Influence of variation in semiflexed knee positioning during image acquisition on separate quantitative radiographic parameters of osteoarthritis, measured by Knee Images Digital Analysis


† Rheumatology & Clinical Immunology, University Medical Center Utrecht, The Netherlands
‡ Image Sciences Institute, University Medical Center Utrecht, The Netherlands
§ Anatomy, University Medical Center Utrecht, The Netherlands
∥ Julius Center for Health Sciences & Primary Care, University Medical Center Utrecht, The Netherlands

SUMMARY

Objective: The clinical application of quantitative measurement of separate radiographic parameters of knee osteoarthritis (OA) might be hampered by a lack of reproducible semiflexed joint positioning during acquisition of radiographs. The influence of systematic variations in knee positioning on measurement of separate quantitative radiographic parameters was studied.

Methods: Five components of knee position during radiographic acquisition (beam height, lower and upper leg extension, internal rotation, and lateral shift) were systematically varied within a clinically relevant range, using three cadaver legs. The influence of these variations on the measurement of the separate quantitative radiographic parameters by Knee Images Digital Analysis (KIDA) was evaluated. Significant changes were validated in vivo. Changes were compared with differences during 2-year follow-up in a radiographic progression cohort of early OA.

Results: Systematic variation in upper and lower leg extension induced changes in the measurement of joint space width (JSW). Lower leg extension also influenced osteophyte area and eminence height measurement. Also bone density measurement was influenced by variation in all five position components. Variations were of clinical relevance compared with 2-year differences in knees with radiographic progression, and were confirmed in vivo.

Conclusions: Variations in semiflexed knee positioning, which are considered to occur easily during image acquisition in trials and clinical practice despite standardization, are of significant influence on the quantitative measurement of most separate radiographic parameters of OA using KIDA. The additional value of quantitative measurement might improve significantly by better standardization during radiographic acquisition; with radiography still being the gold standard for structure-modification in OA.

© 2012 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.

Introduction

Osteoarthritis (OA) is a disabling joint disease that commonly affects large weight-bearing joints like the knee. Structural changes include articular cartilage damage, osteophyte formation, and subchondral bone changes, and are assumed to (at least partly) underlie symptoms of pain and functional disability12. Radiography is still the gold standard for demonstrating structural changes in humans4, since image acquisition is non-invasive, cheap, fast and generally accessible4,5. In the past decades developments have been ongoing on more detailed evaluation to improve sensitivity for detection of structural damage on radiographs. The actual measurement (on a continuous scale) of joint space width (JSW) is increasingly applied6−9, and in recent years digital image analysis tools were developed to increase efficiency and reliability of such measurements6,10,11. Compared with the commonly used Kellgren & Lawrence12 (K&L) grading, the sensitivity to change was improved by actual measurement of JSW13. Digital analysis also enables measurement of additional separate radiographic characteristics of...
knee OA like osteophyte formation\textsuperscript{14} and joint angulation\textsuperscript{14,15}, and even bone density\textsuperscript{16}. The measurement of separate OA parameters might improve the detection of structural damage in an early phase of the disease and might improve the association with clinical symptoms.

When the onset and progression of radiographic OA is evaluated, changes caused by variation in knee positioning during acquisition of the subsequent radiographs may need to be taken into account\textsuperscript{17,18}. Such variation specifically hampers the detection of differences (over time and between individuals) when the radiographic development is subtle, which is generally the case in a slowly progressive disease like OA and specifically early in the disease. Such variation is found to be a confounder for detecting radiographic changes in e.g. hips and hands as well\textsuperscript{19–21}.

Although lack of good alignment influences all methods for evaluation of radiographic damage, particularly when using digital image analysis, reproducible positioning of the knee needs attention since in contrast to conventional subjective grading of OA features, an objective mathematical method does not include the possibility to take into account subjective evaluation of variation in knee positioning between radiographs. It has been reported that variability in JSW measurement is introduced by variations in knee flexion, foot rotation, and beam angle in the extended radiographic view\textsuperscript{22,23}, and by variations in beam height in the tunnel view\textsuperscript{23}.

Therefore, standardization of the radiographic procedure is of great importance. Standardization is commonly aimed at reproducible alignment of the medial tibial plateau, by projection of the anterior rim on the posterior rim. This can be achieved by applying some degree of knee flexion and by inclination of the beam angle. Since verification by fluoroscopy results in increased costs, acquisition time and X-ray exposure, several non-fluoroscopic procedures have been evaluated for the reproducibility of knee joint positioning and the influence on JSW measurement\textsuperscript{24–26}. The semiflexed view according to Buckland-Wright is preferred since this procedure repositions the joint best\textsuperscript{27}, both at the same day\textsuperscript{24} and within a year\textsuperscript{28}.

