

## Whole body simultaneous PET/MRI: One-stop-shop?

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### Abstract

Beginning of this century is hallmarked by arrival of hybrid imaging PET/CT (positron emission tomography/computerized tomography) which has become a standard of care primarily in oncology in a short span of time. Continuous research and development by industry and academia for exploiting the excellent soft tissue contrast, spectroscopy and precise measurement of various functional parameters by magnetic resonance imaging (MRI) with PET has resulted in emergence of whole body PET/MRI. It is expected this new hybrid modality would be warmly welcomed due to high magnitude of functional and morphostructural information at molecular level with low radiation dose which is indeed a point of concern for young and paediatric population. This short technical report for nuclear medicine readers will focus upon the various configuration and acquisition sequences of PET/MRI, attenuation correction and clinical applications of whole body simultaneous PET/MRI.

**Keywords:** Hybrid imaging, PET/CT, PET/MRI, Attenuation correction, Simultaneous PET/MRI.

### Introduction

The concept of hybrid imaging is not new and in last few decades it has transformed from visual integration of anatomical and functional images to software based image fusion (co-registration) and currently integrated imaging systems have become the standard of care. In 1998 concept of PET/CT (positron emission tomography/computerized tomography) was introduced by David Townsend<sup>1,2</sup> and a decade after its prototype introduction, PET/CT has become the modality-of-choice for variety of clinical indications in oncology. Today, over 5,000 PET/CT systems are installed worldwide and up to 90% of all PET-investigations are performed for oncology indications with<sup>18</sup> FDG (fluorodeoxyglucose) being the tracer-of-choice in most of these indications.<sup>3</sup> The profound success of PET lies in the wide range of

biologically relevant probes (PET radiopharmaceuticals), absolute quantification of tracer distribution with good spatial resolution (~4 mm for clinical whole-body systems) and fast throughput.<sup>4</sup> However, radiation dose incurred by CT component of PET/CT (low dose to diagnostic whole body CT) is substantial with an enhanced life time attributable risk for cancer.<sup>5</sup> However, this robust development of PET/CT (nuclear cardiology perfusion scans) has resulted in humongous radiation exposure to public. In 1980 mean radiation dose to an American was 3.6 mSv (3 mSv from background and 0.6 mSv from medical exposure) but in 2006 medical exposure (primarily CT and MPI studies) contributed 3 mSv and no significant change in background source.<sup>6</sup> This trend and its aftermath indeed have created anxiety among various statutory and non-statutory bodies and obviously in public regarding stochastic effects of radiation like cancers and congenital abnormalities. This has indeed fueled the need of exploring new imaging modalities incurring lesser radiation dose to patients without compromising the diagnostic accuracy.

The idea of PET/MRI (positron emission tomography/magnetic resonance imaging) was conceptualized by Simon Cherry and Paul Marsden as early as mid 1990s even before PET/CT was introduced. While performing preclinical hybrid imaging they felt to combine high soft tissue contrast MRI images with molecular information derived by PET.<sup>7</sup> Furthermore, MRI can also provide significant functional data like diffusion weighted MR for assessing ischaemia, contrast based cerebral and myocardial perfusion measurement, and functional MRI (fMRI), spectroscopy and angiography. As photomultiplier tubes (PMTs, basic unit of conventional PET system) can't work in magnetic field, earlier PET/MRI (for small animal imaging) relied on to keep the PMTs at a reasonable distance from the strong magnetic field of MRI unit.<sup>7</sup> This was accomplished by coupling the PET detectors (scintillator) to long optical fibers (4-5 meters) to bring the light to PMTs and read-out electronics outside the magnetic field.<sup>8</sup> However, the major drawback of this design was that the long fibers result in the loss of a significant fraction of the scintillation light, thus affecting the energy and temporal resolution and impairing the overall PET performance.<sup>4</sup> However, continuous research by industry and academia using various modifications in

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detectors and read-out electronic has paved the path of PET/MRI from preclinical arena to clinical and from brain only to whole body clinical scanners various configuration and acquisition protocols.

**PET/MRI Configuration and Acquisition Sequence:** Currently three PET/MRI systems have been launched by 3 major vendors, 2 with sequential and 1 with simultaneous acquisition of PET and MRI data. According to placement of PET and MRI, these can be broadly classified as tandem and integrated configuration.

1) **Tandem Configuration:** In this configuration PET and MRI data are acquired sequentially one after other by two separate scanners mounted in same or two separate rooms. Philip Healthcare's commercially available PET/MRI (Ingenuity TF PET/MRI) consists of two scanners placed in the same room about 2.5 meters apart with imaging table in between to allow the patient to be moved from one scanner to other without getting off the table.<sup>9</sup> GE Healthcare has chosen the "trimodality solution", comprising a top PET/CT scanner, allowing measured attenuation correction, and MRI systems in two adjacent rooms with the patient transferred from one scanner to the other using a dockable table operating as a shuttle.<sup>10</sup> The advantages of the tandem configuration are cost effectiveness as only additional magnetic shielding is required for MR without major modification in PET electronics and use of a sharing bed. Other advantages include lack of claustrophobia due to space between two systems and simplicity of image co-registration.<sup>4</sup> The major drawbacks of the tandem configuration with sequential acquisition are organ motion effects which reduce the precision of quantification, lack of correlation between functional PET and fMRI (particularly in brain studies) and requirement of larger room space.

2) **Integrated Configuration:** In this configuration two modalities are deployed in a single instrument and hence sequential imaging can be acquired. However, this configuration has many technical challenges as high magnetic field prevents the normal functioning of PMTs, interfering front-end electronics of PET and also presence of PET detectors may cause inhomogenities in magnetic fields. After preclinical prototypes and clinical PET/MR for brain only, recently a whole body PET/MRI has been introduced by a vendor (Biograph mMR, Siemens) which can acquire PET and MRI (3 Tesla) simultaneously as PET detector is placed between body and gradients coils of MRI. As a major modification step, PMTs have been replaced with Avalanche Photodiodes (APDs) coupled with Lutetium oxyorthosilicate (LSO).

