ASSESSING MYELOMA BONE DISEASE WITH WHOLE BODY DIFFUSION WEIGHTED IMAGING (WB-DWI): COMPARISON WITH X-RAY SKELETAL SURVEY (SS) AND LABORATORY ESTIMATES OF DISEASE BURDEN

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Target Audience: Radiologists, radiographers, physicists and clinicians with interest in Whole Body Diffusion Weighted MRI (WB-DWI) of myeloma bone disease.

Purpose: Myeloma, a plasma cell malignancy characterised by bone disease, is diagnosed by serum and urinary paraproteins/light chains and clonal plasma cells on bone marrow biopsy. Guidelines recommend x-ray skeletal survey (SS) to screen for bone lesions but evidence suggests that WB-MRI is superior[1,2], although possibly not in the skull and ribs[3]. However, few robust comparisons of WB-DWI and SS have been made. This study aimed to (1) compare the extent of disease identified by WB-DWI with SS by body region and (2) correlate imaging disease burden defined by segmented ADC values with pathological assessment of disease burden.

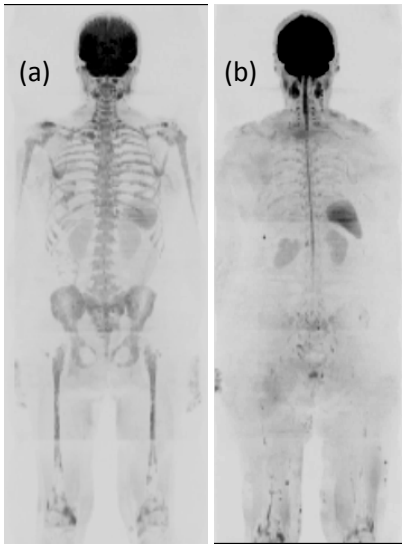
Methods: 20 patients with relapsed myeloma (age 45-73, 8 male, 12 female) underwent WB-DWI and SS before treatment. Serum paraproteins/light chains and marrow histology were recorded. WB-DWI was acquired on a Siemens Magnetom Avanto 1.5T system. 5 stations of a single shot double spin echo echo-planar DW sequence (b =50 and 900s/mm^2 in 3 orthogonal directions) with STIR in free-breathing covered skull vertex to knees in blocks of 50 slices (slice thickness 5mm, no gap, FOV 430mm, phase direction AP, GRAPPA factor 2, TR 14800 ms, TE 66 ms, TI 180 ms, voxel size 2.9x2.9x5 mm, 4 NSA, matrix 150 x 150, bandwidth 1960 Hz per pixel). Morphological imaging was axial T1W spin echo and coronal VIBE Dixon 3D gradient echo sequences. SS radiographs were acquired using a Carestream digital radiography system. Image analyses were undertaken by: (1) Observer Scores, where 2 experienced observers applied a scoring system (1-4) to a categorisation of lesion number (diffuse, >20, 10-20, <10) and largest lesion dimension (>10, 5-10, <5mm) on WB-DWI and SS images and (2) volumetric segmented whole-body ADC histograms of vertebral, sternal, pelvic and femoral bone marrow using Siemens OncoTreat software. Tumor-infiltrated marrow was defined by recording every voxel with an ADC $\geq$774 but $\leq$ 1433mm^2/s[4]. Observer scores for whole skeleton and individual body regions were compared using paired t-tests. Independent samples t-tests compared observer scores and imaging metrics between those with a high or low burden of disease ($\geq$ or < 50% infiltration of plasma cells on bone marrow trephine). Correlation investigated the relationship between observer scores, ADC metrics and laboratory measures of disease burden.

Results: Scores by region and differences between techniques for each observer are shown (Table 1). No patients had a negative WB-DWI score. 3 patients with negative SS scored positively on WB-DWI. Both observers scored WB-DWI significantly more highly than SS in every region ($p<0.05$) except the skull, where observer 1 scored DWI more highly ($p=0.03$) but observer 2 did not ($p=0.8$). There was less observer dependency in WB-DWI than SS scores, although both were significantly different on a per patient basis and in some body regions (Table 1). 20-80% more patients had a positive score by region on WB-DWI than on SS (Table 2).

