

## Visualizing Acute Otitis Media with Non-Invasive OtoSight Technology: Advanced OCT-Based Imaging of the Tympanic Membrane and Middle Ear Effusion Changes across Course of Treatment

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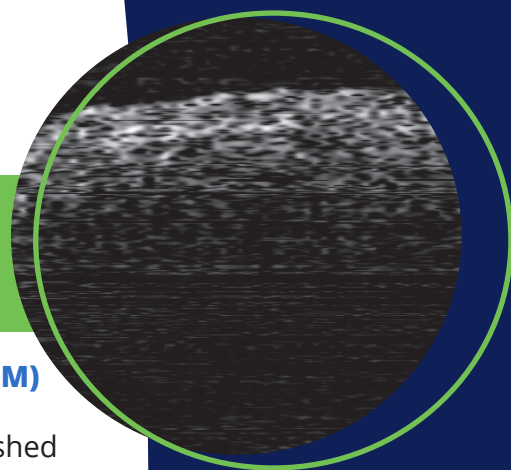
**This is a longitudinal analysis demonstrating how the OtoScan helps to determine the presence or absence of fluid in the middle ear, characterize the type of fluid, visualize the fluid's density, and can do all of this even in the presence of significant wax.**

### I. Challenges in diagnosing and researching Acute Otitis Media (AOM)

The impact of otitis media (OM) on children's health has been well established as the most common driver of pediatric office visits, antibiotic prescriptions, and outpatient surgery performed on children.<sup>1,2</sup> These outcomes in turn raise several key issues, most notably <sup>2,3</sup>:

- **inaccuracy and over-diagnosis** of acute otitis media (AOM) with otoscopy, leading to over-prescription of antibiotics and over-use of tympanostomy tube surgery, and
- concerns regarding **inconsistencies in treatment and follow-up** that can be costly and risky, particularly when it comes to surgery on very young children.

In updating the 2004 AOM guidelines, the American Academy of Pediatrics notes "there is no gold standard for the diagnosis of AOM."<sup>3</sup> As a result, AOM is often over-diagnosed—or sometimes under-diagnosed—by primary care clinicians due to the subjectivity of diagnosing based on interpretations of the tympanic membrane (TM), as well as OM's extensive symptom overlap with other diseases.<sup>1,3</sup> Identifying the presence or absence of middle ear effusion (MEE) plays a critical role when it comes to diagnosing ear infections and determining whether antibiotics are an appropriate course of treatment. The presence of fluid in the middle ear is the most reliable indicator of OM, and accurate assessment of this fluid is crucial in differentiating between AOM and otitis media with effusion (OME). Distinguishing AOM from OME is critical because their respective treatment needs are very different: AOM can be treated with antibiotics, but OME should not.<sup>4</sup> Current practices of diagnosing based on the subjective appearance of the TM often lead to overdiagnosis of AOM and underdiagnosis of OME, which can lead to unnecessary treatments, specifically, the over-prescription of antibiotics and consequent rise in antibiotic resistance.<sup>1,4</sup> When considering treatments that bear risks such as antibiotic resistance or surgery, a clearer way to determine the presence of MEE *in vivo* becomes critical in order to determine the most effective course of action.



Among the challenges of advancing OM research are the fundamental limitations of current clinically used diagnostic technologies and their inability to visualize cellular-scale structural changes in the eardrum and middle ear space *in vivo*. The most common diagnostic tools—otoscopy and otomicroscopy—may enable observation of the eardrum surface, however the picture they provide relies on subjective interpretation and is therefore not always conclusive. The use of an otoscope involves a fair amount of subjectivity in interpreting what the clinician sees on the surface of the TM in order to determine what is happening in the middle ear. Much remains to be learned about TM and middle ear structural changes during OM that otoscopy cannot reliably capture, and the American Academy of Pediatrics notes a need for “devices that more accurately identify the presence of MEE and [TM] bulging that are easier to use than tympanometry during office visits...especially in the difficult-to-examine infant.”<sup>3</sup>

This reliance on interpretation based on heuristic observations of the TM becomes a potential source of confusion in diagnosis. For instance, an image of the TM surface may appear to show the presence of a vesicle or inflammation on the eardrum, however otoscopy is not able to conclusively determine whether the abnormality is a fluid filled bleb without MEE or a bulging monomeric TM with a middle ear full of fluid. As noted above, when it comes to differentiating between AOM and OME, the position, color, and transparency of the TM is used as a proxy to determine the likelihood of MEE presence.<sup>4</sup> The diagnosis, therefore, rests on the clinician’s subjective interpretation of whether the TM is bulging or retracted, which may be difficult to gauge, particularly when examining young children in pain, often with obstructive earwax.

