Nodal volumetric histographic ADC changes associated with successful chemotherapy of adolescent and childhood lymphoma

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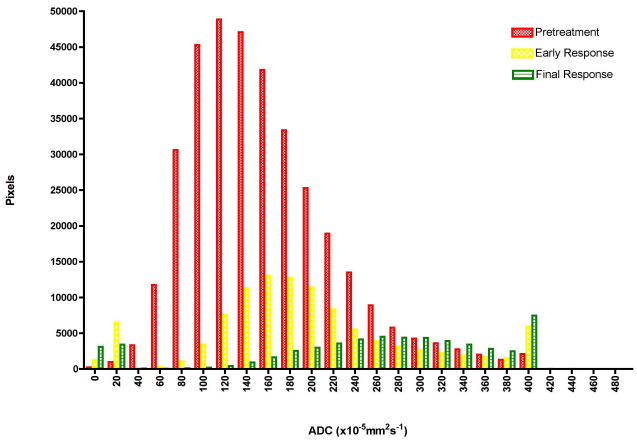
Aim: To investigate nodal volumetric histographic ADC changes associated with successful response to first line chemotherapy of adolescent and childhood lymphoma.

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-2-fuoro-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 [7] and cannot simply identified 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. ADC of lymphomatous nodes is reported to be significantly restricted [8] and has been related to cellular density [9]. However there is little data on whether and how ADC changes following treatment of disease.

Method: Local ethics committee permission was obtained for the study. Eleven patients (6 male) were retrospectively selected from those treated for lymphoma (9 Hodgkin, 2 Non Hodgkin's). Participants were aged between 12 and 18 years, mean age 15.6 years. All patients had undergone initial MRI upon diagnosis and within 72 hours prior to commencement of chemotherapy. Images had been 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). All patients then received two cycles of vincristine, etoposide, prednisolone and doxorubicin (OEPA) as per usual clinical practice at our institution and MRI was re-performed at 2 weeks and 6 months post chemotherapy for early and final response assessment respectively. For each successive MRI study the region of the body covered by diffusion weighted imaging was matched to the pre-treatment MR study. Lymph nodes were identified using b500 diffusion weighted images and STIR-HASTE images, Regions of interest (ROI) were selected on the pre-treatment b500 MR images to encompass all nodal tissue within the imaged volume using Jim 5.0 software's inbuilt ROI contour analysis feature. The ROIs were exported to the corresponding ADC map and ADC values for each individual nodal pixel within the imaged volume obtained. The process was repeated for the early treatment response and final treatment response studies. Nodal volumetric median ADC was computed at each time point. A population histographic ADC response to treatment was plotted (see graph) for the 11 patients. Kruskal-Wallis statistic followed by Dunn's multiple comparison tests was used to assess the change of median ADC between successive MR studies for the population histogram.

Results: Per patient pre-treatment, early response and final response median ADC values ranged between 0.9 - 2.6 x10^{-3} mm^2s^{-1}, 1.4 - 3.5 x 10^{-3} mm^2s^{-1} and 1.9 - 3.2 x10^{-3} mm^2s^{-1} respectively. Population averaged median ADC at pre-treatment, early response and final response was 1.4, 1.8 and 2.7 x $10^{-3}mm^2s^{-1}$ respectively. Change in the population ADC histogram following treatment is illustrated below. There was a significant difference between population histogram median ADC values (Kruskal Wallis $p < 0.0001$) between pre-treatment vs. early response, pre-treatment vs. final response and early response vs. final response (Dunn's $p<0.001$).

Conclusion: Successful treatment of lymphomatous tissue induces a change in histographic ADC appearances. Median ADC values of treated tissue significantly rise following treatment. Further work will prospectively evaluate treatment response by assessment of deviation from population histographic appearances associated with treatment success.



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