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Digital X-ray radiogrammetry better identifies osteoarthritis patients with a low bone mineral density than quantitative ultrasound

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Abstract This study assessed the ability of quantitative ultrasound (QUS) and digital X-ray radiogrammetry (DXR) to identify osteopenia and osteoporosis in patients with knee osteoarthritis (OA). One hundred and sixty-one patients with painful knee OA (81 men, 80 women; age 62.6±9.2 years, range 40–82 years) were included in this cross-sectional study and underwent dual-energy X-ray absorptiometry (DXA) of both hips and the lumbar spine, QUS of the phalanges and calcanei of both hands and heels, and DXR using radiographs of both hands. Unpaired t-test, Mann-Whitney U test, ROC analysis and Spearman's rank correlation were used for comparisons and correlation of methods. Using DXA as the reference standard, we defined a low bone mineral density (BMD) as a T-score ≤ -1.0 at the lumbar spine or proximal femur. In contrast to phalangeal or calcaneal QUS, DXR was able to discriminate patients with a low BMD at the lumbar spine ($p<0.0001$) or hips ($p<0.0001$). ROC analysis showed that DXR had an acceptable predictive power in identifying OA patients a low hip BMD (sensitivity 70%, specificity 71%). Therefore, DXR used as a screening tool could help in identifying patients with knee OA for DXA.

Keywords Bone mineral density · Osteoarthritis · Quantitative ultrasound · Dual energy x-ray absorptiometry · Digital x-ray radiogrammetry

Introduction

Dual-energy X-ray absorptiometry (DXA), quantitative ultrasound (QUS) as measured in the phalanges and calcanei, and digital X-ray radiogrammetry (DXR) of the metacarpals are currently available to assess mineral content and structural properties of bone tissue. DXA is the standard tool to assess patients at risk of osteoporosis and fracture, such as postmenopausal women [1–3]. However, DXA is not an optimal tool for population screening because of limited availability and relatively high costs. Therefore, new techniques with peripheral

measurement sites to select high-risk individuals, who are more likely to benefit from bone mineral density (BMD) measurements by DXA, are under evaluation.

Previous studies have shown that QUS at the calcaneus can predict hip fracture risk in elderly women over 65 years of age and that there is a good relationship between calcaneal broadband ultrasound attenuation (BUA) and incident vertebral fracture and between amplitude-dependent speed of sound (AD-SOS) as measured at the finger phalanges and non-vertebral fractures [3–9]. Furthermore, it has been shown that DXR, as measured at the metacarpals, is able to predict fracture risk at the wrist, spine, and hip in elderly women with a similar exactness as lumbar spine BMD measurements [10]. Recently, many studies have revealed the use of DXR in clinical practice, particularly with respect to rheumatoid arthritis, in the field of paediatrics and for prediction of fracture risk in osteoporosis [11–15].

However, most studies focused on patient populations with a high prevalence of osteoporosis. In contrast, a lower incidence for osteoporosis has been observed in patients with osteoarthritis (OA) and there is an inverse association between the incidence of osteoporosis and OA [16]. Nevertheless, the risk of fracture is not reduced in elderly women with knee OA [17, 18]. Furthermore, screening elderly patients for the presence of osteoporosis will likely include OA patients as well, as OA is the most common form of arthritis and a common problem in the elderly.

The aim of this study was to evaluate the usability of QUS and DXR measurements for screening purposes in patients with OA of the knee, i.e., patients with a low prevalence of osteoporosis. In this study we assessed if QUS and DXR are able to identify patients with a low BMD corresponding to a T-score ≤ -1.0 as determined with DXA of the proximal femur and lumbar spine.

Materials and methods

Patients participating in a 2-year randomised double-blind placebo controlled clinical trial designed to assess the potential structure modifying effects of oral chondroitin sulphate treatment were enrolled in this evaluation. Recent meta-analyses found that treatment with chondroitin sulphate possibly reduces pain and improves function in patients with knee OA [19, 20]. Volunteers participating in this original clinical trial were asked to perform additional bone measurements with DXA, DXR, and QUS. The protocol of this study was approved by the local ethics committee and all patients gave their informed consent for participation. The results of the original clinical trial have been reported elsewhere [21].

