A ROBUST AND EXTENDABLE FRAMEWORK TOWARDS FULLY AUTOMATED DIAGNOSIS OF NONMASS LESIONS IN BREAST DCE-MRI

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ABSTRACT

Diagnosis of breast nonmass lesions, most notably ductal carcinoma in situ, is challenging. Recent studies show that dynamic contrast enhanced MRI achieves high sensitivity in diagnosis of nonmass lesions. Unlike successfully applied to diagnose mass lesions, particularly kinetic features are reported to be less effective in discriminating nonmass lesions. It is even difficult for human observers to differentiate nonmass lesions against the enhancing parenchymal or benign lesions due to their sometimes similar morphology and contrast kinetics. Towards an automated computer-aided diagnosis system of nonmass lesions, we implemented an extendable and completely automated framework that is efficient and modularized, aiming to discriminate detected suspicious regions into malignant and benign. The entire framework consists of five sequentially executed modules: motion correction, segmentation of breast regions, detection of suspicious regions, feature extraction, and knowledge-based analysis of suspicious regions. A preliminary test was performed on a data set collecting 162 nonmass lesions extracted from 67 patients, which achieved an area under ROC curve value of 0.74 for malignant lesions.

Index Terms— Computer-aided diagnosis, CAD, nonmass lesions, DCIS, breast MRI, DCE-MRI

1. INTRODUCTION

Dynamic contrast enhanced MRI (DCE-MRI) has been widely used in breast cancer screening of high risk patients, preoperative staging, and post-treatment follow-up thanks to its high sensitivity. According to the BI-RADS lexicon, based on their morphological characteristics, the lesions are classified into mass, nonmass, and foci [1]. The diagnosis of breast cancer in its intraductal stage might help to prevent from growing to invasive cancers [2]. However, the delineation and diagnosis of nonmass lesions, most notably ductal carcinoma in situ (DCIS), is challenging in breast MRI reading. Clinical evidences show that the kinetic parameters have the potential to distinguish benign and malignant mass lesions more effectively, but failed to demonstrate usefulness in discriminating benign from malignant nonmass lesions [3]. Therefore, the computer-aided diagnosis (CAD) tools strongly relying on kinetic features often failed in detecting and classifying nonmass lesions. In terms of sensitivity and specificity, none of previous trials achieved a performance matching CAD approaches for solid masses [1, 2, 4].

In this work, we present a robust and extendable framework that allows to automate the diagnostic procedure of nonmass lesions in breast DCE-MRI. The aim of this framework is to discriminate detected suspicious regions into malignant and benign. The framework is built with an efficient, robust, and easily extendable workflow comprising all necessary pre-processing and diagnostic decision making modules, e.g., the motion correction of temporal DCE-MRI, the segmentation of breast regions, the detection of suspicious regions or lesion candidates, the feature extraction and validation, and eventually the automatic diagnostic decision making system. Each module of this framework is independently implemented in MeVisLab platform and easily extendable to improve the performance of overall system. The processing pipeline depicting each individual module is shown in Fig. 1. To examine the efficacy of this framework, we conducted a preliminary test using a data set that consists of 67 patients containing 162 nonmass lesions, among of which 131 were pathologically confirmed malignant lesions, and 31 were benign findings. We evaluated the classifier performance in a 10-fold cross validation scheme on that data, and the results are demonstrated.

2. METHODS

2.1. Motion Correction

Automatic correction of image artifacts induced by involuntary motions and muscle relaxation during the image acquisition is essential for the computer-aided diagnosis of breast DCE-MRI. The spatial misalignment of fibroglandular tissues in different temporal images may hamper the morphological and dynamic analysis. The extraction of actual time-intensity curves (TIC) for a specific region of interest (ROI) also relies on the motion compensation. Image registration techniques are employed for this task. To prevent lesion degeneration, the first post-contrast image is commonly chosen as the reference image, and the pre-contrast and other subsequent temporal
images are registered to the reference by minimizing the error with respect to one or more of the available similarity metrics between image pairs, adhering to the constraints imposed by the underlying model. In our work, we use a scheme, which combines a local elastic and global affine transformations into one deformation field [5]. Since only one warping deformation is required, the computational expense on warping interpolation is avoided. The combined algorithm takes the advantages of both elastic and linear affine registration methods and thus allows for compensating both large patient movements and elastic deformation of breast tissues. As illustrated in Fig. 2, our method is able to eliminate the artificial parenchyma enhancement induced by patient motion.

