Whole Body Diffusion Weighted Imaging in Multiple Myeloma; A Comparison of Gaussian and Non-Gaussian Diffusion Models for Quantitative Derived Parameters

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Target audience: Radiologist and oncologist interested in cancer imaging

Purpose: Whole body diffusion weighted imaging (WBDWI) has been used for initial staging and monitoring treatment response of multiple myeloma patients [2]. In the standard diffusion model, the displacement of freely mobile water molecules is considered to have Gaussian distribution, which can be approximated by a mono-exponential decay function of DWI signal intensity with b-value. However, water diffusion behavior in biological tissues is much more complex. For example, DWI signal will be attenuated by both tissue perfusion, resulting in a drop of signals at the lower b-values that is more rapid than predicted by a mono-exponential (ME) model [3]. Several diffusion models (non-Gaussian diffusion models) have been proposed to account for this behavior and provide a more comprehensive analysis of DWI quantitative derived parameters [4]. The purpose of this study is to investigate application of these models for assessment of WBDWI in patients with multiple myeloma.

Material and Methods: Sixteen patients (7 female, 9 male, mean age 54.5 years, range 35-71 years) with biopsy proven multiple myeloma underwent WBDWI imaging as part of a whole body MRI protocol, at diagnosis and after two cycle of chemotherapy. All MRI performed on a 3.0T scanner (Ingenia, Philips, Best, Netherland) using two anterior surface coils, head coil and integrated posterior coil. Free breathing axial diffusion weighted echo planar imaging (DWI-EPI) with spectral attenuated inversion recovery (SPAIR) plus slice selective gradient reversal (SSGR) fat suppression (TR 6371ms, TE 71ms, slice thickness 5mm, pixel bandwidth 3369Hz, acquisition matrix 124*118, SENSE factor 2.5, number of slices 40, 4 b-values; 0, 100, 300 and 1000 s/mm^2) were acquired from vertex to toe. The skeleton was divided into 10 anatomical sites and images were reviewed by two radiologists in consensus. At each anatomical site, a confidence score (1:highly unlikely, 2:Unlikely, 3:Indeterminant, 4: Likely and 5: highly likely) was assigned for detection of myelomatous involvement at pre-treatment. Confidence scores of 4 and 5 were considered as positive for bone marrow involvement for a focal lesion greater than 5mm [5]. A region of interest (ROI) was drawn around the focal lesion on b1000 images and then transferred to b0, 100 and 300 images. Signal intensity (SI) was recorded at each b-value. Three diffusion models were used to fit the signal decay using an in-house MATLAB script: mono-exponential model, stretched model (SE) and diffusion kurtosis model (DKI) [4]. Mono-exponential diffusion coefficient (D_{mono}) and diffusion coefficients for stretched exponential (D_{SE}) and kurtosis models (D_{DKI}) were calculated. All focal lesions were re-evaluated following treatment. The adjusted coefficient of determinant (R^2) was derived for each diffusion model to investigate the accuracy of the fitting. A Kruskal-Wallis test with Dunns multiple post test was used to assess median D_{mono}, D_{SE} and D_{DKI} as well as median R^2 for each decay model. A Mann-Whitney test was applied to determine change in diffusion parameters pre and post-treatment.

