Anatomical and Functional MRI for Radiotherapy Planning of Head and Neck Cancers

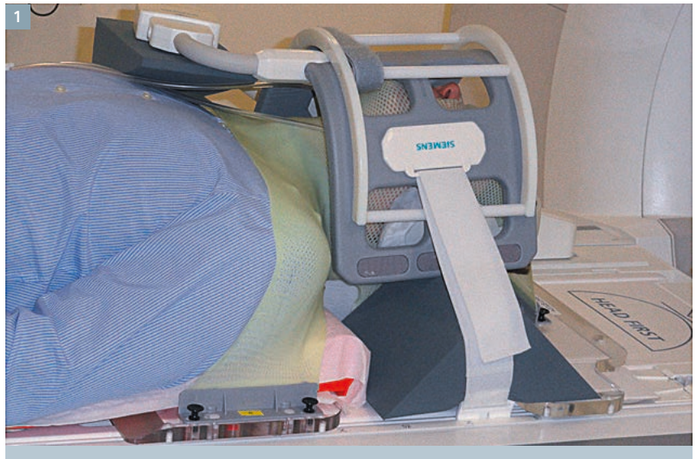
Maria A. Schmidt, Ph.D.; Rafal Panek, Ph.D.; Erica Scurr, DCR(R), MSc; Angela Riddell, MD FRCS FRCR; Kate Newbold, MD MRCP FRCR; Dow-Mu Koh, MD MRCP FRCR; Martin O. Leach, Ph.D. FMedSci

Cancer Imaging Centre, Royal Marsden NHS Foundation Trust and Institute of Cancer Research, Sutton, UK

Introduction

Head and Neck cancers are relatively common: squamous cell carcinoma of the head and neck (SCCHN) has a worldwide incidence of approximately 500,000 cases per annum [1]. Treatment is a combination of surgery, chemotherapy and radiotherapy (RT), devised to maximize the probability of eradicating the disease while retaining organ function [2-5]. Recent technical advances in RT include high-precision conformal techniques such as intensity-modulated RT (IMRT) and volumetric intensity modulated arc therapy (VMAT), which enable dose escalation to lesions without exceeding recommended exposure levels for organs at risk (OAR). However, these techniques require accurate anatomical information to contribute towards improving disease control.

High-resolution Magnetic Resonance Imaging (MRI) has increasingly been used to plan Head and Neck RT [6-10]. MRI and CT images are registered, combining the advantageous soft tissue contrast of MRI examinations and the required CT-based electron density. However, MR images are often distorted due to magnetic field inhomogeneity and non-uniform gradients [11-13], and the use of CT-MR fusion requires geometrically accurate MRI datasets. This article describes the equipment, protocols and techniques used in Head and Neck MRI at the Royal Marsden NHS Foundation Trust to ensure that the MRI examinations undertaken for RT planning purposes achieve the required geometric accuracy.



1 Receiver coil arrangement used at the Royal Marsden NHS Foundation Trust to perform Head and Neck MRI for RT planning. A standard MR-compatible baseboard is employed, enabling the use of a thermoplastic mask. The large flex-coil is positioned above the neck and used in conjunction with elements of the spine array.

High resolution anatomical imaging in the radiotherapy planning position

At the Royal Marsden NHS Foundation Trust clinical Head and Neck MRI examinations for RT planning are undertaken at 1.5T in the 70 cm bore MAGNETOM Aera (Siemens Healthcare, Erlangen, Germany). Patients are scanned in the RT position using an appropriate head rest and thermoplastic shell immobilisation attached to an MR-compatible headboard, modified to remain accurately positioned on the Aera patient couch. In addition to the elements of the posterior spine coil selected at the level of the lesion, a large flex-coil is also placed anteriorly, in line with the tumor, employing a custom-built plastic device to keep the coil curved, following the neck anatomy. This arrangement achieves a high signal-to-noise ratio, allows effective use of parallel imaging and keeps patient comfort in the RT planning position (Fig. 1).

The MRI protocol covers the primary tumor and neck lymph nodes with approximately isotropic T1-weighted sagittal 3D acquisition (TE 1.8 ms, TR 880 ms, 160 x 1 mm slices, 250 mm x 250 mm FOV, 256 x 256 image matrix). Images are acquired post contrast-agent injection (single dose). This dataset is subsequently registered with the RT planning CT examination, and for this reason its geometric integrity is checked periodically with a large linear test object, previously described [14], consisting of sets of straight tubes in three orthogonal directions. Figure 2 shows images of the test object without and with post processing to correct image distortion. The 3D distortion correction built into the scanner software is essential for RT planning, and always used. The maximum displacement found within the volume encompassed by head and neck examinations is less than 1 mm. In addition, the imaging protocol employs a 500 Hz/pixel bandwidth, ensuring chemical shift related displacements in the readout direction remain under 0.5 mm.

