

STEP: SPATIAL-TEMPORAL ENHANCEMENT PATTERN, FOR MR-BASED BREAST TUMOR DIAGNOSIS

Yuanjie Zheng, Sarah Englander, Mitchell D. Schnall, Dinggang Shen

Department of Radiology, University of Pennsylvania, Philadelphia, PA 19104, USA

ABSTRACT

This paper demonstrates the importance of capturing Spatial-Temporal Enhancement Pattern (STEP) for completely characterizing breast tumor in contrast-enhanced MR images. STEP captures not only the dynamic enhancement and architectural features of tumor, but also the spatial variations of pixel-wise temporal enhancement of tumor. Although the latter has been widely used by radiologist during diagnosis, it is rarely considered as important features for computer-aided tumor diagnosis. Notice that, by regarding serial contrast-enhanced images as a single spatial-temporal image, STEP can capture all types of the features within a single framework. In particular, a Fourier transformation is used to extract various temporal enhancement features, followed by moment invariants to capture spatial patterns of each temporal enhancement feature. Experimental results show the better performance of our designed STEP features than many other features available in the literature. The area under ROC curve can reach 0.96 with our STEP features in tumor diagnosis.

Index Terms— Feature extraction, Breast tumor diagnosis, Magnetic resonance imaging

1. INTRODUCTION

Breast magnetic resonance (MR) imaging is emerging as an important complementary diagnostic tool for early detection of breast cancer [1]. Contrast-enhanced MR images show better distinctions between malignancy and benignancy due to their different vascularity and capillary permeability. The main advantage of breast MR imaging lies in its high sensitivity to contrast material enhancement, although its specificity is relatively low [2].

Malignant and benign lesions behave differently in terms of temporal enhancement and spatial structure. For example, *temporally*, malignant lesions usually show early strong enhancement with rapid wash out, whereas benign lesions behave typically a slow increase followed by persistent enhancement [3]. *Spatially*, spiculated border and irregular shapes are important predictors of malignancy, whereas smooth border is more often associated with benignancy [1]. In addition, the spatial variations of pixel-wise temporal enhancements (TE) also show differences between malignancy and benignancy. For example, heterogenous and peripheral internal en-

hancements are important evidence of malignancy, whereas homogenous enhancements are often characterized by benignancy [1].

Dynamic and architectural features of tumor [3, 1, 4, 2, 5] are two main types of features applied in tumor diagnosis. They respectively characterize TE properties and spatial structures of tumor. Dynamic features are typically extracted by averaging a region of interest over the most intensity enhancing part of the tumor on the early pose contrast scans. Architectural features are derived from the spatial tumor region. These indicates that the spatial variations of TE is not accounted for in them, which might affect the overall diagnostic performance. It is generally agreed that the combination of the two different features [3, 1, 6] can further improve the diagnostic performance.

There are various ways to account for spatial variations of TE, however, all of them have limitations. For instance, the tumors were rated manually by experts as homogenous, heterogenous, or being rim in [6, 3, 1]. Unfortunately, manual rating suffers from the inter- and intra- observer variability, and also limits its application in automated tumor diagnosis. Moreover, qualitative rates cannot be as detailed as quantitative ones. On the other hand, although quantitative measures can be accomplished, i.e., using Gilhuijs *et al's* two features including variance of uptake and change in variance of uptake [2], or Chen *et al's* enhancement-variance dynamics features [7], they are relatively simple and much information about the spatial variation of TE is not captured.

In this paper, we propose to extract Spatial-Temporal Enhancement Pattern (STEP) for completely capturing all features about tumor, including TE, spatial structure, and spatial variation of pixel-wise TE. By regarding serial contrast-enhanced images as a single spatial-temporal image, STEP can be captured by many spatial-temporal analysis methods. In this study, we particularly propose using a Fourier transformation to extract various temporal enhancement features, and moment invariants to characterize spatial patterns of each temporal enhancement feature. The experimental results show the better performance of using the proposed STEP features for tumor diagnosis, compared to many features available in the literature.

2. MATERIAL AND METHOD

2.1. Image and Patient Data

Images used in this study were acquired with patients prone in either a 1.5T scanner (Siemens Sonata) or a 3T scanner (Siemens Trio) with use of a dedicated surface breast coil array. The imaging protocol included bilateral fat suppressed T2 weighted images in the sagittal plane and a slab interleaved 3D fat suppressed spoiled gradient echo prior to and after the injection of contrast. A rapid bolus injection of 0.1 mmol/kg Gadopentetate dimeglumine (Omniscan; GE health, NJ) followed by a 10 ml saline flush was administered in all cases. Sequential post contrast acquisitions were acquired for approximately 6 minutes following contrast injection. The spoiled gradient echo sequence had a minimum spatial resolution of 20 cm over a 512×256 matrix and a minimum time of 90 seconds in the sagittal plane and slice thickness of a $2 \sim 3.5$ mm. One slice can contain either 384×384 pixels of $0.47 \times 0.47\text{mm}^2$, or 512×512 pixels of $0.35 \times 0.35\text{mm}^2$, or 896×896 pixels of $0.22 \times 0.22\text{mm}^2$, depending on the scanners or protocols used. In total, there are 31 subjects used in our experiments, including 22 malignant and 9 benign cases diagnosed by a surgical biopsy procedure as gold standard.

