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PET/MR: the Molecular Imaging Dream Team*

Introduction — why PET/MR?

In the last decade, PET/CT (Figure 1) imaging systems have become an essential tool for staging and restaging various types of malignant tutors and have been shown to have a significant impact on patient management [1, 2]. PET/CT also shows exciting potential in predicting the response to treatment for several types of cancer, including metastatic breast cancer [3], lung cancer [4], and lymphomas [5].

The clinical and commercial success of combined PET and CT imaging modality was primarily driven by the complementary character of data derived from each of the imaging modalities: anatomical detail of the CT and metabolic, molecular level information delivered by PET imaging (Figure 2A). In addition, the clinical workflow improvement and ease of use of the combined system cannot be overlooked.

Integration of CT and PET addressed some of the critical questions in diagnosis and staging of the disease: combination of lesions detectability (with FDG PET) and their localization (with CT). It also paved the way for further integration of other imaging modalities. For example, an increasing number of SPECT cameras are being replaced by combined SPECT/CT systems.

With the evolution of MR imaging techniques, MR imaging studies can provide additional diagnostic information regarding soft-tissue analysis, tumour detection, tissue characterization, and functional imaging (Figure 2B). It is not uncommon today for oncology patients to have both PET/CT and MR imaging scans providing complementary diagnostic data [6]. In some cases, the diagnostic value of MR for detection and staging of cancers can be superior to CT studies. This limits the value of the diagnostic CT studies that can be performed in combination with the PET/CT study to a simple anatomical localization and attenuation correction scan.

It is therefore quite rational to anticipate that a hybrid PET-MRI scan could be more valuable in such cases than a PET/CT scan followed by a complementary MRI scan [7]. In addition, whole

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Figure 1. GEMINI TF PET/CT system (Philips Healthcare, Cleveland, Ohio, USA).

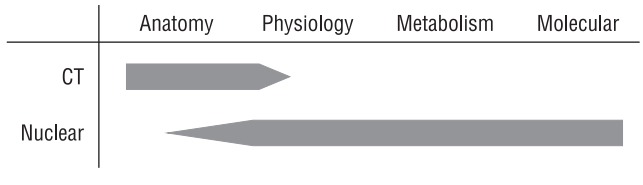

Figure 2A. Anatomical detail is the main strength of CT imaging. Nuclear medicine imaging and PET in particular, provide metabolic information at the molecular level.

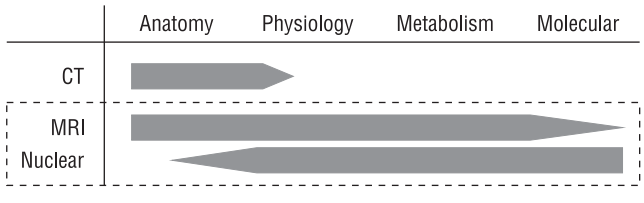

Figure 2B. MR imaging has a unique characteristic combining both anatomical detail and physiological, metabolic information. Combining these strengths of MRI with nuclear medicine imaging enables the study of multiple biomarkers during a single patient examination.

body MRI alone has been reported to have excellent diagnostic performance and has been proposed as an alternative to, or replacement for, PET/CT [8]. Whole body MRI, especially diffusion weighted sequences that showed high sensitivity, are being used increasingly in oncology for initial diagnosis or follow-up staging, as well as assessment of metastases, staging for pregnant woman and children, and follow-up of therapeutic response [9].

This promise to provide a comprehensive picture of patient anatomy (imaged by MR) combined with multi-parameter lesion characterization (imaged by PET and advanced MR imaging techniques) makes an integrated PET/MR system a leading candidate for the molecular imaging "dream team".

