Three-dimensional Analysis for Quantification of Knee Joint Space Width with Weight-bearing CT: Comparison with Non-weight-bearing CT and Weight-bearing Radiography

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Running title:

Weight-bearing 3D joint space analysis
Abstract

Objective:
To compare computer-based 3D-analysis for quantification of the femorotibial joint space width (JSW) using weight-bearing cone beam CT (WB-CT), non-weight-bearing multi-detector CT (NWB-CT), and weight-bearing conventional radiographs (WB-XR).

Design:
Twenty-six participants prospectively underwent NWB-CT, WB-CT, and WB-XR of the knee. For WB-CT and NWB-CT, the average and minimal JSW was quantified by 3D-analysis of the minimal distance of any point of the subchondral tibial bone surface and the femur. Associations with mechanical leg axes and osteoarthritis were evaluated. Minimal JSW of WB-CT was further compared to WB-XR. Two-tailed p-values of <0.05 were considered significant.

Results:
Significant differences existed of the average medial and lateral JSW between WB-CT and NWB-CT (medial: 4.7 vs. 5.1 mm [p=0.028], lateral: 6.3 vs. 6.8mm [p=0.008]). The minimal JSW on WB-XR (medial:3.1 mm, lateral:5.8 mm) were significantly wider compared to WB-CT and NWB-CT (both medial:1.8 mm, lateral:2.9 mm, all p<0.001), but not significantly different between WB-CT and NWB-CT (all p≥0.869). Significant differences between WB-CT and NWB-CT existed in participants with varus knee alignment for the average and the minimal medial JSW (p=0.004 and p=0.011) and for participants with valgus alignment for the average lateral JSW (p=0.013). On WB-CT, 25% of the femorotibial compartments showed bone-on-bone apposition, which was significantly higher when compared to NWB-CT (10%,p=0.008) and WB-XR (8%,p=0.012).
Conclusion:

Combining WB-CT with 3D-based assessment allows detailed quantification of the femorotibial joint space and the effect of knee alignment on JSW. WB-CT demonstrates significantly more bone-on-bone appositions, which are underestimated or even undetectable on NWB-CT and WB-XR.

Keywords

Cone-Beam Computed Tomography

Weight-Bearing

Knee Joint

Osteoarthritis

3-D Imaging

Running headline

Weight-bearing 3D joint space analysis
Introduction

Computed tomography (CT) enables three-dimensional visualization of the osseous structures of the knee joint. Similar to conventional radiography, the presence of subchondral bone cysts, subchondral sclerosis, and osteophyte formations on computed tomography (CT) can suggest cartilage loss, joint degeneration, and osteoarthritis. Joint space narrowing is the fourth classical characteristic of knee joint degeneration. On standard supine multi-detector CT examinations without weight-bearing, however, the extent of joint space width can be underestimated and give a false impression of preserved articular cartilage. Instead, weight-bearing conventional radiographs are commonly performed to assess the degree of joint space narrowing, which is an integral feature of the Kellgren-Lawrence classification system for osteoarthritis. In this regard, reduced JSW is considered an indirect marker of articular cartilage damage. However, also meniscus damage can result in reduced JSW, and measurements on conventional radiographs strongly depend on beam angulations and knee flexion impeding precise assessments, which both may contribute to false conclusions about articular cartilage integrity-based JSW on conventional radiographs. Nevertheless, deceleration of joint space narrowing on conventional radiographs is the only structural endpoint approved by the US Food and Drug Administration to demonstrate the efficacy of disease-modifying osteoarthritis drugs in phase 3 clinical trials.

The introduction of cone-beam CT systems permits upright weight-bearing CT of the knee and ankle joints under physiological conditions. Previous studies have demonstrated that the knee and ankle joint alignments can change significantly between non-weight-bearing and weight-bearing examinations. In these studies, human readers manually quantified the minimal femorotibial joint space widths (JSW) on weight-bearing CT using single locations on single images. More recently, software-based three-dimensional (3D) analysis for
femorotibial JSW quantification have been published, aiding in a more comprehensive assessment of the femorotibial JSW, reducing inter-reader variations and permitting quantification of a variety of joint space parameters. To the best of our knowledge, however, 3D-based joint space assessments comparing weight-bearing and non-weight-bearing CT have not been performed so far, and a lack of knowledge about the value of the addition of weight-bearing to CT and in comparison to weight-bearing conventional radiographs exists.

We hypothesize that the femorotibial JSW on weight-bearing cone-beam CT differs significantly from femorotibial JSW measurements on non-weight-bearing multi-detector CT and weight-bearing radiographs. Therefore, the purpose of our study was to compare computer-based 3D-analysis for quantification of the femorotibial joint space using weight-bearing cone beam computed tomography, non-weight-bearing multi-detector CT, and weight-bearing conventional radiographs.

**Design**

**Participants**

All examinations were acquired during a previously conducted prospective study. Following institutional review board approval, informed consent has been obtained from all participants. A total of 26 participants were included. Inclusion criteria were clinical indication for CT of the knee joint, adult age, and willingness to participate in the study. Exclusion criteria were the inability to bear weight. All included participants were referred for computed tomography by board-certified orthopedic surgeons for the clinical work-up of knee disorders, which were due to osteoarthritis (17/26, 65%), avascular necrosis (4/26, 15%), after anterior cruciate ligament reconstruction (3/26, 12%), after fracture of the intercondylar eminence (1/26, 4%),
and palpable soft tissue abnormality (1/26, 4%). The mean age of the 26 included participants was 57 years (standard deviation [SD] ± 16 years, range 21 - 81 years), consisting of 15 women with a mean age of 59 years (SD ± 14, range 21-76 years) and 11 men with a mean age of 55 years (SD ±19, range 23 – 81).

Image acquisition

Non-weight-bearing CT (NWB-CT) was performed in supine patient position with fully extended knee joints on a clinical 64 slice CT scanner (Brilliance 64, Philips Healthcare, Best, Netherlands), with the following acquisition and reconstruction parameters: tube voltage 120 kV, tube current 150 mAs/slice, pitch factor 0.671, matrix 512 x 512, field-of-view: (16 – 18 cm)³, axial slice thickness 0.67 - 0.9 mm with an overlap of 50% (increment: 0.34 – 0.45 mm), reconstruction kernel: bone, CT dose index \( \text{vol} \) 12.1 mGy, dose length product 193.6 – 217.8 mGy*cm.

Weight-bearing CT (WB-CT) was performed on a clinical cone-beam CT extremity scanner (Verity, Planmed Oy, Helsinki, Finland). The participants were standing on one leg positioned inside the gantry and the other leg resting outside on top of the gantry. The knee joint was in full extension. Following acquisition and reconstruction parameters applied: tube voltage 96 kV, tube current 7.5 mAs, matrix 400 x 400, field-of-view 160 x 160 x 130 cm, voxel size 0.4 mm isotropic, axial slice thickness 0.4 mm, reconstruction kernel: bone, CT dose index \( \text{vol} \) 4.3 mGy, dose length product 55.9 mGy*cm.

