

# ***Optical Biopsy XVII: Toward Real-Time Spectroscopic Imaging and Diagnosis***

**Robert R. Alfano  
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*Editors*

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## Introduction

The SPIE Photonics West Conference, Optical Biopsy, was conceived 17 years ago by Professor Alfano, the founding Conference Chair. His simple aim was, and remains, for photonic engineering and scientific development to realise the optical biopsy for real-time information on cancer and disease detection for screening, early diagnosis, and intra-operative monitoring acquiring clinically relevant data without the need for excision biopsies. Thus, to give clinicians the means to have objective medical and biological data to hand at the point of need, the better to take effective and efficient clinical decisions for curative outcomes. The optical biopsy photonic systems aimed at, ideally, should be compact and provide high resolution tissue imaging within seconds, underpinned by machine learning for diagnostic capability based on morphology or molecular recognition and ideally both.

In our 2019 Optical Biopsy conference, we held two days of oral presentations and discussion. These included sessions on optical bioassay platforms, optical histology, spectroscopic methods, and SWIR (short wave infrared) and (mid-infrared) MIR methods, with lively poster sessions on both days. An average of around 70 attendees, throughout the two days, is indicative of vigorous interest from photonic engineers, scientists, and clinicians. Here follows a synopsis of key papers.

Optical Bioassay Platforms included an invited talk on chip-based Raman spectroscopy for microbial sensing from Jürgen Popp (10873-1, Leibniz Institute, Jena, Germany). The WHO (World Health Organization) has stated that in heading toward a post-antibiotic era, microbial resistance is a serious worldwide threat to public health. Raman bio-assay of body-fluid may give faster, reliable, specific diagnostics to inform therapeutic decision-making. Electrophoresis is used to concentrate pathogens in a capturing unit, on-chip. Lingyan Shi (10873-8, Columbia University, United States) presented her very high standard work on SRS (stimulated Raman), with  $\sim 10^8$ x sensitivity of spontaneous Raman, and outstanding label-free 3D imaging; the novelty was introducing D<sup>+</sup> for H<sup>+</sup> to give tissue signatures in the normally cell-silent vibrational region 4-5 $\mu$ m wavelength.

In the Optical Histology session, high standard work from Virginia University (United States) (paper 10873-10) was on multiparametric photoacoustic microscopy: PAM, which has a unique niche giving label-free imaging with hemoglobin contrast to similar depth as OCT. With a pulsed laser to excite tissue, the absorption gives transient heating and thermoelastic expansion with acoustic emission, for instance, to track brain vasculature (brain cells are invisible to PAM) after stroke.

Day two featured Spectroscopic Methods with innovative, high performance instrumentation for Mueller polarimetric imaging *in vivo* (10873-18, from Ecole Polytechnique and Strasburg University, France) across the visible with multispectral images, wide field, low error, fast acquisition 1-2 s and compact system. Impressive imaging in a hospital setting of cancer margins; collagen orientation is being

detected using liquid crystal alignment. The SWIR and MIR Methods session began with Laura Sordillo (City College of New York, United States, paper 10873-28) who reviewed the state-of-the-art in SWIR, the 4 NIR windows: 650-950 nm, 1100-1350 nm, 1600-1870 nm (so-called: 'Golden Window') and 2100-2300 nm. Light scattering through these windows ranges from none (ballistic photons), to weak (snake-like quasi) to multiple scatter (diffuse scattering). The brain is lipid-rich and 1700 nm is the preferred imaging wavelength. InGaAs IR CCD array suits the third window, which fields the deepest penetration of radiation to see hard wire below chicken tissue. The use of supercontinuum laser for high power, broadband confocal microscopy was discussed. Next up was paper 10873-29 from Birmingham University (United Kingdom) presented by Chris R. Howle; the mod-infrared for wound healing from military injuries like a blast pressure wave, shrapnel, victim-hits-object and flash-burn. FT-(Fourier transform)-IR spectroscopy followed amide B at 3200  $\text{cm}^{-1}$  arising from Fermi resonance of the first overtone of amide II and N-H stretching. Two computational methods applied and machine learning: principal components analysis on normalised spectra, taking first derivative, was found best. For the future, a field-compact technique is being developed based on negative contrast instead of FT-IR. Impressive work by Christian Petersen, a young scientist from Denmark Technical University, was on MIR OCT based on 1.5-2.7 $\mu\text{m}$  MOPA laser pumping of a fluoride glass optical fibre (transparent: 0.9-4.7 $\mu\text{m}$ ) for SC output of 40mW total over 3.6-4.6  $\mu\text{m}$ . For the imaging, a neat solution was to upconvert the radiation to 820-865 nm for Si detection. Tissue was imaged to 8.6 $\mu\text{m}$  depth and 15 $\mu\text{m}$  spatial resolution—a proof of concept study (10873-51). The conference was brought to a close with exciting developments in the MIR spectral domain by two invited papers. First, Stuart D. Jackson, an acknowledged leader in MIR narrow-line fibre lasers reviewed the state of the art and how this can input molecular hyperspectral imaging (Macquarie University, Australia, paper 10873-36). Finally, paper 10873-37 (Nottingham University, United Kingdom) gave an update of MIR molecular imaging using fibre MIR-SC broadband sources showing the state of the art, but still on excised tissue rather than *in vivo*, the ultimate goal.

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