Computer-Aided Diagnosis for Phase-Contrast X-ray Computed Tomography: Quantitative Characterization of Human Patellar Cartilage with High-Dimensional Geometric Features

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Abstract Phase-contrast computed tomography (PCI-CT) has shown tremendous potential as an imaging modality for visualizing human cartilage with high spatial resolution. Previous studies have demonstrated the ability of PCI-CT to visualize (1) structural details of the human patellar cartilage matrix and (2) changes to chondrocyte organization induced by osteoarthritis. This study investigates the use of high-dimensional geometric features in characterizing such chondrocyte patterns in the presence or absence of osteoarthritic damage. Geometrical features derived from the scaling index method (SIM) and statistical features derived from gray-level co-occurrence matrices were extracted from 842 regions of interest (ROI) annotated on PCI-CT images of ex vivo human patellar cartilage specimens. These features were subsequently used in a machine learning task with support vector regression to classify ROIs as healthy or osteoarthritic; classification performance was evaluated using the area under the receiver-operating characteristic curve (AUC). SIM-derived geometrical features exhibited the best classification performance

(AUC, 0.95 ± 0.06) and were most robust to changes in ROI size. These results suggest that such geometrical features can provide a detailed characterization of the chondrocyte organization in the cartilage matrix in an automated and non-subjective manner, while also enabling classification of cartilage as healthy or osteoarthritic with high accuracy. Such features could potentially serve as imaging markers for evaluating osteoarthritis progression and its response to different therapeutic intervention strategies.

Keywords Osteoarthritis · Phase-contrast imaging · Scaling index method · Gray-level co-occurrence matrix · Support vector regression

Introduction

Osteoarthritis (OA) is widely recognized as one of the leading causes of disability worldwide [1–3]. This disorder is characterized by loss of articular cartilage, thickening of the underlying subchondral bone, and osteophyte formation [4]. Diagnostic markers currently used for monitoring OA progression and evaluating the impact of drug intervention, such as joint pain or observation of joint space narrowing on conventional radiography, are only sensitive at advanced stages of the disease. Thus, imaging modalities that could provide early detection and allow visualization of any OA-induced degenerative modifications to the cartilage are of significant medical interest [5].

In this context, phase-contrast imaging (PCI) has emerged as a novel X-ray-based imaging approach owing to its ability to provide enhanced image contrast for visualizing structural details in soft tissue [6]. PCI exploits the fact that X-rays are not just absorbed when passing through matter but also refracted [7, 8]. The phase-contrast effect associated with such refraction can be more pronounced than conventional

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absorption contrast, specifically for the energy range of X-rays used in diagnostic modalities, and for soft tissue types encountered in clinical practice [9]. This allows PCI to be effective in imaging tissue types where conventional absorption contrast is insufficient for soft tissue characterization, notably in breast [10, 11] and cartilage imaging [5, 12–14]. Among the different PCI techniques, we specifically focus on the analyzer-based imaging (ABI) method [8, 15, 16], which has been applied in both *ex vivo* and *in vivo* cartilage studies and demonstrated greatly improved cartilage visualization [14, 17]. In particular, Coan et al. demonstrated the ability of PCI with computed tomography (PCI-CT) using the ABI method to visualize the internal architecture of the cartilage matrix at a micrometer scale resolution in *ex vivo* samples of human patellae [14].

Analysis of PCI-CT images of normal and osteoarthritic cartilage from *ex vivo* human patella specimens revealed specific differences in the internal organization of chondrocytes in the cartilage matrix. In particular, chondrocytes in normal specimens were found to maintain a zone-specific architecture. This was specifically visualized in the radial zone, where the chondrocytes were aligned in a direction radiating outward from the tide mark (Benninghoff's arch [18]). Such chondrocyte organization was absent in osteoarthritic samples; a generalized clustering of cells throughout the matrix was observed instead [14]. This study aims to (1) identify quantitative measures that could characterize such differences in chondrocyte organization in the radial zone, and (2) evaluate their ability to serve as imaging markers for degenerative changes to the cartilage matrix induced by OA.

