Improved diagnostic accuracy of whole body diffusion weighted MRI using computed imaging.

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Introduction: The use of diffusion weighted imaging (DWI) in oncology is gaining popularity for detection of disease. A combination of low diffusion coefficients and long T_2 values in tumours means that signal from suspect malignancies in fat suppressed images acquired at high b-values is hyper-intense compared to normal background tissues [1]. There is still much debate over which imaging b-values are preferable for providing optimal contrast between diseased and healthy tissues as larger b-values provide improved contrast but at the expense of a drop in signal to noise ratio (SNR). A recent methodology known as computed diffusion weighted imaging (cDWI) [2] has demonstrated that improved SNR may achieved at high b-values by acquiring images at multiple b-values, calculating the apparent diffusion coefficient maps and using the results to simulate the signal at a desired b-value. Furthermore, using this technique there is no requirement to decide on the optimal b-value *a priori* as the user can vary the b-value in real time. In our first clinical evaluation of this new technique we compare the diagnostic utility of cDWI, computed at b-values of 1500 and 2000 s/mm^2, with conventional DWI, acquired at 900 s/mm^2, in a small cohort of patients diagnosed with advanced metastatic disease.

Methods: In this pilot feasibility study, we applied the cDWI technique retrospectively to 10 patients who had undergone whole body diffusion-weighted MR imaging (DWIBS), whose images were acquired as part of a prospective study to optimize DWIBS for the detection of metastatic disease. The study was approved by the institutional ethical committee and written informed consent was obtained from all patients. There were 9 males and 1female (mean age = 64.7 years, range = 55 to 76 years). Clinical diagnoses included prostate cancer (n = 8), breast cancer (n = 1) and lymphoma (n = 1). DWIBS imaging was performed on a 1.5T MR imaging system (Avanto, Siemens Healthcare, Erlangen, Germany) using a repetition time of 14,000ms, echo time of 72ms, matrix size of 150x150, slice thickness of 5mm, receiver bandwidth of 1960 Hz/pixel, 4 signal averages, STIR fat suppression with an inversion time of 180 ms and an imaging field of view set to 450x450 mm^2. ADC maps were calculated using b = 0 and 900 s/mm^2 data, which were then used to generate cDWI axial images at b_c = 1500 and 2000 s/mm^2. Maximum intensity projections (MIPs) were generated for the acquired (b = 900 s/mm^2) and computed images (b_c = 1500 and 2000 s/mm^2) where the windowing levels were set to be equivalent for image analysis. These image sets were reviewed randomly by an expert body MR radiologist with seven years experience in body diffusion-weighted MR imaging, blinded to the clinical diagnoses and all imaging findings. For each image set, the following were assessed: image quality (on a 4-point scale: 4 – excellent, 3 – good, 2 – moderate and 1- poor), suppression of background signal (on a 4-point scale) and lesion detection (on a per-region basis for both bone and soft tissue disease using a 5 point scale: 5 – definitely a metastasis, 4 – probably a metastasis, 3 – indeterminate, 2 – probably not a metastasis and 1 – definitely not a metastasis). For skeletal lesions, a focal lesion that showed high signal reflecting impeded diffusion compared to the background or adjacent bone marrow was regarded as definitely malignant. For lymph nodes, a node was deemed definitely involved if it showed impeded diffusion and also measured > 1 cm in maximum short axis diameter. For other soft tissue sites, a focal area of impeded diffusion compared to the background or normal parenchymal tissue was regarded as definitely malignant. Mean scores for image quality and suppression of background signal were computed. Lesion detection of DWIBS was compared with conventional CT imaging (n = 10), radionuclide bone scan (n = 7) and ^{18}FDG-PET imaging (n = 2), ^{18}F-PET (n = 2) performed within two weeks of DWIBS imaging, which were used as the reference standard for the imaging evaluation. Receiver operating characteristics (ROC) analysis was performed and the areas under the curve for the different image sets compared using the variance z-test (Medcalc software, The Nederlands). A malignant lesion that was missed by DWIBS was graded as definitely benign for the purpose of ROC analysis. A p-value of < 0.05 was taken to be statistically significant.