2.2. Methods

2.2.1. Segmentation

The tumors were manually delineated by an experienced radiologist in breast cancer. In this study, for each tumor, a 2D slice with the most obvious tumor and the largest tumor area is selected. Therefore, we finally have 31 samples, each having serial 2D contrast-enhanced images, to train and validate our designed tumor diagnosis system.

2.2.2. Features

Each tumor sample is normalized to have similar size before computing various STEP features, since tumor size seems to be not related to the malignancy or benignancy of tumor according to literature. To achieve this, the eigenvectors of covariance matrix related to the distribution of pixels in each 2D tumor sample are first computed. Then, the 2D tumor sample is rotated by matching its eigenvectors with the predefined axes in the XY plane. Also, it is further rigidly scaled according to the relative value of its ‘larger eigenvalue’ to the predefined size, thus making all samples finally have the same ‘larger eigenvalue’ after normalization. Fig. 1 shows some malignant and benign tumor samples before and after normalization.

From each normalized tumor sample, STEP features are calculated. In particular, for each tumor sample with T serial contrast-enhanced images, Discrete Fourier Transformation (DFT) is first used to capture T Fourier coefficients from 1D TE curve of each pixel in the tumor. Then, moment invariants are utilized to capture the spatial variation pattern of each Fourier coefficient. The details of this STEP feature extraction method are provided next.

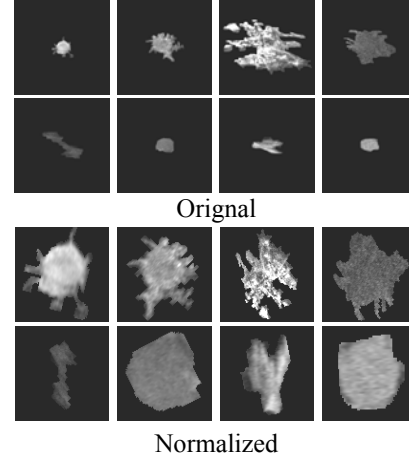


Fig. 1. Tumor samples before and after normalization. For each panel, the top row is malignant, while the bottom row is benign.

The TE is given by:

$$C(x, y, t) = \frac{I(x, y, t) - I(x, y, 0)}{I(x, y, 0)}, t = 1, \dots, T - 1 \quad (1)$$

where (x, y) index the pixels in a 2D tumor image, t means the scanning time, and $I(x, y, t)$ denotes the intensity at position (x, y) and time t .

DFT coefficients are used to completely capture the temporal enhancement features of TE signals on each pixel. We believe, for tumor diagnosis, complete features should be extracted to allow a pattern classification method to determine the important features for classification. Otherwise, some important features might be discarded in the very beginning, i.e., based on so called experiences or a priori knowledge. Fig. 2 shows the maps of the first DFT coefficient, corresponding to the images shown in Fig. 1, respectively.

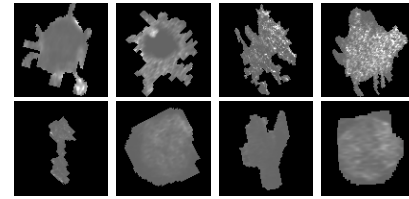


Fig. 2. Maps of the first DFT coefficient, corresponding to the tumor samples shown in Fig. 1.

We select Hu’s seven moment invariants [8] to capture spatial pattern of each DFT coefficient map, although other invariant features can be similarly applied. Notice that these seven features are rotation invariant. That means, the same tumor will have same features, even it is differently positioned in the scanning process. As detailed in [8], Hu’s seven moment invariants are defined as polynomial equation of scale-normalized centralized moments, η_{pq} , which are explained next.

Two-dimensional centralized moments of a $M \times N$ DFT coefficient map $f(x, y)$ around tumor is given as,

$$m_{pq} = \sum_{x=1}^N \sum_{y=1}^M (x - \bar{x})^p (y - \bar{y})^q f(x, y) \quad (2)$$

where

$$\bar{x} = \frac{\sum_{x=1}^N \left(x \sum_{y=1}^M f(x, y) \right)}{\sum_{x=1}^N \sum_{y=1}^M f(x, y)}$$

and

$$\bar{y} = \frac{\sum_{y=1}^M \left(y \sum_{x=1}^N f(x, y) \right)}{\sum_{x=1}^N \sum_{y=1}^M f(x, y)}.$$

The two dimensional scale-normalized centralized moment η_{pq} is defined as:

$$\eta_{pq} = m_{pq} / m_{00}^\gamma \quad (3)$$

where $\gamma = (p + q) / 2 + 1, \forall (p + q) \geq 2$.

