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Title: Advanced Computer-Aided Diagnosis and Prognosis for Breast MRI
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Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) of the breast has become an important tool in patient work-up for breast lesions. Computer-aided diagnosis (CADx) schemes using DCE-MRI have been developed to potentially improve the accuracy with which breast lesions are diagnosed as malignant or benign. However, there are other types of MRI protocols that may generate images that are useful in differentiating malignant from benign lesions. Furthermore, clinicians are concerned not only with the differential diagnosis of the breast lesion, but also with the patients' prognosis which is determined by considering various characteristics of malignant breast lesions.

The overall objective of this research was to expand the potential use of automated computerized analysis of breast MR images for clinical applications by (1) investigating multi-parametric imaging (T2-weighted MRI, high spectral and spatial (HiSS) MRI) to further improve the diagnostic accuracy of CADx and (2) extending automated computerized analysis from diagnostic classification to more complex classification with respect to prognosis. The overall hypothesis to be tested was that, by applying advanced pattern recognition and machine learning techniques, one can achieve efficient diagnostic classification on multi-parametric MR images as well as accurate prognostic classification for the purpose of generating informative prognostic DCE-MR image-based biomarkers for breast cancer.

The main contributions of this research work are summarized as follows: 1) We investigated the incorporation of computerized analysis of T2-weighted MRI images in a DCE-MRI CADx scheme for distinguishing malignant from benign breast lesions. The diagnostic performance of the combination of T2-weighted, T1-weighted DCE, and geometric features was significantly higher than performances using only geometric features, only T1-weighted DCE features, and only T2-weighted features. 2) Automated computerized analysis methods were applied to precontrast HiSS MR images to characterize morphology and evaluate the diagnostic utility of HiSS features. We did not find any statistically significant difference between the performance of HiSS features to that of T1-weighted DCE features, indicating that quantitative analysis of HiSS MRI could potentially provide sufficient information to distinguish benign from malignant lesions without administration of contrast agent. 3) We explored the capability of computerized analysis to characterize histological features of malignant breast lesions including invasiveness, lymph node metastasis, and tumor grade. Specifically, we generated prognostic MRI-based biomarkers by considering three prognostic classification tasks: (i) invasive lesions vs. non-invasive lesions; (ii) lesions with positive lymph nodes vs. lesions with negative lymph nodes, and (iii) Grade 3 lesions vs. Grade 2 lesions vs. Grade 1 lesions. We found that MRI-extracted morphological and kinetic features can accurately distinguish multiple prognostic characteristics of malignant lesions. Additionally, we demonstrated that *N*-class Bayesian artificial neural networks (BANN) can be applied to the three-class tumor grade classification task with similar performance results to the two-class BANN; however, we did not observe any statistically significant difference. 4) We implemented and evaluated different survival prediction methods that integrated the prognostic MRI-based biomarkers (probability of being invasive, probability of being lymph node positive, and probability of being Grade 3). The prognostic image-based biomarkers showed accuracy in survival prediction across two different survival prediction methods (BANN and Cox proportional hazards model) and performed better than using the lesion features directly in survival classification, demonstrating the potential for useful survival information in the integration of the generated prognostic image-based biomarkers.

The results affirm the main hypothesis of this research work. The significance of this research is that it extends automated computerized analysis of breast lesions from DCE-MRI CADx to multi-parametric MRI CADx and prognosis classification. This research provides an effective and accurate computerized scheme that has potential to help radiologists in achieving an improved characterization of breast lesions for the purposes of breast cancer diagnosis and prognosis.