by Dr H Zaidi

Advances in hybrid PET-MR imaging

The development and clinical deployment of hybrid PRT/MRI systems has enabled the assessment of the possibly ground-breaking potential of the approach. Despite this, formidable challenges remain, not the least of which is economic justification.
This article reviews the potential clinical role of hybrid PET/MR systems, describes the currently available equipment and their applications as well as the issues needing to be resolved

RATIONALE FOR AND POTENTIAL CLINICAL ROLE OF HYBRID PET-MR IMAGING

Positron emission tomography (PET) and magnetic resonance imaging (MRI) have become prevailing medical imaging techniques and have proven to be valuable clinical and research tools. However, the inability of PET to provide anatomical information and the difficulties of anatomical MRI to provide molecular signals is considered a major limitation of standalone PET and MR systems [1]. This has motivated the development of software approaches to align PET images with CT or MRI anatomical images [2]. This task proved to be successful in the brain but not in other parts of the body such as the thorax and upper abdomen where the non-rigid motion between the two images owing to different breathing patterns resulting from differences in acquisition times make the registration task difficult to achieve in these regions.

In this context, the development of combined SPECT/CT and PET/CT scanners for clinical imaging rendered possible the acquisition of both structural and functional images [3, 4]. Even though CT has well established benefits in oncological imaging, an extremely attractive substitute to PET/CT is to combine PET with MRI, since the repertoire of MR examinations is greatly complementary to PET [5].

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The combination of PET and MRI, enabling truly simultaneous acquisition, bridges the gap between molecular and systems diagnosis. Since PET and MRI offer richly complementary functionality and sensitivity, integration into a combined system offering simultaneous acquisition will capitalize the strengths of each. Moreover, the dual-modality system would enable the exploitation of the superiority of MR spectroscopy (MRS) to gauge regional biochemical content and to measure the metabolic status or the presence of neoplasia and other diseases [6-8].

Figure 1 shows representative clinical whole-body PET/CT and PET/MR images of a lung cancer patient acquired sequentially on two combined systems, namely the Biograph TrueV (Siemens Healthcare) and the Ingenuity TF PET/MRI (Philips Healthcare). The PET/CT study started 30 mins following injection of 370 MBq of ^{18}F-FDG followed by PET/MRI which was begun about 70 mins later. The lesion detected at PET/CT was also identified by PET/MRI, with 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 further emphasizes the ineffectiveness of PET/CT in some indications, and so emphasizes the potential role of PET/MRI.

The clinical role of hybrid PET/MR imaging is currently encompassing a wide variety of applications and is being performed in some facilities equipped with this technology to answer important clinical questions including those in oncology [6-8], cardiology [8, 9], neurology and psychiatry [10]. Nowadays, a plethora of novel tracers are used routinely for assessing tumour metabolism and other biological and physiological parameters associated with many diseases [11, 12]. These have clearly demonstrated the enormous potential of emerging hybrid technologies in the field of molecular imaging. Some opinions are emerging which advocate the potential benefits of simultaneous PET/MR

