Assessment of Coronary Plaque With Optical Coherence Tomography and High-Frequency Ultrasound

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This study compares the ability of intravascular optical coherence tomography (OCT) and high-frequency intravascular ultrasound (IVUS) to image highly stenotic human coronary arteries in vitro. Current imaging modalities have insufficient resolution to perform risk stratification based on coronary plaque morphology. OCT is a new technology capable of imaging at a resolution of 5 to 20 μm, which has demonstrated the potential for coronary arterial imaging in prior experiments. Human postmortem coronary arteries with severely stenotic segments were imaged with catheter-based OCT and IVUS. The OCT system had an axial resolution of 20 μm and a transverse resolution of 30 μm. OCT was able to penetrate and image near-occlusive coronary plaques. Compared with IVUS, these OCT images demonstrated superior delineation of vessel layers and lack of ring-down artifact, leading to clearer visualization of the vessel plaque and intima. Histology confirmed the accuracy and high contrast of vessel layer boundaries seen on OCT images. Thus, catheter-based OCT systems are able to image near-occlusive coronary plaques with higher resolution than that of IVUS. ©2000 by Excerpta Medica, Inc.

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Optical coherence tomography (OCT) is a new modality for high-resolution, cross-sectional, intravascular imaging.[1] OCT is analogous to B-mode ultrasound but measures back-reflected infrared light instead of acoustical waves. The time for the light to be reflected back, or echo delay time, is used to measure distances. However, because the velocity of light is much greater than the velocity of sound, this time delay is too short to be measured electronically, as in ultrasound. Instead, OCT uses a technique known as low-coherence interferometry, which has previously been described in detail.[1,2] The greatest advantage of OCT is its resolution of 5 to 20 μm, at least an order of magnitude higher than that of high-frequency ultrasound. Already in clinical use for imaging the retina through the transparent structures of the eye,[3] OCT has recently been applied to the more challenging problem of imaging nontransparent tissues.[2,4–8] The present study achieves 2 objectives. First, a direct comparison is made between a catheter-based OCT imaging system and a state-of-the-art intravascular ultrasound (IVUS) system. Second, the study addresses whether OCT has sufficient penetration to image through severely stenotic coronary arteries.

METHODS

Human coronary arteries were obtained within 6 hours of postmortem examination. The sample was stored at 0°C in isotonic saline with 0.1% sodium azide before imaging, and immersed in a saline bath during the process of imaging with IVUS and OCT. After imaging, the artery was fixed, decalcified, sectioned, and stained with hematoxylin and eosin for routine light microscopic examination. Tissue registration was achieved through the combination of sutures, placed in the vessel as markers during pullback, and a visible light-guiding beam that allowed OCT imaged sites to be marked externally with microapplication of dye.

IVUS imaging was performed by an experienced and blinded operator with a 2.9Fr, 30-MHz ultrasound catheter (Microview, CVIS/SciMed, Sunnyvale, California) using the CVIS/SciMed platform. The images were obtained during an automated pullback of the imaging catheter at a rate of 0.5 mm/s after optimization of gain and contrast settings and recorded on videotape (super VHS format).

OCT imaging of the in vitro arteries was performed with a catheter-based system. The OCT system used in this experiment performed imaging with near-infrared light, which had a median wavelength of 1,310 nm and produced an axial resolution of 20 μm. The confocal parameter, or the optics of the catheter, determines the transverse resolution, which is 30 μm at the focal point. The axial resolution has been experimen-

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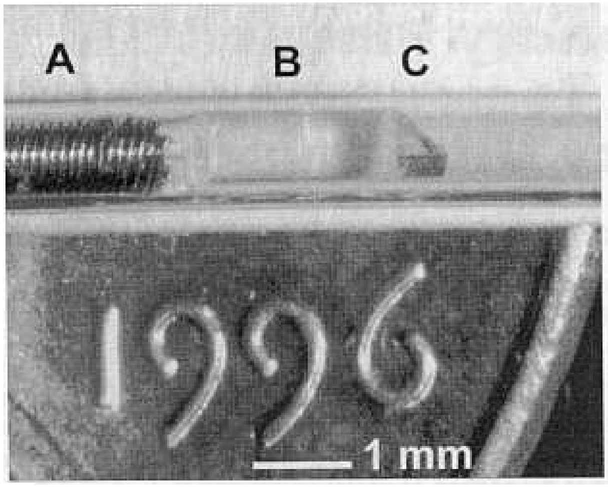

