ORIGINAL ARTICLE

High-Resolution Imaging of the Middle Ear With Optical Coherence Tomography

A Feasibility Study

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Background: Optical coherence tomography (OCT) is a new medical imaging technology that generates cross-sectional images of tissue microstructure with micron-scale resolution. Optical coherence tomography is analogous to ultrasound, measuring the intensity of infrared light rather than acoustical waves.

Objective: To demonstrate the feasibility of using OCT for ultra–high-resolution imaging of the middle ear via ex vivo imaging studies of human tissue.

Design: Images of the tympanic membrane and middle ear were acquired ex vivo, through the ear canal, without perforating the tympanic membrane.

Materials: Four excised intact temporal bones and the auditory apparatus were harvested from cadavers and imaged fresh, without previous fixation.

Results: The resulting images were compared with the gross sample and verified the ability of OCT to delineate relevant structures, such as the tympanic membrane and its sublayers, and the middle ear ossicles, nerves, and tendons at higher resolutions than possible with standard clinical imaging technologies.

Conclusion: The ability of OCT to produce high-resolution images of tissue structure, without contact and in real time, as well as its ability to be integrated with endoscopes, suggests that this technology could become a useful modality for the diagnosis and management of a range of clinical middle ear abnormalities.

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MIDDLE EAR surgery is now performed routinely for conditions varying from congenital abnormalities to trauma and tumors.[1] Significant anatomical variation between patients sometimes necessitates presurgical evaluation of the site of intervention.[2] Several imaging techniques are used to make middle ear surgery safer and more effective. Computed tomography and magnetic resonance imaging, despite their increased acceptance in neurosurgery and their valuable contribution to preoperative assessment, are not suitable for real-time guidance of surgical interventions in the head and neck.[3] Endoscopy, either transmeatic or transtubal, has also been applied in middle ear surgery; however, endoscopes are restricted to imaging the surfaces of tissues.[4-6] A technique that could perform real-time cross-sectional imaging to delineate tissue disease with micron-scale resolution would be a powerful tool in the diagnosis of disease. Optical coherence tomography (OCT) is an emerging imaging technology currently under development that enables noncontact, noninvasive, real-time, cross-sectional imaging of microstructure.[7]

Optical coherence tomography was first applied to image optically transparent structures such as the anterior eye and retina.[8,9] Results of preliminary clinical investigations suggest that OCT is a promising technology for the detection and management of a variety of retinal diseases, including glaucoma and macular edema.[10] Recent advances have enabled the application of OCT to nontransparent tissue.[11-13] Although the imaging depth of OCT is limited by the light scattering and attenuation properties of tissue, image penetrations of 2 to 3 mm can be achieved in most tissues. The resolution of OCT is 1 to 15 µm, up to 2 orders of magnitude higher than conventional ultrasound. Because imaging is being performed near the resolution of histology, over the distance scales of a conventional biopsy, OCT can function as a type of "optical biopsy." Pre-

MATERIALS AND METHODS

Optical coherence tomography is analogous to ultrasound imaging but is based on the detection of infrared light waves that are backscattered or reflected from different layers and structures within the tissue. Unlike sound waves, the speed of light is very high, rendering direct electronic measurement of the echo delay of the reflected light (time for the signal to return) impossible. Measurements can be performed using an interferometric correlation technique known as low-coherence interferometry. In an interferometer, a light beam from an optical light source is split into 2 parts, a reference beam and a sample beam. The reference beam is reflected off a mirror at a known distance and returns to the detector. The sample beam reflects off different layers within the tissue, and light returning from the sample and reference arms recombines. If the 2 light beams travel the same distances (optical path length) to within the coherence length of the light, the 2 beams will interfere. If the path lengths are mismatched, there is no interference. Optical coherence tomography measures the intensity of interference of light backscattered or reflected from different points within the tissue by moving the mirror in the reference arm, which changes the distance that light travels in the reference arm. In **Figure 1**B-C, light from a coherent vs a low-coherent light source are shown, illustrating how low-coherence light can be used to localize backreflection sites and provide the desired high resolution. Two- or 3-dimensional images are produced by scanning the optical beam across the sample and recording the optical backscattering vs depth at different transverse positions. The resulting image is a 2- or 3-dimensional representation of the optical backscattering of the sample on a micron scale. The logarithm of the backscattering signal is represented as a false color or gray-scale image. A schematic of the complete OCT system is shown in **Figure 2**.

