The Development, Commercialization, and Impact of Optical Coherence Tomography

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This review was written for the special issue of IOVS to describe the history of optical coherence tomography (OCT) and its evolution from a nonscientific, historic perspective. Optical coherence tomography has become a standard of care in ophthalmology, providing real-time information on structure and function - diagnosing disease, evaluating progression, and assessing response to therapy, as well as helping to understand disease pathogenesis and create new therapies. Optical coherence tomography also has applications in multiple clinical specialities, fundamental research, and manufacturing. We review the early history of OCT describing how research and development evolves and the important role of multidisciplinary collaboration and expertise. Optical coherence tomography had its origin in femtosecond optics, but used optical communications technologies and required advanced engineering for early OCT prototypes, clinical feasibility studies, entrepreneurship, and corporate development in order to achieve clinical acceptance and clinical impact. Critical advances were made by early career researchers, clinician scientists, engineering experts, and business leaders, which enabled OCT to have a worldwide impact on health care. We introduce the concept of an "ecosystem" consisting of research, government funding, collaboration and competition, clinical studies, innovation, entrepreneurship and industry, and impact - all of which must work synergistically. The process that we recount is long and challenging, but it is our hope that it might inspire early career professionals in science, engineering, and medicine, and that the clinical and research community will find this review of interest.

Keywords: optical coherence tomography, optics, ophthalmic imaging, femtosecond optics

FROM FEMTOSECOND OPTICS TO BIOMEDICAL OPTICS – THE ORIGIN OF OCT

Photographing Light in Flight

Optical coherence tomography is often described as the optical analog of ultrasound, generating images using the time delay and magnitude of light echoes. In fact, OCT had its origins in femtosecond optics. The concept of using echoes of light to see inside biological tissue was proposed more than 40 years ago by Michel Duguay at AT&T Bell Laboratories. Duguay’s pioneering study in 1971 “photographing light in flight” used an ultrafast laser activated optical Kerr shutter to create stunning photographs of propagating light pulses. Although light travels at approximately $3 \times 10^8$ meters per second, it was possible to “freeze” its motion using high speed photography (Fig. 1). The optical...
femtosecond measurement technique, attempting to
‘‘(Arlington, VA, USA), we applied nonlinear cross correlation, a
at the Massachusetts General Hospital (Boston, MA, USA) with
Margolis and A. Oseroff from the Department of Dermatology
visiting from the Politecnico Milano (Milano, Italy), and R.
inside
could
by gating out unwanted scattered light. He suggested that one
behind a scattering screen and partially recovering the image
remarkably close to OCT.

injury and corneal ablation.4,5 Working with S. DeSilvestri,
School (Boston, MA, USA), studying femtosecond laser retinal
Eye and Ear Infirmary (Boston, MA, USA) and Harvard Medical
collaboration with Carmen Puliafito, then at the Massachusetts
femtosecond optics might be used in medicine. We began
with an ex vivo bovine eye. It was natural to ask how
shutter can achieve picosecond resolution using a laser pulse
to induce birefringence (Kerr effect) in a chemical solution
between crossed polarizers. Duguay also demonstrated the
concept of “gated picture ranging” placing the AT&T logo
behind a scattering screen and partially recovering the image
by gating out unwanted scattered light. He suggested that one
could “see inside” biological tissues,2 a concept which is
remarkably close to OCT.

Femtosecond Optics and Ultrafast (A-Scan)
Measurements
Erich Ippen, one of the creators of femtosecond optics, came
to the Massachusetts Institute of Technology (MIT; Cambridge,
MA, USA) from AT&T Bell Laboratories in the mid-1970s and
built a major research program in ultrafast phenomena. One of
the authors (JF) was fortunate to join his team as a doctoral
student. The dye laser was state of the art technology (Fig. 2,
top panel) and generated record short pulses of less than 100
fs, enabling studies in chemistry, physics, and biology.3 Figure 2
(bottom panel) also shows an early optical ranging experiment
with an ex vivo bovine eye. It was natural to ask how
femtosecond optics might be used in medicine. We began
the M. Gustavo Duguay at Massachusetts Eye and Ear Infirmary (Boston, MA, USA) with
Margolis and A. Oseroff from the Department of Dermatology (Vienna, Austria) in 1988.11 Later studies by other groups
demonstrated many applications of low-coherence interferomet-
ery in biological tissues.12–15

