Correlation between Topological Descriptors of the Breast Ductal Network from Clinical Galactograms and Texture Features of Corresponding Mammograms

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Abstract. Mammographic texture has been reported as a biomarker of cancer risk. Recent publications also suggest correlation between the topology of the breast ductal network and risk of cancer. The ductal network can be visualized by galactography, the preferred imaging technique for nipple discharge. We present current results about the correlation between topological and textural properties of clinical breast images. This correlation was assessed for 41 galactograms and 56 mammograms from 13 patients. Topology was characterized using feature extraction techniques arising from text-mining, validated previously in the classification of normal, benign, and malignant galactograms. In addition, we calculated 26 texture descriptors using an automated breast image analysis pipeline. Regression analysis was performed between texture and topological descriptors averaged over all images of the same patient. These data demonstrate a correlation between topology and a subset of texture features with borderline statistical significance due to the limited sample size.

Keywords: Texture analysis, topology descriptors, galactograms, mammograms.

1 Introduction

Previously, we analysed the topological properties of the branching network of breast ducts as visualized by galactography, an x-ray imaging procedure of the contrast-enhanced breast ductal network (1-3). That analysis suggested a correlation between cancer risk and ductal network topology; this correlation also has been supported by evidence from murine cancer models (4). Clinical visualization of breast ducts is, however, not routinely performed; galactography is indicated infrequently, and it mostly commonly reveals benign findings (5, 6).

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On the other hand, texture descriptors of breast parenchyma are known to correlate with cancer risk (7-9). Our work is motivated by a desire to determine whether there is an association between parenchymal texture descriptors and ductal topology. Such an analysis would lead to improved models of breast anatomy, and may lead to a better understanding of breast cancer risk. Currently, breast cancer risk is estimated using patient demographic information and parenchymal texture features extracted from 2D mammograms. The spatial arrangement of breast tissue is, however, three-dimensional, stressing the need to understand the relationship between parenchymal structure and image texture.

The UPenn X-ray Physics Lab has extensive experience with the simulation of breast anatomy and imaging (10, 11). The development of the UPenn breast phantom is predicated upon a set of anatomically justified elements. To that end, we have chosen not to model the parenchymal texture by a random field with statistical properties similar to clinical data. This development process has been incremental, and continues to this day. For example, we have just recently begun to model the hierarchical organization of Cooper's ligaments seen in breast histology slices. A preliminary validation of a model of this small scale tissue detail, published separately in this proceedings, indicates good agreement with clinically estimated texture (12).

This paper presents our current results about the correlation between the ductal topology of clinical galactograms and the parenchymal textural properties of clinical mammograms from the same group of women. Understanding the relationship between mammographic texture and spatial distribution of breast anatomy will help optimize and extend our fully automated software pipeline for breast anatomy and imaging simulation; ultimately, we would like to be able to simulate specific cohorts of women, stratified by age, risk, and other factors.

2 Methods

2.1 Topological Analysis of Galactograms

In this paper, we analysed images of existing, anonymized clinical galactograms of 49 women, obtained from Virginia Commonwealth University. The data collection was performed after IRB review and was HIPAA compliant. Clinical galactograms were digitized from film, and categorized based upon the visibility of the ductal network. Ductal trees were traced manually from galactograms, followed by Prufer encoding of the breadth-first labelled ductal tree nodes (3). Then tf-idf significance weighting (3), originally used in text mining, was performed on the traced and encoded ductal trees. After manually tracing the ductal networks, a subset of 41 galactograms from 13 patients with well-defined ductal trees was selected for further processing and testing.

2.2 Texture Analysis of Mammograms

We measured 26 texture features in 56 digitized mammograms from the 13 selected patients imaged at Virginia Commonwealth University. Texture analysis was performed

using a fully automated software pipeline which extracted a large set of image features from the digitized mammograms (13). The pipeline calculates texture feature maps at points on a regular spatial lattice, determined by two parameters: the window size and the lattice distance. Here we use a window size of 63 pixels, and a lattice distance of 31 pixels. The analysed features are organized into three groups, including (i) descriptors of grey-level histograms, (ii) co-occurrence features, and (iii) run length features. These texture features have been used previously in breast cancer risk assessment studies (9). For the correlation analysis, the texture feature maps were averaged over the whole breast region (excluding the pectoral muscle and air).