Weight-bearing conventional radiography (WB-XR) of the knee joint was performed in full extension in anteroposterior direction with a film-to-focus distance of 1.5 m, 63 kVp, and automated control of the exposure time. The direction of the central x-ray beam was strictly horizontal and centered on the patellar apex. Technical quality characteristics include a
symmetrical presentation of the femoral notch with symmetrical medial and lateral condyles, a partially superimposed fibula head by the lateral tibial condyle, and a streak-like appearance of the lateral tibial plateau. Collimation included the distal femur and proximal tibia, as well as the medial and lateral skin margins.

**Joint space analysis**

On NWB-CT and WB-CT images, the medial and lateral femorotibial joint spaces were separately analyzed using dedicated segmentation and measurement software (Mimics Innovation Suite and 3-Matic, Materialise NV, Leuven, Belgium). Using thresholding and region growing functions, segmentation of the proximal tibia and the distal femur was performed separately. Light smoothing was performed (iterations 6, smoothing factor 1, method: first-order Laplacian smoothing, “compensation” set on “ON”). The area of the mineralized subchondral bone surface of the medial and lateral tibial plateau was identified and manually segmented. The subchondral bone surfaces of the tibial plateau are usually identified by their smooth contour and surrounded by a small limbus, which marks the outer border (besides at the region of the tibial spines). The upper turning point of the limbus was defined to represent the outer border of the segmentation circumferentially. The articular portions of the medial and lateral part extending to the tibial spines were included in the analysis since they are also covered with articular cartilage and therefore are also part of the subchondral bone surface.

The software package allows assessing the minimal distance of any point of the segmented subchondral bone surfaces to the distal femur. In short, for every point on the fixed entity (the subchondral bone surface), the Euclidian distance to any point of the target entity (distal femur) is calculated, which includes thousands of operations for any point on a complex mesh. Once the nearest point is found, the distance between the selected point of the fixed entity to the nearest point of the target entity is measured. The average JSW is the mean of all
minimal distances of any point of the subchondral bone surface, and the minimal JSW is the
lowest value of all minimal distances of any points of the subchondral bone surface.
Furthermore, these quantifications were represented by color-coded maps, indicating the
minimal distance of any point on the medial and lateral subchondral bone surface to the femur
by a spectrum of colors (Fig. 1, Fig. 2). The entire process of segmentation and joint space
analysis took between 5 minutes and 30 minutes.
Grading of osteoarthritis of the knee joint was assessed in all participants on anteroposterior,
standing, weight-bearing conventional knee radiographs in full extension according to the
classification system of Kellgren and Lawrence (KL) for osteoarthritis. The radiographs were
available in our picture archiving and communication system (PACS) for all participants and
performed within three months before NWB-CT and WB-CT. Only one knee per participant
was included in the study. In total, KL grade 0 was present in 1/26 (4%), grade 1 in 2/26 (8%),
grade 2 in 10/26 (39%), grade 3 in 5/26 (19%), and grade 4 in 8/26 (32%) participants.
Osteoarthritis was further categorized into “none/low-grade osteoarthritis” (KL grade 0 to 2,
13/26 (50%) participants) and “high-grade osteoarthritis” (KL grade 3 and 4, 13/26 (50%)
participants). For practical purposes, bone-on-bone apposition was defined as a distance of
less than 0.4 mm between the femoral condyle and the tibial plateau due to the voxel size of
the WB-CT and visual inspection and correlation. In this context, 0.4 mm is considered to
represent the detection limit of this 3D approach for quantitative JSW analysis.
Twentytwo of 26 (85%) participants underwent additional anteroposterior weight-bearing
full-length leg radiographs performed on a biplanar whole-body scanner (EOS imaging system,
EOS imaging Inc., Paris, France), which were evaluated for mechanical leg axis
determination. The four participants (three participants with KL grade 2, one participant with
KL grade 1) without full-length leg radiographs were excluded from the subgroup analysis. The
mechanical leg axis was defined as the angle between the line from the center of the femoral head to the center of the intercondylar notch and the line from the center of the tibial eminence to the tibiotalar joint center. Varus and valgus knee deformities were defined as an angle of more than 3 degrees of the mechanical leg axis in its respective direction, which were present in 12/22 (55%) (KL grade 0 in one, KL grade 2 in three, KL grade 3 in two, and KL grade 4 in six participants) and 10/22 (45%) participants (KL grade 1 in one, KL grade 2 in four, KL grade 3 in three, and KL grade 4 in two participants), respectively.

A fellowship-trained musculoskeletal radiologist performed mechanical leg axis measurements. Grading of knee osteoarthritis was performed, according to Kellgren and Lawrence, by two fellowship-trained musculoskeletal radiologists independently. Disagreements were resolved by subsequent consensus. Two fellowship-trained musculoskeletal radiologists manually measured the minimal medial and lateral femorotibial JSW on WB-XR independently with caliper measurements of the minimal osseous distance between the tibial plateau and femoral condyle. Owing to an excellent inter-reader agreement, the measurements of reader one were randomly chosen.

Furthermore, to assess inter-reader agreement (reproducibility) of minimal and average JSW measurements on WB- and NWB-CT, two fellowship-trained musculoskeletal radiologists (Reader 1: three years experience of bone segmentation and Reader 2: seven years experience of bone segmentation) independently performed all assessments, including bone segmentation and definition of the mineralized subchondral bone surface of the medial and lateral tibial plateau. Results of Reader 1 were also chosen for further analysis and results presentation. All measurements and evaluations were performed on anonymized data sets.
Statistics
Statistical analysis was performed using SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY) and MedCalc version 17.6 (MedCalc Software bvba, Ostend, Belgium). Descriptive statistics were applied. Continuous data are presented with means and standard deviations and categorical data as proportions. Normal distribution was assessed with the Kolmogorov-Smirnoff test. The Wilcoxon signed-rank test and McNemar tests were used to compare joint space parameters of WB-CT, NWB-CT, and WB-XR. Analysis of inter-reader agreement of average and minimal JSW analysis on WB- and NWB-CT was performed using Bland-Altman analyses with limits of agreement method (LoA) and the intraclass correlation coefficient (ICC, absolute agreement, average measures). Inter-reader agreement for minimal femorotibial JSW on WB-XR was calculated with the ICC. Inter-reader agreement for KL-based osteoarthritis grading was calculated with Cohen’s weighted kappa. Kappa-values were interpreted according to Landis and Koch. ICC-values larger 0.9 were considered to represent excellent agreement. Effect size calculation were performed with Pearson’s r (z/N) and interpreted as |0.1| - |0.3| = small, |0.3| - |0.5| = medium, and > |0.5| large effect. Statistical comparison of relative differences of JSW between WB-CT and NWB-CT versus no change was performed with the one-sample t-test. A two-tailed p-value of less than 0.05 was considered to represent significant differences.