We specifically focus on the use of features indicative of local structure and geometry, as computed through the use of the scaling index method (SIM) [19]. To the best of our knowledge, these features have not been previously used for quantitative analysis of cartilage matrix structure as visualized by PCI-CT. This technique has been previously applied to pattern recognition tasks in medical imaging, specifically in estimating the bone strength through analysis of trabecular micro-architecture on CT [20] and MRI [21]. However, results of its application to analysis of point distributions in atomic microscopy [19] and in astrophysical data [22] motivates its use here in characterizing chondrocyte organization. For comparison, we also investigate the use of second-order statistical features derived from gray-level co-occurrence matrices (GLCM) [23], which have also been previously investigated in medical image analytic tasks such as distinguishing pathological patterns on chest CT [24, 25], classifying benign and malignant lesions on dynamic breast MRI [26–28], etc.

We evaluate the performance of features derived from SIM and GLCM in classifying regions of interest (ROI) as being normal or osteoarthritic in an automated manner. This is achieved by extracting these features from ROIs annotated in the radial zone of the cartilage matrix on PCI-CT images,

followed by processing in a machine learning task using support vector regression (SVR) [29], as discussed in the following sections.

Materials and Methods

Samples

The selection of the patellae was based on age of the donor, macroscopic visual inspection and probing of the cartilage surface at autopsy. Donors older than 40 years were *a priori* excluded for harvest of normal samples; no constraint in age was imposed on potential donors for osteoarthritic samples. A smooth, white, and shiny surface across the entire patellar cartilaginous tissue and prompt resilience to manually performed focal indentation probing were the criteria that defined macroscopically normal cartilage. Lack of these criteria in addition to visually perceived defects in the joint surface were used to select osteoarthritic samples. IRB was waived by the Institutional Review Board of the Ludwig Maximilians University, Munich, Germany. Based on these inclusion criteria, two healthy and three osteoarthritic cylinder-shaped osteochondral samples (diameter, 7 mm) were extracted within 48 h postmortem from the lateral facet of 5 human patellae using a shell auger. Cylinders were trimmed to a total height of 12 mm including the complete cartilage tissue and the subchondral bone. The samples were continuously rinsed by 0.9 % saline during extraction, trimming and removal of soiling from sawing. During image acquisition, samples were dipped into a 10 % formalin solution.

PCI Experimental Setup

The ABI setup consisted of a parallel monochromatic X-ray beam, used to irradiate the sample, and of a perfect crystal, the analyzer, placed between the sample and the detector [16]. The analyzer acts as an angular filter of the radiation transmitted through the object and only the X-rays traveling in a narrow angle window close to the Bragg condition are diffracted onto the detector. Before being detected, the beam is modulated by the angle-dependent reflectivity of the crystal (rocking curve), which has a full width at half maximum (FWHM) typically of the order of a few micro-radians. All images were acquired at the half maximum position on one slope of the RC (50 % position), which was chosen to achieve the best sensitivity. Further details of this ABI technique can be found in [6, 14].

Experiments were performed at the Biomedical Beamline (ID17) of the European Synchrotron Radiation Facility (ESRF, France). Quasi-monochromatic X-rays of 26 keV were selected from the highly collimated X-ray beam by means of a double Si (111) crystal system and an additional

single Si (333) crystal [30]. The emerging refracted and scattered radiation from the sample was analyzed with a Si (333) analyzer crystal. Given the laminar shape of the stationary synchrotron beam, images were obtained by rotating and vertically scanning the sample through the X-ray beam [14]. The imaging detector used was the Fast Readout Low Noise (FReLoN) CCD camera developed at the ESRF [31]. The X-rays are converted to visible light by a 60- μm -thick Gadax fluorescent screen; this scintillation light is then guided onto a $2,048 \times 2,048$ pixel ($14 \times 14 \text{ m}^2$) CCD (Atmel Corp, US) by a lens-based system. The effective pixel size at the object plane was $8 \times 8 \mu\text{m}^2$.

