A new approach to improve breast lesion classification from DCE-MRI

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Aims and objectives

Breast cancer is the second most common cancer in the world and the most frequent cancer among women with approximately 1.67 million new cases diagnosed every year. Furthermore breast cancer is the second cause of cancer death in more developed regions after lung cancer (1).

Screening mammography is the only method that has been proven to reduce mortality from breast cancer in asymptomatic women at average risk (2).

At the moment breast magnetic resonance imaging (Breast MRI) is reserved to specific conditions like:

- women at high risk for breast cancer;
- preoperative staging;
- find an unknown primary carcinoma when breast metastasis are incidentally found in absence of evidence of tumor at mammography;
- evaluate the response to neoadjuvant chemotherapy;
- evaluate breast tumor recurrence in operated women or like screening tool in addition to mammography and ultrasound in breast-conserving therapy;
- problem solving in specific situation (e.g. B3 lesions);
- patient with breast implants, either aesthetic or post-mastectomy (3,4).

Optimal dynamic contrast enhancement (DCE) breast MRI protocol is mandatory to get a diagnostic exam. Breast DCE-MRI has a very high sensibility (89-100%) to detect breast cancer but unfortunately despite of an high-quality exam, it suffers of low specificity (30-72%) (5-7).

During last decades many attempts to improve its specificity has been done and at the moment there is a broad agreement about the importance of evaluation for each breast lesion of its morphologic features and enhancement kinetics (5,8).

Traditionally enhancement kinetics analysis of DCE breast MRI is based on a qualitative evaluation of time/signal enhancement curves in voxels of a region-of-interest (ROI). According to a landmark study of Kuhl et al., three different types of time/signal enhancement curves were identified (9) (Figure 1):

- **progressive (Type 1)**: the signal intensity continues to increase over the entire dynamic period;
- **plateau (Type 2)**: the enhancement reach a steady state after the initial phase;
- **washout (Type 3)**: there is a rapid initial enhancement, followed by a decrease of the signal in the intermediate/late phase.
However also with the introduction of qualitative analysis of breast MRI, there is a considerably overlap of kinetic features between benign and malignant lesions of the breast.

Aim of our study was to study a new approach to evaluate the kinetics of the enhancement curves in order to improve breast lesion classification.
Fig. 1: Typical curve shapes for qualitative DCE breast MRI analysis. SI: signal intensity.

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Methods and materials

Patient population and characteristics

In this prospective study 9 women (age: 26-58 years, mean age 46.85 years) with 10 mass enhanced breast lesions. Needle biopsy specimens classified the 10 breast lesions in five ductal carcinomas (stage G3 for three masses and G2 for two masses) and five fibroadenomas. The mean sizes of all breast cancers and benign lesions were 28.32 ± 4.25 mm (range, 8-72 mm), 22.27 ± 3.96 mm (range, 7-107 mm), respectively.

Data acquisition

All MRI examinations were performed using a 1.5 Tesla (T) system (Achieva, Philips Medical System, Eindhoven, The Netherlands). A 7-channel dedicated bilateral breast coil was used. Patients were placed in prone position. The standard clinical breast MRI protocol used at our Institution included the following sequences:

- axial T2-weighted turbo spin echo (TSE);
- axial T2-weighted SPectral Attenuated Inversion Recovery (SPAIR);
- axial Diffusion Weighted Imaging (DWI) with b800;
- axial 3D T1 weighted ultrafast gradient echo sequence with fat saturation (T1 enhanced High Resolution Isotropic Volume Excitation or eTHRIVE) for DCE study.

DCE turbo field echo with 1 pre-contrast (I₀) and 5 post-contrast (I₁₅) series (Figure 2) was performed using a fat-suppressed 3-dimensional volume acquisition sequence in the axial plane (TR 6.9ms, TE 3.4ms, flip angle 10°, field of view 34 × 34 cm, matrix 352 × 352, BW 63.2 kHz, slice thickness 2 mm, spacing between slices 1 mm, voxel size 1 mm³). Before collection of the post-contrast scans, a bolus injection of gadolinium (0.1 mmol/kg) was administered via a previously inserted cubital vein catheter and immediately followed by a 20-mL physical saline solution flush. The injection was administered by using a power injector within 15 seconds. Each series of DCE sequence was acquired with a temporal resolution of 60 seconds. The total scan time for DCE study was approximately 6 minutes.

Data analysis

The pre-contrast series was subtracted from the post-contrast ones (Figure 3).
A ROI was manually placed on each lesion at the level of maximum section area of lesions and was selected to be as large as possible, consistent with minimal contaminations from surrounding unintended normal tissues or fat. Time-intensity enhancement curves (TICs) characterizing suspected lesions were derived from the analysis of 2D and 3D ROIs. More in detail, for the 2D analysis, the ROI was positioned in each corresponding slice in all subtracted volumes and the mean gray-level intensity inside each ROI was computed and used to derive the 2D TIC. For the 3D analysis, the ROI was positioned in each corresponding slice in all subtracted volumes and lesion was segmented in 3D applying a region growing algorithm. The mean gray-level intensity inside each 3D ROI was computed and used to derive the 3D TIC.

