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# Foreword

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There are six articles in this special issue dedicated to multi-modality imaging systems, including two articles on MRI/PET, one on MRI/SPECT, one on MRI/DOT (diffuse optical tomography), one on PET/CT specifically designed for breast imaging, and one on FT (Fluorescence tomography)/CT. While most of these systems are in the developmental phase their future potential can be underlined by one already successful example namely PET/CT. This multi-modality imaging system has already demonstrated its great value in clinical practice. In fact, the majority of newly purchased PET scanners are combined PET/CTs, and the stand-alone PET scanners are expected to be slowly phased out. The most obvious advantage of combining two imaging modalities is to obtain co-registered high spatial-resolution anatomic and functional information. In this issue, the anatomic imaging modalities (MRI and CT) and functional imaging modalities (PET, SPECT, and two optical imaging systems DOT and FT) are combined for various pre-clinical and clinical applications.

Another advantage of multi-modality imaging system is to use the structural information provided by the anatomic imaging modality to enhance the image quality of the functional imaging modality. In case of PET/CT, CT is used to perform attenuation correction for PET reconstruction for more accurate quantification. In MRI/PET or MRI/SPECT, the structural information provided by MRI can also be used for the same purpose. In case of optical imaging, due to the intrinsic limitation of solving an ill-posed reconstruction problem, the use of structural image to provide *a priori* information is critical. It is necessary not only for improving the overall image quality and localization of chromophores/ fluorophores, but also required for quantification of their concentrations.

The first article in this issue is by Wehrl *et al.,* It is a comprehensive review paper describing the developmental history of the MRI/PET scanners in great detail. Six different designs are described in this paper. The first system was a simple combination linking two stand-alone MRI and PET systems with a common patient handling system similar to the current PET/CT systems. This integration is straightforward, but it does not allow simultaneous imaging. For developing a true combined system, since the PET electronics will be affected by the strong magnetic field, one major challenge is to select/optimize the light detectors and the length of the optical fibers to achieve the highest possible signal within the allowed space. The light detectors have evolved from the photomultiplier tubes (PMTs) to Avalanche Photo Diodes (APDs) to Geiger-mode APDs (G-APDs, silicon-photomultipliers (Si-PMs) or solid state photomultipliers (SSPMs)). The advantages and disadvantages of each design were described. This review paper also included a section to discuss the clinical applications of the MRI/PET system particularly in oncology and cardiology. A review of the current use of other stand-alone imaging systems and potential systems that are under development was also provided.

The second paper is by Hamamura *et al.,* to combine a SPECT system with MRI. The system used a cadmium-zinc-telluride (CZT) nuclear radiation detector that can function properly in a high magnetic field. The detector was interfaced with a specialized radiofrequency (RF) coil and tested using a whole body 4.0T scanner. The importance of proper corrections for non-uniform detector sensitivity and Lorentz force effects was considered. Phantom and animal study results were demonstrated. Compared to the MRI/PET, MRI/SPECT is in its infancy. However, the SPECT system can be used to measure different tracers labeled with different isotopes simultaneously, and it can provide unique information targeting different physiological properties. It is anticipated that more MRI/SPECT systems will be developed in the near future.

The third paper is by Boone *et al.,* describing the development of a dedicated PET/CT scanner specifically designed for breast imaging. Although PET/CT has already been used for clinical imaging, it does not provide the required spatial resolution for diagnosis of breast cancer. Furthermore, for screening purposes, the radiation dose has to be comparable to that of screening mammography. Two prototypes have been built. The design and optimization of different hardware and software components were described in detail. The second prototype was also integrated with a PET system that allowed simultaneous PET/CT imaging. There are also dedicated breast-specific gamma camera and PET scanner (Positron Emission Mammography). One can foresee that these systems will be integrated with anatomic imaging systems (e.g. mammography, tomosynthesis, ultrasound) in the near future.

The fourth paper by Barber *et al.,* discusses the development of a fluorescence tomography system integrated with CT (FT/CT). Similarly, the anatomical data from CT provides *a priori* information for the FT reconstruction. In addition, the optical morphological information from absorption and scattering maps were used as *a priori* information in the FT reconstruction to improve the accurate localization and quantification of fluorophore concentration. Phantoms with inclusions containing Indocyanine-Green (ICG) in heterogeneous backgrounds were built for testing, and results demonstrated that with the anatomic *a priori* information and the correction of optical properties, the concentration of ICG could be measured within 15% error. The capability of performing in-vivo fluorescence imaging will provide a very useful tool for cell tracking by labeling them with fluorophores.

The fifth paper is by Hawkes *et al.,*, describing a combined microPET®-MR system. Their design using the split magnet was one of the 6 designs in the review paper by Wehrl *et al.,* The photomultiplier tube (PMT) was used for light amplification, which was incompatible with strong magnetic fields. The use of a long optical fiber may lose a substantial count of photons, not a viable option. Their approach was to construct a split magnet and gradients to locate the magnetic sensitive components, the PMTs, in regions of low magnetic field. A system, a microPET Focus-120 located in a 1T split magnet, has been built, and its performance was compared to previous microPET instruments.

The last paper by Thayer *et al.,* describes the simultaneous measurement of dynamic contrast enhancement kinetics of an MR contrast and an optical contrast agent ICG using the combined MRI/ Diffuse optical tomography (DOT) system. A unique MR compatible fiber optic interface was designed to allow co-registration of MR and DOT data in space and time. High temporal resolution of the hybrid system permits acquisition of data in dynamic mode. ICG binds with albumin and acts like a macromolecular contrast agent. In conjunction with the clinically used gadolinium contrast agents (with small molecular weight), the vascular properties, including vascular volume and permeability, can be measured more accurately to improve the diagnostic accuracy. The capability of measuring enhancement kinetics of MR- and optical-based contrast agents will provide a tool for many other applications in addition to improved diagnosis and specificity.

While multi-modality imaging is moving from its infancy to preclinical and clinical applications for improved diagnosis there have also been new efforts to limit the development of high tech imaging modalities using arguments based on “quality of life” analysis vs. cost. Needless to say almost all of these analyses are based on assumptions that are designed to justify the outcomes. It is the opinion of these authors such efforts are very similar to those unsuccessful ones used to predict the weather or the stock exchange movements. The proof of the pudding is in the amount of lives and expenses saved because of the development of high end imaging technologies such as CT, MRI, PET to name a few without taking into account of the pain and suffering of the patients in the absence of such technologies. An expensive diagnostic procedure may help save even higher medical expenses downstream in addition to saving lives and minimizing pain and suffering. We believe that multi-modality imaging will be here to stay and serve as an effective tool in reducing medical care costs by earlier diagnosis of diseases and assessing the effectiveness of therapy.

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