

## Evaluation of STIR-HASTE whole body MRI for the initial staging of paediatric lymphoma: A correlation with PET/CT

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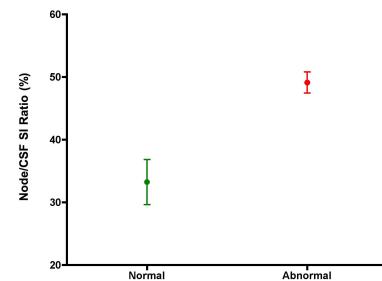
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**Aim:** To compare STIR-HASTE WB-MRI (using size criteria) to a reference of standard of PET/CT for the initial staging of paediatric lymphoma and to evaluate the potential utility of MR node signal intensity for disease assessment in subcentimetre nodes.

**Introduction:** Optimized treatment of lymphoma is dependent upon disease stage. Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) are staged using the Ann Arbor classification system based on a combination of clinical symptoms and imaging assessment of extent of lymph node involvement. CT has a reported sensitivity and specificity for identification for diseased nodal sites of 87.5% and 85.6% [1], based on simple size criteria (positivity defined by nodal short axis > 1 cm). The deficiencies of such size criteria in staging lymphoma are well known, particularly in the pediatric population where benign nodal enlargement is more common [2]. Combined <sup>18</sup>F-2-deoxy-2-fluoro-D-glucose Positron Emission Tomography (FDG-PET) and computerized tomography (CT) staging has been shown to significantly improve diagnostic accuracy [1] by providing a functional as well as structural assessment of nodes. However FDG-PET/CT imparts a significant dose of ionizing radiation, not least given the need for frequent imaging to assess treatment response. Exposure to even small doses of radiation increases an individual's risk of development of malignancy by stochastic effects [3], perhaps many years after the exposure. This is further increased in childhood exposure, given the relatively longer life span of a child as compared to an adult, and increased radio-sensitivity of tissues in childhood [4], [5]. Whole body MRI (WB-MRI) can produce anatomical images for structural evaluation of nodal size akin to CT, furthermore MRI can provide signal intensity measurements which are likely to alter with disease. The purpose of our study was to prospectively compare MR lymphoma staging (using size criteria) with PET/CT staging and to investigate the potential utility of MR STIR-HASTE lymph node signal intensity measurements as an additional parameter in assessing nodal involvement.

**Method:** Local ethics committee permission was obtained for the study. Twenty one consecutive patients (11 male) were recruited. Participants were aged between 8 and 18 years, mean age 15 years. All patients had histologically proven lymphoma and were previously well. As part of routine clinical practice, disease staging was performed using PET/CT and contrast enhanced chest CT. In addition patients were invited to undergo MRI, which was performed within 72 hours of the PET/CT; both prior to treatment. For the MRI study, patients were fasted for four hours before scanning. Bowel motility was reduced by intravenous administration of 0.3mg/kg (maximum 20 mg) of spasmolytic (Buscopan, Boehringer Ingelheim, Germany). Supine images were acquired on a 1.5T Siemens Avanto (Erlangen, Germany) magnet with the manufacturer's body and spine array coils. Axial and coronal Short Tau Inversion Recovery Half Fourier Acquisition Single Shot Turbo Spin Echo (STIR-HASTE) images of the neck, chest, abdomen and pelvis were produced (Axial/Coronal - FOV variable, slices 19/27, stacks 6-8/1, TR 800 ms, TE 60 ms, TI 130 ms, matrix 256 x 256, slice thickness 7 mm, interslice gap 0.7 mm, averages 2, echo train 256, iPAT 2). PET/CT images were acquired using a GE Discovery LS FDG-PET/CT in-line system (General Electric Healthcare, Michigan, USA). Scans were performed using the standard clinical protocol. PET images were reconstructed using CT for attenuation correction. Combined transaxial emission images and CT were reconstructed to a 128 x 128 image resolution (5 mm slice thickness). Anonymized whole body STIR-HASTE images were evaluated by two radiologists in consensus unaware of the PET/CT. For MR staging a nodal size threshold of > 1 cm short axis was used to determine disease positivity. To aid later comparison with PET/CT, the body was divided into 11 nodal (cervical, supraclavicular, infracervical, mediastinal, axillary, splenic hilum, hepatic hilum, retroperitoneal, mesenteric, iliac and inguinal) and 11 extra-nodal (lung, pleura, pericardium, skeletal, chest wall, liver, spleen, kidney, stomach, pancreas and bowel) areas per patient. The PET/CT images were evaluated in consensus by two nuclear medicine physicians, unaware of the MRI, and nodes deemed positive if the short axis diameter on CT > 1 cm and/or if there was focal FDG uptake above the surrounding background [6] or specific uptake value ( $SUV_{max}$ ) > 2.5 [7]. Discrepant sites were jointly evaluated by an independent panel (a radiologist [10 years MR experience] and a nuclear medicine (NM) physician [10 years NM experience]) to exclude perceptual errors. Unweighted Kappa analysis was used to test association between MR and PET/CT nodal and extra-nodal staging. Furthermore, region of interest (ROI) analysis was performed for each individual node/mass on STIR-HASTE images and average node/mass signal intensity / cerebrospinal fluid (CSF) signal intensity ratios determined and correlated with PET/CT assessed involvement at each ROI for MR positive (> 1 cm) and MR negative (< 1 cm) nodal groups. Difference in node / CSF signal intensity ratio between MR and PET/CT positive and negative groups were evaluated.

**Results:** A total of 231 nodal regions were assessed with 76 positive sites identified on PET/CT independent of the MRI. Expert unblinded review revealed two PET/CT perceptual false positive errors making a final total of 74 positive PET/CT nodal regions. Of the 231 extra-nodal sites evaluated only 9 were found to be positive on initial PET/CT assessment, however this number increased to 16 following independent unblinded review. There was very good agreement between MRI and FDG/PET for nodal (Kappa 0.96,  $p<0.0001$ ) and extra-nodal (Kappa 0.86,  $p<0.0001$ ) disease assessment. Node/CSF signal intensity ratios were evaluated at 253 nodes/masses. 201 were positive by both PET/CT and MR (size criteria) and 50 negative by both techniques. The remaining 2 nodes positive on PET were not present on the MR study. Percentage node / CSF signal intensity ratio of MR-PET/CT positive and negative groups are illustrated (see figure - error bars = 95% confidence intervals).



**Conclusion:** Our pilot data suggests that initial staging of lymphoma using WB-STIR-HASTE MRI in the pediatric and adolescent population is possible and that combined use of MRI with PET/CT may improve accuracy for detecting extra-nodal disease extension. Furthermore, node / CSF STIR-HASTE signal intensity ratios differences between normal and abnormal nodes is promising and may prove a useful additional parameter for the 'functional' evaluation of MR size negative (subcentimetre) nodes.

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