

Optical Coherence Tomography of the Tympanic Membrane and Middle Ear: A Review

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Abstract

Objective. To evaluate the recent developments in optical coherence tomography (OCT) for tympanic membrane (TM) and middle ear (ME) imaging and to identify what further development is required for the technology to be integrated into common clinical use.

Data Sources. PubMed, Embase, Google Scholar, Scopus, and Web of Science.

Review Methods. A comprehensive literature search was performed for English language articles published from January 1966 to January 2018 with the keywords “tympanic membrane or middle ear,” “optical coherence tomography,” and “imaging.”

Conclusion. Conventional imaging techniques cannot adequately resolve the microscale features of TM and ME, sometimes necessitating diagnostic exploratory surgery in challenging otologic pathology. As a high-resolution noninvasive imaging technique, OCT offers promise as a diagnostic aid for otologic conditions, such as otitis media, cholesteatoma, and conductive hearing loss. Using OCT vibrometry to image the nanoscale vibrations of the TM and ME as they conduct acoustic waves may detect the location of ossicular chain dysfunction and differentiate between stapes fixation and incus-stapes discontinuity. The capacity of OCT to image depth and thickness at high resolution allows 3-dimensional volumetric reconstruction of the ME and has potential use for reconstructive tympanoplasty planning and the follow-up of ossicular prostheses.

Implications for Practice. To achieve common clinical use beyond these initial discoveries, future in vivo imaging devices must feature low-cost probe or endoscopic designs and faster imaging speeds and demonstrate superior diagnostic utility to computed tomography and magnetic resonance imaging. While such technology has been available for OCT, its translation requires focused development through a close collaboration between engineers and clinicians.

Keywords

tympanic membrane, optical coherence tomography, imaging

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The traditional otoscope and surgical microscope are essential visualization tools for the otolaryngologist, long serving as the premier diagnostic and operative tools for otologic pathology. However, as the optical design of these instruments allows only for the magnification and illumination of the tympanic membrane (TM), there are several weaknesses. Otoscopy can provide visualization of just the lateral surface of the TM, through the narrow field of view afforded by the ear canal, and unless one utilizes an otoendoscope, the full surface of the TM cannot usually be seen in 1 view. In addition, the view is 2-dimensional, resulting in a subjective interpretation of the 3-dimensional (3D) TM shape. Furthermore, visualization into the middle

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ear (ME) is limited, dictated by the translucency of the TM and the severity of any effusion present. Deeper ME structures, such as the round window and stapes footplate, are not visible. These optical limitations play a part in the poor diagnostic accuracy of standard otoscopy for common conditions such as otitis media.¹ Acute otitis media (AOM) is the most common reason for antibiotic prescription of US children,² accounting for up to \$2.8 billion in medical costs a year.³ Diagnosis is made through otoscopic examination findings of TM redness and bulge, with pneumatic otoscopy used to confirm reduced TM mobility. Yet, AOM may be clinically challenging to differentiate from otitis media with effusion (OME), a condition where ME fluid is present but with no bacterial infection, as children with OME typically present asymptotically. Standard otoscopy for OME provides low sensitivity (74%-87%) and specificity (60%-74%),⁴⁻⁶ with some estimates suggesting that OME is misdiagnosed as AOM in up to 30% of children.¹ Underdiagnosis of AOM may lead to lasting hearing morbidity among children, while overdiagnosis may lead to overprescription and antibiotic resistance.^{6,7} While adjunct diagnostic tools, such as pneumatic otoscopy and tympanometry, may provide higher sensitivity and specificity (70%-90%),⁴⁻⁶ they are still recommended to be used in conjunction with otoscopy. For other otologic pathology, such as conductive hearing loss (CHL), identification of the cause is achieved through audiometric testing, as there is currently no clinical tool capable of directly visualizing the location of ossicular chain pathology. Computed tomography (CT) and magnetic resonance imaging (MRI) are used for recurrent or complicated ME pathology and surgical planning. CT is well suited for bony abnormalities and other causes of ME opacification; however, it has poor soft tissue differentiation and associated radiation exposure. MRI normally excels in soft tissue differentiation but lacks the resolution to clearly visualize the thin TM, and imaging is compromised by metal implants and poor patient tolerance. An unmet need exists for a diagnostic tool that can provide real-time high-resolution imaging of the TM and ME with functional information for the clinician to differentiate otitis media types, identify causes of CHL, and assist ME surgical planning.

Optical coherence tomography (OCT) is an established noninvasive, noncontact imaging modality that allows rapid subsurface visualization of tissue microstructure at high resolution. OCT has several advantages over the current imaging standards. The high resolution of OCT (5-15 μm) enables characterization of the thin, low-contrast soft tissue TM and complex ME structures that CT (400 μm), MRI (300 μm), or ultrasound (150 μm at 10 MHz) cannot readily resolve. OCT is readily adapted to handheld probes or surgical microscopes, allowing real-time in vivo imaging without the radiation exposure of CT or the cost of MRI. OCT does not require a transduction medium, as with ultrasound,⁸ making structures in the air-filled ME cavity visible.

In this review, we focus on the current state of the art in OCT for TM and ME imaging and the potential that it has

to improve the quality of otologic diagnostics and surgical planning. Next, the challenges of clinical imaging with OCT in otology are discussed, and we explore how they are being overcome. We conclude by discussing what steps are required to achieve a future where OCT is in common clinical use in otology, learning from the journey that OCT in ophthalmology took to reach widespread clinical acceptance.

Methods

A literature search of the PubMed, Embase, Google Scholar, Scopus, and Web of Science databases was performed to identify all publications from January 1966 to January 2018 with OCT or any other imaging modality to capture TM and ME morphology, according to PRISMA guidelines (**Figure 1**). The key terms “tympanic membrane OR middle ear” and “imaging” returned 515 reports. A separate search with the terms “tympanic membrane OR middle ear” and “optical coherence tomography” yielded 19 reports. The combined 532 abstracts and their reference lists were reviewed with the following inclusion criteria: (1) human or animal TM/ME imaging in vitro, in vivo, or ex vivo with OCT; (2) experimental studies discussing new OCT techniques applied to the TM/ME; and (3) other non-invasive, nonionizing, portable, or handheld TM/ME imaging modalities. Exclusion criteria included (1) non-English language publications and (2) exclusively theoretical studies with no demonstration of OCT or non-OCT techniques in an animal model or human subject. Of the final 36 studies selected, 15 corresponded to exclusively basic research of animals or ex vivo cadaveric temporal bones, while 21 were human in vivo TM/ME imaging studies.

