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Characterizing healthy and osteoarthritic knee cartilage on phase contrast CT with geometric texture features

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Abstract

The current approach to evaluating cartilage degeneration at the knee joint requires visualization of the joint space on radiographic images where indirect cues such as joint space narrowing serve as markers for osteoarthritis. A recent novel approach to visualizing the knee cartilage matrix using phase contrast imaging (PCI) with computed tomography (CT) was shown to allow direct examination of chondrocyte patterns and their subsequent correlation to osteoarthritis. This study aims to characterize chondrocyte cell patterns in the radial zone of the knee cartilage matrix in the presence and absence of osteoarthritic damage through texture analysis. Statistical features derived from gray-level co-occurrence matrices (GLCM) and geometric features derived from the Scaling Index Method (SIM) were extracted from 404 regions of interest (ROI) annotated on PCI images of healthy and osteoarthritic specimens of knee cartilage. These texture features were then used in a machine learning task to classify ROIs as healthy or osteoarthritic. A fuzzy k-nearest neighbor classifier was used and its performance was evaluated using the area under the Receiver Operating Characteristic (ROC) curve (AUC). The best classification performance was observed with high-dimensional geometrical feature vectors derived from SIM and GLCM correlation features. With the experimental conditions used in this study, both SIM and GLCM achieved a high classification performance (AUC value of 0.98) in the task of distinguishing between healthy and osteoarthritic ROIs. These results show that such quantitative analysis of chondrocyte patterns in the knee cartilage matrix can distinguish between healthy and osteoarthritic tissue with high accuracy.

Keywords

phase contrast imaging; cartilage characterization; GLCM; Scaling Index Method; texture analysis; fuzzy *k*-nearest neighbor classifier

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This work is not being and has not been submitted for publication or presentation elsewhere.

1. MOTIVATION/PURPOSE

Osteoarthritis is widely recognized as representing one of the leading causes of disability worldwide and is characterized by progressive damage to the articular cartilage and subchondral bone [1–3]. Its diagnosis requires analysis of cartilage, a tissue type that only yields negligible x-ray absorption contrast. As a result, conventional approaches to diagnosing osteoarthritis involves evaluating indirect cues on radiographic images of the knee joint such as joint space narrowing and increased bone density near the joint. More recently, cartilage thickness and volume have been quantified using ultra-high-field magnetic resonance imaging [4]. However, phase-contrast computer tomography (PCI-CT) recently emerged as a novel imaging approach that provides soft-tissue discrimination in cartilage tissue at a micrometer scale resolution [5]. In this work, we explore the use of texture analysis to quantify differences between healthy and osteoarthritic knee cartilage through differences in chondrocyte organization observed in the cartilage matrix.

Texture analysis involves extracting certain features from a specified region of interest (ROI) which are subsequently used in medical image processing tasks. We investigate the ability of texture features derived from gray-level co-occurrence matrices (GLCM) and Scaling Index Method (SIM) to characterize chondrocyte cell patterns in the radial zone of knee cartilage matrix as visualized on PCI-CT images of both healthy and osteoarthritic samples. GLCM is a texture analysis technique that characterizes gray-level patterns through second-order statistical features. SIM, on the other hand provides a more detailed geometrical description of the underlying gray-level patterns within the ROI, specifically through estimation of local scaling properties. Both methods have been previously applied to other pattern recognition tasks in medical imaging, such classifying between healthy and pathological lung tissue on CT [6], distinguishing between benign and malignant lesions on dynamic breast MRI [7], estimating the bone strength through analysis of trabecular micro-architecture [8], etc. This work is embedded in our group's endeavor to expedite 'big data' analysis in biomedical imaging by means of advanced pattern recognition and machine learning methods for computational radiology, e.g. [9–25].

