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# Multi-dimensional reliability assessment of fractal signature analysis in an outpatient sports medicine population

Mohamed Jarraya[a,b,c], Ali Guermazi[a,b], Jingbo Niu[d], Jeffrey Duryea[e], John A. Lynch[f], Frank W. Roemer[a,b,g,*]

[a] Aspetar, Qatar Orthopaedic and Sports Medicine Hospital, Doha, Qatar
[b] Quantitative Imaging Center (QIC), Department of Radiology, Boston University School of Medicine, Boston, MA, USA
[c] Department of Radiology, Mercy Catholic Medical Center, Darby, PA, USA
[d] Clinical Epidemiology and Training Unit, Department of Medicine, Boston University School of Medicine, Boston, MA, USA
[e] Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
[f] Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA, USA
[g] Department of Radiology, University of Erlangen-Nuremberg, Erlangen, Germany

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ABSTRACT

The aim of this study has been to test reproducibility of fractal signature analysis (FSA) in a young, active patient population taking into account several parameters including intra- and inter-reader placement of regions of interest (ROIs) as well as various aspects of projection geometry.

In total, 685 patients were included (135 athletes and 550 non-athletes, 18–36 years old). Regions of interest (ROI) were situated beneath the medial tibial plateau. The reproducibility of texture parameters was evaluated using intraclass correlation coefficients (ICC). Multi-dimensional assessment included: (1) anterior–posterior (A.P.) vs. posterior–anterior (P.A.) (Lyon-Schuss technique) views on 102 knees; (2) unilateral (single knee) vs. bilateral (both knees) acquisition on 27 knees (acquisition technique otherwise identical; same A.P. or P.A. view); (3) repetition of the same image acquisition on 46 knees (same A.P. or P.A. view, and same unitlateral or bilateral acquisition); and (4) intra- and inter-reader reliability with repeated placement of the ROIs in the subchondral bone area on 99 randomly chosen knees.

ICC values on the reproducibility of texture parameters for A.P. vs. P.A. image acquisitions for horizontal and vertical dimensions combined were 0.72 (95% confidence interval (CI) 0.70–0.74) ranging from 0.47 to 0.81 for the different dimensions. For unilateral vs. bilateral image acquisitions, the ICCs were 0.79 (95% CI 0.76–0.82) ranging from 0.55 to 0.88. For the repetition of the identical view, the ICCs were 0.82 (95% CI 0.80–0.84) ranging from 0.67 to 0.85. Intra-reader reliability was 0.93 (95% CI 0.92–0.94) and inter-observer reliability was 0.96 (95% CI 0.88–0.99). A decrease in reliability was observed with increasing voxel sizes. Our study confirms excellent intra- and inter-reader reliability for FSA, however, results seem to be affected by acquisition technique, which has not been previously recognized.



## 1. Introduction

The fractal dimension or signature of cancellous bone takes into account its composite nature, which is determined principally by trabecular number, spacing, and cross-connectivity (Buckland-Wright et al., 1996; Lynch et al., 1991). Fractal signature or bone texture analysis (FSA) extracted from conventional or digital radiographs has been shown to predict structural outcomes such as radiographic osteoarthritis (OA) progression or future necessity of total joint replacement (Buckland-Wright et al., 1996; Kraus et al., 2013; Woloszynski et al., 2012). However, changes in trabecular bone have also been observed in a post-traumatic setting early in the disease course in young patients (Buckland-Wright et al., 2000). These include thickening of subchondral horizontal trabeculae and may be interpreted by Wolff's law, which states that, in a healthy person, bone will adapt to the loads under which it is placed by undergoing adaptive changes in the internal architecture of the trabeculae (Wolff, 1986). Work done by Kummer has supported the concept of bone adaptation in that bone reacts to

* Corresponding author at: Associate Professor of Radiology, Aspetar, Qatar Orthopaedic and Sports Medicine Hospital, Doha, Qatar, Sports City Road, Doha, Qatar..

*E-mail addresses:* frank.roemer@aspetar.com, frank.roemer@uk-erlangen.de, froemer@bu.edu (F.W. Roemer).

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biomechanical stress via a feedback system with high stress stimulating new bone formation and adaptation and low stress leading to resorption (Kummer, 1995). The radiological architecture of cancellous bone may reflect the direction and local magnitude of stress as manifested by FSA analyses.

These theories and the findings in OA populations suggest that the method may be potentially applied to differentiate young active persons at higher risk from those at lower risk for subsequent knee joint degenerative changes (Buckland-Wright et al., 2000). As FSA has a potential for application in a larger clinical population as a prognostic tool, its applicability in a routine clinical environment needs to be further explored. One potential field of application would be sports medicine as active athletes are potentially at increased risk of premature joint degeneration due to increased biomechanical loading and risk of joint injury (Lohmander et al., 2004; Roos et al., 1994; Roemer et al., 2015). Before one can apply FSA in a sports medicine setting, it is crucial to test the reliability of such a method. This test should – beyond the assessment of observer variability – include parameters of image acquisition. Although FSA has been reported to be a robust method (Lynch et al., 1991), previous studies have shown that fractal indices are affected by the size and shape of the region of interest (ROI) (Shrout et al., 1997).

