From lab to clinic

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Last month I visited my eye doctor, Harold Jacobson, for a routine checkup. After reading rows of ever-smaller letters, just as I had when my eyes were first tested in the 1970s, I asked him what new technology he was most excited about. "Optical coherence tomography," he replied. "It's a game changer!"

Jacobson had bought an OCT scanner after my previous visit, so I got to see the game changer firsthand. As a patient, I briefly looked into a pair of eyepieces. As an ophthalmologist, Jacobson reviewed a wealth of information on the scanner's screen. Beside cross sections of my left and right retinas were charts that characterized how my eyes compared with those of people in my age group. I was impressed.

I was also curious how OCT worked, so I asked Jacobson. His explanation reminded me of another technique, confocal laser scanning microscopy. Like OCT, CLSM builds three-dimensional images by rastering a probe through a transparent object. In CLSM, lenses, beamsplitters, and pinhole apertures ensure that the only strong signal to reach the camera originates from the probe, a tiny focal spot. In OCT, lenses, beamsplitters, and a Michelson interferometer ensure that the only strong signal to reach the camera originates from the probe, a tiny spot where a low-coherence beam constructively interferes with a reference beam.

Confocal imaging was conceived and patented in 1957 by cognitive scientist Marvin Minsky. Given the similarity between CLSM and OCT, I presumed that OCT had its origins in Minsky's invention. In fact, as James Fujimoto and Eric Swanson, two pioneers of OCT, recount in a 2016 review, OCT emerged in the 1970s from ultrafast optics.[1]

In 1971 Michel Duguay devised an ingenious method to gate femtosecond laser pulses and ensure that only pulses that traveled a certain adjustable distance through a sample would be recorded by a camera. Duguay predicted that his optical analog of ultrasound imaging could be used on biological tissue.

What happened in the ensuing decades to bring OCT into my eye doctor's office makes for a fascinating story. Gating femtosecond lasers was unlikely to lead to clinical devices. Fujimoto and others realized that the combination of interferometry and low-coherence light would be cheaper and more practical, especially following Gerard Alphonse's invention in 1986 of the high-brightness, low-coherence superluminescent diode.

One early challenge in developing OCT for ophthalmology was to achieve rastering that was both precisely controlled and fast enough to avoid having to immobilize patients' eyes. As Fujimoto and Swanson describe it, the solution came from appropriating technologies that had been developed for fiber-optic telecommunications and laser gyroscopes—among them, interferometric receivers and galvanic beam steering devices.

The suitability of OCT for ophthalmology was apparent from the start. Whereas most biological tissue strongly scatters light, the eye's fundus, or interior surface, is transparent. What's more, the fundus is readily accessible through the pupil. However, whether ophthalmologists would buy OCT scanners was less clear. Having a new, more effective way of diagnosing diseases is more desirable when doctors can treat the diseases they find. Fujimoto and Swanson point to the development of anti-VEGF therapy for treating macular degeneration as a powerful factor in the clinical adoption of OCT. Not all patients respond to the therapy in the same way, so it's important to monitor their progress.

Jacobson's scanner was made by Carl Zeiss, a 171-year-old company whose revenue last year was €4.88 billion ($5.57 billion). Zeiss invested in OCT in 1994 when it acquired a startup that Fujimoto and Swanson founded with ophthalmologist Carmen Puliafito in 1992. Both entrepreneurship and commercialization are necessary for improving clinical care, write Fujimoto and Swanson, but they are not sufficient. Rather, the success of OCT arose from an ecosystem that also includes government funding, collaboration and competition with research groups around the world, and clinical studies.

Fujimoto and Swanson's paper is freely available online. I urge you to read it.

Reference

1. J. Fujimoto, E. Swanson, *Invest. Ophthalmol. Visual Sci.* **57**, OCT1 (2016). PT