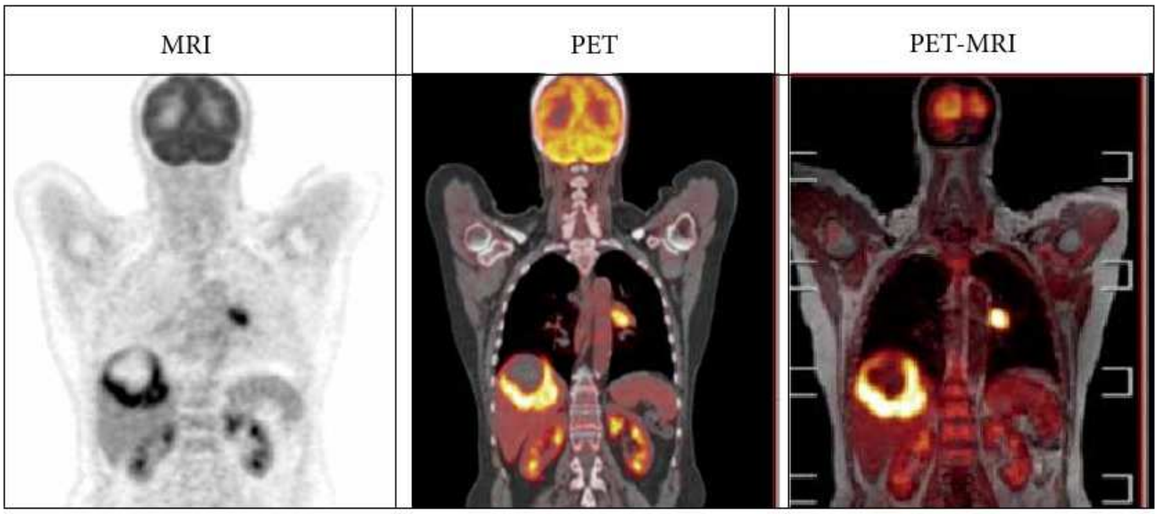

FIGURE 1. Representative clinical whole-body PET (left), PET/CT (middle) and PET/MR (right) images of the same patient acquired sequentially (~70 min time difference) on two combined systems (Siemens Biograph Hirez TrueV and Philips Ingenuity TF PET/MRI, respectively) following injection of 370 MBq of 18F-FDG. Courtesy of Geneva University Hospital.

imaging over PET/CT technology in terms of improvement of tissue characterization. However, many challenging issues still need to be addressed. These include the clinical relevance and clinical/economic justification for this technology.

2. ADVANCES IN HYBRID PET-MRI SYSTEMS

Following the pioneering work and early attempts initiated in the 1990s [13, 14], different trends for PET-MR system design have emerged during the last decade [15-17]. The simplest design follows the configuration adopted for PET/CT where the PET and MR scanners are arranged in tandem, thus enabling sequential data acquisition in space and time. These systems were designed in expectation of the availability of mature and economically viable simultaneous whole-body PET/MRI systems [18].

Two such systems were developed and are now commercially available. The first is the Ingenuity TF PET/MRI (Philips Healthcare, Best, The Netherlands), with time-of-flight Gemini TF PET and Achieva 3T X-series MRI systems, allowing for sequential acquisition of coregistered PET and MR images. The characterisation of the PET subsystem demonstrated no compromise of system performance caused by the presence of the strong MR magnet [19]. In our facility, the system is being mostly used for clinical oncology, focusing on breast cancer, head and neck cancer and prostate cancer. Figure 2 shows a representative PET/MRI study for staging of breast cancer. An alternative proposed by General Electric (GE Healthcare, Waukesha, WI, USA) enabling trimodality imaging (PET/CT/-MRI) uses sequential acquisition on two separate scanners (PET/CT and MR) located in adjacent rooms with a mobile bed that can shuttle the patient from one scanner to the other [20]. This latter solution has the advantage that the two scanners can be operated separately in case of high workload, but presents a major drawback and logistical challenge in terms of coordinating patient transfer from one scanner to the other, and represents a higher risk of patient motion between the two examinations. This design also requires the acquisition of a CT scan for attenuation correction of the PET data, thus resulting in additional radiation dose to the patient.

The most attractive design option is to perform the PET and MRI examinations simultaneously in space and time. This solution has brought to the "insert" concept adopted for both preclinical [21] and brain PET-MR systems design [22], where a small axial size PET insert fits inside a standard MRI scanner. A more challenging solution is the "fully integrated" version, where a dedicated whole body PET scanner is built in a dedicated MRI scanner. This is the most promising option that that can bring to a genuine step forward the adoption of combined PET/MRI systems in clinical diagnosis, therapy and follow-up. The mMR whole-body PET/MRI system (Siemens Healthcare, Erlangen, Germany) is one example of an integrated compact hybrid system. The system was recently deployed in a number of facilities located in Europe and the US for assessment and validation in clinical and research settings [23, 24].