2.3 Hypothesis Testing

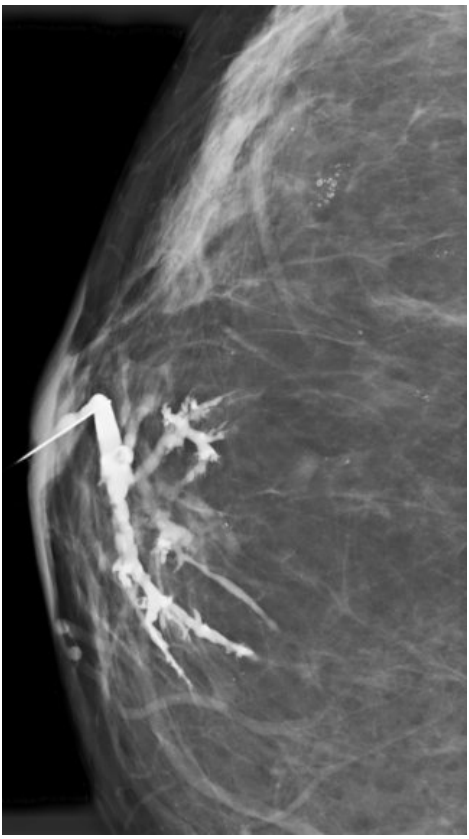
We tested the hypothesis that there is a correlation between mammographic texture features and ductal topology descriptors. To that end, we have calculated the linear regression (14). The goal was to predict values of texture features averaged over all mammograms of the same patient as a function of the topological properties estimated from the corresponding manually-traced ductal networks, averaged over all galactograms of the same patient. Prior to the regression analysis, we combined the tf-idf topological descriptors via principal component analysis (PCA). The regression model considered the first 13 PCA components and the 26 texture features.

2.4 Power Calculations

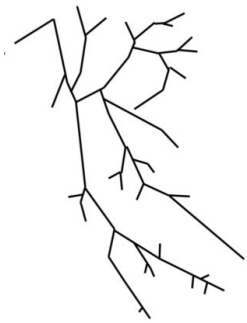
It can be demonstrated that a small sample size (in this case 13 patients), could lead to large estimated p-values and hence rejection of valid linear regression models (large Type II error). To demonstrate the effect of sample size, we simulated an augmented dataset by bootstrapping (15). The bootstrapping was performed by replicating data records, with added Gaussian noise, for each PCA attribute and response variable. The standard deviation of the noise was 50% of the estimated standard deviation of the attributes or response variables.

3 Results and Discussion

Fig. 1 shows an example of a clinical galactogram used in this study (Fig. 1(a)), and the corresponding manually-traced ductal tree (Fig. 1(b)). The Prufer encoding and the tf-idf weights corresponding to the traced tree is also given (Fig. 1(c-d)). The example shown illustrates a breast with a malignant finding. Fig. 2 shows an example of a clinical mammogram from the same woman (Fig. 2(a)) and the corresponding texture feature map (Fig. 2(b)). Shown in this example, is a map of the entropy texture feature.