Despite this standardization, acquiring reproducible radiographs in clinical studies remains difficult. Interestingly, it has never been reported to what extent specific components of the semiflexed knee position (e.g., flexion or rotation) influence the reproducibility of radiographic characteristics other than JSW, like osteophyte area, eminence height, and bone density. The present study evaluated which systematic variations in positioning of the knee toward the X-ray detector have an effect on measurements of separate radiographic parameters using Knee Images Digital Analysis (KIDA\textsuperscript{16}), which is of relevance in the evaluation of structural differences in the process of OA in clinical studies and in clinical practice.

Methods

Cadaver study

Three human cadaver legs (two females and one male: age 76, 76, and 65 years) were prepared for analysis. Although incidence of OA is highest at this age (>65 years), the cadaver legs were not reported as suffering from clinical OA symptoms. These legs were considered suitable for the present evaluation since more and more cohorts focus on very early (pre-clinical) OA (e.g., the Cohort Hip & Cohort Knee (CHECK)\textsuperscript{30} study in the Netherlands and the incidence cohort of the Osteoarthritis Initiative (OAI)\textsuperscript{13} in the United States).

To warrant the mechanical condition of the knee joint as good as possible (like weight-bearing, and ligament/muscle involvement) while keeping the experimental conditions feasible/acceptable, the whole leg including the hip joint was used with the lumbar vertebrae fixed to a framework. This set-up allowed (semi-) weight-bearing during radiography with the possibility to image multiple systematic variations in knee positioning.

Validation in vivo

The significant changes in radiographic parameters by variations in positioning in the cadaver legs were validated in vivo. For each component of knee position two radiographs were acquired of a healthy volunteer, representing the two extremes of the variation in the component of leg positioning. The volunteers (four males and one female) were aged between 50 and 66 years and had no known history of joint disease. The medical ethical committee of the University Medical Center Utrecht approved this study, and volunteers gave written informed consent.

Reference cohort

To evaluate if the changes observed during variation in semiflexed knee positioning were of clinical relevance, they were compared with differences observed in a radiographic progression cohort of individuals with early OA. Radiographs of knees (at baseline and 2-year follow-up) were selected from the CHECK cohort with no radiographic OA (K&L grade < II) at baseline and radiographic OA (K&L grade ≥ II) at 5-year follow-up [310 knees, mean age at baseline: 56 years (range: 44–66)]. In this cohort posteroanterior knee radiographs are taken according to the same semiflexed standardized protocol in 10 centers in the Netherlands. The mean differences from baseline to 2-year follow-up in the separate radiographic parameters of these selected knees were used as a clinical reference.

Radiographic parameters

Posteroanterior radiographs were acquired according to the standardized protocol by Buckland-Wright\textsuperscript{24,32} using a clinical digital radiography system (Digital Diagnost, Philips Healthcare, Best, the Netherlands) at the University Medical Center Utrecht. Acquisition settings were: tube potential of 55 kilo voltage (kV), tube charge of 5 milliamper seconds (mAs), no added tube filtration, and a source image distance of 120 cm. The radiographic protocol and the acquisition settings were accurate according to those used in the CHECK\textsuperscript{30} cohort.

Separate radiographic parameters were quantitatively measured by use of KIDA\textsuperscript{16}, an interactive tool to evaluate radiographic characteristics with low inter- and intra-observer variation\textsuperscript{16,33}. All radiographs were analyzed by one experienced observer (ML) in random order. Analyses revealed minimum, medial, and lateral JSW (in mm), the angle between the femur and tibia in the frontal plane (varus angle in degrees), height of the eminences (mm), osteophyte area (in mm\textsuperscript{2}), in four compartments (lateral and medial femur and tibia), and bone density of the four compartments (expressed in mmAl equivalents)\textsuperscript{16}.

Knee position

For radiographs in the standard position (according to the semiflexed protocol described by Buckland-Wright) the leg was placed in the semiflexed position with the knee leaning against the detector, the first metatarsophalangeal (MTP) joint perpendicular to the detector, and the foot in 75\textdegree exorotation (by use of a foot plate with a triangular wedge)\textsuperscript{24,32}.

