Institution: King's College London

Unit of Assessment: UoA15

Title of case study: Simultaneous PET & MRI

1. Summary of the impact

Positron emission tomography (PET) and magnetic resonance imaging (MRI) are two of the most powerful clinical imaging tools. They provide complementary information that is used in the diagnosis of many diseases and in assessing the effect of current and new therapies. Researchers at King's College London, in an international collaboration, demonstrated for the first time the simultaneous acquisition of PET and MR data and the application of the technique in preclinical models. Simultaneous PET-MR systems significantly improve the quality of patient care by allowing both PET and MR examinations to be performed in a single scanning session and by reducing radiation exposure by a factor of two. This pioneering work has led to clinical whole body simultaneous PET-MR systems recently becoming commercially available and there are currently around 40 PET-MR scanners installed in clinical/research institutions worldwide.

2. Underpinning research

Both PET and MRI have established roles in the routine management of many serious diseases and in biomedical research. Research in the field from KCL is comprised of a body of work mainly carried out between 1996 and 2005 which describes, for the first time, the simultaneous acquisition of data from these two modalities and initial applications in preclinical models.

The main technical challenge in performing simultaneous PET and MRI is that photo-multiplier tubes (PMTs), the standard PET detector technology, will not function in a magnetic field. Work to solve this problem was led by Marsden (1991-present, Professor), Garlick (1985-2010, Senior Lecturer) and Williams (1994-present, Professor), in collaboration with Cherry at UCLA School of Medicine.

The team initially developed a non-imaging system to acquire radiotracer uptake measurements simultaneously with MR spectra from the isolated perfused rat heart in a 9.4T MR spectroscopy magnet. A light pipe transferred light from a scintillation detector placed within the magnet to a PMT placed outside the magnetic field. Changes in the rate of, for example, glucose metabolism, could be correlated with changes in the concentration of various metabolites in the heart in response to interventions such as ischemia or hypoxia [1].

Concurrently, one of the first small animal (non-MR-compatible) PET systems was being developed by Cherry at UCLA. Coincidentally, this system used optical fibres in its design and researchers realised that this approach could be used to extend the KCL non-imaging system to an MR-compatible PET configuration. In collaboration with the UCLA group, a small prototype PET scanner, including all electronics and software to enable its use in real biological experiments, was constructed and demonstrated. The 5.4 cm diameter allowed the detector to be placed within the bore of a spectroscopy magnet and 4m long optical fibres transported light from individual scintillation crystals to three multi-channel PMTs situated away from the magnet. A purpose-designed NMR probe and canullation procedure allowed both coronary beds of the isolated perfused rat heart to be independently perfused and 31P MRS and 18FDG PET signals were obtained from each [2].

The dual modality/dual perfusion system was used in various investigations of myocardial metabolism. For example, it was possible to demonstrate an unexpected differential response of fluorodeoxyglucose (FDG: standard PET tracer) and deoxyglucose (DG: MRS visible) to ischemic and reperfusion interventions [3].

Detailed investigations into the various potential sources of interference between PET and MR were performed. This confirmed that for the prototype system it was possible to acquire PET and MR images simultaneously without any significant artefacts or loss in data quality in either modality [4].

A study demonstrated that simultaneous FDG-PET and MR images of the mouse brain in-vivo could be obtained - an MR-visible fiducial marker aligned with the PET imaging plane was attached to the PET scanner, thus allowing PET and MR image planes to be accurately registered [5].

A further system consisting of four concentric rings of LSO crystals, each coupled to one of eight multi-channel photomultiplier tubes via 3.5m optical fibres, was designed, constructed and demonstrated. This addressed many of the limitations of the prototype demonstrating excellent uniform spatial resolution, increased field-of-view and greatly improved count rate capability [6,7].

PET-MR research has continued at KCL as part of two large EU-FP7 collaborations focusing on novel MR-compatible PET-detector technology, PET-MR interactions/compatibility and the use of simultaneous MR measurements to address the long-standing problem of patient motion in PET. In 2010, KCL researchers described for the first time the use of simultaneously-acquired MR data to correct for non-rigid motion in PET [8] - the recent availability of whole body PET-MR systems will now allow these techniques to be applied in human clinical studies.

3. References to the research

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3. Garlick PB, Medina RA, Southworth R, Marsden PK. Differential uptake of FDG and DG during post-ischaemic reperfusion in the isolated, perfused rat heart. Eur J Nucl Med 1999;26(10):1353-58. Doi: 10.1007/s002590050595
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Grants

Development of a prototype PET scanner to operate inside an MR magnet. Marsden PK & Garlick PB, Special Trustees of Guy's Hospital, £19 558, 1995 -1996

Simultaneous PET+NMR. Marsden PK, Royal Society, £9,418, 1998 –1999

Simultaneous PET+NMR. Marsden PK, Keevil S, Williams SCR. EPSRC, £247,156, 1998 – 2001

Hybrid PET-MR system for concurrent ultra-sensitive imaging (HYPERImage). Shaeffter T, Marsden PK et al. EU-FP7, £513,438 (KCL funding), 2008-2011

SUB nanosecond Leverage In PET/MR iMAging (Sublima). Marsden PK, Schaeffter T et al. EU-FP7, £968,777 (KCL funding), 2011-2015

4. Details of the impact

Researchers at the Division of Imaging Science & Biomedical Engineering, KCL in collaboration with UCLA, devised and demonstrated, for the first time, the basic concepts of simultaneous PET and MRI, including practical implementations of the technique and demonstrations of applications. This work has led to industry collaborations and the development of PET-MR scanners. It has initiated what has become a very large field with considerable commercial and clinical impact.

