High-resolution Proton Density weighted Dixon sequences maximize precision of breast density measurements

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Introduction: Percent-water (%Water) calculation derived from high resolution Dixon fat-water separation techniques has been suggested for a volumetric measurement of breast density; an established risk factor for breast cancer [1]. Recent studies have demonstrated that Dixon %Water calculations differ significantly from percent density measurement derived from clustering algorithms [2], but have not assessed measurement reproducibility or the influence of resolution and T_1/T_2 weighting. Here, we evaluate the reproducibility of %Water measurements from a high-resolution proton-density (PD) weighted two-point Dixon sequence, and error arising at lower spatial resolution and with T_1/T_2 weighting.

Materials & Methods:

MRI Protocols: Ten female volunteers (21–50 yrs) gave their informed consent following Research Ethics Committee approval. Breast images were acquired at 1.5T (Magnetom Aera, Siemens) using the Sentinelle breast coil with Variable Coil Geometry (Invivo). Each volunteer was scanned twice, 30 mins apart, to enable an estimation of measurement reproducibility at the same point within the menstrual cycle. Prior to each scan, lateral breast coils were placed in a standard neutral position to be reconfigured by a different MRI radiographer, and the volunteer was positioned with the nipple aligned to the coil centre.

Image Acquisition: Breast examinations were performed with two high-resolution, two-point Dixon sequences with PD and T_1 weighting (TR=7.34 ms, TE=4.77/2.34 ms, voxel size=1.3×1.3×1.0 mm^3, FA=4° and 18°, respectively), and a low-resolution T_2 weighted two-point Dixon sequence (TR=500 ms, TE=12 ms, FA=180°, voxel size=0.8×0.8×7.0 mm^3) to cover an identical image volume.

Data Analysis: A further PD weighted Dixon image set was generated from the high-resolution sequence with a resolution to match that of the low resolution T_2-weighted sequence. Semi-automated breast volume segmentation was performed on the in-phase PD weighted dataset using in-house software (IDL 8.3, ITTVIS, Boulder, USA) *via* a combination of noise thresholding and erosion, and with a manual straight coronal cut at the most anterior chest wall position. This process generated two volume masks for each breast at high and low spatial resolution. To minimize T_1/T_2 weighting, the difference in fat/water signal was measured for each sequence and a subsequent correction applied; measurements were taken from a standardized 30x30 mm^2 ROI in the centre of the breast (minimising possible coil effects) in a central slice containing fat and water. Dixon %Water was calculated as [(|Water|/|Water + Fat|) x 100].

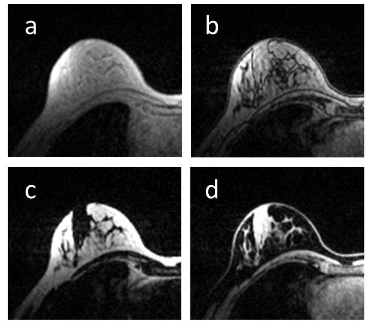

Figure 1: PD weighted Dixon breast images: (a) In-phase; (b) Out-of-phase; (c) Fat-only & (d) Water-only.

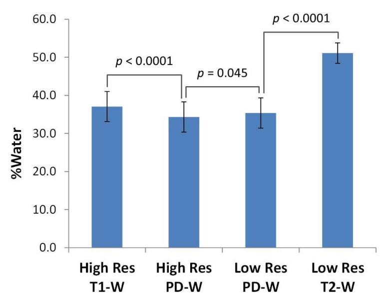

Figure 3: %Water measurements at different resolutions & T_1/T_2 weightings. Error bars represent standard error.

