A Pivotal Time for Hybrid PET/MR Imaging Technology

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INTRODUCTION

PET and MRI are well-established medical imaging techniques that have become valuable clinical and research tools. However, the incapability of PET to provide adequate assessment of molecular and metabolic behavior of tissue has limited the capabilities of PET and MR techniques used separately, each providing different but complementary information. The combination of PET and MRI's complementary data can forseeably enable truly simultaneous acquisition and bridge the gap between molecular and anatomical diagnosis criteria [1].

The first endeavors to perform PET imaging in strong static magnetic fields were inspired by the requirement to reduce the range of positrons before they are annihilated through magnetic confinement of emitted positrons. It was demonstrated through Monte Carlo simulation studies that the transaxial spatial resolution could be improved without affecting axial resolution when a magnetic field collinear with the imager axis is used [2]. This is achieved by the Lorentz force, which acts on the positrons with a velocity vector component perpendicular to the magnetic field such that the positrons will spiral between particle interactions with matter, thus reducing positron range especially for high-energy positron emitting radionuclides. The predicted improvement in spatial resolution for high-energy positron emitters was reported in the reference above to vary between 18.5% (2.73 mm instead of 3.35 mm) for Ga-68 and 26.8% (2.68 mm instead of 3.66 mm) for Rb-82 at a field strength of 7 T.

Surprisingly, prospective developments of hybrid PET/MR systems date from 1994 [3], even before the first peer-reviewed articles on PET/CT appeared. However, hybrid PET/MR developments started with systems dedicated to small-animal imaging as opposed to PET/CT, which was launched mainly for clinical usage. Early designs of MR-compatible PET detector modules were based on the modification of conventional detector blocks of a prototype small animal PET scanner to avoid mutual interference between the 2 systems. This was achieved by coupling the position-sensitive photomultiplier tubes (PMTs) and readout electronics, located at a sufficient distance from the strong magnetic field of a commercial MR imaging scanner, using long (4-5 m) optical fibers [4]. This design inherently has many drawbacks, including the loss of scintillation light through the long fibers, thus producing a weak signal, which negatively impacts energy and timing resolution, impairs crystal identification, decreases PET signal performance, and reduces overall PET scanner performance.

Recent advances in MR-compatible readout technology, such as avalanche photodiodes and silicon photomultiplier tubes, enabled the design and implementation of compact and integrated PET/MR systems, making it possible to acquire simultaneously PET and MR data without compromising system performance on both modalities. These technologic advances enabled the design of more advanced PET/MR units dedicated initially to brain and more recently for whole-body imaging, thus allowing a practical exploration of the clinical potential of this hybrid technology [5].

DESIGN FEATURES OF PET/MR

Subsequent to pioneering work and early attempts discussed in the previous section, different design alternatives of PET/MR systems have materialized during the last decade (Table 1). The most straightforward approach adopted the configuration of clinical PET/CT systems, where separate PET and MR scanners were arranged in tandem to enable sequential data acquisition in space and time. This less challenging design concept was adopted as a first step to gain experience and establish the clinical role of this hybrid modality while waiting for mature and economically practical simultaneous whole-body PET/MRI units to become available [5]. Figure 1 shows potential design concepts of combined PET/MRI systems.

Two commercial units belonging to this category were successfully used in clinical settings for a variety of clinical indications. The Ingenuity TF PET/MRI (Philips Healthcare, Best, the Netherlands), equipped with time-of-flight Gemini TF PET and Achieva 3T X-series MRI scanners, falls in this category and uses a rotating patient handling system to enable sequential PET and MR imaging. Full characterization demonstrated no significant interference between the 2 systems or compromise of PET subsystem performance in the presence of the strong MR

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Table 1. Clinical PET/MR systems comparison

System	Manufacturer	Operation	PET Detector	TOF	MRI	Reference
Biograph mMR	Siemens	Simultaneous	LSO/APDs	No	3T Verio (modified)	[11]
Ingenuity TF	Philips	Sequential	LYSO/PMTs	Yes	3T Achieva	[6]
Unnamed	General Electric	Simultaneous	LYSO/SiPMTs	Yes	3T MR 750w	[13]
Trimodality	General Electric	Sequential	LYSO/PMTs	Yes	3T MR 750w	[8]
BrainPET	Siemens	Simultaneous	LSO/APDs	No	3T Magnetom (modified)	[10]
Brain MGI	Academia	Sequential	LSO-LYSO/PMTs	No	7T Magnetom	[7]