FIGURE 1. A photograph of the OCT catheter. The OCT catheter, shown with a penny and scale bar for comparison, is 1 mm in diameter. The catheter sheath remains stationary while a cable *(A)* rotates an optical fiber that transmits the OCT signal. A rectangular prism *(B)* focuses the light, and the triangular mirror *(C)* reflects the light radially.

tally verified by measuring the reflection from a mirror of the OCT signal (point-spread function).[7] The OCT imaging catheter, shown in Figure 1, is 1 mm in diameter. Inside a stationary sheath, a rotating lens directs light radially to produce a cross-sectional image of the artery. The images were oversampled at a rate of 300 pixels over a 3-mm radial depth for each of 600 radial scans over the circumference of the vessel. At this image size, each cross-sectional image was acquired in approximately 80 seconds. To produce a sequence of OCT images over the entire length of the artery, pullback of the catheter was performed to acquire cross-sectional images at 250-μm intervals.

RESULTS

Consistent with previous work,[2] OCT images of plaque correlate with histopathology (Figure 2). Most significantly, OCT images demonstrate relatively good contrast among the layers of the vessel wall. This allows clear delineation of the tunica intima and tunica media. Histology confirms the presence and morphology of the intimal hyperplasia seen in OCT images of this vessel.

Cross-sectional, catheter-based OCT and ultrasound images from selected sites of an in vitro human coronary artery are shown in Figure 3. OCT images demonstrate superior resolution compared with corresponding high-frequency ultrasound images. In addition to better delineation of the tunicae intima and media, the ability of OCT to demonstrate plaque morphology was particularly noteworthy. In these severely stenotic plaques, imaging was achieved with OCT through the plaque and media to the early adventitia. As expected, IVUS consistently imaged deeper into the adventitia than OCT. However, the IVUS image does not penetrate the plaque any deeper than the OCT image, probably due to the inability of acoustical energy to penetrate calcified tissue. The ability of OCT to penetrate calcified samples has been previously noted.[2] Futhermore, in IVUS images a "ring-down" artifact appears, obscuring portions of the image near the transducer. In OCT images, no ring-down effect was noted, although rings did occur in the image due to internal reflections within the catheter.

DISCUSSION

The greatest advantage of OCT as an imaging modality is its resolution. In this work, OCT demonstrated qualitatively superior delineation of plaque morphology when compared with IVUS, a result that is consistent with the higher resolution of OCT as determined by the point-spread function.[7] The resolution of the current OCT system was 20 μm compared with 110 μm for a 30-MHz IVUS. Should IVUS systems become available at 50 MHz, the maximum resolution would still be no greater than 70 μm.[9] The maximum resolution of OCT appears limited physically only by the diffraction limit of light at 1,300 nm, which is $<$100 nm.[10] OCT systems are already in use with axial resolutions $<$4 μm. These systems may ultimately be of use in cardiology for the identification of subcellular structures.[11] However, to perform imaging at this resolution through a catheter-based approach, a more complex catheter design would be required to compensate for the relatively short confocal parameter.

Additional advantages of OCT are the small, low-cost catheters and the lack of a ring-down effect. Unlike an ultrasound catheter, OCT catheters contain no transducers within their body. They consist of simple light-directing devices (optical fiber, lens, prism, and so forth), making them relatively inexpensive. The ring-down effect in ultrasound systems is well documented as a cause of artifacts in ultrasound images.[12] It results from the finite time required for the transducer to alternate between its signal generation and reception functions. This does not occur with OCT because the source and detector are separate elements. The OCT images in this study do demonstrate an artifact consisting of a series of rings. However, this artifact is distinct from the ring-down effect in that it is caused by refractive index mismatches between components of the catheter, and results in a series of sharp lines that do not obscure the image. This artifact will likely be dramatically reduced with future embodiments as index-matching among catheter components is refined.