Table 1: Water volume and total breast volume from PD weighted Dixon data at different spatial resolutions		
Resolution	**High**	**Low**
Water Volume [cm^3]	427.9 ± 267.3	442.9 ± 275.1
Total Breast Volume [cm^3]	114.2 ± 49.5	122.9 ± 54.5

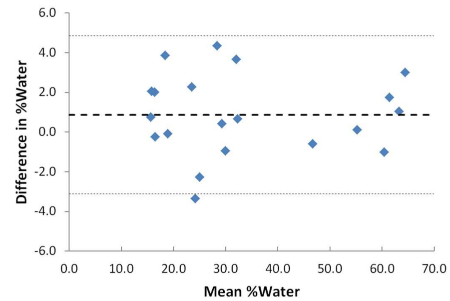

Figure 2: Bland-Altman plot for repeat high-resolution PD weighted %Water measurements. Mean difference and limits of agreement represented by central and outer dashed lines, respectively.

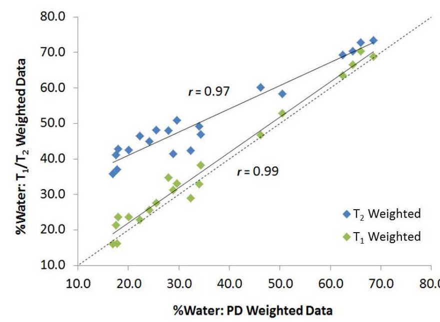

Figure 4: Correlation between low resolution %Water measurement from PD weighted data and T_1/T_2 weighted data.

Statistical Analysis: High-resolution PD weighted data were assumed to provide the most accurate calculation of %Water (*Figure 1*): measurement reproducibility was calculated using Bland-Altman statistics. Differences in coil positioning between volunteer datasets and %Water differences between left and right breasts were evaluated using the paired Student's *t*-test. Values of %Water at low spatial resolution and with T_1/T_2 weighting were compared against high-resolution PD weighted data using the Pearson product-moment correlation coefficient and the paired Student's *t*-test (two-sided α=0.05). Differences in water volume and total breast volume between high and low resolution PD weighted sequences were also assessed using the paired Student's *t*-test.

Results & Discussion: %Water measurement from PD weighted high resolution Dixon sequences was found to have a reproducibility coefficient of 4.0% with no significant difference between the two volunteer datasets (*Figure 2*). No significant difference in coil position was observed between volunteer datasets, with a mean absolute difference in coil position of 1.4 mm anterior-posterior and 1.0 mm left-right, indicating a robust radiographer protocol. The segmentation method is likely to be the largest contributor to measurement error due to differences in chest wall position between the volunteer datasets. No significant difference in %Water was measured between right and left breasts. *Figure 3* displays the differences in %Water measured at different resolutions and T_1/T_2 weightings. Low resolution PD weighted Dixon data over-estimated breast %Water by 1.0% (p=0.045) in comparison with high-resolution PD weighted data. This appeared to arise largely from significant over-estimations in total water volume of 8.7 cm^3 and in total breast volume of 15.0 cm^3 at low resolution (p=0.004 and p=0.006, respectively). Whilst both T_1 and T_2 weighted data were strongly correlated with PD weighted data (r=0.99 and 0.97, respectively) (*Figure 4*), each weighting also resulted in a mean over-estimation of breast %Water by 2.7% (p<0.0001) and 15.8% (p<0.0001), respectively. The over-estimation of %Water due to T_2 weighting was considerably increased at lower breast densities (*Figure 4*).

Conclusions: Significant differences in %Water measurement can arise at lower spatial resolutions and with the introduction of T_1 or T_2 weighting, even with correction for fat/water signal differences. The over-estimation of %Water observed with T_2 weighting is particularly significant considering the measured reproducibility coefficient of 4.0% calculated for this methodology. MRI protocols for Dixon measurement of %Water should be carefully considered in order to ensure the reliability of breast density measurement, with particular relevance to breast density studies performed in a multi-centre setting.

References: [1] Boyd NF, *et al.*; *J Natl Cancer Inst* 2010; 102:1224–1237; [2] Clendenen TV, *et al.*; *J Magn Reson Imaging* 2013; 38:474–481.

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