Tomographic Image Reconstruction

In order to acquire tomographic images with our PCI experimental setup, the cartilage samples were rotated about an axis perpendicular to the incident laminar beam. At the end of each rotation, the sample was displaced along the perpendicular axis to enable imaging of a different region. Unlike conventional CT imaging, the beam and detector were kept stationary. The detector acquisition was synchronized with the sample angular scanning. To reduce the effects of any spatial and temporal X-ray beam inhomogeneities, we then performed a flat field normalization for each angular projection image. A direct Hamming filter backprojection (FBP) algorithm was used for reconstructing tomographic images [32]. For data analysis, coronal slices were reconstructed from the original data and subject to edge-preserving median filtering with a [5 5] sliding window to smoothen noise artifacts. A sample image acquired from one of the specimens is shown in Fig. 1.

Annotation

Chondrocyte patterns were annotated with 2D square ROIs in the radial zone of the cartilage matrix on the reconstructed PCI-CT images of all five specimens. Eight hundred forty-two ROIs were annotated in total, of which 455 were osteoarthritic and 387 were healthy. The annotations were made using a square of 51×51 pixels; ROIs of smaller size (11, 21, ... 41)

Fig. 1 Coronal reconstruction created from axial PCI-CT images of a single cartilage specimen. In this case, the cartilage specimen is osteoarthritic, as seen by the generalized clustering of chondrocytes throughout the matrix

were then extracted without any manual intervention using the same ROI center.

Texture Analysis

SIM is a technique derived from fractal theory that estimates local geometric properties in point distributions and gray-level patterns. While originally developed as a non-linear method for analysis of multi-dimensional arbitrary point distributions through evaluation of the surrounding structural neighborhood [19], this technique has since been extended for application to gray-level ROIs [22].

In any specific ROI, all N pixels are represented by a 3D vector $x_i = (x_i, y_i, g_i)$, $i = \{1, 2, \dots, N\}$, consisting of two spatial dimensions (x_i, y_i) and pixel gray-level intensity $g_i = g(x_i, y_i)$. The application of SIM for a given scale r is treated as an image transform that assigns each pixel within the ROI a local scaling property $\alpha_i = \alpha(x_i, r)$. This scaling property reflects the structural and geometrical properties of the surface formed in the pixel neighborhood defined by r . We use a previously proposed estimator for α that uses a Euclidean distance metric and Gaussian shaping functions, i.e.,

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

where d_{ij} is the Euclidean distance between pixel x_i and neighboring pixel x_j and r is the radius of the Gaussian neighborhood [22]. A limitation of the above estimator is its sensitivity to edge effects owing to artificial geometric properties being imposed by the ROI border. This calls for a conservative scheme to eliminate certain pixels within the ROI, i.e., those closer than $2r$ to the ROI border. In this study, this limitation is overcome by computing the SIM transform for a larger ROI ($N+4r \times N+4r$ pixels) so that the conservative scheme used to eliminate border pixels results in a SIM-processed ROI of the desired size ($N \times N$ pixels).

After the SIM transformation is computed, the resulting distribution of α values characterizes non-linear structural or textural information within the ROI. Different structural components within the ROI are thus assigned α values that reflect the local geometry; all x_i located in a cluster-like neighborhood are assigned an $\alpha \sim 0$, those in a line-like structure $\alpha \sim 1$, those in a plane-like structure $\alpha \sim 2$, and those in a uniformly distributed neighborhood $\alpha \sim 3$, as previously demonstrated through toy models in [21]. Nine percentiles (10th, 20th, ..., 90th) of this distribution are computed and used to generate a 9D geometrical feature vector. Figure 2 shows examples of ROIs extracted from the radial zone of normal and osteoarthritic cartilage samples imaged with PCI-CT. Also shown here are their corresponding SIM transformations for different values of r , the histograms of α values and the

Fig. 2 The top two rows show examples of a normal and osteoarthritic ROIs (*far left*) and the corresponding SIM transformations for radius $r = \{1, 2, 3, 4, 5\}$. In the SIM transformations, *dark regions* correspond to lower magnitudes of α while *brighter regions* reflect higher magnitudes

of α . The *third row* shows the histogram of α values from each SIM transformation; the *fourth row* shows the same distribution but represented by nine percentiles (10th–90th)

9D feature vectors of percentiles used to represent the distribution of α values in the ROI.