3. FUTURISTIC OUTLOOK

The recent introduction of hybrid PET/MRI technology is viewed as a major breakthrough having the potential to prompt a ground-breaking paradigm shift in diagnostic imaging and modernize clinical practice. A number of active research groups in academic and corporate settings are concentrating their efforts towards the

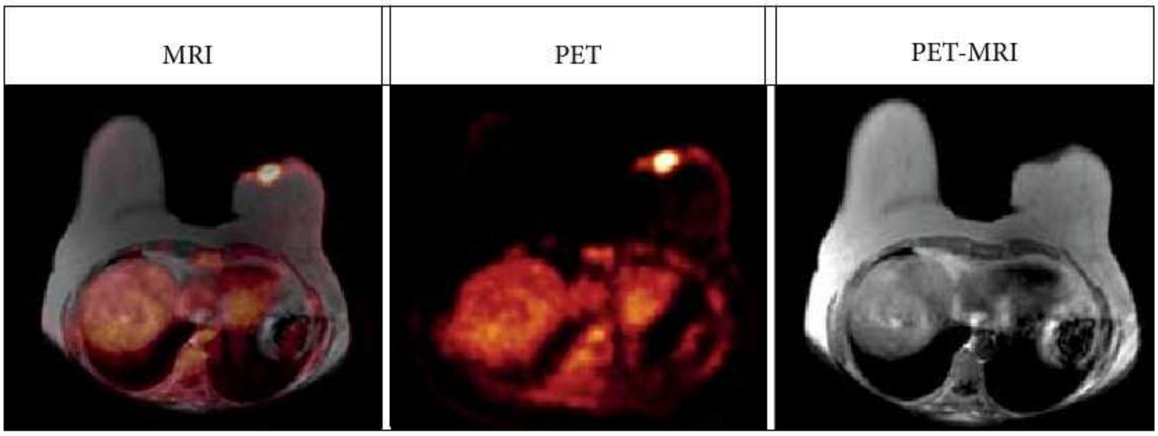

FIGURE 2. Whole body PET/MR study for staging of breast cancer. From left to right, axial planes of low resolution T1-weighted MR scan used for localization and tissue attenuation correction, PET image showing a hypermetabolic lesion of the left breast and fused PET and MR images.

development of stable and compact PET/MRI systems enabling simultaneous imaging using the most highly sophisticated molecular imaging technologies available today.

However, despite the many promising aspects of PET/MRI, many challenges are still facing the success and widespread adoption of this technology, the most relevant being its clinical relevance and economical viability within modern healthcare systems where cost and justification play a pivotal role. The likely clinical deployment of different configurations of hybrid PET/MRI systems in the near future will enable comparative effectiveness research to be performed in order to justify the need for simultaneous PET/MRI as opposed to sequential or even software-based PET/MR image fusion. In addition, the qualifications required of interpreting nuclear medicine physicians and radiologists, residents in training, technologists, and medical physicists will need to be defined and harmonized by interdisciplinary groups representing the various professional societies involved. Finally, new reimbursement guidelines for PET/MRI will also have to be established prior to clinical implementation.

For this technology to realize its full potential, the quantitative capabilities of PET/MRI still require major improvements and validation. The anatomical information provided by MR is currently used with some limitations for attenuation compensation but could also be useful for many other tasks including, motion detection and correction [25], image reconstruction [26], and partial volume correction [27]. Despite the many worthwhile research efforts, the commercial solutions provided for MR-guided attenuation correction are still not satisfactory. As such, this will remain a very hot and active research topic within the next few years.

