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Impressions From BiOS 2013

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Development, Industrial Products UTC Aerospace Systems (Sensors Unlimited Products)

The SPIE annual conferences, BiOS and Photonics West, recently ended for 2013 with a record number of more than 2,000 technical papers presented on biophotonics methods, systems, and applications. The diversity of applications of optical coherence tomography (OCT) continues to expand, with papers featuring new 3D and even 4D imaging capability in the eye, arteries, and lungs. Raman spectroscopy and NIR spectroscopy had significant sessions for biomedical applications, as did diffuse optical tomography (DOT). It is an exciting time for biophotonics, with new companies thinking out of the box to innovate healthcare diagnostics and solutions. It reminds me of the excitement of the 1990s during the expansion phase of digital telecom, as students graduated from the research labs and began applying their knowledge to real-world problems.

Particularly rewarding for me has been seeing the growth of students who I encountered as users of my company's products, who were members of the labs that were early adopters of Sensors Unlimited InGaAs digital linescan cameras for 1.05- and 1.31-micron OCT. For example, Dr. Christine Fleming, now an assistant professor at Columbia University, gave a talk illustrating the use of OCT to position an RF cauterization probe over heart tissue causing abnormal heartbeats, or arrhythmia. A large portion of arrhythmia patients do not respond well to medicine or external pacemakers, solutions that treat the condition rather than curing it. In these cases, RF cauterization can be used to destroy the “miswired” heart muscle tissue, actually curing the problem for those patients. Dr. Fleming’s paper succinctly described the medical problem, the challenges of current methods, and the application of OCT to both locating and monitoring the effective pressure of the probe on the tissue. OCT images show the structural information within the tissue, and in this case, the direction of the fibers that vary in direction from the “normal” tissue. The OCT fiber is also used to recognize the displacement of the blood vessels when the RF probe has the required contact pressure to effectively cauterize the bad tissue fibers (see *figure 1*). Dr. Fleming started studying bio-optics in Dr. Andrew Rollins’ lab at Case Western Reserve University and worked her post-doctorate years in the labs of Dr. Gary Tearney and Dr. Brett Bouma at the Wellman Center for Photomedicine, an affiliate of Massachusetts General Hospital and the Harvard School of Medicine. I am sure that her new posting will enable her to continue to develop healthcare diagnostics with light.

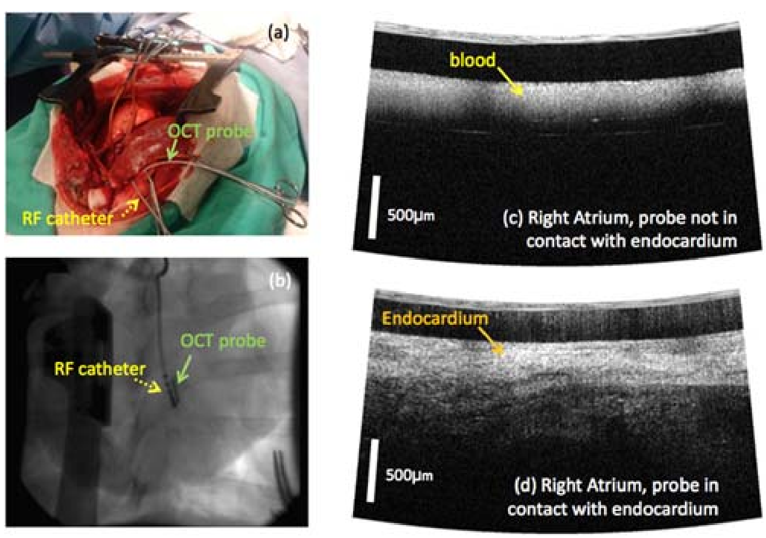


Figure 1: *Permission granted for reuse of this image from* The Journal of Innovations in Cardiac Rhythm Management, *First in vivo Real-Time Imaging of Endocardial RF Ablation by Optical Coherence Tomography* (http://www.innovationsincrm.com/cardiac-rhythm-management/2011/march/55-first-in-vivo-real-time-imaging), *March 2011.*