Future work will focus on reducing catheter size and increasing frame rates. The size of the current 2.9Fr prototype was limited to the radius of a speedometer cable, with the optical fiber itself having a diameter of only 124 μm. It is anticipated that future catheters will have a substantially smaller cross-sectional diameter through the use of smaller mechanical components. The frame rate is primarily determined by how quickly the path length can be changed in the reference arm. The acquisition rate in this study was approximately 80 s/image, which is not sufficient for use in the vascular system. However, clincally rele-

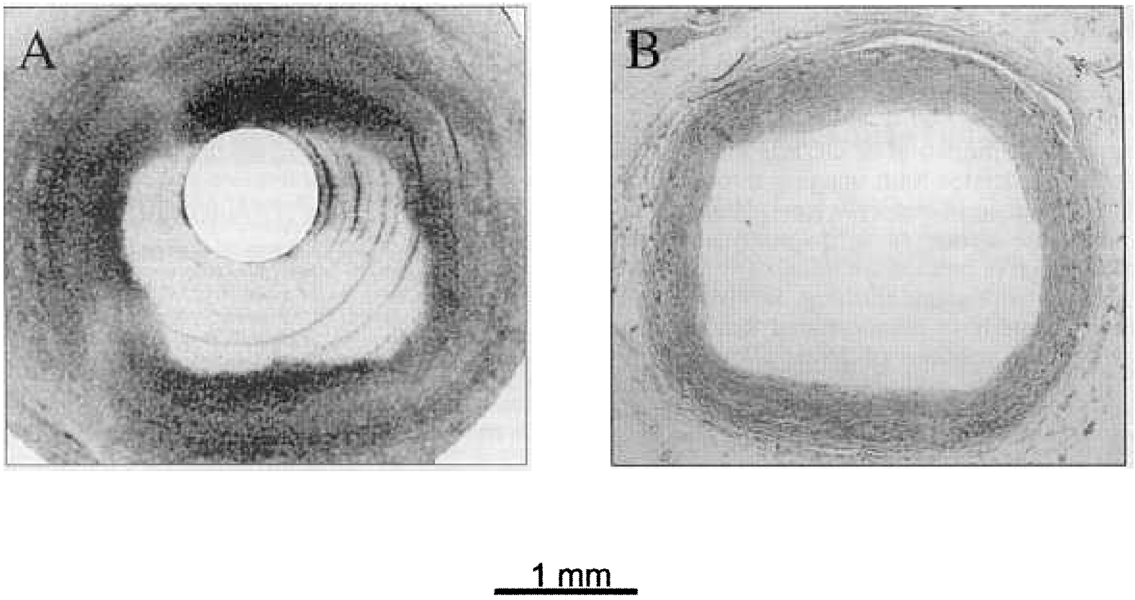

FIGURE 2. A comparison of OCT and histology of a human coronary artery. The OCT image *(A)* is notable for its clear delineation of the tunicae intima, media, and adventitia. Hematoxylin-eosin–stained sections of the artery *(B)* verify the intimal hyperplasia and the resolution of the vessel layers seen on the OCT image.

