



Available online at www.sciencedirect.com



Biosurface and Biotribology 2 (2016) 162-172



Detection and prediction of osteoarthritis in knee and hand joints based on the X-ray image analysis

G.W. Stachowiak, M. Wolski*, T. Woloszynski, P. Podsiadlo

Tribology Laboratory, School of Mechanical and Civil Engineering Curtin University, Bentley, Western Australia 6102, Australia

Received 7 October 2016; received in revised form 16 November 2016; accepted 22 November 2016

Abstract

Current assessment of osteoarthritis (OA) is primary based on visual grading of joint space narrowing and osteophytes present on radiographs. The approach is observer-dependent, not sensitive enough for the detection of the early stages of OA and time consuming. A promising solution is through fractal analysis of trabecular bone (TB) textures on radiographs. The goal is to develop an automated decision support system for the detection and prediction of OA based on TB texture regions selected on knee and hand radiographs. In this review, we describe our progress towards this development which was conducted in five stages, i.e., (i) development of automated methods for the selection of TB texture regions on knee and hand radiographs (ii), development of fractal signature methods for TB texture analysis, (iii) applications of the methods in the analysis of x-ray images of knees and hands, (iv) development of TB texture classification system, and (v) development of ReadMyXray website for knee x-ray analysis. The results achieved so far are encouraging and it is hoped, that once the system is fully developed and evaluated, it will be used to aid medical practitioners in the decision-making, i.e., in designing OA preventative measures, treatments and monitoring the OA progression.

© 2016 Southwest Jiaotong University. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Keywords: Osteoarthritis; Trabecular bone; Fractals; Image analysis; Classification

Contents

1.	Introduction	. 163
2.	Automated bone texture region selection on knee and hand radiographs	. 163
	2.1. Knee radiographs	. 163
	2.2. Hand radiographs	. 164
3.	Development of directional fractal signature methods for bone texture analysis in knees and hands	. 164
	3.1. Knee radiographs	. 164
	3.2. Hand radiographs	. 167
4.	Applications of the methods developed to the analysis of x-ray images of knees and hands	. 167
	4.1. Detection of differences in TB texture between subjects with and without OA	. 167
	4.2. Detection of differences in TB texture between subjects with and without cartilage defects	. 167

Peer review under responsibility of Southwest Jiaotong University.

2405-4518/© 2016 Southwest Jiaotong University. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

^{*}Correspondence to: Department of Mechanical Engineering, Curtin University, GPO Box U1987, Perth, Western Australia 6845, Australia. Fax: +61 8 9266 2681.

E-mail address: marcin.wolski@curtin.edu.au (M. Wolski).

http://dx.doi.org/10.1016/j.bsbt.2016.11.004

	4.3.	Association of baseline bone texture with KJR at 6-year follow up	168
	4.4.	Association of baseline bone texture with incident of knee OA at 30-, 60- and 84-month follow-ups.	168
	4.5.	Detection of differences in TB texture between subjects with and without hand OA	168
5.	Devel	opment of bone texture classification system	169
6.	Devel	opment of ReadMyXray website	169
7.	Sumn	nary	170
Ac	knowle	dgements	171
Ret	ference	s	171

1. Introduction

Osteoarthritis (OA) is a debilitating and costly disease to all societies across the globe [1]. As people live longer and the populations rapidly age, this cost is continuously increasing and OA becomes an important issue that cannot be ignored. One way of mitigating this cost is through early detection and, more importantly, prediction of OA. To achieve this, new automated diagnosis and prognosis techniques designed to assist the medical personnel in the decision-making must be developed. The techniques would allow for identification of patients on a development pathway to OA. For these individuals, OA management (e.g., exercise, dietary supplements, and lifestyle changes) could be initiated in a timely manner, thus reducing impact of OA on quality of their lives and slowing down its progression [2]. The patients would also benefit from inclusion in clinical trials on disease-modifying osteoarthritis drugs (DMOADs), such as strontium ranelate and bisphosphonates [3,4]. The two DMOADs showed promising results in animal models of OA. Strontium ranelate was found to reduce cartilage and bone pathology, while bisphosphonates could prevent bone remodeling and preserve its structural integrity.

Latest imaging techniques such as magnetic resonance imaging (MRI) and computed tomography (CT) are routinely used in medical examinations. Classical x-ray technique, even though more than 100 years old, is cheap, fast, easy to use and still provides valuable information about changes occurring in human bones [5]. Current OA assessment is based primarily on visual grading of joint space narrowing (JSN) and osteophytes using atlases, e.g., the Osteoarthritis Research Society International (OARSI) atlas [6] or Kellgren-Lawrence (K-L) grading scheme [7]. The individual grading is time consuming, prone to high intra- and inter-rater variability, and is not sensitive enough to detect changes occurring in joints at the early stages of OA [8-10]. For example, it was shown that about 11-13% of cartilage volume can be lost before JSN of grade one is observed on radiographs [8], and cartilage defect occur before radiographic OA or knee joint pain are present [11].

