Optical coherence tomography: current and future clinical applications in otology

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Purpose of review

This article reviews literature on the use of optical coherence tomography (OCT) in otology and provides the reader with a timely update on its current clinical and research applications. The discussion focuses on the principles of OCT, the use of the technology for the diagnosis of middle ear disease and for the delineation of in-vivo cochlear microarchitecture and function.

Recent findings

Recent advances in OCT include the measurement of structural and vibratory properties of the tympanic membrane, ossicles and inner ear in healthy and diseased states. Accurate, noninvasive diagnosis of middle ear disease, such as otosclerosis and acute otitis media using OCT, has been validated in clinical studies, whereas inner ear OCT imaging remains at the preclinical stage. The development of recent microscopic, otoscopic and endoscopic systems to address clinical and research problems is reviewed.

Summary

OCT is a real-time, noninvasive, nonionizing, point-of-care imaging modality capable of imaging ear structures *in vivo*. Although current clinical systems are mainly focused on middle ear imaging, OCT has also been shown to have the ability to identify inner ear disease, an exciting possibility that will become increasingly relevant with the advent of targeted inner ear therapies.

Keywords

diagnostic imaging, ear inner, ear middle, optical coherence, otology, tomography

INTRODUCTION

Optical coherence tomography (OCT) is an imaging modality that uses the reflection and scattering of light by biological tissue to generate high-resolution ($\leq$15 μm) in-vivo images. OCT was initially described in 1991 as a novel method in the imaging of the retina and coronary arteries [1]. Subsequently, OCT has become standard of care in the management of arterial plaques and disease of the eye, particularly macular degeneration and other diseases of the retina [2–4]. Further technological advances have seen OCT applied across diverse fields of medicine, including dermatology, dentistry, gastroenterology and otolaryngology [4–8]. In 2001, a study on cadaveric temporal bones was the first to demonstrate the feasibility of OCT for noninvasively visualizing clinically important middle ear structures by generating 15 μm resolution images through an intact tympanic membrane [9]. OCT systems have since been integrated into a variety of devices to allow real-time otologic examination of patients and specimens. OCT has been incorporated into microscopes, otoscopes, rigid endoscopes and flexible endoscopes/fibers [10,11,12▪▪,13▪▪].

PRINCIPLES OF OPTICAL COHERENCE TOMOGRAPHY

The basic components of an OCT scanner (Fig. 1) include a low coherence light source, beamsplitters (to split and recombine light into a reference arm and sample arm) and photodetectors. Optical interference data is used to obtain the optical reflectance as a function of depth along a line and two-dimensional or three-dimensional (3D) images are formed when the light beam is raster scanned across samples. OCT produces images that are very similar in appearance to ultrasonography images but at about 10x to 100x higher resolution (Fig. 2). In an

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KEY POINTS

- OCT can provide high-resolution, real-time images and vibration measurements in a noninvasive manner but has a limited depth of penetration into tissue.
- Otoscope and microscope OCT systems have been validated for the diagnosis of middle ear diseases, such as acute otitis media, otitis media with effusion, otosclerosis and other ossicular diseases.
- Although not yet ready for clinical use, intracochlear OCT offers a promising approach for the diagnosis of sensorineural hearing loss and the guidance of intracochlear therapies.

ultrasound image, the depth of the tissue displayed corresponds to the 'time of flight' for the reflected sound pulse. In OCT, reflected light from the sample is interfered with reference arm light in the interferometer. The interference pattern obtained in this way can be processed to obtain the reflectivity of tissues as a function of axial depth.

The original OCT systems used a technique retrospectively named time-domain OCT in which the length of the reference arm was varied to scan axially in depth (Table 1). Modern OCT systems use a fixed reference arm and perform spectrally resolved measurements of the interference signal. There are two ways this is commonly done, called spectral domain and swept source. As compared to time domain optical coherence tomography (TD-OCT), both these methods offer faster scanning times, higher sensitivity and better signal-to-noise ratios [14]. Technological advances have made 3D reconstructions of patient's middle ear anatomy possible in the clinic setting (Supplemental Video 1, http://links.lww.com/COH/A20).

MIDDLE EAR DIAGNOSIS

The most commonly studied clinical applications of OCT in otology have involved imaging of the tympanic membrane and middle ear space [14]. In-vivo studies have demonstrated changes in the tympanic membrane thickness, biofilm formation and effusion with various states of otitis media. A larger series focusing on the utilization of OCT in assessment of otologic patients highlights some of the issues in uptake of the technology [15]. Acquisition of adequate OCT images was only possible in 70.8% of examinations and can be hindered by narrow or curved external auditory canals (EACs). OCT is only capable of visualizing the middle ear through the tympanic membrane and cannot fully penetrate through bone or soft tissue thicker than about 1 mm. Thickened or cartilage grafted tympanic membranes can also be an impediment to imaging the middle ear space.