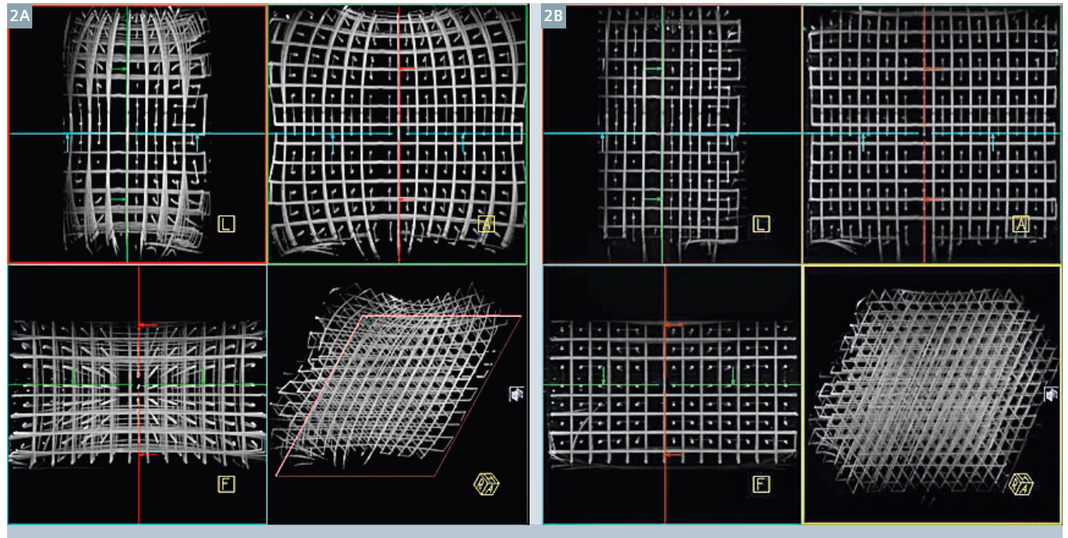
Having characterized the geometric integrity of the protocol employed, it is also essential to characterize any further distortion associated with the distribution of magnetic susceptibility values within the subjects. In Head and Neck a large number of air-tissue interfaces in the vicinity of the tumors gives rise to localized magnetic field inhomogeneity, detrimental to the geometric integrity of the images. For this purpose, the field inhomogeneity in this region was estimated in five Head and Neck subjects. Transaxial gradient-echo images were acquired with fat and water in phase (TE values 4.76 and 9.53 ms), and the phase images were subtracted. The local field inhomogeneity was measured after phase unwrapping. Displacements associated with the airways were mostly under 0.5 mm with this sequence. Displacements only reach 1 mm in the vicinity of dental implants, and only very few pixels are affected.

Functional imaging

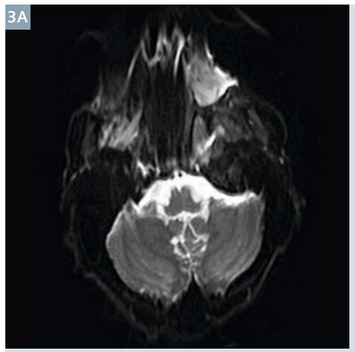
In addition to the clinical service providing anatomical images for RT planning, functional MRI is also employed to characterize lesions pre and post treatment and to investigate prediction of treatment response both at 1.5T (MAGNETOM Aera) and 3T (MAGNETOM Skyra). In RT planning, the ultimate aim of functional imaging techniques is to identify radioresistant disease and thus provide a biological target volume for dose boosting. Geometric accuracy is therefore essential to allow correct registration of functional MR images with anatomical MRI and CT datasets. In Head and Neck cancers, both diffusion-weighted imaging (DWI) and Dynamic Contrast-Enhanced (DCE) MRI have been explored [15-21].

Diffusion-weighted imaging with readout segmentation of long variable echo-trains (RESOLVE): EPI-based DWI is sensitive to the mobility of water molecules and to their environment. In cancer, cell proliferation is often associated with an increase in cell density and in extracellular space tortuosity. This leads to lower values of the Apparent Diffusion Coefficient (ADC), compared to healthy tissues [22-23]. ADC values have thus been used for tumor detection, prediction and assessment of treatment response.