Thus, the aim of this study has been to test the reliability of FSA measurements on digital radiography of the knee joint in a cohort of patients referred to a sports medicine department including several dimensions such as intra- and inter-observer reliability, the influence of repeated image acquisition using the same imaging technique and the variability of measurements using uni- vs. bilateral and anterior–posterior (A.P.) vs. posterior–anterior (P.A.) image acquisitions.

## 2. Materials and methods

### 2.1. Patients

The local institutional review board approved the study design and granted exempt status (Anti Doping Lab Qatar, IRB number EX2014000008).

The study was based on a search performed within the hospital picture archiving communication system (PACS) to find knee radiographs within a 2-year period from January 2011 to December 2012. Altogether, 685 consecutive patients between the ages of 18 and 36, who had presented to the outpatient clinic of a secondary referral center for sports medicine were included. These patients had complained of chronic or subacute pain, but must not have suffered acute knee trauma within the last four weeks as verified by the patients' clinical records. Patients with remote trauma or previous surgery were not excluded as these patients may have altered bone structure that would diversify and enrich the reliability datasets, but knees with metal hardware due to anterior cruciate ligament reconstruction overlapping the ROI were excluded. Data on the prevalence of radiographic features of OA in the same patient population have recently been presented (Roemer et al., 2015).

### 2.2. Image acquisition

Digital radiographic images were acquired with a standard clinical fluoroscopy system and a film–focus distance of 180 cm. Each participant had weight-bearing single and/or bilateral knee radiographs. The X-ray beam was directed in the A.P. and/or the P.A. direction. For achievement of optimal quality, infrequently different angulations had to be applied such that the medial tibial plateau is aligned with the radiographic beam and appears horizontal (Piperno et al., 1998). In line with previous publications,

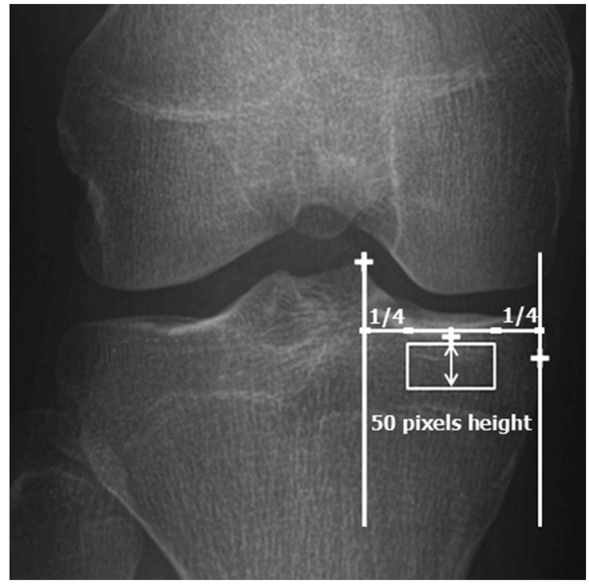


**Fig. 1.** Example of region of interest (ROI) placement for fractal signature analysis (FSA) in the subchondral medial tibia. The horizontal distance of the ROI was set at the middle two quarters of the distance between the medial tibial spine and the medial tibial border (rectangle). The peripheral quarter was excluded to avoid the periarticular osteopenia adjacent to marginal osteophyte formation.

the focus of the current analyses was the medial tibial plateau (Kraus et al., 2013; Wolski et al., 2010). In addition, all radiographic images were then evaluated by a musculoskeletal radiologist (MJ) for quality assurance, particularly as to quality of visualization of the joint space of the medial tibiofemoral compartment, specifically whether the tibial plateau posterior and anterior margins overlapped. Whenever the tibial plateau margins nearly touched or overlapped the medial femoral condyle the radiographic view was considered suboptimal and the corresponding knee was excluded from analysis. Altogether, 8% of the knees ($n = 60$) were excluded from the study due to insufficient image quality.

### 2.3. Fractal signature analyses

Landmarks were placed manually for each X-ray view separately by a musculoskeletal radiologist with 5 years of experience in musculoskeletal imaging research (MJ). These placements were blinded to the other X-ray view of the same knee and landmark placement. Landmarks included the most medial tibial border excluding osteophytes, the medial tibial spine, and the deepest point of the medial cortical plate (Fig. 1). The ROIs were then automatically generated from the selected landmarks with the horizontal distance of the ROI set at the middle two quarters of the distance between the tibial spine and tibial border. The peripheral quarter of the tibia was excluded to avoid common periarticular osteopenia adjacent to marginal osteophyte formation, similar to previous studies (Mills et al., 2008). Rather than using a pre-defined horizontal distance we opted for proportional placement at the middle two quarters to take into account the individual variability of the tibial plateau width. A standard vertical distance of 7.15 mm of the ROI deep to the cortical plate landmark was selected. Other than placing the landmarks, no manual adjustment was performed. FSA was calculated in the horizontal and vertical dimensions in 10 horizontal and vertical dimensions ranging from 0.286 mm to 1.573 mm according to the method by Buckland-Wright et al., 1996.

Multi-dimensional assessment included:

(1) A.P. vs. P.A. views on 102 knees performed by one observer (MJ)