Prediction of lymphoma response to chemotherapy: Evaluation of pre-treatment MR derived ADC and PET derived SUV as prognostic biomarkers

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INTRODUCTION: Predicting the response of cancers to treatment may have considerable clinical benefit. Diffusion weighted imaging (DWI) allows assessment of cellular density within a tumour [1]. Effects of chemotherapy are known to relate to cellular density [2]. Furthermore metabolic activity has also been related to cellular density [3]. The aim of this study was to explore the ability of pre-treatment quantitative DWI and 2-deoxy-2-fluoro-D-glucose (^{18}F-FDG) positron emission tomography (PET) – computed tomography (CT) for predicting treatment response following chemotherapy in paediatric and adolescent patients with lymphoma.

METHODS: Thirty-two patients (≤18 years) with histological confirmed lymphoma underwent PET-CT and contrast enhanced chest CT, which was the standard staging protocol at our institution. For the purposes of the study, patients additionally underwent MRI within 7 days of the PET-CT and prior to commencing treatment. All patients received two cycles of vincristine, etoposide, prednisolone and doxorubicin (OEPA). Early response to treatment after two cycles of OEPA (14 to 17 days after chemotherapy) was evaluated by PET-CT, contrast enhanced chest CT and repeat MRI.

MRI: MRI was performed with the patient in the supine position using a 1.5T Avanto (Siemens, Erlangen, Germany) magnet with the manufacturer's body and spine array coils. Bowel motility was reduced by intravenous administration of 0.3mg/kg of hyocine butylbromide (Buscopan, Boehringer Ingelheim, Germany) immediately prior to abdominal imaging. Imaging of the neck, chest, abdomen, and pelvis was performed using axial and coronal short inversion time inversion-recovery (STIR) Half Fourier Single Shot Turbe Spin Echo (HASTE), as previously described [4]. Diffusion weighted imaging (DWI) was performed in the axial plane using a combined STIR - Echo Planar Imaging (EPI) technique with diffusion gradients applied in 3 orthogonal directions at each 'b' (0, 300 and 500 s/mm^2) value.

Image analysis was performed using Jim 5.0 (Xinapse Systems, Leicester, England) software. Two radiologists in consensus on STIR-HASTE images visually confirmed the anatomical site (limited in cranio-caudal length to 10 cm) of greatest volume of nodal tissue. All nodal tissue within the anatomical site was selected using the Jim 5.0 region of interest (ROI) toolkit on b300 images. ROI boundaries were located to precisely follow and remain inside nodal contours. Total nodal volume within the anatomical location was recorded. ROIs were transferred onto b0 and b500 datasets. Mean signal intensity for the entire volume of nodal tissue was determined for each b-value. The apparent diffusion coefficient (ADC) for the nodal tissue was determined by performing a least squares fit of b0, 300 and 500 signal intensity.

Residual nodal tissue was identified and ROIs redrawn at the same anatomical site on post-treatment b300 images using the technique as described above. Percentage residual volume of nodal tissue was calculated by comparison of total ROI volumes prior to and following treatment.

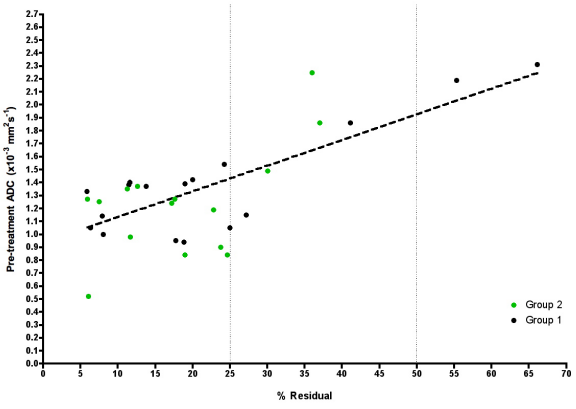
PET-CT: Data were acquired by using a dedicated combined ^{18}F-FDG PET-CT in-line system (GE Healthcare Technology, Waukesha, WI, USA). A standard PET-CT protocol was employed as previously described [4]. Combined transaxial emission images of ^{18}F-FDG PET and CT were reconstructed to a resolution of 128 x 128 and a thickness of 5 mm. PET-CT images were displayed conventionally on a GE workstation. An automated ROI was drawn around the entire nodal volume and ^{18}F-FDG uptake was expressed as the maximum standardized uptake value (SUV_{max}). Automation was performed using a standard ROI analysis tool provided with the scanner, using a thresholding method. A threshold of 42% of the maximum value was set as the default setting in keeping with the manufacturer's recommendation and the literature [5].

Group 1 (investigation): For the initial seventeen patients studied (Group 1), ADC and SUV_{max} measurements were correlated using linear regression analysis with percentage residual tissue volume following treatment.

Group 2 (Validation): For the subsequent fifteen patients (Group 2), the utility of correlated pre-treatment quantitative parameters to predict disease response (as determined by % residual nodal volume) was assessed.

RESULTS: There was a strong positive linear correlation between pre-treatment ADC and percentage residual tissue volume following 2 cycles of chemotherapy (Group 1 R^2 = 0.70). Using a pre-treatment ADC cut-off of 1.43 x10^{-3} mm^{2}s^{-1} MRI had a 100% sensitivity and specificity for differentiating complete (≤25% residual volume) from incomplete response (>25 residual volume) to chemotherapy within the validation group.

There was no significant correlation between SUV_{max} and percentage residual nodal volume following therapy (Group 1 R^2 = 0.1).



CONCLUSION: Pre-treatment ADC correlates positively with residual tissue volume following 2 cycles of OEPA in paediatric and adolescent lymphoma. Our results indicate that assessment of pre-treatment ADC maybe useful in predicting chemotherapy response.

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