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Using quantitative image analysis to classify axillary lymph nodes on breast MRI: A new application for the Z 0011 Era

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ABSTRACT

Purpose: To assess the performance of computer extracted feature analysis of dynamic contrast enhanced (DCE) magnetic resonance images (MRI) of axillary lymph nodes. To determine which quantitative features best predict nodal metastasis.
Methods: This institutional board-approved HIPAA compliant study, in which informed patient consent was waived, collected enhanced T1 images of the axilla from patients with breast cancer. Lesion segmentation and feature analysis were performed on 192 nodes using a laboratory-developed quantitative image analysis (QIA) workstation. The importance of 28 features were assessed. Classification used the features as input to a neural net classifier in a leave-one-case-out cross-validation and evaluated with receiver operating characteristic (ROC) analysis.
Results: The area under the ROC curve (AUC) values for features in the task of distinguishing between positive and negative nodes ranged from just over 0.50 to 0.70. Five features yielded AUCs greater than 0.65: two morphological and three textural features. In cross-validation, the neural net classifier obtained an AUC of 0.88 (SE 0.03) for the task of distinguishing between positive and negative nodes.
Conclusion: QIA of DCE MRI demonstrated promising performance in discriminating between positive and negative axillary nodes.

1. Introduction

Breast MRI is often used in the clinical staging of patients with newly diagnosed breast cancer for defining extent of disease in the breast, detecting contralateral cancers [1], and detecting adenopathy. Axillary and internal mammary lymph nodes are readily detectable on MRI, and T2 weighted sequences and post-contrast dynamic sequences can both demonstrate the size and morphology of axillary lymph nodes. With these high-resolution sequences, the axillae can be viewed three dimensionally and a high level of anatomic detail is discernable. Such images are especially useful for determining architectural details of lymph nodes such as cortical size, morphology and the presence or absence of a fatty hilum (Fig. 1).

Quantitative image analysis (QIA) is an area of active research and includes rather well-established applications, such as computer-aided detection (CADe), and applications not yet available for everyday clinical use, such as computer-aided prognosis. Within radiology, and especially within the subspecialty of breast imaging, CADe has become mainstream for some imaging modalities and is often integrated within clinical workstations. On mammograms, CADe serves as a "second reader" and is used to detect masses and calcifications that could indicate the presence of invasive or in situ carcinoma [2].

In this paper, we investigate the potential of computer-aided prognosis through axillary lymph node assessment in breast MRI. Currently, most commercially available software is more limited in its abilities and performs volumetric assessment of defined lesions, which can aid in surgical planning. Similarly, in cases where the patient will receive neoadjuvant chemotherapy, comparison measurements performed before and after therapy can be used as an imaging biomarker for response [3]. The use of more sophisticated QIA for breast MRI, however, remains an area of active research both for tumor classification [4], and for staging and prognosis [5]. In previous research studies, promising performance was obtained using image-based biomarkers for computer analysis of breast lesions in MRI, whereby the computer performed segmentation, extraction of morphologic and kinetic characteristics (features), and

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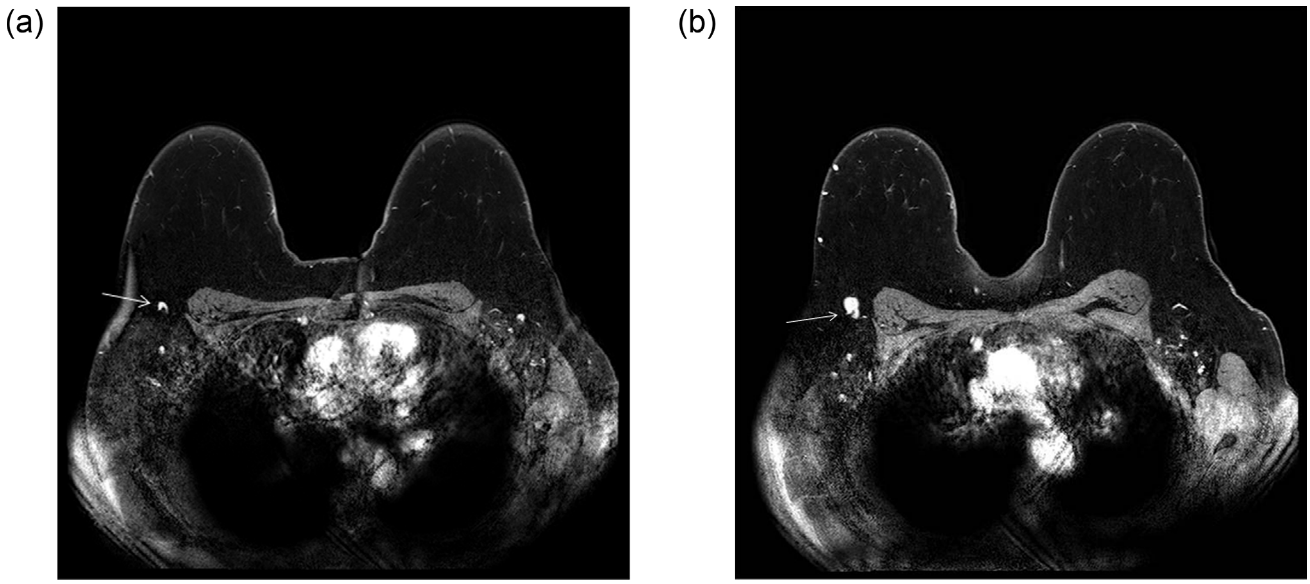