Preciado *et al.* [12▪▪] recently used OCT to detect middle ear effusions with high accuracy (90.6%), sensitivity (90.9%) and specificity (90.2%) in children prior to myringotomy and ventilation tube insertion. The study authors asserted that when

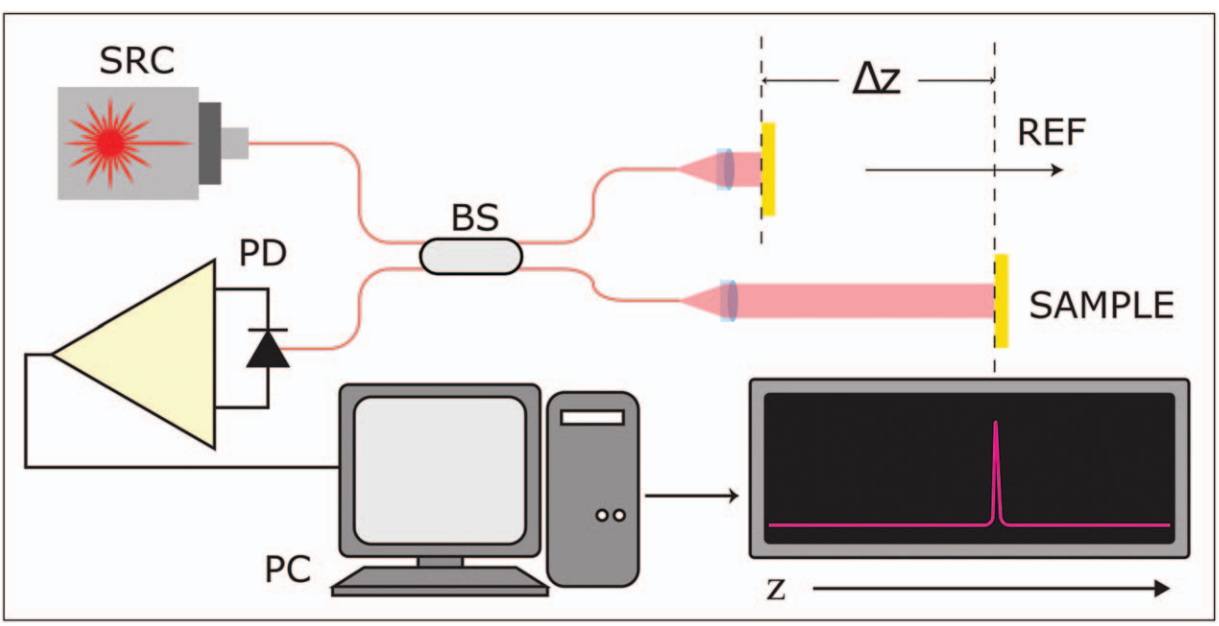

FIGURE 1. Original diagram of a basic time-domain OCT system. The TD-OCT system uses movement of the reference arm mirror to enable axial scanning of a sample/tissue. BD, beamsplitter; PC, personal computer; PD, photodiode; REF, reference arm; SRC, light source; Z, axial depth.

