Changes in lesion T2 and volume predict response of malignant breast lesions to neoadjuvant chemotherapy

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Introduction

Neoadjuvant chemotherapy is generally an effective way of shrinking locally advanced malignant breast lesions before surgery. However, some patients do not respond to the treatment, and require further chemo- or radiotherapy after the standard course of drugs. The ability to predict non-response would thus enable an early change of treatment and prevent unnecessary toxicity. Measurements of tumour size were found not to give a clear indication of response until after the 3rd treatment cycle.[1] A recent study found that a combination of the absolute changes in lesion water T_2 and extracellular-extravascular tissue volume fraction after the 2nd cycle accurately predicted ultimate response.[2] That study used a spectroscopic method to measure lesion T_2, which is generally more complex and gives a much lower spatial resolution than imaging. Furthermore, it did not consider earlier changes in these parameters, so it is not known if predictions could be made before the 2nd cycle. Therefore we report here an investigation into both imaging and spectroscopic methods of measuring the water T_2 of malignant breast lesions, and their utility in predicting response after the 1st and 2nd cycles of treatment, both alone and in combination with lesion volumes.

Methods

Examinations were performed on 37 patients with invasive ductal carcinoma enrolled in a study monitoring lesion response to 4 or 6 cycles of neoadjuvant chemotherapy, using a 1.5T scanner (GE Signa Infinity) and a bilateral breast coil (Machnet). Patients were scanned before treatment, 1-8 days after their 1st cycle, and 2-3 weeks after their 2nd and last cycles. All data were collected after contrast administration. Lesion volume measurements were made by an experienced radiologist or radiographer by tracing the lesion boundary on the post-contrast fat-suppressed images using image analysis software developed in-house. Treatment response was defined as a reduction in the tumour volume of at least 65% after the last cycle of chemotherapy.[3] Two methods of obtaining lesion T_2 were used. Imaging (all patients): 4 axial slices through the lesion were acquired with a fast double spin echo sequence (TR/TE = 1000/30,60,90,120ms). T_2 maps were generated from the images, and ROIs drawn in the lesion and sampled to produce the lesion T_2. Spectroscopy (27 patients): single voxel ^{1}H MR spectra were acquired from the lesion of each patient (voxel size 0.5-11.6cm^3) using PROBE-P TE-averaging (TR 1.5s, initial TE 35ms, 64 steps of 2.5ms, 4 water-suppressed and 2 unsuppressed acquisitions per TE). Spectral processing included 2.5Hz Gaussian line broadening, zero-filling to 4K points, Fourier transformation, and phasing. Monoexponential T_2 fitting of the unsuppressed water signal was then performed in SAGE (GE Healthcare) to obtain the lesion water T_2. The changes in volume (V) and T_2 between the 2nd cycle time point and the 1st cycle and pre-treatment time points were analysed by taking the ratios V_2/V_1, V_2/V_0, $T_{2,2}/T_{2,1}$, $T_{2,2}/T_{2,0}$, as well as the product of these ratios, i.e. $(T_2\times V)_1 = T_{2,2}/T_{2,1}\times V_2/V_1$ and $(T_2\times V)_0 = T_{2,2}/T_{2,0}\times V_2/V_0$, and using ROC curves to see which gave the best result.

Results and Discussion

The mean±SD pre-treatment lesion water T_2 for imaging and spectroscopic methods were 75±15ms and 77±17ms respectively. A paired sample t-test on 106 T_2 data where both methods were carried out in the same examination showed no significant difference between imaging and spectroscopic values ($p>0.1$). As for early prediction of treatment response, an independent sample t-test on the baseline T_2 showed no significant difference between responders and non-responders, while a Spearman's rank correlation test showed no correlation between normalised final lesion volume and normalised lesion T_2 at the 1st cycle time point (all $p>0.1$). Table 1 shows the results of predicting response after the 2nd cycle. Firstly, it is clear that changes between the pre-treatment and 2nd cycle time points are more predictive of response than those between the 1st and 2nd cycle time points. Secondly, using a combination of lesion volume and T_2 is better at predicting response than either parameter alone. The best parameter appears to be imaging $(T_2\times V)_0$, which has a similar PPV but much improved NPV compared to V_2/V_0. Figure 1 shows the relationship between the $(T_2\times V)_0$ cut-offs and the data, and illustrates how this parameter could be useful in helping oncologists decide whether to change a patient's treatment halfway through. The fact that the imaging method of obtaining the parameter works better than the spectroscopic method also means that this could be easily implemented in the clinical setting, as not many clinical scanners have the required software to acquire and process spectra.

	Param.	AUC	Cut-off	PPV	NPV	χ^2 p
	V_2/V_1	0.86	0.80	86.4%	72.7%	<0.01
	V_2/V_0	0.91	0.64	95.0%	73.3%	<0.001
Imaging	$T_{2,2}/T_{2,1}$	0.66	0.96	80.0%	53.8%	>0.05
Imaging	$T_{2,2}/T_{2,0}$	0.75	0.97	89.5%	62.5%	<0.025
Imaging	$(T_2\times V)_1$	0.86	0.68	89.5%	64.3%	<0.025
Imaging	$(T_2\times V)_0$	0.94	0.70	95.5%	84.6%	<0.001
Spectro	$T_{2,2}/T_{2,1}$	0.83	0.94	81.8%	66.7%	>0.05
Spectro	$T_{2,2}/T_{2,0}$	0.76	0.89	88.9%	62.5%	>0.05
Spectro	$(T_2\times V)_1$	0.88	0.79	85.7%	88.9%	<0.01
Spectro	$(T_2\times V)_0$	0.93	0.60	91.7%	76.9%	<0.01

Table 1: Results of using lesion water T_2 and volume to predict response after the 2nd cycle. The cut-off values for each parameter were determined from the respective ROC curves, and lesions with values above that cut-off were considered non-responsive. A χ^2 test was also performed for each parameter using the cut-off obtained.

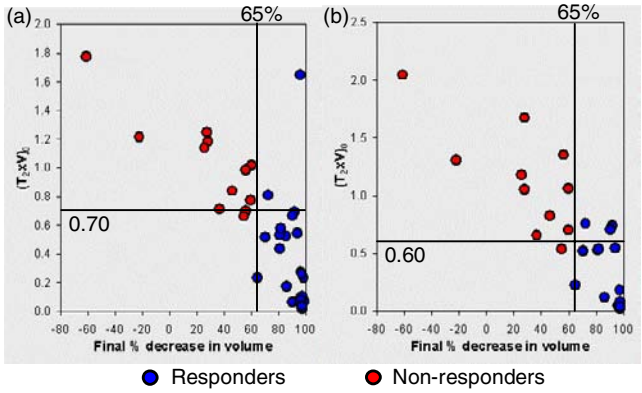

Figure 1: Plot of (a) imaging and (b) spectroscopic $(T_2\times V)_0$ against final percentage decrease in volume, showing the relationship between the two cut-off $(T_2\times V)_0$ values and the data.

Conclusion

For locally advanced malignant breast lesions, the ratio of the product of the lesion T_2 and volume after the 2nd cycle of neoadjuvant chemotherapy to those pre-treatment is a good predictor of ultimate lesion response.

References

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