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ORIGINAL RESEARCH

Accuracy and Reproducibility of Radiographic Knee Joint Space Narrowing Measurements Referenced to the Mid-Coronal Plane

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ABSTRACT

Introduction: Knee joint space narrowing (JSN) is a primary outcome measure in the progression of knee osteoarthritis and its treatment. JSN is most frequently determined from radiographs relying on the radiographic shadow of the anterior or posterior margins of the tibial plateau. Several studies address the confounding issues related to use of the anterior and posterior margins of the tibial plateau. An alternative strategy is to identify the mid-coronal plane of the tibial plateau and use that as a reference for measuring JSN.
Methods: Radiographs with precisely defined changes in joint space width (JSW) were created from CT imaging of cadaver knees. The mid-coronal plane of the knee was used to measure JSW and calculate JSN. Radiographs and data from the Osteoarthritis Initiative study were used to assess reproducibility and compare mid-coronal plane measurements of JSN to previously reported methods.
Results: The average absolute error in the measured versus known medial JSN was below 0.2 mm. The reproducibility was similar to previously published methods. There was a strong correlation between the mid-coronal plane measurements of JSN and JSN calculated using previously reported methods. There were several discrepancies between the two methods, suggesting that JSN for individual cases may depend on the method used to measure JSN.
Discussion: This study describes an alternative to using the margins of the tibial plateau when calculating JSN. JSN measurements based on the mid-coronal plane of the knee, where cartilage changes are more likely to occur, may have advantages.
Keywords: Knee osteoarthritis; Joint space narrowing; Radiographic imaging.

INTRODUCTION

Knee joint space narrowing (JSN) has been reported or discussed in many publications; for example, a Google Scholar search in September 2015 for only the exact phrase "knee joint space narrowing" returned 57 citations since January 2014. Joint space measurements are currently considered the "anchor evidence" in clinical trials of osteoarthritis (OA) treatments [1]. Recent consensus recommends JSN as a primary structural metric

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in osteoarthritis clinical trials [2,3]. JSN measurements are most commonly made from standing anterior-posterior (AP) or semi-flexed, weight-bearing, posterior-anterior (PA) radiographs. Joint space width (JSW) is measured from radiographs as the distance between an anatomic landmark on the tibia and an anatomic landmark on the femur. This measurement is repeated on a radiograph obtained at a later time point and JSN is calculated by subtracting the JSW measurements.

The anterior and posterior margins of the tibial plateau are typically the most prominent radiographic features used to identify the tibial joint surface on AP or PA radiographs (Figure 1). Most published methodologies for measuring JSN use the

