

A Multiple Classifier System for Classification of Breast Lesions Using Dynamic and Morphological Features in DCE-MRI

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Abstract. In this paper we propose a Multiple Classifier System (MCS) for classifying breast lesions in Dynamic Contrast Enhanced-Magnetic Resonance Imaging (DCE-MRI). The proposed MCS combines the results of two classifiers trained with dynamic and morphological features respectively. Twenty-one malignant and seventeen benign breast lesions, histologically proven, were analyzed. Volumes of Interest (VOIs) have been automatically extracted via a segmentation procedure assessed in a previous study. The performance of the MCS have been compared with histological classification. Results indicated that with automatic segmented VOIs 90% of test-set lesions were correctly classified.

Keywords: breast DCE-MRI, multiple classification system, morphological and dynamic features.

1 Introduction

Breast cancer is the most common cancer among women in the Western world. To date it is the second leading cause of cancer death in women (after lung cancer) and is estimated to cause 15% of cancer deaths [2]. Therefore, screening for early diagnosis of breast cancer is of great interest.

The currently widespread screening method is RX mammography [1]. However, this method has some drawbacks: it uses ionizing radiation; it is not adequate for young women because of high density breasts; detection of breast lesions is difficult because of the lack of functional information, moreover no 3D information is available but the whole breast is projected on one or two planes. Although Magnetic Resonance Imaging (MRI) has some limitations such as long scanning time, cost, possible side effects of contrast media injection, the emerging methodology of Dynamic Contrast Enhanced-MRI (DCE-MRI) has

demonstrated a great potential in screening of high-risk women, in staging newly diagnosed breast cancer patients and in assessing therapy effects [2] thanks to its minimal invasiveness and to the possibility to visualize 3D high resolution dynamic (functional) information not available with conventional RX imaging.

Therefore MRI, and in particular DCE-MRI, is gaining popularity as an important complementary diagnostic tool for early detection of breast cancer [3].

In the analysis of breast lesions on MRI, radiologists agree that both *morphological* and *dynamic* features are important for distinguishing benign from malignant [6,5]. On the one hand, morphological features aim to quantify lesion margins characteristics, and are well assessed in the breast-MRI lexicon [6]: round shape and smooth margin for the benign lesions; more irregular shape for the malignant lesions. On the other hand, dynamic features, have shown a great potential in quantifying vascularity of tumors: malignant lesions usually show early enhancement with rapid wash out, whereas benign lesions typically show a slow increase followed by persistent enhancement [6].

Many recent works have attempted to take advantage of morphological features and dynamic information in a separate manner: dynamic information has been used for segmentation of volume of interests (VOIs) [13,12,11], while morphological features of the VOIs have been used for lesion classification [10,7,6]. For example, Nie et al. [4] demonstrated that quantitative analysis of morphology and texture features of breast lesions was feasible, and these features could be selected by artificial neural network to form a classifier for differential diagnosis. Agner et al. [9] showed that using a probabilistic boosting tree (PBT) classifier in conjunction with textural kinetic features good performances could be yielded but when the feature set included both textural kinetic and morphologic features the performances were lower. Tzacheva et al.[8] reported good performances using morphological features and MLP classifier on 14 breast lesions; Zheng et al. [10,18] has investigated the use of a feature set comprising dynamic, spatial, and morphological features with a linear classifier on 31 subjects.

To the best of our knowledge, a Multiple Classification System for classification of breast lesions using dynamic and morphological features in DCE-MRI has not been presented yet, although the idea of combining multiple classifiers is not new. For example, Keyvanfard et al. [21] proposed a multi classifier system composed of three classifiers that used dynamic features to classify breast lesion in DCE-MRI, but in their study morphological features were not used.

The aim of the present study is to propose a Multiple Classification System (MCS) for classification of breast lesions using both dynamic and morphological features in DCE-MRI.

The proposed MCS combines the results of two classifiers trained with dynamic and morphological features respectively. As classifiers, we used the best suited for the problem at hand, according to our previous studies [16].

Twenty-one malignant and seventeen benign breast lesions, histologically proven, were analyzed. Volumes of Interest (VOIs) have been both manually extracted by an expert radiologists and automatically extracted via a segmentation procedure assessed in a previous study. Both dynamic and morphological

features were extracted. The performance of the MCS have been compared with histological classification.