Fig. 1. (a) Normal morphology right axillary lymph node (arrow) on an axial post-contrast T1 fat saturated subtracted sequence. Note the normal appearing enhancement of the lymph node and normal appearance of the fatty hilum with density similar to the background fat. (b) Abnormal right axillary lymph node (arrow) on a post-contrast T1 fat saturated subtracted axial image: Enlarged nodal size and near complete loss of the fatty hilum are seen.

subsequent classification [6–9]. In this study, we investigated whether a QIA scheme utilizing a digital analysis of lymph nodes imaged on breast MRI is able to distinguish between lymph nodes that were positive for metastasis ('positive' nodes) and those that were negative for metastasis ('negative' nodes). In the future, such a scheme, if successful, could potentially help guide clinical management in the axilla.

2. Methods

This study was an institutional review board-approved, HIPPA compliant study, with waiver of informed consent. A retrospective review was performed on 66 cancer patients who underwent staging MRI at our institution between 2006 and 2010.

MR images were obtained by using 1.5 and 3.0 T systems depending on clinical availability. MRI was performed with a dedicated breast coil and the patient in the prone position (Table 1). Contrast material was injected IV (0.1 mmol/kg of gadodiamide [Omniscan, GE Healthcare]) and followed by a 20-mL saline flush at a rate of 2 mL/s. The same contrast material/protocol was used for all systems.

A database from 66 cancer patients was retrospectively collected for the assessment of QIA of axillary lymph nodes on MRI (Table 1). Analysis was performed on 154 negative lymph nodes and 38 positive lymph nodes, identified a posteriori by a board certified expert radiologist with 9 years of experience. Review of surgical pathology reports, radiology reports, and ultrasound images were used to establish the 'gold standard' of positivity or negativity for these lymph nodes. All axillary lymph nodes of the patients with negative sentinel lymph node biopsy were considered negative. All metastatic lymph nodes proven by ultrasound guided core needle biopsy were regarded as positive for metastasis. To correlate between the biopsy proven metastatic axillary LNs on ultrasound (US) and LNs shown on MRI, the same radiologist identified each metastatic axillary LN on MRI by comparing MR images with images from the US guided biopsy. When multiple lymph nodes (>8) were proven positive for metastasis at axillary lymph node dissection, highly suspicious lymph nodes on MRI (up to three lymph nodes per patient) were presumed positive for metastasis.

The methodology involved several steps which were all automated except for MR image acquisition (as detailed above) and the identification of the image locations of lymph nodes. The steps in the methodology not specific to the current application have been described extensively elsewhere [10,11] and are briefly summarized here for clarity. An expert board-certified radiologist identified the locations of axillary lymph nodes visible in the MR images. The lymph nodes were then automatically segmented) using a method previously developed for breast tumors [10]. Subsequently, computer-extracted MR-based features were calculated to characterize the lymph nodes. The feature set describing each node consisted of 28 features, including 5 kinetic curve assessment, 4 variance of kinetics, 14 enhancement texture, and 5 morphological features (Fig. 2a and Table 2). For the task of distinguishing between nodes positive for metastasis and those negative for metastasis, each feature was assessed individually to gain insight into which type of feature was relevant for this task. Subsequently, all features were used in combination through the use of a classifier to predict which nodes were positive and which were negative for metastasis. We used a Markov-Chain Monte-Carlo Bayesian Neural Net classifier [12] (MCMC-BNN) within leave-one-case-out cross-validation. Leave-one-case-out cross-validation is an accepted training and testing method with the aim to minimize database bias (overtraining) of a classifier. Here, for N cases, in each cross-validation a single case was assigned as the testing case and the remaining N-1 cases were used for classifier training. This process was repeated N times until all cases had served a test case.

Hence, the novel aspects of the current study included (a) the application of a 3D segmentation method, which was previously developed on breast tumors [10], for the segmentation of axillary lymph nodes (Fig. 2b), (b) the use of computer-extracted features (mathematical descriptors) to quantitatively characterize the nodes from MR image data [6–8,13], and (c) a neural network classifier to distinguish between nodes that were positive for metastasis and nodes that were negative for metastasis.

Performance was assessed both qualitatively – using box plots – and quantitatively using receiver operator characteristic (ROC) analysis with the area under the ROC curve (AUC) as the figure of merit [14,15]. The performance of individual features was assessed to gain insight into their relative importance for the