The depth resolution in OCT is defined by the property referred to as the coherence length of the light source. A mathematical description yields:

$$\Delta z = \frac{2\ 1n(2)}{\pi}\ \frac{\lambda^2}{\Delta\lambda} \quad (1)$$

where Δz is the resolution, λ is the wavelength, and $\Delta\lambda$ is the bandwidth, ie, the wavelength range, of the light source.[21] Image depth resolution is inversely proportional to the bandwidth of the light source. The experiments reported herein were performed using a superluminescent source operating at a wavelength of 1310 nm, with a bandwidth, $\Delta\lambda$, of 50 nm. The 1310-nm wavelength in the near infrared has reduced optical scattering and tissue absorption and thus allows deeper imaging in scattering tissues. The bandwidth of the light source yields a 15-µm depth resolution.

Transverse resolution, perpendicular to the depth dimension, is defined by the smallest focused spot size that the optics can produce on the specimen, similar to microscopy. Transverse resolution trades off with the confocal variable, ie, depth of focus. Transverse resolution is determined by the following relationship:

$$\Delta x = \sqrt{\frac{2b\lambda}{\pi}} \quad (2)$$

where b is the confocal variable and λ is the wavelength of the source.[22] The combination of optics and focusing conditions used for the experiments reported herein resulted in a 10- to 20-µm transverse resolution. The penetration is approximately 2 to 3 mm in scattering tissue and is limited by light scattering and attenuation.[23]

In addition to its high resolution, several features of OCT suggest it will be a powerful imaging technology for the diagnosis of a wide range of pathological conditions. First, unlike ultrasound, OCT does not require a transducing medium, and imaging can be performed directly through air. Second, unlike computed tomography or magnetic resonance imaging, OCT can be performed in or near real time, allowing information on tissue microstructure to be obtained within the dynamic environment of an endoscopy or surgical suite. Third, OCT is compact and portable, an important consideration for a clinically viable device. Finally, OCT is fiber optic based, allowing relatively easy integration with bronchoscopes and endoscopes without significant changes in device diameter.

Samples for this study were obtained from cadavers and were imaged fresh without previous fixation. This avoided changes in optical properties associated with fixation. The specimens were placed in a Petri dish and irrigated with isotonic saline solution to prevent dehydration during imaging. The OCT probe was 15 mm from the tympanic membrane (TM), a working distance that can be adjusted according to the imaging optics used. The acquisition of each image required between 10 and 30 seconds depending on the size (number of pixel elements) of the image. Because the OCT beam is invisible, tissue registration was performed with a visible light guiding beam. The samples were then dissected, and the TM was removed to reveal the underlying structures. Microscopic examination of the samples enabled verification of tissue identity and in most instances allowed identification of sources of tissue contrast in the OCT images.

vious studies[13-18] with OCT have included identification of abnormalities in the cardiovascular system and the gastrointestinal, urinary, and reproductive tracts, in addition to studies of neural tissue and cartilage. A small catheter-endoscope system also has been developed that allowed high-resolution imaging to be performed internally in a rabbit model.[19,20]

This study demonstrates the feasibility of using OCT for ultra–high-resolution imaging of the middle ear in ex vivo studies of human tissue. Images were obtained that demonstrated the ability of OCT to image microstructural features and demarcate tissue layers and bony structures. Microstructure was compared with gross appearance to confirm the image interpretation and verified the ability of OCT to delineate features that could be used in the diagnosis of disease or as anatomical markers. The ability of OCT to generate 3-dimensional images with resolution in the range close to that of histopathological examination in real time supports the hypothesis that this optical technology will become a powerful modality for