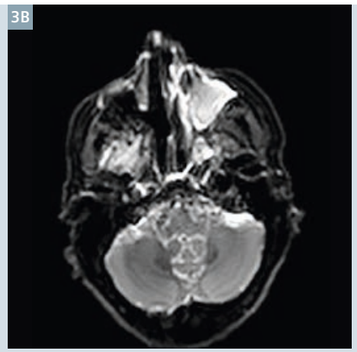
EPI in regions adjacent to air-tissue interfaces is known to suffer from poor geometric integrity [24]. Because this affects Head and Neck studies, strategies to reduce the echo-train length were sought. In addition to parallel imaging, the RESOLVE technique was also employed to acquire multi-shot DWI using a navigator signal to enable accurate multi-echo combinations. In Head and Neck studies, DWI with RESOLVE was employed, covering the volume of interest to identify restricted diffusion within primary lesions and affected lymph nodes.



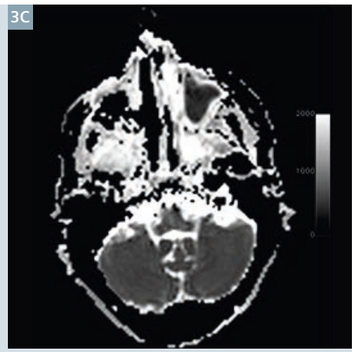
2 Images of the Linear Test Object (described by Doran et al. [14]) acquired using a 3D T1-weighted sequence with bandwidth 500 Hz/pixel, without distortion correction **(2A)** and with 3D distortion correction **(2B)**. Each picture shows three maximum intensity projections (sagittal, coronal and transaxial) and a 3D view of the test object.



Standard DWI (b=0)

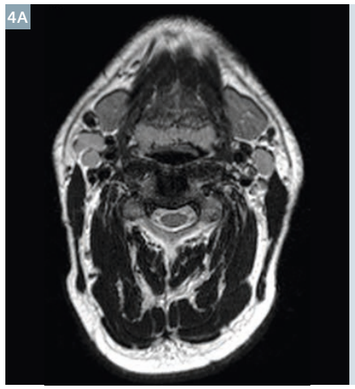


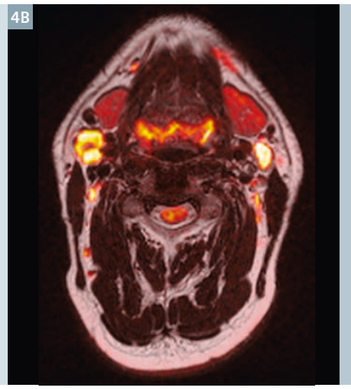
RESOLVE DWI (b=0)



RESOLVE ADC

3 A comparison of conventional single shot DWI **(3A)** and RESOLVE DWI **(3B)** in a head examination. The ADC calculated with the RESOLVE DWI **(3C)** retains the geometric integrity. Standard DWI parameters: TE 98 ms, TR 7000 ms, receiver bandwidth 1040 Hz/pixel, matrix 192 x 192, FOV 230 mm x 230 mm, 3 averages, slice thickness 4 mm. RESOLVE DWI parameters: TE 58 ms, TR 5700 ms, receiver bandwidth 950 Hz/pixel, matrix 128 x 128, FOV 240 mm x 240 mm, slice thickness 4 mm.





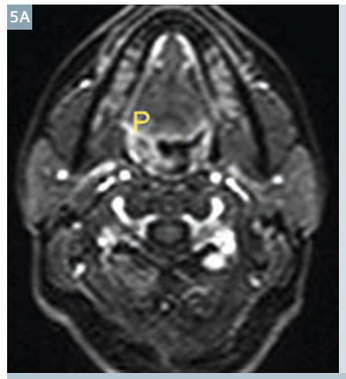
4 Head and Neck T2-weighted image **(4A)** with co-registered RESOLVE diffusion-weighted image **(4B)**. Restricted diffusion (high intensity) can be observed in nodes, spinal cord, tonsils and submandibular glands with no apparent geometrical distortion.