Compared with the standard position, five separate components of knee positioning were systematically varied (Fig. 1). The choice and the range of variation of the position components were based...
on expert opinion (FL/AM). The knee position was varied by systematically changing one position component while the rest of the leg remained in the standard position. Variations were done in both directions [e.g., more extension (+) and more flexion (−) compared with standard position]. Per component the position was varied in fixed steps (one radiograph per step) which were of similar size for all cadaver legs and which were considered to be in a clinically relevant range. ‘Beam height’, ‘lower leg extension’ (shifting the foot forwards/backwards on the panel), and ‘lateral shift upper leg’ (frontal plane) were changed in steps of 1 cm. ‘Internal rotation’ (transversal plane) and ‘upper leg extension’ were changed in steps of approximately 5° as measured by a goniometer. After radiographic acquisition the measurement of ‘upper leg extension’ was verified by angle measurement on standard photographs, which were taken from a lateral view simultaneously with the radiographs. On these photographs the knee extension angle was measured between bars that were fixed to the bone (by pins through soft tissue) on the lateral side of the femur and of the tibia.

Results

Influence of variation in knee positioning on radiographic parameters

In Table I per component of knee position that was varied regression coefficients (β) and P-values are provided which represent the change in outcome per unit change in positioning, in bold in case of significance according to the above described criteria and in normal font in case of non-significance according to these criteria.

Joint space

Varying the ‘beam height’ (−3 to +3 cm) did not influence minimum JSW, medial JSW, and lateral JSW. Increasing the beam height induced a significant decrease in varus angle (−0.12° varus angle per cm beam height; Table I). The effect is not considered clinically relevant, since the change in the cadaver legs was considerably smaller than the mean difference (increase) of 0.77° in knees with radiographic progression (Table II).

Systematically varying the ‘upper leg extension’ (130°–180°) significantly influenced the lateral JSW and varus angle (−0.20 mm and −0.25° per 5°) more extension [Table I and Fig. 2(A)]. The decrease in lateral JSW is in accordance with the decrease in varus angle, meaning a relative decrease in lateral JSW compared to medial JSW. These effects were verified in vivo, showing a decrease in lateral JSW similarly to the cadaver legs (−0.21 mm per 5°) and a decrease in varus angle of −0.08° per 5° (smaller than cadaver legs). The variation in ‘upper leg extension’ on lateral JSW is considered clinically relevant, since this change was only slightly smaller than the 0.27 mm difference during 2-year follow-up in individuals with early OA that progressed from K&L grade < II to ≥ II (Table II).
The variation in ‘lower leg extension’ by shifting the foot forward (from −3 to +3 cm) on the foot plate induced a slight but systematic increase in minimum JSW and medial JSW (both +0.07 mm per cm). The decrease in lateral JSW (−0.18 mm per cm) and varus angle (−0.32° per cm) is considered in accordance with the increase in medial and minimum JSW (since the medial compartment is commonly smallest). These effects were also found in vivo, and specifically the increase in minimum and medial JSW was substantial (per 5°: +0.17 mm for minimum JSW, +0.24 mm for medial JSW, −0.03 mm for lateral JSW, and −0.31° for varus angle). Particularly the increase in minimum JSW [+0.07 mm per cm; Table I and Fig. 2(B)] is clinically relevant when compared with the mean difference of 0.11 mm in knees with radiographic progression.

‘Internal rotation of the upper leg’ (−20 to +15°) and ‘lateral shift of the upper leg’ (−3 to +3 cm) had no clear systematic influence on the measurement of JSW and varus angle on radiographs.

### Osteophyte area

Osteophyte formation in these (relatively) healthy knees was minimal, and at the medial femur of all three cadaver legs no osteophyte area was present. Only by systematically increasing ‘lower leg extension’ (shifting the foot forward) the osteophyte area increased significantly in the medial tibia [0.49 mm² per cm; Table I and Fig. 2(C)]. An increase in osteophyte area in this compartment was also found in vivo (+0.22 mm² per cm). The change is of limited clinical relevance however, since this is clearly smaller than the difference over 2 years of 1.33 mm² in medial tibia osteophyte area in knees with radiographic progression (Table II). Variations in the other position components did not significantly influence the quantitative measurement of osteophyte area. Clearly, the effects may be underestimated due to the minimal osteophyte area in these healthy individuals.

### Eminent height

The height of the tibial eminences was significantly influenced by variation in ‘lower leg extension’, not surprisingly because of their position on the tibia [Table I and Fig. 2(D)]. This effect was confirmed in vivo, with a change of similar size on the lateral eminence (per cm change −0.21 mm in vivo compared with −0.17 mm in cadaver per cm). The influence on the lateral eminence measurement was considered clinically relevant since the change caused by systematic repositioning was only slightly smaller than the difference of 0.27 mm in knees with progression during 2-year follow-up (Table II).