The first studies at MIT were performed by an Electrical
Engineering and Computer Science (EECS) undergraduate,
John Apostolopoulos, and are described his 1989 Bachelor’s
thesis, “Micro-meter multi-layer structure analysis via femto-
second interferometry” (unpublished). Figure 4 (left panel)
from the thesis shows a modified Michelson interferometer
with dual balanced detection that was built and tested. A
compact and low-cost, low-coherence laser diode was used
profile by second harmonic generation as the time delay is
scanned, generating an A-scan. The laser operated at 625-nm
wavelength and generated 65-fs pulses, achieving an axial
distance resolution of approximately 15 μm (in tissue). Figure 2
(bottom panel) shows a first experiment with a bovine eye ex
vivo and Figure 3 (right panel) shows a femtosecond A-scan of a
rabbit eye in vivo9. Sensitivities of −70 dB or 10−7 of the incident
intensity were achieved. We tried to see inside tissue (skin), but
failed. Sensitivities were insufficient to image most biological
tissues which have high optical scattering, so we focused on the
eye because the anterior eye and vitreous are transparent.
Current OCT systems achieve 1000× higher sensitivities of −100
dB or 10−10. We also later learned to use longer 1300-nm
wavelengths, which reduce attenuation from scattering.7

Measuring Echoes (A-Scans) With Low-Coherence Interferometry
Although femtosecond optics is a powerful technology, we
suspected that it might be possible to measure light echoes
using interferometry, which has better scalability and lower
cost. Low-coherence or white-light interferometry was first
described by Sir Isaac Newton and in the 1980s it was used in
optical communications to characterize optical fibers and
waveguide devices.8–10 The first biological application of low-
coherence interferometry, measuring axial eye length, was
reported by Fercher et al. at the Medical University of Vienna
(Vienna, Austria) in 1988.11 Later studies by other groups

declared many applications of low-coherence interferomet-
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FIGURE 1. Photographing light in flight 1971. (Left) A high-speed laser optical shutter is created using a CS2 cell between crossed polarizers. An
intense laser pulse induces transient birefringence (the Kerr effect) and opens the shutter. (Center) An ultrashort laser pulse propagating through a
cell of milk and water, “frozen” by ultrahigh speed photography. The shutter speed was 10 ps. (Right) “Gated picture ranging” sees only the image
light to recover an image behind scattering material. These early studies suggested that high speed optical gating could be used to “see inside”
biological tissues. 5 Reprinted with permission from Duguay MA, Mattick AT. Ultrahigh speed photography of picosecond light pulses and echoes.
Appl Opt 1971;10:2162–2170. © 1971 Optical Society of America.
instead of a femtosecond laser, however, the experimental concept was remarkably similar to nonlinear cross correlation. The light beam is split into a reference path with a scanned distance/time delay, while a second beam is directed onto the tissue. Echo time delays and magnitudes are measured by interfering with the reference beam. Using short-coherence length/broadband light, interference only occurs when the reference time delay matches the echo delay and scanning the reference delay generates an A-scan. The thesis described potential ophthalmic applications including two-dimensional (2D) scanning to map the eye, but the sensitivity of this implementation was limited and it was not possible to obtain ophthalmic data. At that time, it was not clear that interferometry was going to be a good solution. Interferometry is notoriously sensitive to vibrations and bulk optics requires careful alignment to avoid signal loss from fringe averaging.

**The First OCT Images**

David Huang, then an MD/PhD student, continued research on low-coherence interferometry, ultimately demonstrating measurements in biological systems in 1991. Figure 4 (right panel) shows an A-scan of the anterior chamber of an ex vivo bovine eye with a 10-μm axial resolution using an approximately 800-nm low-coherence laser diode. Sensitivities of ~100 dB or 10^{-10} of the incident intensity were achieved. Transverse scanning the beam yielded information on different structures, such as the lens and iris. Interferometry measures electrical field (E) rather than intensity (I) (Intensity ~ E^2) and detects the product of the echo signal and reference electrical fields, so that weak echoes are “amplified” by the strong reference field. This is known as heterodyne gain and is used in optical communications.