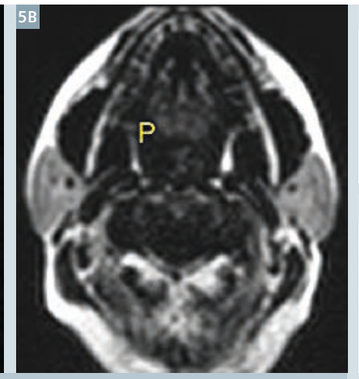
Figure 3 compares DWI acquired without and with the RESOLVE technique for a Head subject, in a slice comprising air spaces. The clear improvement in geometric integrity achieved with RESOLVE DWI allows the registration of anatomical and functional images, thus allowing the use of DWI in RT planning for Head and Neck cancers (Fig. 4).

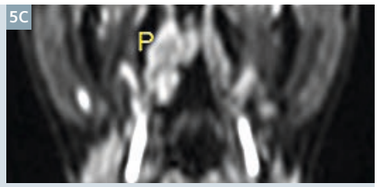
Dynamic contrast-enhanced MRI with CAIPIRINHA-VIBE and TWIST view-sharing*:
In dynamic contrast-enhanced (DCE)-MRI a series of 3D T1-weighted images is acquired to monitor contrast-agent uptake following an intravenous injection of contrast-agent. Using reference images, this technique can be quantitative and provide a dynamic calculation of T1 for each voxel. This enables pharmacokinetic modelling, providing information on tumor microcirculation, vascularity, blood volume and vessel permeability [25, 26]. This quantitative approach to DCE requires high temporal resolution to maintain accuracy. However, this conflicts with the need for high spatial resolution in RT planning applications.

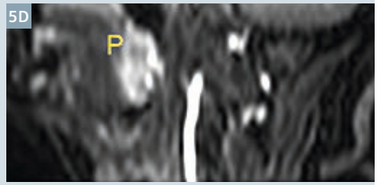
The combination of flex-coil and spine coil elements has been used for DCE employing TWIST view-sharing and CAIPIRINHA reconstruction to produce high resolution images (voxel size 2 mm isotropic x 44 slices, CAIPIRINHA parameters: 2x2) with 2.5 s temporal resolution (TWIST parameters: A = 33% B = 33%). An example of TWIST/CAIPIRINHA DCE with a generous superior/inferior coverage to include both primary site and local involved lymph nodes is shown in figure 5. Isotropic voxels allow for a good 3D delineation of a biological target volume. In addition, Dixon reconstruction of fat and water images also provides information on fat content within the imaged volume, which might be important in the context of tumor response to treatment. Figure 6 shows T1-weighted water-Dixon signal change after Gd injection for a given representative slice containing a primary tumour. Last frame shows K**trans** map within the region of interest.

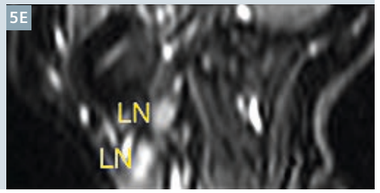
* Work in progress. The product is still under development and not commercially available yet. Its future availability cannot be ensured.