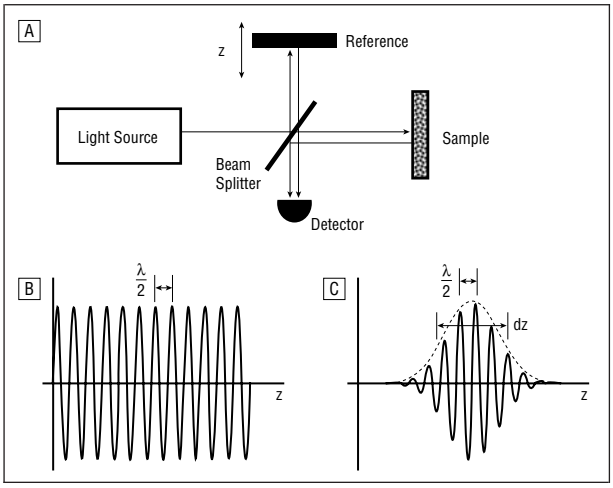

Figure 1. *Low-coherence interferometry principles. Basic Michelson interferometer (A) and interference patterns, resulting from the reference arm mirror movement, using a coherent (B) and low-coherent (C) source. This technique measures the echo delay (time for a reflected light beam to return) to yield the optical backscattering in the specimen vs depth. z indicates location of the reference mirror; dz, depth resolution.*

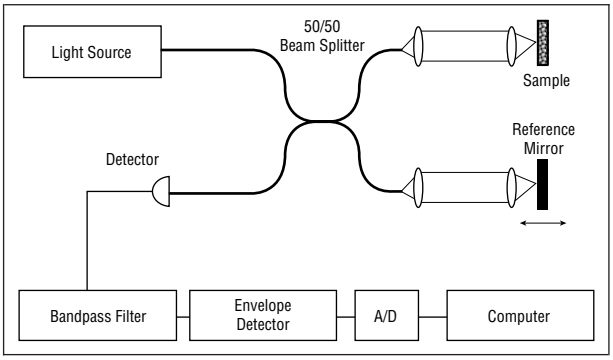

Figure 2. *Schematic of the fiber optic implementation of the optical coherence tomography system. Optical coherence tomographic images are generated by performing successive measurements of optical backscattering vs depth at different transverse positions on the specimen. A/D indicates analog-to-digital conversion circuitry.*

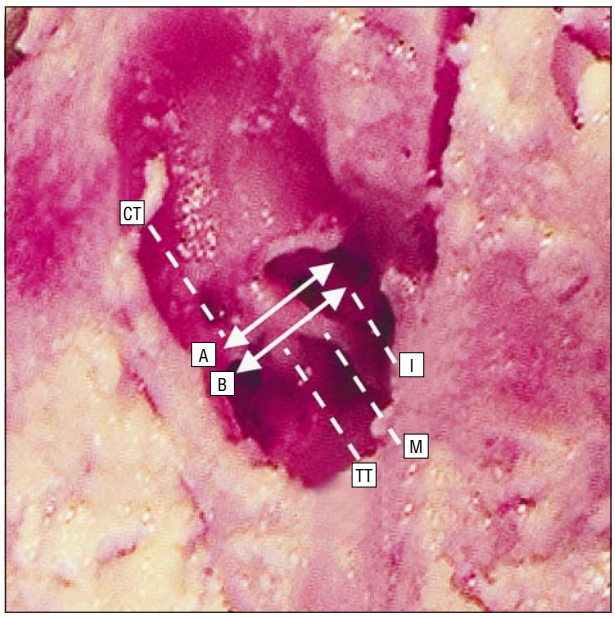

Figure 3. *Typical specimen with the tympanic membrane dissected after optical coherence tomographic imaging to expose the structures of the middle ear. M indicates manubrium of malleus; I, long process of incus; CT, chorda tympani nerve; TT, tendon of tensor tympani muscle; and solid lines A and B, imaging planes of the images in Figure 4.*

the diagnosis and monitoring of conditions of the middle ear.

RESULTS

Multiple transverse OCT images were acquired through the intact TM over a 5×5-mm area spaced 40 µm apart. **Figure 3** shows a typical specimen with the TM dissected after OCT imaging. Images were displayed on a logarithmic intensity scale, with the least backscattered areas shown in white and the most backscattered areas shown in black.

