# Molecular Markers and DCEMRI of Breast Cancer: Relationship with Kinetics in Invasive Ductal Carcinoma

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**Introduction:** Molecular markers such as estrogen receptor (ER), progesterone receptor (ER), and human epidermal growth factor receptor 2 (HER2/neu) are very important for predicting outcome and guiding treatment choices for breast cancer patients. Her2/neu positive and ER negative lesions tend to have poorer prognosis, and targeted therapies are available for Her2/Neu and ER positive lesions. Since kinetics of contrast media uptake and washout measured by dynamic contrast enhanced MRI are related to the underlying physiology and biology of lesions, it is possible that kinetic parameters could be used as surrogates for molecular markers. This would have the advantage that receptor status could be evaluated non-invasively and with high spatial resolution, which would be important in choosing subsequent therapy and guiding biopsy. Some prior reports have shown greater enhancement and washout for ER negative lesions, but have not studied PR or HER2/Neu status [1,2]. The purpose of this study was to perform a systematic evaluation of the kinetic characteristics of 145 invasive ductal carcinoma (IDC) lesions classified by ER, PR and Her2/Neu status.

**Methods:** 138 patients with 145 histologically proven IDC lesions with known ER, PR and Her2/Neu status were selected for IRB approved review. These lesions were classified as: ER positive (n=101), ER negative (n=44), PR positive (n=76), PR negative (n=69), Her2/Neu positive (n=25) and Her2/Neu negative (n=120). One pre and five post-contrast images were acquired in the coronal plane using 3D $T_1$-weighted SPGR (TR/TE = 7.7/4.2 msec, flip angle = 30°, slice thickness = 3 mm, in plane resolution = 1.4 mm, 68 sec acquisition). To generate the kinetic curve, an experienced radiologist traced a small region of interest (ROI) around what was perceived to be the most enhancing part of the lesion on the first post-contrast image. The kinetic curve represents the signal intensity in the ROI over time. Subsequent analysis of kinetic curve shape was made according to the BI-RADS lexicon: initial rise (rapid, medium, slow) and delayed phase (persistent, plateau, washout). In addition, several quantitative parameters were derived from the kinetic curves: initial enhancement percentage $E_1=100x(S_1-S_0)/S_0$, the time to peak enhancement $T_{peak}$, and the signal enhancement ratio $SER_1 = (S_1-S_0)/(S_{last}-S_0)$, where $S_0$ is the pre-contrast signal intensity in the ROI, $S_1$ is the signal intensity at the first post contrast injection time point and $S_{last}$ is the signal intensity at the last post contrast point[3]. A $SER_1 > 1.1$ indicates washout relative to the first post contrast point, while $9.9 < SER_1 < 1.1$ represents a plateau curve.

**Results:** Overall, 92% of lesions showed rapid initial enhancement, and 74% exhibited washout curves. The classification of the initial intensity increase and delayed phase according to BI-RADS lexicon did not differ significantly based on ER, PR and Her2/Neu status. The average values for the kinetic parameters were: $E_1$=307%, $SER_1$=1.13, $T_{peak}$=2.37 minutes. As shown in **Table 1**, ER negative lesions had a larger $E_1$ and $SER_1$, and a shorter $T_{peak}$ compared with ER positive lesions, with $p$ values < 0.03 for all parameters. Based on the $SER_1$ values, ER positive lesions exhibited plateau curves on average, while ER negative lesions showed a strong washout. PR negative lesions exhibited a stronger washout compared with PR positive lesions, with $p$ value < 0.02, but the other kinetic parameters did not show statistically significant differences. Her2/Neu negative and positive lesions were statistically equivalent.

**Discussion:** The kinetic characteristics of ER/PR negative lesions and ER/PR positive lesions showed some statistically significant differences ($p$ <0.03), with ER negative lesions exhibiting the highest $E_1$, $SER_1$ and the shortest $T_{peak}$ compared with all other categories. Previous reports have demonstrated that higher $SER_1$ values correlated with higher vascularity[3]. This implies that ER and PR negative lesions possess higher vascularity compared to their positive counterparts. These results also suggest that PR and in particular ER status may be related to tumor angiogenesis in a way that Her2/Neu status is not. If these preliminary results can be validated in a larger trial with more detailed kinetic analysis, this would suggest that reliable surrogates for these molecular markers can be measured non-invasively, in real-time and with high spatial resolution by MRI. DCEMRI could be used to guide biopsies and assess the spatial distribution of hormone receptors—in larger lesions it is difficult and time consuming for the pathologist to asses the receptor status in the whole lesion. Although preliminary, this study may point to a role for DCEMRI in evaluating hormone receptors and selecting appropriate hormone based therapy.

| | ER –ve (n=44) | ER +ve (n=101) | PR –ve (n=69) | PR +ve (n=76) |
|---|---|---|---|---|
| $E_1$ (%) | 351±19 | 288±16 | 328±18 | 287±18 |
| $SER_1$ | 1.36±0.12 | 1.03±0.04 | 1.25±0.08 | 1.03±0.04 |
| $T_{peak}$ (min) | 1.83±0.17 | 2.61±0.16 | 2.13±0.17 | 2.59±0.18 |

**Table1:** Kinetic parameters for ER/PR positive and negative lesions (mean ± standard error on mean).

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[3] Esserman et al. Breast J. 1999 Jan; 5(1): 13-21.