Combined PET-MR examinations have directly improved patient experience. The innovation has immediately reduced the need for multiple examinations and so reduced the number of patient hospital visits. There is also a two-fold reduction in radiation dose from PET-MR compared with PET-CT, which is particularly important for paediatric studies. The beneficiaries of both the direct clinical use of PET-MR, and any new therapies that it helps bring to the clinic more rapidly, are patients with a wide variety of serious illnesses including cancer, and neuropsychiatric and heart diseases.

Combined PET-MR examinations also result in logistical benefits. Historically PET and MR data have been obtained on different occasions and often in different hospital departments, which can be challenging for the patient workflow. The logistical and patient experience benefits of performing PET and MR examinations in the same session have recently been demonstrated (Catalano et al 2013).

The clinical and research applications of simultaneous PET-MR are now being developed and evaluated worldwide, as evidenced in, for instance, a 2012 review paper by Martinez-Möller that cites both Buchanan et al. 1996 and Garlick et al. 1997 when discussing the introduction of the first preclinical combined PET/MR systems [14].

PET-MR is the most complex imaging technology to date with scanners costing around £3-4M. Initial sales have mainly been to large clinical/research institutions. Siemens launched a CE marked system, the Biograph mMR [9] in 2010, which has now been installed in 40 academic hospitals around the world, with numbers increasing. Company-sponsored talks recognise the pioneering work of KCL when discussing the background to their current technology [10,11].

The three main multinational medical imaging companies – Siemens, General Electric (GE) and Philips – have all developed, or are in the process of developing, whole body human simultaneous PET-MR scanners. GE has announced that they will have a system available in early 2014 and Philips is involved in various R&D projects in this area. KCL work is acknowledged by the manufacturers as the first development of the technology showing its feasibility (see letters from Siemens and Philips [12]) and is referenced in a number of company patents and patent applications. For instance, a patent filed by GE on ‘Exclusion of compromised PET data during simultaneous PET-MR acquisition,’ [13] cites Garlick et al. 1997; Marsden et al. 2002 and Slates et al. 1999.

Similarly, numerous recent leading review articles regarding clinical PET-MR acknowledge KCL’s contribution. For instance, Herzog et al [15] acknowledge ‘the pioneering work of S. Cherry and P. Marsden dealing with the first simultaneous MR-PET scan.’ Similarly, Pichler et al. [16], when discussing the idea to combine PET and MRI state that, ‘Simon Cherry and Paul Marsden saw the need for PET/MRI in small-animal imaging studies to add anatomic landmarks with high soft-tissue contrast to the molecular information delivered by PET.'

Both Siemens and GE expect significant impact through the use of PET-MR in oncology and neuropsychiatry. Both application areas have double-digit growth rates (15-25%) with a strong trend towards therapy assessment (Biotech report 2008). In particular, the National Cancer Institute in the United States is currently standardising PET and MRI procedures for cancer therapy assessment, and it is projected that by 2015 response monitoring will grow from 14% to 48% of all PET procedures (Biotech report 2008).

The future potential of PET-MR is widely acknowledged as evidenced by the specific EU Framework 7 call in this area [17], which was awarded to a consortium including KCL. Due to the only very recent availability of human whole body systems, work evaluating the many potential applications and advantages of PET-MR is only just beginning to emerge, including clinical utility and advantages obtained from MR-based motion correction [18,19].

5. Sources to corroborate the impact

Company related sources

9. Siemens Biograph mMR Product Brochure http://healthcare.siemens.com/magnetic-resonance-imaging/mr-pet-scanner/biograph-mmr
10. 'MR-PET technology', B Pichler (U. Hospital Tuebingen) at the 7th MAGNETOM World Summit in Shenzhen, China. Marsden and Cherry acknowledged as pioneers of PET/MRI at 4:48-5:41: http://www.healthcare.siemens.com/magnetic-resonance-imaging/magnetom-world/clinical-corner/clinical-talks/7th-magnetom-world-summit-pichler
11. 'Technical aspects of BrainPET', C. Catana, (Mass. Gen. Hospital, Boston) at the 2nd Ultra High Field User Meeting in Leipzig, Germany. Marsden and Cherry acknowledged as pioneers of PET/MRI at 3:14-3:27: http://www.healthcare.siemens.com/magnetic-resonance-imaging/magnetom-world/clinical-corner/clinical-talks/7t-uhf-catana
12. Letters from Siemens and Philips on file and at: http://www.kcl.ac.uk/medicine/research/divisions/imaging/ref.aspx
13. US Patent 7847552B2, Exclusion of compromised PET data during simultaneous PET-MR acquisition. Filed 10.1.2007. Published 7.12.2010. General Electric Company.

Review articles acknowledging KCL role

14. Martinez-Möller et al. Workflow and scan protocol considerations for integrated whole-body PET/MRI in oncology. J Nucl Med 2012;53(9):1415-26. Doi: 10.2967/jnumed.112.109348.
15. Herzog et al. The current state, challenges and perspectives of MR-PET. *Neuroimage* 49 2072-82. 2010.
16. Pichler et al. PET/MRI: paving the way for the next generation of clinical multimodality imaging applications. J Nucl Med 2010;51(3):333-6. Doi: 10.2967/jnumed.109.061853

Sources illustrating general expansion and interest in PET-MR

17. 'Sublima' Framework 7 Programme project: http://cordis.europa.eu/projects/rcn/94257_en.html ; http://dev-sublima.keepwebsimple.de/
18. Buchbender et al. Oncologic PET/MRI, Part 1: Tumors of the Brain, Head and Neck, Chest, Abdomen, and Pelvis. Journal of Nuclear Medicine. 2012, 53(6):928-938
19. Würslin et al. Respiratory motion correction in oncologic PET using T1-weighted MR imaging on a simultaneous whole-body PET/MR system. J Nucl Med. 2013 Mar;54(3):464-71.