An important factor to consider in extracting such SIM-derived geometric features is the normalization of the gray-level values within the ROI. Of particular interest is the fact that the Euclidean distance between neighboring pixels is calculated with their spatial and intensity dimensions. Since no intrinsic scaling uniquely defines the relationship between these two attributes, we treat the gray-level scaling factor as a free parameter that can be optimized to maximize the separation between normal and osteoarthritic ROIs. Thus, every ROI is pre-processed with a min–max normalization to scale the values in the interval $[0, 1]$ and subsequently multiplied with a scaling factor before the SIM transform is applied. We investigate such SIM-derived features for different values of this scaling factor, $SF = \{0.5, 1, 10, 100\}$ and different radii, $r = \{1, 2, 3, 4, 5\}$.

GLCMs allow for a more statistical characterization of gray-level patterns within an annotated ROI. GLCMs in the four principal directions (0° , 45° , 90° and 135°) are extracted from normal and osteoarthritic ROIs, after pre-processing them to quantize the gray-level values in each ROI to 32 values, as described in [23]. These directional GLCMs are summed element-wise resulting in one non-directional GLCM which serves as the basis for extracting the least correlated and most frequently used statistical features, i.e., absolute value, entropy, contrast, energy, correlation and homogeneity [33]. These features are used, both individually and combined as a 6D feature vector, to characterize the patterns within the annotated ROIs. The inter-pixel distance d is a free parameter; a suitable choice for it was investigated here.

Local GLCM (loc-GLCM) features were also investigated in this study to enable characterization of local spatial properties with GLCM-derived features. This involved computing

GLCM features as described earlier, but on a pixel-wise basis based on the surrounding local neighborhood. As with SIM, nine percentiles (10th, 20th, ... 90th) of the distribution of each GLCM feature are computed and used to generate a 9D loc-GLCM feature vector. This approach combines free parameters from both SIM and conventional GLCM, i.e., the radius of the inter-pixel distance d , the number of gray-levels that the local neighborhoods were quantized to, and the radius of the local neighborhood r . A suitable choice for these parameters was guided by experiments performed with features derived from conventional GLCM and SIM.

Statistical moments of the gray-level distributions within the ROIs, i.e., mean and standard deviation, were used both individually and combined as a 2D vector to serve as a baseline for comparison with features derived from GLCM and SIM.

Classification

The extraction of ROI characterizing features was followed by a supervised learning step where these ROIs were classified as

normal or osteoarthritic. Here, support vector regression with a radial basis function kernel was used for the machine learning task [29]. The SVR implementation was taken from the libSVM library [34].

To accommodate practical limitations imposed by the small size of the patient population used in this study's cartilage specimen extraction, we specified the following patient constraints to the supervised learning step—(1) ROIs from the same patient were not simultaneously used in both training and test sets, and (2) the same number of ROIs were used from every patient to ensure that the classifier did not get over-trained on patterns from a specific patient. Based on these constraints, each iteration of the supervised learning step involved randomly sub-sampling 100 ROIs from each of the five patients and randomly designating one each of the healthy and osteoarthritic subjects as the test set (the other samples comprised the training set). Such a strategy also ensured that training sets used in different iterations of supervised learning were not identical despite the patient constraint.