2.2. Breast Segmentation

To decrease false positive findings, a precise segmentation of the breast is a fundamental step to facilitate further diagnostic tasks. We previously implemented a fully automatic segmentation method specially designed for processing non-fat suppressed breast MRI [6]. The key observation of this method is that the pectoralis muscle and breast-air boundaries exhibit smooth sheet-like surfaces in 3D, which can be simultaneously enhanced by a Hessian-based sheetness filter [7]. The enhancement strength of the designed Hessian-based filter correlates with the shape and contrast information of the structures, which means that structures with non-specific shapes and lower contrast will be suppressed. The method consists of four major steps: enhancing sheet-like structures, segmenting the pectoralis muscle boundary which defines the lower border of the breast region, segmenting the breast-air boundary which delimits the upper border of the breast region, and extracting the region between the upper and lower borders which eventually captures the area of breast tissue. The accuracy and robustness of this method are evaluated by extensive tests conducted with the data from different sites. Combined with the motion correction, breast masks obtained from pre-contrast images can be used to mask subsequent temporal or subtraction images, which dramatically increases the accuracy in detecting suspicious regions, since it removes many resembling enhancements patterns elsewhere, most notably in the heart.

2.3. Detection of Suspicious Regions

Suspicious regions (or lesion candidates) are defined as abnormal contrast enhancement patterns found in DCE-MRI. The types of suspicious regions could be malignant, benign or other tissue caused by parenchyma enhancement. The accumulation of contrast agent in areas with leaky vascularity is reflected by hyper-intense signals in T1-weighted DCE-MRI. Contrast agent accumulates in the vicinity of a lesion which triggers fast (hence leaky) vascular growth to feed its excessive oxygen needs. Nonmass lesions often exhibit mild enhancement compared to invasive cancers, in fact even to be obscured with normal parenchymal enhancement or benign lesions. However, a key clinical observation is that the enhancement of nonmass lesions is often asymmetric: it appears unilateral. Oppose to nonmass lesions, parenchyma enhancement and some benign lesions enhance bilaterally. This distinctive enhancement characteristic previously led us to develop a detection algorithm of suspicious regions by investigating the asymmetry characteristics of left and right breasts [8].

The method investigates and compares the symmetry
properties in each 2D slice of a given 3D subtraction image. First, the probabilistic distribution of intensity transition patterns in one breast is learned. An intensity transition pattern in a 2D slice is simply an intensity pair of two neighboring pixels. The probabilistic distribution is approximated by analyzing a 2D histogram summarizing the occurrence rate of each unique pattern. Then, the learned probability map is applied to the contralateral breast. The rare transition patterns with extremely low probabilities are considered as suspicious. By applying a threshold with a value of almost close to zero (0.01 in this work) on probability map, we obtain a binary mask of suspicious regions. The same learning strategy is repeated inversely through all slices until all suspicious regions are captured. Figure 4 depicts the successive steps of this detection algorithm [8].

Fig. 4. Detection of lesion candidates. Left: maximum intensity projection (MIP) of the subtraction image, showing the extent of disease. Middle: the suspicion map shows dark areas of ‘low probability’ events. Right: lesion candidates obtained by thresholding. [8]

2.4. Feature Extraction

2.4.1. Kinetic features

Kinetic features interpret the characteristics of time-intensity curves extracted from suspicious regions. Many clinical studies prove that the kinetic features are of great diagnostic values in discriminating malignant from benign lesions for mass lesions. However, most kinetic features tend to be less descriptive in diagnosing nonmass lesions, because statistically the differences of kinetic features between malignant and benign nonmass lesions were not found [3]. Later studies on larger populations suggested that only the parameters associated with wash-out phase are useful in distinguishing nonmass lesions [1]. In this work, we carefully choose a set of features that are documented to be most salient in diagnosing nonmass lesions. We calculate the uptake rate, the wash-out rate, the maximum enhancement and time-to-peak from a dynamic sequences. The uptake rate and wash-out rate quantify the change of contrast agent density by computing the slopes of intensity change over time in wash-in and wash-out phases. Normally, a higher wash-out rate indicates a higher likelihood of malignancy, or of invasive lesions. Moreover, the enhancement strength correlates with contrast agent concentration and thereby with the leakiness of the vasculature, and the time-to-peak value (describing the duration to maximum enhancement) indicates how leaky the vasculature is. For each suspicious lesion, we average the voxels whose feature values are sufficiently prominent, i.e., above the 80th percentile of this feature’s values.

