A REGISTRATION FRAMEWORK FOR EVALUATION OF T1, T2 AND DWI SIGNAL INTENSITIES IN MULTIPLE MYELOMA

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Abstract: **Objective.** In this study we point out the Diffusion-Weighted Imaging (DWI) role in the diagnosis of multiple myeloma (MM), comparing its signal values (SV) (Sommer et al., 2010) with the standard imaging modalities T1, T2. We further evaluate how SV change in relation with the percentage of plasma cells infiltration evaluated through bone marrow biopsy (BMB).

Methods. Since March 2008 23 patients with average age of 61 ($\pm$ 11) years old, 11 females and 12 males, have been investigated before their own therapy with a whole body MRI protocol, concerning a whole body T1, a whole body T2 and a whole body DWI and a BMB. An experienced radiologist defined for each patient two volume of interests (VOIs): onto the main lesions and on healthy bones (Femur and Homerus). After that, we have subdivided the full population by a clinical threshold of 25% on cells infiltration percentage; then, we analysed statistical differences in the 2 groups (A, B).

Results. We found out that DWI voxels intensities in group A (infiltration $\leq 25\%$) were higher than group B, this gap had to be considered statistically different ($P \leq 0.05$).

1 INTRODUCTION

Although conventional radiography is still the standard widely approved staging procedure for newly diagnosed and relapsed multiple myeloma (MM) (Sommer et al., 2010), whole-body MRI (WB-MRI) using T1- and T2-weighted contrast images has proved evidence of its advantages over conventional skeletal survey (Ghanem et al., 2006). In this scenario the whole-body DWI imaging is being attracting interest as a tool for the investigation of MM lesions (Sakurada et al., 2009). This study analyses the great potential of DWI in MM diagnosis, comparing T1, T2, DWI and correlating their values with clonal cells infiltration in bone marrow. When different MRI methodologies have to be compared, relevant role is plaid by registration which allows the comparative analysis among modalities. In this work we present a registration framework to align T1, T2 and DWI MRI acquisition. The framework was designed for the evaluation of signal intensities in Multiple Myeloma lesions.

2 MATERIAL AND METHOD

2.1 Patients

The analysed patients form a subset of a study on whole-body MRI for multiple myeloma lesions started in May 2008 at the national cancer institute of Milan (INT). The study considers only patients at diagnosis or at relapse after disease response (CR or PR) lasting at least 6 months. The study was approved by the local ethics committee and all patients gave their written informed consent before being included. Globally, we analysed 23 patients (12 males and 11 females, median age 61 years, age range 44, 81 years). Patients underwent a whole-body MRI scan consisting of whole-body standard MRI (T1 and T2) and Diffusion weighted MRI. None of the patients had major artifacts on DW imaging that warranted their exclusion from the study. After or immediately before the MRI exams the patients underwent to bone marrow biopsy (BMB).

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2.2 Imaging Protocol

MRI examinations were performed on a 1.5 T MR imaging scanner Siemens Avanto (Erlangen-Germany) using 6 array coils (head, neck, abdominal, torso, pelvic and legs). Whole body images were created composing different volumes: T1 and T2 were acquired coronally in 3 - 5 steps, EPI DWI images were acquired axially in 8 - 10 steps depending on patients' height.
The coronal T1-weighted *tse2d1rr2* sequence was performed with TR 550, TE 9.5, voxels size $\sim$ 1 x 5 x 1 mm, $\sim$ 1 mm gap, a field of view (FoV) of 500 x 500 mm, a matrix of $\sim$ 500 x 500 , two NEX, TA 2.40 minutes.
Coronal T2-weighted *spcir3d1345ns* sequence was performed with TR 4000, TE 367, voxels size $\sim$ 1 x 5 x 1 mm, $\sim$ 1 mm gap, a FoV of 500 x 500 mm, a matrix of $\sim$ 500 x 500 , two NEX, TA 4 minutes.
Axial Echo-planar DW imaging was performed with 4 b-values (50, 400, 800, 1000 $\frac{s}{mm^2}$), *ep2ddiff*: TR 7900, TE 81, voxels size $\sim$ 2.5 x 2.5 x 6 mm, $\sim$ 1 mm gap, a FoV of 400 x 400 mm, a matrix of $\sim$ 160 x 160, two NEX, TA 3 minutes (table 1).

The total acquisition time was 30 min, chest and abdominal T1 and T2 sequences were acquired during breath-hold; all others sequences were acquired during free breathing. No contrast agent was applied.

Table 1: Principal sequence features parameters.

Features	T1	T2	DWI
Orientation	Coronal	Coronal	Axial
TR	550	4000	7900
TE	9.5	367	81
Voxels size	1x5x1	1x5x1	2.5x2.5x6

2.3 Image Data Analysis

To evaluate different tissues property on different MRI modalities we need to create 3D volumes and register them among modalities. Registration of a whole-body volume has many challenges such as the huge size of the matrix, the anisotropy of the volume, the breathing of the patients etc .... We propose a registration framework which is explained in the next section.