Results
Average joint space width
Table 1 presents the average JSW of the medial and lateral femorotibial compartments of the WB-CT and NWB-CT. The average JSW of the medial (p = 0.028, effect size: -0.431) and lateral (p = 0.008, effect size: -0.518) joint space was significantly lower on WB-CT (medial: 4.7 mm ± 1.5 [standard deviation], lateral: 6.3 mm ± 2.0) than on NWB-CT (medial 5.1 mm ± 1.2, lateral:
6.8 mm ± 1.7) (Fig. 3, Fig. 4). Compared to NWB-CT, WB-CT showed in 9% a lower JSW in the medial and 11% a lower JSW in the lateral compartment.

This difference changed substantially with respect to the leg axis: In the subgroup of participants with varus leg axis, the average JSW of the medial compartment decreased significantly by 21% from NWB-CT to WB-CT (3.7 mm ± 1.3 vs. 4.7 mm ± 1.7, p = 0.004, effect size: -0.805). In participants with valgus leg axis, the average JSW of the lateral compartment decreased significantly by 11% from NWB-CT to WB-CT (5.7 mm ± 2.5 vs. 6.5 mm ± 2.1, p = 0.013, effect size: -0.693) (table 1).

**Minimal joint space width**

Table 2 presents the minimal JSW of WB-CT, NWB-CT, and WB-XR. The minimal JSW of WB-CT was significantly lower in comparison to WB-XR with 1.8 mm ± 1.5 vs. 3.1 mm ± 2.0 (p < 0.001, effect size: -0.706) for the medial compartment and 2.9 mm ± 1.8 vs. 5.8 mm ± 2.1 (p < 0.001, effect size: -0.869) for the lateral compartment. In contrast, no significant differences were present for the medial (1.8 mm ± 1.5 vs. 1.8 mm ± 1.1, p = 0.989, effect size: -0.003) and lateral 2.9 mm ± 1.8 vs. 2.9 mm ± 1.5 (p = 0.869, effect size: -0.031) minimal JSW between WB-CT and NWB-CT.

Table 2 also shows the minimal JSW for WB-CT, NWB-CT, and WB-XR with regards to the leg axis. On WB-CT, the minimal JSW of the medial compartment was significantly lower compared to NWB-CT in participants with varus leg axis with 0.9 mm ± 1.2 vs. 1.5 mm ± 1.0 (p = 0.011, effect size: -0.703). Compared to WB-XR, the minimal JSW of WB-CT was significantly lower for the medial (0.9 mm ± 1.2 vs. 2.2 mm ± 1.4, p = 0.004, effect size: -0.790) and lateral (2.9 mm ± 1.6 vs. 6.2 mm ± 2.2, p = 0.003, effect size: -0.827) compartment in participants with varus leg axis, and also for the lateral compartment in participants with valgus leg axis.
(2.6 mm ± 2.3 vs. 5.5 mm ± 2.2, p = 0.005, effect size: -0.777). For all other comparisons, no significant differences existed (all p > 0.086).

Table 3 presents the proportions of compartments with a total loss of the JSW with bone-on-bone apposition and a highly reduced JSW of less than 1 mm for the entire patient cohort, the subgroup with none/low-grade osteoarthritis, and the subgroup of high-grade osteoarthritis.

For the entire patient cohort and patients with high-grade osteoarthritis, significantly more femorotibial compartments demonstrated bone-on-bone apposition on WB-CT in comparison with NWB-CT (25% vs. 10% [p = 0.008] and 46% vs. 19% [0.016] respectively) and WB-XR (25% vs. 8% [p = 0.012] and 46% vs. 15% [0.021], respectively). Similarly, for the entire patient cohort and patients with high-grade osteoarthritis, significantly more femorotibial compartments demonstrated a highly reduced JSW of less than 1 mm on WB-CT compared to NWB-CT (both p = 0.016) and WB-XR (p = 0.001 and 0.002, respectively). For the subgroup of patients with none/low-grade osteoarthritis, no significant differences existed for any comparison (all p = 1). Furthermore, no significant differences existed between NWB-CT and WB-XR comparisons for total joint space loss and reduction of JSW of less than 1 mm (all p > 0.109).

For radiographic measurements of the minimal femorotibial JSW on WB-XR, the inter-reader agreement between both readers was 0.993 (95% confidence interval: 0.985 to 0.997) for the medial, and 0.988 (95% confidence interval: 0.973 to 0.995) for the lateral compartment.

Joint space widths and osteoarthritis grade

Table 4 shows the average and minimal JSW of WB-CT and NWB-CT for participants with high-grade and none/low-grade osteoarthritis. For participants with high-grade osteoarthritis, the average JSW of the lateral compartment was significantly lower on WB-CT than NWB-CT (5.9
mm ± 2.4 vs. 6.6 mm ± 2.0, p = 0.016, effect size: -0.669) but not on the medial compartment (3.7 mm ± 1.4 vs. 4.4 mm ± 1.1, p = 0.075, effect size: -0.494). No significant differences existed for the minimal JSW between NWB-CT and WB-CT for participants with high-grade osteoarthritis (both p ≥ 0.248). For participants with none/low-grade osteoarthritis, no significant differences in average or minimal JSW existed between NWB-CT and WB-CT (all p ≥ 0.073).

Figure 5 demonstrates the box plots of relative changes in the percentage of the average femorotibial JSW between NWB-CT and WB-CT for the medial and lateral compartments. For the entire subgroup of participants with high-grade osteoarthritis, the range of relative JSW changes were wider (mean: 86% ± 21%; range: 38% – 121%) in comparison to participants with none/low-grade osteoarthritis (mean: 96% ± 10%; range: 73% – 114%). For both the medial and lateral compartment, the relative change was significantly different versus a hypothesis of no change in patients with high-grade osteoarthritis (p = 0.031 and p = 0.032, respectively), but not in patients with none/low-grade osteoarthritis (p = 0.248 and 0.104, respectively).

The inter-reader agreement for KL-based osteoarthritis grading was very good (kappa: 0.82; 95% confidence interval: 0.71 to 0.94).

**Inter-reader agreement of WB- and NWB-CT assessments**

Results of Bland-Altman analysis and ICC calculations for demonstration of inter-reader agreement for WB- and NWB-CT assessments are given in table 5 and supplementary table 1 and 2.