Note that $f(x, y)$ for background pixels is always zero in equation (2).

Using definitions given in [8], we compute $H = 7$ moment invariants from each of T DFT coefficient maps. Finally, $H \times T$ STEP features are obtained for each tumor. Notice that, if using higher order moment invariants derived in the literature [9, 8], we can have more STEP features.

Fig. 1 and Fig. 2 show that malignant and benign lesions differ in shapes, margins, enhancements, and spatial variations of enhancement. For example, larger spatial variations of enhancement are related to malignancy. All of this information will be captured by STEP features.

2.2.3. Features Selection and Classification

It is worth noting that not all $H \times T$ STEP features are useful for tumor diagnosis. Some of them might be confounding or irrelevant to diagnosis. Therefore, it is important to use a feature selection method to select a best set of features for tumor diagnosis.

In this paper, a hybrid feature selection proposed in [10] is employed. It involves ranking the features by a Pearson correlation based bagging strategy, and applying the SVM-RFE algorithm [11] on a subset of the features after the most irrelevant features are removed according to the ranking. SVM-RFE algorithm can find a subset of features, which optimizes the performance of the classifier.

Support vector machine (SVM) [12] is selected for classification because it is regarded as one of the best pattern classifiers available in literature. Gaussian radial basis function is employed as the kernel.

Leave-one-out cross-validation is used in the classification process. It involves using a single subject from the original data as the validation data, and the remaining subjects as the training data. This is repeated such that each subject is used once as the validation data.

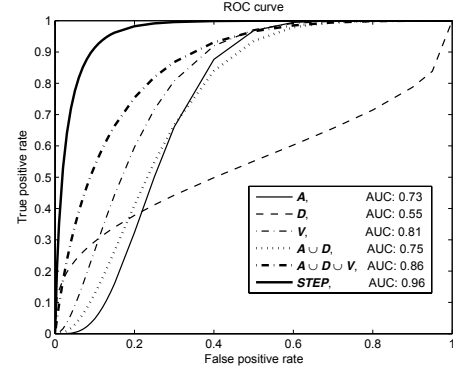


Fig. 3. ROC curves for the uses of different sets of features for tumor classification, along with their corresponding AUC values.

3. RESULTS

To compare the performances of our STEP features with general dynamic and architectural features in tumor diagnosis, we select some existing features which were shown effective in the literature.

For the dynamic features, we select the standard deviation of enhancement (D_1), maximum washout (D_2) [13], the maximum uptake (D_3), uptake rate (D_4), washout rate (D_5) [7], and the two features (D_6) and (D_7) extracted from the enhancement curve modelled by the Hayton-Brady pharmacodynamic model in [14]. Notice that the dynamic features are all computed from the average intensities over the tumor area at every time point.

For the architectural features, we select the compactness (A_1) [13], circularity (A_2) [7], irregularity (A_3), eccentricity (A_4), rectangularity (A_5), and entropy of radial length distribution (A_6) [5].

The features that can account for spatial variations of TE are the variance of uptake (V_1), change in variance of uptake (V_2), margin gradient (V_3), variance of margin gradient (V_4), variance of radial gradient histogram (V_5) [2], the maximum variation of enhancement (V_6), the enhancement-variance increasing rate (V_7), the enhancement-variance decreasing rate (V_8), and the enhancement-variance (V_9) at the first post-contrast frame [7].

We use $A = \{A_1, A_2, \dots, A_6\}$, $D = \{D_1, D_2, \dots, D_7\}$, and $V = \{V_1, V_2, \dots, V_9\}$ to denote the three different types of features, respectively. The classification performances of each of these three types of features $\{A, D, V\}$, each of their two combinations $\{A \cup D, A \cup D \cup V\}$, and the STEP features are compared using the same feature selection and leave-one-out technique based classification procedure. The fitted receiver operating characteristics (ROC) curves and their areas under the curves (AUC) are depicted in Fig. 3. The best classification accuracy and corresponding sensitivity & specificity values are listed in Table 1.

By combining general dynamic and architectural features

Feature	Accuracy(%)	Sensitivity	Specificity
A	83.9	0.95	0.56
D	71.0	0.95	0.11
V	83.9	0.91	0.67
$A \cup D$	83.9	0.95	0.56
$A \cup D \cup V$	87.1	0.95	0.67
STEP	93.6	1.00	0.78

Table 1. The best classification accuracy, along with corresponding sensitivity and specificity, for different sets of features used in tumor diagnosis.

