Institution:
King's College London

Unit of Assessment:
UoA 15

Title of case study:
MR-guided Cardiovascular Catheterisation in Children

1. Summary of the impact

We have developed a new technique of performing cardiac catheterisation in children and adults with congenital heart disease. This has led to the commercialisation of hybrid MRI and X-ray cardiac catheterisation laboratories, a new scientific technique for studying cardiac physiology and pathology and most importantly is being routinely used in clinical practice as it dramatically reduces X-ray radiation exposure (by a factor of 8) and improves the accuracy of physiological measurements leading to better clinical decision making and impact.

2. Underpinning research

The translation of MR-guided cardiac catheterisation from an engineering concept to a clinical reality, required a number of scientific challenges to be addressed. These are described in this section [1-5] and were carried out by Razavi (2000-present, Lecturer and subsequently Professor) and Hill (2000-2005, Senior Lecturer and subsequently Professor) as well as later work by Razavi and Schaeffter (2006-present, Professor) in the Division of Imaging Sciences & Biomedical Engineering at KCL.

The first research challenge was to develop an MRI and X-ray cardiac catheterisation laboratory with the appropriate technical, work-flow and safety features to allow clinical MRI cardiac catheterisation [1]. This involved modification of the MRI and X-ray systems to allow a floating table-top to move between the two modalities, shielding of the image intensifier to minimise distortion and the set up of a work flow to safely monitor and move an anaesthetised patient into an MRI scanner and perform cardiac catheterisation procedures.

The second challenge, was developing safe devices that could be used to perform cardiac catheterisation procedures in patients [2,3,4,5]. Previous research had focused on showing feasibility without tackling the safety issues. The catheters and devices used in those studies had a real risk of heating in an MRI scanning environment and so causing damage to heart and vessels. We devised four potential safe techniques of performing catheter and device visualisation and have moved two of these techniques into clinical practice.

The first technique used passive visualisation of a non-braided balloon angiographic catheter filled with carbon dioxide producing a negative contrast in a steady state free procession real-time sequence [2]. Optimising the echo time and spatial resolution allowed us good visualisation while performing various catheterisation manoeuvres at 5-10 frames per second in a pulsatile flow phantom. We were then able to show feasibility in 20 patients and demonstrate catheter guidance to all the major vessels and left and right-sided cardiac chambers.

The second technique involved using 19F nuclear magnetic resonance in conjunction with proton imaging [3]. This has the advantage of being able to automatically track the catheters when they move out of plane. Using a standard angiographic balloon catheter filled with the blood substitute perfluorooctylbromide (PFOB) and a limited bandwidth excitation at the resonances of the CF2 groups of PFOB, we found that sufficient signal could be received to facilitate tip tracking during catheter motion and length visualisation for various catheter configurations.

The third technique involved using multiple tuned quadrature fiducial markers attached to a non-braided standard catheter with an interleaved real-time interactive sequence with varying flip angles [4]. We were able to show good visualisation and tracking of the length of the catheter in a postile flow phantom with minimal heating.

The fourth technique involved a fibreglass guide wire with a nitinol tip and tiny iron splints affixed along the distal 10 cm for passive visualisation [5]. This underwent bench testing, feasibility in a large animal model and, following Medicines and Healthcare products Regulatory Agency approval, was used for performing cardiovascular interventions in patients with congenital heart disease.

3. References to the research

1. Cardiac catheterisation guided by MRI in children and adults with congenital heart disease. Razavi R, Hill DL, Keevil SF, Miquel ME, Muthurangu V, Hegde S, Rhode K, Barnett M, van Vaals J, Hawkes DJ, Baker E. Lancet 2003 Dec 6;362(9399):1877-82
2. Visualization and tracking of an inflatable balloon catheter using SSFP in a flow phantom and in the heart and great vessels of patients. Miquel ME, Hegde S, Muthurangu V, Corcoran BJ, Keevil SF, Hill DLG, Razavi RS. Magnetic Resonance in Medicine 2004 May;51(5):988-95
3. Catheter tracking and visualization using 19F nuclear magnetic resonance. Kozerke S, Hegde S, Schaeffter T, Lamerichs R, Razavi R, Hill DL. Magnetic Resonance in Medicine 2004 Sep;52(3):693-7
4. Interactive MR imaging and tracking of catheters with multiple tuned fiducial markers. Hegde S, Miquel ME, Boubertakh R, Gilderdale D, Muthurangu V, Keevil SF, Young I, Hill DL, Razavi RS. J Vasc Interv Radiol 2006 Jul;17(7):1175-9
5. Magnetic resonance-guided cardiac interventions using magnetic resonance-compatible devices: a preclinical study and first-in-man congenital interventions. Tzifa A, Krombach GA, Krämer N, Krüger S, Schütte A, von Walter M, Schaeffter T, Qureshi S, Krasemann T, Rosenthal E, Schwartz CA, Varma G, Buhl A, Kohlmeier A, Bücker A, Günther RW, Razavi R. Circulation Cardiovascular Intervention. 2010 Dec;3(6):585-92