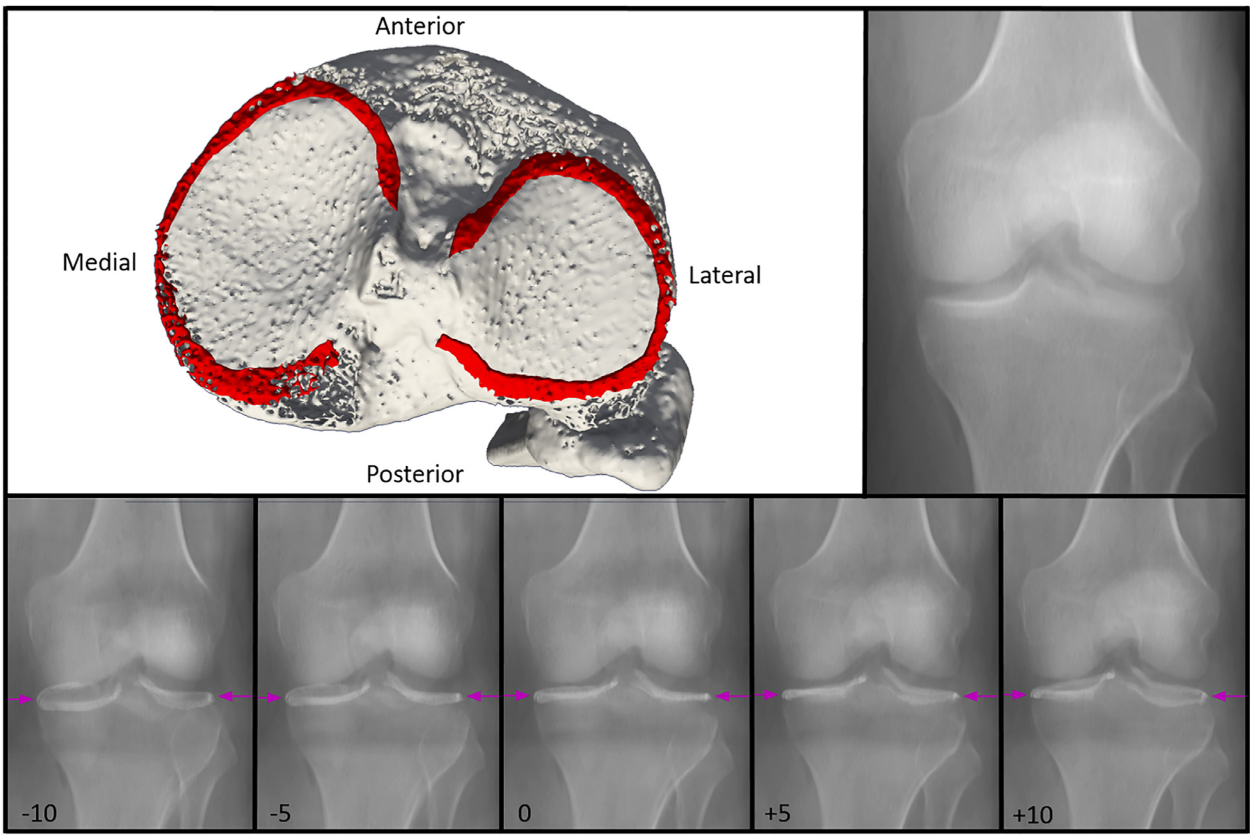

Figure 1. To demonstrate that the anterior and posterior rims of the tibia plateau form the most prominent radiographic features seen in a PA radiograph, a PA radiograph was simulated from a thin-slice CT examination of a cadaver knee (upper right corner). The PA radiograph was simulated with the central X-ray beam tilted +10 deg with respect to the plane of the medial tibial plateau. The typical radiographic features of a tibial plateau can be clearly identified. The rim of the tibia plateau was then isolated (shown in red on the upper left, looking down on the tibial plateau) and digitally set to a density corresponding to cortical bone. A series of simulated radiographs was then simulated representing a central X-ray beam tilted -10, -5 , 0, +5, and +10 deg from the plane of the medial tibial plateau. These rim-enhanced radiographs are shown along the bottom of the figure. Comparing the right-most of the rim-enhanced simulated radiographs along the bottom to the original simulated radiograph in the upper right, it can be seen that the radiographic lines seen in a typical PA radiograph are due to the anterior and posterior rims of the tibial plateau. The magenta arrows on the lower row of images show where the anterior and posterior rims of the tibial plateau meet on the lateral- and medial-most aspects of the tibia plateau. These meeting points are used to identify the mid-coronal plane.

radiographic shadow of these margins as a reference for JSN measurements [4-6]. When the knee is viewed in the sagittal plane, the anterior and posterior borders of the tibial plateau can be several centimeters anterior or posterior to the actual region where the femoral condyles contact the tibial plateau during standing (Figure 2). Contact between the femur and tibia is typically close to the mid-coronal plane of the knee joint. Intuitively, that is where JSW would ideally be measured when using 3D imaging (MRI or CT). Measurements made from 2D radiographs can only estimate depth perpendicular to the plane of imaging. A measurement made close to the point of contact between the femur and tibia may better represent JSN.

The mid-coronal plane of the knee joint can be identified from AP or PA radiographs by looking for specific anatomic landmarks. The primary goal of the present study was to determine the accuracy of radiographic JSN measurements based on the mid-coronal plane of the knee joint. Accuracy was determined using a precisely defined "gold standard." The secondary goal was to compare JSN