Discussion

OCT Working Principles, Development, and Clinical Application

OCT is conceptually analogous to ultrasound imaging, utilizing the time-of-flight information of light waves (time to reach an object and return back) to localize tissue structures in depth. Unlike measurement in ultrasound, in which sound wave echoes can be measured directly, OCT measurement is indirect, utilizing the principles of low-coherence interferometry.⁹⁻¹¹ OCT systems typically have a resolution of 5 to 15 μm and are capable of capturing 3D volumetric data on the order of seconds.¹² However, 3D acquisition of whole volumes at near video rate¹³ and 1- to 2- μm resolutions have been demonstrated.¹⁴ The lateral field of view is typically 5 to 15 mm, and depending on the optical scattering and absorption properties of the tissue, the use of near-infrared light allows OCT to achieve 1 to 3 mm of depth penetration.

OCT was first demonstrated in 1991 when it was used to capture cross-sectional images of the retina and coronary artery in vitro,¹⁵ and early support from industry led to the first commercial ophthalmic OCT system, released in 1996 by Carl Zeiss Meditec, Inc.^{11,16} However, clinical adoption was slow and proved difficult; limited funding and clinical

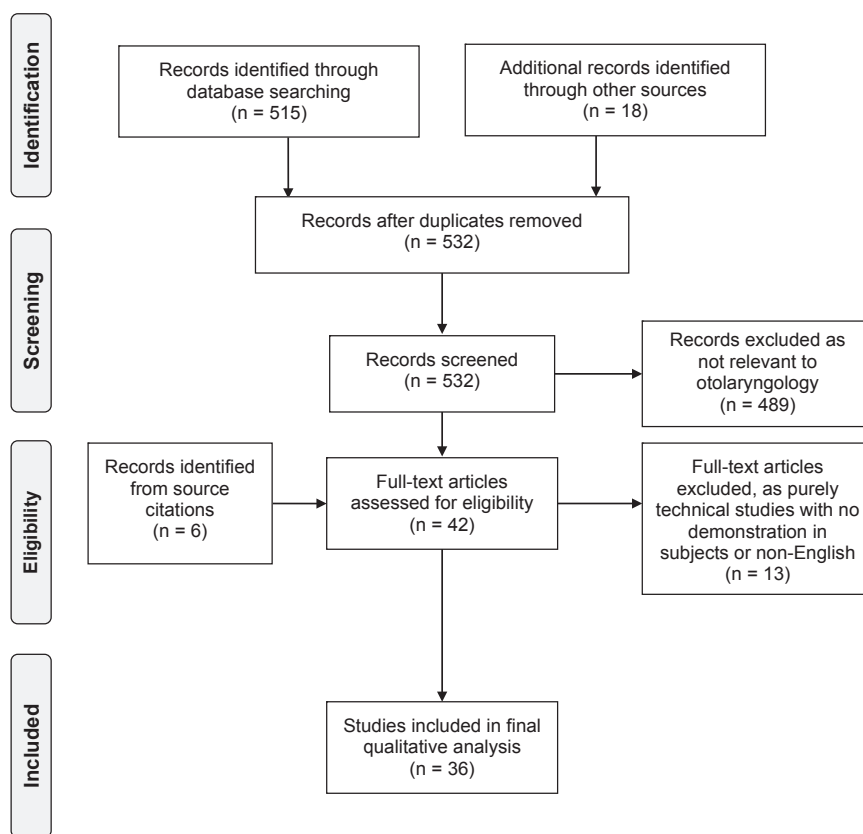


Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) flowchart summarizing the search results and the application of eligibility criteria.

interest almost halted its development in 2001.¹⁷ It required significant perseverance from researchers and clinicians with limited funding (who nonetheless produced a large volume of clinical data) to achieve Food and Drug Administration approval of an OCT system by Optovue in 2006, by which time >20 million ophthalmic OCT procedures had already been performed worldwide.¹⁷ Presently, OCT is a key diagnostic technology in ophthalmology, with >30 million ophthalmic OCT procedures performed worldwide per year, a utilization rate comparable to that of MRI and CT.¹⁷ OCT research continues to be an area of rapid development, as demonstrated by the increasing number of publications with the keywords “optical coherence tomography” published per year (**Figure 2**).

The feasibility of OCT imaging for the TM and ME was first demonstrated in 2001 (**Figure 3a**)¹⁸ when normal ME structures were imaged in 4 ex vivo temporal bones. The trilaminar nature of the TM could be visualized, as well as the manubrium of the malleus and tensor tympani tendon, and the authors proposed that the higher-resolution, real-time, and contactless nature of OCT held potential for “diagnosis and presurgical evaluation of middle ear abnormalities.”¹⁸ However, despite the widespread clinical adoption and commercial success of OCT in ophthalmology, it was another decade before a marked interest developed in OCT technology for TM and ME imaging in otology, where the first in vivo application was to intraoperatively differentiate

cholesteatoma¹⁹ (**Figure 3b**) from inflamed mucosa and the first portable handheld TM OCT imaging device was described.²⁰

In otolaryngology, “optical biopsy,” or noninvasive probe-based OCT characterization of tissue pathology, promises to reduce tissue trauma, pathology results, and patient waiting times and potentially eradicate the need for tissue biopsy altogether.²¹ OCT can delineate several pathologic lesions, such as hyperkeratosis, dysplasia, neoplasia, and inflammation; however, the end goal is differentiation between clinically similar areas (eg, dysplasia vs carcinoma in situ) rather than simple normal versus abnormal tissue.²¹ To date, OCT has focused on examining the laryngeal mucosa for the differentiation of benign and invasive vocal cord cancer, through evaluating basement membrane integrity, epithelium thickness, and lamina propria structure.^{22,23} Beyond the larynx, OCT has been used to examine the subglottic epithelium changes in prolonged mechanical ventilation in pediatric and neonatal patients.²⁴ In rhinology, OCT has been used to examine changes to the nasal septum mucosa following septoplasty, different types of rhinitis, and decongestant use.²⁵⁻²⁷

OCT Imaging of the TM

The recent focus of clinical OCT imaging of the TM (see **Table 1** for the last 5 years; for all studies used for this review, see Supplemental Table S1 in the online version of the article) has

