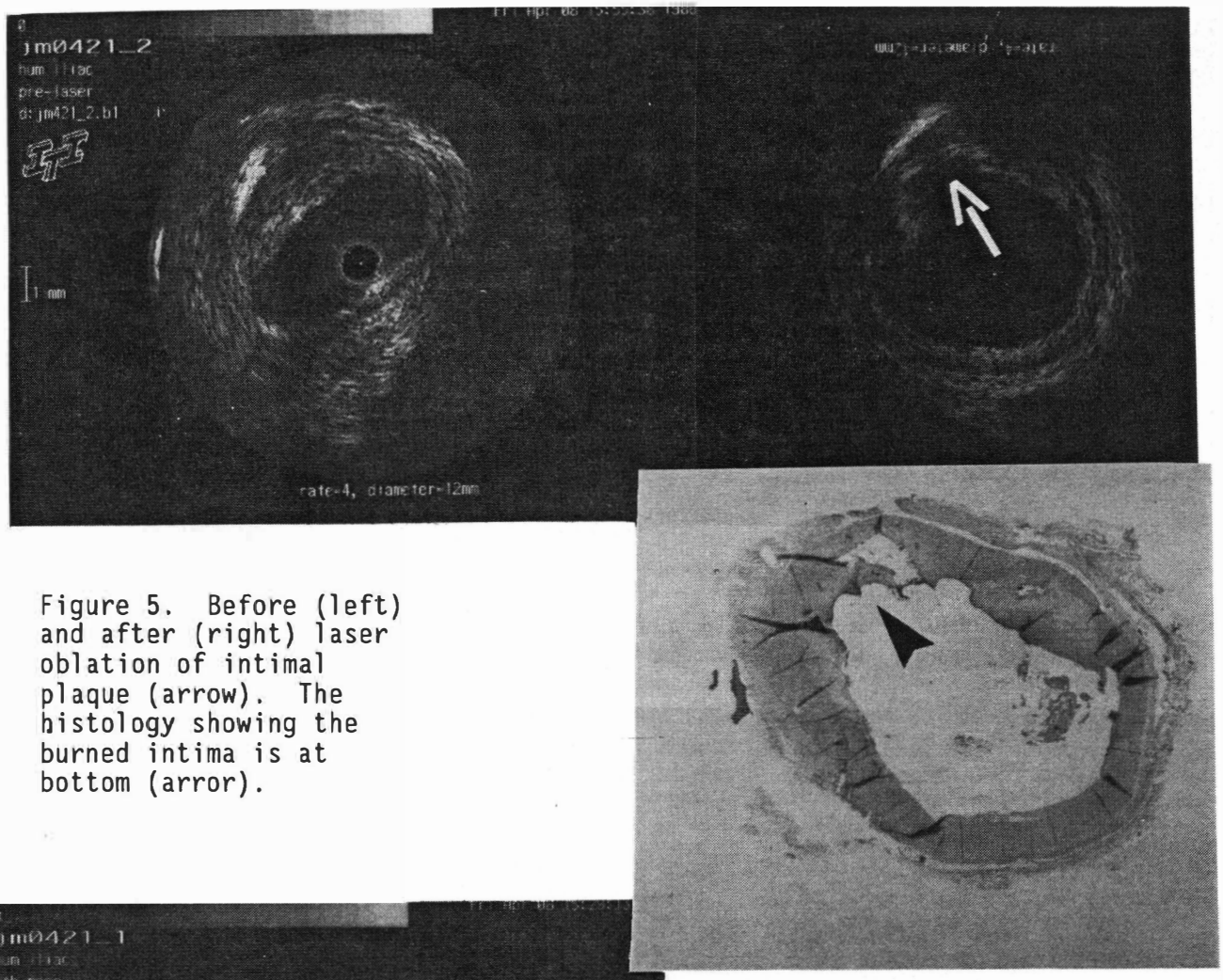

Figure 5. Before (left) and after (right) laser oblation of intimal plaque (arrow). The histology showing the burned intima is at bottom (arror).

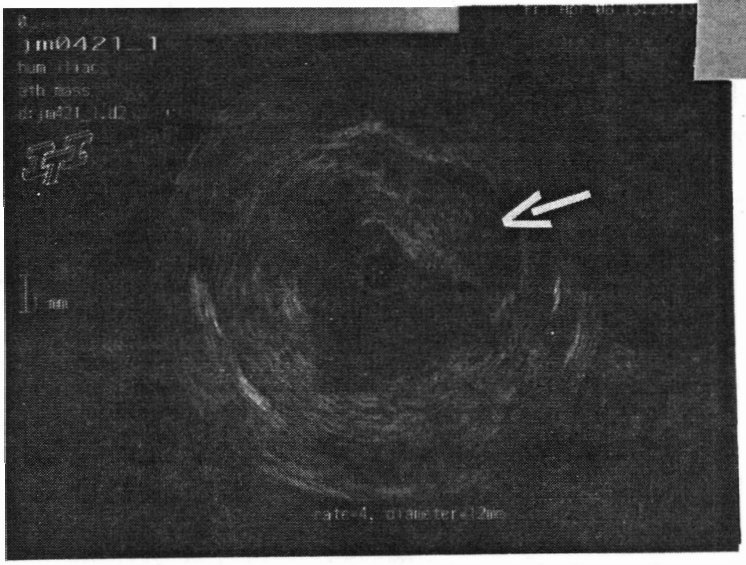

Figure 4. Arrow indicates echolucent zone which was filled with liquid material on gross examination.