Results: cDWI resulted in images of good image quality and excellent background suppression. The mean image quality score for b_c-900, b_c-1500 and b_c-2000 images were 2.6, 2.7 and 2.8 respectively. The mean background suppression scores were 2.9, 3.8 and 4.0 respectively. The b_c-2000 images resulted in the highest image quality and background suppression scores. By ROC analysis, assessment of the b_c-2000 images on their own resulted in the highest diagnostic accuracy (Az = 0.96; 95% CI: 0.95 – 0.97) for detecting metastatic disease compared with standard imaging tests. The diagnostic accuracy of reading b_c-2000 images was significantly higher ($p < 0.01$, variance z-test) than reading the b900 (Az = 0.90; 95% CI: 0.88 – 0.93) or b_c1500 images (Az = 0.92; 95% CI: 0.91 – 0.94), which could be attributed to improved background suppression and increased lesion conspicuity (**Fig 2**). In **Fig 1**, DWIBS maximum intensity projection inverted grayscale (MIP) images were derived from acquired b = 900 s/mm^2 images, as well as cDWI images at b_c = 1500 s/mm^2 and b_c = 2000 s/mm^2. The figure illustrates improved signal suppression from normal structures and enhanced lesion conspicuity on the high b-values cDWI images

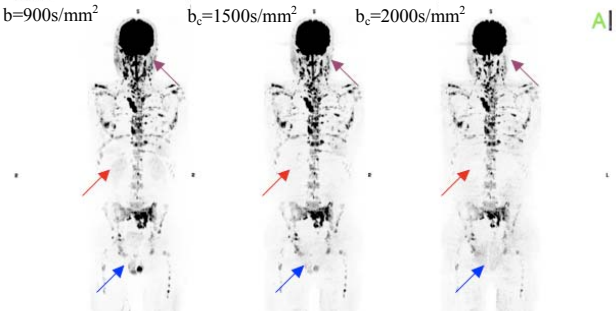

Figure 1. Maximum Intensity projections of DWI/cDWI images generated for a male patient with prostate cancer. The use of higher b-values afforded with cDWI provide improved background signal suppression from tissues such as the testes (blue arrows), kidneys (red arrows) and salivary glands (plum arrows)

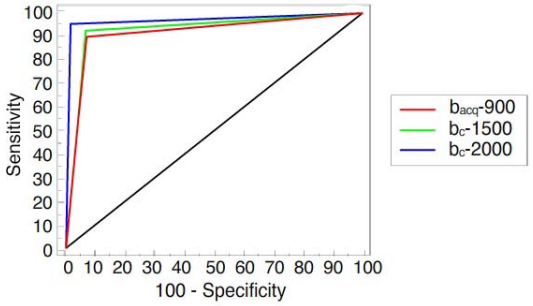

Figure 2. Receiver operator characteristic curves for the evaluation of b = 900, b_c = 1500 and b_c = 2000 s/mm^2 images. The highest diagnostic accuracy (Az = 0.96) was achieved when evaluating the b_c = 2000 s/mm^2, which was statistically higher than the results achieved using either the b = 900 (Az = 0.90) or b_c = 1500 s/mm^2 (Az = 0.92) images ($p < 0.01$, variance z-test).

Conclusion: When we applied the cDWI to our small cohort of cancer patients to test the feasibility of the technique for improving lesion detection, we found that cDWI, particularly at b_c = 2000 s/mm^2, resulted in images of high image quality, with good background signal suppression and lesion conspicuity. The interpretation of b_c = 2000 s/mm^2 images alone resulted in significantly higher diagnostic accuracy (Az = 0.96) compared with evaluation of the b = 900 s/mm^2 (Az = 0.90) or b_c = 1500 s/mm^2 (Az = 0.92) images. Previous studies have shown a high diagnostic accuracy of the DWI technique for staging malignancies such as lung cancer [3] and uterine cervical cancer [4] compared with ^{18}FDG-PET/CT. However, one of the limitations encountered in some DWIBS studies appears to be its diagnostic specificity [5]. cDWI can potentially enhance the diagnostic specificity of the technique by improving signal suppression from normal tissues that may mimic disease.

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