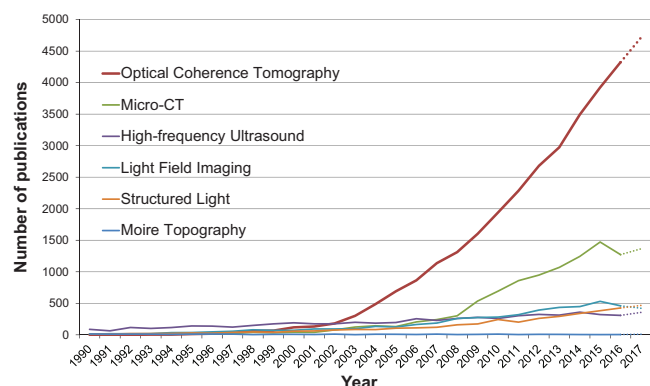


Figure 2. Plot of the number of PubMed publications with “optical coherence tomography” or other imaging modalities as keywords from 1990 to 2016, showing the rapid development of research interest in optical coherence tomography. The dashed lines represent data extrapolated for 2017 based on the number of publications as of September 2017. micro-CT, micro-computed tomography.

been on improving the diagnosis of OM, where handheld OCT probes (**Figure 4a**) have demonstrated the ability to detect the presence of biofilm behind the TM, which is suggestive of chronic OM.^{28–30} Using OCT-detected biofilm to diagnose chronic OM, 1 study with 20 patients reported higher diagnostic sensitivity (83% vs 74%) and specificity (98% vs 60%) over standard otoscopy.²⁸ TM thickness is a proposed metric to differentiate between chronic and acute OM, assisting earlier detection and guiding antibiotic management. OCT measures the overall TM thickness, which is the sum of the TM and biofilm layer thickness.^{31,32} For 34 pediatric patients, acute OM correlated to a

thicker TM, while chronic OM had normal TM thickness but greater biofilm and overall TM thickness, suggesting that the TM tissue returns to relatively normal thickness levels in chronic OM but the overall TM remains thicker due to an increased biofilm layer.^{31,32} In terms of a follow-up diagnostic tool, in a recent prospective series of 25 pediatric patients with chronic or recurrent OM who were undergoing myringotomy and tympanoplasty tube placement, 4 of 6 who were available at 6-month follow-up demonstrated clearance of ME biofilm based on handheld OCT imaging, which correlated with clinical findings.³³ For OME, standard and pneumatic otoscopy provides qualitative assessment of TM bulging and effusion. As such, OCT has been proposed as a tool to assess the degree and turbidity of effusion in OME to quantify severity of chronic OM and monitor resolution of infection.³⁴ To build on this, by coupling OCT and pneumatic otoscopy into a single device, quantitative assessment of TM compliance has been achieved, as determined by minute deflections of the TM and as demonstrated in a pilot study of 15 patients (16 imaged ears) wherein average compliance across 10 healthy ears ($6.1 \mu\text{m}/\text{mm Hg}$) was higher and statistically different from 4 ears with OME ($1.4 \mu\text{m}/\text{mm Hg}$).³⁵

By adapting OCT to the surgical microscope, it has been used to detect microanatomic changes found in the TM layers of patients with chronic myringitis.^{36,37} OCT can visualize the loss of the trilaminar TM structure, the loss of outer epithelial layer integrity, and the separation of outer and inner TM layers occurring in chronic myringitis—information not visible with an operating microscope.³⁶ The high signal intensity of keratin distinguishes it from normal or inflamed ME mucosa (**Figure 3b**); this may assist the surgeon to detect and remove any residual cholesteatoma buried within mucosal tissue that could be missed with a

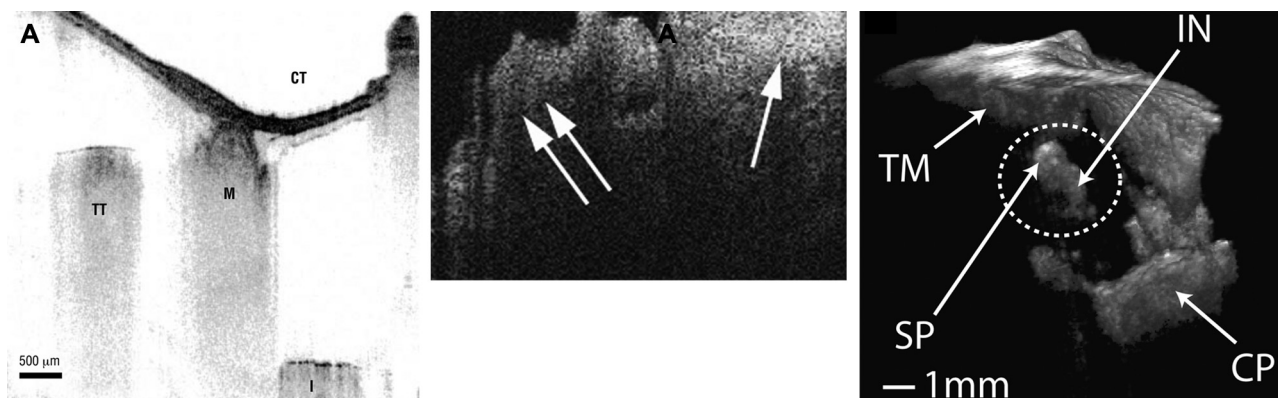


Figure 3. (a) First optical coherence tomography (OCT) image of the normal tympanic membrane and middle ear, taken ex vivo through the ear canal of a cadaver temporal bone in 2001 (adapted from Pitris et al¹⁸). (Reproduced with permission from Pitris C, Saunders KT, Fujimoto JG, Brezinski ME. High-resolution imaging of the middle ear with optical coherence tomography: a feasibility study. *Arch Otolaryngol Head Neck Surg*. 2001;127:637-642. Copyright © 2001 American Medical Association. All rights reserved.) CT, chorda tympani; I, incus; M, malleus; TT, tensor tympani muscle. (b) An intraoperative OCT image showing cholesteatoma (single arrow; confirmed by histology) with its characteristic hyperintensity due to overlying keratin adjacent to inflamed middle ear mucosa (double arrow; adapted from Djalilian et al⁵⁸). (Reproduced with permission from Djalilian HR, Rubinstein M, Wu EC, et al. Optical coherence tomography of cholesteatoma. *Otol Neurotol*. 2010;31(6):932-935.) (c) In vivo 3-dimensional OCT volumetric reconstruction of a patient's middle ear with a stapes prosthesis (SP) crimped along the long process of the incus (IN). The 3-dimensional render allows visualization of the cochlear promontory (CP) inferiorly and tympanic membrane (TM) superiorly (adapted from MacDougall et al⁴⁶). (Republished with permission from MacDougall D, Farrell J, Brown J, Bance M, Adamson R. Long-range, wide-field swept-source optical coherence tomography with GPU accelerated digital lock-in Doppler vibrography for real-time, in vivo middle ear diagnostics. *Biomed Opt Express*. 2016;7:4621-4635.)

