The role of apparent spin-spin relaxation in assessing response to treatment in breast cancer patients undergoing neoadjuvant chemotherapy

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

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

Introduction. Traditionally response to treatment has been assessed via tumour size measurements. Unfortunately assessment of response via this approach is a relatively late event. Earlier methods of response assessment are urgently required, as these methods will enable cessation of ineffective treatments thereby minimising unnecessary toxicity and cost of a failing treatment. This work evaluates the possible role of the apparent spin-spin relaxation rate (R2*) has in response assessment. R2* is believed to reflect the tissue oxygenation levels due to the endogenous BOLD contrast. Since hypoxic tumours are more resistant to treatment (radiotherapy and chemotherapy) and that following successful tumour cell kill a vascular shutdown is anticipated, resulting in reduced oxygen delivery. Consequently it was believed R2* could predict treatment response at an earlier time-point than tumour volume.

Methods. 33 biopsy proven breast cancer patients receiving neoadjuvant chemotherapy were scanned prior to and post 1st 2nd and final treatment cycles. Response classification was based upon eventual tumour volume reduction in line with RECIST. To calculate R2* values gradient echo images were acquired with four different TE values (9, 18, 27 and 36ms), all other parameters were as follows: TR 220ms, flip 40°, 20x20cm FOV, 4mm slice, 0.4mm gap, 256x256 matrix and 4 averages. The resulting gradient of a plot of the log of the signal intensity against the TE gave the R2* value. To calculate tumour R2* values pixel-by-pixel R2* maps were generated, fig. I. ROI's were then drawn around the tumour, individual pixel values within the tumour ROI were averaged. Since R2*=R2+R2' a change in R2 could account for an altered R2* therefore R2 was calculated in a similar manner to R2* utilising a fast spin echo (TE 30, 60, 90, and 120ms TR 4000ms ETL 12).

Results. No significant differences ($p > 0.05$) were noted prior to or post 1st cycle between response groups. However, at the 2nd cycle time-point significant differences were noted between response groups for tumour volume ($p = 0.002$), R2* ($p = 0.009$) and R2' ($p = 0.014$). ROC analysis revealed the diagnostic accuracy for percentage change (pre to 2nd cycle) in tumour volume and R2* demonstrated similar figures (volume, AUC 0.905, 95% CI 0.796 – 1.000, R2* AUC 0.855, 95% CI 0.725 – 0.985). Indeed the Hanley McNeil test revealed no significant difference between the AUC of either parameter $z = 0.59$ $p = 0.56$. Percentage change in R2* (mean 41.33%) was greater than R2 (mean 11.27%) for responders ($p = 0.004$), whilst for non responders no significant difference ($p = 0.282$) was noted R2* (mean -5.03%) R2 (mean -0.74).

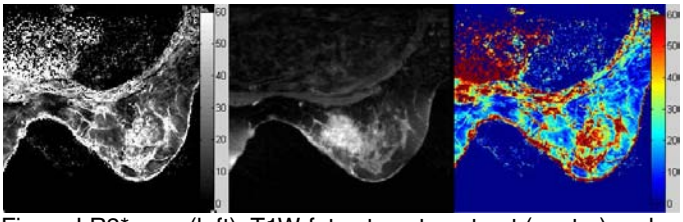

Figure I R2* map (left), T1W fat sat post contrast (centre) and R2* map colour (right)

Parameter	Response	Pre	2nd Cycle
		Mean ± SD	Mean ± SD
R2* (s^{-1})	Responder	27.21 ±6.66	36.09 ±7.42
	Non responder	30.16 ±6.80	28.49 ±6.48
R2 (s^{-1})	Responder	12.21 ±1.52	13.50 ±1.67
	Non responder	12.70 ±1.53	12.59 ±1.50
R2' (s^{-1})	Responder	15.00 ±5.92	22.59 ±7.28
	Non responder	17.46 ±5.97	15.90 ±5.47

Table I R2*, R2 and R2' pre and post 2nd cycle

Conclusion. These results demonstrated that for the cohort of patients studied that R2* values prior to and post 1st cycle did not help in predicting response to neoadjuvant chemotherapy. These results indicate that there was no difference in the tumours tissue oxygenation levels between the response groups prior to treatment. Following the 2nd cycle time-point significant differences were noted between the response groups. Responders demonstrated elevated R2* values in keeping with reduced oxygen delivery following a treatment induced vascular shutdown. Whilst R2* values for non-responders remained fairly static. While a change in R2 was apparent for responders it seems unlikely that this change fully accounted for the change in R2*. It is further noted that the percentage change (pre to 2nd cycle) in R2* performed as well as the percentage change in tumour volume in predicting response, however R2* values did not indicate response prior to tumour volume.