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3D measurement of joint space narrowing in the knee from stereo radiographs using statistical shape models
Three dimensional measurement of joint space narrowing in the knee from stereo radiographs using statistical shape models

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Abstract

Introduction
An important measure for the diagnosis and monitoring of osteoarthritis of the knee is joint space narrowing (JSN), which is assessed from plain radiographs by measuring longitudinal changes in the minimum joint space width (mJSW). Conventional 2D mJSW measurements require alignment of the X-ray beam with the surface of the medial tibial plateau. We propose a newly developed mJSW measurement technique from stereo radiographs using 3D statistical shape models (SSM) of the tibia and femur and evaluate its sensitivity to changes in the mJSW and its robustness to variations in patient positioning and bone geometry.

Method
A validation study was performed using cadaver specimen for which the actual mJSW could be varied using a micromanipulator. For comparison purposes, the mJSW was also assessed from plain radiographs using the conventional 2D measurement method. To study the influence of SSM model accuracy, the 3D mJSW measurement was repeated with bone models obtained from CT scans.

Results
The SSM-based measurement method was more robust than the conventional 2D method, showing that the 3D reconstruction indeed reduces the influence of patient positioning. Both methods showed comparable sensitivity to changes in mJSW. The CT-based measurement was more accurate than the SSM-based measurement, (smallest detectable differences 0.55 vs. 0.82 mm respectively) indicating that the modelling error of the SSM is probably an important contributor to SSM measurement accuracy.

Conclusion
In conclusion, the proposed measurement method is not a substitute for the conventional 2D measurement as it is more complicated to conduct and its improvements on measurement accuracy are marginal. However, further improvement of the model accuracy and optimization technique can be obtained and will stimulate applicability.
7-1 Introduction

Osteoarthritis (OA) of the knee imposes a major health care burden with a reported prevalence of more than 18% in the 65 to 74 year age group in the European Union\[86\]. OA is associated with cartilage degeneration and loss, joint inflammation, and swelling of the joint. Patients experience pain, stiffness and limited mobility\[87\].

OA progression is most frequently evaluated using plain radiographs for their low costs and availability. A variety of features are used to assess the stage of OA, such as the appearance of osteophytes and subchondral sclerosis\[74, 88\]. Cartilage loss associated with OA is estimated by detecting joint space narrowing (JSN). This is measured based on longitudinal changes in the minimum joint space width (mJSW), i.e. the shortest visible distance between the femoral condyle and the tibial plateau.

A limitation of plain radiographs is that measurements are conducted in projection views that are prone to parallax effects. As a result, alignment of the X-ray beam with the surface of the medial tibial plateau (MTP) is crucial in order to obtain a reliable reading of the joint space\[89, 90\]. Standardization protocols have been developed to optimize alignment, such as the fixed-flexion (FF) view, the metatarsophalangeal view and the modified Lyon Schuss view\[91, 92\]. An alternative measurement approach could be to reconstruct the three-dimensional (3D) bone geometry around the knee joint from planar images. This reconstruction has the advantage that geometric measurements such as the mJSW are invariant to the projection angle. This reduces the influence of variation in patient positioning or bone geometry and improves the accuracy and precision of the measurement.

We therefore developed a technique, in which this 3D reconstruction is created from 3D shape models of the tibia and femur and 2D/3D matching in Roentgen Stereophotogrammetric Analysis (RSA)\[32, 34\]. Afterwards, the mJSW is measured with a similar technique used for the measurement of polyethylene wear in total knee prostheses\[72\]. A particular challenge of this 3D reconstruction is that patient-specific 3D models of the tibia and femur are not readily available. To solve this, 3D statistical shape models (SSMs) of the tibia and femur were developed. An SSM is a deformable model that incorporates shape variations of an object class from a training
set of examples. These models could be used to produce accurate reconstructions of 3D patient-specific bone shapes based on 2D image information [93].

In this study, the feasibility of this newly developed mJSW measurement technique was investigated. A validation study was performed using cadaver specimen for which the actual mJSW could be varied using a micromanipulator. For comparison, the mJSW was also measured in conventional plain radiographs with optimized medial tibial plateau alignment, using an image-based semi-automatic measurement technique [94]. To study the influence of model accuracy, the 3D mJSW measurement was repeated with bone models obtained from CT scans and with the SSMs.