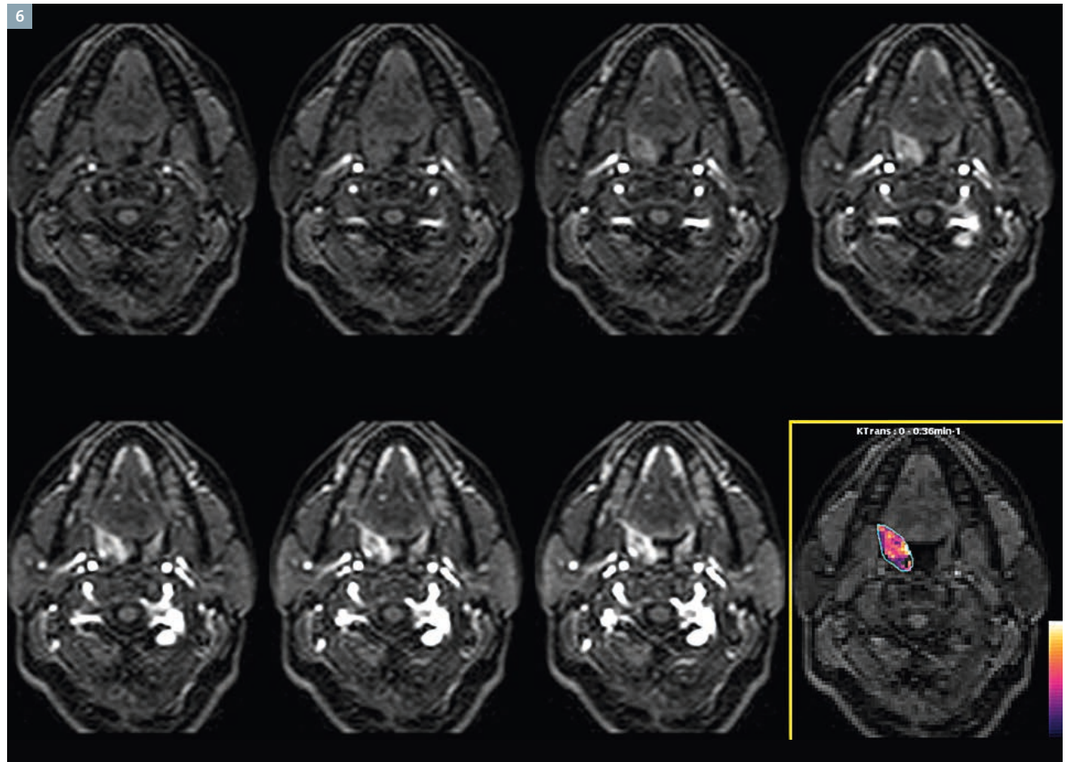








5 Post-contrast water **(5A)** and fat **(5B)** Dixon images of patient with squamous cell cancer of the head and neck. Isotropic voxels allow for a good assessment of primary (P) and nodal (LN) tumour site (**5C–E**; coronal and sagittal image reconstruction). DCE protocol: Flip angle 4/24 degrees, TR 7.2 ms, TE_1 2.4 ms, TE_2 4.8 ms, 2 mm isotropic resolution in 44 slices, temporal resolution 2.5 s (TWIST: A = 33%, B = 33%, CAIPI: 2 x 2).



6 T1-weighted Dixon/water signal change after contrast agent injection, showing progressive enhancement and washout of Head and Neck cancer lesion. Last frame shows K**trans** for a region of interest over a primary tumor site.

Conclusion

Geometrically accurate anatomical and functional imaging for RT planning of Head and Neck cancers were acquired in the RT planning position in standard clinical scanners; this service was developed to meet the clinical and research needs of the users, using custom built coil positioning devices and test objects.

Acknowledgments

The authors wish to thank D. Nickel, R. Kroeker and P. Ravell (Siemens Healthcare) for the provision of the works-in-progress package WIP771 (VIBE with View Sharing TWIST). The authors acknowledge the support of CRUK and EPSRC to the Cancer Imaging Centre at ICR and RMH in association with MRC & Department of Health C1060/A10334, C1060/A16464 and NHS funding to the NIHR Biomedicine Research Centre and the Clinical Research Facility in Imaging. This work was also supported in part by Cancer Research UK Programme Grants C46/A10588 and C7224/A13407. MOL is an NIHR Senior Investigator.

Radiotherapy Planning where MR data is the only imaging information is ongoing research. The concepts and information presented in this article are based on research and are not commercially available. Its future availability cannot be ensured.

Contact

Dr. Maria A. Schmidt
MRI Unit
Royal Marsden NHS
Foundation Trust
Downs Rd
Sutton SM2 5PT
UK
Phone: +44 (0)20 8661 3353
maria.schmidt@icr.ac.uk

