ROI impact on the characterization of knee osteoarthritis using fractal analysis

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Abstract— **This paper presents a preliminary study of the influence of the positioning of Regions Of Interest (ROI) for the characterization of bone texture on radiographs for the diagnosis of knee OsteoArthritis (OA) progression. Characterization of the bone texture is of great interest to doctors because it would improve the prognostic in the clinical routine. In general, studies mainly focus on the descriptors while neglecting the choice of ROI positioning. Using fractal descriptors, the objective of this work is to highlight the impact of the ROI for the diagnosis of knee OA by considering the couple (descriptor, ROI). This study was performed over 1054 knees from 616 subjects composed of stable and progressor patients. Achieved statistical tests demonstrated the importance of the choice of the ROI to improve the clinical diagnosis.**

Keywords— **Texture, Fractal analysis, Region of interest, Osteoarthritis**

I. Introduction

Osteoarthritis (OA) is described as a group of mechanical abnormalities involving articular cartilage loss and subchondral bone changes. Up to now, the magnetic resonance imaging (MRI) is the most relevant tool to describe the complex interaction between the articular and periarticular tissues leading to the whole joint failure that characterize OA [1]. But this examination remains expensive in terms of cost and availability compared to the X-ray radiography. The standard method to assess OA progression consists of measuring the joint space narrowing (JSN) on sequential plain radiographs. This measure gives quite good results but has its own limitations in terms of reproducibility and accuracy since the joint space width (JSW) measure is extremely sensitive to the patient positioning [2].

Recent studies have shown that changes in the subchondral bone are present even in the early stages of the pathology [3], [4]. Moreover the 3D bone structure can be directly evaluated on a 2D plain radiography as shown by Pothuaud [5] and Jennane [6], [7].

These findings led to a renewed interest for the characterization of the subchondral bone texture [8], [9], [10], [11], [12] on X-ray radiographs. Several ways for describing this trabecular texture have been used, as the shape parameters [13], dissimilarity [11], fractal dimension [10] or fractal signature [13].

Fractal analysis is a popular method due to its robustness against common radiographic problem such as exposure or pixel size variations [14]. It was introduced in the trabecular bone characterization of OA joints in the early 1990's [14]. Since this first use, it has been shown using the MRI that the fractal dimension (FD) reflects histomorphometric parameters such as porosity and connectivity [5].

There are many studies in the literature about the diagnosis of knee OA [9], [14] and it is accepted that the FD can be used as a marker of radiographic knee OA. The strength of the FD is that it can detect reduced scale defects invisible to the human observation and help the decision in doubtful situations. This accuracy is also useful for the prediction of knee OA progression. However the diagnosis in clinical routine is still performed on radiography by experienced rheumatologists and mostly based on subjective criterions (*e.g.* Kellgren-Lawrence (KL) scale [15], Osteoarthritis Research Society International (OARSI) grading scale [16]).

There are up to now three studies that use fractal analysis to predict the evolution of knee OA [17], [13], [10].

Messent et al. [17] assessed the changes in the trabecular bone for 40 patients with preexisting OA in medial compartment over 24 months. They used the FD at multiple scales detected by the fractal signature analysis (FSA) [18] to predict the JSN decrease and found significant differences between stable patients and progressors ($p < 0.05$).

Kraus et al. [13] confirmed the results of Messent et al. over a larger dataset (138–vs–40 patients) for a longer period (3–vs–2 years) and added traditional covariates (age, sex, body mass index, knee pain) to boost the classification rates (evaluated using the receiver operating characteristic (ROC) and its area under the curve (AUC) = 0.79–vs–0.75 with 248 knee radiographs).

Woloszynski et al. [10] also involved non-preexisting OA and were able to differentiate early and late progressions. They also introduced a new method for the computation of the FD named Signature Dissimilarity Measure [19] based on the variogram. They obtained similar results as previous studies for late progression (AUC = 0.77 with 68 knee radiographs) and encouraging results for the early progression (AUC = 0.75 with 135 knee radiographs).

