Improved morphological information using the Dixon technique in conjunction with DWI for detection of bone metastases

M. D. Blackledge[1], D. Brown[1], T. Wallace[1], N. Tunariu[1], M. O. Leach[1], D. M. Koh[1], and D. J. Collins[1]
[1]CR-UK and EPSRC Cancer Imaging Centre, Institute of Cancer Research and Royal Marsden Hospital, Sutton, Surrey, United Kingdom

Introduction: The detection and follow-up of bone metastases *in vivo* remains a major diagnostic challenge. Metastatic disease can spread to the bony cortex or infiltrate bone marrow, the latter being less easily detected by conventional imaging. Although widely used, skeletal scinitgraphy (SS) suffers from many disadvantages including low resolution and poor sensitivity [1], leading researchers to explore other modalities such as PET/CT and MRI. Takahara et al [2] proposed whole body diffusion-weighted MR imaging with background signal suppression (DWIBS) as a method for disease detection. This technique uses fat-suppressed, high b-value diffusion weighted imaging (DWI) to suppress signal from protons which move freely within tissue, leaving high signal intensity from cellular tissues with relatively hindered diffusion (e.g. tumour tissues and certain normal anatomical structures) and those with prolonged T2-relxation times. Studies have shown superior sensitivity of the technique compared with both SS and PET/CT although it may be less specific because certain benign tissues can mimic tumours [3]. Another disadvantage of the technique is that it can be difficult to localize tumours due to the lack of anatomical information and so acquiring anatomical images that can be fused with DWIBS in a fashion similar to PET/CT is helpful. Acquisition of such anatomical images should ideally be fast because of the already long scan time required for DWIBS (typically 30-40 minutes). Such images should also have high resolution, good contrast and preferably, provide alternative quantitative information that may be extracted for further tissue characterization. Although various groups have used a combination of T1 and STIR imaging for disease evaluation, these scans do not provide quantitative information. The aim of this technical development was to investigate the use of multiple whole body two point Dixon imaging as a method to acquire high quality whole body anatomical images and quantitative T_1 maps in conjunction with DWIBS. Furthermore, we assess the quality of alignment between Dixon and DWIBS images acquired at the same sitting.

Method: ***Dixon imaging*** - Spoiled gradient echo images are acquired at two echo times; one where signals from fat and water are in phase (4.76ms at 1.5 T) and another where they are out of phase (2.38ms at 1.5T), denoted here by Sin and Sout respectively. Water only and fat only images may then be derived as Swater = Sin + Sout and Sfat = Sin – Sout, from which the water and fat ratios may be calculated by Rwater = Swater/(Swater + Sfat) and Rfat = Sfat/(Swater + Sfat) respectively. Our current protocol consists of images acquired coronally on a 1.5T siemens 'Avanto' scanner over 3 stations with a 45x26x45cm3 field of view and a 5 cm overlap, using a breath hold protocol lasting 21s per station, an in-plane resolution of 2.35x2.35mm2 and slice thickness of 5mm. The entire body is typically imaged in 3 consecutive 21-second breath-holds. Water and fat only images are produced using the native Siemens software and stations are then combined into whole body coronal images. Further, we acquire two sets of Dixon images using optimised flip angles of 3º and 22º [4] so that whole body T1 maps may be calculated using the well known method of Fram [5]. ***DWIBS*** – Whole body diffusion weighted images are acquired axially throughout the body in 50 slice stations with no overlap using b-values of 0 and 900s mm-2 (NSA = 1 and 3 respectively). Other imaging parameters include TE = 72ms, TR = 14s, resolution = 2.5x2.5mm2, slice thickness = 5mm and an inversion time (TI) of 180ms for STIR fat suppression. ***Alignment*** – To assess the degree of alignment between Dixon imaging and DWIBS we applied a range of linear registration methods between the low b-value and in phase images. The following three-dimensional transformations were applied alone and in combination: translation (t), scaling (s), rotation (r) and fully affine (a). The optimum transformation matrix was found using an amoeba search algorithm [6] to maximize the mutual information (MI) between both imaging modalities. The final MI value was recorded as a quantitative measure of alignment for each transform combination and was also calculated for the case where no registration was applied (n). Registration was performed in four patient data sets, each of which had multiple skeletal metastases from primary prostate cancer, and the mean MI value was calculated for the population (see figure 2).