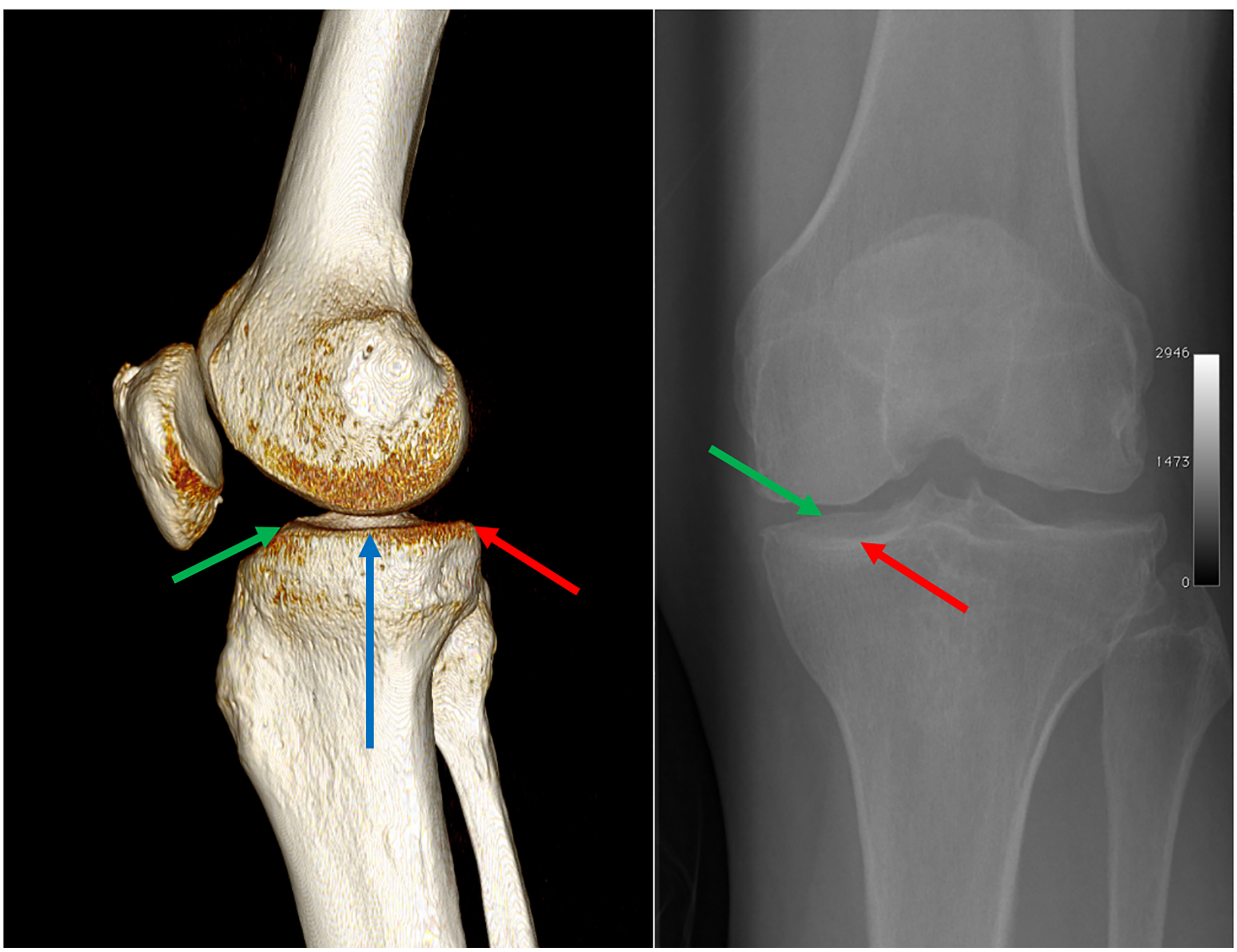

Figure 2. On the left is a view of a knee joint from the side, reconstructed from a CT examination. The anterior rim (green arrow), the posterior rim (red arrow), and the approximate mid-coronal plane (blue arrow) of the tibial plateau are marked. Ideally, joint space width would be measured where the femoral condyle is closest to the tibial plateau (blue arrow). On the right is a typical PA fixed-flexion radiograph where the radiographic shadows of the anterior and posterior rims of the tibial plateau can be seen on the medial side.

measurements based on the mid-coronal plane to previously reported JSN measurements made in reference to the radiographic shadows of the rims of the tibial plateau.

MATERIALS & METHODS

The mid-coronal plane JNS measurement

The mid-coronal plane of the tibia is identified by following the radiographic contour of the anterior and posterior rims, and identifying where they meet at the lateral- and medial-most aspects of the tibial plateau (Figure 3). A line is then drawn between the lateral- and medial-most aspects of the tibial plateau. In practice, these lines are mentally identified and not actually drawn on the images. The length of the line between the lateral- and medial-most points is used to define the width of the tibial plateau. Points are marked on this line that are 20% of the width medial to the lateral-most edge, and 20% lateral to the medial-most edge (Figure 3). These points are where the lateral and medial JSN is measured. Duryea et al. in 2010 reported improved responsiveness of JSN measured at fixed locations [6]. An additional line is drawn that touches the caudal-most points on the medial and lateral femoral condyles. Points are placed on this femoral condyle line, corresponding to the locations where the medial and lateral JSNs are to be measured. These points are placed along lines perpendicular to the points marked on the mid-coronal plane tibial line. Note that these points do not always identify the point where the condyle appears to be in closest apposition to the tibial plateau. The purpose of these points and the measurement methodology are to reliably measure JSN and provide a standardized JSW measurement across subjects and time points,

