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Volumetric Characterization of Human Patellar Cartilage Matrix on Phase Contrast X-Ray Computed Tomography

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Abstract

Phase contrast X-ray computed tomography (PCI-CT) has recently emerged as a novel imaging technique that allows visualization of cartilage soft tissue, subsequent examination of chondrocyte patterns, and their correlation to osteoarthritis. Previous studies have shown that 2D texture features are effective at distinguishing between healthy and osteoarthritic regions of interest annotated in the radial zone of cartilage matrix on PCI-CT images. In this study, we further extend the texture analysis to 3D and investigate the ability of volumetric texture features at characterizing chondrocyte patterns in the cartilage matrix for purposes of classification. Here, we extracted volumetric texture features derived from Minkowski Functionals and gray-level co-occurrence matrices (GLCM) from 496 volumes of interest (VOI) annotated on PCI-CT images of human patellar cartilage specimens. The extracted features were then used in a machine-learning task involving support vector regression to classify ROIs as healthy or osteoarthritic. Classification performance was evaluated using the area under the receiver operating characteristic (ROC) curve (AUC). The best classification performance was observed with GLCM features correlation (AUC = 0.83 ± 0.06) and homogeneity (AUC = 0.82 ± 0.07), which significantly outperformed all Minkowski Functionals ($p < 0.05$). These results suggest that such quantitative analysis of chondrocyte patterns in human patellar cartilage matrix involving GLCM-derived statistical features can distinguish between healthy and osteoarthritic tissue with high accuracy.

Keywords

phase contrast imaging; patellar cartilage; Minkowski functionals; gray-level co-occurrence matrix; texture analysis; support vector regression

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

1. MOTIVATION/PURPOSE

Phase-contrast X-ray computed tomography (PCI-CT) has recently emerged as a novel imaging approach that provides soft-tissue contrast in cartilage tissue at a micrometer scale resolution [1]. Osteoarthritis (OA), which is one of the leading causes of disability worldwide, is an ideal candidate for PCI-CT as early detection of degenerative cartilage structural changes associated with this disease could potentially result in improved prognosis [2]. The ability of PCI-CT to visualize the differences in chondrocyte organization between healthy and osteoarthritic patellar cartilage has been previously demonstrated [1]. With the aim of developing segmentation tools for automated quantification of healthy and diseased cartilage, we explore the performance of volumetric texture features in characterizing chondrocyte organization in the cartilage matrix.

Previous studies have demonstrated the effectiveness of 2D texture features in capturing differences between healthy and diseased patellar cartilage samples [3]. Extending this approach to 3D, we use volumetric texture features derived from Minkowski Functionals and gray-level co-occurrence matrices (GLCM) for characterizing chondrocyte organization. Minkowski Functionals describe global topological characteristics of underlying gray level patterns while GLCM-derived second order statistics can characterize texture in gray scale images. Both approaches have been applied in different medical image analysis studies [4,5]. 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. [6–36].

The goal of this work is to evaluate and compare the performance of these descriptors to characterize chondrocyte patterns to adequately discriminate between healthy and osteoarthritic samples of cartilage in 3D, as discussed in the following sections.

2. DATA

Our dataset consists of 2 (1 healthy and 1 osteoarthritic) cylindrical osteochondral samples with 7mm diameter. These were extracted within 48 hours of postmortem from the lateral facet of the human patella using a shell auger. The cylinder height was trimmed to 12mm including the complete cartilage tissue and portions of the subchondral bone. The samples were continuously rinsed with 0.9% saline during all the procedures. They were kept in 10% formalin solution during image acquisition.

These samples were subject to PCI-CT imaging with an analyzer-based imaging (ABI) scheme at the European Synchrotron Radiation Facility (ESRF, France). A highly collimated X-ray beam was produced by a 21-pole wiggler after monochromatization by the means of a double Si (111) crystal system and an additional single Si (333) crystal [37]. The analyzer used for the experiments was a single Si (333) crystal. Quasi-monochromatic X-rays of 26 KeV were used. The imaging detector used was the Fast Readout Low Noise (FReLoN) CCD camera developed at ESRF [38]. The X-ray beam was converted to visible spectrum by a 60 μm thick Gadox fluorescent screen. This light was guided onto a 2048×2048 pixel

14×14 m^2 CCD (Atmel Corp, USA) by a lens-based system. The effective voxel size was $8 \times 8 \times 8 \mu m^3$. Further details about the experimental setup can be found in [1].