Results: In total, 292 focal lesions were identified in all patients. Median D_{mono} at pre-treatment was 0.75 mm^2/s (median 0.75, interquartile range (IQR): 0.57-1.18) compared to 0.66 a.u. (IQR: 0.43-1.16) for D_{SE} and 1.3 a.u. (IQR: 0.86-1.7) for D_{DKI}. There was a statistically significant different between all three diffusion coefficients ($p<0.05$). Post-treatment the diffusion coefficient values increased for all models ($p<0.05$), with median coefficients of 1.2 mm^2/s (IQR: 0.63-2.0), 1.24 a.u. (IQR: 0.52-1.83) and 1.75 a.u. (IQR: 1.0-2.2) for mono-exponential, SE and DKI decay models (figure 1). The median adjusted coefficient of determinant for pre-treatment diffusion coefficient estimation was 0.89 (IQR: 0.85-0.99), 0.99 (IQR: 0.99-1.0) and 0.97 (IQR: 0.97-1.0), for mono-exponential, SE and DKI models, respectively. For post-treatment diffusion coefficient estimation, the median R^2 was 0.92 (IQR: 0.92-0.99), 0.99 (IQR: 0.99-1.0) and 0.98 (IQR: 0.98-1.0) for mono-exponential, SE and DKI models. There was a statistically significant difference between mean R^2 of all decay models at pre-treatment ($p<0.05$). Post-treatment, there was a statistically significant difference between R^2 of mono-exponential fit, compared to SE and DKI models ($p<0.05$).

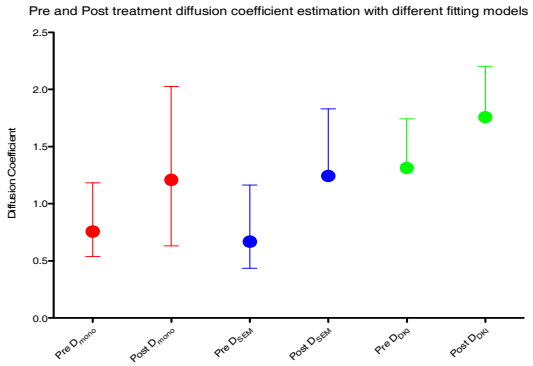

Figure 1: Median (interquartile range) pre and post-treatment diffusion coefficient values for mono-exponential (red), SE (blue) and DKI (green) fitting

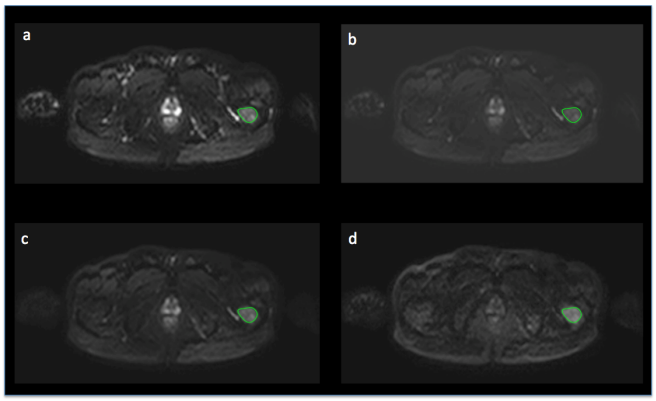

Figure 2: Represented ROI of a left femoral head focal lesion on b0 (a), b100 (b), b300 (c) and b1000 (d)

Discussion and Conclusion: Despite being widely adopted in the clinical setting, apparent diffusion coefficient estimates using a mono-exponential diffusion model fit to multiple b-value DWI does not capture the complex water diffusion behavior in biological tissue. Other models have been proposed to take into account the non-Gaussian diffusion behavior as well as perfusion effect of low b-value DWI. This study reports the first application of SE and DKI to whole-body imaging of patients with multiple myeloma and comparison with the standard mono-exponential model. SE and DKI models demonstrate greater fitting accuracy. Furthermore, whilst diffusion coefficient values are significantly difference between each of the decay models, as previously reported [2], the diffusion coefficient values from focal bony lesions demonstrate a significant increase following treatment for all models. SE and DKI models may provide a more robust method of quantifying diffusion parameters on WBDWI.

References: [1] Fechtner et al, 2010. Radiology 257:195-204 [2] Giles et al, 2014. Radiology 271:785-794 [3] Dikaios et al, 2014. MRM 71: 2105-2117 [4] Yuan et al, 2014. PLoS ONE 9(1):e87024 [5] Hillengass et al, 2010. J Clin Oncol 20:1606-1610