A promising solution to this problem is through application of fractal analysis to the trabecular bone (TB) texture radiographic images. The reasons are following: (i) TB changes at the early stages of OA [12,13], (ii) TB exhibits fractal properties, i.e., it is self-similar over a range of scales [14,15], (iii) TB texture images selected on 2D radiographs are directly related to the underlying 3D bone structure [16], and (iv) OA changes have been detected on TB texture images using fractal methods [17,18]. In this work

we focus on OA in knee and hand joints, since these joints are most commonly affected by the disease.

In this paper, the progress towards the development of the detection and prediction of OA based on TB texture images is summarized. The work conducted has been divided into five stages, i.e.: (i) development of automated methods for the selection of TB texture regions on knee and hand radiographs (ii), development of fractal signature methods for the bone texture analysis in knees and hands, (iii) applications of the methods developed to the analysis of x-ray images of knees and hands, (iv) development of bone texture classification system, and (v) development of dedicated website for the automated analysis of x-ray images of knee joints.

2. Automated bone texture region selection on knee and hand radiographs

In the first stage, an automated methods for the selection of TB texture regions of interest (ROI) on knee [19] and hand [20] x-ray images were developed. Currently, the bone regions are usually selected manually by a trained observer which is time-consuming and observer-dependent.

2.1. Knee radiographs

The method developed selects two square ROIs on an x-ray image on the TB immediately under the medial and lateral cortical plates of the tibia without the need for a human operator (Fig. 1(a)). The method has three major components: image preprocessing, delineation of cortical bone plates and location of the ROIs. In the first component, image is resized to 512×512 pixels, its contrast is adjusted, edges are enhanced, and knee borders together with the joint space line are found. In the second component, active shape models (ASMs) are used to delineate superior borders of the medial and lateral cortical tibia plates. The final component consists of placing the ROIs under the cortical borders and performing horizontal and vertical adjustments of their positions so that they do not overlap periarticular osteopenia, subchondral bone sclerosis and fibula head (only lateral ROI). The accuracy of the method in the selection of the regions was compared against gold standard ROIs selected manually by an experienced radiologist on 132 knee x-ray images. The agreement with the gold standard was evaluated by means of similarity index (SI). SI is an overlap measure between the region selected by the automated method and the corresponding gold standard region. It takes values between 0 (no overlap) and 1





b



Fig. 1. X-ray images of (a) knee and (b) hand with selected TB texture ROIs (white squares). Hand image adapted from OAI database.

(entire overlap). In general, values of SI ≥ 0.70 indicate excellent agreement [21]. The results obtained showed that the method developed is accurate and reliable (SI ≥ 0.81). However, errors in ROI selection can occur. These errors could be due to low contrast between knee and background and the deformation of knee bones. For such cases, a special user interface was developed to enable manual adjustment of ROIs.

2.2. Hand radiographs

For hand radiographs, automated selection of bone regions is far more difficult than for knee joints. Compared to tibia, finger bones and subsequently ROIs are much smaller, e.g., 20×20 pixels as opposed to 256×256 pixels for knee ROIs. Also, there are more bones in hand, i.e. regions to be selected (16 in hands as opposed to 2 in knees). In addition finger bones have varying orientations with respect to the image horizontal axis. There is no such problem with knees. The method developed selects square ROIs above and below cortical plates of the 2nd-5th distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints as these joints are often affected by OA. For one hand, all together 16 ROIs (2 regions per joint) are selected (Fig. 1(b)). The ROIs selection is executed in four stages: (i) x-ray image segmentation into hand and background, (ii) identification of the 2nd-5th finger regions, (iii) localization of centre points of distal phalanges heads and DIP, PIP and metacarpophalangeal (MCP) joints, (iv) location of the ROIs under and above the DIP and PIP joints. The accuracy of the method developed was evaluated using gold standard ROIs selected manually by a trained observer on 40 hand x-ray images. Effects of hand translation, rotation, finger separation and flexion were tested. It was found that the selection of the ROIs on hand radiographs using the new method is accurate and reliable (SI \geq 0.7). Nevertheless, in some isolated cases the selection of ROIs can be inaccurate, especially for hand radiographs with severe OA or non-anatomical structures present (e.g., rings). Thus, a mouse pointer tool was developed to adjust the regions' position and orientation if necessary.

3. Development of directional fractal signature methods for bone texture analysis in knees and hands

In the second stage, methods for the analysis of the ROIs selected on knee and hand radiographs were developed. The methods would have to be not only sensitive enough to differentiate between healthy and osteoarthritic joints, but also be able to detect minute changes occurring in TB due to OA, i.e., to detect an early development of OA.

As bone texture images exhibit anisotropic and multiscale nature (i.e., their characteristics change with direction and scale) we decided to use fractal signature (FS) based techniques, principles of which were originally developed by Peleg [22]. FS is a set of fractal dimensions (FDs) calculated at individual scales (i.e., trabecular image sizes) while FD is the most popular fractal measure of texture roughness. High (low) FD values indicate rougher (smoother) textures.

