The use of texture analysis in breast magnetic resonance imaging: differentiation of ductal and lobular carcinoma

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Introduction and Aims: Breast Magnetic Resonance Imaging (MRI) is becoming more routinely used as a complementary imaging modality to conventional x-ray based mammography and ultrasound in the identification and diagnosis of breast cancer. The main reasons for its increase in use are the excellent sensitivity and negative predictive value of the contrast-enhanced dynamic images. While the sensitivity is around 100% [1], the reported specificity in the differentiation of malignant from benign disease is still unclear with reports varying from 40-92% [1, 2].

Texture analysis is a computer-assisted method of statistically evaluating the grey-level pixel intensity distributions within an image using various models in order to infer information that may not be visually apparent. It has been successfully applied in many branches of medical diagnostics and more recently it has been used to increase the specificity of breast MRI examinations [3, 4]. The underlying histology of the two most common breast cancers is fundamentally different. Lobular cancers tend to consist of single file cells that spread diffusely through the tumour stroma, while ductal cancers tend to grow as solid sheets or nests that invade the stroma. Thus, it was proposed that it may be possible to use texture analysis not only to identify regions of abnormality within normal breast tissue, but also to classify the type of malignancy present.

This study considers a group of patients who were referred for a breast MRI on the basis of a known malignancy, which had been pathologically confirmed prior to the radiological examination as either invasive ductal carcinoma or infiltrative lobular carcinoma. We aimed to identify whether texture analysis could reliably be used to determine whether tissue was normal or malignant, and whether it was possible to differentiate between the two types of invasive cancers.

Methods: A total of 57 patients were imaged on a 16-channel 1.5 Tesla (T) MRI scanner (Avanto; Siemens, Erlangen) using a 4-channel breast matrix coil. A 3-dimensional Fast Low Angle SHot (FLASH) volumetric sequence was acquired axially through both breasts with an acquisition time of 62s (TR/TE= 3.52/1.24 ms, α= 6°, ST= 0.83 mm, FoV= 320×320 mm, matrix= 384×384, BW= 650 Hz/px, iPAT×2, 192 slices). The complete dynamic acquisition consisted of 8 volumes (total imaging time of 8 minutes 17 seconds), with 2 volumes acquired prior to contrast injection, and contrast injected immediately at the end of the second volume acquisition. All patients received a 0.1mmol/kg dose of Dotarem (Guerbet Laboratories, France) injected at 2.0 ml/s, followed by 20ml saline solution. Regions of contrast uptake were identified using subtracted volumes and all analysis was performed on the 2 minute post contrast subtracted volume.

Texture analysis was carried out using MaZda version 4.7 [5]. The three central slices of the lesion were identified first and circular regions of interest (ROI) were then drawn both within the lesion and in an area of normal breast tissue. The ROI's drawn within the enhancing lesions were drawn as large as possible, without straying from the region of enhancement, in order to maximise counting statistics. Gray level normalisation was carried out using a $\mu\pm3\sigma$ regime (μ- grey level mean, σ- grey level standard deviation) to minimise the effect of image brightness and contrast on texture analysis outcome. Texture features were calculated as derived from the auto-regressive model (ARM), co-occurrence matrix (COM), absolute gradient (GRA), run-length matrix (RLM) and wavelet transform (WAV). The best 30 features were automatically calculated by MaZda using a combination of the Fisher coefficient, Mutual Information and the Probability of Error.

Classification of malignant vs. normal tissue and ductal vs. lobular carcinoma was carried out using Weka, version 3.6.2 [6], with a 10-folds cross validation routine and k-nearest neighbour (k-NN) classification, using k=1. The number of incorrectly identified vectors was represented as the percentage of misclassified vectors. In addition to considering all models, the COM and RLM features were also considered separately as these were found to contribute most to the best 30 automatically selected features.

As well as data classification, statistical analysis was performed on the individual texture feature values calculated by MaZda, to assess the significance level of the classification between lobular and ductal carcinoma. For this, a Mann Whitney U test was performed on the data in SPSS (version 18, IBM corp.; Armonk, NY), with a p-value less than 0.05 considered as significant. The contribution of individual features from the COM and RLM model for describing lobular and ductal carcinoma were also compared using student t-tests in order to determine whether some individual features provided a better description of the cancer types.