Table 1. Studies from the Last 5 Years Reporting OCT for TM or ME Imaging.^a

First Author (Year)	Imaging Setting	Sample	Ear Structure Imaged	OCT		Resolution, μm	
				Imaging Role / Purpose	Type	Transverse	Axial
Jang (2013) ⁵¹	Ex vivo	20 guinea pigs, chronic TMP model	TM	Evaluate thickness of an experimental TM repair scaffold	SD-OCT	—	8
Chang (2013) ⁵⁴	Ex vivo	3 chinchillas TBs	TM + ossicular chain	3D vibrational patterns of TM and ossicular chain in physiologic and pathologic ear	SD-OCT	25	12
Van der Jeught (2013) ⁴⁹	Ex vivo	6 human TBs (5 healthy, 1 with retraction)	TM	Determine the 3D full-field thickness distribution of 5 TMs	SD-OCT	<10	<10
Nguyen (2013) ²⁹	In vivo (outpatient)	6 patients (1 healthy, 5 with chronic OM)	TM	Detection of bacterial biofilm on TM	SD-OCT	—	3.1
Rutledge (2013) ⁵⁰	Ex vivo	1 chinchilla TB + 1 human TB	TM	Determine collagen fiber size and arrangement	SD-OCT	—	—
Burkhardt (2014) ⁵⁶	Ex vivo	1 freshly excised human TM	TM	Doppler OCT for vibration behavior of 3D TM	SS-OCT	13	9
Guder (2015) ³⁶	In vivo (outpatient)	47 patients (11 myringitis, 13 retraction, 12 TM sclerosis, 11 perforation)	TM	Thicker TM in chronic myringitis vs normal and other TM pathology	SD-OCT	23	10
Pawlowski (2015) ⁴²	Ex vivo	1 mouse TB	ME + ossicles	Development of a miniature tunable OCT endoscope	SD-OCT	—	—
Cho (2015) ³¹	In vivo (outpatient)	39 patients with chronic OM + 6 healthy (22 TMs imaged)	TM	Characterization of TM biofilm and effusion	SD-OCT	10	6
Hubler (2015) ³⁹	In vivo (outpatient)	1 patient	TM	TM thickness measurement to detect biofilm	SD-OCT	15	2.4
Monroy (2015) ³²	In vivo (outpatient)	34 pediatric patients with OM	TM	Thicker TM in acute OM but normal thickness in chronic OM	SD-OCT	15	4
MacDougall (2016) ⁴⁶	Ex vivo + in vivo (outpatient)	1 human TB + 1 patient	TM + ossicular chain	Real-time, full-ME 3D scan and trans-TM Doppler vibrography	SS-OCT	<40	<40
Pande (2016) ⁴⁰	In vivo (outpatient)	6 healthy patients (7 TMs imaged)	TM	Mapped full-field TM thickness distribution	LCI	—	—
Park (2016) ⁵⁵	Ex vivo	5 human TBs	TM + ossicular chain	Vibration patterns of the TM, ossicles	PS-SD-OCT	15	12
Oh (2016) ⁸⁹	In vivo (animal)	5 mice + 5 rats	TM + ME	In vivo imaging of ossicular chain through intact TM	SS-OCT	13	7

(continued)

Table 1. (continued)

First Author (Year)	Imaging Setting	Sample	Ear Structure Imaged	OCT		Resolution, μm	
				Imaging Role / Purpose	Type	Transverse	Axial
Monroy (2017) ³⁴	Ex vivo + in vivo (outpatient)	1 human TB + 1 patient with ME effusion	TM + ME	Measurement of viscosity and diffusion coefficient of ME effusion	SD-OCT	15	4
Pande (2017) ⁹⁰	In vivo (outpatient)	1 patient	TM	Low-cost probe for TM thickness measurement	LCI	—	5.2
Jang (2017) ⁹¹	Ex vivo	14 rats, TMP model	TM	Thickness of an experimental TM repair scaffold	SD-OCT	—	8
Park (2017) ⁶³	In vivo (outpatient)	1 patient	TM	Clockwise, diagonal scanning for increased lateral scanning range	SD-OCT	15	—
Choi (2017) ⁹²	Ex vivo	1 excised dehydrated mouse, TM	TM	Vibrational measurements in wide field of view	MFS-OCT	5.04	1.8
Shelton (2017) ³⁵	In vivo (outpatient)	12 patients (16 TMs imaged)	TM	Pneumatic otoscope for TM compliance normal vs ME effusion	LCI	—	5.6
Park (2017) ⁴¹	In vivo (outpatient)	120 patients (only 85 successful images, however)	TM	TM perforation margin thickness, and monitor TM graft healing	LCI	15	15
Monroy (2017) ³³	In vivo (outpatient and intraoperative)	25 patients	TM	Confirm biofilm clearance posttubule placement	SD-OCT	15	2.4

Abbreviations: 3D, 3-dimensional; LCI, low-coherence interferometry; ME, middle ear; MFS-OCT, multifrequency-swept OCT; OCT, optical coherence tomography; OFDI, optical frequency domain imaging; SD-OCT, spectral-domain OCT; SS-OCT, swept-source OCT; TB, temporal bone; TM, tympanic membrane; TMP, tympanic membrane perforation.

^aDashes (—) indicate not reported.