David Huang showed that multiple A-scans could be displayed as a false color or gray scale image (B-scan), demonstrating the first OCT images in Science 1991. Similar concepts were also independently described by Tanno et al. in a Japanese patent, but to our knowledge were not demonstrated or published in the scientific literature. Figure 5 shows OCT images of ex vivo retina and coronary artery with corresponding histology. Imaging was performed with 15-μm axial resolution (in tissue) at 830 nm, and images are displayed using a log false color scale spanning approximately ~60 to ~90 dB. The retinal image shows the optic nerve head and nerve fiber layer with postmortem retinal detachment. The coronary image shows fibrocalcific plaque (right) and fibroatheromatous plaque (left). After 20 years, we had finally realized Duguay’s 1971 suggestion to see inside human tissue. Ophthalmic and intravascular imaging later emerged as the two largest clinical OCT applications.
beam, and a visible aiming beam, about the pupil to access a large retinal area (Fig. 6). This example underscores the importance of advanced engineering, which is required to bridge the gap between benchtop studies in an academic department and clinical feasibility studies. The community has recognized need for collaboration between fundamental scientists and clinician scientists, but the importance of advanced engineering is often unappreciated.

The First In Vivo Human Retinal Images

The first in vivo retinal images were obtained in 1993 by our collaborative group, Swanson et al.19 including Michael Hee, then an MD/PhD student and Joseph Izatt, then a postdoctoral associate. Retinal imaging was also demonstrated independently by the Medical University of Vienna, Fercher et al.20 The MIT study used the prototype (Fig. 6), which had a high-speed scanning delay (160 mm/s) enabling rapid image acquisition and real-time display, including software correction of axial eye motion. Figure 7 shows an in vivo human retinal image with 15-μm axial resolution at 840-nm wavelength. The nerve fiber layer and other architectural features could be visualized with higher resolution than previously possible. The first in vivo images of the anterior chamber were also demonstrated shortly thereafter by our group, Izatt et al. 21 We were excited, but the ultimate clinical use was unclear.

Figure 3. Early demonstration of femtosecond optical ranging (A-scans). (Left) Femtosecond echoes of backscattered light (signal) are detected using nonlinear cross correlation, mixing the signal with a delayed reference pulse. (Right) Measurement of corneal thickness in an in vivo rabbit eye, showing an axial scan (A-scan) of backscattering versus depth. An axial resolution of 15 μm (in air) was achieved using 65 fs pulses at 625-nm wavelength. Detection sensitivity was −70 dB or 10−7 (Ref. 6). Reprinted with permission from Fujimoto JG, De Silvestri S, Ippen EP, Puliafito CA, Margolis R, Oseroff A. Femtosecond optical ranging in biological systems. Opt Lett. 1986;11:150–152. © 1986 Optical Society of America.

Figure 4. Low coherence interferometry can measure optical echoes with more scalability and lower cost than femtosecond optics. (Left) Drawing from Bachelor’s thesis by John Apostolopolous (MIT 1989) showing a schematic interferometer for measuring multilayer structures in the eye [Reprinted with permission]. (Right) Measurement from Huang et al.16 demonstrating A-scans of the anterior chamber in an ex vivo bovine eye. A 10-μm axial resolution was achieved using a low-coherence diode light source at approximately 800 nm. Detection sensitivity was −100 dB or 10−100 (Ref. 16). Reprinted with permission from Huang D, Wang J, Lin CP, Puliafito CA, Fujimoto JG. Micron-resolution ranging of cornea anterior chamber by optical reflectometry. Lasers Surg Med. 1991;11:419–425. © 1991 Wiley-Liss, Inc.
Clinical Studies at New England Eye Center Suggest the Potential of OCT

Using the MIT prototype, we began clinical studies in the mid-1990s, working with Carmen Puliafito and Joel Schuman at the New England Eye Center (NEEC) of Tufts University School of Medicine (Boston, MA, USA). Michael Hee was an expert programmer and using the Apple Macintosh, he developed OCT examination protocols including circumpapillary scanning to assess glaucoma\textsuperscript{22,23} and radial scanning to map macular edema\textsuperscript{24,25}. These methods extracted quantitative information from images and were an important step toward objective assessment of progression and response to therapy. These protocols were later adopted in commercial OCT instruments and continued as clinical standards for decades. Michael Hee published over 30 papers during his doctorate and his 1997 thesis, \textit{"Optical coherence tomography of the eye",}, continues to be a reference on OCT ophthalmic design. These examples of undergraduate and doctoral research demonstrate that it is possible to make powerful contributions even at an early career stage.

