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Introduction: Feature Issue on Phantoms for the Performance Evaluation and Validation of Optical Medical Imaging Devices

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Abstract: The editors introduce the Biomedical Optics Express feature issue on "Phantoms for the Performance Evaluation and Validation of Optical Medical Imaging Devices." This topic was the focus of a technical workshop that was held on November 7–8, 2011, in Washington, D.C. The feature issue includes 13 contributions from workshop attendees.

OCIS codes: (000.1200) Announcements, awards, news, and organizational activities; (110.0110) Imaging systems; (120.0120) Instrumentation, measurement, and metrology; (170.0170) Medical optics and biotechnology; (180.0180) Microscopy; (290.0290) Scattering; (300.0300) Spectroscopy

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The impetus of the clinical applications of optical medical imaging technologies has become critical in recent years. One of the key advantages of the optical imaging approach is its minimal invasiveness, which allows for safe practices and enables progressive *in vivo* optical diagnostics and treatment [1–12]. The large variability in key tissue optical properties, such as refractive index, scattering coefficient, and absorption coefficient, in biological media has been of major interest for achieving reliable diagnoses of disease and for quantifying specific features in the tissues [13–18]. In addition, recent studies have demonstrated that many optical imaging modalities are complementary to conventional radiation imaging techniques. Therefore, multimodal approaches combining optical and radiological imaging techniques have been explored [19–21].

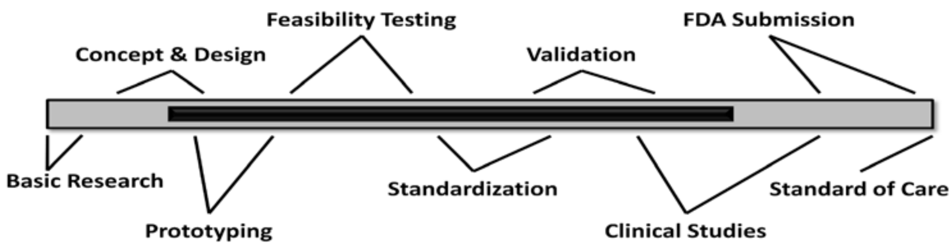

Fig. 1. Translational research map of medical devices from the basic research state to practical application in clinical settings.

As illustrated in the translational research map in Fig. 1, optical medical imaging devices are initially developed in basic research fields, mostly in academia, in order to perform proof-of-principle experiments, designing prototypes for conceptualization of the imaging capability, and testing the feasibility of the measurement concepts. Advancing optical medical imaging technologies from concept to reality requires characterization, calibration, and validation tools [22,23]. These tools would include artifacts or virtual tissue standards (known as "phantoms") that test and optimize hardware, software, and applications; provide training to users; and ensure comparability of measurements across instruments and institutions [24–26].

The phantoms are "materials or artifacts that are used to test and evaluate the measurement performance of different measuring systems for specific tasks," and their specific properties may vary depending on their use, such as device validation and inter-laboratory comparisons [27]. In other words, in addition to their primary use for proof-of-principle studies, phantoms are used for benchmarking system performance and ensuring data consistency across multiple instruments and even vendors. In general, the application-dependent properties of the ideal phantoms are discussed elsewhere [28]. Phantoms used for regulatory clearance and quality assurance during clinical trials and field use will have to be fabricated to the same quality as the biomedical optical devices they are serving. In addition, their physical properties will have to be accurately known, and, for the most effective quantitative applications, they may be traceable to the international system (SI) of units [29].

On November 7–8, 2011, in Washington D.C., The Catholic University of America, with the support of the National Institute of Standards and Technology, hosted a workshop on "standards for phantoms for the performance evaluation and validation of optical medical imaging devices." During this workshop, 20 invited speakers gave technical presentations to address measurement challenges in quantitative optical medical imaging and the use of phantoms to accelerate the broad employment of optical imaging devices. The technical discussions focused on the use of phantoms for standards in optical coherence tomography and in reflectance/transmission mode spectroscopic imaging technologies: (1) to achieve measurement standards in optical medical imaging devices and potential incorporation of phantom-based test methods into biophotonic imaging standards and FDA guidance documents (Jeeseong Hwang, Albert Cerussi, Joshua Pfefer, and Bruce Drum); (2) to resolve measurement challenges towards quantitative clinical applications of optical imaging devices (Guillermo Tearney, Jessica Ramella-Roman, Ron Xu, David Allen, Joseph Rice, Edward Livingston, and Maritoni Litorja); (3) to overcome barriers and take opportunities towards standards with ideal phantoms (Pete Tomlins, Steve Jacques, Irving Bigio, Elizabeth Hillman, Jean-Pierre Bouchard, and Guy Lamouche). There were also presentations to review recent phantom research efforts ("The history of tissue-simulating phantoms" by Brian Pogue and "Phantoms and quantitative optical diagnostic imaging" by Scott Prahl) and to address future directions ("Phantoms for the future" by Robert Nordstrom) as well. This feature issue of *Biomedical Optics Express* showcases selected contributions made by speakers and attendees to this workshop. The key highlights of contributed papers in this feature volume are briefly presented below.