Ex vivo OCT images of the human middle ear taken through the auditory canal as consecutive cross sections perpendicular to the malleus, from the neck to the manubrium, are shown in **Figure 4**. The TM can be identified, and the layered nature of that tissue is also evident. Also visible are the manubrium of malleus, the long process of incus, the chorda tympani nerve, and the tendon of the tensor tympani muscle.

Volume reconstruction of a data set of ex vivo OCT images of the human middle ear is shown in **Figure 5**. The set consisted of 142 images spanning a total volume of 5×5×5 mm. The data were then rendered using simple projection algorithms included in an image processing package (NIH Image; National Institutes of Health, Bethesda, Md). The 3-dimensional nature of the structures identified in Figure 4 is visible from different viewing angles. False color was used to highlight different structures for clarity.

COMMENT

This work demonstrates the feasibility of OCT for cross-sectional and 3-dimensional imaging of middle ear structures without the need to perforate the TM. Images correlated well with gross anatomy. The primary focus of this study was to demonstrate the feasibility of OCT imaging of normal tissue. Additional studies will be required to examine the ability to assess different abnormalities and pathological conditions in vitro and in vivo.

The advantage of OCT is that cross-sectional imaging of structures in the middle ear can be performed noninvasively through the intact TM. However, because the TM is not optically transparent, the image quality is less than if the structures were directly optically accessible by myringotomy. Transverse resolution degrades when structures are imaged behind the TM because of optical scattering and aberration effects. There is a decrease in signal for structures imaged behind the TM because of optical scattering. Attenuation of the optical signal limits the depth of penetration of imaging in most solid tissues to 1 to 2 mm. These effects are observed in the OCT images shown in Figure 4. Increased scattering in superficial structures can also prevent light from reaching lower structures, resulting in "shadowing," similar to that observed in ultrasound imaging. Shadowing artifacts are ob-

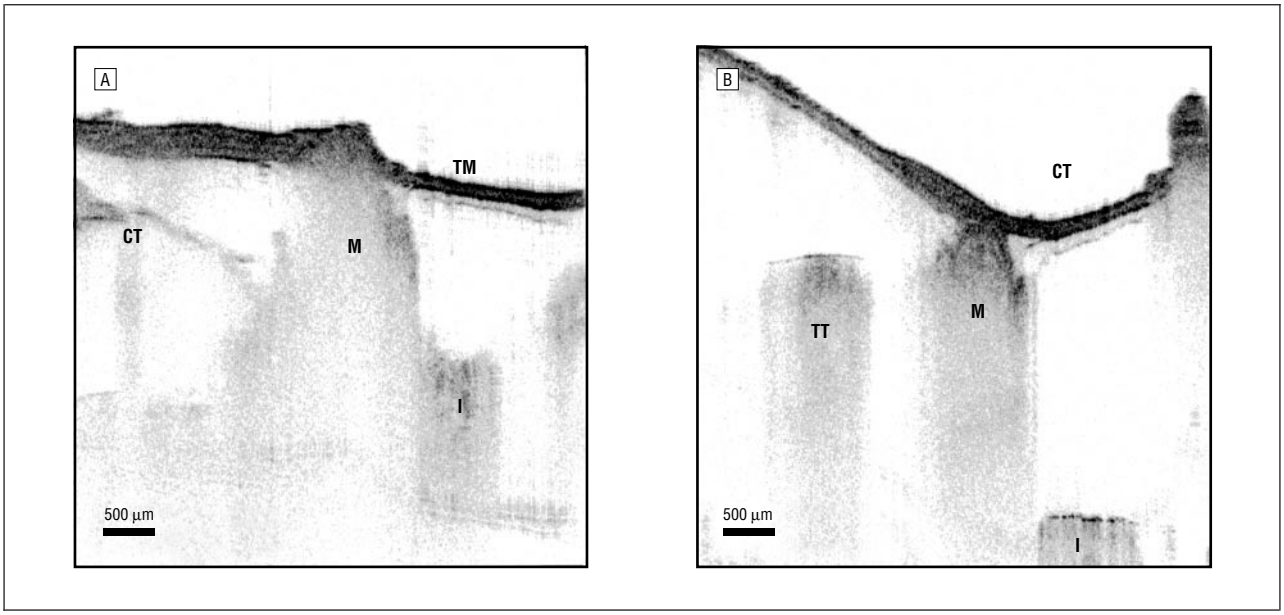

Figure 4. *Ex vivo optical coherence tomographic images of the human middle ear taken through the auditory canal at successive distances from the head of the malleus. The tympanic membrane (TM) can be identified, and the layered nature of that tissue is also evident. Also visible are the manubrium of the malleus (M), the long process of incus (I), the chorda tympani nerve (CT), and the tendon of the tensor tympani muscle (TT) (image size, 5× 5 mm; resolution, 15 µm).*