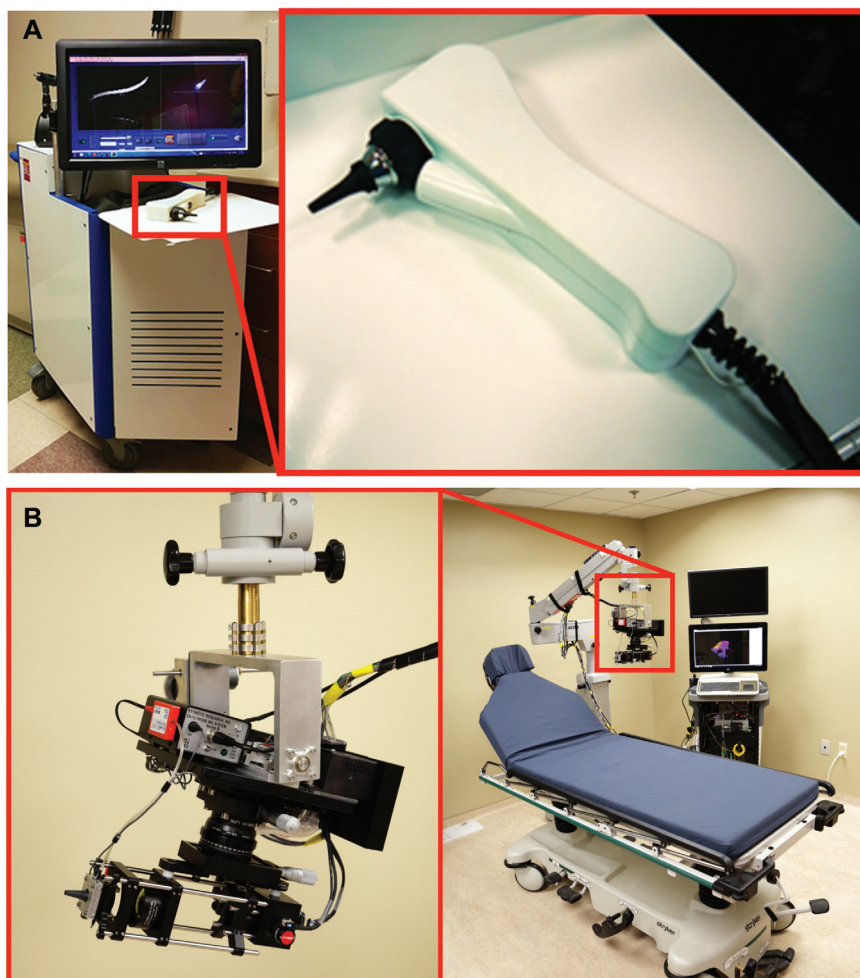


Figure 4. (a) A noninvasive handheld optical coherence tomography probe developed primarily for the purpose of measuring tympanic membrane thickness to assess for biofilm presence and characterize middle ear (ME) effusion viscosity to differentiate otitis media types (adapted from Monroy et al³³). (Republished with permission from Monroy GL, Pande P, Nolan RM, et al. Noninvasive in vivo optical coherence tomography tracking of chronic otitis media in pediatric subjects after surgical intervention. *J Biomed Opt.* 2017;22:1-11.) (b) An optical coherence tomography system mounted onto a surgical microscope arm with coupled Doppler vibrography for real-time whole-ME 3-dimensional volume reconstruction and ME diagnostics (adapted from MacDougall et al⁴⁶). (Republished with permission from MacDougall D, Farrell J, Brown J, Bance M, Adamson R. Long-range, wide-field swept-source optical coherence tomography with GPU accelerated digital lock-in Doppler vibrography for real-time, in vivo middle ear diagnostics. *Biomed Opt Express.* 2016;7:4621-4635.)

standard operating microscope.³⁸ Mapping and tracking the changes in TM thickness of the entire TM with in vivo OCT can describe retraction pocket depth and confirm increased thickness of the white, chalky patches in tympanosclerosis.^{39,40} A handheld OCT-based otoscope was recently used to monitor healing of inserted grafts following tympanoplasty, assessing the interface contiguity between graft and native TM and demonstrating the thinning over time that temporalis fascia grafts undergo during healing.⁴¹ In the same patient series of 120 patients, OCT also provided precise measurements of TM perforation margin thickness (thicker in chronic perforations), matching the otoendoscopic estimates of margin thickness from 3 otologists, which suggested that otoendoscopy is reliable for perforation margin assessment.⁴¹ For assessment of TM retraction severity, however, OCT was superior in differentiating

intermediate-stage TM retraction, unlike concurrent otoendoscopy findings where it was indistinguishable to other severity stages, demonstrating another potential application of OCT as an complementary objective tool in otology.⁴¹

OCT Imaging of the ME

The opacity and reflectivity of the TM hamper optical imaging into the ME cavity by attenuating the signal and creating shadowing artifacts. As such, most OCT clinical imaging of the ME to date has been performed intraoperatively, where the TM has been removed. OCT imaging of the ME has been applied in the form of a 1-mm fine endoscope catheter that can be passed through an existing TM perforation to characterize ossicular chain morphology and vibrational characteristics.⁴² OCT can be mounted onto the articulating arm of a surgical microscope (**Figure 4b**),

where it has been used to measure distances for stapes prosthesis implantation, thereby avoiding mechanical measurement (which risks breaking the stapes footplate or remaining chain) and allowing confirmation of prosthesis position below the TM and in relation to the long process of the incus at follow-up (**Figure 3c**), which is hard to assess with otoscopy.⁴³ Intraoperative OCT has also characterized the morphology of the stapes footplate, identifying sclerotic changes to the elastic suspension of the stapes footplate in patients undergoing stapedectomy for otosclerosis.^{44,45} Moving forward, OCT holds greatest value with its use in combination with other modalities for functional diagnostics (eg, laser Doppler vibrometry; **Figure 4b**) and with other acquisition methods, such as phase-sensitive OCT, where it has demonstrated the potential for real-time in vivo ME diagnostics and vibrometry.^{46,47} However, patient motion must be addressed, as 1 study revealed that in OCT Doppler vibrometry imaging of live patients, motion due to respiration, heartbeat, or muscle movement caused motion artifact several orders of magnitude larger than physiologic TM displacement, thereby degrading image sensitivity.⁴⁶