An image volume of $1120 \times 1124 \times 805$ was acquired for each specimen and subsequently trimmed to eliminate background regions. A total of 496 VOIs, measuring $25 \times 25 \times 25$ were extracted from the radial zone of the cartilage matrix in these two samples (256 healthy, 240 diseased).

3. METHODS

3.1 Feature analysis

Minkowski Functionals are used to characterize morphological properties of binary images i.e. shape (geometry) and connectivity (topology) [39]. An n -dimension pattern is characterized by $n+1$ Minkowski Functionals. For our 3D analysis here, the four Minkowski Functionals are *Volume*, *Surface*, *Mean Breadth*, and *Euler Characteristic*. *Volume* gives the number of white voxels in a binary VOI. *Surface* records the number faces between the white voxel regions and the black background. *Mean Breadth* represents the curvature of the white voxel regions. *Euler* characteristic is a measure of connectivity between the white voxel regions in the VOI. Mathematically these are extracted as follows.

$$\text{Volume} = n_c,$$

$$\text{Surface} = -6n_c + 2n_f,$$

$$\text{Mean Breadth} = 3n_c - 2n_f + n_e,$$

$$\text{Euler Characteristic} = -n_c + n_f - n_e + n_v,$$

where n_c is the number of cubes, n_e is the number of edges, n_f is the number of faces and n_v is the number of vertices. As these features are defined for binary patterns, the VOIs are first subject to thresholding at different gray levels, and then features are computed from these binary VOIs (Fig. 2). In this study, we have also explored the effect of binarizing the VOIs using different number of thresholds to compute the Minkowski Functionals. Hence the topological feature vectors are of dimension N , where N is the number of thresholds used.

GLCM features, as first proposed by [40], represent a variety of second order statistical measures that capture the spatial relationship between gray levels in an image. The least correlated and most commonly used features have been used for this study, namely - absolute value, entropy, contrast, energy, correlation and homogeneity [42]. For each VOI, gray levels were quantized to 32 values prior to the GLCM calculation (in 13 principal directions). From the computed GLCMs, the previously mentioned 6 features were computed and used both individually and combined as a 6D feature vector to evaluate their

ability to classify healthy and osteoarthritic VOIs in this study. Details of the exact computation of these features can be found in [40]. For this study we have also explored the effect of inter-pixel distance when computing the GLCM. For this purpose, we extracted GLCM features from matrices computed with inter-pixel distances 1 through 5.

3.2 Classification

The extracted feature vectors were divided into 60% training and 40% test datasets, and support vector regression [41] with a radial basis function kernel was used for the machine-learning task. The training phase employed a sub-sampling cross-validation strategy; the free parameters of the classifier (cost parameter and shape parameter of radial basis function) were optimized using the training set. The optimized classifier is then used to predict class of VOIs for the independent test set. For measuring the performance of the classifier, the area under the receiver operating characteristic (ROC) curve (AUC) was used. This procedure was repeated 50 times to get the AUC distribution for each texture feature vector used. As there are multiple features involved and hence multiple comparisons, the Holm-Bonferroni correction was used to achieve an overall significance level of $p < 0.05$.

Texture feature extraction, classifier and statistical analysis were implemented using MATLAB 2010a (The Mathworks, Natick, MA).

4. RESULTS

The results obtained using different number of thresholds (5, 10, 15, 20, and 25) have been compared. As can be seen from Fig. 3, the best performance is obtained using 20 thresholds. Further increasing the number of thresholds to 25 yields no significant change in performance. The results using 15 thresholds are also quite close to the best performance, though they are not significantly better ($p > 0.01$).

The free parameter inter-pixel distance for GLCM features plays an important role in the amount of information each feature can capture. A comparison of performance when increasing the inter pixel distance is shown in Fig. 4. With pixel distance 1, the results are best with AUC values having a mean of 0.83. As inter pixel distance increases the performance of the classifier degrades substantially.