Given the many papers presented at the conference, the varied communication styles, as well as the room acoustics, one is often straining to understand, or at least to grasp, the main point of complex slides and concepts, hoping to study the conference proceedings when they are published weeks later. So I must honor one speaker who I heard twice (in a very small sample of the papers I was able to attend). Dr. Lida P. Hariri of Massachusetts General Hospital is a pulmonary pathologist M.D. and a researcher Ph.D. who is developing biophotonic methods to move pathology from the stained slide era into digital imaging.

A standout presenter, in one of the sessions Dr. Hariri described the very wide array of diseases affecting the lungs. She illustrated the clues that differentiate one disease from another that are present in the stained pathology slides. She spoke with clarity over the air conditioning fans, leading the audience step-by-step through the evolution of pathologist knowledge of the diseases and the separate knowledge of the surgeon's changing needs. Currently, surgeons may wait for hours in the operating room or for days post-biopsy to learn enough information from the extracted tissue to decide whether a patient has cancer and then to determine the best treatment. Where once it was enough to say a tissue sample had cancerous cells, now the surgeon needs to know the type and quantity in order to decide whether to go back in for more tissue, select and start administering the most appropriate chemo drugs, design a radiation treatment plan, or some combination of treatments - or even to end treatment entirely. Dr. Hariri's slides brought the audience along with her words, providing context and meaning to support the story she was telling. She spoke with confidence and style and showed herself to be a great example of a medical doctor with a research doctorate - a rare breed that uniquely abounds in biophotonics. Many leaders in this field whom I have had the privilege to meet and work with combine these two educational titles with being natural, down-to-earth people who make you glad you met them.

The hardware part of the conferences was also exciting, with the OCT world impressed by the achievements demonstrated by prototype swept laser sources (tunable lasers with sweep speeds of 100 to 1000s of kHz line rates). These speeds enable capturing faster and larger 3D image volumes of tissue and even 4D videos. The vertical-cavity surface-emitting laser (VCSEL)-based sources combined speed with incredible free-ranging depth in air (which is reduced in tissue as a result of the tissue's index of refraction). Though the presentations documented impressive results, the practical limitations of digitizing speeds and computer bandwidth unfortunately force tradeoffs between speed, resolution, and imaging depth to produce results similar to spectral domain OCT systems based on photodiode arrays and spectrometers. Furthermore, water absorption limits imaging in tissue to just millimeters of depth, minimizing the value of ultra-long-range image capture promised by swept laser sources.

At BiOS 2013, my company showed a new line of 2048-pixel InGaAs linescan cameras with line rates of 76 and 150 kHz. Recent publications by the University of Washington (Dr. Ruikang Wang's group) demonstrated imaging depth of 6.1 mm in free space, which translates to over 3 mm in the retina and at 10-micron depth resolution. By using a 1050 nm light source, they documented imaging morphological details beyond the traditional OCT depth captured with the shorter 840 nm wavelength used by current commercial ophthalmic OCT systems. Their full-range, complex Fast Fourier transform, or FFT, method was then used to double the range depth to 12 mm[i], sufficient to image the whole anterior of the eye, from the tip of the cornea to the bottom of the lens in one capture (see *figure 2*). This new capability will provide cataract surgeons with a comprehensive assessment of the eye both before and after replacement of the lens.

