# Quantitative contrast media concentration and proton density images

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**Introduction:** Development of quantitative, reproducible methods for dynamic contrast enhanced MRI (DCEMRI) would greatly improve diagnostic accuracy. Here we demonstrate the use of phantoms to increase the accuracy of contrast media concentration measurements. Phantoms were inserted in a breast coil to calibrate and standardize breast MRI measurements. Signal from the phantoms was analyzed to produce images of contrast media concentration as well as MRI-detectable proton density.

**Methods:** We designed calibration phantoms, consisting of color-coded tubes filled with gadodiamide solutions (0.05, 0.1, 0.2, 0.3, 0.4, 0.5 mM, Omniscan) and 70% deuterated water, that were placed into a breast coil. 23 patients were scanned in a 16-channel bilateral breast coil at either 1.5 T or 3T (Philips Achieva 1.5T and 3T-TX) under an IRB approved protocol. We acquired a variable flip angle (VFA) gradient echo series (3D spoiled gradient echo, flip angles = 5,10,15,20°, TR/TE = 10/2.4ms), and a $T_1$-weighted dynamic series (3D turbo field echo with fat-sat) before and after a gadodiamide injection (0.1mmol/kg).
The VFA data were fit to find $T_1$ and proton density values for each voxel. Using the known $T_1$ values in the phantom we corrected the nominal flip angles and created a proton density map. Under the experimental conditions, $1/T_1$ is approximately proportional to signal intensity. This allows us to convert signal intensity to concentration of contrast media using the following[1]

$$C(t) = \frac{PD_{phantom}}{PD_{tissue}} \cdot \frac{1}{F \cdot r_1} \cdot (S_{tissue}(t) - S_{tissue}(0)) \quad \text{Eqn. 1}$$

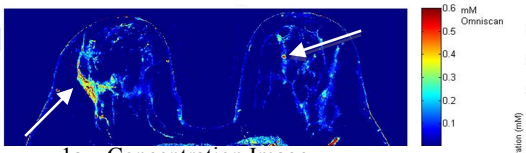
Where 'C(t)' is contrast media concentration as a function of time, 'F' is determined from the calibration phantom, using the known $T_1$ values in the phantom compartments and their measured signal; $S_{tissue}(t)$ and $S_{tissue}(0)$ are the signals at each time point and before contrast injection respectively; and '$r_1$' is the relaxivity of the contrast agent. A correction for the tissue-to-phantom proton density (PD) ratio is applied.

**Results:** Representative peak concentration values, measured for ROIs in lesions, are in Table 1. The ratio of proton density in the tissue to that of pure water was 0.20 - 0.31. Figure 1 compares a difference image with a concentration image at the time of peak enhancement. Although the two images are similar - there are significant differences in contrast - some examples are indicated by arrows. The plot of enhancement vs. concentration (Fig. 2) shows that a single value of enhancement corresponds to a range of concentrations - suggesting that signal enhancement alone does not provide an accurate measure of contrast media concentrations.

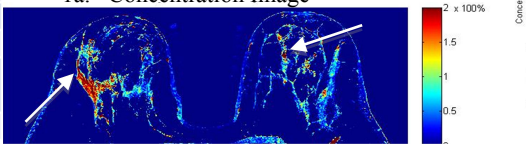
**Discussion:** The pulse sequence used for the present study is not easy to model accurately due to effects of spectrally selective fat saturation. Yet, the present approach can convert subtraction images into concentration images. Due to the use of the calibration phantoms, acquisition of quantitative images required only the addition of a VFA series to the clinical examination; adding less than 10 minutes to the scan time, which means this method can easily be implemented in a clinical environment. The MRI-detectable proton density in tissue was low and highly variable, suggesting a large, broad component of the water signal; this may be a novel source of diagnostically useful information. Peak concentration values found thus far suggest a correlation with malignancy.

**Conclusions:** The present approach can convert subtraction images into quantitative concentration images, even if a good mathematical model is not available. The concentration images have the potential to provide standardized, quantitative information that is independent of acquisition parameters, allowing for standardization across different scanners and institutions. The method additionally provides MR-detectable proton density, potentially a novel source of diagnostic information, and native $T_1$ maps.

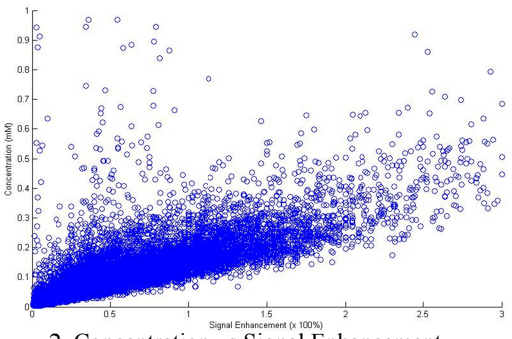
| Lesion Type | Concentration |
|---|---|
| DCIS | 0.64mM |
| Mucinous Cancer | 0.59mM |
| DCIS | 0.47mM |
| IDC | 0.45mM |
| Benign enhancing focus | 0.41mM |
| Fibroadenoma | 0.39mM |
| ADH Biopsy site enhancement | 0.32mM |
| Fibroadenoma | 0.30mM |




1a. Concentration Image




1b. Signal Enhancement Image




2. Concentration vs Signal Enhancement

[1] Medved, M., et al. JMRI, 20: 122–128, 2004