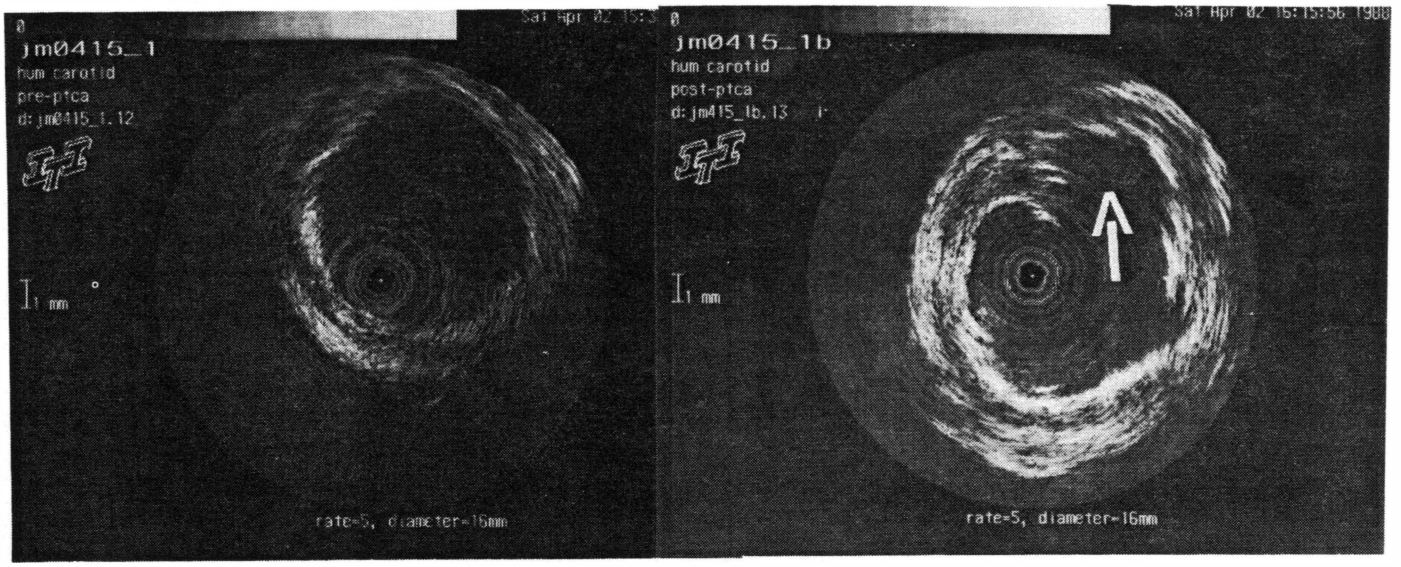

Figure 6. Before (left) and after (right) balloon dilatation of artery. Arrow indicates tear in intima.

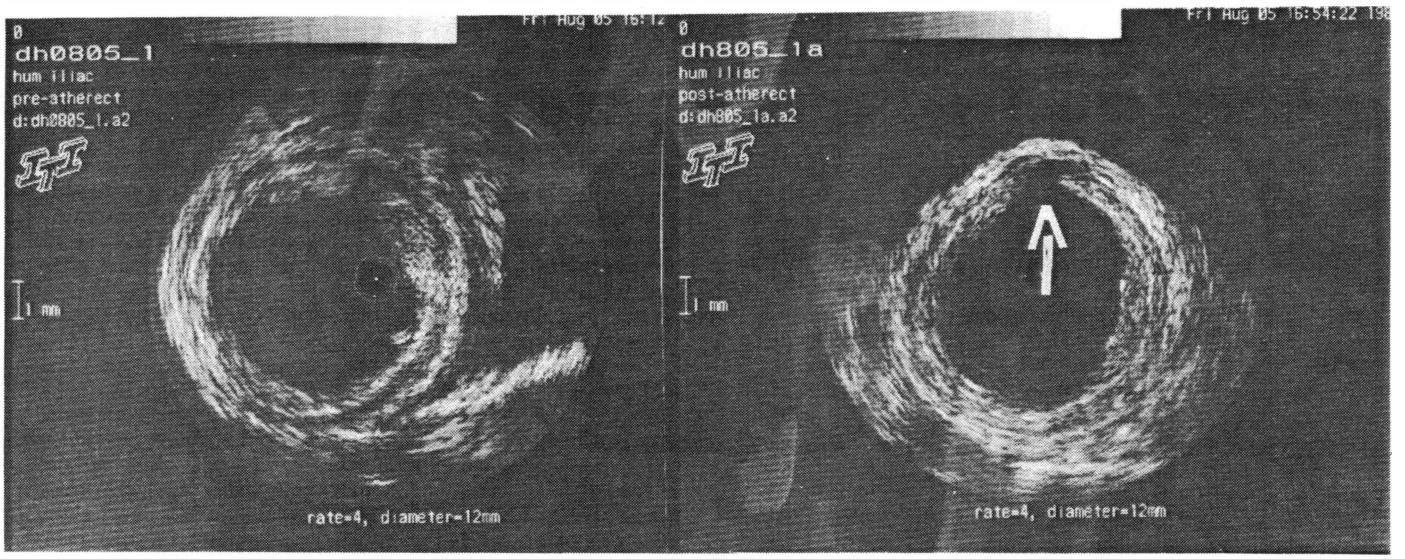

Figure 7. Before (left) and after (right) a single cut by an atherectomy catheter through the intima. The removed tissue is indicated by the arrow.