

#### **Research activities** 1. Conference attendance 2014 – 2016

#### SICOT 2014

Orthopedic Surgery and Traumatology (Oral), Rio de Janeiro, 19.11.2014

#### ASBMR 2015

Bone and Mineral Research (Oral) Seattle, 09.10.2015

#### AUSBMR 2015

Bone and Mineral Researc (Poster), Vienna, 03.12.2015

#### **ORTHOMED 2015**

Orthopedics in medicine (Oral), Florence, 10.12.2015

#### ECR 2016

Radiology (Oral), Vienna, 02.03.2016

#### Osteologie 2016

Osteology (Oral), Essen, 03.03.2016

#### OARSI 2016

Osteoarthritis (2x Poster), Amsterdam, 31.03.2016

#### ISBI 2016

Biomedical imaging, (Poster), Prague, 13.04.2016

#### WCO-IOF-ESCO 2016

Osteoporosis, Osteoarthritis and musculoskeletal diseases (2x Poster), Malaga, 14.04.2016

#### XVIII Congresso Português de Reumatologia 2016

Rheumatology (2x Oral), Vilamoura, 04.05.2016

#### ECTS 2016

European Calcified Tissue Society (2x Poster), Rome, 14.05.2016

#### EULAR 2016

Rheumatic disease (2x Poster), London, 08.06.2016

#### GOTS 2016

Orthopedic traumatic sports medicine (Oral), Munich, 17.06.2016

#### ICRS 2016

Intl Cartilage Repair Society (2x Poster), Sorento, 24.09.2016

#### ÖGO Kongress 2016

Orthopedics and orthopedic surgery (Oral), Villach, 29.09.2016

#### Knochen & Muskel 2016

Bones and Muscles (Oral), Berlin, 11.11.2016





#### 2. Submitted Abstracts

- [1.] A novel method for the assessment of joint space width and subchondral bone micro architecture
- [2.] Computer-assisted diagnosis and monitoring of degenerative bone diseases
- [3.] Automated ROI placement and trabecular-driven orientation for radiographic texture analyses of calcaneus
- [4.] A clinical study to examine thresholds of joint space width and joint space area for identification of knee osteoarthritis
- [5.] A novel feature selection algorithm based on bone micro architecture analysis to identify osteoarthritis
- [6.] Combining radiographic texture parameters increases tibiofemoral osteoarthritis detection accuracy: Data from the Osteoarthritis
- [7.] A Novel Method for identifying radiographic baseline risk of Osteoarthritis using an anisotropy-based Texture Analysis Algorithm: Data from the Osteoarthritis Initiative





#### 3. Selected Abstracts:

### 3.1. A novel method for the assessment of joint space width and subchondral bone micro architecture

Ljuhar R§, Norman B§, Ljuhar D§, Hladuvka J¥, Canhão H‡, Branco J‡, Rodrigues A‡, Gouveia N‡, Fahrleitner-Pammer A†, Dimai HP†

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#### Objective

Assessment of osteoarthritis (OA) of the knee usually involves AP and lateral radiographs to evaluate medial and lateral joint spaces, but perspective errors and low reproducibility are limiting factors. In addition to joint space width, subchondral bone area may provide important information on the status of OA.

However, no adequate standard has been developed so far to quantify subchondral changes. The method described here combines assessment of joint space width (JSW) and texture analysis of the adjacent subchondral bone micro architecture to discriminate between patients with and without OA.

#### Methods

The study included 274 standardized knee radiographs from 110 patients with OA, and 164 controls. Knee joint space analysis was performed at the medial and lateral compartment, applying an entropy based algorithm for automated detection of critical landmarks and joint space contour. Furthermore, subchondral bone texture was assessed by using fractal analysis at predefined regions of the proximal tibia. A matrix of 3x8 ROIs was used to gain sufficient textural information (FIG.).

Self-similarity of the texture, reflecting 2D projection of the 3D trabecular structure, has been used to calculate the Bone Structure Value (BSV) which provides indirect information on bone quality.

#### Results

Comparing mean BSVs of the control and the OA group of selected 89 female patients, a statistical significant deviation of 7.04% (p<0.01) in mean values was determined with an odds-ratio of 2.89 (95% CI, 1.2-6.89). A combination of JSW & BSV showed a further increase in discriminative power between the controls and OA patients.

Differences in BSV were found between left/right knee and male/female. Furthermore, a rising BMI was identified to be linked to lower BSV values.





#### Conclusion

The novel method described here is sufficient to discriminate between subjects with and without OA. Furthermore, fractal analysis alone may provide information on bone quality aspects. Future work should therefore focus on the potential role of bone micro architecture algorithms to serve as a fracture risk assessment tool. Such algorithms could serve as early disease predictor of not just OA but also additional degenerative bone diseases like osteoporosis.





