# Quantitative DCE-MRI Assessment of Breast Cancer Therapeutic Response: How Long Is the Acquisition Time Necessary?

Mohan Jayatilake[1], Xin Li[1], Alina Tudorica[1], Karen Oh[1], Nicole Roy[1], Stephen Chui[1], and Wei Huang[1]

[1]Oregon Health & Science University, Portland, OR, United States

**Purpose:** Quantitative dynamic contrast-enhanced (DCE) MRI has been shown to be an important imaging biomarker for early prediction of breast cancer response to neoadjuvant chemotherapy (NACT) (1,2). The commonly adopted DCE-MRI acquisition time ($T_{acq}$) is 8 min or longer. However, breast cancer patients undergoing NACT are generally quite ill with compromised immune system. Consequently, the relatively long $T_{acq}$ causes significant amount of patient discomfort, often resulting in motion artifacts in the acquired images and low-quality data. Therefore, without sacrificing the ability of DCE-MRI for discriminating responders from non-responders, shorter $T_{acq}$ should be used to reduce patient discomfort and obtain good-quality data. A recent simulation study (3) shows that a DCE-MRI $T_{acq}$ value of 4.6 min is usually sufficient to derive stable $K^{trans}$ and $v_e$ pharmacokinetic parameters from DCE-MRI signal intensity time-course data of most curve features. In this study, by analyzing DCE-MRI data with shortened $T_{acq}$ generated from the acquired data with a long $T_{acq}$, we sought to determine, for the purpose of evaluating breast cancer response to NACT, if the DCE-MRI $T_{acq}$ can be significantly reduced.

**Methods:** Eleven women with locally advanced breast cancer underwent NACT before definitive surgeries. They consented to research DCE-MRI studies that were performed at time-point zero ($TP_0$) - before NACT, at $TP_1$ - after first NACT cycle, at $TP_2$ – midpoint of NACT (usually after three NACT cycles), and at $TP_3$ - after NACT completion. Axial bilateral DCE-MRI images with fat-saturation and full breast coverage were acquired using a 3T Siemens scanner, with a 3D gradient echo-based TWIST sequence (4), $10^o$ flip angle, 2.9/6.2 ms TE/TR, a parallel imaging acceleration factor of two, 30-34 cm FOV, 320x320 matrix size, and 1.4 mm slice thickness. The total DCE-MRI $T_{acq}$ was ~ 10 min for 32-34 image volume sets with 18-20 s temporal resolution. Gadolinium contrast agent (ProHance®) IV injection (0.1 mmol/kg at 2 mL/s) was carried out following acquisitions of two baseline image volumes. Tumor ROIs were drawn by experienced radiologists. The ROI and pixel-by-pixel (within the ROI) DCE time-course data were then subjected to both the Standard (Tofts) Model (SM) (5) and the Shutter-Speed Model (SSM) (6) analyses as previously described (7) to extract pharmacokinetic parameters. The SSM accounts for the finite intercompartmental water exchange kinetics (6). The whole tumor mean parameter values were calculated as the weighted (by ROI pixel number) averages of the ROI values from each of the image slices covering the entire tumor.

Pathology analyses of the surgical specimens and comparisons with pre-NACT biopsy specimens revealed that three patients were pathologic complete responders (pCRs) while the other eight were non-pCRs. We found that the tumor mean $K^{trans}$ (SM and SSM) and $k_{ep}$ (SM and SSM) values after the first NACT cycle (at $TP_1$), as well as their % changes ($TP_1$ relative to $TP_0$), were able to discriminate the 3 pCRs from the 8 non-pCRs. To determine whether DCE-MRI acquisitions with shorter $T_{acq}$ are still effective in predicting therapy response, data points from the actually acquired DCE-MRI time-course data of one pCR and one non-pCR were incrementally dropped from the far end of the time course before undergoing



**Fig.1a**

**Fig.1b**

the same SM and SSM analyses, simulating a $T_{acq}$ range of ~ 10 min to ~ 3 min. The raw data from the two patients were selected for these analyses because their tumor mean $K^{trans}$ and $k_{ep}$ values derived from the full $T_{acq}$ data were close to the means of the pCR and non-pCR groups, respectively, and thus were representative.

**Results:** Fig. 1a shows the column graphs of $TP_1$ tumor mean $K^{trans}$ (SM and SSM) and $k_{ep}$ (SM and SSM) values of the pCR (blue) and non-pCR (red) at varying $T_{acq}$, while **Fig. 1b** shows the corresponding % changes ($TP_1$ relative to $TP_0$) of these metrics. The vertical scales are kept the same in Fig. 1a for each parameter between the two models. Some $K^{trans}$ (SSM) and $k_{ep}$ (SM) values are out of scale at small $T_{acq}$. The $TP_1$ $K^{trans}$ (~0.04 $min^{-1}$) and $k_{ep}$ (~0.06 $min^{-1}$) parameter values of the pCR were nearly identical between the SM and SSM analysis: characteristic for tumor with diminished angiogenesis (7). These values remain stable for $T_{acq}$ as short as 3-4 min. For the non-pCR, the $K^{trans}$ (SSM) value (~0.08 $min^{-1}$) derived from the full $T_{acq}$ acquisition was substantially greater than the $K^{trans}$ (SM) value (~0.05 $min^{-1}$). This is expected for a tumor with presumably still elevated angiogenesis (7) after one NACT cycle. As a result, $K^{trans}$ (SSM) provides better separation of the pCR from the non-pCR. The non-pCR $K^{trans}$ and $k_{ep}$ parameter values remain stable for $T_{acq}$ as short as 5.5-6 min before being artificially increased with further $T_{acq}$ shortening. The latter actually "artificially" enhances discrimination of the two responses albeit with increased uncertainty in data fitting. Fig. 2 shows the pCR and non-pCR $TP_1$ tumor $K^{trans}$ (SSM) color maps obtained at varying $T_{acq}$, demonstrating clear difference between the two



**Fig.2**

breast tumors even at $T_{acq}$ as short as ~ 2.4 min. The % changes in $K^{trans}$ (SM and SSM) and $k_{ep}$ (SM and SSM) remain robust measures of therapy response in the entire simulated $T_{acq}$ range (Fig. 1b), with no less than 20% difference between the pCR and the non-pCR.

**Discussion and Conclusion:** A recent review (8) indicates that the $K^{trans}$ parameter is the dominant DCE-MRI biomarker that is useful for assessment of cancer therapeutic response. The results from this study suggest that for typical responder and non-responder breast tumor $K^{trans}$ or $k_{ep}$ values after one NACT cycle, a DCE-MRI $T_{acq}$ of 5-6 min is sufficient to achieve the goal of early prediction of therapeutic response when either parameter is used as the discriminatory biomarker. Therefore, any breast DCE-MRI acquisition time beyond the 6-min mark is probably unnecessary for the purpose of assessing therapy response. A shorter $T_{acq}$ can speed-up DCE-MRI protocol, reduce patient discomfort, and minimize the possibility of motion.

**References:** **1.** Marinovich *et al. The Breast* 2012;21:669-677. **2.** Ah-See *et al. Clin cancer Res* 2008;14:6580-9. **3.** Wang *et al. Proc ISMRM* 2010;18:4811. **4.** Tudorica *et al. Magn Reson Imaging* 2012;30:1257-67. **5.** Tofts *et al. JMRI* 1999;10:223-32. **6.** Li *et al. Magn Reson Med* 2005;54:1351-9. **7.** Huang *et al. Radiology* 2011;261: 394-403. **8.** O'Connor *et al. Nat Rev Clin Oncol* 2012;9:167-77.