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Characterization of spatiotemporal changes for the classification of dynamic contrast-enhanced magnetic-resonance breast lesions

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ABSTRACT

Objective: The early detection of breast cancer is one of the most important predictors in determining the prognosis for women with malignant tumours. Dynamic contrast-enhanced magnetic-resonance imaging (DCE-MRI) is an important imaging modality for detecting and interpreting the different breast lesions from a time sequence of images and has proved to be a very sensitive modality for breast-cancer diagnosis. However, DCE-MRI exhibits only a moderate specificity, thus leading to a high rate of false positives, resulting in unnecessary biopsies that are stressful and physically painful for the patient and lead to an increase in the cost of treatment. There is a strong medical need for a DCE-MRI computer-aided diagnosis tool that would offer a reliable support to the physician's decision providing a high level of sensitivity and specificity.

Methods: In our study we investigated the possibility of increasing differentiation between the malignant and the benign lesions with respect to the spatial variation of the temporal enhancements of three parametric maps, i.e., the initial enhancement (IE) map, the post-initial enhancement (PIE) map and the signal enhancement ratio (SER) map, by introducing additional methods along with the grey-level co-occurrence matrix, i.e., a second-order statistical method already applied for quantifying the spatiotemporal variations. We introduced the grey-level run-length matrix and the grey-level difference matrix, representing two additional, second-order statistical methods, and the circular Gabor as a frequency-domain-based method. Each of the additional methods is for the first time applied to the DCE-MRI data to differentiate between the malignant and the benign breast lesions. We applied the least-square minimum-distance classifier (LSMD), logistic regression and least-squares support vector machine (LS-SVM) classifiers on a total of 115 (78 malignant and 37 benign) breast DCE-MRI cases. The performances were evaluated using ten experiments of a ten-fold cross-validation.

Results: Our experimental analysis revealed the PIE map, together with the feature subset in which the discriminating ability of the co-occurrence features was increased by adding the newly introduced features, to be the most significant for differentiation between the malignant and the benign lesions. That diagnostic test – the aforementioned combination of parametric map and the feature subset achieved the sensitivity of 0.9193 which is statistically significantly higher compared to other diagnostic tests after ten-experiments of a ten-fold cross-validation and gave a statistically significantly higher specificity of 0.7819 for the fixed 95% sensitivity after the receiver operating characteristic (ROC) curve analysis. Combining the information from all the three parametric maps significantly increased the area under the ROC curve (AUC) of the aforementioned diagnostic test for the LSMD and logistic regression; however, not for the LS-SVM. The LSMD classifier yielded the highest area under the ROC curve when using the combined information, increasing the AUC from 0.9651 to 0.9755.

Conclusion: Introducing new features to those of the grey-level co-occurrence matrix significantly increased the differentiation between the malignant and the benign breast lesions, thus resulting in a high sensitivity and improved specificity.

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1. Introduction and background

Among the different types of cancer, breast cancer has one of the highest incidences in the female population and is one of the most common causes of death worldwide. While there is much uncertainty about the causes of breast cancer, medical experts agree that, with an early detection, the chances of survival are much higher. Therefore, screening programs have been established in many countries to increase the number of cancers detected in the early stages. The dynamic contrast-enhanced magnetic-resonance imaging (DCE-MRI) modality has demonstrated an extremely high sensitivity in interpreting (diagnosing) breast cancers. Moreover, its false-negative rate is lower compared to other imaging modalities. One of its major disadvantages is the moderate specificity, meaning that a relatively large number of the benign tumours are falsely classified as malignant (false positives), contributing to unnecessary biopsies. Physicians are looking for ways to reduce the patient trauma associated with biopsies (or other over-treatments) and health-insurance companies are looking for ways to reduce the costs associated with unnecessary procedures.

DCE-MRI offers four-dimensional data about suspicious breast lesions, three-dimensional spatial and one-dimensional temporal data obtained after the contrast agent administration. The high permeability of the tumour capillaries allows the contrast agent to diffuse out of the capillaries into the interstitial space, leading to a stronger enhancement of the tumour compared to the surrounding breast tissue, which is critical for an accurate breast-cancer diagnosis.