Over 5000 patients were imaged at NEEC under support from the National Institutes of Health in the mid-1990s and the collaborative team investigated OCT in retinal disease and glaucoma\textsuperscript{22–30}. Carmen Puliafito organized the first OCT atlas \textit{"Optical coherence tomography of ocular diseases"} in 1996\textsuperscript{31}, which provided a framework for interpreting OCT of retinal pathologies.

Entrepreneurship and Corporate Investment

In order to impact clinical care, entrepreneurship and commercialization are critical. In 1992, we (Puliafito C, Swanson E, Fujimoto J) founded an MIT startup company, Advanced Ophthalmic Diagnostics (AOD), to commercially develop ophthalmic OCT. Although the technology, clinical, and regulatory barriers were high and there was limited evidence that OCT would be accepted by the ophthalmic community, there was a strong belief, even at this early stage, that OCT would be impactful and that a startup would expedite its impact on patient care. After 2 years, the company was acquired by Humphrey Zeiss with working prototypes and

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**Table.** Milestones in the Development of OCT in Ophthalmology

| Year  | Event                                      |
|-------|--------------------------------------------|
| 1970  | Photographing light in flight and “seeing inside” tissue |
| 1987  | Demonstration of femtosecond optical ranging (A-scans) |
| 1991  | Demonstration of OCT in vitro             |
| 1992  | First OCT startup company                 |
| 1993  | First in vivo images of the retina         |
| 1994  | Humphrey Instruments (Zeiss) acquires startup |
| 1995  | Clinical studies (glaucoma, AMD, diabetic retinopathy) |
| 1996  | First commercial ophthalmic OCT device (Zeiss) |
| 1999  | Approximately 180 units sold              |
| 2000  | Second generation ophthalmic OCT instrument |
| 2001  | Approximately 400 units sold              |
| 2002  | Third generation Stratus OCT              |
| 2003  | Demonstration of FD OCT sensitivity advantage |
| 2004  | ~10 million OCT procedures world wide     |
| 2005  | OCT becoming a standard of care           |
| 2006  | Approximately 6000 Stratus OCT systems sold |
| 2006  | Lucentis FDA approved for exudative AMD    |
| 2006  | Spectral-domain OCT enters the ophthalmic market |
| 2010  | Cumulative procedures pass ~100 million world wide |
| 2014  | Commercial OCTA introduced                |

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\textbf{Figure 5.} The first OCT images from Huang et al.\textsuperscript{17} Imaging was performed at 830-nm wavelength with 15-\textmu m axial resolution in tissue and displayed on a log false color scale spanning –60 to –90 dB of the incident intensity. (A) Optical coherence tomography of the human retina ex vivo and corresponding histology. Optical coherence tomography shows the optic nerve head contour with retinal nerve fiber layer visible as a high scattering layer. (B) Optical coherence tomography of human artery ex vivo and corresponding histology. Optical coherence tomography shows fibrocalcific plaque (right three-quarters of specimen) and fibroatheromatous plaque (left).\textsuperscript{17} After 20 years, we were able to realize Duguay’s proposal to “see inside” tissue. Reprinted with permission from Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. \textit{Science}. 1991;254:1178–1181. © American Association for the Advancement of Science.
fundamental patents; the founders of AOD continued to work with Zeiss to accelerate commercialization. Zeiss’ acquisition of OCT was led by John Moore, then President of Humphrey Zeiss, who took the visionary step to back product development with substantial financial and corporate resources. An engineer, Jay Wei, was in charge of the development effort and led the commercial development. By 1996, just 2 years after acquiring AOD, Zeiss released its first regulatory cleared commercial OCT unit.

THE LONG ROAD TO CLINICAL ACCEPTANCE

OCT Development is Almost Canceled

Although the first OCT instruments became commercially available in 1996, clinical adoption was slow and in 1999 only a total of ~180 units were sold. A second generation instrument (Fig. 8) with improved ergonomics was introduced in 2000, but in 2001 only 400 instruments were sold. Concurrent with this, John Moore left Humphrey Zeiss and we heard that new management was considering abandoning OCT. We struggled to present clinical and business arguments for continued investment. Fortunately, Zeiss continued development and the third generation instrument, Stratus OCT, was introduced in 2002. Stratus OCT had similar resolution, but faster speeds of 400 A-scans per second, increasing image pixel density and quality. The technical, clinical, and market knowledge gained from the AOD prototype, Zeiss OCT1 and OCT2 systems, combined with the advances of Stratus OCT drove OCT to become an important clinical tool, with utilization and sales growing dramatically. By 2004, the estimated number of cumulative OCT imaging procedures worldwide surpassed 10 million (Table).