(a)



(b)

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[ 1  1  3  4  6 10 10  6 11 16 16 11 17 24 24 17 25 34
 34 47 50 50 47 25  4  7 12 18 26 26 18 27 38 38 49 49
 27 12  7 13 20 28 28 20 29 29 13 21 30 30 21  3  5  5]
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(c)

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[0.00 0.11 0.45 0.36 0.40 0.50 0.71 0.00 0.50 0.77
 1.04 0.77 0.97 1.11 0.83 0.00 0.00 1.04 1.55 1.27
 1.45 1.19 0.00 0.00 1.27 0.00 0.00 0.00 0.00 0.00
 0.00 1.27 0.00 0.00 1.66 1.55 0.00 0.00 1.55 0.00
 0.00 1.45 0.00 2.04 2.19 1.66 0.00 1.90 0.00 0.00
 2.19 0.00 0.00 0.00 0.00 1.55 0.00 0.00 0.00 3.36]
```

(d)

Fig. 1. Illustration of the topological descriptors of the breast ductal network. Shown are: (a) a clinical galactogram with malignant finding; (b) the corresponding manually-traced ductal tree; (c) the Prufer encoding; and (d) the tf-idf weights corresponding to the ductal tree.

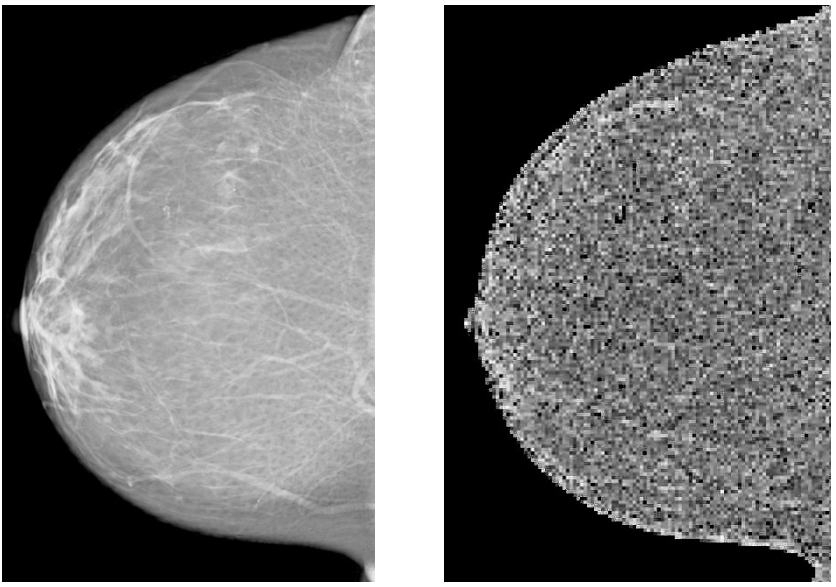

Fig. 2. The clinical mammogram of the patient from Fig. 1 (left) and the corresponding map of the entropy texture feature (right)

Fig. 3 shows the regression analysis results. A borderline statistical significance was observed for three texture features (features 9-11, p-values between 0.05 and 0.1); three additional features (features 17, 20, 24) had p-values between 0.1 and 0.15. It is likely that statistical significance was not achieved due to the limited sample size; thus, we are prevented from drawing a definitive conclusion about the correlation between texture and topology. The observed results, however, suggest a possible correlation between topological descriptors and several texture features. The bootstrap analysis of a hypothetically enlarged dataset with a sample size of 26 suggests that a statistically significant regression (at a significance level of 0.05) could be achieved between various texture features and topological descriptors. Fig. 3 shows the p-values from the bootstrap analysis.

The potential for inter-correlation between individual texture features was accounted for by applying PCA before performing the regression analysis, as PCA uses orthogonal transformations to convert the original data into a set of linearly uncorrelated variables. The bootstrap analysis performed in this paper to estimate the effect of sample size, assumed the noise in the enlarged data set to have a standard deviation equal to 50% of the standard deviation in individual sample data.

The results presented in this paper are based upon an initial analysis of 13 patients. We are currently analysing a larger set of clinical breast images; we expect to double the sample size in the near future. If the linear dependence between the texture and topology is confirmed (as suggested from our initial analysis and supported by bootstrapping), texture descriptors could be used as a proxy for topology, since the ductal network is not routinely visible in clinical images. Identifying texture features, or