We are specifically interested in characterizing the chondrocyte organization in the radial zone of the cartilage matrix where previous work has shown that OA-induced damage disrupts the alignment of chondrocytes [5]. The goal of this work is evaluate whether statistical and geometrical features, extracted using GLCM and SIM respectively, can adequately characterize chondrocyte patterns in the radial zone of the cartilage matrix to enable discrimination between healthy and osteoarthritic cartilage. For this purpose, texture features are extracted from ROIs placed on PCI-CT images and used in a machine learning task that attempts to predict the class of the ROI. Sample ROIs as used in this study are shown in figure 1.

2. DATA

Two osteochondral cylindrical samples of diameter 7 mm and height 12 mm were extracted from the lateral facet of the patella of 2 patients, one healthy and one osteoarthritic, within 48 hours post-mortem. These samples were subject to PCI-CT with an analyzer-based

imaging (ABI) technique, where a parallel monochromatic beam of synchrotron radiation (X-rays of energy 26keV) was used to irradiate the sample. Each bone-cartilage sample was irradiated while rotating about an axis perpendicular to the incident beam, and a projection image was acquired at each angular step. The sample was then vertically displaced at the end of each rotation in order to scan its entire volume. An analyzer crystal was positioned between the sample and the detector to convert the tiny X-ray refraction angles into observable intensity differences. The images were acquired at the ID17 biomedical beamline of the European Synchrotron Radiation Facility (ESRF, France). Further details about the experimental setup used to acquire these images can be found in [5].

Axial images of dimensions 1124×1124 and in-plane resolution of $8\mu\text{m} \times 8\mu\text{m}$ were reconstructed by using a direct Hamming filtered-back projection algorithm. 805 such images were obtained from each specimen and reformatted to yield slices in the coronal plane. 404 regions of interest (ROI) of dimensions 51×51 pixels, capturing chondrocyte patterns, were annotated by an experienced radiologist in the radial zone of the cartilage matrix on these coronal slices. 233 of these ROIs were healthy while the remaining 171 were osteoarthritic. An example of a PCI-CT image acquired from the osteoarthritic sample with a square ROI in the radial zone is shown in figure 2.

3. METHODS

3.1 Texture analysis

For a certain ROI with number of gray-levels G , a matrix of dimensions $G \times G$ can be generated indicating the frequency with which any two specific gray-levels occur at a certain distance d apart in a certain direction. For the 2-D scenario, such a gray-level co-occurrence matrix (GLCM) can be generated in four principal directions i.e. 0° , 45° , 90° and 135° . These frequencies can be normalized to yield the joint probability of gray level values occurring as neighboring pairs. For each directional GLCM, the element at a certain row i and column j indicates the frequency at which gray level values i & j occur as neighboring pairs *in that specific direction*. The non-directional GLCM obtained by summing these directional matrices form the basis for several second-order statistical measures that serve as texture features; these are outlined in [26–27]. One free parameter of GLCM analysis is the inter-pixel distance d that is used in generating the GLCMs; $d = 1$ was used for computing GLCMs in this work.

Scaling Index Method (SIM) characterizes the structure observed in a ROI through geometric features that estimate the local dimension [28]. While originally developed as a non-linear method for analysis of multi-dimensional arbitrary point distributions through evaluation of the surrounding structural neighborhood, this technique has since been extended for application to gray-level ROIs [29].

In this study, the 2D ROI is treated as a 3D volume where the gray-level intensity is treated as the third dimension. Now, for each pixel x_i in the ROI, the local dimension is calculated as –

$$\alpha(x_i, r) = \frac{\sum_{j=1}^N (d_{ij}/r)^2 \exp \left[-(d_{ij}/r)^2 \right]}{\sum_{j=1}^N \exp \left[-(d_{ij}/r)^2 \right]}$$

where d_{ij} is the distance between the i^{th} pixel (centre) and the j^{th} pixel (neighbor), r is the neighborhood radius and N is the number of pixels contained in the neighborhood. This transform essentially assigns each pixel a local scaling property $\alpha(x_i, r)$ in a neighborhood determined by the radius r . While the radius r is a free parameter, it was empirically fixed, i.e. $r = 5$, in this study.