Patients and design of the original clinical study

Between March 1996 and May 1999, a total of 300 patients of both gender were recruited by the Department of Rheumatology and Institute of Physical Medicine of the University Hospital Zurich through advertisements in the local newspapers and posters placed at various locations at the University of Zurich. All patients recruited had both radiological and clinical signs of knee OA according to ACR criteria [22]. Patients with a grade 1, 2 and 3 according to the Kellgren and Lawrence scoring system were eligible for study entry [23]. In the scoring system described by Kellgren and Lawrence, a grade 0 indicates a definitive absence of radiological changes of OA (on conventional X-ray images). Such changes include the formation of osteophytes on the joint margins, the presence of periarticular ossicles (mainly seen at the distal and proximal interphalangeal joints), the narrowing of joint cartilage associated with sclerosis of subchondral bone, small cystic areas with sclerotic walls usually situated in the subchondral bone, and an altered shape of the bone ends (particularly in the head of the femur) [23]. A grade 1 indicates minimal or doubtful changes and grade 2–4 indicate changes which are definitely present with increasing severity.

Exclusion criteria were patients younger than 40 or older than 85 years, pregnancy or lactation, initial radiological signs of severe OA (Kellgren and Lawrence radiological score 4), chondrocalcinosis, secondary OA after trauma and patients after rupture of the anterior cruciate ligament, signs of skeletal hyperostosis, rheumatoid arthritis or psoriasis, arthropathy due to metabolic diseases, Paget's disease, previous surgical intervention less than 6 months before study onset or a planned surgery within the next two years. Furthermore, patients with known hypersensitivity to chondroitin sulphate, asthma, severe diseases of the liver or the kidneys or a malignant disease, and the use of any medication that could affect bone metabolism, such as steroids, or a known abuse of pharmaceuticals were excluded.

There were no differences between the 161 patients volunteering for this evaluation and the 300 knee OA patients of the original clinical trial regarding body weight, height, body mass index (BMI), i.e., body weight in kg ÷ (height in m)^2, age, gender distribution, and clinical and radiological signs of OA. The details regarding medication and follow-up examinations for this 2-year randomised double-blind placebo controlled clinical trial have been previously described [21].

For this study, all DXA, QUS, and DXR measurements were acquired on the same day at study inclusion of the patient. The radiographs of both hands used for DXR measurement were also taken on the day of study inclusion.

DXA measurements

The DXA measurements were performed on the supine patient at the following sites: lumbar spine (L2–L4) and both hips with a Hologic QDR 4500 A and C device (Hologic Inc., Waltham, MA). The lumbar spine measurement was taken exclusively from dorsal projection. At the lumbar spine regions of interest (ROI) in the vertebral body L2–L4 and in the hip regions of interest in the proximal femur including a total ROI, Ward's triangle, femoral neck, and trochanter were evaluated. For this evaluation we used the total hip BMD value, since this is the preferred measurement for monitoring patients. Prior to the study, the DXA devices were cross-calibrated using a spine phantom and daily quality controls using the same phantom were performed during the whole study period, according to the recommendations of the manufacturer. A 1.5% variability from the mean value was considered a tolerable variation of the DXA measurements between the two DXA devices and 0.5% variability for the longitudinal quality control of each individual device. In an own evaluation, the short-term precision (CV%) of the mean BMD measurement of L2–L4 with repositioning of the patient as done in 10 postmenopausal women was 1.2%.

All measurements and quality control were done by the same two experienced technicians (experience of 7 and 10 years) during the whole study period.

BMD was given as absolute values in g/cm^2, and as Z and, T-score values. The Z-score corresponds to the number of standard deviations from the mean value that was defined by the range of BMD of an ethnically comparable age and gender-matched reference population. The T-score corresponds to the number of standard deviations from the mean of a gender-matched reference population of young adults defined as the Peak Bone Mass, as provided by the manufacturer. In agreement with the International Society for Clinical Densitometry (ISCD) guidelines, osteopenia or osteoporosis were defined according to the lowest measured value in either spine or hip. In this study we used the total values of the L2–4 measurement at the spine and the value of the total hip region. Osteopenia, as defined by the WHO classification, corresponds to a T-score value between −1.0 and −2.5. Osteoporosis was defined a T-score value of −2.5 and lower.