## **II. OtoSight Middle Ear Scope Technology**

The foundation of OtoSight technology lies in Optical Coherence Tomography (OCT), a non-invasive imaging modality, analogous to ultrasound, which allows a clinician to see through the eardrum and assess the middle ear. Instead of sound waves, however, OCT uses near-infrared light to provide 2-D views inside living tissue. OtoSight Middle Ear Scope technology provides clinicians with a safe, efficient diagnostic tool for office visits, producing images in real time, similar to an ultrasound.

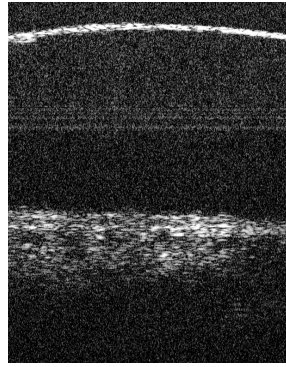
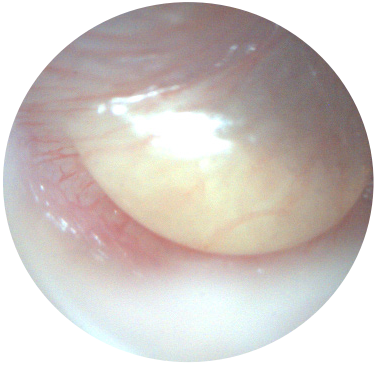
OtoSight technology provides a clinician with a digital otoscopy view, as well as an OtoScan: an image to accurately visualize, in high resolution, a view of the eardrum and middle ear, in depth. Based on the strength of the signal reflected, it is possible to detect boundaries of bubbles or pockets, as well as to determine whether those pockets are filled with air or fluid. For instance, a denser and brighter OtoScan signal behind the TM corresponds to the high turbidity fluid characteristic of AOM, while a less dense/bright signal corresponds with the low turbidity fluid indicative of OME. The images produced by OtoSight technology can also help clinicians distinguish between TM thickening and TM layer separation, providing a clearer picture of how the ear is impacted by a particular infection.<sup>5</sup>

## **III. Longitudinal study based on OtoSight Middle Ear Scope Technology imaging**

The subject of this study was a 29-year-old male with a history of OM in childhood. He presented with a unilateral bulging erythematous TM and the presence of MEE. The subject had experienced a recent mild otalgia, lasting less than 48 hours, but no fever. He did report significant hearing loss. The subject was diagnosed with unilateral AOM and prescribed a 10-day course of Augmentin.

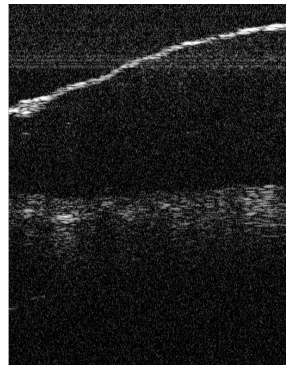
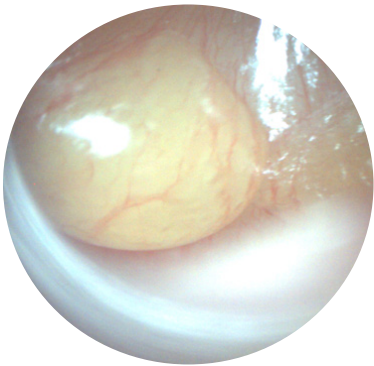
Throughout the course of treatment, daily imaging was conducted to longitudinally track cellular-scale structural changes of the TM and middle ear in order to observe whether the depth-resolved view through the TM provided by the OtoScans affords additional information regarding AOM pathology. The subject was longitudinally imaged daily using OtoSight technology over a 3-week period, starting with the detection of the infection through the 10-day course of antibiotics and for an additional 10 days to track and confirm resolution of the infection.

