Key Considerations in the Purchase of Advanced Ophthalmic Diagnostics: *The Evolution of OCT Technology*

Shareef Mahdavi | SM2 Strategic | Pleasanton, CA

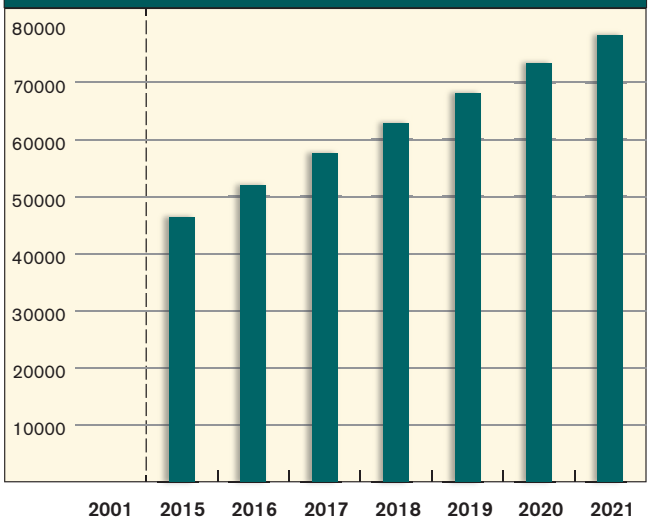
Among medical specialties, ophthalmology has earned distinction for rapid advances in both diagnostic and surgical capabilities, in part due to the overwhelming success of cataract surgery as a procedure that transformed ophthalmology into a distinct specialty (evolving from its status as EENT (Eye, Ear, Nose and Throat) where most procedures now take place in a surgery center or medical office rather than in a hospital. Innovation has extended to all parts of the eye, most notably the cornea (e.g., laser vision correction) and the retina with its multiple approaches to imaging ultrafine structures.

With the rise of new therapeutic treatments for macular degeneration, diabetic retinopathy, and glaucoma, the need for more sophisticated tests to both diagnose and monitor disease progression has driven demand for optical coherence tomography. Invented in 1991 through a collaboration of researchers and clinical ophthalmologists (J. Fujimoto, E. Swanson, D. Huang, A. Fercher, C. Hitzenberger, J. Schuman), Optical Coherence Tomography (OCT) was commercially introduced by Zeiss in 1996.

Within five years, the original Time Domain based technology was supplanted by Spectral Domain, which was significantly faster with much better resolution. During the following 15 years, OCT grew rapidly and had commercial versions from more than a dozen manufacturers. Market Scope estimates that with more than 50,000 units in use worldwide, OCT accounts for 20% of all ophthalmic diagnostic equipment purchased, with retinal evaluation as a whole commanding nearly 38% of all spending. Over the next 4-5 years, demand for OCT devices is expected to continue to be strong, with an installed base increasing more than 50% to 78,000 units. See Figure 1.

This report, commissioned by Zeiss, covers key considerations for ophthalmic practices and institutions deciding how to invest in OCT technology going forward.

Figure 1: Worldwide Number of OCT units in use, 2001–2021
(data courtesy of Market Scope)



Roles on the Path to Commercialization

The next generation of OCT, known as Swept Source OCT (SS-OCT), shows promise to continue enhancing the capabilities of retinal and choroidal imaging and eventually will deliver better sensitivity and depth of imaging along with increasingly sophisticated algorithms for analysis. SS-OCT shows a potential to provide clinicians with more answers earlier in the quest to preserve eyesight for their retinal disease and glaucoma patients.

Multiple manufacturers, including Zeiss and Topcon, have announced development programs around this technology, which has potential to create a significant improvement in speed, resolution and depth of imaging. Given the cost of the equipment, as well as associated maintenance and upgrades, clinicians should pay close attention to the variables affecting development, commercialization and ultimate acceptance of this new technology.