DXR measurements

DXR was performed using a Sectra Pronosco X-posure system (Version 2.0; Sectra Pronosco Inc., Vedbaek, Denmark). With this device conventional radiographs of the hands can be digitised and regions of interest at the second, third and fourth metacarpal bone are automatically drawn to measure the cortical bone volume based on volumetric equations from a cylindrical bone model [24]. The bone mineral content and density can be calculated from this measurement (metacarpal BMD) [25]. In addition, the system provides a porosity index analysed from the intensity profile of the metacarpal bones and yielding information on the presence of lacunar holes within the cortical bone. At the time of planning this study the role of the metacarpal index, a parameter which is automatically calculated by the DXR system, was less clear and, therefore, not considered for this evaluation. Radiogrammetry using this device has been shown to have a good correlation with forearm BMD, as measured with DXA, and the ability to predict fracture risk [26, 10]. Furthermore, a high short-term precision (CV%) with a coefficient of variation of between 0.4% and 0.65% have been reported [26, 27]. In an own evaluation, the short-term precision with repositioning of the same single hand radiograph of 10 postmenopausal women was 0.25%.

For this study both hands of a patient were x-rayed and high resolution radiographs were exposed with the digital information. The hand radiographs were then scanned using a UMAX PowerLook 110 scanner which has an optical resolution of 1200×2400 dpi (height × width, dots per inch). All measurements of hand radiographs were performed by a single scientific collaborator (N.Z.). The mean values of the metacarpals of the left and right hands were used for the comparisons with other methods and the parameters BMD, porosity and the T-score were analysed.

QUS measurements

The QUS measurements of both heels were acquired on an Achilles+ device, which uses a water-bath at 37° as a coupling medium (GE Lunar, Madison, WI, USA). The Achilles+ generates a band of frequencies from 200 to 600 kHz. The device measures the speed of sound (SOS) expressed in m/s and the BUA expressed in dB/MHz. In addition, the Achilles+ system automatically calculates the stiffness index (SI) of the heel bone using the following formula: SI=(0.67×BUA)+(0.28×SOS)−420. SI provides T-scores that can be compared with axial BMD measurements and is considered to be able to identify patients with osteoporotic fractures better than BUA or SOS [28].

The mean values of the left and right heel were used for comparison with other methods and the parameters SI, SOS, BUA and the T-score were analysed. In a recent phantom study, the short-term precision of this device was comparable to that of DXA with a CV% of approximately 0.5% for the BUA parameter [29]. In the same study, the CV% of SOS was approximately 0.3% and 1.9% for SI [29]. In an own evaluation, the short-term precision with repositioning the heel as measured in 10 postmenopausal women was 0.2% for the SOS and 0.5% for the BUA measurements.

QUS was also measured at the distal metaphysis of the proximal phalanges of fingers II, III, IV and V on each hand

using the DBM Sonic 1200 device (IGEA, Capri, Italy). The transducers are positioned on the lateral surfaces of the finger using gel as coupling material. This device generates an ultrasound signal with a frequency of 1.25 MHz and measures the SOS when the signal reaches minimal amplitude of 2 mV (i.e., AD-SOS) and is expressed as m/s. Furthermore, the pattern of the signal received is analysed and information such as the relative peak amplitude, peak regression and trend of SOS in the four phalanges are combined to provide the 'ultrasound bone profile score' (UBPS) as described by Wüster et al. [30]. The mean values of the phalanges of the left and right hand were used for the comparisons with other methods and the parameters SOS and UBPS were analysed. The short-term precision as described by the CV% has been reported to be 0.58% for AD-SOS and 0.59% for UBPS [31]. In an own evaluation, the short-term precision with repositioning of the device on the same phalanges as measured in 10 postmenopausal women was 1.9% for AD-SOS and 1.4% for UBPS. All measurements and quality control for both devices were done by the same two experienced technicians (experience of 7 and 6 years) during the whole study period.

Statistics

The mean value and standard deviation for normally distributed values, or in case of non-normal distribution, the median value and range for the measured parameters are given. Confidence intervals are given at the 95% level.

Unpaired t-test was used to test for differences between the patients for normally distributed parameters. The Mann-Whitney U test was used for data without normal distribution. The results of DXA, QUS, and DXR measurements were further compared for obese (BMI of ≥30 kg/m^2) and non-obese patients using the Mann-Whitney U test with a Bonferroni correction for multiple measurements. The mean DXA, DXR or QUS values as obtained from the left and right hand, hip, or heel respectively, were used for correlation of the results of the different methods using Spearman's rank correlation.