combinations of texture features, which have the strongest correlation with topology could improve the understanding of texture-based risk biomarkers.

If, however, the increased sample size does not confirm the correlation between topology and texture, it could suggest that topology may carry risk-related information independent from texture descriptors. This could potentially lead to an improvement in the accuracy of breast cancer risk estimation techniques, assuming a clinically feasible method for the visualization and characterization of breast ducts (e.g., MRI or tomosynthesis) is available.

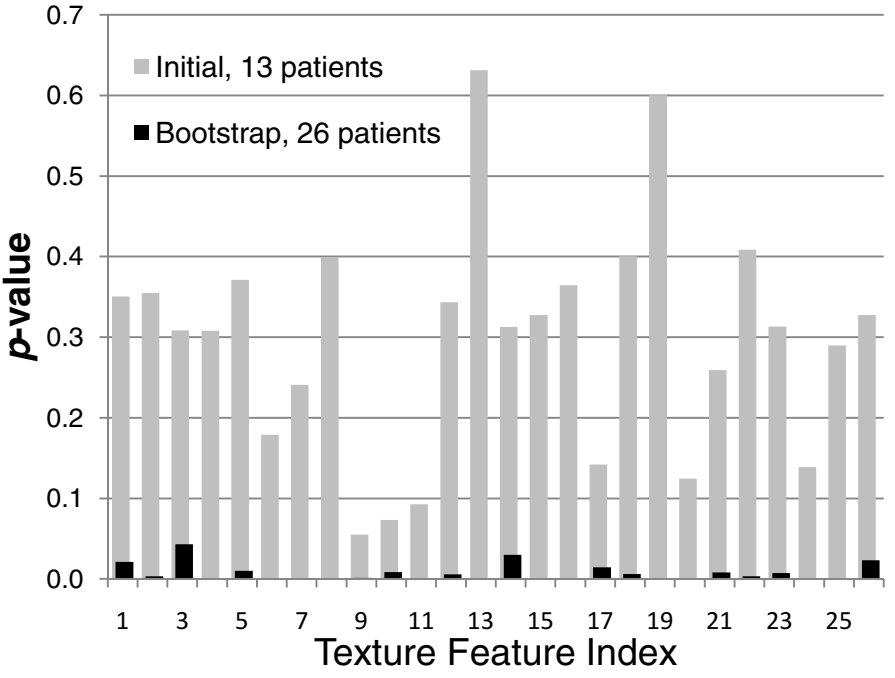

Fig. 3. *p*-value for the regression of individual texture features (averaged over all mammograms of the same patient) as a function of principal component analysis (PCA) components for the topological descriptors (tf-idf weights, averaged of all the traced ductal networks of the same patient). Shown are the results of the initial analysis of 13 patients, as well as the bootstrap results modelling a dataset of 26 cases.

It is worth noting the limitations of the current study. First, the ductal trees analysed in this paper were manually-traced from digitized galactograms. The manual tracing was performed by one person (a third-year medical student with experience in breast imaging). We believe that manual tracing did not compromise the analysis. In our previous study of ductal topology, we observed relatively low variations (a root-mean-square fractional error on the order of 2%) in estimated topological features due to manual tracing (2).

Additional potential limitations include the use of average texture descriptors, and the inter-correlation between individual descriptors of texture (or topology). In this paper, the regression analysis was performed using texture features averaged over the breast region in each mammographic image. These average values may suppress the differences in feature histograms calculated over mammographic images. In the future, we may repeat the analysis based upon other histogram moments, or using the full histogram as the texture descriptor.

4 Conclusion

We have performed a regression analysis between topological descriptors of the breast ductal network extracted from previously acquired, anonymized clinical galactograms, and texture descriptors estimated from corresponding clinical mammograms. Ductal networks were extracted from galactograms by manual tracing. The texture features were estimated using a fully automated image analysis pipeline. Initial analysis of clinical images from 13 women suggests correlation with borderline significance for a subset of texture descriptors. The identified subset of texture descriptors could hypothetically be used as proxy for ductal topological properties. Analysis of a larger number of clinical cases is ongoing.

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