Accessing Changes of Functional Dynamic Magnetic Resonance Imaging in Locally Advanced Breast Cancer Patients undergo Neoadjuvant Chemotherapy

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Introduction: Neoadjuvant chemotheraphy (NACT) is currently standard treatment for women with late stage disease, which is frequently locally advanced (LABC) [1]. Research evidence has suggested that clinical responders have a better prognosis than do nonresponders [2]. Therefore, recognition of a patient's resoponse to NACT is important issue for optimal and cost-effective management. The ability of identify nonresponders early after the start of the chemotherapy would be great clinical benefit because patient can undergo alternative therapy and avoiding the unresponsive toxic therapy. Dynamic contrast-enhanced MR (DCE-MRI) is able to distinguish malignant from benign by recognized differences in contrast enhancement uptake and evaluate some of the functional effect, such as tissue perfusion and permeability of tumor vascularity, to be studies in vivo [3]. Therefore, this ability of DCE-MRI can be used as a functional method for monitoring the pathophysiological response to therapy. In this work, two-compartment model proposed by Buckkey et al.[4] was applied in DCE-MRI to monitor the sequential chemotherapy response of patient with LABC. We aim to find the perfusion parameters which are sensitive to chemotherapy response.

Material and Methods: MRI scanning: This study enrolled 6 LABC subjects with good chemotherapy response (female, mean age = 53.50 ± 7.12 years). 3 times longitudinal MR scans,when before, during theraphy and before surgery, were performed to follow tumor change for each patient. All DCE-MRI examinations were performed using a 1.5T MR system (Siemens Sonata). Axial images were acquired using a FLASH 3D imaging sequence to include whole breasts. Imaging parameters were as follows: TR/TE = 3.65/1.76 ms; flip angle = 12°; FOV = 20×20 cm; matrix size = 192×192; slice thickness = 2 mm. The interval time between each measurement will be 12 seconds and total acquired time will be 8 minutes. Bolus Gd-DTPA injection with a total dose of 0.1 mmole/kg via auto-injector at a rate of 2.5ml/sec was followed by a 20 ml saline flush at the same rate. **Data Analysis:** The data of dynamic images will be transferred to a personal computer, and analyzed pixel-by-pixel using a pharmacokinetic two-compartment model. An equation, described the mathematical relation of signal in tissue with bolus injection, based on this pharmacokinetic model is obtained:

$$\frac{S(t)-S_0}{S_0} = A \bullet \frac{k_{out}}{(k_{out}-k_{el})}(\exp(-k_{el}t)-\exp(-k_{out}t))$$

On the model equation, the quantitative parameters are estimated from signal time curve using non-linear least square fitting. There are three kinetic parameters in this model: the amplitude of uptake A, exchange rate kout , and washout rate kel. ROIs based on dynamic T1WI subtracted by initial T1WI, and circled on whole tumor by a 5-year experienced radiologist. Five perfusion parameters: A, Kout, Kel, AK (A × Kout) and peak signal enhancement ratio (SIgEnh), their average values in ROIs were calculated. The tumor size was also computed. Statistical analysis was performed with linear relationship correlation between tumor size and five parameters.