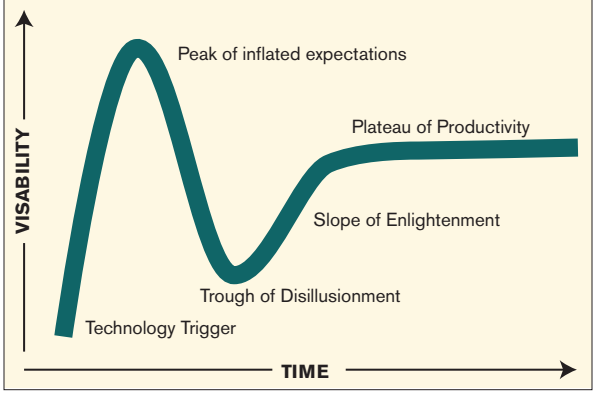
The Role of Hype

Given the rapidly increasing number of articles, peer-reviewed papers and presence at the 2017 ARVO meeting, the level of excitement among clinicians is understandable. Publicly, both Zeiss and Topcon have acknowledged that Swept Source is the future of OCT and have introduced instruments that can be purchased. There is an audible buzz among researchers about what Swept Source could mean in terms of improved diagnostic and monitoring capability; this early support is indeed critical to maintain project funding and gain initial experience while the technology goes through iterations of improvement.

There is a difference, however, between a research-level device and one that is ready for use in the clinic. Clinical research is a key step that allows a technology to be properly vetted before becoming commercially available. A review of the literature demonstrates that many unknowns exist regarding the clinical benefit of Swept Source, especially when compared with currently available Spectral Domain.

As of yet, there is no clear-cut advantage in terms of resolution, image quality, or speed (see next section). Most papers published to date can be summarized as "Swept Source is new and exciting but hasn't yet demonstrated any meaningful improvement in ability to diagnose." Regardless, SS-OCT is receiving significant visibility and is subject to a great deal of hype in the media. This phenomenon is common with potential technology breakthroughs as illustrated by the Hype Cycle. Originally developed by research firm Gartner, it provides a framework to understand how even the announcement of a new technology can lead to huge expectations. If not met, those failed expectations lead to disillusionment. Over time, the technology gets understood and next-generation versions are able to meet customer requirements and achieve market acceptance. *See Figure 2*.

Figure 2: Hype Cycle: The change in expectations for new technology
(Source: Gartner Research)



The Role of Speed

With light-based technology, speed matters. The original Time Domain OCT (TD-OCT) operated at 400 Hz, meaning it could perform 400 axial scans per second. That seems fast until you realize that Spectral Domain OCT (SD-OCT) now performs at 70 kHz, or 70,000 axial scans per second. The faster speed translated to a direct clinical benefit by allowing three dimensional imaging of retinal structures, and increasing the decision-making capabilities of retina and glaucoma specialists, as well as general ophthalmologists and optometrists.

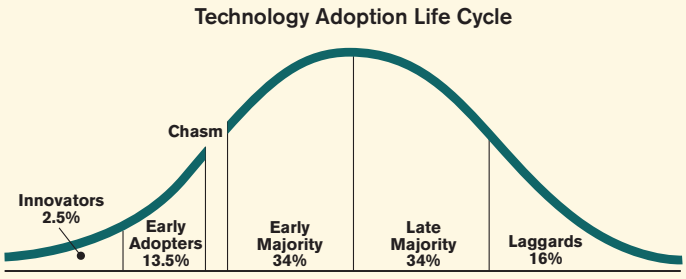
Swept Source OCT currently operates at 100 kHz. Researchers indicate that to achieve a meaningful improvement in clinical value similar to what occurred between TD-OCT and SD-OCT, Swept Source OCT devices will need to scan at 400 kHz. While this is technically feasible, commercial availability of the 400 kHZ laser source from photonics suppliers is estimated to be 18-24 months away (i.e., early 2019).

The Role of Being First

Author and Venture Capitalist Geoffrey Moore's book *Crossing the Chasm* offers another framework to describe the diffusion of technological innovation and how the path towards widespread commercial acceptance of any new technology (which in medicine would equate to "standard of care") is neither smooth nor guaranteed. The very first users of a technology are known as Innovators, risk takers who want to be able to tinker, experiment and determine a product's benefits by accessing a technology as soon as its available. The next wave of customers, known as Early Adopters, want to be involved in setting standards for a product, giving it a chance to achieve mainstream acceptance with Early and Late Majority users. By virtue of the number of units in use worldwide, Spectral Domain has gained mainstream acceptance. *See Figure 3*.

The ability of Swept Source to cross the chasm and become used by the majority of doctors remains to be seen. As the technology gains acceptance, many manufacturers will be drawn to the category and seek to incorporate this laser source into their OCT devices. As discussed in the next section, the first two manufacturers to announce Swept Source are taking very different directions to the market.