### 3.2. Computer-assisted diagnosis and monitoring of degenerative bone diseases

Ljuhar R§, Norman B§, Ljuhar D§, Nehrer S†, Riedl M#, Hladuvka J¥, Stiassny F‡, Wetzl C‡, Westhauser C‡

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#### Objective

Osteoarthritis (OA) is a degenerative, slowly developing joint disease and characterized by pain and functional disability. It results from a loss of joint cartilage and changes in the subchondral bone area. OA represents one of the leading causes for long-term pain and disabilities associated with musculoskeletal disorders.

Many studies have confirmed that OA has a substantial impact on socioeconomic burden. Thus, early predictors and ways to observe the progression of this disease are highly demanded.

However clinical detection relies heavily on subjective experience to condense the continuous features into discrete grades. Traditional radiographic imaging techniques primarily focus on semi-quantitative assessment methods like the Kellgren & Lawrence Score (KL) and quantitative measurements of Joint Space Width (JSW) based on radiographs. These disease parameters have proven to be highly physician-dependent with subjective interpretation results. Consequently, a new method for a computer-assisted diagnosisand monitoring of degenerative bone diseases like OA is introduced.

#### Methods

In a first step, the image set of 274 radiographs was clinically examined by three radiologists based on the visual assessment of the radiograph using a standard DICOM Viewer. Additionally, the physicians had to score four parameters according to KL and do a manual JSW measurement.

The physicians were separated from each other during the assessment to avoid any inter-observer influence on the results. To be able to do an intra-observer variability evaluation, 5 images were duplicated twice (placed at random order within the sample size).

All images were anonymized with new image IDs. Using a computer-assisted software application (i3a Technologies, Vienna, Austria) the same image sample was analyzed.

Based on the identification of distinct landmark points placed on the outer edge of the tibia, the joint space width as well as area (JSW/A) was calculated. KL scoring was performed using the computer-assisted i3a grading tool.





All results were stored in a database and printed reports were obtained, documenting JSW, JSA distribution, KL scores and patient information.

#### Results

Regarding inter-observer variability of KL scoring, a difference of 1 and higher in any of the given KL categories (JSW, Sclerosis, Deformity & Osteophytes) was present in at least 62% of cases. Looking at Total KL score among all three physicians, just 14% of cases showed inter-observer agreement. More than 50% had a Total KL score discrepancy of 3 and above. The Total KL score deviation has been found to be 2.5on average and a maximum of 7.

To evaluate the intra-observer variability, given scores per physician for the five identical radiographs were compared. Each of the identical radiographs received different KL scores. The highest intra-observer variability in terms of KL scores was found to be 2.

Just one physician assessed the identical radiograph correctly in 3 out of 5 times; the other two had consistent results in 2 out of 5 and 1 out of 5 times.

In comparison, a significantly higher rate of reproducibility in regard to KL scoring was observed when using the computer-assisted method. The inter- and intra-observer variability as well as the deviation in mean Total KL scores were both reduced. In 93% of cases, no physician-guided correction of JSW/A assessment was required.

#### Conclusion

Manual assessment and diagnosis of patients affected by OA has shown to be highly subjective and physician-dependent.

Inter- and intra-observer variability can be observed when comparing manual assessments of radiographs. As a result, disease diagnosis and assessment can significantly be influenced by subjective variables.

Computer-assisted methods have shown to deliver considerable better results, especially when building and monitoring the OA diagnosis on KL grades. The fully automatic system described in this work annotates the radiograph based on distinct landmark points, providing the physician with independent information for the classification of OA patients.

Future work should focus on shape-recognition features which can deliver an automatic KL grade suggestion.





#### 3.3. Automated ROI placement and trabecular-driven orientation for radiographic texture analyses of calcaneus

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#### Abstract

Radiographic texture analysis of calcaneus has been recently extensively researched for automated discrimination between osteoporotic and healthy subjects. Existing work concentrates on design of texture descriptors and assumes already available texture patches previously defined by human experts.

In this paper we address the missing link to complete the automatic workflow – localization and orientation of regions of interest (ROIs) the texture patches are sampled from. We exploit the shape of calcaneus to define ROI position and the structure of trabecula to define its orientation.

We evaluated our automated method on 361 high-resolution radiographs. Comparison to user-defined ROIs reveals localization discrepancy of 1.85 \_ 1.06 mm and deviation in orientation of -1.81 \_ 7.31 degrees.





#### 3.4. A clinical study to examine thresholds of joint space width and joint space area for identification of knee osteoarthritis

Ljuhar R§, Norman B§, Ljuhar D§, Haftner T§, Hladuvka J¥, Bui Thi Mai P¥, Canhão H‡, Branco J‡, Rodrigues A‡, Gouveia N‡, Nehrer SΠ, Fahrleitner-Pammer A†, Dimai HP†

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#### Objectice

Osteoarthritis (OA) is a degenerative, slowly developing joint disease and characterized by pain and functional disability. Although clinical indications of OA can vary among different definitions there is a general agreement that the disease is associated with cartilage narrowing and the development of osteophytes and sclerosis within the subchondral bone.