### Day 1:



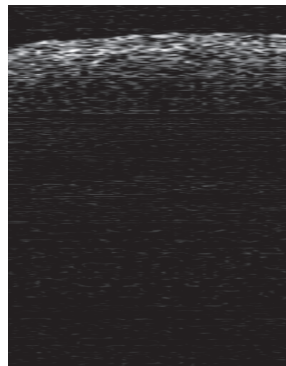
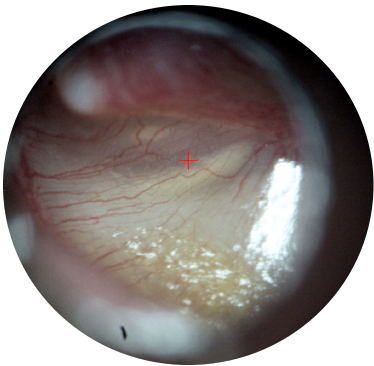
On **Day 1** of the study, the OtoScan showed what appeared to be epidermal layer separation in the TM and the presence of highly dense and bright OtoScan signal indicative of purulent MEE behind the TM. From the otoscopy image, several bulges appeared on the TM, consistent with a vesicle. The OtoScan, however, showed that these structures appeared to be neither solid nor filled with purulent fluid. The absence of a signal between the outer boundary of the vesicle and the TM show that these vesicles formed on the surface of the TM were more likely pockets of air or blebs filled with a very clear transudate that does not reflect the near-infrared light.

### Day 2:



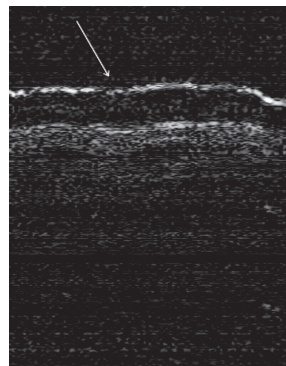
The images from **Day 2** were taken approximately 12 hours after the subject started the course of Augmentin. They showed transformation in the size and location of the blebs. From the otoscopy images, it would appear the vesicles had merged, however the topography observed in the OtoScan showed that while the vesicles had pressed into each other, a thin boundary was still visible between them. The OtoScan also showed signs that the MEE directly behind the TM was slightly less bright/dense than Day 1, and therefore likely starting to dissipate.

### Day 3:



On **Day 3**, on the OtoScan the vesicles appeared to deflate, and the otoscopy images also showed the vesicles starting to shrink.

### Day 4:

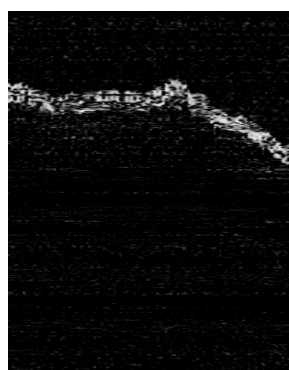
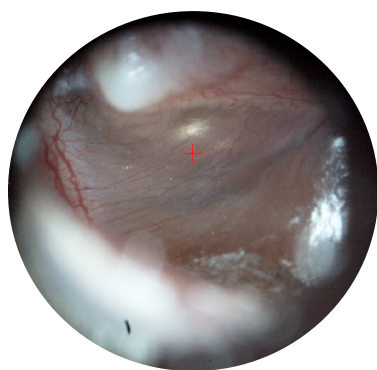


Starting on **Day 4**, the continual decrease in brightness and density of the MEE signal on the OtoScan would be indicative of continued resolution of the purulence. This trend would continue for the next three days. While there was little change in the otoscopy images from **Days 4-6**, the OtoScans show that each day the fluid reflectance signal became progressively weaker, indicating that the fluid was becoming less purulent.

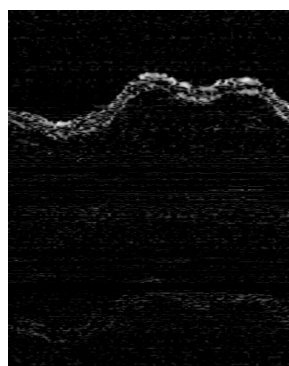
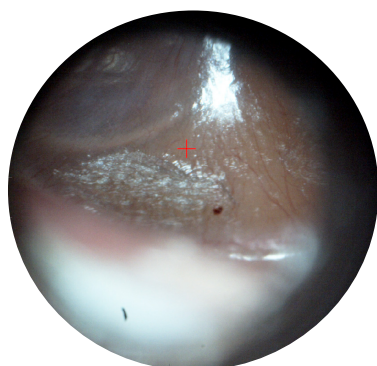
Also visible is the scab/crust on the external portion of the TM. This is visible on the OtoScan by the thin line above the TM (see arrow).