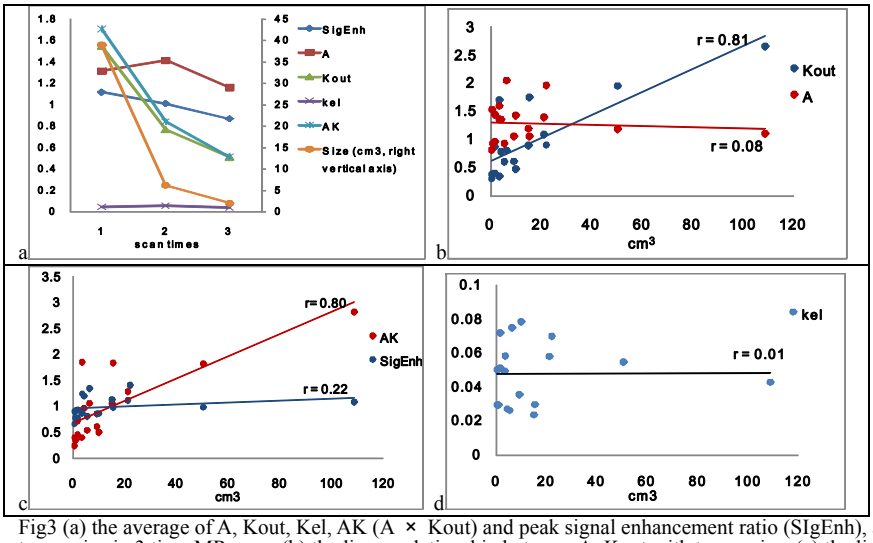

Fig3 (a) the average of A, Kout, Kel, AK (A × Kout) and peak signal enhancement ratio (SIgEnh), and tumor size in 3 time MR scan. (b) the linear relationship between A, Kout with tumor size. (c) the linear relationship between AK, SigEnh with tumor size. (d) the linear relationship between Kel with tumor size.

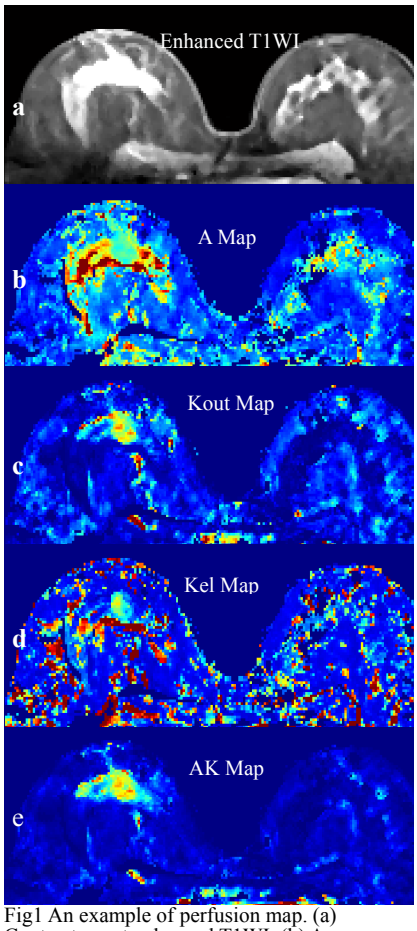

Fig1 An example of perfusion map. (a) Contrast agent enhanced T1WI. (b) A map. (c) Kout map. (d) Kel map. (e) AK map.

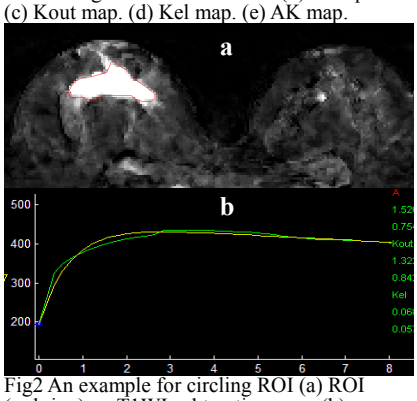

Fig2 An example for circling ROI (a) ROI (red ring) on T1WI subtraction map. (b) Enhanced curve (green) and fitting curve by model (yellow) in ROI.

Results : Fig 1 shows a case of perfusion maps and contrast agent enhanced T1WI. Fig 2 shows the ROI analysis and enhanced time curve. Fig 3(a) illustrates the longitudinal perfusion parameters and tumor size change in 3 time scans. Fig 3(b), (c) and (d) plot the linear relationship between five parameters and tumor size, and the correlation coefficients (r) are displayed.

Discussion : There are a lot of pharmacokinetics model to analyze and quantify DCE-MRI [5]. For accurate quantification, more complicated models are developed and more input data are necessary such as the arterial input function (AIF) and T1 map. But more input data could lead to error during computing parameters if they don't well control, for example AIF location. Sometimes simple model is more practicably used in clinical examination. In this study, the simple model was applied in DCE-MRI and we found the perfusion parameters (Kout and AK) are highly related with the change of whole tumor size during the chemotherapy. This finding might be helpful in further research in the pathophysiological responsiveness of breast tumor treatment.

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