7-2 Materials and Methods

7-2-1 Data

Five human, cadaveric legs with no visible pathology were selected from the Department of Anatomy of the Leiden University Medical Center (Table 7-13). All ligaments and soft tissues including cartilage were dissected so that only the naked tibia and femur remained.

Table 7-13. Main characteristics of the cadaveric specimen. Age is expressed in years.

<table>
<thead>
<tr>
<th>index</th>
<th>Gender</th>
<th>Age</th>
<th>Leg Side</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>91</td>
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</tr>
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<td>Right</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>63</td>
<td>Right</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>93</td>
<td>Left</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>84</td>
<td>Right</td>
</tr>
</tbody>
</table>

7-2-2 Models

3D CT models from cadaver bones

3D surface models of the cadaveric bones were created from helical CT scans (Toshiba Aquilion 64, Toshiba Medical Systems Ltd., Tokyo, Japan). The bones were arranged in such a way that their long axes were aligned parallel to the CT
The bones were separated using foam padding in order to simplify the digital delineation of the bones. The scans were obtained at 120 kV and 130 mA with a slice thickness of 1.0 mm and a pitch of 0.8 mm per revolution. The scans had a resolution of 512 by 512 by 641 voxels with a voxel size of 0.78 by 0.78 by 0.8 mm.

Image segmentation was employed using Amira software (FEI Visualization Science Group, Bordeaux, France). A voxel mask was created to separate the bones from the background in the CT images using a threshold-based approach. The mask was converted into a triangulated surface model using a marching cube algorithm [95]. The average triangle edge length of the models was 1.7 mm.

Statistical Shape models
An SSM is a deformable model of shape that learns the mean shape and likely shape variations of an object class based on a training set. It can generate new shapes using the formula, $x = \bar{x} + \Phi b_x$, where $\bar{x}$ is the mean shape of the training set, $\Phi$ is the set of eigenvectors (modes of variation) that is based on the covariance matrix of the training set and $b$ is the set of shape parameters, one for each eigenvector. Thus, $b_x$ stands for the set of parameter values corresponding to the generated shape $x$ [96].

In this work two SSMs were used to model the distal femoral and proximal tibial bones, truncated to the region near the knee joint (each approximately 12 cm in length). The two models originate from a previous study where they are described in detail [97]. The training sets consisted of 62 polygonal surface models that were created from CT data using a level-set segmentation. Correspondence in the training sets was achieved using a non-rigid registration with the Elastix software [98]. Note that the five cadaver bones from this study are not included in the training set.

The eigenvector sets of the SSMs were truncated so that only those modes remained that describe 95% of the eigenvalue sum. For both models 33 modes of variation remained. For each mode $j$, the corresponding shape parameter $b_j$ was allowed to vary between $\pm 3$ times the standard deviation (SD) of the corresponding eigenvalue ($-3 \text{SD}_j \leq b_j \leq 3 \text{SD}_j$) when generating new shapes.
To test the goodness of fit, the models were fitted to each of the 3D surface models of the cadaveric bones using 3D/3D matching and the root mean square point-to-surface distance was computed. The root mean square point-to-surface distances ranged between 0.49 and 0.74 mm, which indicates that results are similar to earlier studies using SSMs[97].

7-2-3 mJSW measurement methods

In this section, the mJSW measurement methods are described for the SSM-based measurement, the conventional 2D measurement and the CT based measurement (Figure 7-23).

![Figure 7-23. Schematic view of the intermediate steps of the mJSW measurement methods. The steps start with the original images and end with the feature that is used to compute the mJSW. The 3D reconstruction step also includes the model optimization, which differs between the SSM-based and CT-based measurements.](image)

SSM-based measurement

The SSM-based measurement is conducted using RSA image pairs. In essence, a 3D reconstruction of the femur and tibia is created, in which the mJSW is measured.

First, image calibration and edge delineation are done using a standard analysis in Model-based RSA software (v4.0, LUMC, Leiden, Netherlands). In this analysis, candidate edges are detected with a canny-edge-detection algorithm and a selection
is made semi-automatically. To avoid correspondence problems, only those edges were selected that a) represented the outer object contours and b) belonged to the region that the SSM could represent (i.e. the distal part of the femur and proximal part of the tibia).