In theses studies, authors mostly focus on the descriptors and their predictive ability, but as in many image-based characterization methods, the choice of the ROI has its advantages

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Table 1: Characteristics of the cohort

	0-months	48-months
Age, years	62.3 ± 8.9	66.3 ± 9.0
Body mass index, kg/m^2	29.5 ± 4.6	29.4 ± 4.8
♀, no. (%)	629 (60)	629 (60)
♂, no. (%)	425 (40)	425 (40)
OA knees, no. (%) *	693 (65)	848 (80)
JSN grade, no. (%) **		
0	537 (51)	475 (45)
1	353 (34)	291 (27)
2	150 (14)	197 (19)
3	14 (1)	91 (9)

* Knees with radiographic OA defined as a KL grade ≥ 2.
** JSN grade in the medial compartment defined using the OARSI grading scale.

Table 2: Populations distributions

		KL_{T_0} *	$\Delta JSN_{T_0 \to T_1}$ **	no. (%)
Early	developers	≤ 1	≥ 1	57 (16)
	controls	≤ 1	$= 0$	304(84)
Late	progressors	≥ 2	≥ 1	186 (27)
	stables	≥ 2	$= 0$	507 (73)

* KL grade at first observation.
** JSN grade increase in the medial compartment between both observations.

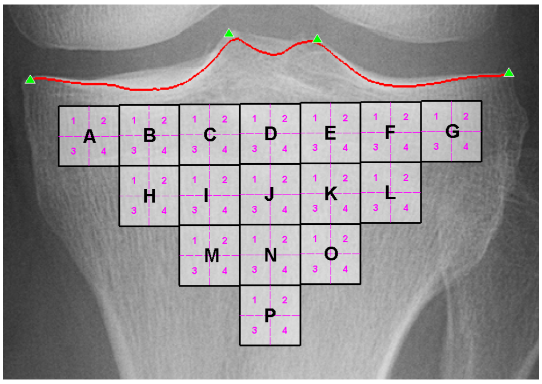

Fig. 1: Segmented tibia and ROIs positioning

and drawbacks and might be determinant.

The present work aims to prove that the ROI can also impact significantly the ability of a descriptor to characterize knee OA development and to provide a background for future studies on knee OA prediction.

II. Material & Methods

Patients.: Data for these analyses are from the OsteoArthritis Initiative (OAI) public use datasets. This database contains X-ray fixed flexion knee radiographs of 4796 patients followed over 72 months. This study is multi-center and multi-equipment. To minimize the bias we only kept the images obtained by the most common modality: the computed radiography. With this restriction, and using only the KL-graded and OARSI-graded part of the database we felt to a subset of 1054 knee radiographs which belong to 616 different patients acquired 48 months apart. This population was composed of 252 men and 364 women. Among these subjects there were 693 knees with OA at baseline and 848 knees with OA after 48 months (see Table 1).

This population was divided into 4 categories according to the KL and OARSI grades and based on the study of Woloszynski et al. [10]. The preexisting knee OA defined as a KL grade ≥ 2 separated the population into two populations called "early" and "late". The progression of the knee OA is evaluated as an increase of the OARSI JSN grade in the medial compartment over the 48 months. Using the JSN grade, the first population "early" was divided into two sub-populations: controls (KL$\leq$ 1 & $\Delta JSN_{T_0 \to T_1} = 0$) and developers (KL$\leq$ 1 & $\Delta JSN_{T_0 \to T_1} \geq 1$). The second population called "late" was also divided into two sub-populations: stables (KL$\geq$ 2 & $\Delta JSN_{T_0 \to T_1} = 0$) and progressors (KL$\geq$ 2 & $\Delta JSN_{T_0 \to T_1} \geq 1$) (see Table 2) .

Image segmentation.: For knee osteoarthritis characterization there is no standard about ROI extraction and each study defines its own ROI [12], [17]. In our implementation, in order to define common ROIs, we placed manually 4 anatomical markers (medial and lateral tibial bounds plus the medial and lateral tibial spines, marks in Figure 1) on the knee radiographs. Using the geodesic distance [20] we developed an original algorithm. The geodesic distance was used to determine the brightest path going through the markers. In case of multiple paths, the euclidean distance was used as a criteria to select the shortest one. This path was retained as the tibial plate (highlighted line in Figure 1) and used as a reference for the placement of the ROIs.