($A \cup D$) for tumor diagnosis, the AUC value is improved a little, compared to the cases of using these two features independently. However, the best classification accuracy is not improved, compared to the case of using architectural features (A) alone. Notice that the spatial variation of contrast is very important in distinguishing between malignant and benign lesions. The combination of this type of features with dynamic and architectural features ($A \cup D \cup V$) significantly improves the AUC value, classification accuracy and specificity. This result shows that TE, architectural structure, and spatial variation of TE all play an important role in distinguishing between malignant and benign lesions.

Obviously, the STEP features performed best in all experiments. The AUC value, classification accuracy, sensitivity and specificity all show significant improvement.

Only 3 STEP features were elected by feature selection, which are the 6th moment invariant of the 2nd DFT coefficient map, the 1st moment invariant of the 1st DFT coefficient map, and the 2nd moment invariant of the 4th DFT coefficient map, respectively.

4. CONCLUSION

The tumor properties, including temporal enhancement, architectural structure, and spatial variations of pixel-wise temporal enhancement (TE) within a tumor area are all important in distinguishing between malignant and benign lesions. However, in most computer-based diagnosis algorithms, features capturing these properties are intuitively defined, which may result in loss of some useful discriminating information due to the limitation of the observers. On the other hand, the previously proposed features for spatial variation of TE are very simple, thereby limiting the extraction of more complex variations.

Accordingly, we have proposed a framework of extracting Spatial-Temporal Enhancement Pattern (STEP) for completely characterizing tumor. Although a particular method has been proposed in this study, i.e., using DFT to capture pixel-wise temporal enhancement features and Hu's seven moment invariants to describe the spatial pattern of each DFT-based enhancement feature, other advanced spatial-temporal analysis methods are also applicable. For effective tumor diagnosis using SVM, it is important to employ an effective feature selection method (with cross-validation) to select a best

set of features for classification. This study shows that the extracted features should be as rich as possible, and the importance of each feature in classification should be determined by a combined feature selection and classification method, not simply by a subjective or intuitive way as widely used in many breast tumor diagnosis algorithms. That is the reason why STEP features performed better than the combination of some existing features capturing all of the three properties of tumor in our experiments. The four STEP features selected by feature selection were best in our experiments, but they are not easy to be found through a subjective way.

5. REFERENCES

- [1] M.D. Schnall et al., "Diagnostic architectural and dynamic features at breast mr imaging: Multicenter study," *Radiology*, vol. 238, pp. 42–53, 2006.
- [2] K.G.A. Gilhuijs et al., "Computerized analysis of breast lesions in three dimensions using dynamic magnetic-resonance imaging," *Med Phys*, vol. 25, pp. 1647–1654, 1998.
- [3] B.K. Szabo et al., "Dynamic mr imaging of the breast: Analysis of kinetic and morphologic diagnostic criteria," *Acta Radiol*, vol. 44, pp. 379–386, 2003.
- [4] D.M. Ikeda, "Progress report from the american college of radiology breast mr imaging lexicon committee," *Magn Reson Imaging*, vol. 9, pp. 295–302, 2001.
- [5] C. Tanner et al., "Classification improvement by segmentation refinement: Application to contrast-enhanced mr-mammography," in *MICCAI'04*, vol. 3216.
- [6] B.K. Szabo et al., "Neural network approach to the segmentation and classification of dynamic magnetic resonance images of the breast: Comparison with empiric and quantitative kinetic parameters," *Acad Radiol*, vol. 11, pp. 1344–1354, 2004.
- [7] W. Chen et al., "Computerized interpretation of breast MRI: Investigation of enhancement-variance dynamics," *Med Phys*, vol. 31, pp. 1076–1082, 2004.
- [8] M.K. Hu, "Visual pattern recognition by moment invariants," *IRE Transactions on Information Theory*, pp. 179–187, 1962.
- [9] S. O. Belkasim et al., "Pattern recognition with moment invariants: A comparative study and new results," *Pattern Recognit*, pp. 1117–1138, 1991.
- [10] Y. Fan et al., "Classification of structural images via high-dimensional image warping, robust feature extraction, and svm," in *MICCAI'05*, 2005, pp. 1–8.
- [11] I. Guyon et al., "Gene selection for cancer classification using support vector machines," *Machine Learning*, vol. 46, pp. 389–422, 2002.
- [12] V. N. Vapnik, *The Nature of Statistical Learning Theory*, Springer, 1995.
- [13] C. Tanner et al., "Does registration improve the performance of a computer aided diagnosis system for dynamic contrast-enhanced mr mammography," in *ISBI'06*.
- [14] X. Chen et al., "Simultaneous segmentation and registration of contrast-enhanced breast MRI," in *IPMI'05*, vol. 3565.