Figure 3: Technology Adoption: Segmenting Different Customer Buying Behavior
(Source: Geoffrey Moore, *Crossing the Chasm*)



The Role of Research

Topcon: "Go Commercial" Topcon initially developed SS-OCT as a research tool but has since made it commercially available to clinical practices that want access to the technology. They are on their second OCT hardware platform to accommodate Swept Source since initial launch in 2012. While this may well appeal to an Innovator mindset as described above, use of this particular technology beyond research is fraught with risks beyond financial cost. One key concern is the interpretation of data. At present, there is no reference point or baseline data available to compare images taken via SS-OCT with those previously

taken via SD-OCT. In this scenario, the clinician is limited to his own experience rather than being able to tap into the collective wisdom of a larger group of peers.

Zeiss: "Lab to Lane" By contrast, Zeiss has specifically chosen to limit access to its SS-OCT platform to researchers who seek to help understand and validate the clinical potential of Swept Source. Zeiss has formalized this approach through the launch of the Advanced Retina Imaging (ARI) Network, which represents a global collaboration of leading clinicians with Zeiss scientists and engineers. Formed at ARVO in 2016, the ARI Network allows clinicians to push boundaries in their own research as well as provide the ground rules for how to best develop and use SS-OCT in a clinical setting. In its first year alone, research on Swept Source OCT by ARI Network members led to 34 papers and posters presented at the 2017 ARVO meeting.

From the perspective of technology adoption, the latter approach from Zeiss seems better positioned to help Swept Source achieve mainstream adoption once commercially available.

"It's a marvelous piece of technology, and we can see things we have never seen before. While it's primarily a research tool right now, my prediction is that it's going to become the standard-of-care instrument within the next few years" commented Philip Rosenfeld, MD, PhD. Dr. Rosenfeld is a professor of ophthalmology at Bascom Palmer Eye Institute and also serves as chairman of the ARI Network.

The Role of Software

Microprocessor-based equipment revolutionized ophthalmic diagnostics forever, both in automation of tasks to ensure consistency (e.g., automated perimetry) and in the ability to instantly analyze results against prior tests and/or against large databases. As hardware becomes increasingly sophisticated, a device's software becomes more like a "brain" to help clinicians interpret data. This is especially true in OCT, where repeatability (the ability to take the same test and get the same result) becomes crucial to understanding whether a change in a test result is real or an artifact. In essence, the ability to detect change is what separates value found in OCT devices, providing the clinical confidence needed to initiate or adjust therapy.
A prime example has been the launch of Zeiss AngioPlex OCT Angiography, a software solution that expands the capabilities of Zeiss OCT platforms to perform Angiography non-invasively without injecting dye. This software brings hardware-like functionality by improving motion tracking to increase test-to-test reliability; this is accomplished via precise location of reference structures.

Launched in 2015, OCT-A is gaining rapid adoption among retinal specialists as a primary means of testing for macular disease. When compared with Fluorescein Angiography, OCT-A is far faster and more convenient to both physician and patient. OCT-A takes less than a minute versus up to a half hour (for intravenous dye to be administered and take effect). The ability to see in vivo retinal structures is unparalleled. While not yet a full replacement for FA and FAF (e.g., FA is able to detect leakage, and certain patients have conditions that present challenges in obtaining quality OCT images), OCT-A shines in assessing retinal vascular disease and choroidal neovascularization.

"In essence, the ability to detect change is what separates value found in OCT devices, providing the clinical confidence needed to initiate or adjust therapy."

The power of software to expand the capabilities and usefulness of a diagnostic device such as OCT should not be underestimated. As described in the next section, Zeiss AngioPlex plays another key role in serving to bridge hardware that is available today with what is coming in the future.

The Role of Platform Compatibility

Given the Zeiss heritage and resulting market leadership in retinal imaging, the development of Swept Source OCT presents a significant challenge to satisfying the needs of both a large installed base and an emerging technology. Again, software plays a key role as the AngioPlex platform serves both current SD-OCT technology and emerging SS-OCT technology (PLEX Elite 9000). The same AngioPlex algorithm is used on both OCT platforms.

What this means for clinicians is a clear path forward in terms of accessing state-of-the-art technology for their patients. AngioPlex makes the translation of data collected on either platform seamless, as the differences between the SD and SS modalities are adjusted for continuity of detecting meaningful changes. This requires a significant investment by the manufacturer that pays off in the clinic in several meaningful ways. First, doctors are able to interpret data confidently regardless of platform. Second, data from patients referred to multiple clinics can be interpreted to maintain continuity of care in the analysis and treatment.