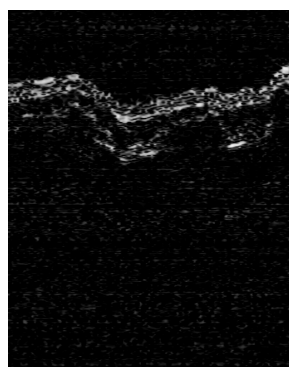
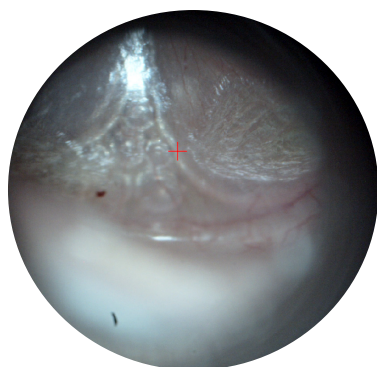
### Day 7:



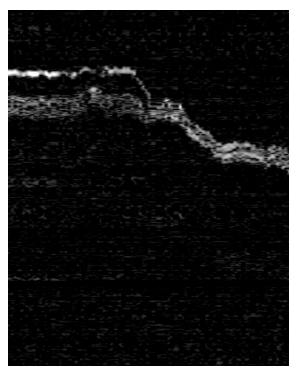
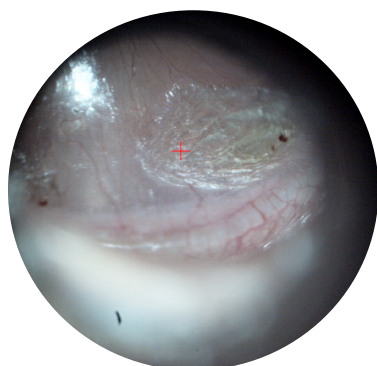
### Day 8:



### Day 9:



### Day 10:



**Day 7** marked a significant difference on both the otoscopy and OtoScan images. The OtoScan confirmed a decrease in MEE turbidity on Day 7 that continued to decrease into **Day 8**.

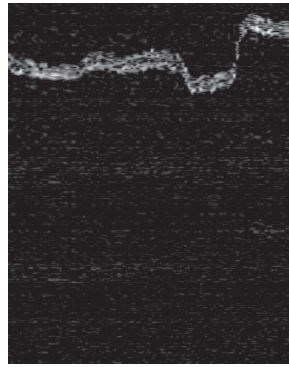
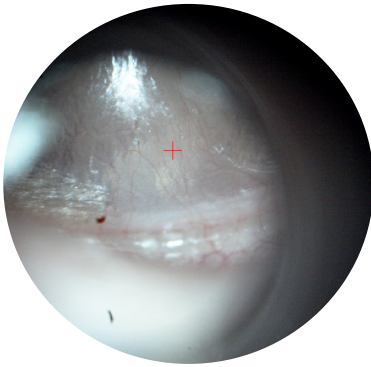
**Day 9** then saw the appearance of multiple bubbles in the MEE, clearly visible on the otoscopy images. The OtoScan confirmed that these bubbles were located in the MEE. At this point the subject reported a noticeable improvement in hearing, though not yet fully restored. When swallowing or chewing, the subject noted a crackling sound consistent with successful valsalva maneuver performance.

On the final day of antibiotic treatment, **Day 10**, the subject reported fully restored hearing, and the OtoScans showed no remaining traces of MEE. The OtoScans confirmed the absence of MEE and, the air pockets on the TM surface were visibly deflated. The lack of MEE signal in the OtoScans provides a clear sign that despite the appearance of a slightly thickened TM—likely due to lingering swelling from the infection and its resolution—eustachian tube function had returned, an indicator that the 10-day course of Augmentin had resolved this case of AOM.

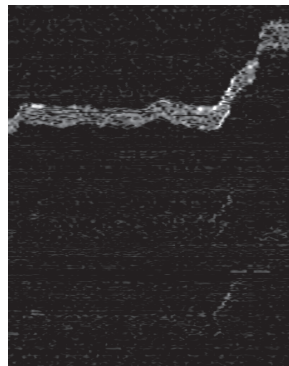
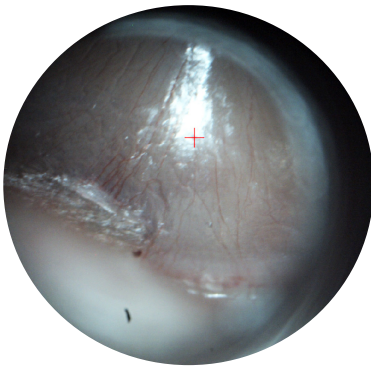
In order to persistently follow up after the treatment, the subject continued with daily ear imaging to monitor ear health resolution and confirm the lack of MEE recurrence. On **Day 15**, otoscopy imaging looked fairly similar to Day 10, however OtoScans showed that the TM was continuing to heal, and the vesicles had continued deflation compared to Day 10. OtoScans still showed the absence of MEE and therefore no AOM recurrence. Finally, on **Day 21**, the TM appeared to be completely healed in both the OtoScans and otoscopy images.