The paper is organized as follows: in section 2.1 we describe the characteristics of the subjects enrolled in the study; in section 2.2 we give details on the data acquisition via DCE-MRI; in section 2.3 we show how the volumes of interest (VOIs) have been selected manually and automatically; in section 2.4 we illustrate the main characteristics of the features used; in section 2.5 we present the proposed multiple classifier system: in particular we summarise the characteristics of the classifiers used, together with the classifiers for dynamic features and morphological features respectively and the combination scheme. We subsequently report the performances of the system proposed in section 3 and finally we compare our results to the literature in section 4.

2 Materials and Methods

2.1 Patients Selection

38 women (average age 46 years, range 16-69 years) with benign or malignant lesions histopathologically proven were enrolled. 21 lesions were malignant and 17 were benign. The lesions were subdivided in two groups: training-test (12 benign and 16 malignant) and test-set (5 benign and 5 malignant).

2.2 Data Acquisition

The patients underwent imaging with a 1.5 T scanner (Magnetom Symphony, Siemens Medical System, Erlangen, Germany) equipped with breast coil. Turbo spin echo T2-weighted axial images (TR/TE: 4000/56 ms; flip angle: 180 degrees; field of view 340 x 340 mm x mm; matrix: 384 x 385; thickness: 2 mm; gap: 0; 56 slices spanning entire breast volume) and Turbo spin echo T1-weighted fat sat axial images (TR/TE: 564/12 ms; flip angle: 90 degrees; field of view 350 x 350 mm x mm; matrix: 512 x 256; thickness: 2 mm; gap: 0; 40 slices spanning entire breast volume) were acquired for morphological imaging.

DCE T1-weighted FLASH 3-D coronal images were acquired (TR/TE: 9.8 / 4.76 ms; flip angle: 25 degrees; field of view 330 x 247 mm x mm; matrix: 256 x 128; thickness: 2 mm; gap: 0; acquisition time: 56 s; 80 slices spanning entire breast volume). One series was acquired before and 9 series after intravenous injection of 2 ml/kg body weight of a positive paramagnetic contrast medium (Gd-DOTA, Dotarem, Guerbet, Roissy CdG Cedex, France). Automatic injection system was used (Spectris Solaris EP MR, MEDRAD, Inc., Indianola, PA) and injection flow rate was set to 2 ml/s followed by a flush of 10 ml saline solution at the same rate.

2.3 VOI Segmentation

Manual. Manual ROI selection slice-by-slice was performed by an expert radiologist taking into account both morphological (Turbo spin echo T2- and T1

weighted images) and functional imaging (DCE T1 weighted images) based on the fat-suppressed image obtained subtracting the basal pre-contrast image from the 5-th post-contrast image. Per each patient all the slices including the lesion have been used. The segmentation was performed with OsiriX v.3.8.1 (fig. 1).

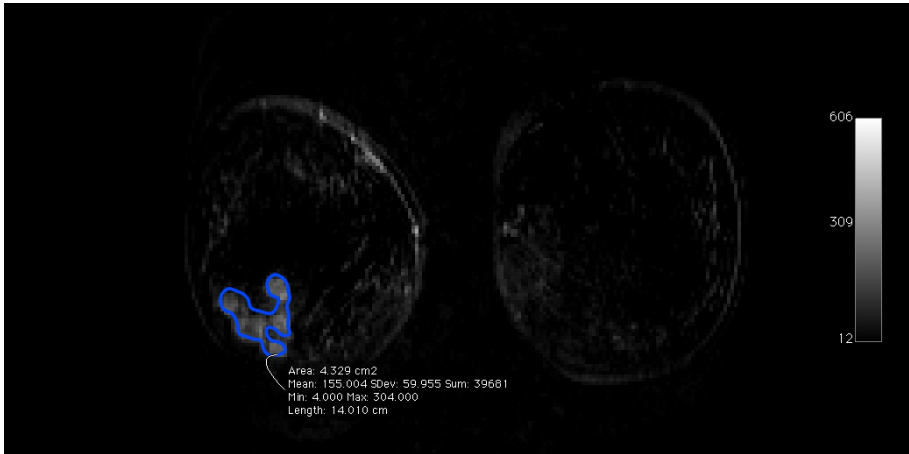


Fig. 1. Manual Segmentation

Automatic. In automatic selection the first step was the overall breast mask segmentation by means of Otsu thresholding of the parametric map obtained considering the pixel-by-pixel SOD followed by hole-filling and leakage removal by means of morphological operators as in a previous study [15]. Successively, **automatic** VOI segmentation has been obtained with pixel by pixel classification of dynamic features by using an MLP classifier.