Grants:

- Jan 2001 - Dec 2004 Centre for Magnetic Resonance Imaging and Intervention; EPSRC Joint Research Equipment Initiative HEFCA; £1,382,993. The Charitable Fund for Guy's and St Thomas' Hospital; £200,000. Evelina Heart fund (The Charitable Fund for Guy's and St Thomas' Hospital); £42,925. Evelina Children's fund (The Charitable Fund for Guy's and St Thomas' Hospital); £20,000. Philips Medical Systems UK; £293,967. Philips Medical Systems NL; £643,000.
- March 2002 - Sept 2005 Use of an interventional MRI system for diagnostic and interventional cardiac catheterisation of patients with congenital heart disease; The Charitable Foundation of Guy's and St Thomas' Hospital; £493,000.
- March 2004 - Feb 2007 Magnetic Resonance Imaging assessment of pulmonary vascular disease; The Charitable Foundation of Guy's and St Thomas' Hospital; £193,000.

4. Details of the impact

Around one child in a hundred is born with a congenital heart defect. Depending on the severity of the condition, some children will require cardiac catheterisation as a diagnostic tool or as a curative treatment. To guide the procedure, images are recorded throughout using X-ray, exposing children to radiation. Research has shown that children who undergo even a single procedure are at an increased risk of developing tumours and cancer in later life [6]. Children are especially vulnerable to the oncogenic effects of radiation. Tissues and organs that are growing and developing are more sensitive to radiation effects. Moreover, the oncogenic effects of radiation require a long latent period (decades) that varies with the type of malignancy. Therefore children have a longer lifetime risk of developing radiation-induced cancers.

MRI is a completely radiation free imaging technique and can provide much better characterisation of cardiovascular anatomy than it is possible with x-ray. As described above, we developed the technical, work-flow and safety features and the catheter visualisation techniques needed to carrying out the first in-man MRI-catheterisation procedures in patients with congenital heart disease [1]. This new clinical technique that allows simultaneous measurement of invasive pressure and physiological measurements such as flow and volume has enabled new avenues of

research and insights into human cardiovascular physiology and pathology [7-14].

We have also shown that this technique has significant benefits for patients. Firstly, it reduces the X-ray radiation dose by a factor of eight, which is very important particularly as the majority of patients undergoing catheterisation for congenital heart disease are children [7, 15]. Secondly, it improves the accuracy of physiological measurements like the measurement of pulmonary-vascular resistance (PVR) [8,9] – important in making decisions about treatment such as judging whether the risk of going ahead with palliative or corrective surgery is justified. The previous technique has a bias of up to 54% with limits of agreement from 154% to -66%.

In congenital heart disease, making decision on whether to proceed with surgical palliation or other interventions, versus continuing conservative management, can often be very difficult. This is because there is not population-based data on outcomes, because of the complexity and large variation in the type of abnormality. Having more accurate measurement of physiology, only made possible by the technologies we have developed, means that now we can start to make decisions on the basis of these measurements and, for example, know that PVR of over 4 dyne.sec/cm^5 in children with a uni-ventricular circulation and over 6 dyne.sec/cm^5 in a bi-ventricular circulation, would be too high risk to move forward with palliative or corrective surgery [7, 15].

We have worked with Philips Healthcare to develop the concept of a combined MRI and X-ray clinical cardiovascular catheterisation laboratory (the first research challenge described in section 2) which has led to the CE marking and commercial release of the first such product by Philips Healthcare in 2004 [15]. Based on the concept we developed, similar systems have subsequently been released by Siemens and GE [15]. These systems are installed in 15 leading academic health science centres across the world and are used for cutting edge clinical research and for the care of complex patients such as those with congenital heart disease.