For the 3D analysis, the ROI was positioned in each corresponding slice in all subtracted volumes and lesion was segmented in 3D applying a region growing algorithm. The mean gray-level intensity inside each 3D ROI was computed and used to derive the 3D TIC.

For each curve we computed the standard parameters (slope of the initial (wash-in WI) and of the delayed (wash-out WO) phases, percentage enhancement of the delayed phase (SI)) (10,11):

\[ WI = \frac{(I_2-I_1)}{(t_2-t_1)} \]

\[ WO = \frac{(I_{end}-I_2)}{(t_{end}-t_2)} \]

\[ SI = \frac{(I_{end} - I_{mean(2,3)})}{I_{mean(2,3)}} \times 100 \]

Since none of these parameters describes the percentage enhancement of second part of the initial phase we formulated and computed a new index indicating the fast enhancement of the initial phase as:

\[ E_{WI} = \frac{I_1}{I_{peak}} \times 100 \]

In addition experimental data were fitted using different approaches (Figure 4):

- a sigmoidal model: \( I(t) = \frac{A}{1+e^{-Ct}} A1+e^{-C\cdot t} \) leading to two additional parameters, A and B;
- two linear models:
\[ I_{in}(t) = a_{in}t + b_{in} \]
\[ I_{delayed}(t) = a_{delayed}t + b_{delayed} \]

to simulate the initial and delayed phases respectively, leading to four additional parameters \((a_{in}, b_{in}, a_{delayed}, b_{delayed})\).

These parameters were used to classify each lesion and the result of such classification was compared with each other.
**Fig. 2:** Schematic representation of the MRI protocol for DCE acquisition

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**Fig. 3:** Example of the subtraction step: the pre-contrast volume (I₀) is subtracted from the post-contrast volume (I₂ in the example) and the subtracted volumes (S₂ in the example) were then used for the following process.

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Fig. 4: Different models applied to simulate the TIC (in blue the original data, in red the sigmoidal model and in green the two linear models).

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Results

In Figure 5 we show two examples of the TICs obtained in two breast lesions classified as benign (Figure 5a) and malign (Figure 5b), together with the corresponding sigmoidal and linear models.

Parameters from linear and sigmoidal TIC models were not able to correctly classify the lesions. Based on the parameters derived from experimental data, the analysis in 2D did not allow to correctly classify one malignant lesion that was misclassified as benign (lesion #3, see Table 1).

Analysis in the 3D domain allowed to correctly classify all the lesions (Table 2).

In Figure 6 we show the TICs for lesion #3 obtained applying the 2D (left panel) and the 3D (right panel) analysis. The values of the standard parameters computed in 3D (WI changed from 0.19 to 0.18, WO from 0.009 to 0.003, SI% from 4.5 to 0.9) did not allow to classify correctly lesion #3. Conversely $E_{WI}$ underwent a change of 10%. The value of this parameter in all malignant lesions showed a significantly higher value (range: 29-40) with respect to benign lesions (range: 0.4-21) (p<0.05). Importantly, considering exclusively this new index indicating fast percentage enhancement of the late wash-in, we were able to correctly classify all the lesions.
Fig. 5: (a) Example of the TIC (blue) obtained in a benign breast lesion and the corresponding sigmoidal model in red and the two linear models for the initial and delayed phases in green; (b) example of the TIC (blue) obtained in a malign breast lesion and the corresponding sigmoidal model

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**Table 1:** Parameters computed from the analysis of the TICs performed in the 2D domain.

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### Table 2: Parameters computed from the analysis of the TICs performed in the 3D domain.

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**Fig. 6:** TICs for lesion #3 obtained applying the 2D (left panel) and the 3D (right panel) analysis

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Conclusion

Since there is a considerably overlap of kinetic features between breast benign and malignant lesions from DCE MRI, in order to improve breast lesion classification, in this study we propose a new approach to evaluate the kinetics of the enhancement curves.

The results of the TIC analysis in the 2D and 3D domain using the standard parameters computed from experimental data did not increase the performance of the analysis.

Also the use of sigmoidal and linear models to fit experimental data was not successful.

Since none of the standard parameters was able to describe the increase of the enhancement of the late wash-in phase, we designed this new index as the ratio between the mean gray-level intensity in the first subtracted volume and the maximum value of the TIC in the detected ROI. This index was computed both in the 2D and 3D analysis.

Results showed a correct classification of all lesions exclusively using this index computed in the three dimensional domain.

The standard parameter WI computes the slope of the increase between the second and the first mean gray-level intensity computed in the manually selected ROI. The index $E_{WI}$ we propose computes a measure of the increase of the enhancement in the second part of the wash-in phase: given a certain value for $I_{peak}$, higher is the mean gray-level intensity in the first subtracted volume $I_1$, and higher is the value of this parameter highlighting a higher enhancement in the first part of the wash-in phase. We expect a malignant lesion to capture the contrast medium immediately after its injection and therefore high values for $E_{WI}$ may be predictive of a cancerous diagnosis.

Obviously this hypothesis needs to be tested on a larger population of breast lesions also including carcinomas different from ductal ones. These preliminary results showing to improve the diagnostic performance of TIC curve analysis for breast malignant lesion identification, ensure further investigations.
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References


