Dynamic Contrast Uptake Analysis in the Breast by Linear Combination

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Introduction: Dynamic Contrast Enhanced (DCE) breast imaging is has been used successfully to discriminate many benign and malignant breast lesions [1,5]. Studies have shown the diagnostic importance of the exchange parameter (k_{21}) in the two compartment model [1,2]. Least squares (LS) based curve fitting is often used to estimate k_{21}. However this approach suffers from poor noise characteristics and long computation times. In this work we improve on the LS curve fitting post-processing approach with a faster linear combination (LC) method.

Theory: The two compartment model characterizes contrast uptake by a lesion. The model characterizes flow from two compartments (the plasma compartment and the lesion) with the k_{21} parameter [2]. High values of the exchange parameter indicate that contrast can flow freely between the two compartments while low values of the exchange parameter indicate restricted flow of contrast to the lesion. For analysis a series of MR images are acquired at different times after contrast injection. The LC method then compiles the parameter map by linearly combining the time series on a pixel by pixel basis (as in: $\Sigma_i a_i$ Image(i)). Prior to applying the linear combination, the time series is normalized and the start of enhancement is estimated using thresholding based on a 3 σ deviation from pre-contrast images. This increases robustness to normal variations in vascular activity. The weights of the linear combination are found using regularized least squares optimization to give a near linear mapping from the k_{21} parameter to LC scores in the diagnostically important k_{21} region (k_{21} from 0.1 l/min to 10 l/min) [1]. This is used to design a family of LC filters covering a range of contrast arrival times t_0. For each subject the appropriate filter is chosen based on t_0 (Fig. 1).

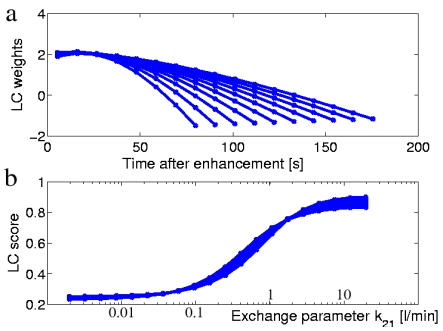

Figure 1: (a) Weights used for the linear combination (LC) method a family of filters is designed to account for variation in t_0. (b) Mapping of exchange parameter values to LC values. The mapping is approximately linear over the diagnostically important range (k_{21} from 0.1 l/min to 10 l/min) [1].

Methods: For comparison a numerical LS based fitting method was designed that fits the time series to the two compartment model using a Broyden-Fletcher-Goldfarb-Shanno (BFGS) based quasi-Newton method (`fmincon` in Matlab) [3]. Dynamic data was acquired on a 1.5T scanner (GE Medical systems) with dedicated phased array breast coil (MRI Devices inc) using a 20 interleave TR/TE = 38/12.3 ms spiral sequence with a 40 ° flip angle, 20 cm single breast FOV interpolated onto a 256 by 256 matrix. The 3D spiral sequence was repeated every 10.6 s starting 40 s before contrast injection and imaging the wash-in phase up to 2 min 40 s after contrast injection. 0.1 mmol/kg Gd-DTPA was the agent injected at 2cc/sec, and followed by a 20 cc saline flush using a power injector. A high resolution water selective 3DSSMT TR/TE = 33/9 ms, 20 cm FOV, 512 by 192 was acquired after the 3D spiral sequence. To test the diagnostic performance of the LC method, both the LC method and the LS fitting method were used to analyze dynamic enhancement of 56 lesions (30 malignant and 26 benign) that were subsequently excised. Prior to analysis the time series was integrated over a region of interest (ROI) encompassing the entire lesion yielding a single LC and LS score for each lesion. To compare the computational effort required for the k_{21} fitting method and the LC method 10 random cases out of the 56 lesions were further analyzed. Both methods were run serially on a P4 Linux machine. For each of those lesions the contrast to noise ratio (CNR) of the lesion was measured on both parameter maps using ROIs over the lesion, background and benign breast tissue. All computations were done using Matlab © by the MathWorks, MA.

Results: Shown in Fig. 2 are the LC and LS parameter maps. The lesion CNR is 2 for the LC parameter map but only 0.1 for the LS k_{21}-map. The area under the ROC curve was 0.88 (95% conf. interv. 0.84 to 0.92) for LC and 0.83 (95% conf. interv 0.79 to 0.85) for the LS fitting method. Lesion CNR was on the average 1.1 for malignant and 0.4 for benign lesions for the LC method and 0.15 for malignant and 0.15 for benign for the LS fit method. Computation time for the LC method was on the average 28.56 s (std. dev. 0.07s, min 28.47s, max 28.72s) and for the LS fit method on the average 4h (std. dev. 8m, min 3h 45m, max 4h 12m). On the average the LC method was 505 times faster than the LS k_{21} fitting method.

Discussion: There is not a statistically significant diagnostic performance difference between the LC method and the LS fit method, although there was a trend indicating slightly better diagnostic performance of the LC method (p-value < 0.1). The speed increase is highly significant. The LC method is 450 times faster (p-value < 0.001). On the average malignant lesion CNR is 7 times higher for LS, and benign lesion CNR is 3 times higher for LC. Statistically CNR measurements indicated a strong trend for higher CNR for the LC method although this was not significant (p-value < 0.05). The LC method is a fast, promising alternative to LS k_{21} based fit methods.

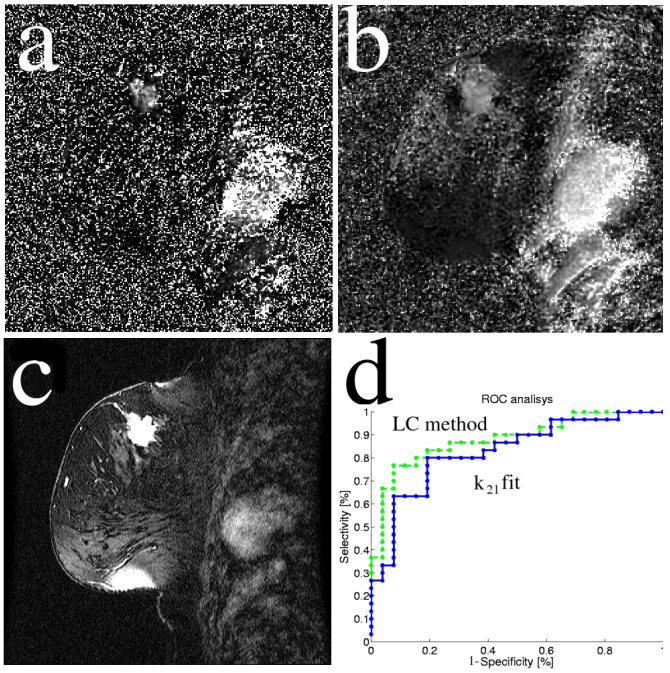

Figure 2: (a-c) Images of a patient with invasive ductal carcinoma. (a) Traditional LS k_{21} parameter map (CNR=0.1) (b) LC parameter map (CNR=2) (c) high resolution 3DSSMT post contrast image (d) ROC curve using ROI data of 57 lesions (30 malignant, 26 benign) for both the conventional k_{21} fitting method, and the LC method.

References:

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