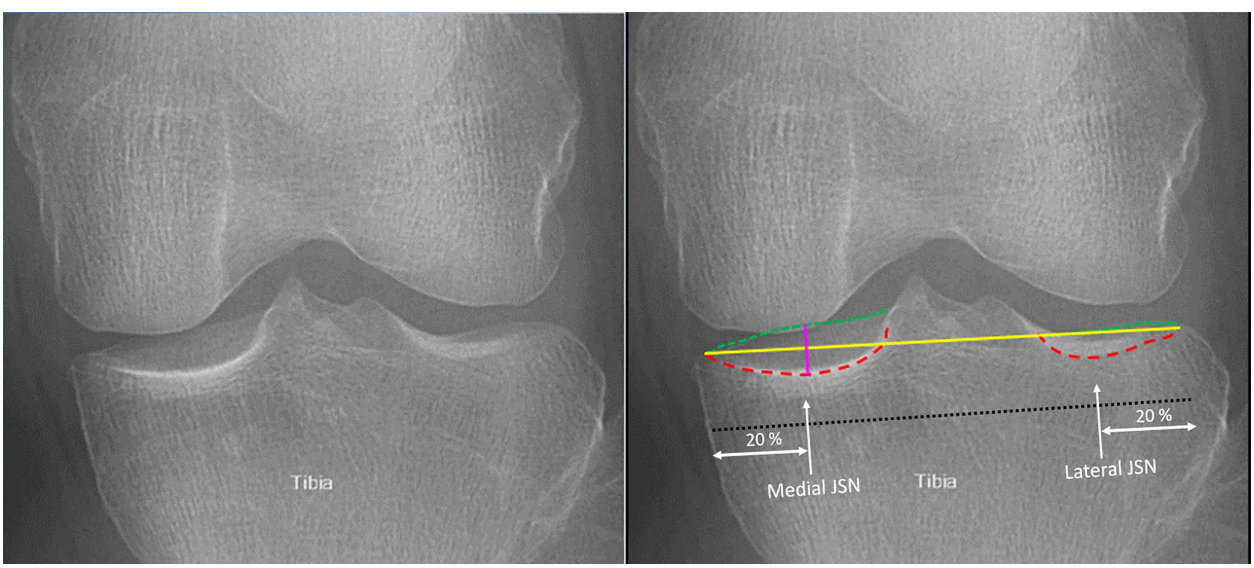

Figure 3. The mid-coronal plane is identified by tracing the radiographic shape of the anterior rim (green dotted lines on right image), tracing the radiographic contour of the posterior rim of the tibial plateau (red dotted lines), identifying points where the anterior and posterior rims meet on the lateral- and medial-most aspects of the tibial plateau, and drawing a line connecting these points (yellow line). The original radiograph is on the left. The magenta line on the medial compartment on the right side shows the intermargin distance. The dotted black line shows the medial-lateral width of the tibial plateau. The white arrows show where medial and lateral JSN was measured.

even though the JSW measurement may not correspond to what appears as the minimum JSW in any one radiograph.

All of the lines and points described above were drawn and positioned digitally using the interface to the Quantitative Motion Analysis (QMA®, Medical Metrics, Inc; Houston, TX) software. Note that these lines and points are placed only on the baseline radiograph. After stabilization of the femur and tibia, the software calculates the positions of lines and points on the subsequent radiographs. This eliminates errors from a human operator attempting to identify the same landmarks on multiple images. The QMA® software has been previously validated for measuring knee joint space laxity and for measuring intervertebral motion [7,8]. Using the QMA® software, the tibia and femur are stabilized using computer-assisted pattern recognition technology. This technology uses all available radiographic information about each bone to achieve stabilization. After stabilization, the baseline and follow-up radiographs can be alternately displayed, and the tibia or the femur (depending on what is selected), will remain in a constant position on the computer display. This allows for verification of stabilization and visualization of the relative motion. Note that when the central X-ray beam is parallel to the tibial plateau, the anterior and posterior rims of the tibial plateau overlap and JSN measurements would be the same as if a tibial rim were used as a reference when measuring JSN. Also note that if the central X-ray beam is oblique to the tibial plateau, the anterior and posterior borders may appear to move between time points when the mid-coronal plane is stabilized. Thus, some discrepancy between mid-coronal plane measurements and tibial rim-based measurements would be expected.

The QMA® stabilization technology produces mathematical transformation matrices that are used to determine the relative position of the tibia and femur in each radiograph, and to calculate the change in position of the femur and tibia between time points, and then to calculate JSN at the medial and lateral measurement locations (Figure 3).

Assessment of measurement accuracy

The tibia and fibula were digitally removed from thin-slice (0.625 mm), high resolution (0.31 mm/pixel) CT imaging of semi-flexed knees from three adult male cadavers (CT imaging obtained by contract with Advanced Technology in Orthopedics, Houston, TX). All overlying soft tissues (skin, fat, muscles, etc) were intact when the CT images were obtained. The CT images were first interpolated to 0.275 mm isotropic resolution to provide higher resolution simulated radiographs. The tibia and fibula were then digitally added back to the CT data after applying precise cranial or caudal displacements. This provided known amounts of JSN. JSN (as well as mild joint space widening) of between 0 and 3.5 mm was simulated in 0.5 mm increments. Small (1-3 deg) rotations in the transverse plane were also applied to some of the images to simulate variability in patient positioning and central X-ray beam orientation. The modified CT images were then used to create PA radiographic images of the knee, using digitally reconstructed radiograph (DRR) software that is extensively used for radiation treatment planning (Plastimatch DRR, url: www.plastimatch.org/drr.html). The radiograph-like images created using DRR simulated X-ray scatter and X-ray parallax, which are primary sources of error in radiographs. The central X-ray beam path was varied from perfectly co-planar with the medial tibial plateau and up to 15 deg oblique to the medial tibial plateau (Figure 4). Obliquity of the X-ray beam with respect to the tibial plateau is referred to as out-of-plane (OOP) in this paper.