OCT Imaging as a Research Tool

OCT is a key research tool in experimental ME and hearing research, as researchers can remove the external auditory canal (EAC) to closer image the TM and view its medial side.⁴⁸ Using OCT to characterize the thickness distribution of the ex vivo TM has assisted hearing researchers in creating better mathematical and finite element models of ME biomechanics and has a role to play in surgical prosthesis and graft modeling.^{49,50} As an imaging tool, OCT has been used as a tool to assess the healing of experimental grafts in mouse models⁵¹ and, in another study, to assess the “fit” and placement of a film patch (with an integrated strain gauge that was used to detect TM movement) on a normal TM.⁵² With high-sensitivity optical microangiography and OCT, 3D volumetric representations of blood flow in the cochlea of mice have been created.⁵³ Crucial to the study of ME biomechanics, OCT has been used to visualize sound-induced TM and ossicular motion at different frequencies and for different pathologies, such as stapes fixation and incudostapedial disruption, with the clinical goal to translate OCT as an adjunct to ME diagnostics.⁵⁴⁻⁵⁷

Challenges of Clinical TM and ME Imaging with OCT

The shape of the EAC and position of the TM present a challenge for endoscopic design. OCT requires a clear line of sight, which is difficult in the narrow, angled EAC. This is further complicated as imaging the whole surface of the TM and the visually obscured regions of the ME cavity (eg, sinus tympani) is often desired.⁵⁸ Presently, visualization requires a conical ear speculum to retract the tragus and align the conchal cartilage to straighten the EAC, and it often requires the removal of wax. The inferior (43° to the horizontal plane) and medial (34° to parasagittal plane) projection of the TM⁵⁹ means that the inferior and anterior quadrants are situated deeper relative to the axis of the EAC

and are thus in a different focal plane if approached directly along the axis of the EAC. OCT is thus required to have a focal depth and imaging range of 3 to 4 mm for the TM and 10 mm for the ME,⁴⁶ which is achievable but at a significant cost to transverse resolution. While OCT devices do not cause ear canal discomfort through pain or heat, the need for patients to remain completely motionless to reduce motion artifact may be challenging, particularly in uncooperative young children.

To image the ME cavity, the imaging beam must first pass through the TM, backscatter off an ME structure, and pass back through the TM to the detector—a challenge worsened in cases of pathologic thickening or calcification of the TM.^{19,60} As light needs to pass through the TM twice, up to 89% of original incident photons are scattered, resulting in a source signal loss of up to 19 dB, as found in ex vivo analysis of normal TM.⁶⁰ In addition, the reflectivity of the TM can obscure weaker reflections of other ME structures, though when compared with signal loss due to scattering, these are considered negligible.⁶⁰ Capturing the full volume of the ME through the intact TM is challenging but has been performed in ex vivo temporal bones^{18,55} and live patients.⁴⁶ The ME can also be imaged through a perforation with a fine endoscope⁴² or, as demonstrated for cochlea imaging, a flexible, thin, catheter-based OCT.⁶¹ However, the requirement for myringotomy to place a catheter may prove too invasive for routine diagnostic use; hence, a noninvasive approach is still preferred.

Ideally, an OCT imaging device for the TM and ME will have a wide field of view (at least 8 mm to capture the entire TM annulus in 1 view), a large depth of focus (to accommodate the tilted TM), and an adequate working distance (to avoid accidental contact with TM); it will also be forward facing (to ensure en face TM imaging), thin or flexible and endoscopic (to navigate past the narrow EAC isthmus), and rapidly scanning (to increase patient comfort and reduce the impact of hand motion tremors). However, this is challenging, as increasing the depth of focus or increasing the working distance to improve the field of view compromises transverse resolution and because unintentional probe tip movement caused by the patient or operator introduces motion artifact.⁶² One approach to overcoming the narrow field of view afforded by the tight ear canal has been to build a composite image of the full surface of TM from various OCT images taken with the ear specula, otoscope, and patient's head in different positions.⁴⁰

Last, an attractive feature of OCT is the ability to rapidly visualize detail in 3D. Most demonstrations of OCT in otology to date have been 1- or 2-dimensional due to the challenge of motion artifact and limited penetration depth into the ME. It is also challenging to present the 3D volumetric reconstruction OCT data as a live view, as it requires rapid computing power. However, real-time 3D OCT was recently demonstrated through a system with orthogonal galvanometer mirror scanners mounted on a microscope arm (**Figure 4b**).⁴⁶ This system was the first to demonstrate the ability to capture the entire ME volume of a live patient, at

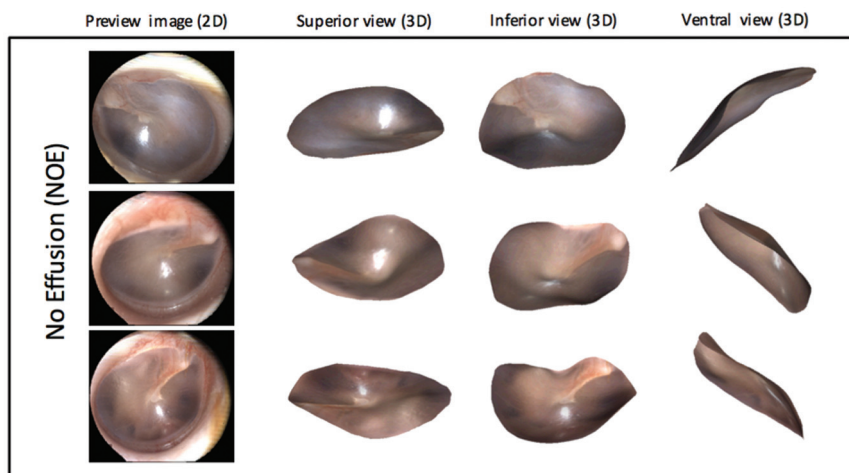


Figure 5. Lateral surface of the tympanic membrane as reconstructed from light field imaging (adapted from Bedard et al⁷³). (Republished with permission from Bedard N, Shope T, Hoberman A, et al. Light field otoscope design for 3D in vivo imaging of the middle ear. *Biomed Opt Express*. 2017;8:260-272.)

a distance, and (excitingly) with the incorporation of laser Doppler vibrography. This is a significant step in translating OCT into an ME imaging and functional diagnostic tool for CHL, as it will allow the live, dynamic assessment of ossicular and TM vibrational patterns in response to sound.⁴⁶ Another group achieved 3D visualization through a wide-field, diagonal-scanning handheld device that overcame motion artifact by crossing over the same location with each scan.⁶³