For the average JSW measurement of the entire patient cohort and the medial compartment, the mean difference (bias) was -0.06 mm for WB-CT and 0.02 mm for NWB-CT. The LoA were
±0.35 mm for WB-CT and ±0.52 mm for NWB-CT. Similar values were found for the lateral compartment of the entire patient cohort with a mean difference of -0.06 mm and LoA of ±0.49 mm for WB-CT, and 0.04 mm and LoA of ±0.5 mm for NWB-CT (table 5). Subgroup analysis of patients with high-grade OA and none/low-grade OA revealed similar numbers for average JSW assessment for both compartments on WB-CT and NWB-CT (supplementary table 1).

For the minimal JSW measurement of the entire patient cohort and the medial compartment, Bland-Altman analysis showed a mean difference of 0.0 mm with LoA of ±0.26 mm for WB-CT, and -0.01 mm with LoA of ±0.11 mm for NWB-CT. Similar values were found for the lateral compartment of the entire patient cohort with a mean difference of 0.0 mm and LoA of ±0.05 mm for WB-CT, and 0.0 mm and LoA of ±0.1 mm for NWB-CT (table 5). Subgroup analysis of patients with high-grade OA and none/low-grade OA revealed similar numbers for minimal JSW assessment for both compartments on WB-CT and NWB-CT (supplementary table 2).

The ICC between both readers showed excellent agreements for WB-CT and NWB-CT for both compartments and all patient groups with values ≥ 0.975 for all assessments (table 5 and supplementary table 1 and 2).

**Discussion**

We compared a 3D analysis for femorotibial JSW quantification using WB-CT compared to NWB-CT and WB-XR. We found that the average and minimal femorotibial JSW can differ significantly between WB-CT, NWB-CT, and WB-XR. WB-CT identified significantly more joint space reductions and bone-on-bone apposition, which were underestimated or not detected by NWB-CT and WB-XR.
A major finding of this study was the significantly higher number of participants demonstrating a total loss of JSW with bone-on-bone apposition on WB-CT compared to NWB-CT and WB-XR. Bone-on-bone apposition indicates high-grade or full-thickness opposing cartilage loss and often supports an indication for joint replacement, which may not be detected with NWB-CT and WB-XR in a relevant number of patients. To date, however, WB-XR is the established method of choice for joint space evaluation, even though limitations of detection of early osteoarthritis are well known. A potential limiting factor of our study results is the performance of WB-XR in full extension, which is considered to be inferior to semi-flexed WB-XR for JSW analysis in patients with high-grade osteoarthritis and also to a lower extent in patients with none/low-grade osteoarthritis. This may have influenced the detection of bone-on-bone apposition in our study, which can be referred to a restricted joint space visualizations compared to the also in full leg extension performed WB-CT. Since WB-CT also detected significantly more compartments with bone-on-bone apposition than NWB-CT, this indicates the necessity of combining CT with weight-bearing to gather the precise extent of joint space reduction on examinations performed in full leg extension. Replacing WB-XR with WB-CT in a clinical setting could prevent underestimating high-grade osteoarthritis and may prevent underuse or delayed total knee replacement and concomitant disabilities and chronic diseases. However, the lower cost, higher availability, and lower radiation dose are advantages of WB-XR that require careful consideration when using WB-CT.

A 3D approach for assessing the minimal JSW of the medial femorotibial compartment on WB-CT compared to WB-XR was already evaluated in a former study. On 35 knee examinations, an underestimation of about 2 mm of the minimal medial JSW on WB-XR compared to WB-CT was found. In our study, the minimal JSW of the medial compartment was significantly lower by 1.4 mm on WB-CT compared to WB-XR. A relevant difference between both studies is the
level of knee flexion during examinations, which limits comparability. All examinations were performed in full knee extension in our study, while the published study performed examinations in knee flexion of 15 – 30°.

Besides the minimal JSW, also the average JSW can demonstrate significant differences between WB-CT and NWB-CT. The assessment of the average JSW represents a second quantification parameter of the femorotibial JSW, which is the average of the minimal femorotibial distances of each voxel of the subchondral bone surface of the tibial plateau. Combining the 3D software-based joint space evaluation and standing WB-CT allows characterization and quantification of the femorotibial joint space under physiological conditions, permitting comprehensive joint space analysis, which NWB-CT or WB-XR cannot achieve.

MRI is often the preferred method for the non-invasive assessment of cartilage integrity. However, patients with contraindications, claustrophobia, or inability to sustain the longer acquisition times may not undergo MRI. In addition, access to MRI is limited in many regions worldwide, and MRI is more expensive than CT. CT arthrography provides an alternative for assessing the surface and thickness of the joint cartilage, overcoming many of the limitations of MRI. However, the invasive nature and the associated risk of infection, bleeding and allergic reactions, prolonged procedure time, and pain of CT-arthrography are drawbacks that require careful consideration.

Furthermore, the intraarticular high-density contrast media impedes Hounsfield unit-based automated bone segmentation and may hamper the suitability of this technique for custom-made implant design or 3D visualization based on volume rendering technique. In addition, native NWB-CT is already often part of the work-up of severe osteoarthritis to assess osseous
anatomy, quality of bone stock, and planning of surgery. Therefore, WB-CT may offer an alternative for this patient group combining more accurate cartilage assessment and the traditional advantages of native CT for bone assessment. A study published in 2016 performed medial femorotibial 3D-based JSW-assessments on WB-CT compared to MRI. In this study, a greater surface area with reduced JSW on WB-CT correlated well with medial tibial cartilage damage on MRI, underlining the potential of 3D-based femorotibial JSW assessments on WB-CT as a surrogate marker for cartilage integrity.

Our results show that the mechanical leg axis should be taken into consideration on an individual basis. Varus leg axis reduces the medial JSW and increases the average lateral JSW, whereas the opposite is true for knees with valgus leg axis. Consequently, the average JSW of the entire study cohort was different from the groups of varus and valgus leg axis. This is also a common finding on WB-XR and applies in the same manner to femorotibial joint space assessments with WB-CT.

To the best of our knowledge, this is the first study performing 3D-analyses of the joint space for comparison of the femorotibial JSW of WB-CT and NWB-CT. However, a recent study performed a 3D approach of the foot and ankle for comparison of geometric measurements between WB-CT and NWB-CT. The authors concluded that automated 3D analyses are more precise and reproducible than 2D assessments and better identify differences in bone configurations between WB-CT and NWB-CT. Furthermore, the femorotibial JSW has been compared previously with manual two-dimensional measurements obtained from a single image at a single position. Manual measurements may be prone to higher inter-reader variability and only permit the assessment of the minimal femorotibial JSW, whereas an automated, software-based 3D approach for JSW quantification may minimize the individual influence on the assessments and offers the possibility for quantification of the average JSW.
The here presented three-dimensional approach for JSW quantification demonstrated a high inter-reader agreement for all measurements. The performed Bland-Altman analysis demonstrated mean differences close to zero and LoA ranging from ±0.4 to ±0.6 mm for average JSW measurements and of ±0.1 to ±0.3 mm for minimal joint space measurements. These numbers suggest a high reproducibility of these JSW analysis techniques and compare well to a previous publication on a similar topic, which however differed in their technical approach\textsuperscript{20}. Still, both studies underline the reproducibility and high accuracy of software-supported 3D-approaches for JSW quantification based on CT data.