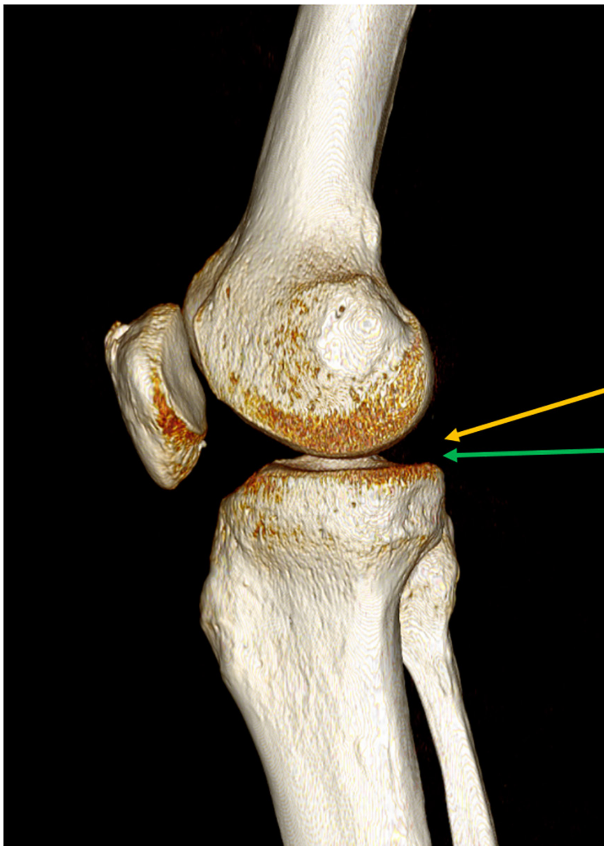

Figure 4. Schematic of the central X-ray beam orientation when it is co-planar with the tibial plateau (green arrow) and when it is 15 deg oblique to the tibial plateau (orange arrow).

Seventy pairs of X-rays generated with the DRR program were analyzed using the QMA® software. Each pair of X-rays had two different, precisely defined amounts of separation between the tibia and femur. To represent various amounts of OOP, the central X-ray beam was directed 2-4 deg OOP in 20 pairs (mild OOP) and was 10-15 deg OOP in 20 pairs (severe OOP). The central X-ray beam was directed co-planar to the medial tibial plateau in the remaining 30 pairs. The analyst conducting the stabilization of the tibia and femur was blinded to the known JSN or the amount of applied OOP. The analysts who completed the stabilization had received extensive training on use of the QMA® software, and had passed a training and certification program for stabilization of the femur and tibia. JSN was then calculated by the QMA® software in both the medial and lateral compartments. The errors in the measured JSN were determined as the difference from the applied displacement of the tibia with respect to the femur.

Comparison of mid-coronal plane medial JSN to medial JSN reported in the OAI study

In addition, paired baselines of 1, 2, 3, and 4 year follow-up radiographs of 37 subjects enrolled in the Osteoarthritis Initiative (OAI) study were used to measure medial JSN by using the mid-coronal plane method and those measurements were compared with medial JSN reported in the OAI public use data sets. Radiographs and JSW data were obtained from the OAI database which after registering with the OAI, is available for public access at http://www.oai.ucsf.edu/. Cases were selected to uniformly span the full range of JSN at 4 years as calculated from the JSW reported in the OAI study data. The radiographic scaling of the images was determined using the markers in the OAI images, in accordance with the OAI guidance documents In the OAI study, multiple different JSW measurements were available. To facilitate a direct comparison between methods, the JSW measured at a point 20% (of the tibial width) lateral to the medial edge of the tibia was used. This corresponds to the 0.2

measurement location in the first figure of Duryea et al. (6). In the reliability testing reported on the OAI website, the intraclass correlation coefficient (ICC) for the original and repeat measurements of JSW measured at the medial 20% location was 0.987, and the limits of agreement between repeated measurements were -0.339 and 0.319 mm. JSN was calculated from the JSW measurements reported in the OAI database. Agreement between JSN measured by the mid-coronal plane method and JSN reported in the OAI data were assessed by linear regression analysis and intraclass correlation (Stata version 13; College Station, TX).

Assessment of the reproducibility of mid-coronal plane JSN

To assess intraobserver variability of the mid-coronal plane JSN measurements, three trained analysts independently stabilized the tibia and femur from 18 paired baseline and 4-year radiographs from the OAI study. JSN was calculated by the QMA® software. Variability was assessed using descriptive statistics and Bland-Altman limits-of-agreement analysis (Stata version 13; College Station, TX).

RESULTS

The simulated radiographs were of lower quality than typically obtained in clinical practice or in the OAI study (Figure 5). This did not prevent stabilization of the mid-coronal plane using QMA®, although stabilization is easier using actual radiographs. The absolute error in the measured JSN measured was dependent on compartment (medial or lateral, $p=0.0004$) and on the amount of OOP applied relative to the medial tibial plateau on the simulated radiographs ($p<0.0001$, Figure 6). When the central X-ray beam was oriented to be co-planar with the tibial plateau, absolute errors relative to the known narrowing averaged 0.1±0.08 mm (medial and lateral compartments combined). In the medial compartment, including all levels of OOP, the average error was 0.17±0.16 mm. The largest errors (0.78±0.58 mm) were with JSN measured in the lateral compartment when the X-ray beam was >10 deg from the plane of the medial tibial plateau. Note that OOP was applied to the radiographs relative to the medial compartment of the tibial plateau. The OOP was greater in the lateral compartment than in the medial compartment in some radiograph pairs.