Other Imaging Modalities of the TM and ME

Advanced imaging tools are likely to play an important role in planning TM and ME surgery by measuring the size and shape of biomaterials used in reconstruction. The need for this information has been driven with the advent of 3D bio-material printing.⁶⁴ Although it has been demonstrated that OCT technology can provide topographic data, advances in other imaging modalities may provide solutions. Historically, endoscopic photography to achieve “entire” TM images was first performed in 1967,⁶⁵ and fluorescein angiography via endoscopy was later used to visualize TM microvasculature and demonstrate temporalis fascia graft revascularization 2 to 4 weeks posttympanoplasty.⁶⁶ Structured light imaging is a 3D scanning technique where patterned light (often vertical bars or grids) is projected on an object and, depending on how these patterns deform about the surface, its depth and surface topography can be recorded.⁶⁷ When adapted into a handheld otoscope⁶⁸ or into a surgical binocular microscope,^{67,69} structured light is an effective and low-cost approach to acquiring the 3D surface topography of the lateral TM. An older low-cost technique used to map the TM surface is Moiré topography, an established profilometry technique that creates contour maps from the overlapping interference patterns of coherent light from 2 sources.^{70,71} Surface topography has also been captured through a light field otoscope based on a plenoptic camera (**Figure 5**): an imaging technology that positions an

array of microlenses in front of a conventional image sensor to detect the direction and intensity of light rays, as opposed to the sole intensity of a conventional camera.^{72,73} More rudimentary, the lateral surface of the TM can be reproduced by 3D scanning with photogrammetry of cast impressions of the TM and deep ear canal; however, this is a more invasive approach than noncontact imaging.⁷⁴⁻⁷⁶

Accurate modeling of the TM shape is crucial to ME biomechanics and finite element modeling.⁷⁷ Confocal laser microscopy has been used to create a thickness distribution map in cat TM and demonstrate the extent of thickness variability among human TM samples.^{78,79} Micro-CT is a widely used high-resolution imaging tool for finite element modeling for the ME bony structures and cochlear hydrodynamics, and recent use of iodine potassium iodide as a contrast agent increased resolution to sufficiently visualize the thin TM.⁸⁰⁻⁸³ However, micro-CT is not yet clinically ready for patients or larger-sized objects. Last, high-frequency ultrasonography has demonstrated potential utility in ex vivo human cadaver TM as an ME diagnostic and monitoring tool through real-time vibrometry, though disadvantaged to OCT by its need for saline as an imaging medium.⁸

Implications for Practice

In its current state, OCT for clinical imaging in otology is still far from reaching broad clinical use. In some respects, it offers significant value over existing imaging modalities (CT, MRI, and micro-otoscopy), but many pathologic conditions of the TM and ME do not require diagnostic imaging beyond micro-otoscopy. At its inception, retinal OCT provided an image that could not be achieved with any other technique, and yet it still required 5 to 10 years to fully reach clinical use. For otology, while CT and MRI do not provide the high resolution of OCT, they can still provide imaging sufficient for the accurate radiologic diagnosis of causes of ME opacification, including cholesteatoma, glomus tympanicum, ME schwannoma, congenital

Table 2. TM Imaging Modality Types.

Imaging Modality	Resolution, μm	Penetration Depth	Measured Value	Utility for TM and ME Imaging
Optical coherence tomography	5-10	1-3 mm	Optical scattering	High-resolution, noninvasive measurement, rapid 3D ME and TM capture
Computed tomography	400	NA	Absorbed ionizing radiation	Unable to resolve the thin TM but excels in bony features
Micro-computed tomography	1	NA	Absorbed ionizing radiation	Excellent for small objects, not ready for clinical use
High-frequency ultrasound	30-60 (at 50 MHz)	10 mm	High-frequency ultrasound waves reflected from deep structures	Lower resolution and requires saline as a conducting medium but provides greater penetration depth over OCT
Light field imaging	50-60	None (surface only)	Direction and intensity of light via lens microarray	Acquires TM surface topography but a more costly, early technology
Structured light		None (surface only)	Deformation of projected patterned light (vertical bars)	Real-time profilometry for quantitative TM deformation will assist with otitis media with effusion but limited by the reflectivity of TM
Moiré topography		None (surface only)	Overlapping interference patterns of coherent light	An older method to re-create the 3D surface topography of the TM but is likely inferior in resolution to other modalities
Confocal laser microscopy	5	300-400 μm	3D reconstruction optical slices gained from laser imaging	High-resolution imaging, but limited depth of focus requires a flattened TM and is impractical for in vivo imaging

Abbreviations: 3D, 3-dimensional; ME, middle ear; NA, not available; OCT, optical coherence tomography; TM, tympanic membrane.

malformations, and chronic ME inflammation.⁸⁴ OCT has provided some detailed pictures and functional information, such as biofilm presence, TM thickness, and ossicular chain vibration, but the data provided will hold limited clinical value until validation in larger patient trials.

Yet the future of OCT for otology remains bright. In the future, OCT can play a large role in ME infection diagnosis and management. OCT can detect and quantify ME effusions better than what regular otoscopy allows, which will provide earlier diagnosis and an indication of severity at first diagnosis. A research OCT system costs approximately US \$50,000 to \$100,000, and a clinical OCT device for otology will likely have a cost similar to that of ophthalmic OCT (\$300,000). OCT devices are significantly cheaper than MRI (\$1-\$3 million) and CT (\$1-\$2 million) scanners; however, they are several times more expensive than commonplace clinical tools, such as an outpatient microscope (\$5000-\$10,000), tympanometer (\$2000-\$4000), or otoscope (\$100-\$200). As the drive for lower-cost OCT continues, a price point may be reached where it can be integrated and potentially replace the standard otoscope. Smaller OCT systems will assist clinical translation; OCT “on a chip” aims

to miniaturize OCT to the size of a coin by implementing optical components within integrated silicone photonic chips, and it has reached proof of concept.⁸⁵ OCT elastography and vibrometry will develop as tools to measure effusion viscosity, which may be used to determine the pathogenesis of OM. Biofilm clearance may be used as a metric of antibiotic responsiveness or success of tympanoplasty tube placement. Specific otopathogenic bacterial species may be identified through Raman spectroscopy, allowing directed antibiotic therapy.⁸⁶ For hearing diagnostics, OCT vibrography will assist in identifying causes of CHL within the TM and ossicular chain. For surgical follow-up, the high resolution of OCT will allow the monitoring of tympanoplasty graft healing and integration at the microscopic level.