While automated, software-based, 3D quantification can overcome reader-related variations in measurements, preparing the data set for automated analysis is more time-consuming. Two-dimensional measurements can be made within a few seconds, whereas the software-based 3D analysis requires segmentation of the femur and tibia and the definition of the tibial subchondral bone surfaces. In our study, the entire analysis could be achieved in as fast as five minutes; however, it also required up to 30 minutes in some patients. These variations were induced by the bone segmentation process, which was the most time-consuming analysis factor. In particular, inferior image quality with increased image noise and artifacts may require manual correction and prolongate segmentation time. Automated segmentation algorithms with optional support of artificial intelligence may aid in accelerating this process in the future.

Our study has limitations. First, the inclusion criteria were based on indications for NWB-CT of the knee, which was not exclusive for suspected osteoarthritis. Although not all participants were examined due to clinically suspected cartilage loss, we believe the prevalence of osteoarthritis was sufficient in our cohort to evaluate the difference in JSW between the three modalities. Second, full-length leg radiographs of the entire lower extremity were only
available for 22/26 (85%) participants, which limited evaluation of the association between JSW and leg axis to a subset of participants. Third, our knee radiography series included anteroposterior views in full extension, which is the standard technique in our institution. However, flexed posteroanterior views may also be included, which can also visualize joint space reduction related to posterior femorotibial cartilage space loss that may escape detection on anteroposterior views [34]. Fourth, WB-CT was not performed on a physiological bipedal stance but with the examined leg inside the scanner gantry and the contralateral leg placed on top of the scanner housing in a kneeling position. Even though some weight is placed on the contralateral leg, this may differ from a physiological bipedal stance and may have influenced comparisons to conventional radiographs in bipedal stance.

In conclusion, combining WB-CT with 3D-based assessment allows detailed quantification of the femorotibial joint space and the effect of knee alignment on JSW. WB-CT demonstrates significantly more bone-on-bone appositions, which are underestimated or even undetectable on NWB-CT and WB-XR.

Author contributions

Fritz, Benjamin: Conception and design, analysis and interpretation of the data, drafting of the article, critical revision of the article for important intellectual content, final approval of the article, statistical expertise, collection and assembly of data.

Fritz, Jan: Analysis and interpretation of the data, critical revision of the article for important intellectual content, final approval of the article, collection and assembly of data.

Fucentese, Sandro F: conception and design, critical revision of the article for important intellectual content, final approval of the article.
Pfirrmann, Christian W A: Conception and design, critical revision of the article for important intellectual content, final approval of the article, administrative, technical, or logistic support, collection and assembly of data

Sutter, Reto: Conception and design, analysis and interpretation of the data, critical revision of the article for important intellectual content, final approval of the article, administrative, technical, or logistic support.

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Siemens AG, GE, QED, BTG, IBL, Synthetic MR, Boston Scientific Mirata Pharma

Fucentese, Sandro F: Consultant for Medacta International SA

Pfirrmann, Christian W A: Nothing to disclose

Sutter, Reto: Nothing to disclose
References


Figure legends

Fig. 1: Non-weight-bearing (A) and weight-bearing (B) CT of the right knee joint in a 64-year-old woman with osteoarthritis. The left (coronal) and middle (sagittal) images demonstrate joint space narrowing of the medial compartment with a minimal joint space width of 1.0 mm on non-weight-bearing CT and a sizeable area of bone-on-bone apposition on weight-bearing CT (minimal joint space width: 0 mm) (arrows). The right column demonstrates the color-coded joint space width quantifications projected onto the medial and lateral tibial surfaces. Yellow and green colors indicate higher grade joint space narrowing of about 1 mm and less, which involves a substantially larger area on weight-bearing CT than on non-weight-bearing CT. The average joint space width of the medial compartment was 4.7 mm on non-weight-bearing CT and 2.8 mm on weight-bearing CT.

Fig. 2: Non-weight-bearing (A) and weight-bearing (B) CT of the left knee joint of a 76-year-old woman with osteoarthritis (Kellgren-Lawrence grade 4). The sagittal images (left column) demonstrate joint space narrowing of the lateral compartment (arrows), which is much narrower on weight-bearing CT than non-weight-bearing CT. The right column images demonstrate quantification of the joint space width with color-coding, projected onto medial and lateral tibial articulation of the plateau. Green and yellow colors indicate high-grade joint space narrowing of about 1mm and less, which involves a substantially larger area on weight-bearing CT than on non-weight-bearing CT.

Fig. 3: 76-year-old woman with medial joint line pain of the right knee. Anteroposterior weight-bearing radiograph (A) shows osteoarthritis of the medial compartment with joint space narrowing, osteophyte formations, and subchondral sclerosis (Kellgren-Lawrence grade 2). (B) Non-weight-bearing CT shows a mildly reduced medial femorotibial joint space (black arrows) (average joint space width: 3.1 mm; minimum joint space width: 1.6 mm), which is similar to the weight-bearing CT (C) (average joint space width: 3.3 mm; minimum joint space width: 1.5 mm), indicating partial
preservation of cartilage. The osteophytes of the intercondylar region do not demonstrate osseous contact (hollow arrows).

Fig. 4: 65-year-old man with medial joint line pain of the left knee joint. Anteroposterior weight-bearing radiograph (A) shows advanced osteoarthritis of the medial compartment with mild joint space narrowing, osteophytes, subchondral sclerosis, and bony deformity (Kellgren-Lawrence grade 3). Non-weight-bearing CT (B) shows preserved joint space width of the medial femorotibial joint space (arrow in B) (average joint space width: 6 mm; minimum joint space width: 2.4 mm). In contrast, weight-bearing CT (C) shows bone-on-bone apposition in the medial compartment (black arrow in C) due to full-thickness cartilage loss (average joint space width: 2.7 mm; minimum joint space width: 0 mm).