2.3.1 3D Reconstruction and Registration

Whole-body examination was obtained by partial MRI scans of sub-volumes; the first step was to rebuild a unique 3D whole-body volume from the sub-volumes acquired by T1 and T2 sequences. The sub-

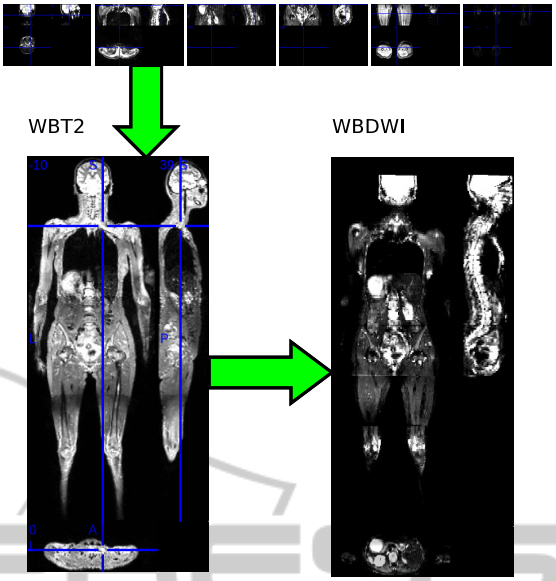

Figure 1: Reconstruction of whole-body DWI, each DWI sub-volumes is aligned on the reconstructed whole-body T2.

volumes were spatial combined and voxels averaged in the overlapped areas. In addiction, to compensate possible deformation due to patient breathing a non-rigid registration between T1 and T2 was performed using the T2 as reference imaging.

Conversely the 3D Volume reconstruction for the DWI was obtained by the affine registration of each DWI sub-volume with the reconstructed whole-body T2. An affine registration was used in this purpose and overlapped voxels were averaged. The procedure is described by figure 1. To optimize computation time, the registration parameters were calculated for b50 volumes and then applied to the other volume acquired with different b-value. Finally to remove possible local misalignment, a non-rigid registration was performed between whole-body T2 and DWI at lowest b-value (50 $\frac{s}{mm^2}$). All non-rigid registration were performed with IRTK software (Schnabel et al., 2001) using a multi-resolution optimization with free-form deformations based on multi-level B-splines (Lee et al., 1996) (Lee et al., 1997).

The total time for reconstruction and registration was roughly 15 minutes for each patient. The accuracy of the registration was visually scored by an expert radiologist. None of the registered volume was classified as non acceptable or erroneous by the radiologist.

Our framework subdivides the registration task in two parts: a global transformation and a local one. This kind of solution is usually adopted in breast MR Images to model the movement of the tissues (Rueck-

ert et al., 1999). The global motion model describes the overall motion of the sub-volume and is compensated by an affine transformation, which has 12 degrees of freedom, describing rotations and translations scaling and shearing.

For the local registration, through which we try to compensate the local deformation of the sub-volume (i.e. breathing movement on rib cage), we selected a free form Deformations model (FFD), based on B-splines (Rueckert et al., 1999). The basic idea of FFD is to deform an object by manipulating an underlying mesh of control points. The resulting deformation is applied to the entire 3-D object and produces the final transformation.

For both the models we used normalised mutual information as voxels similarity measure and a working resolution of 5 x 5 x 5 mm for the global registration while a thinner mesh for the local model 2 x 2 x 2 mm.

2.3.2 Image Quantification

An experienced radiologist identifies for each patients 2 volumes of interest: within the main lesions (in the surrounding of the BMB) and on healthy bone (Femur and Homerus). The selection was performed in one of the image modalities, usually on b1000 DWI images as suggested by the literature (Khoo et al., 2011) and easily transferred to the other as the volume was registered previously, averaged values inside the ROI were computed for each image modality.

2.3.3 Statistical Analysis

Comparison between intensity of healthy bone and lesions was performed using a Wilcoxon's signed-rank test, the level of significance was set to $P = 0.01$.

In addition, the patients were categorised in two groups based on the percentage of clonal cells in bone marrow resulting from the BMB exam; group A had an infiltration percentage $\leq 25\%$ and group B $> 25\%$. An infiltration greater than 25% is for oncologist clinicians a typical threshold that decides for treatments on patients. Mean values of the voxels intensities were compared using Mann-Whitney rank-sum test, to reveal the differences between the two groups, the level of significance was set $P = 0.05$.

3 RESULTS

Median signal intensity and 25^{th} and 75^{th} percentile are reported in table 2, the same data are shown in box-plot of figure 2. In all the modalities a statistical significance $P < 0.001$ was observed between the voxels values in the healthy ROI vs the lesions ROI.