Breast-cancer diagnosing with DCE-MRI is a time-consuming and demanding task for the radiologist due to the multi-dimensionality of the data. The diagnostic finding, for any suspicious enhancement, is generated by a visual examination of the kinetic, textural and morphological patterns of malignancy using descriptors specified in the BI-RADS (Breast Imaging-Reporting and Data System) lexicon [1]. Interpretation of the textural and morphological patterns (features) results in a diagnosis that frequently suffers from inter- and intra-observer variability [2]. This makes the performance of the diagnosis very dependent on the level of experience of the radiologist [3,4]. As a result, recent researches have focused on developing automated DCE MR image-analysis methods aimed at helping radiologists to detect and diagnose breast cancer, particularly those radiologists experienced in mammography reading (diagnostic) but inexperienced in interpreting the breast MRI [5].

The first step in diagnosing the breast MRI is to classify the lesion as a mass (focal lesion) or a non-mass-like enhancement. The BI-RADS breast MRI lexicon gives the following clear definitions for the mass and non-mass-like enhancement: "Mass—A mass is a three-dimensional space-occupying lesion that comprises one process, usually round, oval, lobular, or irregular in shape"; "Non-mass-like enhancement—Enhancement of an area that is not a mass. This includes enhancement patterns that may extend over small or larger regions, and whose internal enhancement characteristics can be described as a pattern discrete from a normal surrounding breast parenchyma."

Malignant and benign mass lesions in the DCE-MR images exhibit three spatiotemporal differences: (i) differences in the temporal enhancement (kinetic), (ii) differences in the spatial morphology (shape and margin) and spatial variation of the signal intensity (texture) and (iii) differences in the spatial variation of the temporal enhancements.

The differences in the temporal-enhancement curves occur due to the hyper-vascularity and increased permeability of the malignant lesions compared to the benign lesions, leading to a faster diffusion of the contrast agent into and out of the interstitial space (strong wash-in and wash-out) compared to the benign cases (characterized by moderate wash-in and either a persistent or steady post-contrast phase) [6–9]. The temporal-enhancement curves are characterized by kinetic features which provide quantitative indices of malignancy. These quantitative parameters showed the potential to differentiate between the malignant and the benign lesions, as pointed out in the literature [10,11].

Furthermore, while the malignant breast lesions tend to have a spiculated margin and an irregular shape suggesting an invasion into the surrounding breast tissue together with the heterogeneous grey-level intensity distribution (texture), the benign lesions usually have a well-circumscribed and smooth margin with a round or oval shape and a more homogeneous texture. In past, the texture and shape analyses were applied to spatial variations of the signal intensity in 2D images and in 3D lesion volumes in order to quantify the heterogeneity and to differentiate between the malignant and the benign breast lesions. These analyses provided promising results [12–16].

Additionally, the uptake of the contrast agent in breast lesions is often spatially varying. By averaging, as used in the clinical practice, the resulting averaged kinetic curve can be misleading [17]. For this reason, pixel-mapping methods [18] for the spatial analysis of the pixel-wise temporal-enhancement heterogeneity have been proposed for standardization of the DCE-MRI breast-cancer diagnosis [19–22].

The pixel-mapping methods display quantitative enhancement information for every pixel in the observed lesion as a colour map (the three-time-point method [19]) or a grey-level map. The advantage of these methods is in not requiring manual selection of the region of interest – ROI (as in the region-based methods) in order to obtain a temporal-enhancement information, thus reducing the possibility of overlooking a diagnostically significant part of the lesion.

In clinical diagnostic procedures, the specificity rate is relatively lower compared to the sensitivity rate because of the physician's concern about the missed breast cancers. Additionally, the specificity rate for diagnosing breast cancer is lower among women with clinical factors associated with an increased breast-cancer risk (e.g., family history of breast cancer) because the physician may interpret breast abnormalities more cautiously among these women.

For effective clinical use of the computer-aided diagnosis tools and for offering reliable support to a physician's decision, the system should provide a higher specificity rate than the one clinically obtained; however, without reducing the sensitivity rate.

This paper describes an automated approach to the DCE-MRI mass breast-lesion classification of manually segmented lesions on benign and malignant tumours by applying a textural analysis on pixel-mapping grey-level maps.

The paper is organized as follows. Upon providing introduction and the background of the aim of our study, Section 2 reviews the related work on the DCE-MRI breast-lesion classification. Section 3 describes the population samples (lesions) analyzed in our study, the applied texture analysis methods and the concept revolving around classification procedure. Section 4 explains the applied experimental procedure and Section 5 describes the statistical data analysis. Section 6 reports our experimental results for DCE-MRI breast-lesion classification performance. Section 7 summarizes the main findings of our study, outlines its limitations and determines areas for our future work. Finally, Section 8 draws the conclusions of our study.

2. Related work and motivation

Many authors tried to alleviate the impact of noise on the pixel-mapping methods used to capture the spatial changes of temporal