5. NEW AND BREAKTHROUGH WORK

The ability of PCI-CT to acquire high-resolution images that can capture chondrocyte organizational differences in healthy and osteoarthritic samples of the human patellar cartilage has been documented in previous work [1]. Previous studies have investigated the use of 2D texture features for classifying healthy and osteoarthritic ROIs annotated in the radial zone of patellar cartilage matrix, as visualized in PCI-CT [3]. Given the need for quantification of healthy and osteoarthritic regions within a patellar cartilage sample, we explore the performance of volumetric texture features in characterizing chondrocyte organization in the cartilage matrix. Here, we explore the use volumetric topological texture features derived from Minkowski Functionals and second-order statistical features derived

from GLCM for classifying VOIs extracted from patellar cartilage as healthy or osteoarthritic.

Our results suggest that GLCM outperforms Minkowski Functionals at the machine learning task. This suggests that the global characterization of the patterns in the VOI provided by Minkowski Functionals is not effective in distinguishing between the two classes of patterns. GLCM on the other hand focuses on local gray-level variations, which contributes to better classification performance. We also note that GLCM correlation exhibits the best classification performance. This feature incorporates the linear dependency of gray levels in a neighborhood, which is measure of how closely related the pixels in the VOI are. In an osteoarthritic sample, the chondrocytes are more clustered and show a more predictable pattern, which is sufficiently characterized by correlation. Among the Minkowski Functionals, comparable classification performance is noted with surface, mean breadth and Euler characteristic. Volume exhibited the worst performance, which indicates its inadequacy in characterizing complex chondrocyte patterns in the cartilage matrix. We have also explored the effect of different free parameters (number of thresholds for Minkowski Functionals and inter-pixel distance for GLCM) in this study. Increasing the number of thresholds does not contribute to improved performance beyond a certain extent (see Figure 3). And as noted in Figure 4, the performance of the classifier significantly declines as the inter pixel distance increases.

The use of such volumetric features could contribute towards segmentation of cartilage into healthy and diseased regions, which can be used to quantify the percentage of the radial zone affected by OA. Such PCI-CT based imaging markers could assist in diagnosis and disease progression monitoring of OA, while also enabling quantification of response to different therapeutic intervention strategies.

6. CONCLUSION

We have proposed an automated approach for classification of healthy and osteoarthritic patellar cartilage VOIs based on volumetric textural characterization of the chondrocyte organization in the radial zone of cartilage matrix, as visualized by PCI-CT images. Our results suggest that GLCM feature correlation achieves high classification performance in this task when compared to topological features derived from Minkowski Functionals. We conjecture that such volumetric analysis can extend towards texture feature-based segmentation of an entire volume of cartilage into healthy and diseased, thereby giving an imaging based diagnostic marker for tracking disease progression and response to therapeutic intervention.