6 patients had a high burden of disease and 12 a low burden (2 bone marrow samples were unquantifiable). For both observers, WB-DWI total scores per patient were higher in those with a high compared to a low disease burden (Observer 1: mean±SD: 48.8±7.0, 38.6±14.5, Observer 2: mean±SD: 37.3±13.5, 30.4±15.5), but the differences did not achieve significance ($p=0.06$, $p=0.35$). The volume of tumor infiltrated marrow ranged from 35.4-554.8 cm^3 (mean±SD: 241.3±155.1 cm^3). There were no significant differences in whole skeleton ADC metrics between those with a high or low disease burden ($p=0.97$ [mean ADC], 0.46 [median ADC]). WB-DWI observer scores and segmented tumor volume did not correlate significantly with either the proportion of plasma cells on bone marrow trephine or serum paraprotein concentration.

TABLE 1	Obs 1 scores (mean ± SD)		Obs 2 scores (mean ± SD)		Paired t-test Obs 1 & Obs 2 (p)	
Region	WB-DWI	SS	WB-DWI	SS	WB-DWI	SS
Skull	5.3±3.5	3.1±2.3	2.3±2.9	2.5±1.6	**0.005**	0.09
C Spine	5.8±2.7	3.3±3.5	4.6±3.3	0.7±1.2	**0.02**	**0.004**
D Spine	6.9±1.9	5.2±3.5	6.5±2.1	0.8±1.6	0.39	**<0.0001**
L Spine	6.5±2.1	3.8±3.6	4.8±3.2	1.0±1.4	**0.01**	**0.001**
Pelvis	5.8±2.6	2.4±2.9	5.1±2.7	1.4±1.9	0.27	0.08
Ribs/Other	7.3±1.3	2.8±2.7	6.1±3.0	1.3±1.7	0.05	**0.002**
Long Bones	5.4±2.8	2.1±2.0	4.9±2.9	1.7±1.6	0.30	0.31
Total	42.4±12.8	22.2±15.5	33.9±14.4	9.1±7.7	**0.001**	**0.0002**

TABLE 2	Obs 1 % pts scoring + (no. pts)			Obs 2 % pts scoring + (no. pts)		
Region	WB-DWI	SS	Diff WB-SS	WB-DWI	SS	Diff WB-SS
Skull	75 (15)	75 (15)	0	55 (11)	80 (16)	-25
C Spine	95 (19)	60 (12)	35	80 (16)	35 (7)	45
D Spine	100 (20)	75 (15)	25	100 (20)	20 (4)	80
L Spine	95 (19)	60 (12)	35	95 (19)	35 (7)	60
Pelvis	90 (18)	50 (10)	40	90 (18)	40 (8)	50
Ribs/Other	100 (20)	65 (13)	35	85 (17)	40 (8)	45
Long Bones	85 (17)	65 (13)	20	85 (17)	60 (12)	25
Total	100 (20)	85 (17)	15	100 (20)	85 (17)	15



WB-DWI in 2 female patients >65yrs with (a) high disease burden of 80% clonal cells on bone marrow biopsy and (b) low disease burden of 20-25% clonal cells; appearances suggest greater disease extent in the former

Discussion and Conclusions: WB-DWI demonstrated more lesions in all body regions except the skull. There was a smaller observer dependency in WB-DWI than SS scores; the skull was the only region where WB-DWI scores were significantly different but SS scores were not. However WB-DWI scores were also significantly different between observers in the cervical and lumbar spine. Greater experience of WB-DWI may improve results further, unlike SS where observer dependency is limiting despite years of experienced interpretation. Small patient numbers meant that significant differences in WB-DWI scores or ADC metrics between those with a high or low burden of disease were not seen, although previous reports indicate that these correlations exist[5].

References: (1) Dinter et al,2009, Ann Hematol, 88:457-64; (2) Horger et al, 2011, *Acta Radiologica*, 52:881-8; (3) Regelink et al, 2013, *BJH*, 162:50-61 (4) Padhani et al, 2013, AJR, 200(1):163-70; (5) Messiou et al, 2013, ISMRM e-poster 4150.

Acknowledgments: 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 Clinical Research Facility in Imaging and Biomedical Research Centre, Dr. P. Gall & Dr. T Feiweier at Siemens Healthcare for providing the OncoTreat software and WIP DWI sequence & Dr. M. Blackledge at Institute of Cancer Research for optimisation of shimming techniques used in the acquisition.