System design

In 2010, Philips Healthcare introduced the Ingenuity TF PET/MR, an integrated PET/MR hybrid imaging system similar to a PET/CT (Figure 3). The whole body PET-MRI system consists of a GEMINI TF PET system and an Achieva 3T X-series MRI system. The two scanners are separated by approximately 3 metres, with a sliding patient table between the two, allowing sequential imaging in each of the scanners with the patient staying perfectly still on the table. This system design was driven by the requirements of uncompromised performance of both modalities, full whole body imaging capabilities for PET and MR imaging and integrated clinical workflow.

Technical challenges

There are two critical technical areas that have to be addressed when considering an integrated PET/MR scanner:

— possible interference between the two modalities;
— use of MR imaging for the purpose of PET attenuation correction.

Figure 3. The Ingenuity TF PET/MR (Philips Healthcare, Cleveland, Ohio, USA) combines Philips time of flight PET technology (gantry on the left) with Philips Achieva 3T MR system (gantry on the right). Typically, the patient undergoes a fast MR imaging scan for the purpose of anatomical localization and attenuation correction, followed by a PET scan and then any additional MR imaging sequences. The patient table rotates between the scans but the patient remains in the original position. PET imaging is performed with MR coils in place.

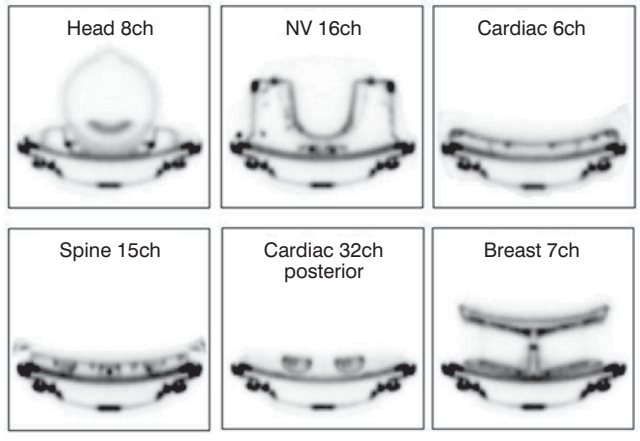

Figure 4. Attenuation correction of PET images using an attenuation map generated from automatic segmentation of whole-body MR images. From left to right: uncorrected PET image, MR attenuation correction sequence, segmented attenuation correction map at 511 keV, attenuation corrected PET image. Patient data courtesy of Prof. Ratib, HUG, Geneva, Switzerland.

Compared to PET/CT, modifications to the PET were made to avoid mutual system interference and deliver uncompromising performance that is equivalent to the standalone systems. System separation, additional shielding of the PET system, and placement of sensitive electronics in a separate equipment room were implimented to minimize possible interference. In particular, the PET gantry was redesigned to introduce magnetic shielding for the photomultipliers (PMTs), which ensured their operation in 'normal' flux levels close to the Earth's magnetic field.

Attenuation correction for clinical imaging represents the biggest challenge facing those working in the field of PET/MRI. Philips implemented a 3-segment approach for generation of MR based attenuation maps (Figure 4).

In addition to image segmentation, one needs to consider the attenuation of the patient table and the coils used for MR imaging. Neither of these is visible on the MR image and have to be inserted by software into the PET attenuation map. Figure 5 shows attenuation maps of different coils available on the Ingenuity TF PET/MR system.

Initial evaluation indicates that PET images obtained from the PET/MR system, reconstructed with default reconstruction method, portrayed good image fidelity qualitatively comparable to PET/CT.

System performance

The PET NEMA results obtained with PET/MR are comparable to typical GEMINI TF PET/CT. System energy and time of flight timing resolution were comparable to PET/CT, confirming the benefit of magnetic shielding to maintain the PMTs in normal flux levels. There is a slight decrease in peak NECR (Figure 6) and a minor increase in IEC background variability, which can be attributed to a thicker patient table used in the PET/MR system. Overall, the results demonstrate that both PET and MRI can function in close proximity without compromising PET imaging performance and quality.