Fig. 3 Illustrating the distribution of percentile curves extracted from normal ROIs (gray area) and diseased ROIs area (dashed lines). The distribution of curves corresponding to each class is enclosed by the standard deviation as a function of the percentiles; the solid lines mark

the mean value. The root mean square difference between the two classes of curves is indicated on the top left corner of each plot. The rows show the SIM features for different radii (R) and the columns for different scaling factors (SF)

In the training phase, models were created from labeled data by employing a random sub-sampling cross-validation strategy where the training set was further split into 70 % training samples and 30 % validation samples—the purpose of the training was to determine the optimal classifier parameters that best captured the boundaries between the two classes of ROIs. The free parameters for the classifier used in this study were the cost parameter for SVR and the shape parameter of the radial basis function kernel. Then, during the testing phase, the optimized classifier predicted the class of ROIs in the independent test set. A receiver-operating characteristic (ROC) curve was generated and used to compute the area under the ROC curve (AUC) which served as a measure of classifier performance on the independent test set. This process was repeated 50 times resulting in an AUC distribution for each feature set.

Statistical Analysis

A Wilcoxon signed-rank test was used to compare two AUC distributions corresponding to different texture features. Sig-

nificance thresholds were adjusted for multiple comparisons using the Holm–Bonferroni correction to achieve an overall type I error rate (significance level) less than 0.05 [35, 36].

Texture, classifier, and statistical analysis were implemented using Matlab 2010a (The MathWorks, Natick, MA).

Results

Free Parameter Exploration

Figure 3 shows the separation achieved by high-dimensional geometric feature vectors derived from SIM between normal and osteoarthritic ROIs for different combinations of radii and scaling factors. The feature vectors were computed from ROIs of size 51×51 pixels. As seen here, adequate separation between the two classes is achieved by different combinations of values for these parameters. We also make note of two observations—(1) better separation is achieved for smaller radii with smaller scaling factors, and vice versa, as indicated by the root mean square difference between the two classes of

Fig. 4 Comparison of classification performance achieved with GLCM when different inter-pixel distances (d) are used for computation of features (ROI size: 51×51 pixels). For each distribution, the central mark

corresponds to the median and the edges are the 25th and 75th percentile. The best results are observed for correlation when $d=1$

percentile curves and (2) the range of α values produced by the application of the SIM transform to the ROI increases as the scaling factor is increased. For purposes of this study, we used $r=1$ and $SF=1$ for further analysis.

Figure 4 shows the classification performance of the GLCM-derived features when computed with different inter-pixel distances ($d=1, 2, 3, 4, 5$). The features were computed from ROIs of size 51×51 pixels. As seen here, the classification performance deteriorated as the inter-pixel distance was increased. The best classification performance was noted with GLCM feature *correlation* (0.90 ± 0.09) for $d=1$.

Classification Performance Comparison

Table 1 compares the classification performance (evaluated on the independent test set) achieved with the statistical moments, GLCM-derived features (using $d=1$) and SIM-derived geometric features ($r=1$ and $SF=1$). The best performance was observed with the SIM geometric feature vector comprising of nine percentiles representing the histogram of α values extracted from the ROI (0.95 ± 0.06). The best performance among conventional GLCM features was observed with the 6D GLCM vector that combined all features (0.92 ± 0.08). Comparable performance to SIM was achieved by all loc-GLCM features (computed with $d=1$ and $r=1$) except

Table 1 Comparison of classification performance achieved with statistical moments, GLCM features and SIM (ROI size: 51×51 pixels)

Technique	Feature	AUC
SIM	9-Percentiles	<i>0.95±0.06</i>
GLCM	Absolute value	0.82±0.10
	Entropy	0.67±0.07
	Contrast	0.81±0.10
	Energy	0.67±0.06
	Correlation	0.90±0.09
	Homogeneity	0.79±0.10
	Combined (6D)	<i>0.92±0.08</i>
Local GLCM	Absolute value	0.93±0.09
	Entropy	0.93±0.10
	Contrast	0.90±0.10
	Energy	0.93±0.09
	Correlation	0.92±0.10
	Homogeneity	<i>0.94±0.08</i>
Statistical moments	Mean	0.57±0.05
	Std	0.55±0.04
	Mean and Std	0.56±0.05

The best results in each category are marked in *italics*. As seen here, the best classification performance is noted with the SIM feature vector but comparable performance is achieved by most loc-GLCM feature vectors

correlation. All texture features were computed from ROIs of size 51×51 pixels. The best feature from SIM, GLCM and loc-GLCM categories outperformed all statistical moments ($p < 10^{-4}$).