Regions of interest.: Our objective is to provide a large-scale prospective study on the impact of ROI placement for the evaluation of knee OA progression. We have defined a new patchwork of multiple ROIs providing a global view of the OA impact over the FD along the bone. The patchwork was composed of a 4-by-7 matrix of squares clamped to the line defined by the lowest points of the medial and lateral tibial plates. The square side length is equal to 1/7 of the tibial width minus an offset of 10% preventing the periarticular malformations. To avoid cortical region of the bone we analyzed only the central squares of this patchwork that creates a reverse isosceles triangle (see Figure 1). The size of the squares was defined as a percentage of the tibial plateau width in order to scale to the patients anatomy allowing the comparison of different morphologies. The 1/7 factor was determined as the best compromise between a good site specificity and an acceptable reproducibility score. This scale choice provided ROIs of approximately 10.5 x 10.5 mm according to the resolution of the images (0.17 mm/pixel).

Texture analysis.: There are several methods in the literature to compute the fractal dimension [21] of a signal and we focused on the variogram method. The lines of each images were modeled using the fractional Brownian motion (fBm) model governed by a single parameter, the Hurst exponent (H) which is linked to the fractal dimension (FD) as

$$FD = E + (1 - H) \quad (1)$$

where E is the Euclidean dimension. This method is based on the work of Istas & Lang [22] who proved that

$$V_k = V_0.k^2 H \tag{2}$$

where V_0 is a constant, k the distance between samples (scale of observation), H the Hurst exponent and V_k the quadratic variations of the signal. The H parameter can be computed by several ways such as the slope of $log(V_k) - vs - log(k)$. For efficient computation H can be determined directly from (2) as :

$$H = \frac{1}{2}.log_k \frac{V_k}{V_1} \tag{3}$$

Based on the study of Messent et al. [17] we defined k=2 corresponding to the minimum resolution of our images (0.17 ± 0.01 mm). In this case :

$$V_1 = \frac{1}{n_j} \sum_{j=0}^{n_j-1} \left(\frac{1}{n_i - 1} \sum_{i=0}^{n_i-2} \left((I(i,j) - I(i+1,j))^2 \right) \right)$$

$$V_2 = \frac{1}{n_j} \sum_{j=0}^{n_j-1} \left(\frac{1}{n_i - 2} \sum_{i=0}^{n_i-3} \left((I(i,j) - I(i+2,j))^2 \right) \right)$$

For this study images were analyzed in the horizontal (0°) and vertical (90°) directions.

III. Results

The H parameter of the fBm estimated using the Variogram method was used to characterize the 16-ROIs of each image of the database. Focusing on the "late" sub-population and using a Student t-test no significant statistical difference was found to separate the subjects (developers and controls) of the "early" sub-population ($p\text{-}value \geq 0.05$). This led us to refine our patchwork in order to be more site specific. Each ROI was divide into 4 sub-ROIs leading to a total of 64 ROIs (see Figure 1). Each ROI and its sub-ROIs (1, 2, 3, 4) were analyzed in the horizontal (H_{0°) and vertical (H_{90°) orientations. Only the results obtained in the vertical orientation (H_{90°) are presented due to their better results in terms of separability.

As can be seen in Figure 2a for the "early" sub-population the H_{90° mean value of control subjects is always higher compared to the H_{90° mean value of the developers whatever the considered ROI. This shows that the OA progression affects the trabecular bone texture quite uniformly. However, the analysis of Student t-test values highlights differences in the separability of the sub-populations. The lowest $p\text{-}values$ were obtained in the medial subchondral ROI A1 ($p\text{-}value = 0.004$) and in several lateral subarticular ROIs K3, L1, L3 ($p\text{-}values = 0.008, 0.005, 0.007$, respectively).

Focusing on the "late" sub-population we performed the same fractal analysis following the same scheme going from 16 to 64 ROIs. First, the same observation as above can be made *i.e.* a higher H_{90° mean value for the stable sub-population than the H_{90° mean value of the progressors (Figure 2b). Contrary to what was observed for the early sub-population, analyzing the large ROIs with the H parameter, $p\text{-}values$ show statistical significant differences between the stable and progressor patients ($6.10^{-5} \leq p - values \leq 9.10^{-3}$). The lowest and highest $p\text{-}values$ were obtained for ROI B located in the medial compartment and ROI O located in the lateral compartment, respectively (Figure 2b). Analyzing the obtained results for the 64 small sub-ROIs, $p\text{-}values$ were less significant than those obtained for large ROIs.