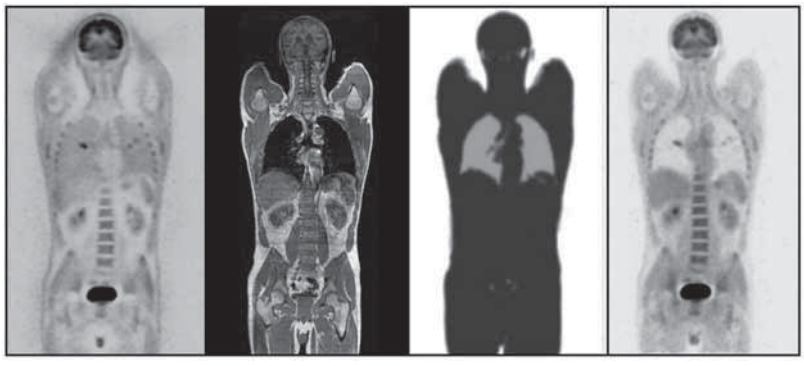

Figure 5. Attenuation templates for the patient table and different MR coils.

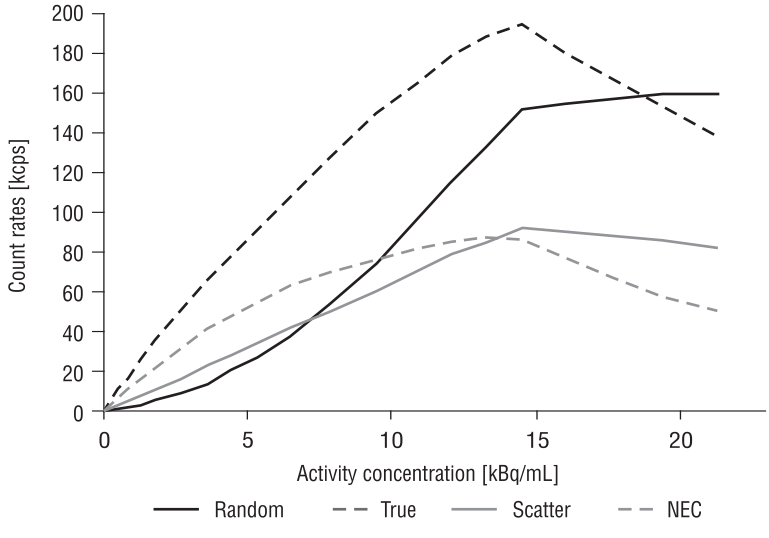

Figure 6. Random, true, scatter, and noise-equivalent count rate curves for Ingenuity TF PET/MR system. NEC [NEC = Trues2/(Trues + Scatter + Randoms)] performance *vs*. activity and scatter fraction measured using the 20 cm diameter × 70 cm long phantom with 555 MBq in a 70 cm line source at 4.5 cm from the central axis of the cylinder.

The Table 1 shows GEMINI TF PET/CT typical NEMA values compared to Ingenuity TF PET/MR. Time of flight timing resolution and energy resolution of the PET/MR system were stable over time and were measured to be 520 ps and 12%, respectively.

The 3T MR system is sensitive to frequencies in the range of 32 MHz to 128 MHz (e.g. for multinuclear). RF noise generated from electronics situated inside the PET gantry shows distinct MR artefacts [10]. While a normal PET system has EMI emissions that meet all regulatory requirements, requirements for MRI are far more stringent. To obviate these issues, PET system modifications were made to move all electronics from the PET gantry to the equipment room, where it is easier to mitigate spurious noise transmissions. The PET gantry contained only the normal crystal/PMT geometry and the first level of signal processing boards. All power and signal cables penetrating the MR walls were filtered through specially designed RF penetration panels to prevent extraneous EMI radiation from entering the imaging suite through the cables. Further, PET acquisition electronics were enclosed in an RF-tight cabinet which provided shielding effectiveness of 40 dB @ 1 GHz frequencies. These design changes allowed the elimination of the effects of the PET system on MR performance and image quality.

