Automated tool to quantitatively assess bone disease on Whole-Body Diffusion Weighted Imaging for patients with Advanced Prostate Cancer

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Abstract

An automated tool has been developed to assess bone disease on Whole-Body Diffusion Weighted Imaging (WBDWI). The tool segments areas of suspected bone disease on the high b-value sequences, transfers the ROIs obtained onto the derived Apparent Diffusion Coefficient (ADC) map and estimates the median global ADC (gADC) and the Total Diffusion Volume (TDV).

Keywords: Metastatic bone disease, WBDWI, transfer learning, atlas-based registration, segmentation

1. Introduction

WBDWI is a recognised technique for monitoring treatment response of metastatic bone disease in patients with Advanced Prostate Cancer (APC) (Padhani et al., 2011). Delineation of disease within WBDWI allows measurement of the TDV and median gADC, the latter being a surrogate imaging biomarker of tumour cellularity (Perez-Lopez et al., 2017). However, this is not feasible in clinical practice due to the time needed for tumour delineation (approximately 1-2 hours) (Blackledge et al., 2016). Therefore, we have developed an automated tool to delineate ROIs that might show same properties than bone lesions on WBDWI in patients with APC.

2. Methods

2.1. Patient Popualtion

A retrospective WBDWI cohort of 40 patients with APC was used to train the segmentation tool (Cohort A). A radiologist with 2+ years of experience in WBDWI performed manual delineation of metastatic bone lesions on WBDWI across this cohort. Every patient underwent baseline and post-treatment scans (range = 8–26 weeks). A second radiologist with 10+ years of experience in WBDWI classified patients as responders/non-responders (10/30) to treatment based on all available clinical data.

2.2. Image Acquisition

WBDWI was acquired using b-values of 50/600/900 s/mm^2 on a 1.5T scanner (MAGNETOM Aera, Siemens Healthcare, Erlangen, Germany), over 4-5 stations from skull base to mid-thigh, with each station consisting of 40 slices with a slice thickness of 5mm.

2.3. Image Processing

The automated tool includes four steps:

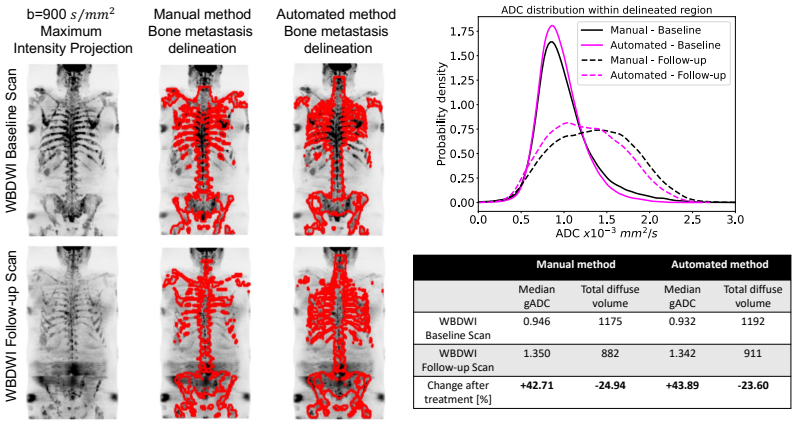
- b=900 s/mm^2 image signal normalisation. An AI-based model with Unet architecture was trained to delineate the spinal cord on WBDWI (Cohort A; 80/20% training/validation split) using a two-channel input: (i) calculated b=0 s/mm^2 image, and (ii) ADC map following mono-exponential fitting across all b-values. Images were normalised to the 90^{th} percentile of b=900 s/mm^2 signal within the spinal cord.
- An atlas-based 3D affine transform followed by diffeomorphic demons registration was performed to delineate the full skeleton on WBDWI. ADC map (target) was registered to an atlas cohort of ADC maps of 15 patients with diffuse Multiple Myeloma (MM) for which entire skeleton was manually defined (Cohort B). A weighted majority voting method was used to determine a probability mask for the skeleton. Moreover, the registration employs a transfer deep-learning model (VGG16) to improve initial alignment between the target and atlas images.
- A machine learning model was trained to derive the ROIs. 18 baseline WBDWI scans of patients with APC (Cohort A) were used for training a xgBoost algorithm to classify healthy/diseased bone voxel-wise. The algorithm was trained using two features, (i) the atlas-derived skeleton probability at each voxel location, and (ii) the normalised b=900 s/mm^2 image.
- Derived ROIs were transferred onto the ADC map to derive the median gADC, TDV (in millilitres), changes in median global ADC ($\Delta gADC$) and TDV (ΔTDV) after treatment.

3. Results

Dice score between the manual and predicted spinal cord mask on test datasets was on average 0.89. A leave-one-out cross validation (LOOCV) was performed to assess the performance of the atlas-based registration assisted with the transfer-deep learning model. Dice score, average Hausdorff distance and Relative Difference (RD) of skeletal volume (following logarithmic transform) between manual defined and automatically derived skeleton mask were 0.65, 2.8 mm, 3.5%, respectively. The software tested on the holdout WBDWI scans showed a RD of median gADC and log TDV of 5.53%(2.17-10.75) and 4.02%(2.77-14.50), respectively. Figure 1 shows one patient with diffuse bone metastases. The ADC and TDV derived from ROIs delineated from a radiologist suggest a response to treatment (increase of ADC and decrease of TDV post-treatment). The accuracy in predicting responders/non-responders in the retrospective cohort was 82.5% (with sensitivity/specificity of 70/86.7%) using a threshold of +25% or -40% for $\Delta gADC$ and ΔTDV (Donners et al., 2018), respectively.

4. Discussion

The software shows good agreement with bone lesion ROIs delineated by a radiologist on test data with running time under 4 minutes. Derived ROIs identified bone areas that show high signal intensity on WBDWI scans for APC patients, as expected. As a result, the segmentation tool showed accurate measures of ADC and TDV, biomarkers that can support clinical assessment of response to systemic treatments.



	Manual method		Automated method	
	Median gADC	Total diffuse volume	Median gADC	Total diffuse volume
WBDWI Baseline Scan	0.946	1175	0.932	1192
WBDWI Follow-up Scan	1.350	882	1.342	911
Change after treatment [%]	**+42.71**	**-24.94**	**+43.89**	**-23.60**

Figure 1: Comparison of manually and automatic derived ROIs with response biomarkers

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