### Bone density

Surprisingly the bone density measurement was influenced by systematic variations in many of the components of knee positioning. By increasing ‘upper leg extension’, bone density in the lateral femur increased with 0.38 mmAl per 5° [Table I and Fig. 2(E)]. The effect of ‘upper leg extension’ on the lateral femur corroborates the effect of ‘beam height’ (−0.31 mmAl per cm). Since increasing ‘beam height’ artificially causes an increase in knee flexion angle, this resulted in decreased bone density. Varying ‘beam height’ did not significantly influence bone density in the...
other compartments. Surprisingly, although the position of the tibia was not changed by 'upper leg extension', also tibial bone density was influenced to a similar extent as in the lateral femur (lateral tibia: 0.38 mmAl and medial tibia: 0.29 mmAl per 5°).

Varying 'lower leg extension' resulted in a significant increase in lateral tibia bone density (0.29 mmAl per cm). No influence on the femur was observed, which is in line with the fact that the femur is not actually varied in position by changing the 'lower leg extension'. Varying 'internal rotation' resulted in a limited increase in bone density measurement in the lateral and medial femur and lateral tibia. This effect corroborates the bone density increase due to 'upper leg extension'. During radiographic procedures (closed chain movement due to fixed foot position) the femur rotates internally and medially (varus) at the last 30° of extension. Similarly, this effect fits the significant increase in bone density in the femur by variation in 'lateral shift upper leg'. Moreover, it supports relatively normal joint kinematics in the cadaver legs. Unexpectedly, but in accordance with 'upper leg extension' and 'internal rotation', 'lateral shift upper leg' induced a bone density increase in the lateral tibial compartment and also in the medial tibial compartment (Fig. 2(F)).

In general, the influence of systematic variation in positioning on bone density measurements was considered of minor clinical relevance since the changes due to systematic repositioning were all smaller than the differences in knees with radiographic progression (Table II). For lateral femur and tibia however, changes in bone density over 2 years in the knees with radiographic progression (1.46 and 1.33 mmAl in 2 years) were only twice that of the systematic variation induced by 1 cm lateral shift (0.79 and 0.73 mmAl, respectively). Surprisingly, when evaluating variation in lateral shift in vivo, the change was in the opposite direction but substantially smaller (−0.07 and −0.13 mmAl, respectively).

**Discussion**

Systematic variation in semiflexed knee joint positioning during image acquisition, and particularly in the extension angle, influenced the quantitative measurement of different radiographic parameters, using KIDA in this study. These clinically relevant changes were confirmed by *in vivo* evaluation. Several of these changes were relevant compared with the detected differences during 2-year follow-up in knees with radiographic OA progression early in the disease.

The clinical relevance of the influence of knee positioning on JSW measurement is confirmed by the commonly reported annual progression rate of joint space narrowing due to OA of around 0.2 mm. Specifically very early in the disease narrowing is probably even less, as shown by the difference of 0.29 mm for medial JSW during 2 years of follow-up, in knees with KL grade progression in the CHECK cohort. Even subtle variations in 'upper leg extension' (5°) and 'lower leg extension' (1 cm shift) influenced the medial JSW measurement with 0.07 mm in the cadaver legs and even 0.24 mm in vivo. Although the Buckland-Wright protocol aims at medial tibia plateau alignment, these changes were only slightly smaller than the 2-year differences in progressive radiographic OA. Less well known is the influence of positioning on lateral JSW and varus angle measurement. Clearly also these parameters are influenced by variations in knee extension (by 'lower' and 'upper leg extension') both in cadaver legs and in vivo. To improve the additional value of digital analyses this needs further attention, as JSW is a commonly applied outcome to evaluate radiographic knee OA.

As expected, the measurement of eminence height is only significantly influenced by 'lower leg extension'. From a mathematical point of view, only 'beam height' might have been of influence additionally. By varying the height of the X-ray beam the eminence height was expected to decrease when shifting up (+) but also when shifting down (−) compared with the standard position, which indeed occurred (data not shown). Although the role of the eminences in the OA process is argued, recent studies (in CHECK) have demonstrated clear progression in eminence height during follow-up (manuscript submitted) and a predictive value of this parameter for progression of disease (manuscript submitted).