There was a high correlation between the mid-coronal plane JSN measurements and currently reported JSN measurements in the OAI study ($R^2=0.84$, Figure 7). The ICC (two-way mixed effects) for correlation between individual OAI and mid-coronal plane measurements was 0.85. The difference between methods (mid-coronal plane JSN minus OAI) was -0.49±0.51 mm (range -2.2 to 0.85 mm). The knee X-rays with the largest difference between the mid-coronal plane-based measurements and the OAI measurements were examined to understand the discrepancy. The discrepancies were most commonly associated with radiographs in which there was a pronounced intermargin difference, which is the distance between radiographic shadows of the anterior and posterior margins of the tibial plateau (magenta line in Figure 3). One advantage of analyzing JSN using QMA® is that the radiographic JSN can be scrutinized

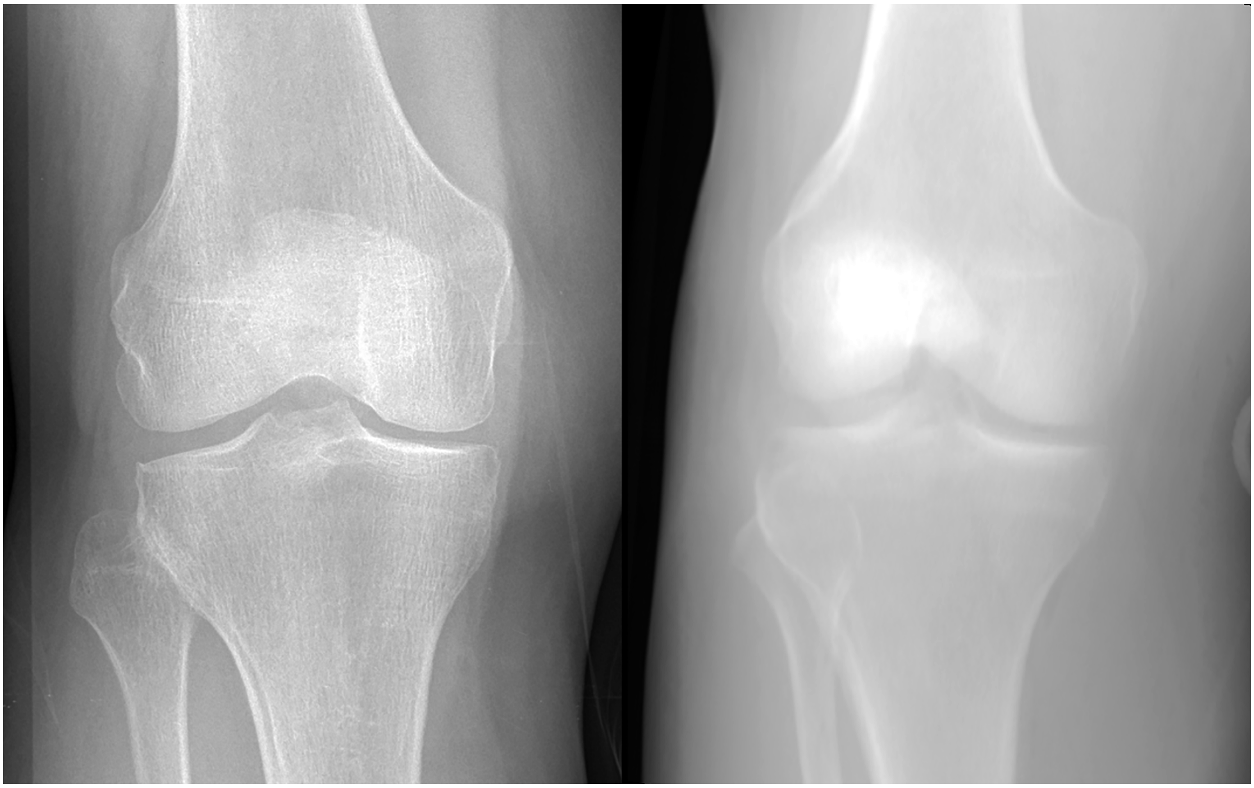

Figure 5. Actual PA fixed-flexion radiograph from the OAI study (on the left), and a radiograph simulated from a CT examination of a semi-flexed cadaver knee (on the right). Note that all the radiographs display in higher quality on monitors used to stabilize the tibia and femur, compared with the quality seen in this figure.

using stabilization. With stabilization, the radiographs taken at different time points can be alternately displayed while keeping either the tibia or the femur in a constant position on the computer display. That facilitates visualization of the true JSN, since the changes in relative position between tibia and femur can be clearly visualized.

The interobserver variability of mid-coronal plane JSN was assessed by assuming that the average JSN for the three analysts was the true JSN for each knee, and then calculating the error in each analyst's measurement relative to the average. The average error was 0.041 mm, -0.0037 mm, and -0.037 mm for analysts 1, 2, and 3 respectively. The Bland-Altman limits of agreement were from -0.46 to 0.48 mm for analyst 1, -0.31 to 0. 28 for analyst 2, and -0.36 to 0.38 for analyst 3.

DISCUSSION

The accuracy of using the mid-coronal plane to measure JSN was determined using simulated radiographs with precisely applied changes to JSW. When the central X-ray beam is co-planar or nearly co-planar with the tibial plateau, the accuracy of the mid-coronal plane approach to measuring JSN is similar to the accuracy reported for methods that use the radiographic shadows of the tibial plateau margins [9]. In the Dupuis et al. study that previously reported the accuracy of radiographic measurements of JSN, the displacement of the tibia relative to the femur was applied by a testing machine [9]. Owing to concern about the reliability of the applied displacements, a roentgen stereophotogrammetric analysis (RSA) was used to measure relative displacements.