Impact of ROI Size

Figure 5 shows the effect of ROI size on the classification performance of the best features from SIM (9-percentiles feature vector), GLCM (combined 6D feature set), and loc-GLCM (homogeneity). While all features exhibited their best results when extracted from ROIs of the largest size, i.e. 51×51 pixels, SIM-derived features exhibited the least amount of deterioration in classification performance as the size of analyzed ROIs was reduced. For ROIs of size smaller than 41×41 , SIM features exhibited significantly better classification performance than GLCM and loc-GLCM features ($p < 0.05$).

Discussion

PCI has been previously demonstrated as a promising image acquisition modality for visualizing structural details of the cartilage matrix with high spatial resolution [12–14]. Coan et al. acquired PCI-CT images of human knee patellae and reported differences between chondrocyte organization in the radial zone of normal and osteoarthritic cartilage matrix [14]. In this study, we investigated the use of features derived from geometrical and statistical approaches, i.e., SIM and GLCM, in characterizing such differences and potentially serving as imaging markers for OA. Our results show that such pattern descriptors can classify chondrocyte patterns as being normal or osteoarthritic with high accuracy.

Fig. 5 Comparison of classification performance achieved with SIM, combined 6D GLCM vector (*GLCM*) and homogeneity (*loc-GLCM*) when extracted from ROIs of different sizes. For each distribution, the central mark corresponds to the median and the edges are the 25th and 75th percentile. As seen here, SIM exhibits the least deterioration in performance as ROI size is reduced

SIM focuses on a detailed characterization of local structure and geometry in gray-level texture maps captured in annotated ROIs. This characterization was computed on a pixel-wise basis within the ROI and resulting distribution of α values contained non-linear structural and geometrical information corresponding to gray-level patterns in the radial zone of the cartilage matrix. In this study, this distribution of α values was represented by its nine percentiles (10th–90th) and such 9D geometrical feature vectors were subsequently processed in a machine learning task. Our results show that such SIM-derived feature vectors were able to distinguish between normal and osteoarthritic ROIs with high accuracy (0.95 ± 0.06). The observed high accuracy stems from differences in the distribution of α values in both classes of ROIs; osteoarthritic ROIs have an increased content of lower α values while healthy ROIs have more α values of higher magnitude. This effect seems to be a consequence of the fact that the chondrocytes are more clustered in osteoarthritic ROIs; the larger amounts of extracellular space present in normal ROIs contribute more gray-level transitions which results in an increase in higher local dimension, and correspondingly higher magnitudes of α values, as seen in Fig. 2.

The impact of free parameters of SIM, i.e. neighborhood radius r and scaling factor SF, on the ability of SIM-derived feature vectors to distinguish between normal and osteoarthritic chondrocyte patterns was also investigated. Experiments performed in this study do not reveal unique candidate values which best separate normal and osteoarthritic ROIs, but instead suggest a specific relationship between these two free parameters. As shown in Fig. 3, for smaller scaling factors (SF=0.5 or 1), smaller values of r provide the best separation between the two classes while the opposite is true for larger scaling factors (SF=10 or 100). This is explained by the fact that pixel intensities are included in the computation of α values. The scaling factor affects the range of gray-level intensities within the ROI, and consequently plays an integral

role in determining the magnitude of the α values computed. Thus, increasing the magnitude of SF increases the range of α values, thereby requiring larger magnitudes of r to adequately capture differences between the two classes of ROIs.

