Using Convolutional Neural Networks for Enhanced Capture of Breast Parenchymal Complexity Patterns Associated with Breast Cancer Risk

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Rationale and Objectives: We evaluate utilizing convolutional neural networks (CNNs) to optimally fuse parenchymal complexity measurements generated by texture analysis into discriminative meta-features relevant for breast cancer risk prediction.

Materials and Methods: With Institutional Review Board approval and Health Insurance Portability and Accountability Act compliance, we retrospectively analyzed "For Processing" contralateral digital mammograms (GE Healthcare 2000D/DS) from 106 women with unilateral invasive breast cancer and 318 age-matched controls. We coupled established texture features (histogram, co-occurrence, run-length, structural), extracted using a previously validated lattice-based strategy, with a multichannel CNN into a hybrid framework in which a multitude of texture feature maps are reduced to meta-features predicting the case or control status. We evaluated the framework in a randomized split-sample setting, using the area under the curve (AUC) of the receiver operating characteristic (ROC) to assess case-control discriminatory capacity. We also compared the framework to CNNs directly fed with mammographic images, as well as to conventional texture analysis, where texture feature maps are summarized via simple statistical measures that are then used as inputs to a logistic regression model.

Results: Strong case-control discriminatory capacity was demonstrated on the basis of the meta-features generated by the hybrid framework (AUC = 0.90), outperforming both CNNs applied directly to raw image data (AUC = 0.63, $P < .05$) and conventional texture analysis (AUC = 0.79, $P < .05$).

Conclusions: Our results suggest that informative interactions between patterns exist in texture feature maps derived from mammographic images, which can be extracted and summarized via a multichannel CNN architecture toward leveraging the associations of textural measurements to breast cancer risk.

Key Words: Digital mammography; breast cancer risk; convolutional neural network; parenchymal texture.

INTRODUCTION

The stratification of breast cancer risk levels is becoming increasingly important and is rapidly evolving beyond the "one-size-fits-all" approach in breast cancer screening to personalized regimens tailored by individual risk profiling (1,2). Starting from the pioneering work of Wolfe (3), studies have consistently shown an association of the breast parenchymal complexity (ie, the distribution of fatty and dense tissues) on breast images with levels of breast cancer risk. In particular, full-field digital mammography (FFDM), which is routinely used for breast cancer screening (4), has demonstrated substantial potential in providing novel quantitative imaging biomarkers related to breast cancer risk. Mammographic density is one of the strongest risk factors for breast cancer (5,6), while studies increasingly support significant associations of breast cancer risk with mammographic texture descriptors (7–9), which reflect more refined, localized characteristics of the breast parenchymal pattern.

In early studies investigating the role of mammographic texture in breast cancer risk assessment (10–14), textural measurements have been estimated within a single region of interest (ROI) in the breast. In an attempt to provide more granular texture estimates, more recent studies have proposed sampling the parenchymal tissue through the entire breast for subsequent texture analysis (15–17). For instance, in a recently

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proposed lattice-based strategy (15), each texture descriptor is calculated within multiple nonoverlapping local square ROIs through the breast, and texture measurements are then averaged over the breast regions sampled by the lattice. In a preliminary case-control evaluation (15), the lattice-based texture features were shown to outperform state-of-the-art features extracted from the retroareolar or central breast region, thereby suggesting that enhanced capture of the heterogeneity in the parenchymal texture within the breast may also improve the associations of texture measures with breast cancer risk. However, by averaging regional texture values, important information about the overall parenchymal tissue complexity might be still missed and, therefore, an improved fusion approach, which retains richer information about texture variability over the breast, might leverage the potential of such granular texture measurements provided by multiple ROIs.