3.1. Knee radiographs

For the analysis of x-ray images of knee joints, we developed the variance orientation transform (VOT) method [23]. The method calculates FS in all possible directions (i.e., directional FS (DFS)) allowing for detailed analysis of multiscale bone texture roughness. Briefly, in the VOT method, absolute differences of grayscale level values are calculated for



Fig. 2. A schematic illustration of the VOT method: (a) a search region that moves across the image, (b) a log-log plot, (c) a rose plot of Hurst coefficients and (d) texture parameters calculated from the plot.

pairs of pixels within a circular search region of a fixed size, which moves across the bone texture image (Fig. 2(a)). The differences between the pixels' grey-scale level values along with the corresponding directions and distances between the pixels are stored. The direction is defined as an angle between a line running through the pair of pixels and the x-ray horizontal axis. For each direction, the variances of the differences stored are plotted in log-log coordinates against distances (Fig. 2(b)). The log-log data points are then divided into overlapping sub-sets of points, a line is fitted to each subset, and its slope is used to calculate the Hurst coefficient (H)at an individual scale. H relates to FD as FD=3-H. The individual scale is represented by the distance associated with the central log-log data point in the corresponding sub-set. At each scale, the Hurst coefficients obtained are plotted in polar coordinates against directions and an ellipse is fitted to the resulting plot (Fig. 2(c)). Using the ellipses fitted, the following bone texture parameters are calculated (Fig. 2(d)):

- Roughest part FS (FSSta). FSSta quantifies the texture roughness in the roughest direction of TB at individual scales. FSSta is calculated as 3-Sta, where Sta is half the minor axis length of the ellipse fitted at a given scale.
- Texture aspect ratio signature (StrS). The parameter measures a degree of bone texture anisotropy at different scales. It takes values between 0 and 1, with lower values representing higher anisotropy. It is calculated as the ratio of the minor to the major axes of the ellipses fitted at different scales.
- Texture direction signature (StdS). It describes dominating texture direction at individual scales. It is defined as an angle between the major axis of the ellipse fitted and the horizontal image axis at each scale.



Fig. 3. X-ray images of (a) normal and (b) osteoarthritic knee joints with marked ROIs (white squares), corresponding (c, d) bone texture images, and (e, f) rose plots of Hurst coefficients, along with ellipses fitted, at scale of 0.55 mm obtained for the regions.

As an example, the VOT method was applied to two bone texture regions selected in the medial compartment of tibia from subjects with and without knee OA (Fig. 3(a) and (b)). Corresponding rose plots obtained for these two regions are shown in Fig. 3(e) and (f), respectively. From the Fig. 3, it can be seen that the plot corresponding to the healthy knee approximates an ellipse, while the plot corresponding to the OA knee exhibits roughly circular shape. This indicates that bone texture roughness in the healthy joint, as compared to the diseased bone, varies considerably with direction, i.e., OA texture is less anisotropic than in the healthy knee [24]. The mean StrS values obtained were 0.72 (OA) and 0.52 (non-OA).

The plots also show that Hurst coefficients calculated for healthy bone are, in general, lower (i.e., higher FDs) than those for OA bone. This means that the healthy bone texture is generally rougher than the OA bone [24]. This agrees with the mean FDSta values obtained for the non-OA and OA subjects, i.e., 2.87 and 2.83, respectively. The means of StdS obtained were 105° (non-OA) and 60° (OA), showing the dominating texture directions, i.e., directions in which bone texture is the smoothest.

The effects of radiographic conditions on the VOT method were evaluated, i.e., radiographic noise, blur, exposure, magnification, projection angle, translation of the ROIs, and image resolution/size [23,25,26]. The results obtained showed that the method is considerably affected by image noise (greater than 5%), blur, magnification, projection angle (more than 10°), and resolution (less than 48×48 pixels).

3.2. Hand radiographs

ROIs selected on hand radiographs are considerably smaller than those on knee radiographs, e.g., 20×20 (hand) vs 256×256 (knee) pixels. We found that the VOT at image sizes less than 48×48 pixels does not provide reliable results as there is not enough data for the analysis [26]. To address this problem, we developed an augmented VOT method (AVOT) [26].

The AVOT method's operating principles are similar to VOT, except that the size of the search region is automatically adjusted to the size of a TB texture ROI, and FSs can be calculated with respect to any reference direction. This was achieved through the application of a recursive multidirectional pixel selection (RMPS) algorithm and a reduction of the marginal subsets of points in the log–log plot from five to three. Details of the algorithm and the reduction procedure are given in [26]. As a result, the AVOT method can reliably calculate FSs of small bone texture regions selected on arbitrary oriented finger bones.