In the cadaver legs and healthy volunteers osteophyte area was hardly present as a characteristic of OA. Irrespectively, small
changes in osteophyte area are considered to be of relevance since osteophyte formation is assumed to occur first when OA develops, as defined in the commonly used K&L grading. When separate features were measured, the formation of osteophytes was found to be important, e.g., in predicting incidence of radiographic OA (manuscript submitted) and in predicting phenotypes of radiographic knee OA progression (manuscript submitted). As for eminence height and JSW, specifically ‘lower leg extension’ influenced osteophyte area measurements. Although the 2-year difference in osteophyte area in knees with progressive radiographic OA exceeds the influence of 1 cm variation in positioning, this difference will be smaller than the change when a shift in positioning of 2 cm is applied.

The influence of variations in all components of knee position on bone density measurement is of interest. Although the effect was smaller than differences during 2-year follow-up in case of radiographic progression, this effect should not be underestimated. Slight variations in positioning may alter projection of compact bone areas which results in significant changes in bone density measurement. On the other hand, the observed changes may also be due to the use of digital image acquisition (in contrast to conventional film-screen acquisition) in which the appearance of the image is influenced by variable automated adjustments of contrast and noise. When the leg is positioned differently, this can influence the projected gray values of the bone and with that the post-processing.

It can be argued that the use of cadaver legs is not representative of clinical practice. Although the set-up was optimized by using a whole leg and a frame which aimed at fixation and similar weight-bearing in all radiographs, knee positioning might be hampered by e.g., the lack of muscle tension. The validation in vivo however, confirmed the observed changes. It should be noted though that only three cadaver joints were imaged and only one validation for each of the extreme variations in positioning was used. It is therefore of relevance to validate the data from the present study, to demonstrate that accurate positioning improves reliability of quantitative analysis of radiographs.

Since strict criteria were applied to distinguish between actual effects owing to systematic variations in knee positioning and random effects (β’s of three cadaver legs in same direction and two P < 0.10), the number of clinically relevant effects was limited. Additionally, the comparison with 2-year differences in an early OA cohort with clear radiographic progression in the knees might have underestimated the clinical relevance of the observed changes. In clinical studies radiographic progression is preferably evaluated already after 1 year, and not all individuals will progress in radiographic OA severity. As such, it is concluded that the presently identified position variations that influence radiographic analyses are the most relevant but probably not the only one. Moreover, in clinical practice the influence might actually be larger since, when a patient is positioned for a radiograph, a combination of small variations in different position components likely occurs instead of a variation in only one component.

Besides technical limitations, variations in knee positioning might be introduced by actual progression of pain or structural damage. Pain may result in limitations in knee movement, forcing different knee positioning during image acquisition. Also weight-bearing on the affected leg might be limited due to pain, which can influence the width of the projected joint space.

Clearly the influence of knee positioning exceeds the variation in the measurements using KIDA, since intra-observer variation was low with these measurements. As such, to benefit from this very robust analysis method, optimal attention of the technicians involved in image acquisition is needed. Although it needs to be evaluated, it is hypothesized that this is also the case for other (digital analysis) methods that quantitatively evaluate radiographic change. So presumably better, new techniques, like the use of molds might need to be developed to improve this standardization.

The present study demonstrates that variations in knee positioning, which can easily occur during acquisition in trials and clinical practice despite standardization, significantly influence the quantitative measurement of most separate radiographic characteristics of OA. Although the parameters measured by digital analysis are sufficiently robust, the surplus value of these quantitative measurements over qualitative grading will pay off only when standardization during image acquisition is improved. Since radiography remains cheap and easily accessible, it is considered of value to further improve standardization of acquisition.

Authors contributions

MK, KV, TH, RB, MV, AM, and FL contributed to conception and design of this study. MK, KV, and TH contributed to the analysis of data. MK, AM, PW, and FL contributed to the interpretation of data. Article drafts were written by MK and critically revised by all authors. The final version of the article was approved by all authors. MK takes responsibility for the integrity of the work as a whole (M.B.Kinds@umcutrecht.nl).

Conflict of interest

The authors declare that they have no conflicts of interest.

Acknowledgments

We acknowledge Willem van Wolferen from the department of anatomy of the University Medical Center Utrecht (UMCU) for his assistance with the preparation of the cadaver legs and the experimental set-up. We thank the healthy volunteers. We acknowledge the radiology department of the UMCU for their cooperation with the acquisition of the radiographs. And we thank Marja Lafeber (ML) for measurements of the radiographs using KIDA.

References


