Size, ADC and T2 signal- a reproducibility study of parametric measurements for classification of nodal disease in paediatric hodgkin's lymphoma

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Target audience: Radiologist and oncologist with an interest in cancer imaging

Background: Positron emission tomography (PET-CT) remains the gold standard imaging modality for staging and treatment response monitoring of paediatric lymphoma despite the associated radiation risk [1]. Anatomical whole body MRI (WB-MRI) offers an alternative non-ionising technique [2] that can be supplemented by diffusion weighted imaging (DWI) assessing cellularity as a surrogate for metabolic activity [3]. In clinical practice classification of nodal status in paediatric Hodgkin's lymphoma relies upon size measurement on CT and/or increased flurodeoxyglucose (FDG) uptake on PET. In order to develop WB-MRI as an alternative modality to PET-CT we investigate the comparative performance and reproducibility of anatomical MRI derived nodal size and signal intensity; and diffusion derived apparent diffusion coefficient (ADC) measurement for determination of nodal disease status.

Material and Methods: Thirty-seven patients (mean age, 15.9 years, range 12.8-18 years) with histologically proven Hodgkin's lymphoma underwent WB-MRI and PET-CT for disease staging prior to treatment. All patients were imaged using a standard paediatric PET-CT protocol [4]. All patients underwent axial WB-T2w imaging (STIR-HASTE, TE/TR=60/800ms, TI=130ms, Slice thickness=7mm, NSA=2, acquisition matrix=256*256, FOV=variable and iPAT=2) augmented by axial WB-DWI (STIR-EPI, TE/TR=77/6000ms, TI=180ms, Slice thickness=4mm, NSA=4, acquisition matrix=128*100, FOV=280, iPAT=2, b-values= 0,300 and 500 s/mm^2). DWI and T2-weighted images were reviewed on an Osirix workstation by two experienced radiologists independently. For analysis the body was divided into 11 nodal stations based on conventional anatomical definitions [5]. For the largest lymph node at each station, the radiologists measured short axis diameter on T2 and b500 DWI, ADC (calculated using Excel Solver by a least square exponential fit of signal intensity values obtained from b0, 300 and 500 s/mm^2 DWI images) and T2 signal intensity (T2-SI). T2-SI was normalized to muscle signal intensity (nT2SI). As a reference standard, PET-CT images were reviewed in consensus by two nuclear medicine physicians and nodal involvement assessed by application of conventional PET-CT positivity criteria [4] for the same anatomical sites as evaluated by the radiologists on WB-MRI. The utility of individual MRI parameters (DWI size, T2 size, nT2-SI and ADC) to predict PET-CT nodal disease status was assessed for each reader by receiver operating characteristic (ROC) area under curve (AUC) analysis. Inter-reader agreement of derived quantitative MRI parameters was assessed using Bland-Altman statistics. Bland-Altman statistics were also used to test the inter-sequence agreement for size measurements performed on b500 DWI and T2-w sequences for each reader.

Results: A total of 291 nodes were evaluated. Of these, 143 were negative and 148 positive for disease by the PET-CT reference. Median quantitative MRI parameters for positive and negative nodes are given in table 1. For reader 1, as a determinant of PET-CT positivity, the ROC-AUC of nodal size (as measured on b500 DWI and T2-w MRI) was 0.90 (95% CI, 0.86-0.94) and 0.89 (95% CI, 0.85-0.93) respectively; and the ROC-AUC of nT2-SI and ADC was 0.80 (95% CI, 0.74-0.85) and 0.79 (95% CI, 0.73-0.84) respectively (Fig.1). The ROC-AUC of nodal size on DWI and T2-w images for reader 2 were 0.88 (95% CI, 0.84-0.92) and 0.89 (95% CI, 0.86-0.93) respectively (Fig.2). The ROC-AUC of nT2-SI and ADC for reader 2 were 0.75 (95% CI, 0.70-0.81) and 0.84 (95% CI, 0.79-0.89) respectively (Fig.2).
There was a positive bias for reader 1 vs. reader 2 of 0.25 cm (95% limits of agreement (LoA): -0.50 to 0.54) and 0.26 cm (95% LoA -0.49 to 0.51) for nodal size measurements made on b500 DWI and T2-w MRI respectively. There was also a positive bias of 0.39mm^{2}s^{-1} (95% LoA -0.74 to 0.8) and 0.56 (95% LoA -1.07 to 1.16) for ADC and nT2-SI respectively for reader 1 vs reader 2. Inter-sequence agreement of nodal size measurements for reader 1 was 0.24 cm (95% LoA: -0.47 to 0.48) and for reader 2 was 0.23 cm (95% LoA: -0.45 to 0.45).

Conclusion: Our results demonstrate that despite a potential inter-reader variability of approximately 5 mm, assessment of short axis nodal diameter either on b500 DWI or T2w MRI provides a good classification of nodal disease status in paediatric patients with Hodgkin's lymphoma. ADC and nT2-SI can independently classify nodal disease status but ROC-AUC is lower than simple size measurement.

	DWI Size (cm)		T2 Size (cm)		ADC (mm^{2}s^{-1})		nT2 SI	
	Reader1 (range)	Reader2 (range)	Reader1 (range)	Reader2 (range)	Reader1 (range)	Reader2 (range)	Reader1 (range)	Reader2 (range)
Positive nodes (n=148)	1.5 (0.2-6.6)	1.6 (0.2-6.6)	1.4 (0.4-6.6)	1.5 (0.3-6.12)	1.1 (0.5-2.5)	1.1 (0.6-2.6)	3.2 (1.1-7.9)	3.6 (1.4-7.3)
Negative nodes (n=143)	0.5 (0.2-6.1)	0.5 (0.3-4.8)	0.5 (0.2-6.1)	0.5 (0.3-4.2)	1.5 (0.8-5)	1.5 (0.2-3.7)	3.1 (1.1-5.7)	2.6 (1.0-5.4)

Table.1: Median (range) values for size measurement on DWI, T2-w MRI and ADC and nT2 SI derived parameters for reader 1 and 2.

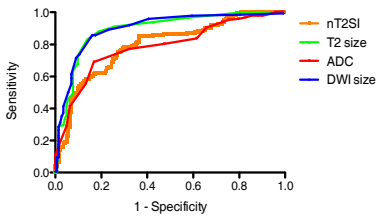

Fig.1: ROC analysis for reader 1

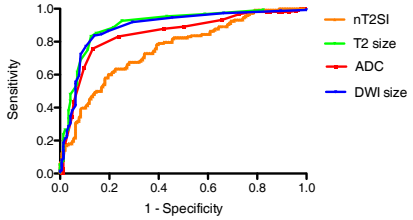

Fig.2: ROC analysis for reader 2

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