Hyperspectral imaging (HSI) [30,31] has the potential to achieve high spatial resolution and high functional sensitivity for noninvasive assessment of oxygen level in cells and tissues [32,33]. However, clinical acceptance of hyperspectral imaging in ischemic wound assessment is hampered by its poor reproducibility, low accuracy, and misinterpreted biology. Ronald Xu *et al.* have proposed a digital tissue phantom (DTP) platform [34] for quantitative calibration and performance evaluation of spectral wound imaging devices. The technical feasibility of such a DTP platform was demonstrated by both *in vitro* and *in vivo* experiments. Samarov *et al.* presented a statistical analysis framework for HSI analysis validation by comparing the performance of two algorithms, the Least Absolute Shrinkage and Selection Operator (LASSO) [35] and the Spatial LASSO (SPLASSO) [36], extracting the abundance fraction of water soluble dyes in mixtures printed on microarray chips that served as HSI test phantoms. The design and fabrication of custom-tailored microarrays [37] for use as phantoms in the characterization of HSI is described by Clarke *et al.* In this work, as the shape of the dye spots in the array results in significant scattering signals, which can be used to test image analysis algorithms, the separation of the scattering signals allows elucidation of individual spectra of different dyes.

In *optical coherence tomography* (OCT) [38,39], Guy Lamouche *et al.* reviewed the development of OCT phantoms that are capable of mimicking a number of tissue properties and discussed durable phantoms that can replicate not only optical properties, but also mechanical and structural properties of a range of tissues. Robert Chang *et al.* reports on a novel fabrication approach to build multilayered optical tissue phantoms that serve as independently validated test targets for axial resolution and contrast in scattering measurements by depth-resolving OCT with general applicability to a variety of three-dimensional optical sectioning platforms, including confocal microscopy and OCT. Varying the dimensions of the scattering microspheres and the thickness of the intervening transparent polymer layers enables different spatial frequencies to be realized in the transverse dimension of the solid phantoms. Anant Agrawal *et al.* have designed, fabricated, and tested a nanoparticle-embedded phantom incorporated into a model eye in order to characterize the point spread function of retinal OCT devices in three dimensions under realistic imaging conditions. This model eye-based phantom can provide retinal OCT device developers and users a means to rapidly, objectively, and consistently assess the point spread function, a fundamental imaging performance metric [40].

For *quantitative evaluation of the wavelength and/or morphology-dependent spectral properties*, including absorption and reduced scattering coefficients of biological tissue layers is important for elucidating light propagation for quantitative optical spectroscopy of tissue layers. Quanzeng Wang *et al.* evaluated a technique based on neural network inverse models trained with radial reflectance data from layered tissue Monte Carlo simulations as an approach for broadband measurement of layered mucosal tissue optical properties. As the sensitivity to surface profile of noncontact optical imaging techniques leads to incorrect measurements of optical properties and consequently physiological parameters, Thu Nguyen *et al.* proposed an experimental method to correct the effect of surface profile on spectral images using three-dimensional (3D) phantoms of semi-identical shape constructed using an inexpensive 3D printer.

Steven Jacques *et al.* demonstrated that a reflectance *confocal scanning laser microscopy* measures the decay of reflected signal as the focus moves deeper into solutions of nanoparticles, absorbing and scattering materials, and typical reflectance standards. These results are mapped into the scattering coefficient and anisotropy of scattering, providing a new approach for measuring tissue optical properties using confocal microscopy. In fluorescence nanoparticle-including optical phantoms for quantitative molecular imaging standards, the optical properties of clustered fluorescent nanoparticles such as quantum dots (QDs) are essential to the design of QD-based optical phantoms. In a report by HyeongGon Kang *et al.*, controlled assembly of a fixed number of QDs into single clusters and multimodal optical characterization and analysis of their dynamical photoluminescence (PL) properties enables the long-term evaluation of the optical properties of QDs in a single or a clustered state. This study is presented in an effort to guide the design and evaluation of QD-based phantom materials [41] for the validation of the PL measurements for quantitative molecular imaging in a variety of biomedical applications.

In *phantoms involving fluid materials*, as noninvasive biophotonic techniques to measure flow in the human vasculature have been developed and employed [42–47], appropriate calibration and validation techniques dedicated to these particular measurements have recently become important. Long Luu *et al.* introduce a fast prototyping technique based on laser micromachining for the fabrication of dynamic flow phantoms to mimic vasculature geometries to accommodate a particular experimental scenario. When using Intralipid phantoms and mimicking tissue scattering properties [48], fiber optic reflectance devices may be used. Stephen Kanick *et al.* investigated the spectral response of specific device configurations, and the findings are important in characterizing the response over a set range of geometrical perturbations involving device configurations such as fiber size and source-detector distance. The results show the need to consider the influence of scattering phase function when using measurements of Intralipid to either characterize or calibrate a reflectance device that collects light close to the source.

Through active scientific interactions among the stakeholders in the field of optical medical imaging, the quality of healthcare could improve. However, the development of suitable working standards that can be used in any clinic to ascertain the working order of measurement instrumentation are necessary to achieve optimal results. When this characterization also addresses natural person-to-person variability of the tissue optical properties, a wide range of tissues types are of clinical interest for data collection. With good measurement practices facilitated by well-designed phantoms, erroneous sources of variability from instruments and measurement protocols can be minimized, isolating the variability of the tissue itself, both within and among individuals. Studies in this feature volume address important roles of optical phantoms to accelerate realization of optical medical imaging techniques in the clinic.

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