Institution: King's College London

Unit of Assessment: UoA 15

Title of case study: Spatiotemporal Undersampling for Highly Accelerated Magnetic Resonance Imaging

1. Summary of the impact

Imaging speed is of critical importance in most Magnetic Resonance (MR) imaging applications. King's College London (KCL) researchers have developed spatiotemporal undersamplings, or "k-t" methods, for three-dimensional (3D) imaging and corresponding image reconstruction methods that have increased the speed of imaging significantly, so that particular scans are now 5-7 fold faster. This has directly impacted the experience of the patient whose overall examination time has been reduced from more than 1 hour to less than 30 minutes depending on the application. The technology has been patented and has been implemented by Philips Healthcare, one of the three major manufacturers of MR equipment. A clinical solution platform for 3D MR cardiac perfusion and quantitative flow imaging, based on the technology developed at KCL, has also been launched by the Swiss company, GyroTools LLC.

2. Underpinning research

Research at the Division of Imaging Science & Biomedical Engineering, KCL has been concerned with addressing a key limitation intrinsic to the image formation process in Magnetic Resonance (MR) imaging and developing a technology to overcome this restriction. As MR relies on a spectroscopic encoding principle, higher resolution inherently prolongs scan time and makes imaging of moving organs and transient processes at high resolution impossible. While parallel imaging methods, as available on commercial MR systems, can address this, they are limited by noise amplification for scan acceleration beyond a factor of three to four, and necessarily require dedicated multi-channel signal receivers.

In contrast, spatiotemporal undersampling, or "k-t" methods, exploit information redundancy present in the data themselves to reduce the density of sampling, and thus scan time, without requiring dedicated receiver arrays. In essence, these methods encode the changes of moving objects from one time instant to the next, rather than imaging the entire object at every time instant. This means MR scans can be accelerated dramatically. In addition to providing more time-saving and cost-efficient scanning, dynamic 3D imaging applications that have hitherto been prohibitively long for a breathhold of the patient have now become clinically feasible. Such methods have been developed at KCL by Kozerke (2002-2003 and 2008-present, Research Fellow and subsequently Professor) together with Razavi (2000-present Lecturer and subsequently Professor).

A major application field of spatiotemporal MR undersampling methods is in diagnosing cardiovascular disease, which remains the major cause of mortality in the Western world, affecting 30% of the population. Ischemic or coronary heart disease is the main contributor to cardiovascular disorders and early diagnosis has been identified as a key strategy for monitoring patients at risk. To assess the ischemic burden of the heart, a non-invasive and cost-effective 3D imaging test is required that provides adequate resolution and coverage.

Based on the fundamental principle of k-t undersampling for 2D imaging, KCL researchers proposed a 3D approach for imaging cardiac motion. Here, it was demonstrated that 4.3-fold scan acceleration can be achieved by extending k-t undersampling to a 3D sampling domain including two spatial and one temporal dimension. In this way, twenty imaging slices at a resolution of 2x2x5 mm^3 could be acquired in a single breathhold (the timeframe required to carry out the exam), hence enabling single-breathhold time-resolved volumetric imaging of the heart at high resolution for the first time [1].

Among a wide range of possible applications of the technology researchers at KCL have focused on developing dynamic contrast-enhanced cardiac perfusion imaging as a diagnostic tool. In order to achieve scan acceleration factors beyond a factor of four to five, they employed a decomposition of the spatiotemporal data into temporal basis functions weighted by temporally independent

spatial weights. Thereby nominal k-t undersampling factors of 10 have been achieved enabling 3D contrast-enhanced cardiac perfusion imaging at unparalleled resolution. KCL researchers were the first to present 3D whole-heart myocardial perfusion imaging in patients and have successfully validated its diagnostic performance against fractional flow reserve measurements, which is regarded as the gold standard for invasive assessment of perfusion. In 53 patients referred for angiography, this technique was shown to accurately detect functionally significant coronary artery disease (CAD). Sensitivity, specificity, and diagnostic accuracy for the detection of significant CAD were 91%, 90%, and 91%, on a patient basis, demonstrating excellent diagnostic performance [2].

