Quantitative analysis of clinical dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) to evaluate treatment response in human breast cancer

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Introduction: Neoadjuvant chemotherapy (NAC) has become more common for treatment of breast cancer prior to surgery. In spite of usefulness of quantitative DCE-MRI in treatment assessment, this technique still has not been adopted in routine clinical practice because of several major practical limitations [1], including: 1) difficulty in obtaining an accurate arterial input function (AIF); 2) the long scanning time needed to acquire 3D data with high spatial resolution and a high signal-to-noise ratio (SNR) for accurate estimation of baseline $T_1(0)$; and 3) often highly variable and even considerable percentage of unphysical results generated by conventional methods due to noise effects. Other practical difficulties include the long computational time associated with the non-linear least square fit method (NLS) commonly used in quantitative DCE-MRI. In this study, we develop a method (T_1-FCM) that combines a fixed-T_1 method, the Fuzzy C-Means (FCM) technique and the reference region (RR) model to overcome the aforementioned difficulties in estimating pharmacokinetic parameters from clinical DCE-MRI without measuring either an AIF or $T_1(0)$, and demonstrate its feasibility to assess treatment response to NAC in patients with breast cancer using routinely acquired clinical DCE-MRI data.

Methods and Materials: All MR studies were performed at a 1.5 Tesla whole-body MR clinical scanner (Signa Excite 1.5T; GE Healthcare, Milwaukee) using a four-channel phased-array breast receive coil. DCE-MRI were obtained with a T_1-weighted fast 3D short TR spoiled gradient echo sequence with fat suppression (TR = 6.65 ms, TE =1.56 ms, flip angle = 15°, slice thickness=3mm, matrix=512×512) before treatment and after two cycles of NAC. The median time interval between pretreatment MR imaging and the start of chemotherapy was 1 day. One pre-contrast and seven post-contrast series were obtained at an interval of 58 seconds. 17 patients with biopsy-proven breast cancer participated in this study, and all gave written informed consent approved by the Human Investigation Committee of participating Institutes. The specific neoadjuvant chemotherapy (NAC) regimen of each patient was determined on an individual basis by their oncologists. Histopathologic response was assessed based on excised surgical specimens according to the scheme proposed by Ogston et al [2]. For the five grades of the scheme, grade 4 or 5 was classified as major histological response (MHR) and grade 1 to 3 was classified as non-major histological response (NMHR). DCE-MRI data were processed by T_1-FCM method with in-house developed software written in Matlab 7.6 (MathWorks, Inc., Natick, MA, USA).

T_1-FCM method includes the following steps: 1) segment tumor area using a FCM-based technique [3] and delineate the RR area (muscle); 2) estimate baseline tumor $T_1(0)$ value using the relationship between $T_1(0)$ in the tumor [$T_{1tumor}(0)$] and $T_1(0)$ in the reference region by the following equation:

$$T_{1tumor}(0) = \frac{T_{1,RR}(0) - \cos\theta \cdot T_{1RR}(0) + \cos\theta \cdot TR - \cos\theta \cdot TR \cdot N_{RR,t} \cdot \frac{S_{tumor}(0)}{S_{RR}(0)}}{N_{RR,t} \cdot \frac{S_{tumor}(0)}{S_{RR}(0)} \cdot (1 - \cos\theta)}$$

where $N_{RR,t}$ is proton density ratio between tumor and RR (ρ_{tumor}/ρ_{RR}). $N_{RR,t}$ can be roughly estimated by the ratio between averaged signal intensity over tumor and that in the RR (SI_{tumor}/SI_{muscle}) and literature T_1 of tumor (1151ms) and RR (869 ms) using FLASH signal intensity equation.

3) Convert signal intensities of tumor and RR to CA concentration $C_t(t)$ ($C_t(t)=1/T_1(t)-1/T_1(0)$); 4) Automatically clustering tumor CA concentration $C_t(t)$ into pre-defined number (number of tumor pixels/60) of clusters by FCM technique; 5) Estimating K_{trans} and V_e for each cluster using RR model [4] with linear regression method [5], and K_{trans} and V_e for each pixel were given by corresponding cluster with the greatest similarity (or the largest membership grade) for the pixel. Tumor volumes of the two measurements were assessed for each patient using a FCM-based technique [3], as well as the median values of K_{trans} and V_e over 3D tumor area.

Results: The average computational time for extracting K_{trans}/V_e from CA concentration $C_t(t)$ by the T_1-FCM method using linear regress was 12 seconds for the 17 patient studies on a Window XP platform with an Intel processor of 2.53 GHz and 2GB RAM memory, compared with 400 seconds for NLS fitting method for five of the 17 patients. FCM automatically groups CA concentration curves with similar patterns into a single cluster, which markedly reduce not only noise effects but also computation time. Preliminary clinical study found a significant difference (p<0.01, Kruskal-Wallis test) in the change of K_{trans} between the MHR group and the NMHR group before treatment and after two cycles of NAC, while failed to show significant difference in the change of volume (p=0.274, Kruskal-Wallis test) and V_e (p= 0.153, Kruskal-Wallis test). Figure 1 shows a typical case from a patient with invasive ductal carcinoma (IDC) by needle biopsy. Tumor volume, histogram of K_{trans} and K_{trans} map are shown before treatment and after two cycles of NAC. Although the change in tumor size was small (12.5%) (Fig. 1A), "hot" K_{trans} pixels decreased dramatically after the treatment (Fig. 1B-D), suggesting a positive response. Final pathological assessment for treatment response was scored as G4 for this patient, confirming our DCE-MRI results.
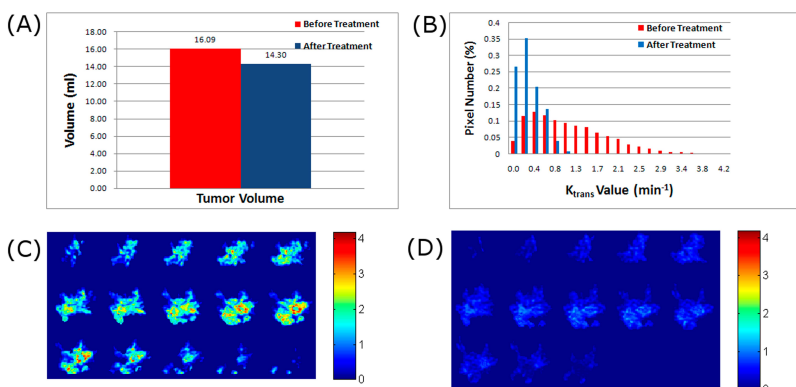

Conclusion: We have demonstrated the feasibility of T_1-FCM method to assess treatment response to NAC in patients with breast cancer using routine clinical DCE-MRI data without measurement of AIF and $T_1(0)$. This method could prove useful for evaluation of breast cancer therapy.

Reference:
1. Yankeelov TE, et al. Current Medical Imaging Reviews 2007;3(2):91-107.
2. Ogston KN, et al. Breast 2003;12(5):320-327.
3. Chen WJ, et al. Acad Radiol 2006;13:63-72.
4. Yankeelov TE, et al. MRI 2005;23(4):519-529.
5. Murase K. Magn Reson Med 2004;51(4):858-862.

Fig.1 Illustration of estimated tumor volume and K_{trans} of a patient with IDC before treatment and after two cycles of NAC. (A) Tumor size (in cm^3) before (red) and after (blue) the NAC; (B) Histograms of K_{trans} before (red color) and after (blue color) the NAC; (C) 3D K_{trans} map before treatment; (D)3D K_{trans} map after the two cycle of NAC.