However, there is no general consensus about the threshold below which the joint space width (JSW) and the respective joint space area (JSA) can be certain indicators for the state of OA.

Therefore this study evaluates these limits to reveal quantitative information about indicators of OA.

#### Methods

The study included 226 standardized knee radiographs from 101 female patients with OA, and 125 controls. All images were acquired in PA direction and standardized positions.

The minimum JSW and JSA were calculated by using the i3a software. 3 physicians assessed the 2D radiographs by using the Kellgren & Lawrence Score and assigned the images to either a Case or Control group.

A knee was assigned to the Case group, if at least two physicians assessed it as being affected by OA. The JSW was defined as the vertical distance from the inferior femur condyle to the superior tibia condyle on both the medial and lateral compartment, obtained from 4 distinct points from each side.

By building a spline curve between the points of each condyle, the upper and lower boundaries of the JSA are defined for each side, whereas the outer points define the horizontal boundaries. For the JSW and JSA, only the minimum value of each variable was taken into account.







#### Results

Considering the minimum JSW, an odds ratio of 5.63 (CI: 3.17 - 9.99) with an accuracy of 70.35% and a sensitivity of 70.30% can be obtained. Every subject that has a minimum JSW below 3.4mm belongs to the Case group. With respect to the minimum JSA, the odds ratio is 3.60 with an accuracy of 65.49% and a sensitivity of 65.35%. Results also show that every subject with a minimum JSA below 50mm2 is being considered to have OA.

#### Conclusion

Based on this study it can be concluded that a JSW below 3.4mm and a JSA below 50mm2 at the knee joint are strong indicators for OA. Thus, for clinical assessments it is suggested to consider these threshold values for diagnostic purposes.

In further studies, symptomatic knee OA should be incorporated to verify whether minimum JSWs and JSAs can also be linked to symptomatic knee pain.





## 3.5. A novel feature selection algorithmbased on bone micro architecture analysisto identify osteoarthritis

Ljuhar R§, Norman B§, Ljuhar D§, Haftner T§, Hladuvka J¥, Bui Thi Mai P¥, Canhão H‡, Branco J‡, Rodrigues A‡, Gouveia N‡, Nehrer SΠ, Fahrleitner-Pammer A†, Dimai HP†

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#### Objective

Texture information of the subchondral bone area of 2D radiographs represents a promising possibility for evaluating the state of osteoarthritis (OA) in addition to traditional clinical means such as visual and semi-quantitative assessments.

Algorithms based on fractal analysis have shown to be capable of identifying differences in trabecular bone structure. However such features are likely to vary within the subchondral bone area. Therefore the appropriate selection of the region of interest (ROI) plays a crucial role for the result of the analysis. Thus, a feature selection algorithm is being applied in order to determine ROIs that enable an optimum discrimination between patients with and without OA. es, Vienna, Austria) the same image sample was analyzed.

Based on the identification of distinct landmark points placed on the outer edge of the tibia, the joint space width as well as area (JSW/A) was calculated. KL scoring was performed using the computer-assisted i3a grading tool.

#### Methods

The study included 152 standardized knee radiographs from 66 female patients with OA, and 86 controls. Subchondral bone micro architecture was assessed by using both fractal analysis and a Shannon Entropy (SE) algorithm at predefined regions of the proximal tibia and the distal femur.

For fractal analysis the distinct parameter Bone Structure Value (BSV) was defined. The selected area of the proximal tibia involved a matrix of 3x8 ROIs, whereas a 2x2 matrix was defined for each condyle of the distal femur. SE and the BSV were calculated for each of the 32 ROIs, respectively. Based on these 64 variables, a feature selection algorithm was applied to determine the variables that showed the best discrimination power between Case and Control subjects.





#### Results

By combining the BSV and SE, the odds ratio increased significantly from 3.08 (95% CI: 1.78-5.30) to 14.82 (95% CI: 6.69-32.83) when using 15 features, and to 39.75 (95% CI: 15.41-102.51) based on 10 features. By using the selected 10 features the accuracy was found to be 0.86.

This showed to be a significant improvement compared to the accuracy achieved when calculating a single mean value for the 3x8 ROIs of the proximal tibia alone (0.62 vs. 0.86).

#### Conclusions

The application of a feature selection algorithm in accordance with the combination of the two texture analysis methods shows a significant improvement with respect to the discrimination power between subjects with and without OA.

The high odds ratios confirm that reliable results can be achieved by combining the BSV and the SE. This novel algorithm for the assessment of bine micro architecture may not only be useful in osteoarthritis subjects but also for the early prediction and assessment of other degenerative bone diseases like osteoporosis and rheumatoid arthritis.