Fig. 5: Box plots presenting difference of the average femorotibial joint space width in percentage between non-weight-bearing and weight-bearing CT for the medial (light grey) and the lateral compartment (dark grey). The ranges of the relative joint space width change were wider for the subgroup of participants with high-grade osteoarthritis in comparison to participants with low grade osteoarthritis. For both, the medial and lateral compartment, the relative change was significantly different versus a hypothesis of no change in patient with high-grade osteoarthritis (p = 0.031 and p = 0.032, respectively), but not in patients with none/low-grade osteoarthritis (p = 0.248 and p = 0.104, respectively).
Tables

Table 1: Average joint space width

JSW = joint space width, WB-CT = weight-bearing CT, NWB-CT = Non-weight-bearing CT, SD = standard deviation. P-values were calculated using the Wilcoxon signed-rank test. Bold font indicates significant p-values.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Compartment</th>
<th>Average JSW WB-CT (SD)</th>
<th>Average JSW NWB-CT (SD)</th>
<th>P-value</th>
<th>Effect size r</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants</td>
<td>Medial</td>
<td>4.7 mm (1.5)</td>
<td>5.1 mm (1.2)</td>
<td>0.028</td>
<td>-0.431</td>
</tr>
<tr>
<td></td>
<td>Lateral</td>
<td>6.3 mm (2.0)</td>
<td>6.8 mm (1.7)</td>
<td>0.008</td>
<td>-0.518</td>
</tr>
<tr>
<td>Varus leg axis</td>
<td>Medial</td>
<td>3.7 mm (1.3)</td>
<td>4.7 mm (1.7)</td>
<td>0.004</td>
<td>-0.805</td>
</tr>
<tr>
<td></td>
<td>Lateral</td>
<td>6.5 mm (1.7)</td>
<td>6.8 mm (1.4)</td>
<td>0.308</td>
<td>-0.283</td>
</tr>
<tr>
<td>Valgus leg axis</td>
<td>Medial</td>
<td>5.4 mm (1.1)</td>
<td>5.2 mm (0.8)</td>
<td>0.241</td>
<td>-0.325</td>
</tr>
<tr>
<td></td>
<td>Lateral</td>
<td>5.7 mm (2.5)</td>
<td>6.5 mm (2.1)</td>
<td>0.013</td>
<td>-0.693</td>
</tr>
</tbody>
</table>
Table 2: Minimal joint space widths

JSW = joint space width, WB-CT = weight-bearing CT, NWB-CT = Non-weight-bearing CT, WB-XR = weight-bearing radiographs. SD = standard deviation. P-values were calculated using the Wilcoxon signed-rank test. Bold font indicates significant p-values.

<table>
<thead>
<tr>
<th></th>
<th>Minimal JSW WB-CT (SD)</th>
<th>Minimal JSW NWB-CT (SD)</th>
<th>Minimal JSW WB-XR (SD)</th>
<th>P-value</th>
<th>P-value [Effect size r]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All participants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial</td>
<td>1.8 mm (1.5)</td>
<td>1.8 mm (1.1)</td>
<td>3.1 mm (2.0)</td>
<td>0.989</td>
<td>&lt;0.001 [-0.003] [-0.706]</td>
</tr>
<tr>
<td>Lateral</td>
<td>2.9 mm (1.8)</td>
<td>2.9 mm (1.5)</td>
<td>5.8 mm (2.1)</td>
<td>0.869</td>
<td>&lt;0.001 [-0.032] [-0.869]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varus leg axis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial</td>
<td>0.9 mm (1.2)</td>
<td>1.5 mm (1.0)</td>
<td>2.2 mm (1.4)</td>
<td>0.011</td>
<td>0.004 [-0.703] [-0.790]</td>
</tr>
<tr>
<td>Lateral</td>
<td>2.9 mm (1.6)</td>
<td>2.7 mm (1.1)</td>
<td>6.2 mm (2.2)</td>
<td>0.480</td>
<td>0.003 [-0.196] [-0.827]</td>
</tr>
<tr>
<td>Valgus leg axis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial</td>
<td>2.1 mm (1.5)</td>
<td>1.8 mm (1.2)</td>
<td>3.6 mm (2.3)</td>
<td>0.086</td>
<td>0.086 [-0.476] [-0.476]</td>
</tr>
<tr>
<td>Lateral</td>
<td>2.6 mm (2.3)</td>
<td>2.9 mm (2.1)</td>
<td>5.5 mm (2.2)</td>
<td>0.114</td>
<td>0.005 [-0.438] [-0.777]</td>
</tr>
</tbody>
</table>
Table 3: Proportion of compartments with highly reduced joint space width

JSW = joint space width, WB-CT = weight-bearing CT, NWB-CT = Non-weight-bearing CT, WB-XR = weight-bearing radiographs. OA = osteoarthritis. P-values were calculated using the McNemar-test. Bold font indicates significant p-values.

<table>
<thead>
<tr>
<th></th>
<th>JSW</th>
<th>WB-CT</th>
<th>NWB-CT</th>
<th>WB-XR</th>
<th>P (WB-CT vs. NWB-CT)</th>
<th>P (WB-CT vs. WB-XR)</th>
<th>P (NWB-CT vs. WB-XR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALL patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone-on-bone apposition</td>
<td>13/52 (25%)</td>
<td>5/52 (10%)</td>
<td>4/52 (8%)</td>
<td></td>
<td>0.008</td>
<td>0.012</td>
<td>1</td>
</tr>
<tr>
<td>&lt; 1 mm</td>
<td>17/52 (33%)</td>
<td>10/52 (19%)</td>
<td>5/52 (10%)</td>
<td></td>
<td>0.016</td>
<td>0.001</td>
<td>0.109</td>
</tr>
<tr>
<td><strong>None/low-grade OA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone-on-bone apposition</td>
<td>1/26 (4%)</td>
<td>0/26 (0%)</td>
<td>0/26 (0%)</td>
<td></td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>&lt; 1 mm</td>
<td>1/26 (4%)</td>
<td>1/26 (4%)</td>
<td>0/26 (0%)</td>
<td></td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>High-grade OA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone-on-bone apposition</td>
<td>12/26 (46%)</td>
<td>5/26 (19%)</td>
<td>4/26 (15%)</td>
<td></td>
<td>0.016</td>
<td>0.021</td>
<td>1</td>
</tr>
<tr>
<td>&lt; 1 mm</td>
<td>16/26 (62%)</td>
<td>9/26 (35%)</td>
<td>4/26 (15%)</td>
<td></td>
<td>0.016</td>
<td>0.002</td>
<td>0.180</td>
</tr>
</tbody>
</table>
Table 4: Joint space width and osteoarthritis

WB-CT = weight-bearing CT, NWB-CT = Non-weight-bearing CT, SD = standard deviation. P-values comparing joint space widths between WB-CT and NWB-CT separate for participants with none/low-grade and high-grade osteoarthritis were calculated using the Wilcoxon signed-rank test. Bold font indicates significant p-values.