OCT Gains Clinical Acceptance

The volume of published clinical data, coupled with technological improvements and reimbursement helped drive the clinical adoption of OCT. A powerful factor in OCT adoption was the development of anti-VEGF therapy for exudative AMD. Anti-VEGF therapy revolutionized the treatment of AMD, but patients had varying responses and OCT became important for identifying markers of treatment response. The concept of linking diagnostics and therapy remains a key point in business development to this day.

The risk that AOD and Zeiss took accelerated the introduction of ophthalmic OCT perhaps by as much as a decade. Although the road to clinical acceptance is long, especially for pioneers who must create both a new technology and a new market, by 2006 when the first Food and Drug Administration (FDA)-approved spectral-domain (SD)-OCT system was introduced by Optovue, commercial OCT ophthalmic system sales were dominated by Zeiss. Over 6000 systems had been sold, with over ~20 million ophthalmic OCT procedures performed worldwide – OCT had become a standard of care.
Fourier-Domain OCT and the Need for Speed

Advances in OCT technology enabled dramatic increases in imaging speeds, further accelerating research progress and market acceptance. These techniques, known as SD-OCT and swept-source OCT (SS-OCT), are subsets of Fourier-domain detection. Early OCT instruments used time-domain detection, a low-coherence light source and interferometer with a scanning reference arm. However, it is possible to detect light echoes in the Fourier domain measuring the interference spectrum with a spectrometer and high speed line scan camera. Spectral-domain OCT was described by Fercher et al. and by Hausler in the mid-1990s. Spectral-domain OCT was also experimentally and theoretically investigated at MIT in 1991 and is described in patents dating from 1995 to 1996, but the results were not published in scientific literature.

The first SD-OCT retinal images were demonstrated in 2002 by Wojtkowski et al. from the Copernicus University (Torun, Poland), working in collaboration with the Medical University of Vienna. There was initial skepticism about SD-OCT because the interference spectrum is sensitive to eye motion and we thought that micron scale motion might cause the fringe averaging and loss of signal. Spectral-domain OCT has the interesting limitation that it works only at high speed; low speed fails because eye motion causes fringe averaging. In 2003, three different research groups independently demonstrated that SD-OCT has a powerful sensitivity advantage over time-domain detection, because it essentially measures all echoes of light simultaneously. Spectral-domain OCT is also closely related to Fourier spectroscopy, which achieves enhanced sensitivity. Sensitivity is enhanced by the ratio of axial resolution to imaging depth. For most OCT systems, this is factor of 50 to 100, enabling a corresponding increase in speed. Spectral-domain OCT drove a boom in OCT research and development.

High speed improved image quality and retinal coverage, a key step toward comprehensive volumetric imaging. In 2003, Jay Wei left Zeiss to found the startup company Optovue and introduced the first FDA-approved SD-OCT instrument in 2006. Spectral-domain OCT is currently the standard for ophthalmic instruments and imaging speeds range from 25,000 to 80,000 A-scans per second. The fundamental concepts of SD-OCT were in the public domain, allowing numerous companies to develop SD-OCT instruments. Competition in the market has fostered innovation, but price and reimbursement pressures create challenges.

SS-OCT Gains 100× in Speed – The Technology of the Future?

The second type of Fourier-domain detection, SS-OCT uses an interferometer with a narrow-linewidth, frequency-swept laser, and detectors to measure interference versus time. Early OCT instruments used time-domain detection, a low-coherence light source and interferometer with a scanning reference arm. However, it is possible to detect light echoes in the Fourier domain measuring the interference spectrum with a spectrometer and high speed line scan camera. Spectral-domain OCT was described by Fercher et al. and by Hausler in the mid-1990s. Spectral-domain OCT was also experimentally and theoretically investigated at MIT in 1991 and is described in patents dating from 1995 to 1996, but the results were not published in scientific literature.