To enable further scan acceleration, KCL researchers have developed k-t undersampling to employ compartment-specific temporal basis functions, weighted by temporally independent spatial weights. In this work, they demonstrated that significant improvements in reconstruction accuracy can be achieved relative to the original k-t imaging formulations. It was shown that prospective nominal undersampling of up to 16 can be realised. As a clinical application, the acquisition of cine flow data in the aorta was demonstrated permitting assessment of 2D velocity images and pulse wave velocities at 100 frames per second in a single breathhold per slice [3].

Extending the application range, sparsity transform k-t principal component analysis has been proposed and demonstrated for flow quantification of the carotid bifurcation. The rationale behind this additional sparsity transform is the fact that blood vessels provide a very sparse and hence compressible representation upon subtraction of the image background. This subtraction is achieved by exploiting the fact that images encoding blood velocities in different spatial directions can be linearly combined such that static background cancels out. Deploying the sparsity transform, velocity root-mean-square errors were found to decrease by 52 ± 14%, 59 ± 11%, and 16 ± 32% in the common, external, and internal carotid artery, respectively [4]. Moreover, by exploiting k-t undersampling technology KCL researchers have been able to assess both kinetic and turbulent kinetic energy using Bayesian analysis. Comparison of peak turbulent kinetic energy measured in patients with aortic stenosis revealed considerable differences relative to the values detected in healthy subjects proving the potential of the method to provide a comprehensive hemodynamic assessment in patients [5].

Both projects [4 & 5] were initiated and supervised by Kozerke while at KCL. The implementations were, however, carried in close collaboration with researchers at ETH Zurich, Switzerland to exploit experimental equipment and resources available at ETH.

3. References to the research

1. Kozerke S, Tsao J, Razavi R, Boesiger P. Accelerating cardiac cine 3D imaging using k-t BLAST. Magn Reson Med 2004;52(1):19-26. Doi: 10.1002/mrm.20145

2. Jogiya R, Kozerke S, Morton G, De Silva K, Redwood S, Perera D, Nagel E, Plein S. Validation of dynamic 3-dimensional whole heart magnetic resonance myocardial perfusion imaging against fractional flow reserve for the detection of significant coronary artery disease. J Am Coll Cardiol 2012;60(8):756-65. Doi: 10.1016/j.jacc.2012.02.075

3. Giese D, Schaeffter T, Kozerke S. Highly undersampled phase-contrast flow measurements using compartment-based k-t principal component analysis. Magn Reson Med 2013;69(2):434-43. Doi: 10.1002/mrm.24273

4. Knobloch V, Boesiger P, Kozerke S. Sparsity transform k-t principal component analysis for accelerating cine three-dimensional flow measurements. Magn Reson Med 2013;70(1):53-63. Doi: 10.1002/mrm.24431

5. Binter C, Knobloch V, Manka R, Sigfridsson A, Kozerke S. Bayesian multipoint velocity encoding for concurrent flow and turbulence mapping. Magn Reson Med 2013;69(5):1337-45. Doi: 10.1002/mrm.24370.

Grants

2000-2006: PIs: Hawkes D, Marsden P From Medical Images and Signals to Clinical Information Inter-disciplinary Research Consortium" EPSRC and MRC, £1,859,379

2009-2011. PIs: Plein S, Kozerke S. Three-dimensional Whole Heart Perfusion MR Imaging, British Heart Foundation, project grant. £195k

2011-2013. PI: Kozerke S. Accelerated Myocardial Perfusion, Metabolic and Contractile Cardiovascular Magnetic Resonance Imaging. FP7 EU Marie-Curie-Fellowship. €180k

2011-2014. PI: Kozerke S. Development of Highly Accelerated Magnetic Resonance Methods for Quantitative Analysis of Perfusion, Metabolism and Function in Cardiac Ischemia. Swiss National Science Fonds, project grant. £465K (In Swiss Francs).