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Joint space width</th>
<th>None/low-grade osteoarthritis</th>
<th>High-grade osteoarthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WB-CT (SD)</td>
<td>NWB-CT (SD)</td>
<td>P-value</td>
</tr>
<tr>
<td>Minimal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial</td>
<td>2.9 (0.8)</td>
<td>2.6 (0.7)</td>
<td>0.073 [-0.431]</td>
</tr>
<tr>
<td>Average</td>
<td>5.7 (0.8)</td>
<td>5.8 (0.8)</td>
<td>0.173 [-0.378]</td>
</tr>
<tr>
<td>Lateral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimal</td>
<td>3.4 (1.2)</td>
<td>3.5 (1.1)</td>
<td>0.834 [-0.058]</td>
</tr>
<tr>
<td>Average</td>
<td>6.6 (1.6)</td>
<td>7.0 (1.4)</td>
<td>0.173 [-0.378]</td>
</tr>
</tbody>
</table>
Table 5: Bland-Altmann analysis and intraclass correlation coefficient of both readers for average and minimal joint space width assessments for the entire patient cohort

WB-CT = weight-bearing CT, NWB-CT = Non-weight-bearing CT; CI = confidence interval; LoA = limits of agreement; ICC = intraclass correlation coefficient.

<table>
<thead>
<tr>
<th>Joint space width</th>
<th>Compart ment</th>
<th>Mean difference (95% CI)</th>
<th>LoA</th>
<th>Lower LoA</th>
<th>Upper LoA</th>
<th>ICC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>medial</td>
<td>-0.06 mm (-0.13; 0.02)</td>
<td>0.35 mm</td>
<td>-0.41 mm (-0.54; -0.29)</td>
<td>0.3 mm (0.17; 0.42)</td>
<td>0.996 (0.991; 0.998)</td>
</tr>
<tr>
<td></td>
<td>NWB-CT</td>
<td>0.02 mm (-0.09; 0.13)</td>
<td>0.52 mm</td>
<td>-0.5 mm (-0.69; -0.32)</td>
<td>0.54 mm (0.36; 0.73)</td>
<td>0.988 (0.972; 0.994)</td>
</tr>
<tr>
<td></td>
<td>lateral</td>
<td>-0.06 mm (-0.16; 0.04)</td>
<td>0.49 mm</td>
<td>-0.55 mm (-0.73; -0.38)</td>
<td>0.43 mm (0.25; 0.6)</td>
<td>0.996 (0.991; 0.998)</td>
</tr>
<tr>
<td></td>
<td>NWB-CT</td>
<td>0.04 mm (-0.07; 0.14)</td>
<td>0.5 mm</td>
<td>-0.47 mm (-0.65; -0.29)</td>
<td>0.54 mm (0.36; 0.72)</td>
<td>0.994 (0.987; 0.997)</td>
</tr>
<tr>
<td></td>
<td>Minimal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>medial</td>
<td>0.00 mm (-0.05; 0.06)</td>
<td>0.26 mm</td>
<td>-0.26 mm (-0.35; -0.16)</td>
<td>0.26 mm (0.17; 0.36)</td>
<td>0.998 (0.996; 0.999)</td>
</tr>
<tr>
<td></td>
<td>NWB-CT</td>
<td>-0.01 mm (-0.03; 0.01)</td>
<td>0.11 mm</td>
<td>-0.12 mm (-0.16; -0.08)</td>
<td>0.1 mm (0.06; 0.14)</td>
<td>0.999 (0.999; 1)</td>
</tr>
<tr>
<td></td>
<td>lateral</td>
<td>-0.00 mm (-0.1; 0.01)</td>
<td>0.05 mm</td>
<td>-0.04 mm (-0.06; -0.03)</td>
<td>0.05 mm (0.03; 0.06)</td>
<td>1 (1; 1)</td>
</tr>
<tr>
<td></td>
<td>NWB-CT</td>
<td>0.00 mm (-0.02; 0.02)</td>
<td>0.1 mm</td>
<td>-0.1 mm (-0.14; -0.07)</td>
<td>0.1 mm (0.06; 0.13)</td>
<td>1 (0.999; 1)</td>
</tr>
</tbody>
</table>
Supplementary table 1: Bland-Altman analysis and intraclass correlation coefficient of both readers for average joint space width assessments for the subgroups with none/low-grade osteoarthritis and high-grade osteoarthritis

OA = osteoarthritis; WB-CT = weight-bearing CT, NWB-CT = Non-weight-bearing CT; CI = confidence interval; LoA = limits of agreement; ICC = intraclass correlation coefficient

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Compartment</th>
<th>Mean difference (95% CI)</th>
<th>LoA</th>
<th>Lower LoA</th>
<th>Upper LoA</th>
<th>ICC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None/Low-grade OA</td>
<td>medial</td>
<td>-0.03 mm (-0.15; 0.09)</td>
<td>0.39 mm</td>
<td>-0.41 mm (-0.62; -0.21)</td>
<td>0.36 mm (0.15; 0.57)</td>
<td>0.987 (0.957; 0.996)</td>
</tr>
<tr>
<td></td>
<td>NWB-CT</td>
<td>0.01 mm (-0.14; 0.18)</td>
<td>0.52 mm</td>
<td>-0.51 mm (-0.79; -0.22)</td>
<td>0.54 mm (0.25; 0.82)</td>
<td>0.975 (0.918; 0.992)</td>
</tr>
<tr>
<td></td>
<td>lateral</td>
<td>0.06 mm (-0.23; 0.11)</td>
<td>0.55 mm</td>
<td>-0.62 mm (-0.91; -0.32)</td>
<td>0.49 mm (0.19; 0.78)</td>
<td>0.993 (0.977 0.997)</td>
</tr>
<tr>
<td></td>
<td>NWB-CT</td>
<td>0.09 mm (-0.07; 0.24)</td>
<td>0.5 mm</td>
<td>-0.41 mm (-0.68; -0.14)</td>
<td>0.58 mm (0.31; 0.85)</td>
<td>0.991 (0.972; 0.997)</td>
</tr>
<tr>
<td>High-grade OA</td>
<td>medial</td>
<td>-0.09 mm (-0.19; 0.01)</td>
<td>0.33 mm</td>
<td>-0.42 mm (-0.59; -0.24)</td>
<td>0.24 mm (0.06; 0.41)</td>
<td>0.996 (0.984; 0.999)</td>
</tr>
<tr>
<td></td>
<td>NWB-CT</td>
<td>0.03 mm (-0.14; 0.19)</td>
<td>0.54 mm</td>
<td>-0.52 mm (-0.81; -0.22)</td>
<td>0.57 mm (0.27; 0.86)</td>
<td>0.985 (0.95; 0.995)</td>
</tr>
<tr>
<td></td>
<td>lateral</td>
<td>-0.06 mm (-0.19; 0.08)</td>
<td>0.44 mm</td>
<td>-0.5 mm (-0.74; -0.26)</td>
<td>0.39 mm (0.15; 0.63)</td>
<td>0.998 (0.993; 0.999)</td>
</tr>
<tr>
<td></td>
<td>NWB-CT</td>
<td>-0.01 mm (-0.17; 0.15)</td>
<td>0.51 mm</td>
<td>-0.53 mm (-0.8; -0.25)</td>
<td>0.51 mm (0.23; 0.79)</td>
<td>0.996 (0.986; 0.999)</td>
</tr>
</tbody>
</table>
Supplementary table 2: Bland-Altmann analysis and intraclass correlation coefficient of both readers for minimal joint space width assessments for the subgroups with none/low-grade osteoarthritis and high-grade osteoarthritis

