# Measuring water T2 and water:fat signal ratios with MR spectroscopy (TEA-PRESS) and chemical shift imaging (IDEAL): preliminary results in phantoms and breast cancer chemotherapy patients

**D. J. Manton[1], G. P. Liney[1], P. Gibbs[1], M. Lowry[1], M. D. Pickles[1], and L. W. Turnbull[1]**

[1]YCR Centre for MR Investigations, Hull, East Yorkshire, United Kingdom

**Introduction:** Breast cancer remains a serious, prevalent disease world-wide, with 44,091 and 178,480 cases reported annually in the UK [1] and US [2] alone, and its incidence is also known to be increasing. Approximately 5% of women diagnosed with breast cancer, primarily those with large tumours, will be offered neoadjuvant chemotherapy (NAC) as a first-line treatment in order to improve the surgical outcome [3, 4]. Unfortunately NAC can be unsuccessful in between 6% [5] and 42% [6] of cases necessitating further chemotherapy or early surgery. In these poor responders, the ineffective therapy will decrease quality of life, increase costs, and may adversely affect disease free survival by delaying initiation of effective treatment. An accurate indication of treatment success is thus clinically important and this is currently provided by change in tumour size as determined by palpation and magnetic resonance imaging (MRI) at around the half-way point of NAC. Change in tumour size may be a relatively late manifestation of response, however [7-11], and a sensitive indicator of early tumour response would permit individual treatment regimes to be adjusted more rapidly, thus sparing patients unnecessary risks associated with prolonged use of potentially toxic, non-efficacious drugs.

MRI and magnetic resonance spectroscopy (MRS) have been shown to provide non-invasive, quantitative measurements which might indicate early response to chemotherapy in human breast cancer or in animal studies involving human breast cancer cell lines. These measurements include a decrease in the water:fat signal ratio [12-13b] and water $T_2$ values [13a-14] derived from proton MRS, an increase in apparent diffusion coefficient (ADC) values for water derived from diffusion-weighted MRI [11], and decreases in neovascular parameters related to blood flow and permeability surface area product derived from dynamic contrast-enhanced MRI [8, 10]. A study has therefore been set up to measure water:fat signal ratio (WFSR) and water $T_2$ values in NAC patients with spectroscopy, the proven technique, and a new, asymmetric three-point chemical shift MRI sequence (IDEAL) to determine whether the greatly increased spatial resolution of MRI is clinically useful.

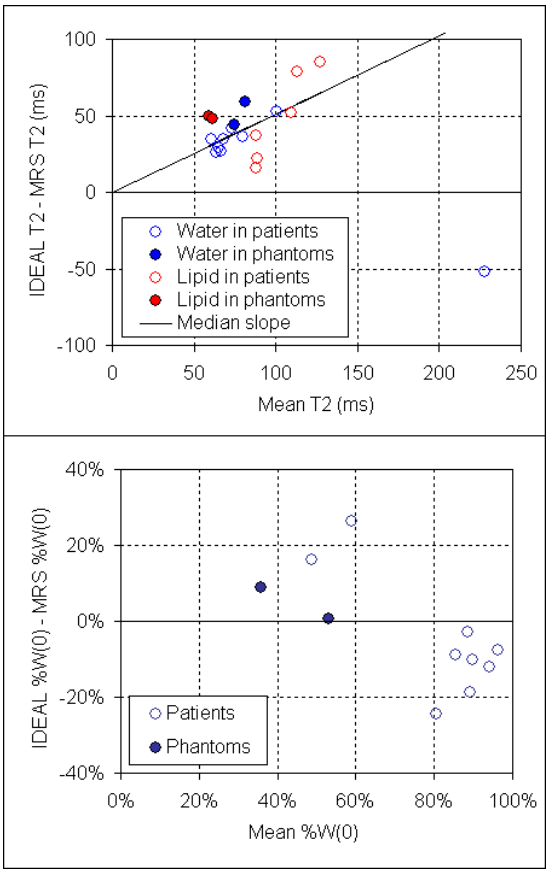
**Methods:** Water and fat $T_2$ values, and water signal fraction (%W = water signal / [ water signal + fat signal ] = 1 / [ 1 + 1 / WFSR ]) have been measured prior to NAC in nine breast tumours. Data were acquired using a 3.0 Tesla GE Signa HDx whole-body MRI scanner and a dedicated, eight channel, phased array breast coil (GE Healthcare, Milwaukee, WI, USA). Similar data were also acquired using a quadrature head coil and two homogenous oil-in-water emulsion phantoms (made using deionised and demineralised water, soya oil, 15 mmol of sodium dodecyl sulphate, an anionic surfactant / emulsifying agent, and 5 g / litre of carrageenan) of known water content (33% and 50%). MRS was carried out using the TEA-PRESS multi-echo sequence (4 s TR, 16 TEs ranging from 30 to 150 ms, 2 excitations per TE, separate water and lipid acquisition frames for optimal chemical-shift induced voxel displacements, total acquisition time *c.* 6', *in vivo* voxel volumes ranging from 0.4 to 10.1 ml) and chemical shift MRI was carried out using the IDEAL sequence (12 axial slices; 4s TR; four separate acquisitions with TEs of 30, 60, 100 and 150 ms; 20 kHz receiver band-width; total acquisition time *c.* 15'; 5 mm slices, 1 mm skip, 36 cm FOV, 320 x 256 matrix zero-filled to $512^2$; 0.00247 ml voxel volume).