4. Applications of the methods developed to the analysis of x-ray images of knees and hands

In the third stage, the potential of the VOT and AVOT methods for the detection and prediction of OA was evaluated in a number of following studies [26-30], i.e.:

- Detection of differences in TB texture between subjects with and without knee OA.
- Detection of differences in TB texture between subjects without radiographic knee OA (K–L grade < 2), but with and without cartilage defects.
- Association of baseline bone texture with knee joint replacement (KJR) at 6-year follow-up.
- Association of baseline bone texture with incident of knee OA at 30-, 60- and 84-month follow-ups, and
- Detection of differences in TB texture between subjects with and without hand OA.

4.1. Detection of differences in TB texture between subjects with and without OA

Initially a pilot study was conducted to evaluate the VOT method abilities to differentiate between OA and non-OA textures in knees [27].

For this study 26 cases and 26 controls were used. Controls were the subjects with (K–L grade ≥ 2) and without (K–L grade < 2) knee OA, respectively. The subjects were individually matched by sex, age and body mass index (BMI). Tibial bone texture ROIs (two per knee joint) were selected on cases and controls knee x-rays, and analysed by the VOT method.

Examples of the ROIs selected on a knee x-ray are shown in Fig. 1(a). Bone texture parameters obtained for cases and controls were compared using paired *t*-test. The results showed that OA textures were smoother and less anisotropic than textures in healthy joints, i.e., that trabeculae in OA joins are thicker and less structured than in non-OA joints. For this study, a database from Lund University (Sweden) was used [31].

4.2. Detection of differences in TB texture between subjects with and without cartilage defects

In this case-control study, the VOT method's sensitivity to pre-radiographic OA bone changes in joints with and without cartilage defects was investigated [28]. Cases (n=28) were subjects with cartilage defects (grade ≥ 2), whereas controls (n=28) exhibited normal cartilage (grade < 2). The subjects were individually matched by sex, age, BMI, whether arthroscopic partial meniscectomy (APM) was performed or not, and APM's location (i.e., medial or lateral compartment). All subjects were without radiographic knee OA (K-L grade < 2). Cartilage defects were identified and graded based on MRI scans [28]. An example of a MRI scan of a knee joint with cartilage defects is shown Fig. 4 [32]. Databases from the University of Western Australia and Monash University (Australia) were used [33]. On each x-ray image, bone regions in the medial and lateral compartment were selected and analysed using the VOT method. Paired t-tests were used to evaluate differences in fractal parameters between cases and controls. The results showed that TB texture was rougher for cases than for controls, suggesting that thinning and fenestration of trabeculae occur in knee joints with early OA (i.e., with cartilage defects). This finding seems to contradict our previous results [27] which showed that OA knees exhibit lower roughness than healthy joints. However, a possible



Fig. 4. Example of grade 2 and grade 3 cartilage defects visible on a MRI scan. Image adapted from [32].

explanation is that TB changes occur in two stages due to OA. In the early OA stage, trabecular structures undergo thinning and fenestration, whereas in the late OA, TB thickens. This explanation is consistent with other studies in which it was shown that early knee OA exhibits bone resorption, while later stages of OA are characterized by bone formation, suggesting non-linear relationship between TB changes and OA severity [34,35].

The results from this study show that the VOT method is sensitive enough to detect pre-radiographic OA bone changes.

4.3. Association of baseline bone texture with KJR at 6-year follow up

In another study, the potential of the VOT method in predicting KJR in patients with OA was assessed [36]. Medial and lateral bone ROIs were selected on knee radiographs of 114 subjects with symptomatic knee OA. A database from Monash University (Australia) was used [29]. 28 subjects (25%) underwent KJR over 6-years. The associations between tertiles of bone texture parameters obtained at baseline and the incidence of KJR were studied using logistic regression. The statistical analyses were performed with adjustment for baseline age, sex, BMI, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, and osteophyte and JSN grades. It was found that in knees exhibiting higher baseline bone texture roughness, the risk of KJR is reduced. This could be the result of the decrease in size of trabeculae and increase in interconnectivity of TB structures due to bone marrow lesions (BMLs). It is known that BML is a risk factor of KJR [37].

These results showed that the VOT method could identify subjects with knee OA who are likely to undergo KJR.

4.4. Association of baseline bone texture with incident of knee OA at 30-, 60- and 84-month follow-ups

Recently, a much wider study, involving 3026 subjects (6052 knees) from the Multicentre Osteoarthritis Study (MOST) [University of California, San Francisco], was conducted [30]. In the study, 894 subjects (626 knees) recruited by University of Alabama (UAB), and 807 subjects (1158 knees) from University of Iowa (UIowa) were used. Associations between baseline TB texture and radiographic OA incidence at three follow-up periods (30, 60 and 84 months) were investigated. At the baseline, subjects were without radiographic knee OA (i.e., K–L grade 0 or 1). There were 195 (22%, UAB) and 303 (26%, UIowa) OA incident knees cumulative to 84 months. OA incidence was defined as K–L grade 2 or more at follow-up.