IV. Conclusion

In this work the impact of ROI placement combined to texture analysis was used for the study of knee OA progression. For texture description we used the fractional Brownian motion model. The H parameter of the fBm was estimated using an efficient method in terms of bias and variance. The ROIs were selected semi-automatically. First, 4 anatomical markers were manually placed on each knee radiograph. Then, the tibial bound was computed automatically using an original method based on the geodesic distance. An original patchwork of 16 ROIs was defined within the medial and lateral compartments on each X-ray image. The size of the rectangle was optimally chosen in such a way that the ROIs were localized avoiding the cortical plate and the fibula bone (Figure 1).

Figure 2 shows that the H parameter decreases with the progression of knee OA ($H_{progressors\&developpers} < H_{stables\&controls}$). The same trend concerning the decrease in H was observed in previous clinical studies.

Results show that location and size of the ROI provide different results for knee OA progression. Better significant results were found for the late progression whatever the size of ROIs (large or small). The resizing of ROIs showed that early prediction depends on the site of observation. This could be explained by the OA process which may be more site specific in the early stages of the pathology. For late stages considering large ROIs is sufficient enough for the diagnosis of knee OA progression. To complete this work, the same analysis should be performed at different stages of the OA progression (12, 24 and 36 months). We believe that such results might improve the prediction of OA progression in the clinical routine and help to define potential progressors subgroup for evaluation of preventive treatments.

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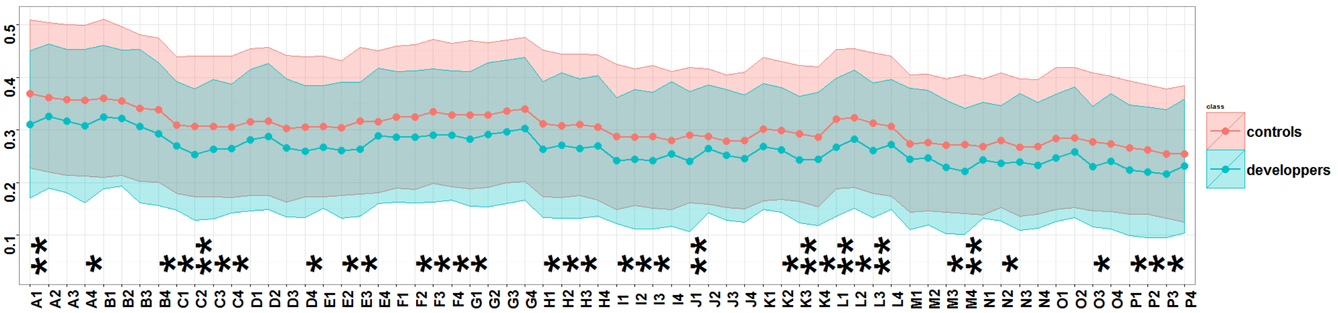
(a) H_{90° for the 64 small sub-ROIs of the early sub-population



(b) H_{90° for the 16 large ROIs of the late sub-population

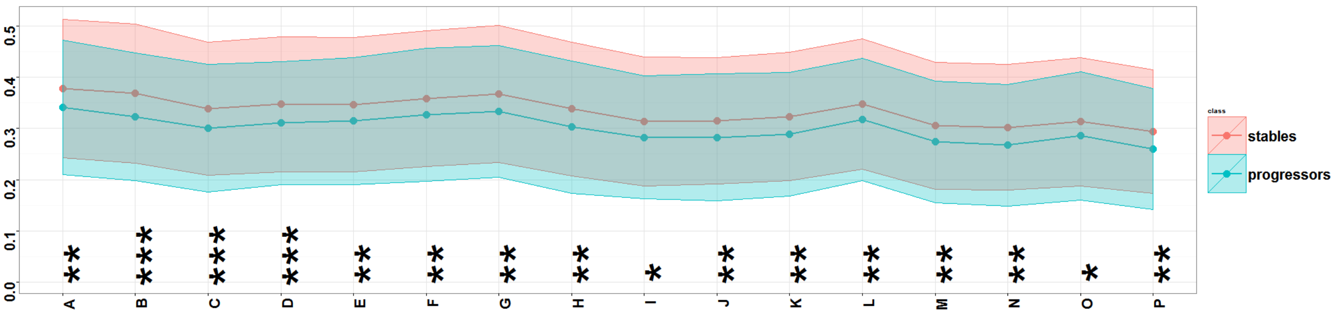


Fig. 2: H_{90° mean values and standard deviation
Significance levels : * p<0.05; ** p<0.01; *** p<0.001

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