Whole body mDixon MRI in multiple myeloma: Quantitative derived parameters changes following chemotherapy

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Target Audience: Radiologists and Oncologists with an interest in cancer imaging

Purpose: Whole body morphological and functional MRI (WBMRI) is being used increasingly for initial assessment and evaluation of treatment response in patients with monoclonal plasma cell disorders [1,2]. In multiple myeloma, there is replacement of the normal fatty marrow cells by neoplastic cells. Currently apparent diffusion coefficient (ADC) is the most common biomarker for assessment of treatment response in multiple myeloma, but alternatively new MRI techniques i.e. Iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) could be employed in quantitative analysis of patients with multiple myeloma [3]. Such imaging techniques would have the advantage of faster acquisition compared to Diffusion Weighted imaging (DWI) and could potentially enable us to better depict the underlying processes. In this study we evaluate the changes of fat and water MRI derived signal intensities in patients with multiple myeloma, compared to healthy volunteers and its subsequent changes after chemotherapy.

Material and Methods: Fourteen patients (5 female, 9 male, mean age 58.9 years, range 45-71) with biopsy proven multiple myeloma underwent whole body MRI imaging on a 3.0T scanner using two anterior surface coils, head coil and integrated posterior coil. As part of a WBMRI protocol, coronal pre and post-contrast 2 points modified Dixon (mDixon) sequences (TR 3.0ms, TE 1.02-1.8, flip angle 15°, slice thickness 5mm, pixel bandwidth 1992Hz, acquisition matrix 196*238, SENSE factor 2, number of slices 120) covering vertex to toe were acquired. The skeleton was divided into 10 anatomical stations (cervical, thoracic and lumbar spine, shoulder girdle, humerus, chest wall, pelvis, femur, skull and tibia, fibula and foot as one station). Pre contrast in phase and post-contrast water only images were reviewed in consensus by two radiologists prospectively for different patterns of bone marrow involvement as previously described [4]. Four pattern of involvement; normal, focal, diffuse and diffuse and focal patterns were allocated. At each anatomical station, a confidence score (1 highly unlikely, 2 unlikely, 3 indeterminate, 4 likely and 5 highly likely) was assigned for detection of myelomatous involvement for focal lesions greater than 5mm [5]. Confidence scores of 4 and 5 were considered as positive for disease. A maximum of 20 focal lytic lesions scored as 4 or 5 on post-contrast mDixon images for each patient were chosen for quantitative analysis of fat fraction and percentage enhancement. A region of interest was contoured around the focal lesion on post-contrast water only mDixon and then transferred to pre and post contrast fat only images as well as pre-contrast water only images. Fat fraction ($SI_{fat}/(SI_{fat}+SI_{water})$) [3] and percentage enhancement ($(SI_{post}-SI_{pre})*100/SI_{pre}$) [7] for focal lesions were derived; where SI_{fat} and SI_{water} is the lesion signal intensity on pre-contrast fat and water only image respectively, and SI_{pre} and SI_{post} is the lesion signal intensity on pre and post-contrast water only image. Mann-Whitney test was used to analyse pre and post-treatment changes of fat fraction and percentage enhancement.
Eight healthy volunteers (4 male, 4 female, mean age: 38.6, range 24-52 years) were imaged at two time points (mean 2 weeks apart) using the pre-contrast mDixon sequence as above. Multiple regions of interest covering head, mid shaft and distal femur, entire iliac crest and sacroiliac joints, entire L4 and T10 spine were drawn for each volunteer at each scanning time point. Signal intensities from fat and water images were derived for each region of interest and fat fraction for each ROI was derived. An interclass correlation coefficient (ICC) analysis was performed to assess repeatability of fat fraction measurement in the healthy volunteer group. A Kruskal-Wallis statistic with Dunns multiple comparison test was performed to assess significant changes of median fat fraction between patients at pre-treatment, patients at post-treatment, and healthy volunteers.

Results: In total, 56 normal ROIs were evaluated in healthy volunteers. The ICC of fat fraction from normal ROIs in healthy volunteers between two time points was 0.99 a.u. (95% CI: 0.98-0.99). The median fat fraction of normal ROI across all healthy volunteers was 0.75 a.u. (interquartile range (IQR) 0.59-0.94).
A total of 248 focal lesions were evaluated in patients. The median fat fraction at baseline was 0.25 a.u. (IQR 0.16-0.37), with a significant increase to 0.42 a.u. (IQR 0.26-0.61) following treatment ($p<0.05$). The median pre and post-treatment fat fraction of lesions in patients were significantly lower than normal ROIs in healthy volunteers ($p<0.05$) (figure 1 and 2). The median percentage enhancement of lesions was not significantly different between pre-treatment and post-treatment studies (153.5% and 157.9% respectively, $p=0.69$).

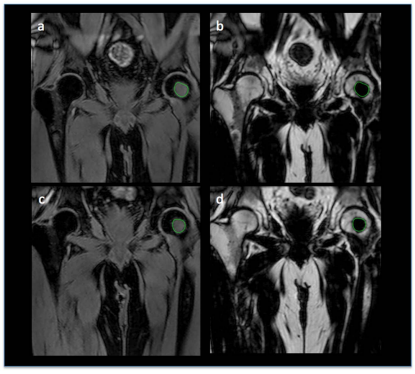

Figure 1: Pre-treatment pre-contrast water (a) and fat only (b) mDixon images and post treatment pre-contrast water (c) and fat only (d) demonstrating a focal lesion, on the left femoral head.

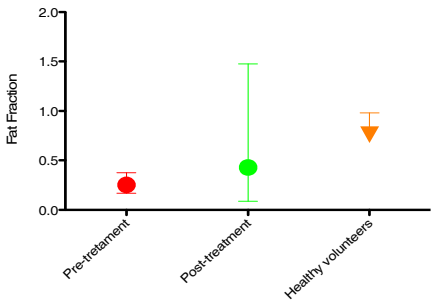

Figure 2: Median and interquartile range of fat fraction in healthy volunteers (orange), compared to patients at pre- and post-treatment (red and green respectively).

Discussion and conclusion: As well as providing a through investigation of the extent of disease, WB MRI is being used for evaluation of treatment response in patients with multiple myeloma. Currently, the most widely used MRI sequence for evaluation of treatment response in oncological malignancies is DWI, which provides ADC as an imaging biomarker. However, problems with ADC quantification and standardisation remain unresolved [8] and scanning times for DWI are relatively lengthy, in order of minutes compared to seconds for mDixon sequence. Whole body mDixon imaging is a fast imaging technique that can potentially provide quantitative imaging biomarker in conjunction with morphological imaging information. Here we demonstrate that fat fraction may provide an alternative robust and sensitive WB MRI biomarker for assessment of treatment response in patients with multiple myeloma.

References: [1] Fechtner et al, 2010. Radiology 257:195-204 [2] Giles et al, 2014. Radiology 271:785-794 [3] Takasu et al, 2012. Eur Radiol 22:1114-1121 [4] Dimopoulos et al, 2009. Leukemia 23:1545-1556 [5] Hillengass et al, 2010. J Clin Oncol 20:1606-1610 [6] Durie et al, 2003. Hematol J 4(6):379–398 [7] Lin et al, 2010. Radiology 254:521-531 [8] Kivrak et al, 2013. Diagn Interv Radiol 19:433-43