Do diffusion changes occur prior to size changes in breast tumours undergoing neoadjuvant chemotherapy?

M. D. Pickles[1], P. Gibbs[1], M. Lowry[1], L. W. Turnbull[1]

[1]Centre for Magnetic Resonance Investigations, University of Hull, Hull, East Yorkshire, United Kingdom

Introduction. Traditionally tumour response has been assessed via tumour size measurements during the course of a treatment. However, changes in this morphologically based measure occur relatively late in the course of a treatment. To enable an earlier assessment of treatment, to facilitate early cessation and cost savings, alternative biomarkers are currently being evaluated. Diffusion weighted imaging (DWI) has been identified by pre-clinical studies to be a likely alternative to tumour size measurements. In these early animal and cell studies alterations in the apparent diffusion coefficient (ADC) were noted prior to changes in tumour size measurements. However, currently only a few studies have translated this work into human studies. This work evaluates tumour diffusion and size changes in patients with breast cancer undergoing chemotherapy.

Methods. 12 patients were scanned during their treatment of neoadjuvant chemotherapy. Patients were scanned either on a 3.0T or 1.5T scanner (GE Healthcare, Milwaukee, WI, USA) in combination with dedicated bilateral breast coils. A change in field strength was necessitated due to limited availability of a 3.0T breast coil. Since ADC values are not field strength dependant this will not have affected the results. However, increased field strength may have affected the accuracy, consequently no patient with mixed field strength examinations was included. Images of both breasts were acquired axially with a single shot dual spin echo EPI sequence with the following parameters: TR 4000ms, fractional TE 74ms (3.0T) or 98ms (1.5T), FOV 340 x 340mm, slice 5mm, gap 1mm, 10 averages, and *b*-values 0 and 700s/mm^2 applied in all three orthogonal directions, see figure I. Following the current guidelines for assessing treatment response as proposed by RECIST lesion longest diameters were calculated at each time-point. To allow comparisons of ADC and longest diameter during the course of treatment, individual patient measurements (ADC or longest diameter) were normalised to their pre-treatment value.

Results. Data form 12 patients is presented for the pre-treatment and 1st cycle time-point, however of the 12 patients currently under investigation 3 have not progressed to the 2nd cycle time-point as yet. Consequently data from 9 patients is presented for this cycle time-point. Figure II graphically illustrates the mean and standard deviation at each time point for both the normalised ADC and the normalised longest diameter measurements. It is clear from figure II that at the 1st cycle time point the mean normalised longest diameter remained fairly static. However, ADC values had already increased at the 1st cycle time point. Additional paired sample t-tests revealed that the difference between the pre and 1st cycle longest diameter measurements were not significant ($p = 0.834$) and demonstrated a significant difference between the pre and 2nd cycle time points ($p = 0.043$). In contrast, for the ADC results significant differences were noted between the pre and 1st cycle ($p = 0.001$) time points and the pre and 2nd cycle time points ($p = 0.004$).

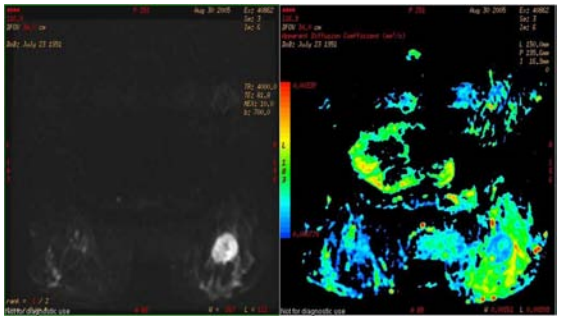

Figure I. b=700s/mm^2 and ADC map of breast lesion

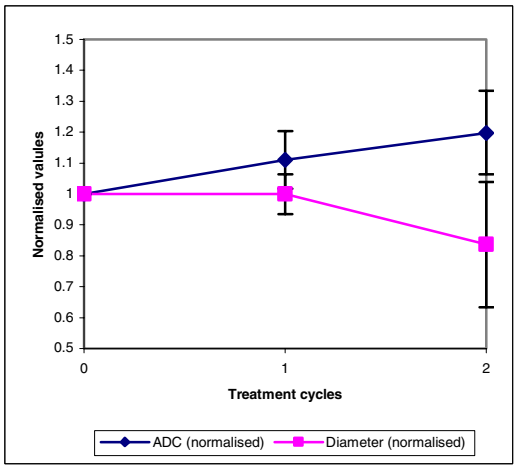

Figure II. Normalised (mean ±SD) tumour ADC and diameter during treatment

Conclusion. The observed increase in ADC prior to a decrease in tumour size measurements, is in keeping with the results of pre-clinical animal and cell studies. Consequently this work supports the hypothesis that, via an increase in water mobility following treatment induced cell damage, ADC can provide an earlier biomarker of response than tumour size measurements. It is believed that the resulting increase in ADC values is as a consequence of cellular damage leading to necrosis.