2.4.2. Morphological and texture features

The diagnostic accuracy of nonmass lesion CAD is expected to be improved by combining morphological and kinetic features [9]. In our work, we hence incorporate a set of distribution descriptors including elongation factor, flatness, eccentricity, principle axis, eigenvalues, skewness, circularity and ellipticity. These features interpret the intrinsic morphological properties of a given suspicious region from different perspectives. Furthermore, we calculate the local binary patterns (LBP) of suspicious regions in subtraction images [10]. One of the advantages of LBP features is their invariance to the absolute enhancement levels.

2.5. Knowledge-based Analysis of Suspicious Regions

In this work, the knowledge-based analysis of lesion characteristics is implemented in a generic machine learning library embedded in the MeVisLab platform [11]. The library enables object based image analysis (as opposed to voxel-based image analysis) and includes rapid classification algorithms. It is based on a relational database to achieve the desired speed. Although not harvested fully in our current work, this frameworks enables the easy inclusion of advanced morphological features, utilizing the modeling of spatial relationships. Unlike other CAD systems, our aim is to investigate the properties of all types of suspicious regions, including malignant, benign and other tissue. Therefore, multi-class classifiers are trained to classify suspicious regions into three classes. Finally, given a new input data, the classifier, which achieves the best performance in training stage, will be directly used as an automated diagnostic tool to classify suspicious regions.

3. RESULTS

To test the diagnostic performance of the proposed framework, we conducted a preliminary test. A total of 162 nonmass lesions in 67 patients were collected retrospectively. The DCE-MRI images were acquired on a 1.5T scanner (Magnetom Vision, Siemens, Erlangen) in Nijmegen, Netherlands. A dedicated breast coil (CP Breast Array, Siemens, Erlangen) was used in prone patient placement. The pixel spacing differed between volumes with values ranging from 0.625 mm to 0.722 mm. The slice thickness was 1.3 mm, and the volume size was 512 x 256 x 120 voxels. TR and TE were 6.80 s and 4.00 s, respectively, at a 20 degree flip angle.
All patients were histologically confirmed by needle aspiration/excision biopsy or surgical removal. Subsequently, the amount of malignant lesions were 131, most of which were diagnosed as DCIS. Other types of malignant lesions included invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), lobular carcinoma in situ (LCIS) and metastasis. On the other hand, benign histologic findings were found in 31 lesions including fibrocystic changes (FCC), adenosis and hyperplasia. One experienced radiologist retrospectively reviewed the histologic reports and identified the reported lesions in each data set by assigning three labels: malignant with 1; benign with 2 and other tissues with 3.

The false positive lesions obtained without pre-processing modules are dramatically decreased by applying motion correction and breast segmentation, eventually resulting 388 suspicious regions comprising 131 malignant lesions, 31 benign lesions and 226 other tissues. Three multi-class classifiers were trained with the detected suspicious samples, including random forest (RF), naive Bayes (NB), and support vector machine (SVM). The trained classifiers investigate the feature vectors of each suspicious region and determine the class labels, which will be compared to the true labels. For each classifier, a 10-fold cross validation scheme was applied on detected 388 suspicious samples. The classification power, expressed as the area under the ROC curve (AUC) is listed in Tab.1.

<table>
<thead>
<tr>
<th>Classifier</th>
<th>other tissue</th>
<th>malignant</th>
<th>benign</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF</td>
<td>0.77</td>
<td>0.74</td>
<td>0.61</td>
</tr>
<tr>
<td>NB</td>
<td>0.79</td>
<td>0.73</td>
<td>0.70</td>
</tr>
<tr>
<td>SVM</td>
<td>0.71</td>
<td>0.68</td>
<td>0.52</td>
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</tbody>
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Table 1. The AUC values associated with different lesion types, which were obtained by RF, NB and SVM classifiers

4. DISCUSSIONS

In this contribution, we present an extendable framework aiming to establish a completely automated diagnostic system particularly for nonmass lesions in breast DCE-MRI. The advantages of this framework lie in its modularized and flexible structures, which eases the improvement and extension of each individual module. We added a set of kinetic, morphological and texture features in discriminating detected suspicious regions into three classes: malignant, benign and other tissue. A preliminary test with a large number of testing cases was conducted to show its potential in making diagnostic decisions. Because kinetic features are less indicative in distinguishing nonmass lesions compare to mass, our focus will lie in further exploring morphological and textural characteristics of lesions. Apparently, the systematic error introduced in each sequential step will affect the diagnostic accuracy eventually, thus the robustness and reproducibility of each module have to be tested further.

5. REFERENCES