The dynamic features used in the classification were sum of intensities difference (SOD), basal signal and relative enhancement slope calculated pixel by pixel on the breast mask: they were used as input of MLP classifier (learning rate = 0.3, momentum = 0.2, and a training time of 100 epochs). The classifier labeled each pixel as *suspicious* or *not suspicious*. The region of interest was obtained by the union of all suspicious pixels.

2.4 Morphological and Dynamic Features

Starting from our previous studies [16,17], we considered a feature set including 54 morphological features and 98 dynamic features, respectively.

The main categories of morphological features included areas, circularity, compactness, complexity, perimeter, radial length, smoothness, roughness, sphericity, eccentricity, volume, rectangularity, solidity, spiculation, convexity, curvature, edge [10,7,6]. For dynamic features the main categories included area, maximum intensity ratio, relative enhancement, relative enhancement slope, basal signal, perfusion index, sum of intensities difference (SOD), wash-in, wash-out, time to peak [13,12,11].

It is well known that training machine learning classifiers with large numbers of morphological features can lead to classifier overfitting, reduces the generalization capabilities of the classifiers and slows down the training process. Therefore, the number of morphological and dynamic features were reduced by a feature selection procedure to remove the unimportant and uninformative morphological features. To keep the loss of information to a minimum we tested Correlation-based Feature Selection (CFS) and Consistency feature Selection method with several search: the forward search, the backward search, the bidirectional search, the greedy search, feature ranking methods.

The dynamic features obtained by selection procedure were the sum of intensities difference (SOD), basal signal and relative enhancement slope [13,12,11].

The morphological features obtained by the selection procedure were instead area, eccentricity, compactness and perimeter.

The classifiers were trained with the morphological and dynamic feature extracted both by manual that automatic VOI segmentation.

2.5 VOI Classification

The proposed Multiple Classifier System combines the results of two classifiers trained separately with dynamic and morphological features respectively (fig. 2): in particular it was considered the weighted sum of probability of malignity and the probability of benignity of the two chosen classifiers as proposed in [20].

The choice of the classifier to be used was based on a previous study [16], where a Decision Trees (DT) and a Bayesian classifier gave us the best results when trained on morphological and dynamic features, respectively.

In order to combine the results of the two classifiers, each suspicious pixel within the VOI has been first classified as *benign* or *malignant* on the basis of the selected dynamic features. The whole VOI has been then classified as malignant if the number of malignant pixels n_m within the VOI was higher than that of benign pixel n_b within the same VOI.

The probabilities of malignant lesion (D_m) and benign lesion (D_b) were calculated as eq. 1:

$$\begin{aligned} D_m &= \frac{n_m}{N} \\ D_b &= \frac{n_b}{N} \end{aligned} \quad (1)$$

where N is the total number of pixels in the lesion.

Morphological features were instead calculated for the whole VOI and were used to classify the lesion in malignant and benign. In this case the probability of malignity and benignity were M_m and M_b respectively.

Finally, the VOI was classified as malignant if $\alpha D_m + \beta M_m > \alpha D_b + \beta M_b$, where α and β were multiplicative coefficients ($\alpha + \beta = 1$) that must be suitably chosen in order to maximize the accuracy (fig. 2). In [20], a leave-one-out procedure is suggested.

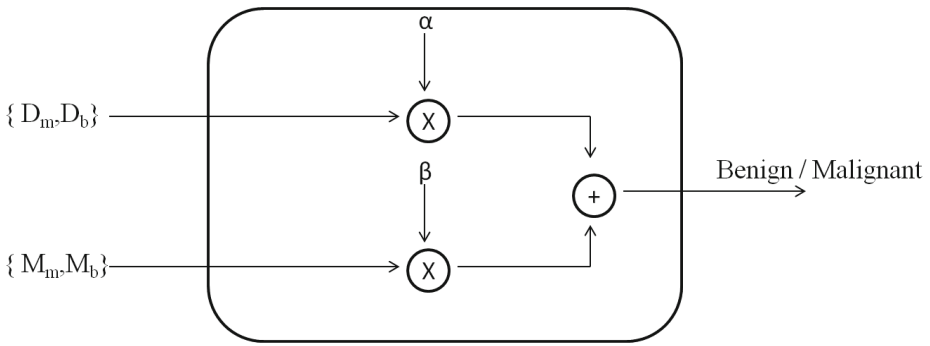


Fig. 2. Multiple Classifier System

3 Results

The results were reported for automatic VOI segmentation that have obtained the better findings. Table 1 shows the results obtained on the test set (10 patients) by the single classifiers that use dynamic and morphological features, respectively. Table 2 reports the performance obtained on the test set (10 patients) by our multiple classifiers system, using automatic VOI segmentation. The acronyms used in this table are the following: MC = Classifier trained with morphological feature; DC = Classifier trained with dynamic feature.

