Investigating the contribution of osteoblastic activity to ADC of bone metastases by correlating changes in ADC with changes in T2* and HU

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Introduction: The unique structure of bone marrow presents particular challenges in interpretation of changes in apparent diffusion coefficient (ADC). Predominantly osteolytic bone metastases have a higher ADC than sclerotic metastases and so that ADC is influenced by the balance of osteoblast and osteoclast activity. Magnetic resonance imaging sequences such as ultra short TE (UTE) enable measurement of signal from sclerotic bone and quantified T2* can be used to assess short T2 components within bone metastases. CT Hounsfield units (HU) can also be used as a measure of density of bone metastases. The aim of this study therefore was to investigate the contribution of osteoblastic activity to ADC of bone metastases from prostate carcinoma undergoing treatment by correlating changes in ADC with changes in T2* and HU.

Methods: Subjects: 16 patients age range 50-83 years (mean age 68.9 years) with histology proven carcinoma of the prostate and bone metastases confirmed on bone scintigraphy or conventional T1W and T2W MRI. Imaging protocols: Patients were imaged at baseline (within 7 days prior to commencement of therapy) and 12 weeks +/-7 days following commencement of chemotherapy. MRI was performed on a 1.5 T Siemens Avanto using an external coil array with subjects positioned supine. Sagittal T1W (590/11msec TR/TE; 400mm FOV; 4mm slice thickness) and T2W (2690/93msec TR/TE; 400mm FOV; 4mm slice thickness) images of the spine and pelvis were acquired. Axial single shot twice refocused spin echo planar images were acquired covering the lumbar spine and pelvis with the following parameters: 3000/80msec TR/TE; FOV 350 mm, slice thickness 5mm, 4 averages, 3 orthogonal directions and b values of 0, 50, 100, 250, 500, and 750 mm²/s with SPAIR fat saturation. Sagittal and axial 2D UTE of the lumbar spine and pelvis was also performed: TR 500ms, FOV 800mm, matrix 512, 4 averages, flip angle 85°, BW 540Hz, fat saturation; 4mm slice thickness, spine elements 5, 6 and 7 and body coils 1 and 2 with TEs 0.07, 7.4 and 9.4ms and 4 averages. CT of the chest, abdomen and pelvis was performed as part of routine clinical staging: GE Lightspeed (GE Healthcare Technologies, Waukesha, WI): Omnipaque 300 100mls at 3ml/s portovenous phase using a Smartprep technique, 16 slice, 1.25mm thick with 5mm reconstructions. Data Analysis: Monoexponential ADC maps using all 6 b values (0, 50, 100, 250, 500, 750 mm²/s) were generated using software taking an average value for the 3 directions of diffusion sensitisation. ADC maps were also generated using b 100, 250, 500, 750 mm²/s (ADCslow). Using T1 MR sequences to aid ROI placement up to 5 regions of interest (ROIs) were drawn around lesions on ADC maps avoiding artefacts. T2* maps were generated using Diffusionview software with a monoexponential fit over 3 echo times. Lesions corresponding to those chosen for DWI analysis were selected and ROIs were drawn on the T2* maps avoiding artefacts. Axial CT images and multiplanar reformats of the lumbar spine and pelvis generated using a bone algorithm were viewed in conjunction with all MRI imaging. Lesions corresponding to those chosen for DWI/T2* analysis were selected. ROIs were drawn on axial images or sagittal reformats as appropriate to correspond with lesions analysed on DWI/UTE imaging. All measurements were made on baseline scans and on the corresponding lesions on the 12 week follow up scans. Statistics: Data were analysed using SPSS (v15) and tested for normality and T2* and HU were investigated using a Pearson’s correlation coefficient.

Results: Mean ROI area of all bone lesions at baseline was 8.0 +/- 4.0 cm². Corresponding pre and post treatment ADC and HU were available on 60 lesions from 16 patients. Corresponding pre and post treatment ADC and T2* were available on 12 lesions from 6 patients.

Figure 1. Percentage change in ADC (x10⁻⁶mm²/s) vs mean HU (a) and percentage change in ADC (x10⁻⁶mm²/s) vs percentage change in T2* (b) show no significant correlation with Pearson correlation coefficients of 0.721 and 0.343 respectively. Plots using % change in ADCslow produced similar results.

Figure 2. The relationship between ADC (x10⁻⁶mm²/s) and HU. Axial CT bone windows of the pelvis and corresponding ADC map pre (a and b) and 12 weeks post chemotherapy (c and d) in a patient with bone metastases secondary to carcinoma of the prostate. The metastatic deposit in the right ischial tuberosity (a, arrow) shows sclerotic healing after treatment (c, arrow) with an increase in HU from 142 to 390HU, as the patient responds to treatment (PSA fell from 84 to 23.9 ng/ml). Corresponding ADC maps show that ADC has risen from 877 to 1700mm²/s x10⁶ despite the increase in bone sclerosis (b and d arrows).

Conclusion: Percentage changes in ADC did not correlate with percentage change in HU or T2*. This may be because inter trabecular distance is beyond the range interrogated by the DWI technique employed in this study and does not affect the ADC measurement. High resolution CT studies indicate a normal inter trabecular distance of anywhere between 2.63 and 3.5mm depending on age and sex (5,6). Intercellular distances however are of the order of µm. Because inter trabecular distance is so large relative to cell size, a marked sclerotic response may be required to bring intratrabecular distances down to a level where it affects intercellular distances and diminishes ADC.