To achieve this future, superior whole-field, real-time 3D imaging with adequate axial resolution to image into the ME will be required. Powerful imaging technology, as summarized in **Table 2**, continues to develop at a rapid pace. Multiparameter imaging such as OCT with vibrometry or elastography in a portable form factor will herald a new era in otologic diagnostic and monitoring imaging. To make

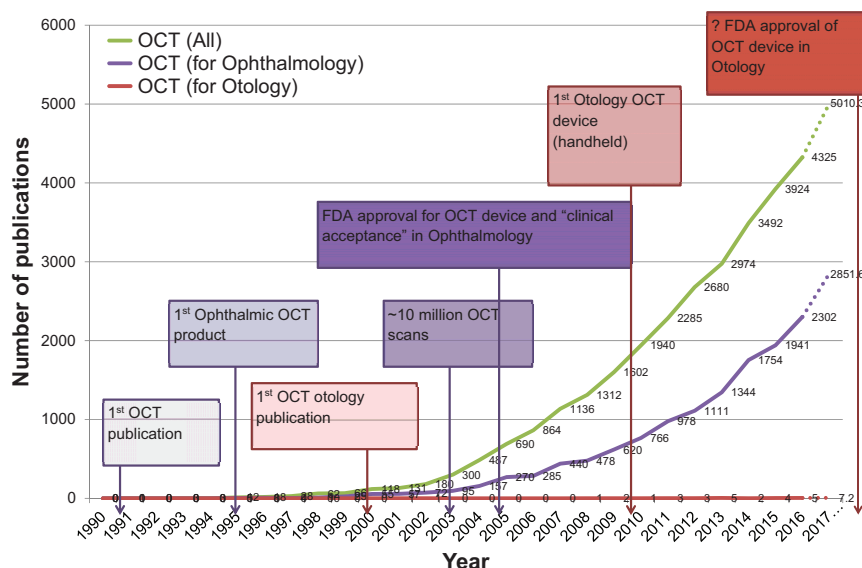


Figure 6. Key milestones in the life cycle of optical coherence tomography (OCT) in ophthalmology (purple) versus OCT in otology (red) as represented by number of publications on PubMed. FDA, Food and Drug Administration.

OCT imaging data relevant to clinicians, clinical practice guidelines for otitis media will require changes to reflect the role of biofilm presence and OCT-based diagnosis.⁸⁷ Further longitudinal studies in geographically varied populations and age groups are required to validate the role of OCT-identified ME biofilm.³³ For ME imaging, increasing the field of view and addressing signal attenuation and artifact production from the TM with faster imaging speed will be key for expanding the role of OCT in the ME and, potentially, inner ear. A database of normal and diseased TM topography and ME imaging may aid machine-assisted diagnosis.⁸⁸

Lessons may be learned from the life cycle and lengthy road to clinical acceptance that OCT took in ophthalmology. OCT for otology finds itself in a position similar to that of OCT for ophthalmology at its early inception >2 decades ago, with various publications demonstrating proof of concept for clinical application yet without clinical acceptance (**Figure 6**). While technological advancements increased OCT imaging speeds, the tipping point in OCT for ophthalmology (as later reflected on by the inventing group of OCT¹⁷) was the development of anti-VEGF therapy for exudative age-related macular degeneration, where OCT played a unique role in identifying treatment response. This gave immediate clinical applicability and linked both diagnosis and therapy. For otology, OCT technology in terms of image resolution and 3D volume acquisition speed surpasses what is clinically needed for diagnostics. However, in the absence of an age-related macular degeneration “tipping point” for otology, clinical acceptance will require focused development to fully utilize the noninvasive, higher-resolution, and imaging speed advantages of OCT. An ecosystem that allows greater interaction among entrepreneurs, government funding institutions, clinician scientists, researchers, and medical device industries will assist this development.¹⁷

Persistence from research groups to optimize OCT for clinical applications will see to a growing body of supporting evidence for OCT use in otology and commercial interest. The threshold for OCT to enter clinical otology has been set higher by the near-sufficient imaging technology in everyday use. The challenge for future development of OCT imaging in otology will be to focus on the advantages that it provides over existing imaging and to provide clinically relevant information to clinicians beyond that from CT or MRI.

Conclusion

As OCT continues to develop as a powerful clinical and experimental imaging modality, the price, user-friendliness, and clinical usefulness of handheld devices must be considered. Otitis media diagnostics and ossicular chain assessment are key areas where OCT may demonstrate benefit, particularly through noninvasive identification of specific otopathogens in biofilm and with integration with other parameters, such as vibrography and elastography for CHL. OCT for otology still requires significant focused development to reach common clinical use. The barriers of signal attenuation and OCT optics are being addressed to image beyond the intact TM with OCT. Moving forward, larger clinical trials focused on the long-term outcomes of OCT-based diagnoses are required to push forth the role of OCT in otology.

Author Contributions

Hsien Ern Ivan Tan, review concept and design, literature search, analysis, and drafting and preparation of entire manuscript, all figures and tables, writing of response to reviewers document; **Peter Luke Santa Maria**, review concept and design, critical review, manuscript revision, influenced direction and flow of manuscript, extensive clinical input to assess relevance of OCT,

final approval of version, feedback on response to reviewers document; **Philip Wijesinghe**, critical review, review concept, manuscript revision, contribution to design and flow of manuscript sections, final approval of version, OCT technical expertise, suggestions for layman explanation for technology, feedback on response to reviewers document; **Brendan Francis Kennedy**, critical review, manuscript revision at each stage, final approval of version, OCT technical expertise, expansion on future trend of OCT technology, feedback on response to reviewers document; **Benjamin James Allardye**, critical review, manuscript revision, perspectives on role of OCT as research tool, input from an materials engineering perspective, final approval of version, feedback on response to reviewers document; **Robert Henry Eikelboom**, critical review, manuscript revision, suggestions of other TM and ME imaging modalities, final approval of version, feedback on response to reviewers document; **Marcus David Atlas**, critical review, manuscript revision, elucidating the clinical needs to create relevance for OCT in otology particularly in the context as a surgical tool, of final approval of version, feedback on response to reviewers document; **Rodney James Dilley**, critical review, manuscript revision, final approval of version, comparisons to ophthalmology, feedback on response to reviewers document, overall flow of manuscript.

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Supplemental Material

Additional supporting information is available in the online version of the article.

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