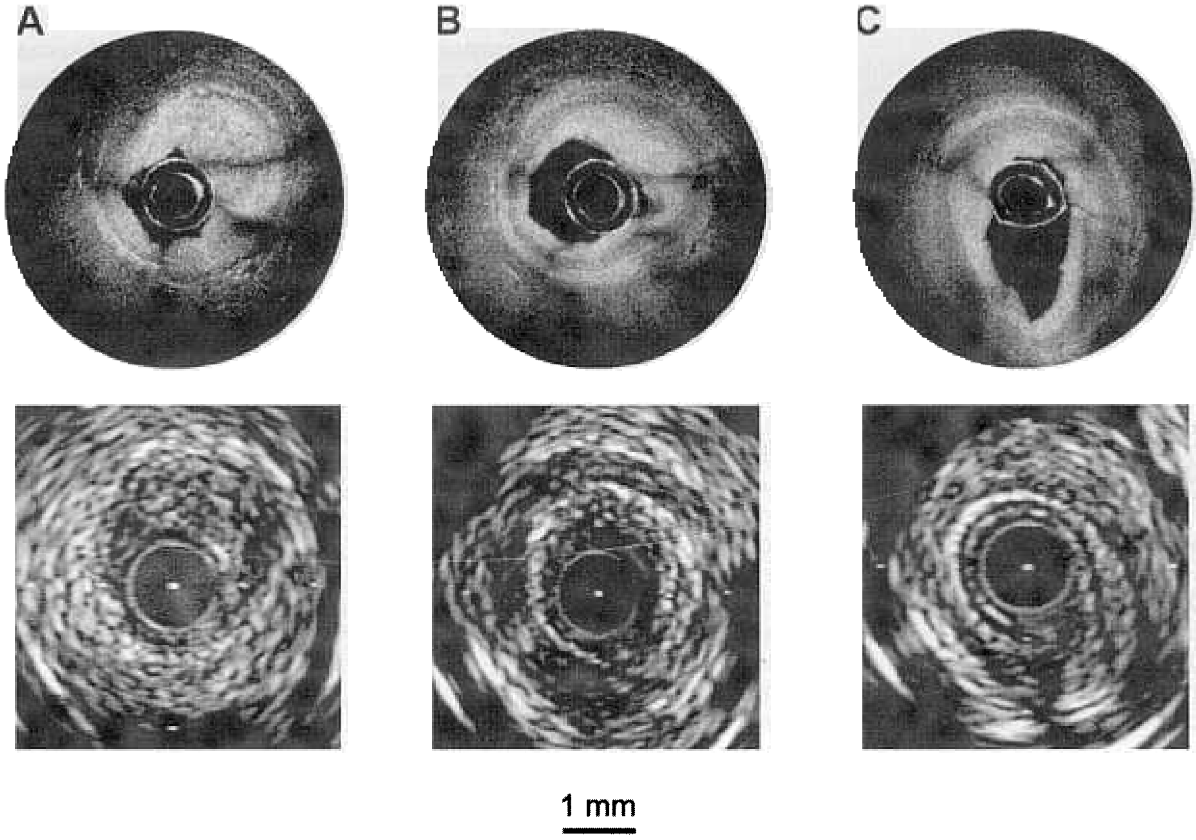

FIGURE 3. Comparison of OCT with high-frequency ultrasound in a human postmortem coronary artery. The OCT images have been inverted for comparison with ultrasound images. The proximal end of the artery *(A)* contains a near-occlusive plaque. Note that OCT is able to image through the full thickness of the plaque. An OCT image from more distal in the vessel *(B)* demonstrates high-resolution delineation of all the layers of the vessel wall. Distal to the stenotic area *(C)*, an OCT image unambiguously identifies the vessel lumen, whereas ring-down artifact obscures the lumen in the corresponding IVUS image.

vant OCT systems with acquisition rates as high as 4 frames/s have been used for in vivo imaging.[8,13] Furthermore, acquisition at a video rate (30 frames/s) is anticipated with future advances in reference arm technology.

The greatest limitation of OCT is the reduced effectiveness associated with imaging through blood.[13] The large number of red cells per volume of blood leads to a large amount of light scattering. Currently, the most effective method for addressing this issue is bulk removal with saline flushing. In vivo, intra-arterial experiments have demonstrated that injection of relatively small volumes of saline allow unimpeded OCT imaging.[13] In addition, it may be possible to improve OCT imaging through blood by index-matching for the red blood cells, thereby reducing light scattering (M.E. Brezinski, unpublished data). If saline injection is ultimately required for in vivo use, clinicians will need to balance the information gained from increased resolution against the increase in procedure time in evaluating the effectiveness of OCT.

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