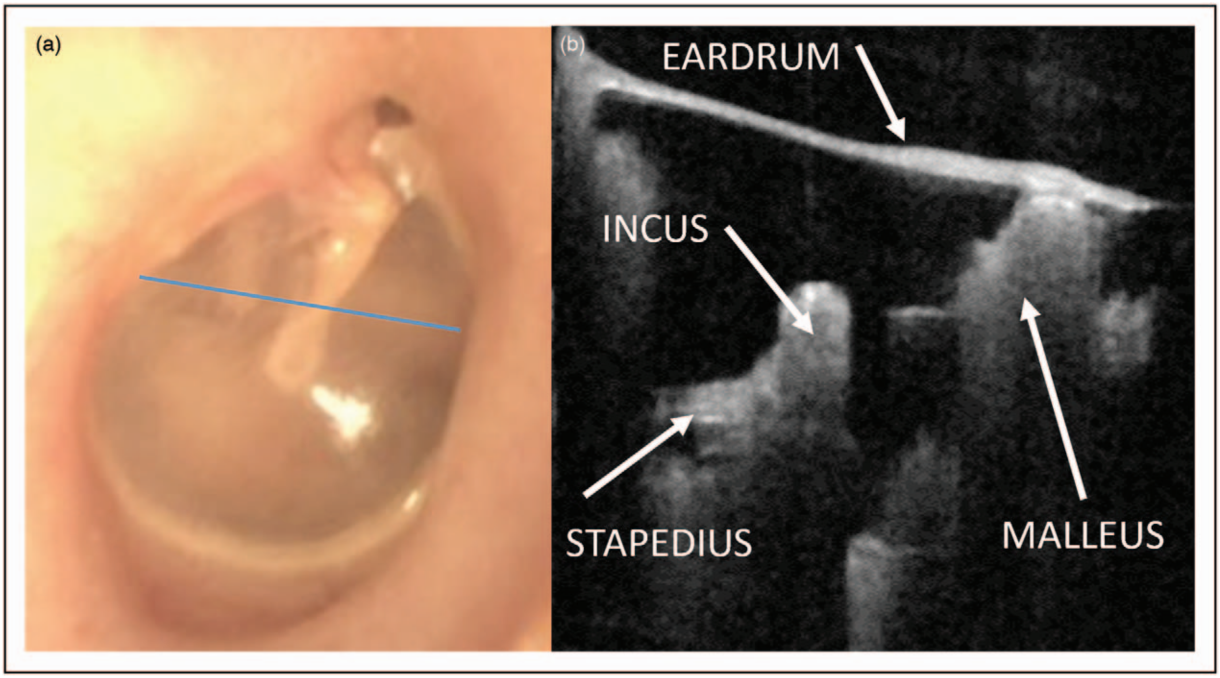

FIGURE 2. Original OCT image of an adult patient in clinic. An OCT image is obtained through the right tympanic membrane of a patient in the clinic. The otoscopic image on the left (A) demonstrates the plane the B-scan OCT image (B) was taken.

compared to traditional techniques, such as tympanometry or pneumatic otoscopy, OCT does not require a seal of the ear canal and could potentially offer greater ease of use. OCT quality was poorer in younger children (2.54 years) compared to older children (5.01 years) likely due to patient cooperation, movement and narrow EACs. The use of automatic OCT classification could potentially further increase the accuracy in diagnosis of otitis media with effusion [16▪]. Further clinical trials showing advantages in OCT's cost, accuracy and ease of use over other diagnostic tools are required before we are likely to see the widespread clinical uptake in otitis media management [17].

OCT Doppler vibrometry (OCT-DV) is an OCT technique capable of measuring the vibration of visible middle ear structures in response to pure tone stimuli through an intact tympanic membrane [18]. MacDougall *et al.* [19▪] compared otosclerosis patients with normal controls via OCT-DV. The sensitivity and specificity for the diagnosis of stapes fixation with OCT-DV were shown to be 100% and 98%, respectively. OCT-DV also offers the possibility of spatially resolved mobility assessment, which could be used, for instance, to distinguish malleus fixation from stapes fixation preoperatively. Reliable preoperative localization of the site of conductive hearing loss could potentially be of great benefit in surgical planning and patient counseling.

Recent advances in phase stabilization and the measurement of vibratory responses with OCT have shown that OCT can detect vibrations of the tympanic membrane and ossicles down to a noise floor of around 5 picometers under clinically realistic

Table 1. Original table comparing some common methods of optical coherence tomography and their basic components

		Fourier domain techniques	
	Time domain	**Spectral domain**	**Swept source**
Light source	Broadband light source (e.g. SLD)		Rapidly tuneable narrowband laser
Detector	Photodiode	Spectrometer	Photodiode
Depth resolution method	Axial movement of reference arm	Spectral information/wavelength of detected light	Change in signal with change in light source wavelength

SLD, super luminescent diode.

scenarios, a level that approaches the threshold of hearing [11]. With this system, OCT has been shown capable of observing and quantifying vibrations from distortion product otoacoustic emissions at the level of the tympanic membrane and incus in awake patients.

So far, few OCT systems have been used intraoperatively in middle ear surgery with only proof of concept studies published thus far. In one implementation, an augmented reality overlay of OCT data onto the operative microscope provided real-time feedback to surgeons during tympanomastoidectomy [20]. Djalilian *et al.* [21] demonstrated that differentiation of cholesteatoma from middle ear mucosa was possible during surgery using a flexible probe TD-OCT system. Future intraoperative middle ear applications of OCT could include accurate middle ear measurements to guide cholesteatoma removal, patient-specific planning of ossicular reconstruction and assessment vibrometric results in the operating room. OCT can be integrated into both surgical endoscopes and into traditional operating microscopes and so can be implemented in the operating room with minimal changes to workflow.

MIDDLE EAR PHYSIOLOGY

Nonclinical studies have benefited from the nondestructive nature of OCT as a research imaging tool in understanding middle ear mechanics and pathophysiology as summarized by Burwood *et al.* [22▪▪]. For example, healed traumatic perforations in a gerbil model were recently mapped by OCT, demonstrating increased thickness and ongoing high-frequency hearing loss after spontaneous perforation closure [23]. OCT offers compelling advantages over laser Doppler vibrometry for cadaveric and animal studies of ear mechanics, including coregistration of 3D structural and vibrometric data and the ability to independently measure the motion of axially separated structures along the same line of sight.