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References

1. Coan P, Bamberg F, Diemoz PC, Bravin A, Timpert K, Mützel E, Raya JG, Adam-Neumair A, Reiser MF, Glaser C. Characterization of Osteoarthritic and Normal Human Patella Cartilage by Computed Tomography X-ray Phase-Contrast Imaging: A Feasibility Study. *Investigative Radiology*. 2010; 45:437–444. [PubMed: 20479648]
2. Braun HJ, Gold GE. Diagnosis of osteoarthritis: Imaging. *Bone*. 2012; 51(2):278–288. [PubMed: 22155587]
3. Nagarajan MB, Coan P, Huber MB, Diemoz PC, Glaser C, Wismüller A. Computer-Aided Diagnosis in Phase Contrast Imaging X-ray Computed Tomography for Quantitative Characterization of *ex vivo* Human Patellar Cartilage. *IEEE Transactions on Biomedical Engineering*. 2013; 60(10):2896–2903. [PubMed: 23744660]
4. Huber MB, Nagarajan MB, Leinsinger G, Eibel R, Ray LA, Wismüller A. Performance of topological texture features to classify fibrotic interstitial lung disease patterns. *Medical Physics*. 2011; 38(4):2035–2044. [PubMed: 21626936]
5. Boehm HF, Raeth C, Monetti RA, Mueller D, Newitt D, Majumdar S, Rummeny E, Morfill G, Link TM. Local 3D Scaling Properties for the Analysis of Trabecular Bone Extracted from High-Resolution Magnetic Resonance Imaging of Human Trabecular Bone: Comparison with Bone Mineral Density in the Prediction of Biomechanical Strength In Vitro. *Investigative Radiology*. 2003; 38(5):269–280. [PubMed: 12750616]
6. Bunte K, Hammer B, Wismüller A, Biehl M. Adaptive local dissimilarity measures for discriminative dimension reduction of labeled data. *Neurocomputing*. 2010; 73(7):1074–1092.
7. Wismüller A, Vietze F, Dersch DR. Segmentation with neural networks. *Handbook of Medical Imaging*. 2000:107–126.
8. Leinsinger, G., Schlossbauer, T., Scherr, M., Lange, O., Reiser, M., Wismüller, A. *Eur. Radiol.* Vol. 16. Springer-Verlag; 2006. Cluster analysis of signal-intensity time course in dynamic breast MRI: does unsupervised vector quantization help to evaluate small mammographic lesions?; p. 1138–1146.
9. Wismüller, A., Vietze, F., Behrends, J., Meyer-Baese, A., Reiser, M., Ritter, H. *Neural Networks*. Vol. 17. Pergamon; 2004. Fully automated biomedical image segmentation by self-organized model adaptation; p. 1327–1344.
10. Hoole, P., Wismüller, A., Leinsinger, G., Kroos, C., Geumann, A., Inoue, M. Analysis of tongue configuration in multi-speaker, multi-volume MRI data; *Proc. 5th Semin. Speech Prod. Model. Data CREST Work. Model. Speech Prod. Mot. Plan. Articul. Model*; 2000. p. 157–160.
11. Wismüller, A. Ph.D. Thesis. Technical University of Munich, Department of Electrical and Computer Engineering; 2006. Exploratory Morphogenesis (XOM): a novel computational framework for self-organization.
12. Wismüller, A., Dersch, DR., Lipinski, B., Hahn, K., Auer, D. *ICANN 98*. Springer; London: 1998. A neural network approach to functional MRI pattern analysis—clustering of time-series by hierarchical vector quantization; p. 857–862.
13. Wismüller, A., Vietze, F., Dersch, DR., Behrends, J., Hahn, K., Ritter, H. *Neurocomputing*. Vol. 48. Elsevier; 2002. The deformable feature map—a novel neurocomputing algorithm for adaptive plasticity in pattern analysis; p. 107–139.
14. Behrends, J., Hoole, P., Leinsinger, GL., Tillmann, HG., Hahn, K., Reiser, M., Wismüller, A. *Bildverarbeitung für die Medizin 2003*. Springer; Berlin, Heidelberg: 2003. A segmentation and analysis method for MRI data of the human vocal tract; p. 186–190.
15. Wismüller A, Dersch DR. Neural network computation in biomedical research: chances for conceptual cross-fertilization. *Theory in Biosciences*. 1997; 116(3):229–240.