The associations of quartiles of baseline fractal parameters calculated using the VOT method with incident OA were evaluated using logistic regression adjusted for age, sex, race, BMI, leg alignment and baseline K–L grade (0 or 1). The analyses were stratified by two radiographic modalities used, i.e., digitized film in the UAB and computer radiography in the

UIowa. Results obtained showed that baseline bone texture parameters are associated with the OA incident at follow-up. Specifically, for subjects from UAB, it was found that the baseline higher medial bone roughness was associated with increased odds of OA incidence at a follow-up. For subjects from UIowa, lower anisotropy of bone textures at baseline was associated with increased odds of OA. The higher roughness of bone texture at baseline in subjects who had incident of OA, as compared to those who did not, could be a result of fenestration and breakage of TB structures due to early OA. The results agree with our previous findings [28] that in knee joints with pre-radiographic OA, bone texture is rougher than in healthy joints.

These results are promising, showing that the VOT method can be used in the development of a system for knee OA prediction.

4.5. Detection of differences in TB texture between subjects with and without hand OA

Hand x-ray images from 40 subjects from the Osteoarthritis Initiative (OAI) database [University of California, San Francisco] were analyzed using the AVOT method. The subjects were individually matched by sex, age, BMI and race [26]. Half of the subjects (i.e., cases) had radiographic OA (approximate K-L grade ≥ 2) in the 5th DIP joint. Controls did not have OA (approximate K-L grade < 2) in the joint. On each hand radiograph, two ROIs were selected, i.e., the first in the base of the 5th distal phalanx and the second in the head of the 5th middle phalanx (Fig. 5). The regions were analyzed with the AVOT method and the differences in the parameters obtained between cases and controls were evaluated using paired t-tests. We found that TB texture was smoother for cases than for controls in the horizontal directions, rougher in the vertical direction, and less anisotropic. These differences might indicate thickening and realignment of trabeculae in the phalanges due to OA.



Fig. 5. X-ray images of (a) normal and (b) osteoarthritic DIP joints with marked bone texture regions $(20 \times 20 \text{ pixels})$. Images adapted from [26].

The results obtained were encouraging, showing that the AVOT method could be used for OA detection in hands. A study with larger number of subjects will be conducted in the future.

5. Development of bone texture classification system

In the fourth stage, we focused on the development of an automated system for the classification of knee x-ray images based on bone textures. To simplify the development, we initially decided to use a signature dissimilarity measure (SDM) method which calculates only three parameters (i.e., overall roughness, anisotropy and direction) [38]. The parameters quantify texture features sensitive to OA changes in trabecular bone. The VOT method calculates a relatively large number of parameters (i.e., 27) which considerably hinders image classification due to the "curse of dimensionality". Full description of the SDM method is given in [38]. Briefly, the method is executed in several steps. First, a scale-space representation of a TB texture image is constructed by convoluting the image data with Gaussian kernels at different scales. Second, the gradient and Laplacian operators are applied over all scales and their extremum values are found. Next, histograms of the differences of the extremum values in different directions are constructed. Using the histograms, the three, mentioned above, parameters are then obtained.

We assessed the performance of the SDM method in prediction of radiographic OA progression and achieved high prediction scores in the sample of patients tested [39]. In the study, we analyzed the radiographs from 105 subjects (90 men and 15 women with a mean age of 54 years) [39]. Altogether, radiographs from 203 knees, 68 with and 135 without radiographic tibiofemoral OA (i.e., K–L grade < 2), were analyzed. Two sets of knee radiographs (baseline and follow-up) were obtained 4 years apart. ROIs of medial compartment tibial TB texture were selected using an automated region selection method. TB texture was then analyzed using the SDM method and three parameters were produced for each ROI: roughness, degree of anisotropy and direction of anisotropy. A logistic regression model based on the parameters was evaluated in the prediction of medial tibiofemoral OA progression defined as an increase in medial JSN grade between baseline and follow-up. The model was adjusted for age, sex, and BMI. For knees with and without pre-existing radiographic OA at baseline, the regression model based on the parameters calculated on medial TB texture had the prediction accuracy of 0.77 and 0.75 area under the curve (AUC), respectively.

We then used the SDM method to develop a dissimilaritybased multiple classifier (DMC) system for the classification of knee x-ray images [40]. The schematic illustration of the DMC is shown in Fig. 6. The DMC consisted of a heterogeneous ensemble of classifiers (linear, quadratic, tree, k nearest neighbors, Parzen and support vector machine). To produce a class for TB texture (e.g., healthy or OA), classifiers in the ensemble were combined using a specially developed probabilistic model [41]. The model selectively combined only those classifiers which performed well on similar TB texture



Fig. 6. A schematic illustration of the DMC system for classification of TB bone textures.

images during system training. We assessed the DMC in the detection of radiographic OA and prediction of radiographic OA progression, and the results were encouraging.

