Correlation between lymph node apparent diffusion coefficient and positron emission tomography standardised uptake value in paediatric patients with lymphoma

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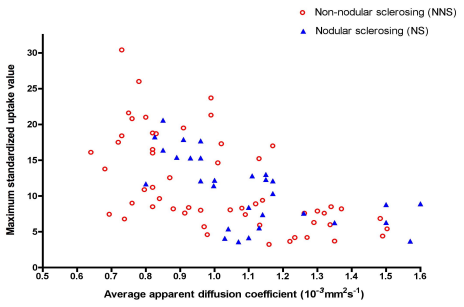
Aim: MRI average apparent diffusion coefficient (ADC_{av}) and positron emission tomography (PET) maximum standardised uptake value (SUV_{max}) have been related to cellular density and metabolic activity respectively. This study investigates the relationship between ADC_{av} and SUV_{max} measured in lymph nodes in paediatric patients with known lymphoma.

Introduction: Lymphoma staging has traditionally been based upon anatomical imaging with contrast enhanced computed tomography using size criteria to distinguish between involved and uninvolved nodal masses. CT has a reported sensitivity and specificity for identification for diseased nodal sites of 87.5% and 85.6% [1]. 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 ^{18}F-2-deoxy-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]. MRI may provide a safer non-ionizing alternative imaging modality for the anatomical assessment of lymphoma and has provided encouraging results in adults [6]. However, tissue often remains at the site of disease following chemo/radiotherapy and cannot be categorised as residual disease based on size alone. In these cases reassessment with PET is crucial, with an increased FDG uptake suggesting active disease and initiating a further course of treatment. Recently, diffusion weighted imaging has been proposed as a potential method of identifying lymphomatous nodes based on qualitative and quantitative assessment of diffusion weighted images [7]. ADC of lymphomatous nodes is reported to be significantly restricted [8] and has been related to cellular density [9]. In theory, cellular density should be related to metabolic activity and as such ADC values could provide a potential surrogate measure of 'functional' activity. However, to our knowledge there are no studies to date investigating the relationship between ADC with PET metabolic activity (SUV_{max}). This study aims to evaluate this relationship as a basis for validating the utility of diffusion weighted MR for 'functional' disease assessment.

Method: Local ethics committee permission was obtained for the study. Nineteen consecutive patients (11 male) were recruited. Participants were aged between 8 and 17 years, mean age 15 years. All patients had histologically proven lymphoma (17 Hodgkin [8 nodular sclerosis subtype], 2 Non Hodgkin's) and were previously well. MRI and PET/CT were performed within 72 hours prior to commencement of chemotherapy. Images were acquired in the supine position using 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 (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) were used to localize disease by two radiologists in consensus. The region (9.2 cm cranio-caudal dimension) containing the greatest number of enlarged (> 1 cm short axis) lymph nodes was selected for diffusion imaging. Diffusion weighted images were acquired in the axial plane using a combined Short Tau Inversion Recovery - Echo Planar Imaging (STIR-EPI) technique with diffusion gradients applied in 3 orthogonal directions at each b (0, 300 and 500) value **(**FOV 280 mm, slices 21, slice thickness 4 mm, interslice gap 0.4 mm, TR 6000 ms, TE 77 ms, TI 180 ms, matrix 128 x 100, averages 4, iPAT 2, total acquisition time 188 s). Trace diffusion weighted images and ADC maps were generated from a Siemens Avanto workstation (Erlangen, Germany). 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). Matched regions of interest (ROIs) were placed on the middle slice of individual nodes / masses on ADC maps and corresponding PET images and ADC_{av} and SUV_{max} at each site recorded. Correlation between ADC_{av} and SUV_{max} values for all lymph nodes / masses was performed using Spearman correlation statistics. Nodular sclerosis disease was assessed separately as it has a distinct cellular structure [10].



Results: Between 1 and 11 (median 4) MRI - PET/CT matched nodes / masses were identified per patient. A total of ninety lymph nodes / masses were assessed (55 non-nodular sclerosing (NNS), 35 nodular sclerosing (NS)). SUV_{max} and ADC_{av} ranged from 3.23 to 30.4 (mean 11.0) and 0.64×10^{-3} to 1.50×10^{-3} (mean 1.01×10^{-3} mm^2s^{-1}) respectively for NNS; and 3.70 to 20.6 (mean 11.2) and 0.83×10^{-3} to 2.30×10^{-3} (mean 1.26×10^{-3} mm^2s^{-1}) for NS respectively. There was a significant negative correlation between ADC_{av} and SUV_{max} for individual subtypes (NNS Spearman's $r = -0.61$, $p < 0.0001$; NS Spearman's $r = -0.62$ $p < 0.0001$) and a significant difference between the mean ADC of NNS and NS subtypes (t-test, $p<0.01$).

Conclusion: The NS subtype has a higher ADC_{av} than NNS. The negative correlation between ADC_{av} and SUV_{max} supports a relationship between cellular density and metabolic activity providing a basis for the potential utility of ADC_{av} values for post treatment disease activity assessment.

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