16. Bunte K, Hammer B, Villmann T, Biehl M, Wismüller A. Exploratory Observation Machine (XOM) with Kullback-Leibler Divergence for Dimensionality Reduction and Visualization. *ESANN*. 2010; 10:87–92.
17. Wismüller, A., Vietze, F., Dersch, DR., Hahn, K., Ritter, H. ICANN 98. Springer; London: 1998. The deformable feature map—adaptive plasticity for function approximation; p. 123-128.
18. Wismüller, A. *Advances in Self-Organizing Maps*. Springer; Berlin Heidelberg: 2009. The exploration machine—a novel method for data visualization; p. 344-352.
19. Meyer-Bäse, A., Jancke, K., Wismüller, A., Foo, S., Martinetz, T. *Eng. Appl. Artif. Intell.* Vol. 18. Elsevier; 2005. Medical image compression using topology-preserving neural networks; p. 383-392.
20. Huber, MB., Nagarajan, M., Leinsinger, G., Ray, LA., Wismüller, A. *SPIE Med Imaging*. Vol. 7624. International Society for Optics and Photonics; 2010. Classification of interstitial lung disease patterns with topological texture features; p. 762410
21. Wismüller A. The exploration machine: a novel method for analyzing high-dimensional data in computer-aided diagnosis. *SPIE Med. Imaging*. 2009:72600G–72600G.
22. Bunte, K., Hammer, B., Villmann, T., Biehl, M., Wismüller, A. *Neurocomputing*. Vol. 74. Elsevier; 2011. Neighbor embedding XOM for dimension reduction and visualization; p. 1340-1350.
23. Wismüller, A. *Advances in Self-Organizing Maps*. Springer; Berlin Heidelberg: 2009. A computational framework for nonlinear dimensionality reduction and clustering; p. 334-343.
24. Huber, MB., Nagarajan, MB., Leinsinger, G., Eibel, R., Ray, LA., Wismüller, A. *Med. Phys.* Vol. 38. American Association of Physicists in Medicine; 2011. Performance of topological texture features to classify fibrotic interstitial lung disease patterns; p. 2035-2044.
25. Wismüller A, Verleysen M, Aupetit M, Lee JA. Recent Advances in Nonlinear Dimensionality Reduction, Manifold and Topological Learning. *ESANN*. 2010
26. Wismüller, A., Meyer-Baese, A., Lange, O., Reiser, MF., Leinsinger, G. *Med. Imaging, IEEE Trans.* Vol. 25. IEEE; 2006. Cluster analysis of dynamic cerebral contrast-enhanced perfusion MRI time-series; p. 62-73.
27. Twellmann, T., Saalbach, A., Müller, C., Nattkemper, TW., Wismüller, A. Detection of suspicious lesions in dynamic contrast enhanced MRI data. *Eng. Med. Biol. Soc; IEMBS'04. 26th Annu. Int. Conf. IEEE*; 2004. p. 454-457.2004
28. Schlossbauer T, Leinsinger G, Wismüller A, Lange O, Scherr M, Meyer-Baese A, Reiser M. Classification of small contrast enhancing breast lesions in dynamic magnetic resonance imaging using a combination of morphological criteria and dynamic analysis based on unsupervised vector-quantization. *Invest. Radiol.* 2008; 43(1):56. NIH Public Access. [PubMed: 18097278]
29. Otto TD, Meyer-Bäse A, Hurdal M, Summers D, Auer D, Wismüller A. Model-free functional MRI analysis using cluster-based methods. *AeroSense*. 20032003:17–24.
30. Varini, C., Nattkemper, TW., Degenhard, A., Wismüller, A. Breast MRI data analysis by LLE. *Neural Networks; Proceedings. 2004 IEEE Int. Jt. Conf*; 2004. p. 2449-2454.2004
31. Huber, MB., Lancianese, SL., Nagarajan, MB., Ikpot, IZ., Lerner, AL., Wismüller, A. *Biomed. Eng. IEEE Trans.* Vol. 58. IEEE; 2011. Prediction of biomechanical properties of trabecular bone in MR images with geometric features and support vector regression; p. 1820-1826.
32. Meyer-Base, A., Pilyugin, SS., Wismüller, A. Stability analysis of a self-organizing neural network with feedforward and feedback dynamics. *Neural Networks; Proceedings. 2004 IEEE Int. Jt. Conf*; 2004. p. 1505-1509.2004
33. Schlossbauer, T., Kallergi, M., Reiser, MF., Wismüller, A., Meyer- Bäse, A., Lange, O., Leinsinger, G. *J. Electron. Imaging*. Vol. 15. International Society for Optics and Photonics; 2006. Segmentation and classification of dynamic breast magnetic resonance image data; p. 13020
34. Nagarajan, MB., Huber, MB., Schlossbauer, T., Leinsinger, G., Krol, A., Wismüller, A. *Mach. Vis. Appl.* Vol. 24. Springer; Berlin Heidelberg: 2013. Classification of small lesions in dynamic breast MRI: eliminating the need for precise lesion segmentation through spatio-temporal analysis of contrast enhancement; p. 1371-1381.
35. Nagarajan MB, Huber MB, Schlossbauer T, Leinsinger G, Krol A, Wismüller A. Classification of Small Lesions in Breast MRI: Evaluating The Role of Dynamically Extracted Texture Features Through Feature Selection. *J. Med. Biol. Eng.* 2013; 33(1) NIH Public Access.

