# Special Section Guest Editorial

## Optical Clearing of Tissues and Cells

In the visible and near-infrared wavelength range, the majority of tissues and blood are low absorbing but highly scattering media. Scattering defines spectral and angular characteristics of light interacting with living objects, as well as its penetration depth. Thus, the deleterious effects of the optical properties of tissues and blood on light-based diagnostic and therapeutic techniques may be effectively mitigated by reducing light scattering. Optical clearing agents (OCAs) have been identified that can reversibly change the light scattering properties of tissues and blood. The challenge remains to elucidate optical clearing mechanisms and to identify properties of agents that are predictive of its optical clearing potential (*a priori*).

In this special section, uses of OCAs are presented that enhance in-depth light and laser beam penetration into naturally turbid tissues and blood *in vitro* and *in vivo* for spectrophotometry, Raman spectroscopy, as well as Fourier transform infrared (FTIR) spectroscopic, second-harmonic generation (SHG), and optical coherence tomography (OCT) imaging techniques. The optical properties of tissues and blood are analyzed as they are transformed from basic multiple scattering to a low scattering mode. It is shown that light reflection, transmission, and scattering can be effectively controlled. Enhanced diagnostic abilities with the use of OCAs are demonstrated based on contrasting of abnormalities, in-depth profiling of tissue and blood, and monitoring of endogenous and exogenous chemical diffusion within tissue.

A few papers in this section describe optical clearing of human and animal skin with comparative studies of permeability and dehydration of intact and photothermally or microneedle perforated skin. Refractive index and cross-polarization measurement techniques were used. The enhancement of optical clearing efficacy of skin by topical application of different alcohols is demonstrated in *in vitro* studies of porcine skin using integrating sphere spectrophotometry. The penetration kinetics of such important OCAs as DMSO and glycerol into porcine skin tissue *in vitro* were studied by FTIR spectroscopic imaging techniques.

Two papers are related to blood vessels and flowing blood optical clearing examination. The short-term and long-term effects of OCAs (glycerol and glucose) on blood vessels in the model of chick chorioallantoic membrane were investigated using speckle contrast imaging. Optical clearing of flowing blood pumped through a round glass capillary with a diameter of 300 or 600 $\mu$m was studied by spectral domain OCT with the application of dextrans as OCAs.

Noise reduction in transcutaneous Raman spectroscopy of murine cortical bone tissue is demonstrated using glycerol mediated optical clearing. Quantitative SHG imaging in striated muscles and tendons is characterized with optical clearing, and corresponding numerical modeling of the optical clearing mechanism is presented.

As a reflection of the great prospects for optical clearing technology in the improvement of OCT imaging modalities, four papers in this section are related to this technology. Three of them are devoted to the study of glucose diffusion, impact, and sensing. In one paper, the differential permeability rate and percent glucose-induced clearing in different regions of rabbit sclera are quantified. In two papers, recent achievements and drawbacks in glucose sensing are discussed on the basis of detecting glucose-induced changes in *in vitro* and *in vivo* experiments and study of the influence of probe pressure on blood glucose monitoring.

Two papers show two other prospective applications of optical clearing technology. They are 3-D imaging of unsectioned specimens for macroscopic gene expression and microvasculature structure using optical transmission/emission tomography and the use of hyperosmotic OCAs for improvement of the laser treatment of cutaneous vascular lesions.

We thank all the authors for their contributions to the special section. As we look forward, we believe that optical clearing, based on reversible reduction of tissue scattering, will be of great interest for biomedical optics research and a promising technique for future developments in the fields of tissue imaging, spectroscopy, phototherapy, and laser surgery.

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