The next step is to optimize the shape parameters as well as the pose parameters of the tibiae and femora. This optimization step is done in MATLAB (R2011a) using a 2D/3D matching algorithm. Validation of this algorithm in previous work found a root-mean-square error of 1.86±0.29 mm for the femoral model[97]. The tibial bone was not included in this validation experiment.

Last, the mJSW is computed as the minimum distance between the tibia and the femur model. This distance is measured in the direction perpendicular to a 0.2 mm by 0.2 mm measurement grid residing in the transverse plane beneath the medial condyle (Figure 7-24). The construction of the measurement grid and the coordinate system of the tibia is based on three landmark regions manually defined on the tibial SSM model. These regions transform with the shape optimization, so that this procedure is required only once.

Figure 7-24. illustration of the grid construction process. A) Three tibia surfaces areas are selected by the used. B) The geometric means of these locations are used to define the coordinate system. C) The measurement grid is constructed beneath the medial condylar surface area aligned with the coordinate system.
2D measurement
The 2D measurement was performed with an automatic technique which has been validated for mJSW measurements in hand radiographs (freely available at www.lkeb.nl). The smallest detectable difference (SDD = 1.96 x SD) ranged between 0.05 mm and 0.354 mm depending on the joint shape[94]. This technique was adopted for the current measurement in terms of image contrast and joint size. Hereto, the proximal (femoral) and distal (tibial) margins of the medial knee joint are delineated using a semi-automatically algorithm specialized for these structures[94]. The user selects the center point of the medial tibial plateau in the image and the algorithm returns the edges of the margins in a 20 mm range. Optionally, the user can provide additional guiding points to correct these edges manually. The shortest perpendicular distance within the interval of delineation divided by image magnification was stored as the mJSW.

CT-based measurement
A CT-based measurement was used to study the influence of model accuracy. This measurement used models based on CT-scans instead of the SSM models. The calibration and edge selection for the CT-based measurement are similar to the SSM-based measurement. In the 2D/3D matching step however, the pose parameters (position, orientation, isotropic scale) of the CT models of the tibiae and femora are optimized using the default 2D/3D matching algorithm in Model-based RSA software.

7-2-4 Experiments
A validation experiment was done using a set-up in which the actual medial mJSW of the cadavers could be controlled with a micro manipulator (Figure 7-25) as part of a positioning device (accuracy 0.01 mm). This set-up was used to acquire both plain radiographs and RSA images under equal, controlled circumstances.

The plain radiographs were acquired with an X-ray imaging system at the Leiden University Medical Center (CXDI-series, 169dpi, 12BPP, Canon, New York, USA). A standing anterior-posterior (AP) view was used with a focus-film distance of 1.2 meters. The image magnification factor was 110%, based on measurements of the bone to detector distances. For the RSA images a mobile X-ray system with the same
device qualifications was added. The detectors were placed in a carbon calibration box (LUMC, Leiden, The Netherlands). The X-ray sources were positioned at 1.5 meters from the detectors and the angle between the X-ray beams was approximately 40°. For both imaging modes the positioning device was placed as close to the detectors as possible.

For each cadaver, first a plain radiograph was acquired with the actual mJSW at 0 mm, i.e. in which there was contact between the medial femoral condyle and the tibial plateau. For this acquisition, the medial tibial plateau was aligned with the X-ray beam. This was achieved by optimizing the positioning of the tibia in the phantom and by adjusting the height of the X-ray tube until the center of the beam (laser
guidance) just skimmed the edges of the plateau. Since alignment was optimized for the medial plateau, the lateral mJSW was not measured in this validation study.

After the first acquisition at 0 mm, the actual mJSW was increased to 2 mm, 4 mm and 6 mm. These values are representative for diseased and healthy adult knees. For each of these distances, 3 exposures were made with varying X-ray tube heights (-5 cm, 0 cm, +5 cm) and 3 exposures were made with varying rotations of the cadaver (-10°, 0°, +10°). Note that when one parameter was varied, the other parameter was in neutral position and the exposure with zero tube height and zero rotation was made twice. In total, 19 exposures were made per cadaver. A schematic with the function of these parameters is shown in Figure 7-25. The range of the parameters was considered representative for actual variations in patient positioning during follow-up studies.