OA = osteoarthritis; WB-CT = weight-bearing CT, NWB-CT = Non-weight-bearing CT; CI = confidence interval; LoA = limits of agreement; ICC = intraclass correlation coefficient

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Comparison</th>
<th>Mean difference (95% CI)</th>
<th>LoA</th>
<th>Lower LoA (95% CI)</th>
<th>Upper LoA (95% CI)</th>
<th>ICC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None/Low-grade OA</td>
<td>medial WB-CT</td>
<td>0.04 mm (-0.05; 0.14)</td>
<td>0.31 mm</td>
<td>-0.27 mm (-0.43; -0.1)</td>
<td>0.35 mm (0.19; 0.52)</td>
<td>0.991 (0.972; 0.997)</td>
</tr>
<tr>
<td></td>
<td>medial NWB-CT</td>
<td>-0.01 mm (-0.03; 0.01)</td>
<td>0.08 mm</td>
<td>-0.09 mm (-0.13; -0.05)</td>
<td>0.07 mm (0.02; 0.11)</td>
<td>0.999 (0.998; 1)</td>
</tr>
<tr>
<td></td>
<td>lateral WB-CT</td>
<td>0.00 mm (-0.02; 0.02)</td>
<td>0.06 mm</td>
<td>-0.06 mm (-0.09; -0.02)</td>
<td>0.07 mm (0.03; 0.1)</td>
<td>1 (1; 1)</td>
</tr>
<tr>
<td></td>
<td>lateral NWB-CT</td>
<td>-0.01 mm (-0.01; 0.04)</td>
<td>0.09 mm</td>
<td>-0.07 mm (-0.11; -0.02)</td>
<td>0.1 mm (0.06; 0.15)</td>
<td>1 (0.999; 1)</td>
</tr>
<tr>
<td>High-grade OA</td>
<td>medial WB-CT</td>
<td>-0.04 mm (-0.09; 0.02)</td>
<td>0.18 mm</td>
<td>-0.22 mm (-0.31; -0.12)</td>
<td>0.14 mm (0.04; 0.24)</td>
<td>0.999 (0.995; 1)</td>
</tr>
<tr>
<td></td>
<td>medial NWB-CT</td>
<td>-0.01 mm (-0.05; 0.04)</td>
<td>0.14 mm</td>
<td>-0.14 mm (-0.22; -0.07)</td>
<td>0.13 mm (0.06; 0.2)</td>
<td>0.999 (0.995; 1)</td>
</tr>
<tr>
<td></td>
<td>lateral WB-CT</td>
<td>-0.00 mm (-0.01; 0.00)</td>
<td>0.02 mm</td>
<td>-0.02 mm (-0.03; -0.01)</td>
<td>0.01 mm (0.01; 0.02)</td>
<td>1 (1; 1)</td>
</tr>
<tr>
<td></td>
<td>lateral NWB-CT</td>
<td>-0.02 mm (-0.05; 0.01)</td>
<td>0.1 mm</td>
<td>-0.12 mm (-0.18; -0.07)</td>
<td>0.08 mm (0.03; 0.14)</td>
<td>1 (0.999; 1)</td>
</tr>
</tbody>
</table>
Figures

Figure 1

Fig. 1: Non-weight-bearing (A) and weight-bearing (B) CT of the right knee joint in a 64-year-old woman with osteoarthritis. The left (coronal) and middle (sagittal) images demonstrate joint space narrowing of the medial compartment with a minimal joint space width of 1.0 mm on non-weight-bearing CT and a sizeable area of bone-on-bone apposition on weight-bearing CT (minimal joint space width: 0 mm) (arrows). The right column demonstrates the color-coded joint space width quantifications projected onto the medial and lateral tibial surfaces. Yellow and green colors indicate higher grade joint space narrowing of about 1 mm and less, which involves a substantially larger area on weight-bearing CT than on non-weight-bearing CT. The average joint space width of the medial compartment was 4.7 mm on non-weight-bearing CT and 2.8 mm on weight-bearing CT.
Figure 2

Fig. 2: Non-weight-bearing (A) and weight-bearing (B) CT of the left knee joint of a 76-year-old woman with osteoarthritis (Kellgren-Lawrence grade 4). The sagittal images (left column) demonstrate joint space narrowing of the lateral compartment (arrows), which is much narrower on weight-bearing CT than non-weight-bearing CT. The right column images demonstrate quantification of the joint space width with color-coding, projected onto medial and lateral tibial articulation of the plateau. Green and yellow colors indicate high-grade joint space narrowing of about 1mm and less, which involves a substantially larger area on weight-bearing CT than on non-weight-bearing CT.
Fig. 3: 76-year-old woman with medial joint line pain of the right knee. Anteroposterior weight-bearing radiograph (A) shows osteoarthritis of the medial compartment with joint space narrowing, osteophyte formations, and subchondral sclerosis (Kellgren-Lawrence grade 2). (B) Non-weight-bearing CT shows a mildly reduced medial femorotibial joint space (black arrows) (average joint space width: 3.1 mm; minimum joint space width: 1.6 mm), which is similar to the weight-bearing CT (C) (average joint space width: 3.3 mm; minimum joint space width: 1.5 mm), indicating partial preservation of cartilage. The osteophytes of the intercondylar region do not demonstrate osseous contact (hollow arrows).
Fig. 4: 65-year-old man with medial joint line pain of the left knee joint. Anteroposterior weight-bearing radiograph (A) shows advanced osteoarthritis of the medial compartment with mild joint space narrowing, osteophytes, subchondral sclerosis, and bony deformity (Kellgren-Lawrence grade 3). Non-weight-bearing CT (B) shows preserved joint space width of the medial femorotibial joint space (arrow in B) (average joint space width: 6 mm; minimum joint space width: 2.4 mm). In contrast, weight-bearing CT (C) shows bone-on-bone apposition in the medial compartment (black arrow in C) due to full-thickness cartilage loss (average joint space width: 2.7 mm; minimum joint space width: 0 mm).
Fig. 5: Box plots presenting difference of the average femorotibial joint space width in percentage between non-weight-bearing and weight-bearing CT for the medial (light grey) and the lateral compartment (dark grey). The ranges of the relative joint space width change were wider for the subgroup of participants with high-grade osteoarthritis in comparison to participants with low grade osteoarthritis. For both, the medial and lateral compartment, the relative change was significantly different versus a hypothesis of no change in patient with high-grade osteoarthritis ($p = 0.031$ and $p = 0.032$, respectively), but not in patients with none/low-grade osteoarthritis ($p = 0.248$ and $p = 0.104$, respectively).