As far as the choice of optimal values for α and β is concerned we report in fig. 3 the percentage of correctly classified lesions vs. α . It is worth to notice that

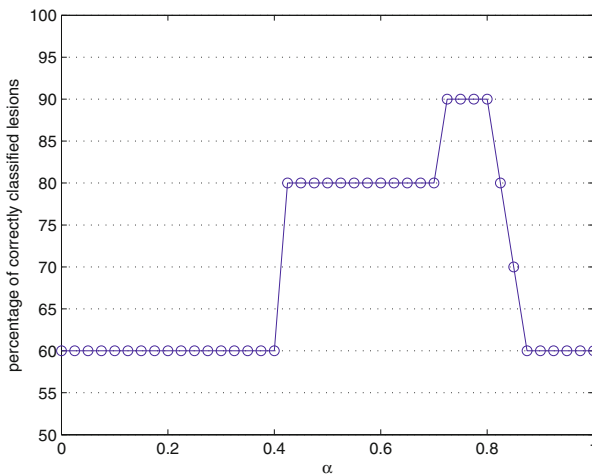


Fig. 3. Performances of the proposed MCS vs α

Table 1. Performance on the test set obtained by the single classifiers

Classifier	Feature	accuracy[%]
Bayes	Dynamic	80.00
DT	Morphological	60.00

Table 2. Performance obtained by the proposed method on the test set

MC	DC	α	β	accuracy[%]
DT	BC	0.75	0.25	90.00

there is an interval ($[0.7, 0.8]$) of values in which high performance can be obtained. The best compromise among sensitivity, specificity and overall accuracy resulted in $\alpha = 0.75$.

4 Discussion and Conclusions

The aim of this study was to propose a Multiple Classifier System (MCS) for classifying breast lesions in Dynamic Contrast Enhanced-Magnetic Resonance Imaging (DCE-MRI).

The proposed MCS combines the results of two classifiers trained with dynamic and morphological features respectively.

Twenty-one malignant and seventeen benign breast lesions, histologically proven, were analyzed. Volumes of Interest (VOIs) have been both manually extracted by an expert radiologists and automatically extracted via a segmentation procedure assessed in a previous study [15]. Both dynamic and morphological features were extracted. The performance of the MCS have been compared with histological classification.

In our previous studies [16] and [17] we analysed the performance of several classifiers (MLP, SVM, Bayes, DT) in conjunction with dynamic and morphological features separately. We observed that manual or automatic selection of the VOI affected the overall performance. In particular, when manual ROIs have been used, higher performance have been obtained (dynamic features with a DT classifier gave 70% accuracy; morphological features with Bayes gave 90% accuracy) with respect to those reported in this paper (dynamic features with DT gave 60% accuracy; morphological features with Bayes gave 80% accuracy), where automatic ROIs segmentation has been performed. This notwithstanding, by suitably combining the two classifiers, we were able to obtain the same results (90% accuracy) obtained by the best single classifier that uses manually extracted VOIs.

The findings of this study are in line with recent literature. In fact, Wedegrtner et al [19] reported a sensitivity of 85% using morphological features and a receiver operating characteristic (ROC) curve for 62 breast lesions but without automatic classification; Tzacheva et al. [8] reported a sensitivity of 90%, a specificity of 91% and an accuracy of 91% using morphological features and

MLP classifier on 14 breast lesions. However, these result must be carefully considered because of the small number of patients and because they did not use an automatic segmentation step. Zheng et al [18] reported a sensitivity of 95% using a combination of temporal, spatial, and morphological attributes and a linear classifier for 31 subjects: even in this study the segmentation step was not completely automatic.

It should be noticed that although previous studies obtained in some cases higher accuracy in comparison to our findings, however, they did not employ a completely automatic multi-classifier system such as the system presented in the present study.

Moreover, further investigation is required for an optimal choice of α and β because as is clear from fig. 3 the specific value could affect the overall accuracy of the system.

In the future, our preliminary study will be extended on a larger number of patients, manual segmentation will be done by multiple readers and morphological, dynamic and texture [7] feature combination will be performed

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