For the detection, in a pilot study [40], knee radiographs from 51 subjects were initially analyzed. Healthy and OA classes were defined as K–L grade 0 in both tibiofemoral compartments in both knees and K–L grades 2 or 3 in at least one tibiofemoral compartment in at least one knee. Prediction of radiographic OA progression was assessed on two sets of knee radiographs taken from 50 subjects 4 years apart. The definition of non-progressive and progressive classes was based on the increase in the sum of tibiofemoral JSN and osteophytes grades between baseline and follow-up. The DMC achieved classification accuracies of 90.51% and 80% (averages over 5 repetitions of two-fold cross validation) for the detection of radiographic OA and prediction of radiographic OA progression, respectively.

The results obtained indicate that detection and prediction of radiographic OA using the classification system developed is possible. Thus, our future research will involve the modifications of the classification system developed to include parameters calculated by the VOT method on knee radiographs. Also, the system will be extended to hand radiographs using parameters calculated by the AVOT method.

6. Development of ReadMyXray website

For the purpose of assisting the medical personnel in knee OA diagnosis we developed ReadMyXray website (http://readmyxray.curtin.edu.au/). The website provides, free of charge, fractal-based assessment of bone texture of knee x-rays. Medical practitioners, researchers and members of a general public can upload knee radiographs for analysis, which are then analysed using the VOT method. A bone roughness

Bone Roughness ReadMyXray

Date: 1 Feb 2014

Email: 1234_my@gmail.com

X-ray and measures in 2013

Anteroposterior x-ray image of knee



Measures Bone region	FD _{MEAN}	FDv	FD _H	FD _{Sta}
1	2.80	2.80	2.81	2.81
2	2.78	2.80	2.77	2.82

Trabecular bone roughness measures

Trabecular bone roughness curves up to 2013



Explanation: For each bone region we produce a plot of roughness coefficients (black dots) to which we fit an ellipse (dotted lines). The roughest part direction is along the line running through the smallest distance across the ellipse (red line). Based on the plot we calculate four basic radiographic measures:



Fig. 7. Example of a bone roughness report from ReadMyXray website.

report is prepared and forwarded to the uploader. An example report is shown in Fig. 7.

Currently, a work is undertaken to extend the website usability for analysis of hand radiographs using the AVOT method and also to enable x-ray image classification by the SDM method for both knee and hand x-rays.

7. Summary

The current research efforts directed towards the development of methods for diagnostic and prognostic purposes of OA were described. The methods include automated selection of TB texture regions on knee and hand radiographs, followed by a numerical analysis of the regions selected and their classification.

Radiographs of knee joints were analyzed using the VOT method. A number of studies were conducted. We found that the method could not only differentiate between OA and healthy knee joints and identify pre-radiographic OA bone changes, but it also could be used in prediction of OA and KJR.

For the analysis of very small images, like those found in hand radiographs, the VOT method was augmented (i.e., AVOT), and successfully applied to hand radiographs. We showed that the method is sensitive enough to show the differences between healthy and OA hand joints.

Classification system of knee bone textures was developed. Initially, for the classification, the bone textures selected were analyzed by means the SDM method. The SDM calculates much lower number of bone texture parameters than the VOT method, thus reducing the complexity of the classification system developed. As the system was shown to have good predictive capability of radiographic OA progression, we are planning to extend it by including support for the VOT method, and also to extend it to hand radiographs analyzed by the AVOT method.

The results obtained show that automated OA detection and prediction based on x-ray images of knee and hand joints is possible. To assist the medical practitioners in knee OA diagnosis we developed ReadMyXray website.

It should be noted that as the imaging technologies advance rapidly, the techniques developed can be adapted to be used in the analysis and classification of MRI images, CT scans, ultrasound images, and others.

Our future work will include development of regression models for prediction of OA in knee and hand joints and evaluation of the models developed in longitudinal and prospective studies. It is also planned to modify and test the methods developed for analysis of other joint disorders than OA, such as rheumatoid arthritis and osteoporosis. Read-MyXray website will be further developed to provide fractalbased assessment and classification of TB textures of not only knees, but also hands and other joints.

Acknowledgements

The authors wish to thank the Curtin University, Department of Mechanical Engineering and the School of Civil and Mechanical Engineering for their support during preparation of the manuscript.

References

- R. Bitton, The economic burden of osteoarthritis, Am. J. Manag. Care 15 (2009) S230–S235.
- [2] E. Kon, G. Filardo, M. Drobnic, H. Madry, M. Jelic, N. van Dijk, et al., Non-surgical management of early knee osteoarthritis, Knee Surg. Sports Traumatol. Arthrosc. 20 (2012) 436–449.
- [3] D.G. Yu, H.F. Ding, Y.Q. Mao, M. Liu, B. Yu, X. Zhao, et al., Strontium ranelate reduces cartilage degeneration and subchondral bone remodeling in rat osteoarthritis model, Acta Pharmacol. Sin. 34 (2013) 393–402.
- [4] G. Mohan, E. Perilli, I.H. Parkinson, J.M. Humphries, N.L. Fazzalari J.S. Kuliwaba, Pre-emptive, early, and delayed alendronate treatment in a rat model of knee osteoarthritis: effect on subchondral trabecular bone microarchitecture and cartilage degradation of the tibia, bone/cartilage turnover, and joint discomfort, Osteoarthr. Cartil. 21 (2013) 1595–1604.
- [5] C. Buckland-Wright, Which radiographic techniques should we use for research and clinical practice?, Best Pract. Res. Clin. Rheumatol. 20 (2006) 39–55.
- [6] R.D. Altman, G.E. Gold, Atlas of individual radiographic features in osteoarthritis, revised, Osteoarthr. Cartil. 15 (2007) A1–A56.