Convolutional neural networks (CNNs) and "Deep Learning" technology (18,19) are able to automatically generate hierarchical representations useful for a particular learning task via neural networks with multiple hidden layers. In the last few years, CNNs have demonstrated a remarkable impact on medical image analysis (20,21), and they are now gaining increasing attention in applications with digital mammography, including primarily mass or lesion detection and characterization (22–25). However, their potential in breast cancer risk prediction remains largely unexplored, with only a few studies having used CNNs to relate mammographic patterns to breast cancer risk (26,27) or breast density (28). Moreover, although CNNs have been primarily applied to raw imaging data, they may also have value as efficient feature-fusion techniques, especially in cases when conventional feature summarization approaches may have limitations.

In this study, we employ a multichannel CNN architecture to fuse parenchymal texture feature maps into discriminative *meta-features* relevant for breast cancer risk prediction. The rationale is that CNNs can also be used as a high-level approach to effectively summarize high-dimensional patterns resulting from handcrafted features such as texture descriptors, for which conventional feature summarization or dimensionality reduction approaches may be limited in capturing the available rich information. Our hypothesis, therefore, is that by capturing sparse, subtle interactions between localized patterns present in texture feature maps derived from mammographic images, a multitude of textural measurements can be optimally reduced to meta-features capable of improving associations with breast cancer. We assess our hypothesis by evaluating these meta-features in a case-control study with digital mammograms, and we also compare their performance to the performances of conventional texture analysis and CNNs when fed directly with raw mammographic images.

MATERIALS AND METHODS

Study Dataset

In this Institutional Review Board-approved, Health Insurance Portability and Accountability Act-compliant study under a waiver of consent, we retrospectively analyzed a case-control dataset of raw (ie, "FOR PROCESSING") mediolateral oblique view digital mammograms previously reported (15,29). Briefly, the cases included women diagnosed with biopsy-proven unilateral primary invasive breast cancer ($n = 106$) at age 40 years or older, recruited by a previously completed, Institutional Review Board-approved, multimodality breast imaging trial (2002–2006; NIH CA85484), in which all women had provided informed consent. For the cases, the contralateral images were analyzed (ie, images from the unaffected breast) as a surrogate for inherent breast tissue properties associated with high breast cancer risk, as done in prior case-control studies of mammographic pattern analysis (15,29–31). Controls were randomly selected from the eligible population of women seen for routine screening over the closest possible overlapping time period at the same institution, and had negative breast cancer screening and confirmed negative 1-year follow-up. Controls were age-matched to cases on 5-year intervals at a 3:1 ratio ($n = 318$), yielding a total sample size of 424.

Image Acquisition

All images were acquired using either a GE Senographe 2000D or Senographe DS FFDM system (image size: 2294×1914 pixels; image spatial resolution: 10 pixels/mm in both dimensions). Prior to further analysis, images were log-transformed, then inverted, and, finally, intensity-normalized by a z-score transformation within the breast region, which was automatically segmented in each image using the publicly available "Laboratory for Individualized Breast Radiodensity Assessment" (29,32). These common preprocessing steps help to alleviate differences between studies via intensity histogram alignment, while also maintaining the overall pattern of the breast parenchyma (17). Additionally, we flipped horizontally the images of right mediolateral oblique views so that the breast is always on the same side of the image.

Revealing Meta-features of Breast Parenchymal Complexity

We developed a hybrid framework which coupled state-of-the-art texture analysis with CNNs (Fig 1). In the first step which follows the previously validated lattice-based strategy for parenchymal texture analysis (15), a regular lattice was virtually overlaid on the mammographic image and a set of texture descriptors were computed on 6.3×6.3 mm^2 (63×63 pixels (2)) local square ROIs centered on each lattice point within the breast. For each image, this step generated a set of 36×30 pixels (2) texture feature maps (each pixel corresponds to an ROI defined by the lattice), one for each texture descriptor that represents the spatial distribution of the corresponding textural measurements as sampled by the lattice over the entire breast.

Our texture feature set included a total of 29 established texture descriptors (Table 1 and Appendix for detailed feature