served in Figure 4 behind dense structures such as the malleus and incus. Finally, there are also depth of field limitations for imaging structures outside the focal plane of the image. Increased depth of field can be achieved by scanning the focus of the lens similar to C-mode scanning in ultrasound.

Improvements in the delivery optics, acquisition rates, and resolution are also necessary to transform the current OCT system into a viable clinical apparatus. Although a bench-top OCT microscope system was used for this study, a variety of other clinical imaging devices have been developed. Optical coherence tomography also has been effectively integrated with an ophthalmologic slitlamp for retinal imaging.[8] Handheld imaging probes have been developed and demonstrated in open-field surgical imaging.[24] These devices are based on the necessary focusing optical elements and galvanometers, which can scan the beam in any direction. Optical coherence tomography delivery optics can be further miniaturized and also integrated with standard otoscopes. An OCT otoscope would allow simultaneous viewing of the ear canal and OCT imaging through the TM at any area within the otoscope's field of view. With such devices, the OCT beam can be delivered to the target tissues in a variety of settings and imaging can be performed through the ear canal or via endoscopic access to the middle and inner ear.

The acquisition rate for images in this study ranged from 10 to 30 seconds per image. This is too slow to prevent motion artifacts in clinical imaging. Recently, OCT systems have been developed that can generate images of 500 to 250 transverse pixels at 4 to 8 frames per second.[20] These high-speed systems have enabled in vivo imaging to be performed in animal models. Image speeds up to video rates are possible; however, there is a signal-to-noise trade-off because signal levels decrease in proportion to imaging speed. Signal can be increased by increasing the incident optical power; however, permissible light exposure levels will ultimately govern the maximum imaging speed and image penetration.

The 15-µm resolution of images used in this study allows imaging of tissue architecture but does not allow cellular-level imaging to be performed. The ability to identify cellular structures would be useful in the assessment of a wide range of disorders. Recently, ultra–high-resolution OCT has been demonstrated using a solid-state laser light source that achieves resolutions on the order of approximately 1 µm.[25] Although these sources are relatively complex and not yet viable for a clinical instrument, robust sources with similar performance characteristics will likely be available in the near future. Therefore, higher-resolution in vivo imaging should be possible in future clinical OCT systems.

The ability of OCT to perform noninvasive imaging of middle ear structures suggests many applications in the diagnosis and presurgical evaluation of middle ear abnormalities. Cross-sectional images and 3-dimensional reconstructures of middle ear structure can be performed. This study focused on imaging through the intact TM to demonstrate feasbility for noninvasive imaging. Imaging with OCT can be performed in bone with depths of up to 2 to 3 mm.[18] If direct optical access to middle ear structures is possible, imaging of cochlear structures might be possible. Optical coherence tomography also has been applied for imaging nerve fascicle structure,[15] and it might be used for guiding surgical interventions involving the seventh and eighth nerve bundles. The image resolution of OCT is higher than that of other standard clinical imaging techniques. In addition, OCT imaging can be performed noninvasively, without contact, and without the need for a transducing medium as in ultrasound. These features, combined with its ease of integration with optical instruments and low cost, suggest that OCT might be a useful technology for diagnostic imaging and surgical guidance in the middle ear.