Table 1. Comparison of values of GEMINI TF PET/CT and Ingenuity TF PET/MR

Specification	GEMINI TF PET/CT	Ingenuity TF PET/MR
Spatial res. 1 cm transverse (FWHM)	4.7 mm	4.7 ± 0.1 mm
Sensitivity 0 cm/10 cm (cps/MBq)	7000/7200	7000 ± 155/7200 ± 142
NECR Max (kcps) — 20 cm	110	90 ± 3

Overall, the system performance demonstrates that both PET and MRI can function in close proximity without compromising PET and MR imaging specifications and image quality.

Clinical applications

The Ingenuity TF PET/MR has been designed to perform uncompromised PET and MR imaging for the entire spectrum of clinical applications. PET/MR as a new imaging modality has great potential to build on and extend the success of PET/CT by being able to provide more insight into relevant tumour biomarkers and better characterize cardiovascular, neurological, and other diseases.

There are two broad clinical applications for PET/MR that can potentially result in enormous benefit for the patient [11]:

— support the entire care cycle (diagnosis-treatment-monitoring) process;
— support the development of drugs by allowing the study of tumour growth and function, as well as the mechanisms of action that make a drug effective.

Screening and diagnosis

For some applications, screening programs could be introduced with a lower risk of exposing the patient population to radiation, by avoiding CT exposure. The excellent soft tissue discrimination and high resolution of MRI complement the sensitivity of PET imaging, making a diagnosis that is more firm, accurate, and reliable. Some preliminary work indicates that high-risk plaque characterization could be a possible application in this phase of the care cycle.

More accurate staging

In some types of cancer, PET/CT demonstrated some limitations for accurate cancer staging. A hybrid PET/MR, based on better soft tissue contrast, improves the potential for accurate tumour staging. MR can also more clearly discriminate the uptake of the PET tracer in areas that are active but not related to the tumour, such as brain, thyroid gland, striated muscle, bone marrow, digestive tract, and genitourinary tract. This could therefore reduce the number of false positives.

Better therapy planning

PET/MR could potentially provide truly individualized therapy planning for patients by providing additional information to better characterize the tumour. Today, PET/CT provides the anatomical extent of the tumour and the sugar metabolism of the tumour (with FDG PET). PET/MR has the potential to evaluate additional biomarkers that may be key in guiding the choice of intervention; examples might include tumour perfusion, angiogenesis, apoptosis, and cell proliferation. The composite picture of these biomarkers would allow the design of a personalized treatment strategy — extremely critical in the era of more targeted and very expensive therapies.

Therapy monitoring

A vital step in the long battle to make cancer a chronic disease could come in the form of accurate, non invasive, and safe patient monitoring. By not using the radiation of CT, PET/MR can allow scans of treated patients to be taken at regular intervals, maximizing the chance of catching any return of the disease early enough to successfully treat it.

Pharmaceutical development

A comprehensive picture of the key biomarkers that are enabled by combined PET/MR could be used to develop novel drugs and therapies. A whole body scanner could be used in early preclinical work, in translating the results into clinical research and eventually clinical practice. The combination of PET and MR imaging in a single system has brought molecular imaging a giant step closer to reality.

Summary

The future of PET/MR appears to be very bright. There are several potential clinical applications awaiting their validation. Preliminary results already demonstrate the value of combined modality in oncology (whole body scanning), cardiology (high-risk plaque assessment), and neurology. The Philips Ingenuity TF PET/MR system is well positioned to provide relevant clinical research data by delivering uncompromised performance in both PET (including time of flight) and MR (comprehensive 3T imaging portfolio). Once again, nuclear medicine is a big part of a new hybrid imaging modality that is well positioned to change the paradigm of imaging: from lesion (disease) detection to characterization.

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