As Table 1 outlines, the information gained from the OtoScans offered more detail than the otoscopy imaging, allowing the clinician to better understand the location of vesicles as well as the presence or absence of MEE. This additional data provided a more thorough understanding of what was happening in the TM and inside the middle ear, as well as further confirmation that appropriate treatment had resolved the infection.

## Day 15:



## Day 21:



**Table 1: Description of OtoScans vs. Otoscopy imaging throughout course of treatment**

	<u>OtoScans</u>	Otoscopy imaging
<b>Day 1</b>	High turbidity shown on <u>OtoScan</u> under the TM represents purulent fluid Epidermal layer separation in the TM	Fluid visible Large vesicles present on or in the TM
<b>Day 2</b>	Signs that highly turbid fluid is starting to dissipate in middle ear Epidermal layer separation in the TM	Fluid visible Vesicles appear to be merging
<b>Day 3</b>	Meniscus from high turbidity fluid visible on <u>OtoScan</u> due to an air pocket in the middle ear Vesicles appear to be deflating on the surface of the TM	Fluid visible in inferior quadrants of TM Vesicles appear to be deflating
<b>Days 4-6</b>	Continual decrease in brightness and density of fluid on <u>OtoScan</u> TM vesicles remain	Fluid challenging to see with otoscopy Little change in vesicle appearance Minimal change across 3 days
<b>Day 7</b>	Low turbidity fluid visible on <u>OtoScan</u> continues to reduce in intensity TM vesicles remain	High turbidity fluid no longer visible Unable to identify level of turbidity in visible fluid
<b>Day 8</b>	Low turbidity fluid visible on <u>OtoScan</u> continues to reduce in intensity TM vesicles remain	High turbidity fluid no longer visible TM appears to be resolving infection TM similar to Days 3-7
<b>Day 9</b>	Multiple bubbles appear on <u>OtoScan</u> denoting resolution of fluid	Bubbles visible TM vesicles remain
<b>Day 10</b>	No remaining traces of fluid on <u>OtoScan</u> TM vesicles remain	Fluid not visible TM vesicles remain
<b>Day 15</b>	<u>OtoScan</u> reveals the absence of fluid in the middle ear TM vesicles nearly resolved	Fluid not visible TM vesicles nearly resolved
<b>Day 21</b>	No trace of fluid or TM vesicles	TM clear and appears healed

## IV. Implications for future research, diagnosis, and treatment

This longitudinal series of images adds to the breadth of findings indicating OtoSight Middle Ear Scope technology is a promising imaging modality that allows for a better understanding of OM and the resultant microstructural changes.<sup>1,6</sup> The additional detail provided by OtoSight technology allows clinicians to see the structure of the TM and middle ear more clearly, which can help improve the efficacy of not only diagnosis, but also treatment management.

As discussed above, current clinical tools are limited and require clinicians to subjectively use the TM as a proxy for what is happening in the middle ear, which can lead to accuracy problems in diagnosis. Being able to directly visualize the contents of the middle ear would allow clinicians to confirm the presence or absence of MEE, an integral first step in both the American Academy of Pediatrics and American Academy of Otolaryngology clinical practice guidelines for AOM and OME, respectively<sup>3,4</sup>, which can help address the current issues of over-diagnosis of AOM and underdiagnosis of OME discussed earlier. OtoSight imaging shows promise in helping clinicians distinguish between a separation of layers in the TM, as opposed to a thickening of the TM, and most importantly, it can identify the presence or absence of MEE in spite of the obscuring effect of TM pathology.

Furthermore, with current clinical diagnostic tools, clinicians also run the risk of misinterpreting whether a case of AOM or OME has resolved. As we saw on the Day 10 images, OtoScans provided an in-depth view allowing the clinician to see the structure of the TM and contents of the middle ear more clearly.

Clinical use of the OtoSight Middle Ear Scope shows promise in three key areas:

- determine the **presence or absence of fluid in the middle ear**
- evaluate the **turbidity of middle ear fluid**
- accurately determine the presence of fluid or air in the middle ear **in the presence of earwax**

The combined images generated by the OtoSight Middle Ear Scope (digital otoscopy + OtoScan) provide a clearer picture of what is happening beyond the surface-level view obtained from standard otoscopy. This holds promising implications for improved accuracy in diagnosis as well as proof of disease resolution when it comes to treatment management.

#### References:

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