The above procedure was repeated acquiring RSA image pairs for each cadaver bone. The mJSW was measured using the 2D measurement in plain radiographs and using the SSM-based and CT-based measurements for the RSA image pairs, resulting in 285 measurements in total.

### 7-2-5 Statistical analysis

From the experiment data, the relative measurement errors were computed as the measured mJSW minus the actual mJSW. To analyze the robustness of the measurements against the variations in position applied in the experiment, the measurement errors per method are shown in a boxplot. Significant differences between the dispersion are tested with Levene’s test.

The sensitivity was evaluated based on the data with mJSW variation only. Measurements with a mJSW of 0 mm and with any tube offset or rotation were excluded, (N = 6 measurements per cadaver). Standard deviations (SD) and the smallest detectable differences (SDD = 1.96xSD) were computed. The SDD is a relevant outcome for OA research, representing the minimum JSN that could be detected [88, 99]. Between-cadaver differences were analyzed with a univariate linear model with the shape index as random factor. Last, data trends were analysed by plotting the measurement errors against the actual mJSW.
Chapter 7

7-3 Results

In the robustness analysis, the measurement errors showed a large difference in dispersion between the measurement methods (Figure 7-26). Generally, the smallest dispersion was found for the CT-based measurement, next for the SSM-based measurement and last for the 2D measurement. These differences were statistically significant for cadaver 2 to 5 (Levene's test, p < 0.01).

![Boxplots presenting the difference between the actual mJSW and measured mJSW in the validation experiment for each method and cadaver shape (N = 19 for each boxplot). The horizontal bar indicates the median difference. The whiskers are set at 1.5 times the interquartile range.](image)

No significant differences or trends were found between the measurement error versus the actual mJSW (Figure 7-27). The results in Table 7-14 show that the SDDs differed significantly between the cadavers for all measurement methods (ANOVA, p < 0.01). More specifically, the SDD of cadaver 1 was relatively high for all measurement methods. The last table column shows the SDDs corrected for between-cadaver effects with the univariate linear model. This shows the corrected SDD is smallest for the CT-based measurement method, followed by the 2D measurement and the SSM-based measurement method respectively.
Figure 7-27. The measurement errors as a function of the actual mJSW (tube offset 0 cm, rotation 0 degree) together with linear trendlines. To improve the readability of the plot, the dots have a slight horizontal offset based on the index of the cadaver bones as illustrated at mJSW = 2 mm.

Table 7-14. The standard deviations and smallest detectable differences of the three measurement methods (with tube offset 0 cm, and rotation 0 degree). In the columns, values are first shown per cadaver and then for the whole dataset.

<table>
<thead>
<tr>
<th></th>
<th>Single cadavers (1 to 5)</th>
<th>Whole dataset*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N = 6</td>
<td>N = 6</td>
</tr>
<tr>
<td>Standard deviation (SD)</td>
<td>2D</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>3D – CT</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>3D – SSM</td>
<td>0.74</td>
</tr>
<tr>
<td>Smallest detectible difference (SDD)</td>
<td>2D</td>
<td>1.15</td>
</tr>
<tr>
<td></td>
<td>3D – CT</td>
<td>1.85</td>
</tr>
<tr>
<td></td>
<td>3D – SSM</td>
<td>1.45</td>
</tr>
</tbody>
</table>

* based on the least square error in the univariate analysis
7-4 Discussion

The purpose of this article was to investigate the application of a SSM reconstruction of the knee to conduct mJSW measurements and assess the feasibility of this measurement method. In a validation study, its sensitivity to changes in the mJSW was evaluated as well as its robustness to variations in knee positioning and bone geometry. For comparison, the mJSW was also measured in conventional plain radiographs. The measurement was repeated with bone models obtained from CT scans to study the influence of model accuracy. In comparison with the conventional 2D mJSW measurement from plain radiographs, the method is more robust (Figure 7-26) with a similar sensitivity over the whole dataset (Table 7-2). Thus, 3D reconstruction reduces the influence of knee positioning as expected. However, we could not establish an improvement in sensitivity, since the SDD of the SSM-based measurement is higher than that of the conventional measurement and CT-based measurement (SDD = 0.82 mm, 0.7 mm and 0.55 mm respectively). The error in the SSM-based measurement can originate from different sources: image calibration error, edge detection error, fitting error (i.e. not finding the global minimum solution) and modelling error. The comparison of results of the SSM-based measurement and the CT-based measurement shows that the CT-based measurement results were more accurate than those of the SSM-based measurement. This indicates that modelling error is probably an important contributor. The modelling error could be reduced by increasing the training set of the shape models. Another option is to improve the 2D/3D fitting and optimization. For example, edge detection can be inaccurate or incomplete when parts of the femoral and tibial silhouettes overlap. This could be solved by searching for better edge candidates in the neighborhood of the SSM silhouette during optimization. In addition, the edge orientation can be used to discriminate between the femoral and tibial edges, which is a technique that already has been studied[36]. Moreover, in clinical practice follow-up images are available. These can be exploited to limit the search space in which the optimization is performed.