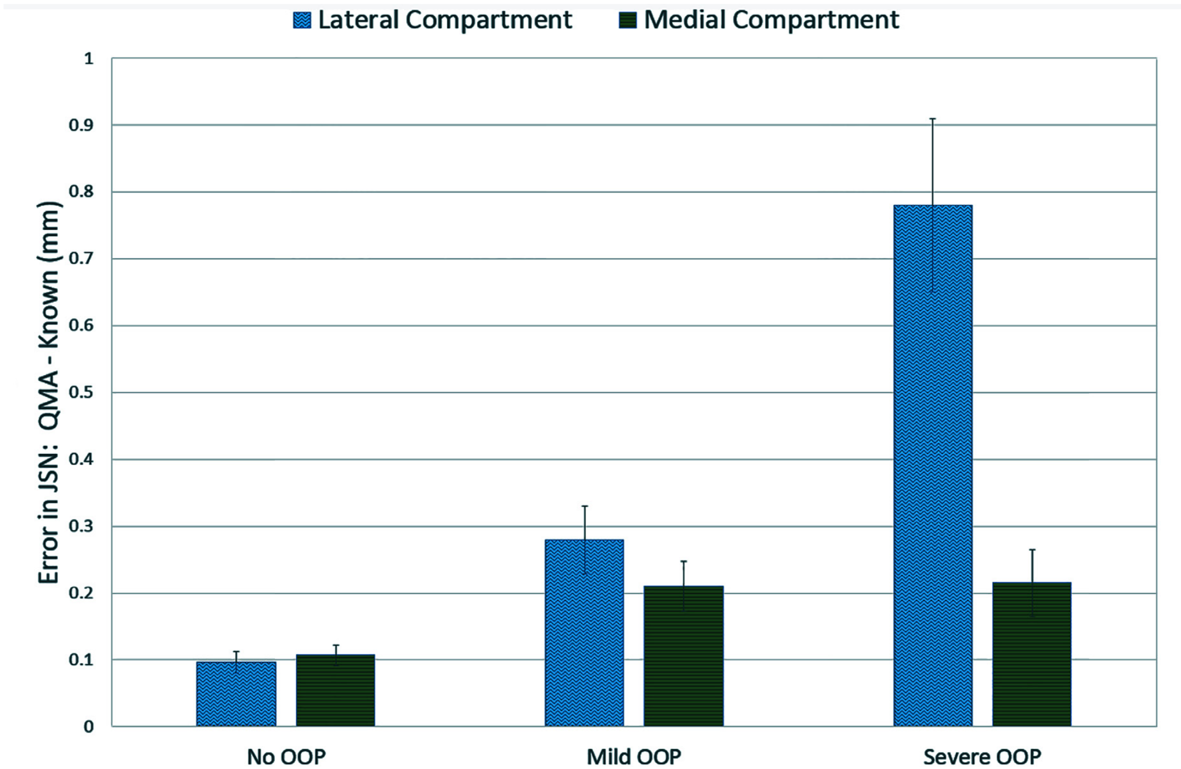

Figure 6. Average absolute error in the JSN measured using QMA® relative to the known JSN that was applied to the knee. The error bars show the standard error. JSN = joint space narrowing; OOP = out-of-plane.

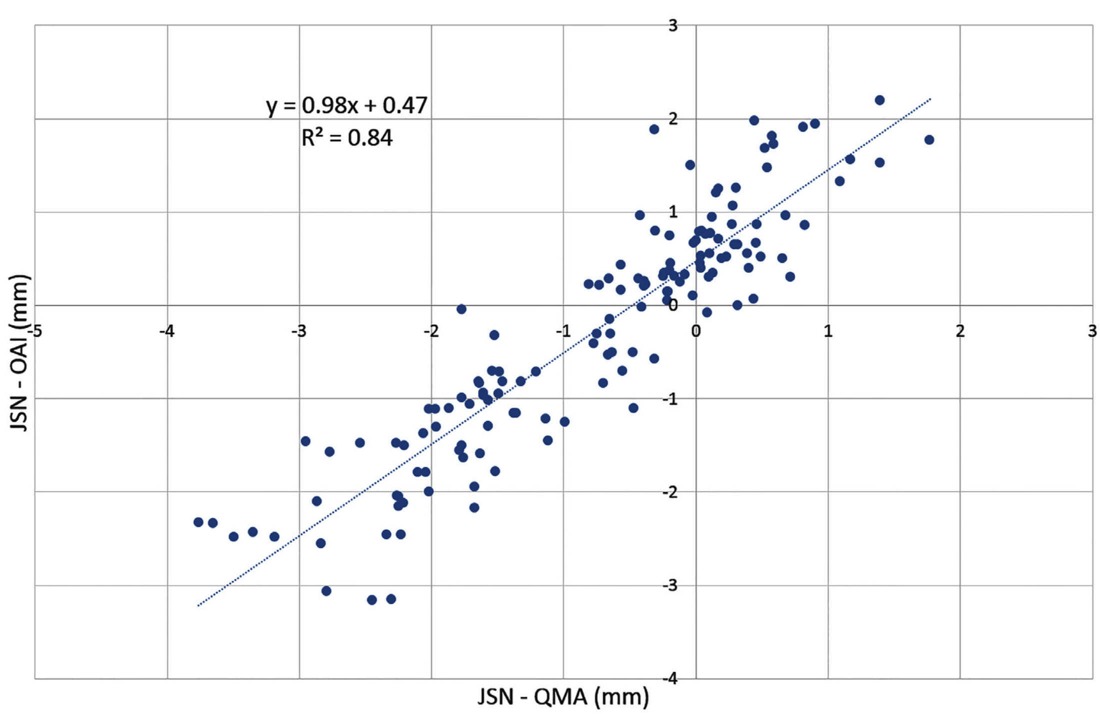

Figure 7. The correlation between the joint space narrowing (JSN) measurements obtained using QMA® with the mid-coronal plane approach and the JSN calculated from the joint space width (JSW) measurements reported in the publicly available Osteoarthritis Initiative (OAI) database.