36. Wismüller, A., Meyer-Bäse, A., Lange, O., Auer, D., Reiser, MF., Sumners, D. J. Biomed. Inform. Vol. 37. Academic Press; 2004. Model-free functional MRI analysis based on unsupervised clustering; p. 10-18.
37. Brankov JG, Wernick MN, Yang Y, Li J, Muehleman C, Zhong Z, Anastasio MA. A computed tomography implementation of multiple-image radiography. Medical physics. 2006; 33(2):278–289. [PubMed: 16532932]
38. Coan P, Peterzol A, Fiedler S, Ponchut C, Labiche JC, Bravin A. Evaluation of imaging performance of a taper optics CCDReLoN'camera designed for medical imaging. Journal of synchrotron radiation. 2006; 13(3):260–270. [PubMed: 16645252]
39. Michielsen K, Raedt H. Integral-geometry morphological image analysis. Physics Reports. 2001; 347(6):461–538.
40. Haralick RM, Shanmugam K, Dinstein I. Textural Features for Image Classification. IEEE Transactions on Systems, Man and Cybernetics SMC-3(6). 1973:610–621.
41. Drucker H, Burges C, Kaufman L, Smola A, Vapnik V. Support vector regression machines. Advances in Neural Information Processing Systems. 1996; 9:155–161.
42. Anys, Hassan, He, Dong-Chen. Evaluation of textural and multipolarization radar features for crop classification. Geoscience and Remote Sensing, IEEE Transactions on 33.5. 1995:1170–1181.

Figure 1. Sample healthy (left) and osteoarthritic (right) volumes of interest of size $25 \times 25 \times 25$ voxels. Volumetric features are used to characterize the gray-level patterns in such VOIs.

Figure 2.

A sample osteoarthritic VOI shown after binarization at 9 different thresholds. Visualization of the internal structure of the binarized VOI is enabled through alpha-transparency settings. The 4 Minkowski Functionals are computed for every such binary VOI.

Figure 3.

Classification performance of 3D Minkowski Functionals at different sets of thresholds (t).

The central marker corresponds to the median of the AUC distribution and the edges correspond to 25th and 75th percentile. As seen here best performance is seen using 15 or 20 thresholds.

Figure 4.

Classification performance of 3D GLCM Features (Absolute Value, Entropy, Contrast, Energy, Correlation, and Homogeneity) for different inter pixel distances (pd). The central marker corresponds to the median of the AUC distribution and the edges correspond to 25th and 75th percentile. As seen here, the best performance is achieved for $pd = 1$.

Figure 5.

AUC distributions obtained over 50 trials using different features. Each plot represents the distribution of values obtained. The box represents the distribution of value between the 25th and 75th percentile and the central line represents the median value of the distribution.

Table 1

Classifier performance comparison using the different features (mean AUC $\pm$ std) achieved with Minkowski Functionals and GLCM features.

Category	Feature	AUC
<u>3D Minkowski</u>		
	Volume	0.54 ± 0.02
	Curvature	0.72 ± 0.06
	Surface	0.74 ± 0.06
	Euler	0.78 ± 0.04
<u>3D GLCM</u>		
	Absolute Value	0.82 ± 0.06
	Entropy	0.69 ± 0.06
	Contrast	0.81 ± 0.08
	Energy	0.69 ± 0.05
	Correlation	0.83 ± 0.06
	Homogeneity	0.82 ± 0.07

Fig. 5 summarizes the classification performance results achieved with the best free parameter for the different feature sets. Our results suggest that the highest classification performance is achieved by GLCM feature correlation (AUC = 0.83 ± 0.06); comparable performance is achieved by GLCM feature homogeneity (AUC = 0.82 ± 0.07). We also note that GLCM feature correlation significantly outperforms all Minkowski Functionals at classifying healthy and osteoarthritic VOIs ($p < 10^{-4}$). Table 1 summarizes the AUC values obtained using all features.