Results and Discussion: There were a total of 83 lesions identified on the MR images from our 57 patients. Of these, pathology findings showed that 46 lesions were invasive ductal cancer, while the other 37 lesions were infiltrative lobular cancer. Regions of interest drawn onto the central three slices of each lesion gave a total of 138 ROI for the ductal group and 111 ROI for the lobular group.

For the ductal cancers, 76% of the features were attributed to the COM model and 20% to the RLM, while for the lobular cancers 73.5% of the features are from the COM model and 23% from the RLM. Therefore, the COM and RLM models are clearly the most efficient texture models for describing invasive breast cancer.

For ductal cancers, the dominating COM features were found to be inverse difference moment, difference variance, difference entropy and sum entropy; and grey level non-uniformity for the RLM model. For lobular cancers, the dominating COM features were found to be difference entropy, entropy, inverse difference moment, sum average and sum entropy; for the RLM model, grey level non-uniformity and run length non-uniformity dominated. For ductal carcinomas, the 'moment' features appeared to be more common than for lobular, however this was not statistically significant. For lobular cancers, the entropy features were more prevalent, which was calculated to be statistically significant compared to the ductal cancers (p=0.028). In general, moment features are generally defined to relate to image homogeneity, while entropy features are a measure of disorder [7]. It is therefore possible that texture findings are able to infer the more dispersed, irregular cellular growing pattern associated with lobular carcinoma.

Classification between normal and malignant tissue was perfect (i.e. no misclassification) for all lesions, thereby suggesting that there are measurable texture differences between normal tissue and malignancy.

	30 best features	COM features	RLM features
% misclassification	4.0%	3.6%	24.9%
Mann Whitney U	p<0.001	p<0.001	p=0.550

Table 1- *Summary of percentage misclassification and Mann Whitney U statistical tests between the lobular and ductal cancer groups*

Considering the differentiation between lobular and ductal cancer using the best 30 features selected by MaZda, classification accuracy was good with only a 4% misclassification rate (see Table 1). Statistical testing of the raw texture feature values showed a significant difference between the values in the two groups as calculated using a Mann Whitney U test ($p<0.001$).

The data was then split to consider the COM and RLM models. For the COM model, the misclassification rate was slightly improved to 3.6%, with $p<0.001$, while for the RLM model the differentiation was relatively poor with almost a quarter of the data being misclassified and no significant difference in the feature values between ductal and lobular cancer (p=0.550).

The error rate of 4% misclassification for ductal and lobular differentiation is relatively low and would be expected to diminish as the sample size increases. The low rate of misclassification for the COM data suggests that these features are heavily represented in the best 30 features selected through MaZda. This is likely to be due to the large number of features associated with the COM model and the use of pixel pairs which results in improved counting statistics. The RLM model resulted in a high rate of misclassification, which may be due to the model being unable to adequately model texture differences between lobular and ductal cancers.

Both the COM and the RLM models were chosen as they were noted to make up most (>96%) of the best 30 features selected by MaZda. For this particular study, it was felt un-necessary to consider the other models for which even higher rates of misclassification would be expected.

Conclusions: Texture analysis has demonstrated perfect classification between normal breast tissue and malignancy in all of our patients. We were also able to reliably differentiate between the two main types of breast cancer- invasive ductal cancer and infiltrative lobular cancer. This technique resulted in a classification accuracy of over 96% and therefore could potentially be useful alongside morphological findings to provide an indication of the type of breast cancer prior to biopsy results becoming available. The COM model was demonstrated to be best for differentiating between lobular and ductal carcinoma.

In describing ductal carcinoma, the COM model is dominated by moment features- representing the homogeneity of the texture, while for lobular carcinoma entropy features are more common- which is significant when compared with the entropy features representing ductal carcinoma (p=0.028). As the entropy features describe disorder of a texture, it is possible that this model better represents the more erratic pathological growth pattern of this cancer type.

References:

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