MRI guided cardiac catheterisation, has been adopted as best practice at the Evelina Children's Hospital, London - one of the ten major paediatric cardiac centres in the UK [7]. The practice has extended its reach nationally and internationally to hospitals such as Great Ormond Street Hospital, London [12], German Heart Centre, Berlin, Germany [13] and Children's National Medical Centre, Washington DC, USA [14] enhancing the quality of care for patients with congenital heart disease.

Our research activities have led to the development of a new commercial product, the hybrid MRI X-ray cardiac catheterisation laboratory, the development of a new technique for assessing cardiac physiology in patients and a better way of performing cardiac catheterisation in children and adults with congenital heart disease, which has been adopted as routine practice at the Evelina Children's Hospital, London and also used in centres around the world.

5. Sources to corroborate the impact

6. Radiation risk from pediatric cardiac catheterization: friendly fire on children with congenital heart disease. Andreassi MG. Circulation 2009;120:1847-9.
7. Diagnostic and interventional MRI catheterization: A 10-year single center experience Tzifa A, Pushparajah K, Valverde I, Bell A, Hussain T, Wong J, Beerbaum P, Greil G, Bellsham-Revell H, Rosenthal E, Krasemann T, Simpson J, Miller O, Qureshi S, Schaffter T, Razavi R. Circulation abstract from Association for European Paediatric Cardiology meeting London May 2013 published Cardiology in the Young 2013 May Volume 23 Supplement 1 page S18
8. Novel method of quantifying pulmonary vascular resistance by use of simultaneous invasive pressure monitoring and phase-contrast magnetic resonance flow. Muthurangu V, Taylor A, Andriantsimiavona R, Hegde S, Miquel ME, Tulloh R, Baker E, Hill DL, Razavi RS. Circulation. 2004 Aug 17;110(7):826-34.
9. Magnetic resonance imaging guided catheterisation for assessment of pulmonary vascular resistance: in vivo validation and clinical application in patients with pulmonary hypertension. Kuehne T, Yilmaz S, Schulze-Neick I, Wellnhofer E, Ewert P, Nagel E, Lange P. Heart. 2005 Aug;91(8):1064-9

10. Measurement of total pulmonary arterial compliance using invasive pressure monitoring and MR flow quantification during MR-guided cardiac catheterization. Muthurangu V, Atkinson D, Sermesant M, Miquel ME, Hegde S, Johnson R, Andriantsimiavona R, Taylor AM, Baker E, Tulloh R, Hill D, Razavi RS. Am J Physiol Heart Circ Physiol. 2005 Sep;289(3):H1301-6
11. Integrated assessment of diastolic and systolic ventricular function using diagnostic cardiac magnetic resonance catheterization: validation in pigs and application in a clinical pilot study. Schmitt B, Steendijk P, Lunze K, Ovroutski S, Falkenberg J, Rahmanzadeh P, Maarouf N, Ewert P, Berger F, Kuehne T. JACC Cardiovasc Imaging. 2009 Nov;2(11):1271-81
12. Comparison of bare metal stenting and percutaneous pulmonary valve implantation for treatment of right ventricular outflow tract obstruction: use of an x-ray/magnetic resonance hybrid laboratory for acute physiological assessment. Lurz P, Nordmeyer J, Muthurangu V, Khambadkone S, Derrick G, Yates R, Sury M, Bonhoeffer P, Taylor AM. Circulation. 2009 Jun 16;119(23):2995-3001
13. Pulmonary vascular resistance, collateral flow, and ventricular function in patients with a Fontan circulation at rest and during dobutamine stress. Schmitt B, Steendijk P, Ovroutski S, Lunze K, Rahmanzadeh P, Maarouf N, Ewert P, Berger F, Kuehne T. Circ Cardiovasc Imaging. 2010 Sep;3(5):623-31
14. Real-time MRI-guided right heart catheterization in adults using passive catheters. Ratnayaka K, Faranesh AZ, Hansen MS, Stine AM, Halabi M, Barbash IM, Schenke WH, Wright VJ, Grant LP, Kellman P, Kocaturk O, Lederman RJ. Eur Heart J. 2013 Feb;34(5):380-9
15. Letters from Philips Healthcare and Siemens Healthcare on file, and presentation slides from Association of European Paediatric Cardiology Meeting, London, May 2013 at: http://www.kcl.ac.uk/medicine/research/divisions/imaging/ref.aspx