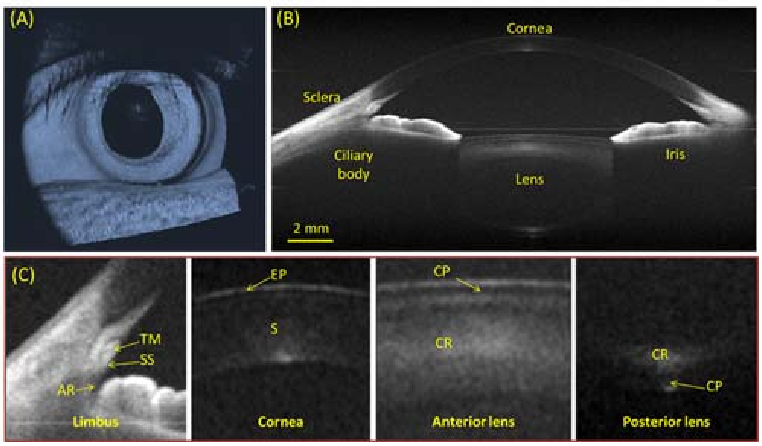
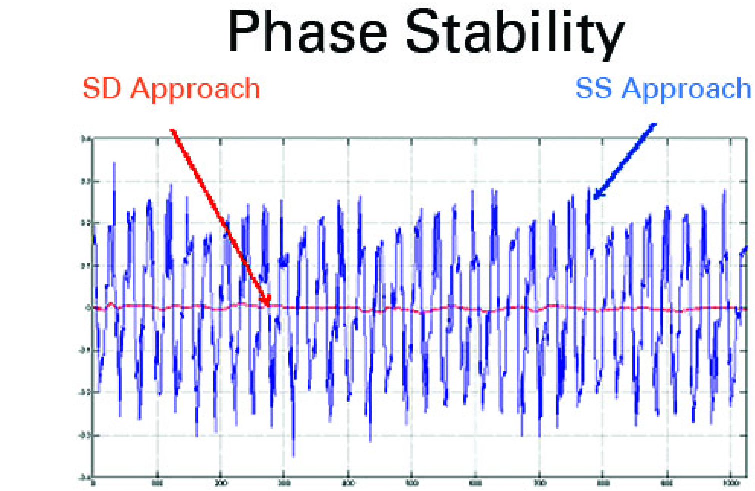
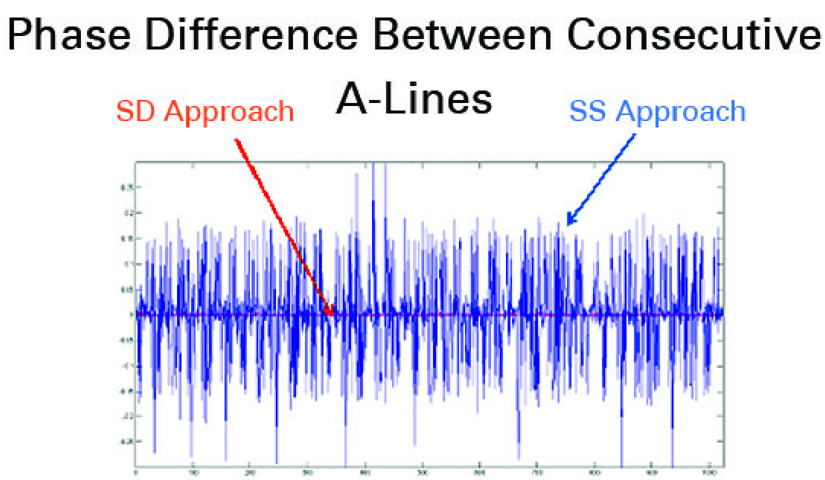


Figure 2: *Images of the anterior segment (front of the eye) captured by the prototype GL2048R-10A InGaAs camera operating at 120,000 A-lines per second. A) Shows a 3D tomogram of the human eye, from the eye lashes through to the lens. B) Shows a B-Scan slice captured in one acquisition, clearly depicting the physical relationship between the top of the cornea down through the bottom of the lens, information useful for cataract surgeons before and after operating. C) Shows the angle formed at the intersection of the cornea with the iris, an important region to detect the obstruction of a drainage canal that could result in glaucoma if left untreated. To the right, details showing the covering of the cornea and its width, the top surface of the lens and its structure, and all the way to the right, detail at the bottom of the lens. Images used with permission from the University of Washington.*