These PET blocks are well shielded to virtually eliminate magnetic field interference in the PET data processing chain and also has integrated cooling feature (water-cooled).<sup>11</sup> The major advantages of this whole body PET/MRI configuration are simultaneous acquisition of PET and MRI which ensures precise alignment, minimal motion artifacts, precise spatial registration and shorter acquisition time. Furthermore, it is cost effective as one room is required for two systems, one cooling system, one operator and increase patients' throughput. However, limited temporal resolution of APD based system makes it incompatible with time of flight (TOF) technique which ensures better signal to noise ratio in PET/CT.<sup>12</sup> A study performed on whole body Biograph mMR (Siemens) has shown negligible interference of PET on MRI.<sup>11</sup> The Biograph mMR has received approval from US Food and Drug Administration (FDA) and European Union too in 2011.

### **Attenuation Correction (AC) in PET/MRI**

In PET attenuation and scatter correction (caused by PET hardware and also by distribution of tracer in soft tissue, bone and air) is mandatory for image resolution and quantification. In stand-alone PET scanner this has traditionally been performed by rotation of a radioactive Ge-68 source (Germanium-68, positron emitter, 511 keV) around the patient and from a number of projections, a topography of attenuation values ( $\mu$ -map) could be reconstructed. Although this was a time-consuming process but was more accurate for soft tissue attenuation correction for 511 keV gamma rays of injected PET tracer.<sup>13</sup> In existing hybrid PET/CT systems, the hardware (e.g. patient table) and the patient's tissue  $\mu$ -map are generated from a fast (potentially low-dose) 3D CT scan and then rescale Hounsfield units to 511-keV linear attenuation coefficients.<sup>14</sup> However, in case of a fully integrated PET/MRI scanner, the small space inside the bore of the magnet and the presence of a high magnetic field render both options unfeasible. In integrated PET/MRI system tissue attenuation has to be obtained in a completely different way. CT attenuation map reflects the distribution of density of different organs, being highest for bone due to high calcium content, which makes attenuation correction straightforward. But MRI signal is governed by the proton density and relaxation mechanisms and has no direct correlation with the tissue density as do CT images. In MRI-based attenuation correction, basic challenge is to find a way to determine tissue density from a set of MR images, for example, by separating different tissue classes and assigning the corresponding linear attenuation coefficients. However, in MR-based

AC, air and bone are depicted in black due to lower water content and quicker relaxation of proton in cortical bone, so that MRI signal disappears before it is sampled.<sup>15</sup> However, ultrashort echo time (UTE) sequence has been used successfully to visualize cortical bone.<sup>15</sup> Currently two methods have been suggested for obtaining attenuation maps from MR images which are template-based<sup>16</sup> and segmentation-based<sup>17</sup> and detail of these is beyond the scope of this article. In Biograph mMR system (only simultaneous PET/MRI system is available), tissue attenuation and scatter correction is performed twice. The attenuation correction of head/neck region is done with UTE while rest body parts by a Dixon technique providing two images where water and fat are 'in phase' and in 'opposed phase'.<sup>18</sup> Recently correlative studies comparing standard uptake values (SUV) measured by PET/CT and simultaneous PET/MRI (Biograph mMR) have shown good correlation.<sup>19,20</sup>

### Clinical Applications

Arrival of whole body simultaneous PET/MRI has taken multimodality imaging a step ahead of PET/CT. Since it has been approved by FDA and European Union, we expect rapid deployment of this modality in clinical arena worldwide. Oncology and cardiovascular diseases are two potential areas where this modality has major clinical applications.

In oncology PET/MRI will be indicated for those tumours (like musculoskeletal, head and neck, brain, breast and liver malignancies) where high soft tissue contrast is required for local tumour assessment (T-staging) and also when whole body staging is needed. It is expected that combination of metabolic information at molecular level by PET with high magnitude of morphostructural details of MRI would be more accurate for assessment of nodal and distant metastases than PET/CT. Based on integrated information provided by PET/MRI about cell metabolism and microenvironment, this will likely be an ideal tool for investigation of new drugs, evaluation of tumour response to these drugs and optimizing treatment strategy.<sup>9</sup> Real time monitoring of radiofrequency ablation of tumour using<sup>15</sup> O-water PET is another potential indication of PET/MRI.<sup>22</sup>

Cardiology seems to have good potential for integrated PET/MRI as simultaneous acquisition of data will allow accurate motion correction. PET/MRI has an established role in the diagnosis of coronary artery disease, detection of hibernating myocardium in patients with congestive heart failure, congenital heart disease and precise estimation of ventricular volumes. MR

angiography with FDG-PET also has great potential for detection of vulnerable plaques of coronaries and other vessels.

Simultaneous PET/MRI also opens new insight into neurology and evaluation of various disorders of brain like early diagnosis of dementia or neurodegenerative disorders, epilepsy and stroke which would have an enormous impact on management and its financial implication. In neuro-oncology simultaneous PET/MRI data would allow improve diagnostic accuracy and might be used for surgery and radiation therapy planning.<sup>23</sup>

Whole body simultaneous PET/MRI offers a powerful "one-stop shop" modality of anatomical, functional and molecular imaging technologies potentially superior to PET/CT, PET alone or MRI alone for certain clinical applications. However, comparative studies to evaluate clinical indications of whole body simultaneous PET/MRI based on diagnostic performance, feasibility, and cost relative to existing modalities is necessary before routine clinical PET/MRI becomes a reality.

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