Hybrid MR - Optical Imaging

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The potential high synergy that exists between MR and optical imaging has prompted over the past 10 years the development of systems and methods that can visualize both optical and MR contrast *in-vivo*. Attaining high versatility in sensing hemoglobin, vascular agents and several cellular and sub-cellular components and processes, hybrid MR -optical imaging has been perceived as a possible way to enhance the information contained in the MR examination. Similarly, the unsurpassed anatomical and functional contrast and the high resolution imparted by MRI have been seen as a necessary vehicle for the propagation of optical imaging to non-invasive pre-clinical and clinical applications.

Today, MR-optical systems largely remain on the sidelines of clinical use and are implemented mostly for proving feasibility in pilot studies. Interestingly, the primary reasons behind the slow clinical propagation are not associated with issues of light penetration in tissues. Light is known to attenuate one to two orders of magnitude for every centimeter of propagation in tissue in the near-infrared spectral region. With these attenuation metrics, highly sensitive detectors have been shown capable of imaging through several centimeters of tissue, for example through the human breast for cancer imaging, in brain functional studies or for visualizing hemo-dynamics in exercising muscles. There are however two major impediments that explain the so far difficulty in the widespread use of optical and hybrid systems. *First*, original optical methods did not appropriately accommodate for the intricacies that arise from the strong scattering of photons propagating in tissues. Photographic and trans-illumination approaches produced results that were highly modulated by the geometry and the spatially varying tissue optical properties. Along the same lines, original tomographic approaches attained low resolving power as they did not adequately treat the known "ill-posed" nature of the inverse optical problem and the optical heterogeneity of tissue. *Second*, the original intended use of optical imaging as a diagnostic method for cancer, based on oxy- and deoxy-hemoglobin content, did not impart detection sensitivity and specificity that was better than that of established radiological modalities and possibly infused the field with hesitation as to the practical value of clinical MR - optical imaging.

Significant advances in optical imaging technology for imparting high imaging fidelity *in-vivo* and developments in fluorescence probes that can report on a large range of biomarkers *in-vivo* breathe new potential for the hybrid method. Two major approaches are currently taken for hybrid imaging reflected in

1. the development of hybrid optical/MR systems, and
2. the development of hybrid optical/MR reporter probes.

Collectively these approaches are increasingly applied in small animal imaging and attain great potential for clinical propagation as well. Hybrid imaging systems can be used to examine different biomarkers of tissue function, disease and treatment under identical placement conditions or simultaneously, largely enhancing the versatility of the combined approach to examine complex pathways and physiological and molecular alterations. In addition, dual modality probes are used for the *ex-vivo* confirmation of MR findings using standard laboratory optical techniques, such as histology, but their *in-vivo* use is also emerging for performing co-registration of optical and MR findings not by virtue of a common imaging system but due to the exact co-localization of the hybrid reporter agent used.

This talk summarizes the diverse current applications of hybrid MR-optical use and describes the hardware and physical advancements that lead to new performance landmarks for the optical method and to a new outlook for the hybrid approach. Issues of simultaneous vs. stand alone operation are also examined. Based on these developments and the pre-clinical current evidence we predict areas with immense potential for the clinical propagation of MR-optical hybrid systems, probes and methods.