The overlying skin and soft tissues had been removed (although the immediate periarticular structures were maintained), so the radiographic quality would likely have been excellent with radiographs obtained with the central X-ray beam co-planar with the tibial plateau. It is not known how the presence of soft tissues or variability in orientation of the central X-ray beam with respect to the tibial plateau would have affected the accuracy reported by Dupuis el al. [9].

With the exception of the Dupuis et al. study [9] that used laboratory-quality radiographs, the accuracy of JSN measurements is not commonly reported, and there are no direct data to document that the mid-coronal plane approach improves measurement accuracy with clinical-quality radiographs when the central X-ray beam is not nearly co-planar with the tibial plateau. Nevertheless, the accuracy of the mid-coronal plane may be sufficient for the goals of some studies that require knee JSN measurements. The accuracy required for various clinical study designs has yet to be established.

Only a small proportion of patients lose significant joint space in some studies of knee joint osteoarthritis or of treatments for knee OA [10-12]. The average rate of JSN is small in most studies [11,13]. It is therefore important to accurately identify all subjects with a significant change in joint space. Conversely, a study in which treatment goal is to improve knee health would benefit from identifying all cases with a true improvement in JSW. A study comparing treatment options for knee OA will require a smaller sample size if the measurements of JSN are both accurate and repeatable. In large population-based studies, the natural history of JSN or treatment effect on JSN can be documented using appropriate large sample statistics, even if the measurement reliability is limited. However, in a study where JSN might be used to identify a positive treatment effect in each subject, or to identify treatment failures, an accurate measurement is desirable for each subject. Multiple publications describe the reproducibility of JSN methodology [14-16]. Reproducibility is undeniably important. However, reproducibly getting the wrong measurement is not helpful, so accuracy should also be documented.

Assessment of measurement accuracy is difficult owing to the challenge of finding a "gold standard" that can be used as a reference. It is difficult to experimentally measure motion between the tibia and femur in living subjects, so physical measurements of motion are generally limited to ex vivo cadaver studies, eg Thompson et al. [7]. Some of the available options for experimentally measuring relative motion between bones may have similar measurement error to radiographic measurements and thus are a suboptimal "gold standard." It is for this reason that a virtual simulation of JSN was used in our study as the "gold standard."

If all radiographs could be attained such that the radiographic contours of the posterior and anterior margins of the tibial plateau are superimposed and cannot be individually identified, the method described in this paper would not be needed. Unfortunately, uniformly perfect radiographs would require that a fluoroscopy system be available to determine the optimum central beam orientation with respect to the knee in each subject [17]. This is not practical in many studies. The intermargin distance is the distance between the anterior and posterior rims of the tibial plateau on the PA or AP radiograph. The intermargin distance was shown to influence JSN measurements using methodology that relies on the rims of the tibial plateau [18]. Some studies prospectively define a rule that the intermargin distance must be under a threshold level such as 1.0 or 1.5 mm [19,20]. Without careful control of how the radiographs are obtained, this restriction may eliminate a substantial number of radiographs within a typical clinical study. The data reported in this paper suggest that use of the mid-coronal plane when measuring JSN may reduce the dependency of the JSN measurements on OOP, although severe OOP will increase error in the JSN measurements.

The data show that OOP had a much greater effect on the JSN measured in the lateral side of the knee. This is likely due to OOP being applied relative to the medial plateau. The actual amount of OOP relative to the lateral plateau was not controlled and was dependent on the anatomy of the knees.

There was a strong correlation between JSN measurements reported in the OAI study, and JSN measured using the mid-coronal plane method. This correlation would support that in a study with a large sample size, with a study hypothesis that is addressed by comparing the mean and standard deviation in JSN between groups, either method for measuring JSN would likely provide a similar answer to the research question. If the study design requires classifying each subject as a success or failure in part based on JSN, the method used to measure JSN may prove significant.

Limitations of the study include calculating measurement accuracy using simulated radiographs that were of lower quality than typically used in clinical practice. However, it might be expected that the accuracy would improve with better-quality radiographs.

CONCLUSIONS

The radiographic projection of the anterior or posterior border of the tibial plateau is commonly used to measure JSN. Anatomically, in the sagittal plane, these borders are distant from the point where JSN would be measured if using 3D CT or MRI data. JSN accurately and reproducibly measured near the mid-coronal plane of the knee may be more effective in clinical research. This study supports that measurements of JSN about the mid-coronal plane of the knee can be accurately and reproducibly obtained and may potentially avoid errors in measurements made using the anterior or posterior borders of the plateau as reference.

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