Are Kinetic Parameters related to Prognostic Indicators in < 2.0 cm Invasive Ductal Carcinomas?

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Introduction: Tumor size is strongly correlated with prognosis in breast cancer—the larger and more advanced a tumor, the worse the prognosis. In addition, there are other factors that contribute to prognosis, for example lesions that are estrogen receptor (ER) negative, poorly differentiated (nuclear grade III) or have positive lymph nodes tend to have poorer outcome. These other prognostic indicators are in turn correlated with tumor size: advanced tumors frequently exhibit positive nodes, ER negativity and poorer differentiation. Since kinetics of contrast media uptake and washout measured by MRI are related to the underlying physiology and biology of lesions, it is possible that kinetic parameters could be used as surrogates for prognostic indicators. Prior studies have found that lesions with poorer prognosis have more suspicious enhancement kinetics[1], but these studies have included large tumors; it could be that the kinetic patterns they have found are simply a reflection of the tumor size, rather than being correlated to specific markers. The purpose of this study was to separate the effect of lesion size from the assessment of the relationship between MR parameters and certain prognostic indicators. We evaluated the morphologic and kinetic characteristics of 71 small T1 (< 2.0 cm) invasive ductal carcinoma (IDC) lesions, and classified these findings by ER status, nuclear grade and node invasion.
Methods: 71 patients with 71 histologically proven T1 IDC lesions were selected for IRB approved review. Grade classification: 15 grade I, 32 grade II and 21 grade III, with 3 unclassified. 19 were ER negative and 47 ER positive lesions with 5 unclassified. 18 were node positive and 47 node negative, with 6 unknown. Dynamic MR protocol: 1 pre and 5 post-contrast images using a T1-weighted SPGR with 68 second timing resolution. Analysis of kinetic curve shape and morphology was made by an experienced radiologist according to the BI-RADS lexicon. In addition, several quantitative parameters were derived from the kinetic curves:

$$E_1 = 100 \times \frac{S_1 - S_0}{S_0},\ E_{peak} = 100 \times \frac{S_{peak} - S_0}{S_0}, SER = \frac{S_1 - S_0}{S_{last} - S_0},$$

where $\mathbf{E_1}$ and $\mathbf{E_{peak}}$ are the initial and peak enhancement percentages, respectively, **SER** is the signal enhancement ratio (a measure of washout), and $\mathbf{T_{peak}}$ is the time to peak enhancement.
Results: The predominant MR morphology was homogeneous(44%) mass-like enhancement(87%), with a round shape(51%), irregular margins(51%), and average size=1.6 cm. 93% of kinetic curves exhibited 'rapid' initial uptake and 69% a delayed phase 'washout'. Mean kinetic parameters: $\mathbf{E_1}$=304%, $\mathbf{E_{peak}}$=346%, **SER**=1.12, $\mathbf{T_{peak}}$=147sec. Node negative lesions were significantly smaller on MRI than node positive lesions (p=0.001), but did not exhibit statistically significantly different enhancement kinetics. Grade III lesions exhibited stronger washout (**SER**=1.34) compared with grade I and II lesions (**SER**=0.98, p=0.03). ER negative lesions showed a stronger washout (**SER**=1.40) compared with ER positive (**SER**=0.97, p=0.01) lesions.
Discussion: We have found that enhancement kinetics in < 2.0cm cancers were associated with ER status and grade, but did not depend on whether the cancer had spread to lymph nodes. Compared with ER positive and grade I and II lesions, ER negative and poorly differentiated tumors showed stronger washout. Previous reports have demonstrated that higher **SER** values correlated with higher vascularity[2]; our results suggest increased vasculature in small aggressive tumors compared to small less aggressive tumors. By considering only small cancers, our results suggest that kinetic parameters are related to certain prognostic indicators irrespective of lesion size. An improved understanding of kinetic and morphologic presentation of small IDC lesions, and the characteristics of poorly differentiated and ER negative lesions, may improve interpretation of DCEMRI exams. If these preliminary results can be validated in a larger trial with more detailed kinetic analysis, they would suggest that reliable surrogates for these molecular markers can be measured non-invasively, in real-time and with high spatial resolution by MRI. Although preliminary, this study may point to a role for DCEMRI in guiding biopsies, selecting hormone based therapy and assessing lesion differentiation.

References:
1. Szabo et al, Eur Radiol. 2003 Nov; 13(11): 2425-35.
2. Esserman et al, Breast J 1999 Jan; 5(1): 13-21.