APDs = avalanche photodiodes; SiPMTs = silicon photomultiplier tubes; TOF = time of flight

magnet [6]. A similar design concept was also developed for high-resolution neuromolecular imaging in high magnetic field by docking separate PET (Siemens' high-resolution research tomograph) and 7-T MR imaging units together with a shared common bed to integrate both modalities [7]. The second system designed by General Electric (GE Healthcare, Waukesha, WI, USA) enables trimodality imaging (PET/CT/MRI) through sequential imaging on separate PET/CT and MR systems placed in adjacent rooms. A mobile patient handling system shuttles the patient from one scanner to the other [8]. One of the motivations behind this design is the capability to operate both scanners separately in case of high clinical workload. However, the major obstacle of this design is the additional complexity of the logistics and the high risk of patient motion during transfer from one examination room to the other. Another drawback is that an additional CT scan is required for correction of photon attenuation, thus increasing the radiation dose to the patient.

Despite the usefulness of sequential PET/MR systems for many applications that do not require simultaneous imaging, the objective targeted since the inception of hybrid PET/MR technology is to perform simultaneous PET and MRI imaging in space and time. Two main design concepts were followed to reach this goal in both academic and corporate settings: use the PET detector ring as an "insert" inside a standard MRI scanner or use a "fully integrated" compact version where a dedicated whole body PET scanner is built in a dedicated MRI scanner. This design concept is expected to take combined PET/MRI a genuine step forward toward its adoption in clinical diagnosis, therapy monitoring, and follow-up. In the latter design a small axial-size PET insert is fitted inside a standard clinical MRI scanner. This solution was adopted for the design of hybrid systems dedicated to small-animal [9] and brain [10] imaging. Despite the challenges associated with this technology and some inherent limitations (implementation of time-of-flight capability not possible on slow avalanche photodiodes-based readout technology), this design concept was taken further with appropriate modifications to build an integrated compact hybrid system dedicated to whole-body PET/MRI imaging. This first commercial system, launched on the market called the Biograph mMR, is manufactured by Siemens Healthcare (Erlangen, Germany) [11] and was recently

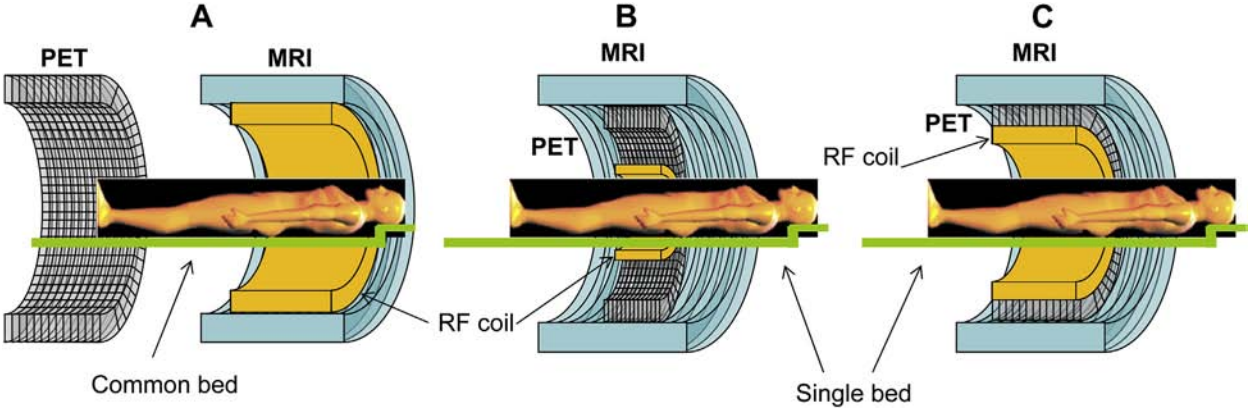

Fig 1. Schematic cross-sectional views of potential designs for combined PET/MR imaging systems: (A) tandem design with two imagers mounted back-to-back (similar to that in PET/CT instrumentation) to allow sequential rather than simultaneous acquisition, (B) insert design with PET imager inserted between radiofrequency coil and gradient set of MR imager, and (C) fully integrated design with two imagers in same gantry. Radiofrequency (RF) coil, gradient set, PET imager, and patient bed are shown for all configurations. Adapted with permission from [5].