Finally, the learning curve to move from one type of OCT platform to another is significantly less than it would be without shared software. AngioPlex allows the accumulated user experience from the SD-OCT platform to transfer over to the SS-OCT platform in the future. This can be thought of as "clinical future proofing."

The Role of Price and Total Cost of Ownership

With any new technology, the first to buy any new technology are also most likely to pay a higher price than future buyers. That same construct applies to the hardware for SS-OCT, which is in its infancy. An example of this in the OCT category is Topcon's Atlantis platform, which was first launched in 2012 but has since been replaced by the Triton platform. The hardware change indicates that an upgrade was not feasible and required a complete replacement of the platform. This phenomenon is not uncommon with novel technology, as a great deal is learned in the first few iterations of hardware.

The example above illustrates the importance of TCO or Total Cost of Ownership, a concept popularized to quantify the costs over time of owning an automobile and is also widely used in computer and software industries. As applied to Optical Coherence Tomography, clinicians need to factor more than the original cost of the equipment. Service, upgrades, and supplies are the more obvious line items affecting total cost. Less obvious are soft costs including learning curves for doctors as well as technicians and opportunity costs such as extra time required to perform a test or conduct analysis on one platform versus another.

In the Topcon example, TCO may have doubled for the earliest users due to obsolescence of the first iteration of hardware. Additional cost components may be incurred due to Topcon's use of separate processors for image capture (the device) and image analysis (external computer); anecdotal evidence suggests that additional time is required to acquire, process and analyze images.

In the Zeiss example, TCO may well be reduced by the shared software across hardware platforms and the fact that Zeiss has limited the commercial availability of its PLEX Elite 9000 until it meets expectations around scanning speed as well as clinical utility.

Further, AngioPlex makes the transition from one hardware platform to the other much easier to digest financially. An investment today in SD-OCT makes sense given its compatibility with SS-OCT. The ARI Network plays a key role in achieving this compatibility; while tasked with understanding the clinical value offered by Swept Source, findings from that effort are planned to flow through to CIRRUS users via AngioPlex.

Similar to what we saw in terms of clinical compatibility, the Zeiss approach to hardware and software can be thought of as "financial future proofing."

Commentary

Having spent more than 30 years in the commercialization of ophthalmic devices, SM2 Strategic has obtained a unique vantage point in understanding the factors that serve as drivers as well as barriers to technology adoption. Without question, Zeiss has a lot at stake in terms of how it navigates the commercial issues surrounding a technology upgrade to a market segment where it has market leadership. Their history, size and presence all suggest that they will expand commercial availability of Swept Source technology beyond clinical research when it is ready and will continue to take care of the customer as they have for decades. Although their SS-OCT platform was the first to receive FDA clearance, they made a conscious decision to delay a wide release until a sufficient body of clinical understanding emerges. They also learned from the early days of OCT — when Time Domain was rapidly supplanted by Spectral Domain — of the importance of ensuring a new technology is ready for primetime. Even with Spectral Domain as the dominant approach, there are customers who still use the original Time Domain offering (Stratus). This reality simply underscores what Geoffrey Moore was trying to convey: consumer behavior (including ophthalmologists) exhibit a range of characteristics when deciding on the timing of purchase. Adoption of any new technology occurs over time, not overnight. Swept Source OCT is no different in this regard.

The advent of the ARI Network should prove highly valuable in the coming years. First, it is a novel approach to R&D. Second, its collaborative network sets the foundation for a method to rapidly learn and share findings. Finally, it goes far beyond a user group meeting and becomes a continuously available resource for new and existing users to learn how to use the technology responsibly.

OCT is an evolving case study around the timing of adoption of technology. The early research work that began in Boston in the early 1980s took a decade to coalesce and another decade to reach commercial viability. Swept Source shows great promise, but in the context of OCT's history in the diagnosis of ocular pathology, more development is required before it should be adopted in a busy clinical setting.

Shareef Mahdavi *advises physicians on technology adoption, providing insight into the decision criteria necessary for evaluation. His research extends to practice economics and patient experience in ophthalmology and other medical specialties with a strong private-pay focus. Website: www.sm2strategic.com*