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Because SS-OCT performance depends on the swept laser, advances in laser technology became critical. The development of Fourier domain mode locking (FDML) in 2006 by Huber et al. provided a novel approach for breaking laser tuning speed limits. Early FDML lasers achieved record speeds of 370,000 A-scans per second in nonophthalmic applications. This technology enabled multiple ophthalmic as well as endoscopic/catheter-based applications and ophthalmic imaging with greater than 1 million A-scans per second was demonstrated, a speed increase of greater than 100×.

In addition to research systems, commercial swept lasers also made critical advances. The commercial short cavity swept laser (Axscan Technologies, Billerica, MA, USA) enabled intravascular as well as ophthalmic applications. Retinal imaging with approximately 5- to 6-μm axial resolution at 1050 nm was demonstrated at 100,000 and 200,000 A-scan per second. The vertical cavity surface emitting laser (VCSEL) improved both imaging speed and range. Figure 10 shows wide-field retinal and choroidal imaging using SS-OCT at 580,000 A-scans per second. A 12 × 12-mm region of the retina with 1000 × 1000 A-scans can be imaged in approximately 2 seconds. The high A-scan density enables high-resolution en face OCT images.

Swept-source OCT has the advantage that it does not require a spectrometer and line scan camera. Swept-source OCT can operate at long wavelengths, achieve faster imaging speeds, and longer imaging range than SD-OCT. Long
wavelengths at 1050 nm have less attenuation from ocular opacities and improved image depth. Commercial SS-OCT instruments are now available and operate at over 100,000 A-scans per second. At the time of this writing, market acceptance in ophthalmology is limited because of high costs, lack of clinical and normative data, as well as uncertainties caused by rapid technology evolution. However, SS-OCT is dominant over SD-OCT in other clinical specialties such as cardiology, dermatology, and gastroenterology. Finally, it is important to point out that SS-OCT can ultimately be built using photonic integrated circuit technology and will eventually become much lower cost and more compact than SD-OCT.

**THE IMPACT OF OCT**

**The Ecosystem of Technology Development**

The commercialization and growth of OCT over the past 25 years has been highly impactful scientifically, clinically, and economically. Many factors helped drive this success, starting...
Government funding allowed researchers to pursue creative ideas and the collaborative and competitive process of scientific research rapidly moved OCT forward from the first publication in Science in 1991.\(^{17}\) Figure 12 shows National Institutes of Health and National Science Foundation funding for grants listing OCT in the title or abstract with cumulative funding totaling approximately $590 million. If the search criterion is reduced to OCT in the title (not abstract), the cost drops to less than $100 million and is probably more indicative of the cumulative US OCT research funding for OCT technology, a small amount compared to return on investment.

Figure 13 (right panel) is based on data from (found in the public domain) www.octnews.org using a combination of automated search, machine learning, and manual editing to track OCT topics over the past approximately 10 years. From 1991 to 1998 the number of publications grew from 1 to 123 and by 2015 it grew to over 21,000, with worldwide participation of scientists, engineers, and clinicians from approximately 500 organizations.

**Publications as a Marker of Fundamental and Clinical Research**

Figure 14 shows the growth in OCT-related publications over the past 25 years included in PUBMED, color coded by category. There has been dramatic growth to over 3000 publications per year with growth catalyzed by the availability of commercial systems. There are commercial instruments for ophthalmology, cardiology, dermatology, gastroenterology, and digital pathology. Ophthalmology is the largest category, followed by cardiology and the general technology category.

There has been tremendous innovation in OCT over the past 25 years. Innovation often occurs at the boundaries of fields where there is a leveraging of ideas, knowledge, and technology from one field into another. The clearest example in OCT is the use of technology and ideas from fiber optic telecommunications. All of the lasers, detectors, many of the system concepts, and fiber optic components themselves came from telecom. Without the billions of dollars of development in this and other industries, OCT would not be where it is today and could not advance to the exciting applications where it will go in the future. Optical coherence tomography is a rich combination of optical/mechanical design, electronics, software, medical devices, and clinical medicine. The multidisciplinary nature of OCT is one of the reasons there has been so much innovation and will continue to drive future advances. For example, photonic integrated circuits are a major focus in telecommunications and are now being explored to improve performance and dramatically reduce the size and cost of OCT systems.\(^{62}\) These advances should allow OCT to further penetrate existing markets, but also to enter new, cost-sensitive markets and importantly, allow this technology to serve people in less developed economies.
Clinical Adoption and Impact

