Assessment of whole-body DWI combined size and ADC criteria for determination of nodal disease status in paediatric Hodgkin's lymphoma

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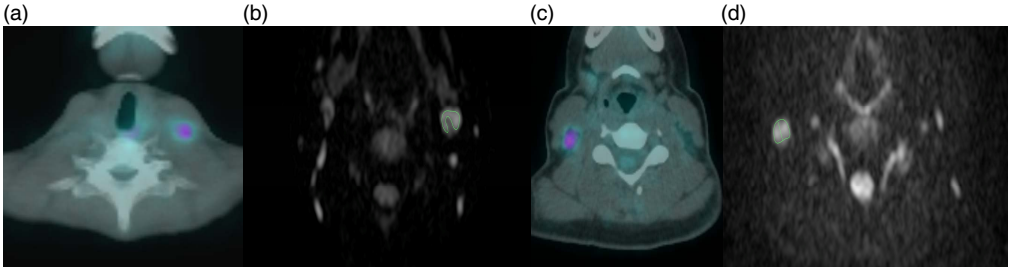
Target audience: Radiologists and paediatric oncologists with an interest in using MRI for cancer staging.

Purpose: Despite the associated radiation exposure and its potential consequences [1], PET-CT remains the gold-standard for staging of paediatric Hodgkin's lymphoma [2]. Whole-body (WB) MRI anatomical assessment of disease shows promise as an alternative staging modality, but fails to detect disease within small (sub-centimeter) lymph nodes [3]. Diffusion-weighted imaging (DWI) derived apparent diffusion coefficient is reduced in lymphoma involved nodes and a cut-off value of 1.2 mm^2s^{-1} has been proposed for nodal classification [4]. This study evaluates four separate WB-DWI criteria based on a combination of nodal size and ADC criteria for classification of lymph node disease status in paediatric patients with known Hodgkin lymphoma; and aim to determine whether addition of ADC criteria to conventionally used size threshold improves test performance.

Methods: Thirty-eight patients (mean age, 15.35 years; range, 12.8-18 years) that underwent both PET-CT and WB-DWI between 2009 and 2012 for initial staging of histologically proven Hodgkin's lymphoma were selected from our local database for study inclusion. Axial WB-DWI images were acquired using STIR-EPI sequence (TE=77ms,TR= 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). All patients were also imaged using a standard paediatric PET-CT protocol [5]. WB-DWI images were evaluated by a paediatric radiologist; the body was divided into 11 nodal stations based on conventional anatomical definitions [3] and the short axis diameter and ADC (calculated using Excel Solver by a least squares exponential fit of signal intensity values obtained from b0, 300 and 500 s/mm2 diffusion weighted images) of largest lymph node at each station measured. Four separate criteria of positivity were evaluated: (i) where a node was ≥ 1-cm short axis irrespective of ADC; (ii) where a node ADC < 1.2 mm^2s^{-1} irrespective of nodal size; (iii) where an individual node short axis diameter was ≥ 1-cm irrespective of ADC, and when the short axis diameter was < 1-cm and the ADC is <1.2 mm^2s^{-1}; and (iv) where an individual node ≥ 1-cm and the ADC is < 1.2 mm^2s^{-1}. PET-CT images were reviewed in consensus by two nuclear medicine physicians based on the same anatomical body divisions as for WB-MRI evaluation and the largest node at each body location classified as positive or negative for disease based on conventional PET/CT staging criteria [6].



Results: 322 nodes (and thereby nodal sites) were identified across all patients on WB-DWI and matched with PET-CT. Median nodal size was 6.4 cm (range, 0.2-12.6 cm) and median nodal ADC was 2.7 mm^2s^{-1} (range, 0.4-5 mm^2s^{-1}). 51.6% (166/322) nodes were >= 1-cm and 48.4% (156/322) < 1-cm in short axis diameter.

Figure1: Patient 1: (a) positive left cervical node on PET-CT;(b) corresponding DWI short axis diameter= 0.7, ADC=0.8
Patient 2: (c) positive right cervical node on PET-CT; (d) corresponding DWI short axis diameter=0.5, ADC=1.0

The sensitivity, specificity, PPV and NPV for the four positivity criteria were: (i) 81.2%, 85.4%, 86% and 80%; (ii) 78.9%, 65.5%, 72% and 73%; (iii) 68.5%, 97.3%, 96.6% and 73.1%; and (iv) 85.9%%, 48.3%, 65.3% and 75.2% respectively. Figure 1 shows examples of two patients with nodes less than 1-cm (i.e. negative by definition (i)) but positive based on ADC < 1.2 mm^2s^{-1} (i.e. positive by definition (iii)); corresponding to PET-CT positive sites.

Discussion: The deficiencies of using size criteria alone for the assessment of nodal disease are well documented [3]. We evaluated the application of different combinations of size and ADC criteria to define nodal disease and found that using an ADC threshold alone (i.e. irrespective of size, definition (ii)) reduced sensitivity, specificity, PPV and NPV of nodal classification compared with size criteria alone (definition (i)). The "best" combined performance was achieved where ADC criteria were applied in combination with size criteria for nodes < 1-cm in short axis (definition (iii)) improved the specificity and PPV to 97.3% and 96.6% respectively (Figure1); whilst exhibiting a modest drop in sensitivity and NPV to 68.5% and 73.1%. The comparison of test performance based on sensitivity and specificity statistics should be guided by the clinical situation in which the test is to be applied. In the case of paediatric Hodgkin lymphoma, the misclassification of nodal status whether positive or negative, has the potential to alter disease stage and thereby result in under or over-treatment.

Conclusion: The study shows that sole ADC based classification of nodal disease status is not as effective as the conventional size alone classification. The study highlights that whilst the performance characteristics of WB-DWI can be altered based on positivity thresholds derived from size, ADC or combined criteria; the increase in specificity afforded by combined criteria classification comes at the cost of reduced sensitivity. Further evaluation is necessary to prospectively evaluate the clinical impact of combined criteria on Ann-Arbor staging.

References: 1. Ufford et al. AJR. **2011** 106:662-669 **2.** Darge et al. EJR. **2008** 68:289-298 **3.** Punwani et al. Radiology. **2010** 255:182-190 **4.** Punwani et al. Cancer Biomarker. **2010** 7:249-259 **5.** Alessio et al. **2009** 50:1570-1578 **6.** Kleis et al. EUR J Nucl Med Mol Imaging **2009** 36:23-36