## 3.6. Combining radiographic texture parameters increases tibiofemoral osteoarthritis detection accuracy: Data from the Osteoarthritis

T. S. Haftner<sup>1</sup>, R. Ljuhar<sup>2</sup>, H. P. Dimai<sup>3</sup>, D. Ljuhar<sup>2</sup>, J. Hladuvka<sup>4</sup>, S. Nehrer<sup>1</sup>

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#### Objective

Changes to the subchondral trabecular bone are characteristic features of tibiofemoral osteoarthritis and can be identified by radiography-based analysis techniques.

Texture descriptors are usually constrained to regions of interest on the subchondral bone of the tibia.

Here, we describe a method that involves gathering additional texture information from the lateral and medial condyles of the distal femur. The investigated algorithm selects an optimal combination of different texture descriptors in order to increase tibiofemoral osteoarthritis detection accuracy based on conventional radiographs.

#### Methods

This study was performed using data from the Osteoarthritis Initiative (OAI). The image dataset was restricted to female, Caucasian, right knee exams of the same modality.

Participants which had a KL-Score higher than 1 were assigned to the Case group,

whereas people with a KL-Score lower than 2 represented the Control group, totaling 501 patients. Based on selected images, texture analysis was performed by using the Bone Structure Value, the Shannon Entropy and six other indicative features describing texture roughness and anisotropy.

Our framework selects an optimal combination of these different texture parameters from six different regions for evaluation with various classifiers.

#### Results

By taking the combination of four instead of just a single feature, the classification between Cases and Controls was increased from 62.58% to 72.32%, regarding the Area under Curve. Results show that the most significant discrimination can be achieved by selecting both regions from the medial tibia as well as the lateral femur. From a statistical point of view the Linear Discriminant Analysis yields the best accuracies with respect to the selected OAI-dataset.





#### Conclusions

This framework shows a novel and promising method for the detection of osteoarthritis based on radiographic information only.

The method described reveals new possibilities to achieve higher discriminative power between Case and Controls by combining significant texture-based features.

Future work will focus on applying the combined tibia/femur analysis mask to additional datasets to further validate and improve the discriminative power also in regard to early disease prediction.



# 3.7. A Novel Method for identifying radiographic baseline risk of Osteoarthritis using an anisotropy-based Texture Analysis Algorithm: Data from the Osteoarthritis Initiative

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- <sup>4</sup> Medical University Graz, Graz, Austria

#### Background

Osteoarthritis (OA) is the most common form of arthritis and affects in a disproportinal way the knee. Recent research developments in imaging options showed that OA is not just a joint disease but also involves progressive changes in the subchondral/subarticular bone area of the tibia.

Besides the accepted methods of measuring the joint space width, assessments of the trabcular bone structure in selected regions of interest (ROI) of the knee based on conventional x-rays may be offering an alternative method for quantifying the risk and progression of the disease.

#### Objective

The accepted method for assessing OA - Joint space width (JSW) and Joint Space Area (JSA) measurements - have limited capabilities with respect to early identification and reproducible follow-ups of the disease. The objective of this abstract is to evaluate

trabecular bone structure as area

for early identification of OA risk, applying texture anisotropy algorithms and subsequently comparing the results to standard JSW and JSA measurements.

#### Methods

This study was performed using data form the Osteoarthritis Initiative. The image data set was restricted to female, Caucasian, right knee exams of the same modality which had a KL grade of 0 at the baseline exam with a deteriorating KL grade  $\geq$ 2 at 96 months follow up. 22 CASES fulfilled these criteria with matching 22 CONTROLS with no signs of OA at 96 months follow up.

The selected region of interest (ROI) for the analysis of the radiographic texture encompassed four ROIs in the subchondral tibia and one additional ROI in each femur condyle – in total 6 ROIs. For each individual ROI, the degree of texture anisotropy was calculated and compared between case/controls. In addition,





JSW/JSA were calculated in both groups using a software-based method (i3a Technologies).

#### Results

Whereas the JSW and the JSA measurements did not yield any significant differences with respect to their mean values (Cohen's d = 0.139 and 0.028), the calculated texture parameters showed that differences in values between Cases and Controls can be found in ROI1 and 2 with Cohens'd values of 0.625 and 0.831. With respect to selected patient groups, the differences in anisotropy results were significant using these texture parameters.

#### Conclusions

Our results indicate that using the selected radiographic texture parameters, an early identification of patients at risk for developing OA using conventional x-rays can be achieved. This may offer an additional method for quantifying the risk of baseline OA.

This is supported by the Conhen's d values that are by definition relatively large (0.625 and 0.831). Ongoing research focuses on larger sample set validation and the use of such algorithms for additional applications, such as the early identification of patients at risk for fractures.