The validation experiment showed that a 3D reconstruction improves the robustness of the measurements against variations in patient positioning, which was simulated using different tube offsets and rotation angles of the knee. Although this comparison
is useful, the robustness found for the 2D measurement cannot be extrapolated directly to clinical practice as measurement protocols are often employed reducing variability. Also, images that violate certain specifications (such as a high inter-margin distance) are retaken, further reducing variations in viewing angles. These protocols reduce variations in patient positioning and viewing angles by reducing inaccuracies in mJSW measurements in clinical practice.

A curious finding was that cadaver 1 showed relatively high measurement errors for all methods. This could be caused by bone abnormalities in the medial joint shape. As can be seen in Figure 7-28, a bulge was present in the femoral bone as well as a large inter-margin difference in the tibial plateau. Although the CT-based measurement does incorporate this bulge, results still show high measurement errors, indicating that other factors influence the measurement results.

Figure 7-28. Screenshot of the contour delineation for the 2D measurement in one of the examinations for cadaver 1.
The reproducibility of the 2D mJSW measurement has been evaluated in several other studies. Dupuis et al. found an SD of 0.08 mm to 0.11 mm in a cadaver study[100], which is a remarkably high precision. Conrozier et al. reported an SD of 0.14 mm for the reproducibility when fluoroscopy-assisted radiographs were used[90]. Except for the first cadaver specimen, the results in our study are comparable with an SD ranging between 0.10 and 0.20 mm.

Only cadaver knees without signs of OA were used in this validation study, because it was designed as a proof of concept of the measurement method. For patients with OA, modelling the femoral and tibial bones will be more challenging, because of abnormal shapes and the formation of osteophytes. The optimization of shape and pose parameters in the SSM-based measurement can be adjusted for such aberrations. For example, semi-automatic or automatic detection of the corresponding regions can be introduced, followed by the assignment of different weights to these regions in the 2D/3D matching algorithm.

More sophisticated imaging techniques such as MRI and CT are considered as a more reliable alternative than planar radiographs for the estimation of cartilage loss[101, 102]. However, these methods are more costly, more time-consuming and require experience and special equipment. Given that the modelling error can be further improved, the SSMs can provide a good alternative. Moreover, SSMs can provide quantitative information on the bone morphology. This has proven its value in the identification of risks and in the diagnosis of skeletal diseases[93, 103]. For example, the risks for hip fractures, the progression of osteoarthritis of the hip and the need for total hip replacement can be estimated by analysing the shape of the femur using a SSM model[104-106]. Likewise, a SSM-based reconstruction of the knee can be used to combine shape analyses and geometric measurements such as the mJSW, which can be valuable for OA-related research[107].

This study focused only on the validation of the mJSW measurement, but the 3D reconstruction has other contributions as well. For example, the 3D location of the mJSW could be determined and correlations between progression of joint space narrowing and (changes in) the 3D bone geometry can be studied. Also, alternative metrics such as the median or mean joint space distance could be investigated.
These metrics are probably less susceptible to noise or outliers than the mJSW, but often do require a standardized definition of the tibial margin based and deviate from the current definition of JSW.

In conclusion, the proposed measurement method is not a substitute for the conventional 2D measurement. The marginal improvement in measurement accuracy does not outweigh the increase in measurement complexity. However, further improvement of the model accuracy and optimization technique can be obtained. Combined with the promising options for applications using quantitative information on the bone morphology, SSM based 3D reconstructions of natural knees are interesting for further development.

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