References

1 Parkin DM, Bray F, Ferlay J, Pisani P. Estimating the world cancer burden: Globocan 2000. International Journal of Cancer. 2001;94(2):153–6.
2 Bentzen SM, Trotti A. Evaluation of early and late toxicities in chemoradiation trials. J Clin Oncol 2007; 25:4096-4103.
3 Harrington KJ, et al. Interactions between ionising radiation and drugs in head and neck cancer: how can we maximise the therapeutic index? Curr Opin. Investig Drugs 2002; 3: 807-11.
4 Lefebvre JL, et al. Larynx preservation clinical trial design: key issues and recommendations - a consensus panel summary. Int J Radiat Oncol Bioi Phys. 2009; 73: 1293-303.
5 Kazi R, et al. Electroglottographic comparison of voice outcomes in patients with advanced laryngopharyngeal cancer treated by chemoradiotherapy or total laryngectomy. Int J Radiat Oncol Bioi Phys. 2008; 70: 344-52.
6 Ahmed M, Schmidt M, Sohaib A, Kong C, Burke K, Richardson C, Usher M, Brennan S, Riddell A, Davies M, Newbold K, Harrington KJ & Nutting CM. The value of magnetic resonance imaging in target volume delineation of base of tongue tumours – a study using flexible surface coils. Radiother Oncol 2010; 94, 161-7.
7 Bhide SA, Ahmed M, Barbachano Y, Newbold K, Harrington KJ & Nutting CM. Sequential induction chemotherapy followed by radical chemo-radiation in the treatment of locoregionally advanced head-and-neck cancer. Br J Cancer 2008; 99, 57-62.
8 Gregoire V et al. Radiotherapy for head and neck tumours in 2012 and beyond: conformal, tailored, and adaptive? Lancet Oncol. 2012; 13(7), pp.e292-300.
9 Nuyts S. Defining the target for radiotherapy of head and neck cancer. Cancer Imaging.2007;7(Special Issue A):S50–S55.
10 Newbold K, Partridge M, Cook G, Sohaib SA, Charles-Edwards E, Rhys-Evans P, et al. Advanced imaging applied to radiotherapy planning in head and neck cancer: a clinical review. Br J Radiol. 2006 Jul 1;79(943):554–61.
11 Wang D & Doddrell DM. Geometric distortion in structural magnetic resonance imaging. Current Medical Imaging Reviews 2005; 1: 49-60.
12 Wang H, Balter J & Cao Y. Patient-induced susceptibility effect on geometric distortion of clinical brain MRI for radiation treatment planning on a 3T scanner. Phys Med Biol. 2013; 58: 465-77.
13 Reinsberg SA, Doran SJ, Charles-Edwards EM & Leach MO. A complete distortion correction for MR images: II. Rectification of static-field inhomogeneities by similarity-based profile mapping. Phys Med Biol 2005; 50: 2651-61.
14 Doran SJ, Charles-Edwards L, Reinsberg SA & Leach MO. A complete distortion correction for MR images: I. Gradient warp correction. Phys Med Biol. 2005; 50: 1343-61.
15 Thoeny HC, de Keyzer F & King AD. Diffusion-weighted MR imaging in the head and neck. Radiology, 2012; 263(1): pp.19-32.
16 Vandecaveye, V. et al. Evaluation of the larynx for tumour recurrence by diffusion weighted MRI after radiotherapy: initial experience in four cases. The British Journal of Radiology 2006; 79: 681-687.
17 Sumi M, Sakihama N, Sumi T, Morikawa M, Uetani M, Kabasawa H, et al. Discrimination of metastatic cervical lymph nodes with diffusion-weighted MR imaging in patients with head and neck cancer. AJNR Am J Neuroradiol 2003; 24(8):1627-34.
18 Powell C, Schmidt M, Borri M, Koh DM, Partridge M, Riddell A, Cook G, Bhide S A, Nutting CM, Harrington KJ & Newbold KL. Changes in functional imaging parameters following induction chemotherapy have important implications for individualised patient-based treatment regimens for advanced head and neck cancer. Radiother Oncol. 2013; 106, 112-
19 Quon H, Brizel DM. Predictive and prognostic role of functional imaging of head and neck squamous cell carcinomas. Semin Radiat Oncol. 2012 Jul; 22(3):220–32.
20 Wang P, Popovtzer A, Eisbruch A, Cao Y. An approach to identify, from DCE MRI, significant subvolumes of tumours related to outcomes in advanced head-and-neck cancer. Medical Physics. 2012; 39(8):5277–85.
21 Srinivasan A, Mohan S & Mukherji SK. Biological imaging of head and neck cancer: the present and the future. AJNR Am J Neuroradiol. 2012; 33(4), pp. 1-9.
22 Padhani et al. Diffusion-Weighted Magnetic Resonance Imaging as a Cancer Biomarker: Consensus and Recommendations, Neoplasia 2009; 11(2):102-125.
23 Galbán CJ et al. The parametric response map is an imaging biomarker for early cancer treatment outcome. Nature medicine, 2009;15(5): pp.572-6.
24 Jezzard P. Correction of geometric distortion in fMRI data. Neuroimage 2012; 62: 648-51.
25 Walker-Samuel S, Leach MO, Collins DJ. Evaluation of response to treatment using DCE-MRI: the relationship between initial area under the gadolinium curve (IAUGC) and quantitative pharmacokinetic analysis. Phys Med Biol. 2006 Jul 21; 51(14):3593–602.
26 O'Connor J P B, Jackson A , Parker G J M and Jayson G C. DCE-MRI biomarkers in the clinical evaluation of antiangiogenic and vascular disrupting agents. British Journal of Cancer 2007; 96: 189–195. doi:10.1038/sj.bjc.6603515.