Optical coherence tomography is a standard of care in ophthalmology and there are approximately 30 million ophthalmic OCT procedures per year worldwide, which equates to an OCT procedure every few seconds, on par with other major imaging modalities such as magnetic resonance imaging, computed tomography, and positron emission tomography. However, OCT is also used in many other specialties including cardiology, dermatology, and gastroenterology. Cardiovascular disease is the number one killer in the industrialized world and OCT is advancing the understanding of cardiovascular disease, helping develop new treatments, and aiding in clinical decision making; there are now approximately 100,000 intravascular OCT procedures per year. Cancer is the second leading cause of death. Optical coherence tomography is increasingly being used to understand, diagnose, and guide treatments of several forms of cancer. While translation is still in early stages, preliminary results look promising. There are commercial systems in dermatology to diagnose skin cancer (the most common cancer), in gastroenterology to assess esophageal cancer (the fastest growing cancer in the United States), in digital pathology, and several companies are in trials for real-time breast cancer surgical margin assessment (breast cancer affects > 10% of women worldwide).

Economic Impact

Figure 15 shows the growing number of system companies that entered the OCT space over the past 25 years. Approximately 40% of these companies are associated with institutions receiving government funding for OCT research.
and this is an indicator that government funding is having a positive translational impact on society. In addition, approximately 75% of the OCT companies (blue dots) are, or originated as, startups. Zeiss and St. Jude are today the market leaders in their respective segments. The risks that these business took accelerated the introduction of OCT by perhaps as much as a decade.

and this is an indicator that government funding is having a positive translational impact on society. In addition, approximately 75% of the OCT companies (blue dots) are, or originated as, startups. This is a clear testament to the positive impact entrepreneurship can have on expediting translation of research into clinical care. Many of these startup companies have been acquired by larger companies, including the first two OCT startup companies. The first startup was in ophthalmology in 1992 growing out of an MIT/Tufts collaboration (founded by Puliafito C, Fujimoto J, and Swanson E) and was acquired 2 years later by Zeiss who applied significant finances and resources to bring ophthalmic OCT to market. The second startup was in 1998 growing out of an MIT/Harvard collaboration (founded by Swanson E, Fujimoto J, and Brezinski M) in cardiology and was eventually acquired by St. Jude Medical (Little Canada, MN, USA) 10 years later. Zeiss and St. Jude are today the market leaders in their respective segments. As mentioned earlier, the risks that these business took accelerated the introduction of OCT to ophthalmic and cardiovascular patient care by perhaps as much as a decade.

Figure 16 shows estimated OCT system revenue (including biometry), which is approaching $1 billion/year. Since the first commercial product was released in 1996, cumulative revenue has likely exceeded $5 billion. It is interesting to compare government investment in OCT research over the past decade to total tax receipts related to employment-related taxes, corporate taxes, and other taxes from the commercialization of OCT. Such a comparison is indicative of the return on investment for government sponsored research. Perhaps the most important return is the improvement in clinical care, reducing morbidity and mortality, and improving quality of life for the millions of people who have had OCT diagnostics or guided treatment. It is challenging to estimate the total tax receipts paid by OCT system suppliers directly or indirectly by employees of these companies because there are many forms of taxes and authorized taxing agencies across federal, state, and local governing bodies, as well as different tax policies in different countries. One approach to estimate tax receipts is to extrapolate the findings of Price Waterhouse Coopers66 to estimate both taxes borne directly by the company and taxes collected by the company as a pass through (e.g., employee personal income tax withholdings). This indicates a return of over $500 million in government tax receipts. Additional significant tax receipts are collected through indirect employment in the supply chain and at the clinical installations around the world operating OCT systems.

Another measure of economic impact is to estimate the number of direct and indirect jobs created by the OCT marketplace. To estimate employment data, 70 OCT system and component companies were contacted and asked to supply their individual historic OCT direct employment per year since the time that OCT efforts started at that company. Companies were asked to include any OCT linked job in any discipline such as research and development, engineering, manufacturing, marketing, sales, general and administrative expense.67 Figure 17 shows the resulting statistics. By the end of 2016, the OCT industry will have provided approximately 20,000 person-years of cumulative direct high quality jobs. It is important to note that there are many other OCT component and subsystem related supply chain jobs that could easily represent a doubling in the employment number shown. Another major source of employment not included in our
History of Optical Coherence Tomography

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