REFERENCES

1. Pichler BJ, Kolb A, Nagele T, Schlemmer HP. PET/MRI: paving the way for the next generation of clinical multimodality imaging applications. J Nucl Med. 2010;51:333-36.
2. Hill DL, Batchelor PG, Holden M, Hawkes DJ. Medical image registration. Phys Med Biol. 2001;46:R1-45.
3. Hasegawa BH, Gingold EL, Reilly SM, Liew SC, Cann CE. Description of a simultaneous emission-transmission CT system. Proc SPIE. 1990;1231:50-60.
4. Beyer T, Townsend D, Brun T, Kinahan P, Charron M, Roddy R, et al. A combined PET/CT scanner for clinical oncology. J Nucl Med. 2000;41:1369-290.
5. Zaidi H, Mawlawi O. Simultaneous PET/MR will replace PET/CT as the molecular multimodality imaging platform of choice. Med Phys. 2007;34:1525-28.
6. Buchbender C, Heusner TA, Lauenstein TC, Bockisch A, Antoch G. Oncologic PET/MRI, Part 1: Tumors of the brain, head and neck, chest, abdomen, and pelvis. J Nucl Med. 2012;53:928-38.
7. Buchbender C, Heusner TA, Lauenstein TC, Bockisch A, Antoch G. Oncologic PET/MRI, part 2: bone tumors, soft-tissue tumors, melanoma, and lymphoma. J Nucl Med. 2012;53:1244-52.
8. von Schulthess GK, Kuhn FP, Kaufmann P, Veit-Haibach P. Clinical positron emission tomography/magnetic resonance imaging applications. Semin Nucl Med. 2013;43:3-10.
9. Wehrl HF, Sauter AW, Judenhofer MS, Pichler BJ. Combined PET/MR imaging-technology and applications. Technol Cancer Res Treat. 2010;9:5-20.
10. Catana C, Drzezga A, Heiss W-D, Rosen BR. PET/MRI for neurologic applications. J Nucl Med. 2012;53:1916-25.
11. Valliant JF. A bridge not too far: Linking disciplines through molecular imaging probes. J Nucl Med. 2010;51:1258-68.
12. Wester H-J. Nuclear imaging probes: from bench to bedside. Clin Cancer Res. 2007;13:3470-81.
13. Christensen NL, Hammer BE, Heil BG, Fetterly K. Positron emission tomography within a magnetic field using photomultiplier tubes and lightguides. Phys Med Biol. 1995;40:691-97.
14. Shao Y, Cherry SR, Farahani K, Meadors K. Simultaneous PET and MR imaging. Phys Med Biol. 1997;42:1965-70.
15. Delso G, Ziegler S. PET/MRI system design. Eur J Nuc Med Mol Imaging. 2009;36:86-92.
16. Zaidi H, Del Guerra A. An outlook on future design of hybrid PET/MRI systems. Med Phys. 2011;38:5667-89.
17. Vaska P, Cao T. The state of instrumentation for combined positron emission tomography and magnetic resonance imaging. Semin Nucl Med. 2013;43:11-18.
18. Torigian D, Zaidi H, Saboury B, Udupa J, Kwee T, Karp J, et al. PET-MRI: Technical aspects and potential clinical applications. Radiology 2013 in press
19. Zaidi H, Ojha N, Morich M, Griesmer J, Hu Z, Maniawski P, et al. Design and performance evaluation of a whole-body Ingenuity TF PET-MRI system. Phys Med Biol. 2011;56:3091-106.
20. Veit-Haibach P, Kuhn F, Wiesinger F, Delso G, von Schulthess G. PET–MR imaging using a tri-modality PET/CT–MR system with a dedicated shuttle in clinical routine. Magn Reson Mat Phys Biol Med. 2013:in press.
21. Judenhofer MS, Wehrl HF, Newport DF, Catana C, Siegel SB, Becker M, et al. Simultaneous PET-MRI: a new approach for functional and morphological imaging. Nat Med. 2008;14:459-65.
22. Kolb A, Wehrl HF, Hofmann M, Judenhofer MS, Eriksson L, Ladebeck R, et al. Technical performance evaluation of a human brain PET/MRI system. Eur Radiol. 2012;22:1776-88.
23. Delso G, Furst S, Jakoby B, Ladebeck R, Ganter C, Nekolla SG, et al. Performance measurements of the Siemens mMR integrated whole-body PET/MR scanner. J Nucl Med. 2011;52:1914-22.
24. Drzezga A, Souvatzoglou M, Eiber M, Beer A, Ziegler S, Furst S, et al. First clinical experience of integrated whole-body MR/PET. Comparison to PET/CT in patients with oncological diagnoses. J Nucl Med. 2012;53:845-55.
25. Ouyang J, Li Q, El Fakhri G. Magnetic resonance-based motion correction for positron emission tomography imaging. Semin Nucl Med. 2013;43:60-67.
26. Bai B, Li Q, Leahy RM. Magnetic resonance-guided positron emission tomography image reconstruction. Semin Nucl Med. 2013;43:30-44.