- [7] J.H. Kellgren, J.S. Lawrence, Radiological assessment of osteo-arthrosis, Ann. Rheum. Dis. 16 (1957) 494–502.
- [8] G. Jones, C. Ding, F. Scott, M. Glisson, F. Cicuttini, Early radiographic osteoarthritis is associated with substantial changes in cartilage volume and tibial bone surface area in both males and females, Osteoarthr. Cartil. 12 (2004) 169–174.
- [9] K.D. Brandt, R.S. Fife, E.M. Braunstein, B. Katz, Radiographic grading of the severity of knee osteoarthritis: relation of the Kellgren and Lawrence grade to a grade based on joint space narrowing, and correlation with arthroscopic evidence of articular cartilage degeneration, Arthritis Rheum. 34 (1991) 1381–1386.
- [10] C. Ding, F. Cicuttini, J. Jones, How important is MRI for detecting early osteoarthritis?, Nat. Clin. Pract. Rheumatol. 4 (2008) 4–5.
- [11] M.F. Sowers, C. Hayes, D. Jamadar, D. Capul, L. Lachance, M. Jannausch, et al., Magnetic resonance-detected subchondral bone marrow and cartilage defect characteristics associated with pain and X-ray-defined knee osteoarthritis, Osteoarthr. Cartil. 11 (2003) 387–393.
- [12] M. Ding, A. Odgaard, I. Hvid, Changes in the three-dimensional microstructure of human tibial cancellous bone in early osteoarthritis, J. Bone Jt. Surg. 85 (2003) 906–912.
- [13] S.K. Boyd, R. Müller, J.R. Matyas, G.R. Wohl, R.F. Zernicke, Early morphometric and anisotropic change in periarticular cancellous bone in a model of experimental knee osteoarthritis quantified using microcomputed tomography, Clin. Biomech. 15 (2000) 624–631.
- [14] N.L. Fazzalari, I.H. Parkinson, Fractal dimension and architecture of trabecular bone, J. Pathol. 178 (1996) 100–105.
- [15] I.H. Parkinson, N.L. Fazzalari, Methodological principles for fractal analysis of trabecular bone, J. Microsc. 198 (2000) 134–142.
- [16] R. Jennane, R. Harba, G. Lemineur, S. Bretteil, A. Estrade, C. L. Benhamou, Estimation of the 3D self-similarity parameter of trabecular bone from its 2D projection, Med. Image Anal. 11 (2007) 91–98.
- [17] J.A. Lynch, D.J. Hawkes, J.C. Buckland-Wright, Analysis of texture in macroradiographs of osteoarthritic knees using the fractal signature, Phys. Med. Biol. 36 (1991) 709–722.
- [18] V.B. Kraus, S. Feng, S. Wang, S. White, M. Ainslie, A. Brett, et al., Trabecular morphometry by fractal signature analysis is a novel marker of osteoarthritis progression, Arthritis Rheum. 60 (2009) 3711–3722.
- [19] P. Podsiadlo, M. Wolski, G.W. Stachowiak, Automated selection of trabecular bone regions in knee radiographs, Med. Phys. 35 (2008) 1870–1883.
- [20] M. Wolski, M. Englund, G.W. Stachowiak, P. Podsiadlo, Automated selection of trabecular bone texture regions on hand radiographs, in: Proceedings of ISMRM Workshop on Imaging Based Measures of Osteoarthritis, Pacific Grove, CA, USA, 2015.
- [21] A.P. Zijdenbos, B.M. Dawant, R.A. Margolin, A.C. Palmer, Morphometric analysis of white-matter lesions in mr-images – method and validation, IEEE Trans. Med. Imaging 13 (1994) 716–724.
- [22] S. Peleg, J. Naor, R. Hartley, D. Avnir, Multiple resolution texture analysis and classification, IEEE Trans. Pattern Anal. Mach. Intell. 6 (1984) 518–523.
- [23] M. Wolski, P. Podsiadlo, G.W. Stachowiak, Directional fractal signature analysis of trabecular bone: evaluation of different methods to detect early osteoarthritis in knee radiographs, Proc. Inst. Mech. Eng. H 223 (2009) 211–236.
- [24] P. Podsiadlo, L. Dahl, M. Englund, L.S. Lohmander, G.W. Stachowiak, Differences in trabecular bone texture between knees with and without radiographic osteoarthritis detected by fractal methods, Osteoarthr. Cartil. 16 (2008) 323–329.
- [25] M. Wolski, P. Podsiadlo, G.W. Stachowiak, A new method to measure trabecular bone texture on hand radiographs: data from the Osteoarthritis Initiative, Osteoarthr. Cartil. 22 (2014) S257–S258.
- [26] M. Wolski, P. Podsiadlo, G.W. Stachowiak, Directional fractal signature methods for trabecular bone texture in hand radiographs: data from the Osteoarthritis Initiative, Med. Phys. 41 (2014).
- [27] M. Wolski, P. Podsiadlo, G.W. Stachowiak, L.S. Lohmander, M. Englund, Differences in trabecular bone texture between knees with and without radiographic osteoarthritis detected by directional fractal signature method, Osteoarthr. Cartil. 18 (2010) 684–690.