The resulting distribution of α values, as seen in the SIM transformations and SIM histograms shown in Figure 2, contain non-linear textural information that characterizes the underlying gray-level structure. We represent such distributions as a 9-D feature vector consisting of the 9 quantiles extracted from the distribution α values; this 9-D feature vector is subsequently processed in a classification task. An illustrative example is shown in Figure 3 for examples of healthy and osteoarthritic ROIs extracted from PCI-CT studies, as well as their corresponding SIM transformations and SIM histograms.

3.2 Classification

Calculation of the texture feature vectors is followed by a machine learning step where patterns are characterized as control or treated through supervised learning. In this study, a fuzzy k -Nearest Neighbor (k -NN) classifier proposed by Keller, Gray et al. that models learning through density estimation was used for the classification task [30]. A fuzzy k -NN classifier assigns “fuzzy” class memberships or weights to the training data neighbors of any given test data point based on their distance from that particular test data point; label assignment is now based on weight thresholds rather than a simple majority evaluation of the k nearest neighbors. In the training phase, models are created from labeled data – the purpose of the training is to determine the optimal classifier parameters (the number of nearest neighbors k for example) that best capture the boundaries between the two classes of cartilage patterns.

In this study, 70% of the data was used for the training phase while the remaining 30% served as an independent test set. The training phase employs a ten-fold cross-validation strategy where each data-point serves as a validation case in one cycle and as a training case in other cycles; the free parameters of the fuzzy k -NN classifier are optimized here. Then, during the testing phase, the optimized classifier predicts the label of lesions of unknown character in the testing dataset and an ROC curve is generated and used to compute the area under the curve (AUC). This process is repeated 50 times resulting in an AUC distribution, and a Wilcoxon signed rank test was used to compare AUC distributions corresponding to different features. Both texture and statistical analysis were implemented using Matlab 2008b (The MathWorks, Natick, MA).

4. RESULTS

Table 1 and Figure 3 shows the classifier performance obtained when both GLCM and SIM texture feature vectors that characterize chondrocyte patterns are extracted from ROIs placed on the radial zone of the knee cartilage matrix. The highest AUC value was observed with the SIM feature vector (0.98 ± 0.01). Similar performance was achieved by GLCM Correlation features f3 (correlation), f12 (information measure of correlation I) and f13 (information measure of correlation II).

5. DISCUSSION

While PCI-CT has been shown as an effective technique at visualizing the cartilage matrix of the human knee patella, quantitative measures are required to consistently capture differences observed in the chondrocyte cell patterns in the radial zone of the cartilage matrix in the presence or absence of osteoarthritis. This investigation shows some preliminary work to showcase the role that texture analysis can play in quantitatively discriminating between ROIs extracted from healthy and osteoarthritic cartilage matrix. As presented in this work, texture features that characterize these chondrocyte cell patterns through second-order statistics (GLCM) or through geometrical features derived from estimating local scaling properties (SIM) can be used to classify ROIs extracted from PCI-CT images of the cartilage matrix as belonging to healthy or osteoarthritic samples with high accuracy. Such texture features, in conjunction with PCI-CT imaging, have significant potential in serving as bio-markers for capturing progression of osteoarthritis in the human knee patella.