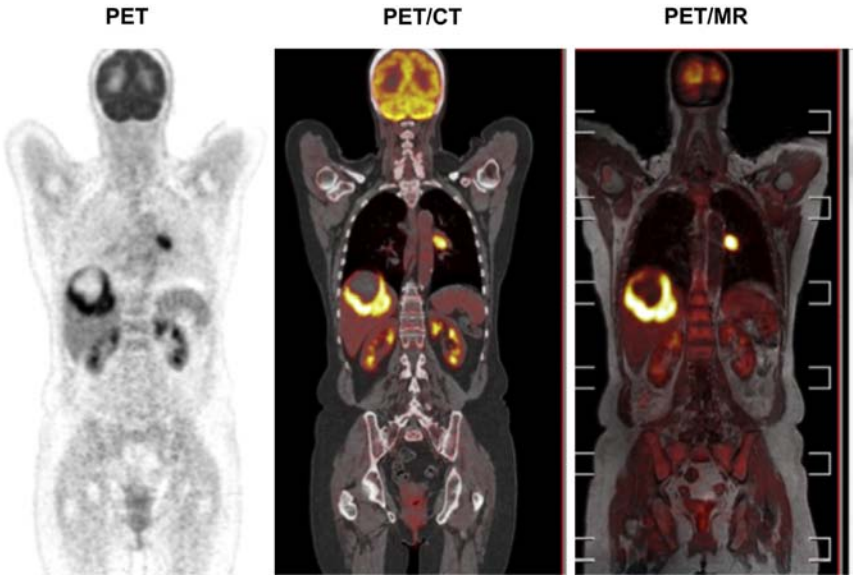

Fig 2. Representative clinical whole-body PET (left), PET/CT (middle), and PET/MR (right) images of the same patient acquired sequentially (~70 minute time difference) on 2 combined systems (Siemens Biograph Hirez TrueV and Philips Ingenuity TF PET/MRI, respectively) following injection of 370 MBq of ^{18}F-FDG. Courtesy of Geneva University Hospital.

deployed in a number of European and North American facilities for assessment and validation in clinical and research settings, leading in a short time to numerous initial reports on its clinical applicability [12]. More recently, some very preliminary results about the integrated PET/MR system being actually developed by General Electric were presented at the 2013 Society of Nuclear Medicine and Molecular Imaging meeting [13].

Figure 2 shows representative clinical whole-body PET/CT and PET/MR images of a lung cancer patient acquired sequentially on 2 combined systems, namely Biograph TruePoint 64 (Siemens Healthcare) and Ingenuity TF PET/MRI (Philips Healthcare). The PET/CT study started 30 minutes after injection of 370 MBq of ^{18}F-FDG followed by PET/MRI, which started about 70 minutes later. The lesion detected at PET/CT was also identified by PET/MRI, with a small difference between PET/CT and PET/MRI uptake ratios, owing to differences in uptake time. However, the better soft tissue contrast observed on MRI is obvious and far superior to PET/CT in cases where soft tissue analysis is required, thus emphasizing the potential role of PET/MRI.

CONCLUSION

Hybrid PET/MR imaging is currently viewed as a major technological breakthrough having the potential to trigger a groundbreaking paradigm shift in clinical diagnostic imaging as it holds praise to bringing sweeping change. A number of active research groups in academic and corporate settings are currently focusing on the development of compact and stable PET/MRI systems allowing simultaneous imaging using the most advanced molecular and anatomical imaging technologies currently available. However, despite the advances and technical achievements, some challenges still face the success and widespread adoption of PET/MR technology. These include the establishment of an evidence-based clinical role for this modality and its cost-effectiveness in the context of an economically challenged health care system, where cost and justification play a pivotal role. The deployment in the clinic of a number of hybrid PET/MRI systems beyond the critical mass with different design configurations will enable comparative and cost effectiveness research to be carried out to justify the need for simultaneous PET/MRI as a replacement for sequential, software-based PET/MR image fusion and more widely adopted PET/CT imaging. In addition, the required qualifications of interpreting nuclear medicine physicians and radiologists, residents in training, technologists, and medical physicists will need to be defined and harmonized by interdisciplinary task groups representing the various professional societies involved. Finally, PET/MR studies will require appropriate reimbursement by health insurances and by national health systems.

For this technology to realize its full potential in clinical and research settings, the quantitative capabilities of PET/MRI still need

to be improved and validated in large clinical studies The anatomical information provided by MRI is currently used for attenuation compensation but could also be useful for many other tasks, including motion detection and correction, image reconstruction, and partial volume correction. Despite the many worthwhile research efforts, more robust and accurate MR-guided attenuation correction strategies still need to be developed and validated. This will remain a very hot and active research topic for the next few years. It is foreseen that more accurate and robust measurements of absolute tissue metabolic activity could bring an additional strength to hybrid imaging in the future.

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