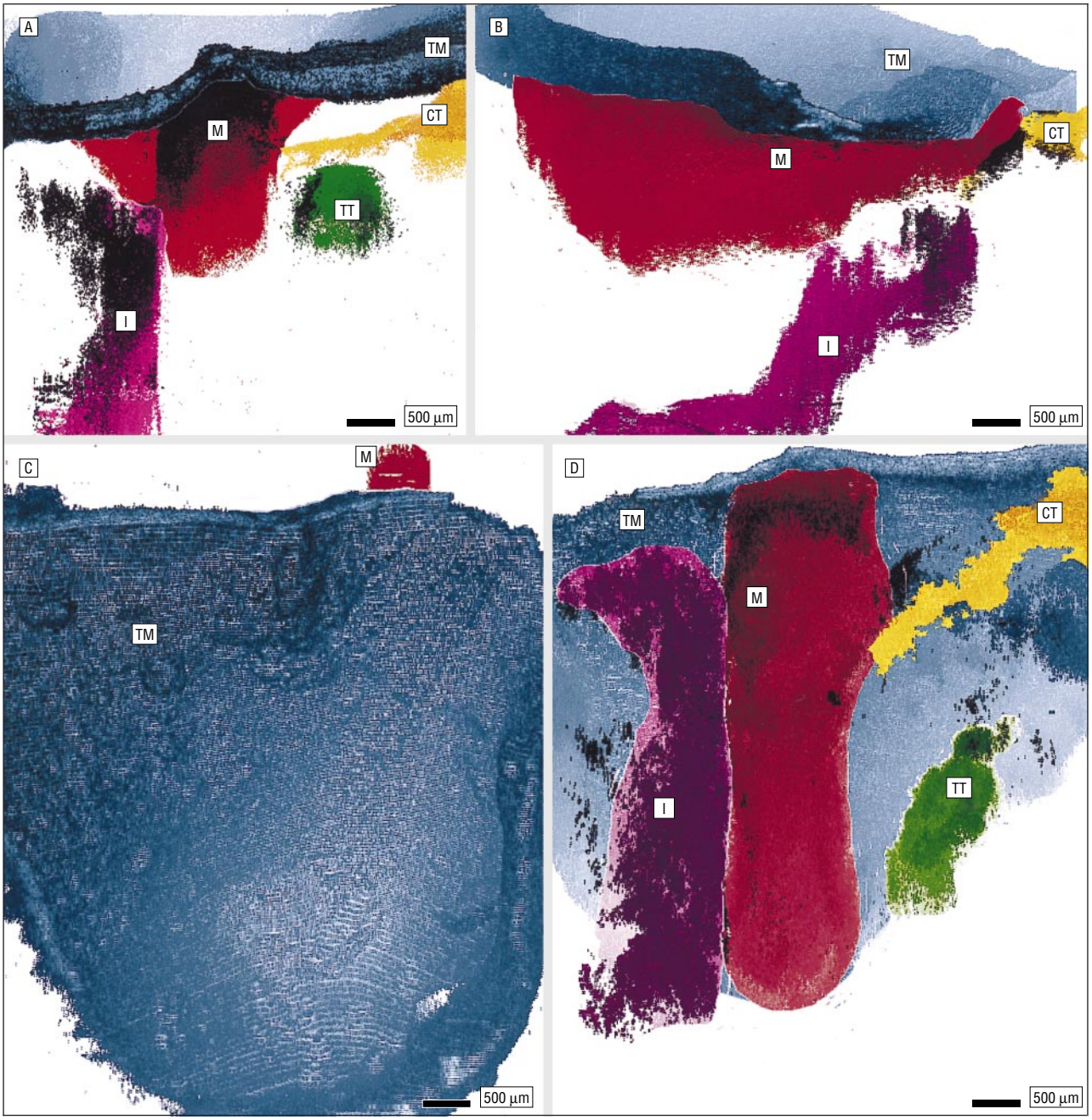

Figure 5. *Volume reconstruction of a data set of ex vivo optical coherence tomographic images of the human middle ear. The 3-dimensional nature of the structures identified in Figure 4 are visible from different view angles: superior (A), coronal (B), lateral (C), and medial (D). The tympanic membrane (TM), the manubrium of the malleus (M), the long process of incus (I), the chorda tympani nerve (CT), and the tendon of the tensor tympani muscle (TT) can be identified (volume size, 5× 5× 5 mm; 142 cross-sectional images; resolution, 15 µm).*

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