Spectroscopic data were analysed using GE's SAGE/IDL package (SNR-weighted coil element FID combination, 3 Hz Gaussian apodisation, zero-filling from 2048 to 4096 time-domain points, FFT and DC baseline correction) and water and dominant lipid (1.3 p.p.m.) peaks were quantified by means of peak amplitudes (heights). $T_2$s and $T_2$-corrected amplitudes ($a_0$s) were obtained from the amplitude-TE curves within SAGE/IDL. IDEAL data were analysed using in-house software developed using MATLAB (The MathWorks, Inc., Natick, MA, USA). All %W values were calculated with $T_2$ correction (i.e. at zero TE, using $a_0$s; $\%W_0$).

**Results:** As hoped, the greatly increased spatial resolution of IDEAL compared to MRS permitted lesion heterogeneity to be determined.

Lipid content was too low to permit accurate lipid $T_2$ determination in 3 patients, therefore 19 $T_2$ data were available for analysis (9 patient water, 2 phantom water, 6 patient lipid & 2 phantom lipid). IDEAL yielded $T_2$ values which were systematically elevated (for 18/19 data) compared to those obtained by TEA-PRESS (the assumed gold standard), as shown by the Bland-Altman limits of agreement (difference *versus* mean) plot on the right (top). A line on the plot representing the median gradient appears to fit the data quite well which suggests that IDEAL $T_2$ data could be corrected using a simple calibration formula (corrected $T_2$ = measured $T_2 \times 0.59$).

Eleven $\%W_0$ data were available and IDEAL appeared to overestimate low values and underestimate high values, as shown by the limits of agreement plot on the right (bottom).




**Conclusions:** To the authors' knowledge, this abstract represents the first reported use of IDEAL to quantify water $T_2$ and water:fat signal ratio in breast cancer patients. Although the increased spatial resolution of IDEAL has permitted lesion heterogeneity to be determined, the clinical benefit of this will only become apparent after a number of women have completed NAC.

The systematic overestimation of $T_2$ by IDEAL presents a potential stumbling block to successful clinical application, although it appears that a simple calibration correction is possible. Also, it is the change in $T_2$ which is clinically relevant and IDEAL would still be able to quantify $T_2$ change fairly reliably despite the presence of grave systematic errors. Correction for the more complex systematic errors in $\%W_0$ would be more problematical, however. Investigations are underway to determine the underlying reasons for the systematic errors demonstrated by IDEAL, which should permit a more thorough, theoretical correction of the data (rather than an empirical one).

**[1]** Cancer Research UK. Cancer stats reports. (2006). **[2]** Ries LAG, *et al.* (eds). SEER Cancer Statistics Review, 1975-2004, National Cancer Institute. Bethesda, MD (2007). **[3]** Swain SM, *et al.* Cancer Research 47, 3889-3894 (1987). **[4]** Hortobagyi GN, *et al.* Cancer 62, 2507-2516 (1988). **[5]** Denis F, *et al.* EJSO 30, 1069-1076 (2004). **[6]** Londero V, *et al.* Eur Radiology 14, 1371-1379 (2004). **[7]** Padhani AR. Eur J Cancer 38, 2116-2127 (2002). **[8]** Hayes C, *et al.* NMR in Biomedicine 15, 154-163 (2002). **[9]** Chenevert TL, *et al.* Molecular Imaging 1, 336-343 (2002). **[10]** Wasser K, *et al.* Eur Radiology 13, 80-87 (2003). **[11]** Pickles MD, *et al.* Magnetic Resonance Imaging 24, 843-847 (2006). **[12]** Jagannathan NR, *et al.* NMR in Biomedicine 11, 414-422 (1998). **[13a]** Manton DJ, *et al.* Br J Cancer 94, 427-435 (2006). **[13b]** Manton DJ, *et al.* Br J Cancer 94 1554 (2006). **[14]** Tan PC, *et al.* Magnetic Resonance Imaging 26, 26-34 (2007).