Results: Shown in figure 1 is an example of the acquisition scheme outlined above performed on a patient diagnosed with multiple skeletal metastases. DWIBS images were fused on top of water only Dixon images acquired using a 22º flip angle and T1 maps were generated using the 'in phase' Dixon images. Note the lower water proportion observed in T12 (green arrow) indicating a high concentration of fat. This corresponds well with the location of a 'cold spot' observed in the DWI (green arrow in (a)), possibly indicating relative sparing of this vertebral body. Figure 2 is a plot of the mean population MI values (shown on the y-axis) calculated for the different transformation combinations (as presented on the x-axis). No significant difference was found for alignment quality between the different transform types indicating that there is good spatial correlation between the two modalities without the need for registration.

Figure 1

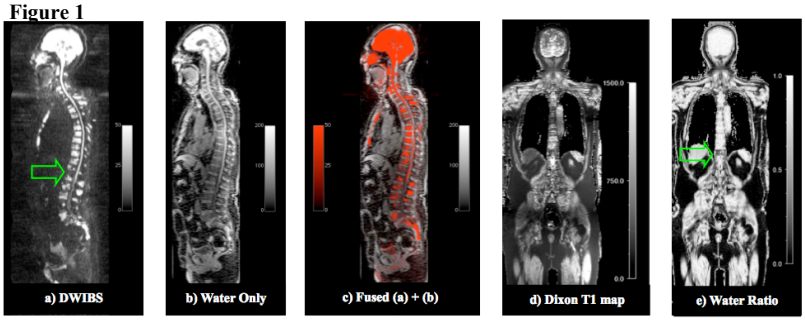

Figure 2

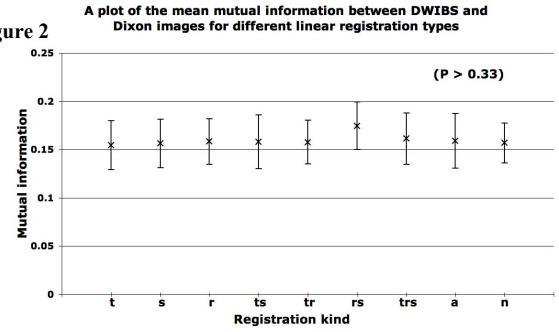

Figure 1. (a) A sagittal reconstruction of a DWIBS image acquired using a b-value of 900 s/mm^2. Note the appearance of 'hot spots' observed along the vertebral column and sternum that indicate the presence of extensive bone metastases. **(b)** A sagittal reconstruction of a water only image acquired using the Dixon imaging protocol. **(c)** A fused reconstruction of both (a) and (b) with DWIBS signal being shown in red. **(d)** A T1 map obtained using the acquired Dixon images with increased T1 in metastases. **(e)** A water ratio image as derived from the proton density Dixon acquisition. **Figure 2**. A plot of mean population MI value for each transformation type. t = translation, s = scaling, r = rotation, a = affine, n = no registration.

Conclusions: We suggest the use of the two point Dixon technique for acquiring anatomical matched images for use with high b-value, whole body diffusion weighted imaging of bone metastases. Dixon imaging provides high resolution images with excellent contrast in short acquisition times and also allows for the calculation of other useful quantitative maps in the form of water/fat ratio and T1 values. We have performed the same protocol on 3 other patients and have observed similar results in all cases. Furthermore, we have demonstrated that there is intrinsically good alignment between both image sets provided they are acquired in succession. Slight mismatches were observed in some of the soft tissues such as kidneys and liver and it remains to be seen whether other non-rigid registration techniques could improve alignment. However in the case of rigid tissues such as the skeleton good spatial correlation can be expected. It is hypothesized that through the combination of well registered multiple tissue parameters afforded using these images, the specificity of DWIBS as a modality for screening and segmenting bone metastases can be improved and is the subject of on-going investigation.

References: [1] Gulenchyn *et al.*, Clin Nucl Med, 12(1):45-6, 1987. [2] Takahara *et al.*, Radiat Med. 22(4):275-82, 2004. [3] Nakanishi *et al.,* Magn Reson Med Sci, 6(3):147–55, 2007. [4] Miyazaki *et al.*, Proc 17th Ann. Meeting ISMRM 2009 (4443). [5] Fram et al., Mag Res Imag. 5(3):201-8, 1987. [6] Numerical recipes in C: The art of scientific computing (2nd edition).

Acknowledgements: We acknowledge the support received from the CRUK and EPSRC Cancer Imaging Centre in association with the MRC and Department of Health (England) grant C1060/A10334, also NHS funding to the NIHR Biomedical Research Centre. We also acknowledge Dr T. Feiweier (Siemens Medical Sector) for developing the DWI sequence.