As shown in this work, texture analysis can be used in combination with machine learning to predict the source of an ROI extracted from a PCI-CT image, i.e. as being healthy or osteoarthritic, with high classification performance. The highest classification performance with GLCM was observed through its correlation features, specifically f3 and f13. This appears to be a result of lower density and clustering of chondrocytes in the cartilage tissue, specifically in the radial zone of healthy cartilage and the smaller size of such cells. This resulting exhibition of more extracellular space corresponds to some uncorrelated noise in the PCI-CT images. As a result, the correlation values obtained for the osteoarthritic ROIs are higher than those obtained for healthy ROIs. The effectiveness of SIM in distinguishing between healthy and osteoarthritic ROIs can be attributed to its capturing geometrical properties of local neighborhoods. As seen in Figure 2, the chondrocytes are more clustered in the radial zone of osteoarthritic cartilage leading smaller local dimensions being evaluated at most pixels. This is also reflected in the corresponding SIM histogram that represents the distribution of α values computed from the SIM transformation. However, chondrocytes in healthy cartilage are less clustered owing to their alignment in a specific direction (radiating outward from the tidemark). As a result, a high local dimension is evaluated at a larger number of pixels.

While this preliminary study shows some promising results for capturing difference between healthy and osteoarthritic cartilage patterns in PCI-CT images using texture analysis, it does have some drawbacks which will be addressed in future studies. The current setup includes

only two specimens, one extracted from a healthy donor and the other one from an osteoarthritic donor (post-mortem). It is desirable to include more cartilage specimens in future studies as having ROIs from the same patient in the training and testing phase of the machine learning step could lead to some bias in the results. The current study also uses a fixed size for the ROIs extracted from the PCI-CT images i.e. 51×51 pixels. The choice of this size is arbitrary and future studies can investigate whether the size of the ROI analyzed has an impact on the classification performance obtained with different texture features.

6. CONCLUSION

This study explored the role that texture features can play in characterizing chondrocyte patterns in the radial zone of human patellar cartilage matrix as visualized on PCI-CT images. Our results show that texture features derived from both GLCM and SIM can classify ROIs extracted from images of healthy and osteoarthritic samples with high classification performance.

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Figure 1.

Regions of interest extracted from the radial zone of healthy and osteoarthritic knee cartilage matrix. The goal here is to classify these ROIs as belonging to either class based on quantitative analysis of the difference observed in chondrocyte patterns through texture analysis. Note that the above ROIs encompass an area of $0.4 \times 0.4 \text{ mm}^2$.

Figure 2.

Coronal reconstructed image from the osteoarthritic sample used in this study. Note the absence of chondrocyte alignment in the radial zone. The red square indicates an example annotated ROI in this region that is used for further analysis.

LEFT: Healthy and Osteoarthritic ROIs of knee cartilage matrix captured from PCI-CT images. MIDDLE: ROIs after being processed with SIM ($r = 5$); color-coded (color bar on extreme right) based on local dimension estimates. RIGHT: SIM histograms of both ROIs. As seen here, such SIM histograms can capture differences between healthy and osteoarthritic ROIs.

Figure 3.

Comparison of classification performance between GLCM and SIM in the task of classifying a certain ROI as healthy or osteoarthritic. The central mark corresponds to the median while the edges are the 25th and 75th percentile. The results marked red are those obtained when GLCM features are used in the classification task while those marked in blue are obtained with SIM.

Table 1

Classification performance (mean $\pm$ std) achieved with features derived from GLCM and SIM. The highest classification performance is observed with SIM, as well as with GLCM features related to correlation (bold).

Features	AUC
GLCM.f1	0.74 $\pm$ 0.03
GLCM.f2	0.96 $\pm$ 0.01
GLCM.f3	0.98 $\pm$ 0.01
GLCM.f4	0.69 $\pm$ 0.04
GLCM.f5	0.97 $\pm$ 0.01
GLCM.f6	0.67 $\pm$ 0.04
GLCM.f7	0.67 $\pm$ 0.04
GLCM.f8	0.70 $\pm$ 0.04
GLCM.f9	0.71 $\pm$ 0.04
GLCM.f10	0.95 $\pm$ 0.02
GLCM.f11	0.96 $\pm$ 0.02
GLCM.f12	0.98 $\pm$ 0.01
GLCM.f13	0.98 $\pm$ 0.01
SIM	0.98 $\pm$ 0.01