INNER EAR IMAGING: CLINICAL APPLICATIONS

Imaging of the labyrinth is limited by its location deep in the temporal bone and surrounding thick otic capsule. Traditional clinical imaging modalities, such as x-ray computed tomography and MRI, lack the resolution and contrast required to assess intracochlear structures or ability to measure real-time inner ear physiology. Synchrotron radiation phase contrast imaging (SR-PCI) has provided increased nondestructive visualization of cochlear microstructures in human temporal bones *ex vivo* [24,25]. SR-PCI could replace traditional histology as the gold standard in postmortem examination of cochleae but unlikely to supplant OCT for *in vivo* or vibrometric measurements.

An important limitation of OCT technology is its poor penetration in soft and bony tissues (<2 mm). Although the osseous labyrinth has been partially observed through the promontory in transtympanic in-vivo OCT, the limited penetration of OCT in bone is likely to preclude noninvasive, high-resolution imaging of the entire cochlea in humans [11]. It could be that invasive strategies, such as using a transtympanic probe to image the inner ear via a cochleostomy or round window, may allow better visualization of human intracochlear structures, but this has not yet been demonstrated *in vivo*. For ex-vivo studies, decalcification of the temporal bone or the use of optical clearing agents offers viable pathways to imaging inside the cochlea, but these are methods that are likely not translatable to clinical use.

One possible future intraoperative application of OCT is its potential use in guiding cochlear implant insertion to reduce insertion trauma. OCT light can be delivered and received on an optical fiber that could be inserted along with the cochlear implant electrode to provide visual feedback to the surgeon during insertion and then retracted once the implant is in place [26]. Alternatively, cochlear implant insertion can be monitored from the round window. Starovoyt *et al.* [13▪▪] demonstrated that anatomical structures in the hook region of a human cochlea could be visualized in this way via a standard cortical mastoidectomy and posterior tympanotomy in human cadaveric specimens.

INNER EAR IMAGING: INSIGHTS INTO ANATOMY AND PATHOPHYSIOLOGY

The ability to image the unopened healthy rodent cochlea with OCT systems has had a significant impact on current understanding of cochlear function and anatomy [22▪▪]. The thin promontory bones and reduced dimensions of the rodent ear allow better penetration into the cochlea than is possible in humans, including noninvasive measurements of the motion of the organ of Corti in gerbil and mouse [27,28]. Other groups have imaged the in-vivo gerbil cochlea via the round window and demonstrated measurement of the basement membrane displacement [29]. As compared to traditional laser Doppler vibrometry techniques for measuring cochlear vibration, OCT offers a lower level of invasiveness that makes damage to the cochlea less likely, and coregistered imaging that allows precise targeting of intracochlear structures on a cellular or even subcellular level [30]. The ability of OCT to resolve the differential motion of axial structures has led to improved understanding of the role of differential motion of the tectorial membrane and basilar membrane in stimulating hair cells and cochlear amplification [31].

Although the diagnosis of inner ear pathology remains elusive, OCT imaging is poised to be an important tool for differentiating various causes of sensorineural hearing loss in the future. Continued development of noninvasive, cellular-level imaging is necessary to correlate our histopathological understanding of sensorineural hearing loss with in-vivo data [32▪]. A combination of nontraumatic perilymph sampling, OCT imaging and genetic testing may someday guide novel targeted therapies for sensorineural hearing loss [33,34]. This could be analogous to the way ophthalmological surgeons use real-time intraoperative OCT to ensure the correct location of subretinal gene therapy injections [35].

EUSTACHIAN TUBE IMAGING

Many of the underlying mechanisms of Eustachian tube dysfunction remain poorly understood and can be difficult to demonstrate with traditional imaging [36]. Renewed interest in accurate diagnostic tools has been ignited by the increasing application of Eustachian tube balloon dilation. Luminal OCT has been widely used within the coronary arteries to provide intraluminal and transluminal imaging [2]. Along similar principles, Schuon *et al.* [37▪▪] investigated the viability of an OCT catheter in obtaining images from within the lumen of the Eustachian tube on cadaveric sheep heads *ex vivo*. The peritubal structures were delineated to a rough depth of 2 mm from the mucosal surface. Insights into Eustachian tube biomechanics, intraluminal and extraluminal pathology may be possible with further refinement of this OCT imaging technique.

CONCLUSION

OCT provides a unique method for the imaging of ear structures. Multiple OCT systems have been validated for the diagnosis of middle ear conditions, whereas many others remain under investigation. Widespread clinical adoption will ultimately depend on cost, ease of use and improvement over traditional management paradigms. The application of OCT systems in nonclinical research will continue to provide important insights into the microscopic function of the ear.

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Conflicts of interest

RA has an interest in Audioptics Medical Inc., a spinout company working to commercialize OCT technology for middle ear diagnostics. TM has no conflicts of interest to declare.

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