As seen in Table 1, loc-GLCM features (computed for $r=1$ and $d=1$) yield comparable performance to SIM-derived geometrical features while significantly outperforming most conventional GLCM counterparts. This suggests that local evaluation of spatial descriptors defined through geometry or GLCM-derived statistics can significantly improve performance in classifying healthy and osteoarthritic ROIs. The ability of such loc-GLCM features to distinguish between the two classes of is further illustrated in Fig. 6 for features homogeneity and entropy. As seen here, more regions with high local entropy and low local homogeneity are noted in osteoarthritic patterns than in healthy patterns which could be related to chondrocyte organization in these ROIs. This could be a consequence of chondrocytes being more clustered in osteoarthritic ROIs which could result in more regions with high local entropy and low local homogeneity. Finally, we note that the highest performance in this subset of features was observed with GLCM feature correlation; combining all features did not present a significant improvement in performance over using correlation alone. This could again be related to the fact that the chondrocytes are more clustered in the osteoarthritic ROIs, thereby yielding larger correlation values.

We also studied the impact of ROI size on the classification performance of different features. As seen in Fig. 5, classification performance of all features deteriorates as the ROI size decreases. However, SIM-derived feature vectors are more robust to changes in ROI size than other features. Of particular interest is the observation that SIM-derived feature vectors exhibit a high classification performance (0.94 ± 0.07) when extracted from ROIs as small as 21×21 pixels. This suggests that such geometric feature vectors could play a role in segmentation tasks for automated annotation of normal and

Fig. 6 Median probability distribution (normalized histogram) of healthy and osteoarthritic distributions corresponding to loc-GLCM features entropy (*right*) and homogeneity (*left*). As seen here, such histograms are able to capture differences between the two classes of patterns

osteoarthritic regions. One such approach to segmentation could involve assigning a normal or osteoarthritic label to every pixel in the radial zone based on geometric features computed from the surrounding neighborhood. This would be useful in quantifying the percentage of the radial zone affected by OA, especially in cases where some portions of the cartilage remain healthy, thereby serving as an imaging marker for tracking osteoarthritic progression. This will be explored in further detail in future studies.

We acknowledge a limitation of this study with regard to its small number of patients (five) from whom cartilage specimens were extracted for image acquisition and processing. As a result, the classifier was trained with a smaller subset of patients and could be over-trained to the limited variations of healthy and osteoarthritic patterns found in these subjects. Future studies should include more patients to ensure that the classifier is trained with a potentially larger variation of healthy and osteoarthritic patterns. Future studies could also investigate improvements to the characterization of the radial zone through volumetric analysis as the techniques used in this study, i.e. SIM and GLCM, can be extended for processing 3D volumes of interest (VOI).

Finally, we also note a practical limitation with the experimental setup used in this study concerning the reliance of the imaging technique on synchrotron radiation. This use of a stationary radiation source restricts PCI-CT imaging to ex vivo specimens rather than cartilage tissue in vivo. In this regard, future research will need to focus on implementing PCI methods with high brilliance and high-energy compact X-rays sources that are currently under development [37–39]. These technologies currently show significant promise for transferring PCI-CT imaging from synchrotron radiation facilities, which offer highly collimated, high fluence, and partially coherent X-rays, to a clinical environment.

Conclusion

This study evaluates the performance of geometrical features in characterizing radial zone chondrocyte organization of the cartilage matrix in ex vivo human patella specimens visualized by PCI-CT. The results of this work suggest that geometrical features derived from SIM can distinguish between healthy and osteoarthritic ROIs with high accuracy. The automated and non-subjective manner in which such cartilage matrix descriptors are extracted and the high classification performance they exhibit could indicate a future role for such features as imaging markers for evaluating OA progression and responses to therapeutic intervention when PCI-CT is integrated in a clinical imaging environment. However, larger controlled trials need to be conducted in order to further validate the applicability of such geometric features in a clinical setting.

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