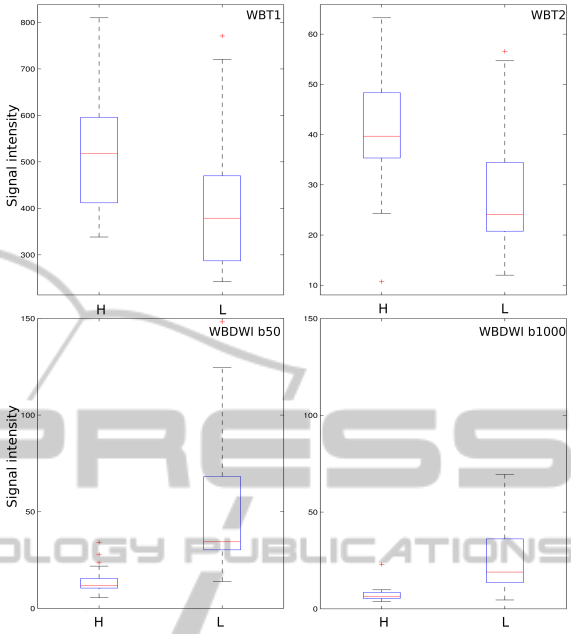

Figure 2: Voxels intensity of the 2 ROI healthy bone marrow (H) and lesions (L) in T1, T2 and DWI (b50 ,b1000).

The second comparison between group A and group B is shown in figure 3, it shows the difference between the voxels values of the 2 groups (BMB$\leq$ 25% and BMB $>$ 25%), significant difference is observed between group A and group B in the all the DWI imaging in particular in all the cases signal intensity was lower in the group B (Koh and Collins, 2007) (Khoo et al., 2011). Conversely no significant differences were observed in T1 and T2 imaging even if a trend for lower value of lesions is observed.

4 CONCLUSIONS

Whole-body DWI imaging is a powerful tool for the staging of patients with multiple myeloma (Padhani et al., 2009) (Sommer et al., 2010). The new technique allows for fast whole-body imaging with low technical and operational efforts. DWI sequences can improve the accuracy of focal MM lesions identification in patients newly diagnosed. A decrease of DWI voxels values evaluated at the same b-value can be potentially related to an high grade myeloma with cells infiltration percentage higher than 25% ($P \leq 0.05$).

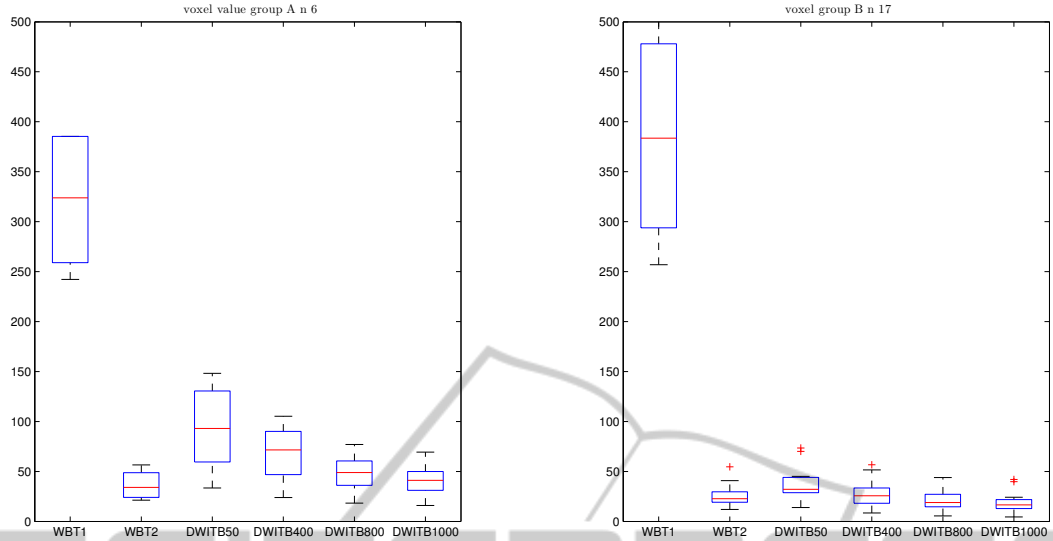

Figure 3: Ranksum test on T1, T2 and DWI (b50, b1000) voxels values in patient from group A and B.

Table 2: Median and quartile of lesion (L) and healthy bone marrow (H) pixel values of the different techniques.

techniques	$median_L$	$q\ 25_L$	$q\ 75_L$	$median_H$	$q\ 25_H$	$q\ 75_H$
T1	397	287	470	517	412	596
T2	28.3	20.8	34.4	40.2	35.3	48.3
DWIb50	49.2	30.3	68.2	14.1	10.5	15.4
DWIb1000	23.7	13.5	36.2	7.31	5.36	8.49

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