4. Details of the impact

King's College London's k-t method for 3D imaging as described in Kozerke et al. 2004 was patented and subsequently licensed to Philips Healthcare [6]. KCL implemented the technology on Philips clinical MR systems and the fundamental implementation became available on MR systems as a clinical product option in 2007/08 [7,8]. Today the method is available on 80% of all high-end MR systems for cardiovascular imaging around the world. Philips says of the technology that "k-t BLAST represents a quantum leap in the speed of cardiac MRI. Up to 5 times faster than other methods, k-t BLAST substantially reduces cardiac MRI scan times, while retaining excellent image quality. k-t BLAST makes cine cardiac MRI in a single breath hold a reality, and is the fastest cine cardiac MRI in the industry" [7].

During an MR scan, patients need to hold their breath and often several (2-5) repeat scans are required to obtain all data covering the target anatomy. The whole breath holding process may be particularly difficult for patients with cardiovascular disorders or other illnesses affecting lung function. Using the k-t technology, significant speed-up of a range of key MR imaging protocols has been achieved in practice, directly impacting patient experience. Total scan times are reduced by four to ten times to benefit patient comfort and compliance. Many dynamic MR imaging protocols now require only a single breathhold rather than multiple repetitions. As a result, the quality and consistency of data are directly improved hence requiring fewer repeat scans and the overall exam times are significantly reduced.

In addition to these benefits, k-t methods have enabled some key diagnostic protocols. Of particular importance has been the possibility to acquire whole-heart 3D MR perfusion data in patients for the first time. Data from KCL patient studies [2] have proven the diagnostic performance and accuracy of the method in a single centre study. These results have led to on-going multi-centre trials in Germany, Switzerland and the UK to assess the diagnostic performance of quantitative whole-heart 3D perfusion imaging, relative to Fractional Flow Reserve measurements as the invasive reference [9]. Based on these clinical data there is already sufficient evidence that 3D perfusion imaging is at least as good as single photon emission computed tomograohy (SPECT), while reducing the cost of the exam by at least two-fold. In addition the MR method does not employ ionising radiation, hence protecting the patient from radiation risks [9] and permitting longitudinal monitoring in a safe and non-invasive manner.

Recognising the potential of KCL research in spatiotemporal undersampling for cardiac perfusion imaging, GyroTools LLC, a Swiss-based company, developed and distributed efficient image reconstruction codes that formed the basis of the on-going multi-centre perfusion trial. The software was made available to selected sites starting in 2009. In 2012 GyroTools LLC and PMOD Technologies joined forces to develop and launch a clinical perfusion solution, including kinetic modelling for quantitative myocardial blood flow assessment, based on MR spatiotemporal data undersampling (10a).

Clinical results from perfusion imaging with k-t methods have led to further work on improving

stratification of patients. Using the method devised it has become possible to quantify energy efficiency in the cardiovascular system by assessing both kinetic and turbulent kinetic energy in larger vessels [5]. It has been demonstrated that this allows for a quantitative assessment of the hemodynamic consequences of stenotic heart valves. In conjunction with the GTFlow flow analysis package offered by GyroTools LLC, a powerful flow imaging solution is offered (10b).

5. Sources to corroborate the impact (indicative maximum of 10 references)

6. Patent WO2005003804/EP1651975/US2006208730/. K-t blast and k-t sense magnetic resonance imaging. Publication date: 13.1.2005: http://www.google.com/patents/WO2005003804A1?cl=en

7. Philips Healthcare, Best, The Netherlands http://www.healthcare.philips.com/main/products/mri/innovations/freewave/

8. Letter of corroboration from Philips Healthcare on file and at: http://www.kcl.ac.uk/medicine/research/divisions/imaging/ref.aspx

9. Manka R, et al. Multicenter evaluation of dynamic three-dimensional whole-heart myocardial perfusion imaging for the detection of coronary artery disease defined by fractional flow reserve. J CARDIOV MAGN RESON 2013;15(Suppl 1):O103 doi:10.1186/1532-429X-15-S1-O103: http://www.jcmr-online.com/content/15/S1/O103

10. GyroTools LLC, Winterthur, Switzerland
    a. Perfusion imaging brochure: http://www.gyrotools.com/products/GTPerfusion_2013.pdf
    b. Flow imaging brochure: http://www.gyrotools.com/products/ktPCAFlow_2013.pdf
    c. Letter of corroboration from GyroTools on file at: http://www.kcl.ac.uk/medicine/research/divisions/imaging/ref.aspx