- [28] M. Wolski, G.W. Stachowiak, A.R. Dempsey, P.M. Mills, F.M. Cicuttini, Y. Wang, et al., Trabecular bone texture detected by plain radiography and variance orientation transform method is different between knees with and without cartilage defects, J. Orthop. Res. 29 (2011) 1161–1167.
- [29] F.M. Cicuttini, G. Jones, A. Forbes, A.E. Wluka, Rate of cartilage loss at two years predicts subsequent total knee arthroplasty: a prospective study, Ann. Rheum. Dis. 63 (2004) 1124–1127.
- [30] P. Podsiadlo, M. Nevitt, M. Wolski, G. Stachowiak, J. Lynch, I. Tolstykh, et al., Baseline trabecular bone and its relation to incident radiographic knee osteoarthritis and increase in joint space narrowing score: directional fractal signature analysis in the MOST study, Osteoarthr. Cartil. 24 (2016) 1736–1744.
- [31] H. Roos, M. Laurén, T. Adalberth, E.M. Roos, K. Jonsson, L. S. Lohmander, Knee osteoarthritis after meniscectomy: prevalence of radiographic changes after twenty-one years, compared with matched controls, Arthritis Rheum. 41 (1998) 687–693.
- [32] A.E. Wluka, Y. Wang, M. Davies-Tuck, D.R. English, G.G. Giles, F. M. Cicuttini, Bone marrow lesions predict progression of cartilage defects and loss of cartilage volume in healthy middle-aged adults without knee pain over 2 yrs, Rheumatology 47 (2008) 1392–1396.
- [33] P.M. Mills, Y. Wang, F.M. Cicuttini, K. Stoffel, G.W. Stachowiak, P. Podsiadlo, et al., Tibio-femoral cartilage defects 3–5 years following arthroscopic partial medial meniscectomy, Osteoarthr. Cartil. 16 (2008) 1526–1531.
- [34] T. Hayami, M. Pickarski, Y. Zhuo, G.A. Wesolowski, G.A. Rodan, L. T. Duong, Characterization of articular cartilage and subchondral bone changes in the rat anterior cruciate ligament transection and meniscecto-mized models of osteoarthritis, Bone 38 (2006) 234–243.

- [35] D.L. Batiste, A. Kirkley, S. Laverty, L.M.F. Thain, A.R. Spouge, D. W. Holdsworth, Ex vivo characterization of articular cartilage and bone lesions in a rabbit ACL transection model of osteoarthritis using MRI and micro-CT, Osteoarthr. Cartil. 12 (2004) 986–996.
- [36] P. Podsiadlo, F.M. Cicuttini, M. Wolski, G.W. Stachowiak, A.E. Wluka, Trabecular bone texture detected by plain radiography is associated with an increased risk of knee replacement in patients with osteoarthritis: a 6 year prospective follow up study, Osteoarthr. Cartil. 22 (2014) 71–75.
- [37] S.K. Tanamas, A.E. Wluka, J.P. Pelletier, J.M. Pelletier, F. Abram, P. A. Berry, et al., Bone marrow lesions in people with knee osteoarthritis predict progression of disease and joint replacement: a longitudinal study, Rheumatology 49 (2010) 2413–2419.
- [38] T. Woloszynski, P. Podsiadlo, G.W. Stachowiak, M. Kurzynski, A signature dissimilarity measure for trabecular bone texture in knee radiographs, Med. Phys. 37 (2010) 2030–2042.
- [39] T. Woloszynski, P. Podsiadlo, G.W. Stachowiak, M. Kurzynski, L. S. Lohmander, M. Englund, Prediction of progression of radiographic knee osteoarthritis using tibial trabecular bone texture, Arthritis Rheum. 64 (2012) 688–695.
- [40] T. Woloszynski, P. Podsiadlo, G. Stachowiak, M. Kurzynski, A dissimilarity-based multiple classifier system for trabecular bone texture in detection and prediction of progression of knee osteoarthritis, Proc. Inst. Mech. Eng. H 226 (2012) 887–894.
- [41] T. Woloszynski, M. Kurzynski, P. Podsiadlo, G.W. Stachowiak, A measure of competence based on random classification for dynamic ensemble selection, Inf. Fusion 13 (2012) 207–213.