Another of the U of W publications demonstrated the value of the rock-solid stability of the spectral-domain (SD) design. Here, blood flow in the tissues is measured by overlapping the depth scans to capture shifts of the blood cells, detecting the Doppler frequency shift due to the velocity of the blood. The parallel detection of all wavelengths simultaneously provides superior system phase stability compared to swept sources (SS) where each wavelength is captured sequentially. SS-OCT systems also suffer from variations and non-linearity in line-to-line acquisition, causing instabilities that have to be compensated for by additional hardware or software (see *figures 3a and 3b*). This compensation in turn reduces the net 3D imaging rate to below that implied by the advertised line rates. The University of Washington papers, on the other hand, demonstrated 100 dB[ii] OCT sensitivity in reference conditions, while acquiring at 120 kHz via medium Camera Link.





Figures 3a and 3b: *Figure 3a (top) illustrates the difference between the wide fluctuations of phase stability in a commercial swept source OCT system compared to that of a Spectral-Domain system (photodiode array with fixed grating spectrometer). Figure 3b (bottom) illustrates the phase difference between consecutive A-lines recorded by the same two systems.*

Another system characteristic worth considering when choosing between SS-OCT and SD-OCT system designs is the cost of total ownership. SD-OCT systems have no moving parts, and the detectors are qualified for very long lives. The high-speed swept sources change their wavelengths with microelectromechanical systems (MEMS); these are moving parts, though on a micron scale. Many of the high-speed systems have had reliability issues for the early-adopter researchers, which is not surprising considering the number of cycles that quickly accumulate. Telecommunications system analysis of tunable lasers in 2008 projected lifetimes of 1.5 e+12 cycles, but at a frequency of 200 Hz. However, at the rate of 100 kHz, this number of cycles would accumulate in just one half year of continuous operation or 5 years of operation if the source is turned off between 10-minute sessions with a rate of 3 per hour, 5 days per week for 48 weeks a year. This assumes no derating as a result of the very high repetition rate of SS-OCT sources. In contrast, the solid state detectors and super-luminescent diodes (SLDs) used in spectral domain OCT have lifetimes of a decade of continuous operation.

Though new device reliability will improve over time, for those making system design decisions now, the maturity of processes should be compared. Though VCSELs have been in volume production for a long time, the producers of high-speed tunable lasers are only at the beginning of developing their production processes. As those experienced with the semiconductor economics know, when a facility has processed only tens of wafers, yield is low, and costs per unit are high. Mature semiconductor processors, such as those at the UTC Aerospace Systems (Sensors Unlimited Products) facility in Princeton, NJ, have 20 years of experience processing InGaAs wafers. Thus, the new GL2048 family of high-speed linescan cameras has both a cost and reliability advantage over the still developing swept source producers (see *figure 4*).

Producers of medical OCT systems require high reliability, repeatability, stability, and affordable key components. With a design goal of greater than 10-year life, the GL2048 product line is positioned to fill that requirement.

Figure 4: *UTC Aerospace Systems' (Sensors Unlimited Products) new GL2048-10A InGaAs-SWIR camera breaks new ground for SD-OCT when used at the center wavelengths of 1.05, 1.31, or 1.55 microns by delivering A-line rates of >76,000 lines per second, which is near the maximum for Base Camera Link interfaces.*

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i Peng Li, Lin An, Gongpu Lan, Murray Johnstone, Doug Malchow, and Ruikang K. Wang, "Extended imaging depth to 12 mm for 1050-nm spectral domain optical coherence tomography for imaging the whole anterior segment of the human eye at 120-kHz A-scan rate," *Journal of Biomedical Optics*, 18(1), 016012, January 2013

ii Lin An, Peng Li, Gongpu Lan, Doug Malchow, and Ruikang K. Wang, "High-resolution 1050 nm spectral domain retinal, optical coherence tomography at 120 kHz, A-scan rate with 6.1 mm imaging depth," *Biomedical Optics Express*, Vol. 4, No. 2m p245, 1 February 2013

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