Furthermore, receiver-operating characteristics were calculated to assess the predictive power of the different screening methods. The areas under the curve were calculated with the 95% confidence interval.

Results

Patients and results of DXA

All patients participating in the original trial were asked to undergo additional DXA, DXR and QUS measurements. One hundred sixty-one out of the 300 initially included knee OA patients volunteered for at least one additional measurement. The patient characteristics are listed in Table 1. Only 25 out of the 161 patients had a BMI of less than 25 kg/m^2 and 42 patients were obese, i.e., they had a BMI of ≥30 kg/m^2 (19 male, 23 female; BMI between 30.0–46.9 kg/m^2). Ninety-four patients were overweight with a BMI between 25.1 and 29.9 kg/m^2. There were 119 non-obese patients (61 male, 58 female; BMI between 17.7 and 29.9 kg/m^2).

The results of DXA measurements are listed in Table 2. DXA measurements revealed a decreased BMD (T-score value −1 or lower) at the lumbar spine or hip in 84 patients (52% of all patients; 72 patients in the lumbar spine and 36 patients in at least one hip). Osteoporosis was found in 21 patients (13% of all patients; 19 in the lumbar spine and 4 in the hip).

Mann-Whitney U test revealed a difference of lumbar spine BMD (1.086±0.151 vs. 0.998±0.157 g/cm^2) and mean hip BMD (1.046±0.127 vs. 0.939±0.142 g/cm^2) between the 42 obese and the 119 non-obese patients. The obese patients had significantly higher total lumbar spine BMD (p=0.004, significance level p=0.007 after Bonferroni correction) and higher mean hip BMD (p=0.0001) than the non-obese patients.

Results of DXR measurements

Results of DXR measurements were available in 154 patients (76 male, 78 female; Table 3). The DXR parameters BMD and porosity showed an excellent correlation between the metacarpals of the left and right hand as tested with Spearman's rank correlation (p<0.0001 for both parameters). There was no significant difference between the left and right hand metacarpal

Table 1 Patient characteristics

		Men (n=81) (mean±SD; range)	Women (n=80) (mean±SD; range)
Age	years	62.6±9.4 40–82	62.2±9.1 41–79
Age, postmenopausal women (n=72)	years		64.0±7.6 48–79
Age, pre-menopausal women (n=8)	years		46.1±4.3 41–54
Body size	cm	174.8±6.3 160–196	162.1±6.5 147–178
Body weight	kg	84.2±12.5 62–119	73.5±14.9 45–115
Body mass index	kg/m^2	27.5±3.7 20.5–39.8	28.0±5.8 17.7–46.9

Characteristics of 161 volunteer patients participating in the placebo controlled double-blind study undergoing screening with DXA, DXR, and QUS. 90% of the women were postmenopausal.

Table 2 DXA measurements

n=161 patients		Mean±SD	Range
Lumbar spine total BMD	g/cm^2	1.021±0.159	0.580–1.450
Lumbar spine T-score		Median −0.7	−4.5–+3.3
Lumbar spine Z-score		Median +0.5	−3.4–+4.0
*Left hip total BMD	g/cm^2	0.971±0.146	0.530–1.320
Left hip T-score		Median −0.2	−3.4–+1.9
Left hip Z-score		Median +0.6	−2.6–+3.3
*Right hip total BMD	g/cm^2	0.961±0.150	0.460–0.135
Right hip T-score		Median −0.3	−4.0–+2.1
Right hip Z-score		Median +0.6	−3.3–+2.9

* The left hip was measured in 157 patients; the right hip was measured in 155 patients

porosity (paired t-test, p=0.11; 95% CI for mean difference −0.4–+0.04).

Mann-Whitney U test revealed a significant difference for the BMD parameter, but not the porosity, between patients with a normal and those with a low BMD at the vertebral spine or hip (Table 3).

Mann-Whitney U test revealed no significant difference for the BMD parameter (0.587±0.080 vs. 0.602±0.078 g/cm^2; p=0.28) and the porosity (4.774± 0.974 vs. 4.828±0.0915%; p=0.78) between 40 obese and 114 non-obese patients.

Results of QUS measurements

Results of QUS of the phalanges of both the left and right hand were available in 97 patients (48 male, 49 female; Table 4), and QUS of the left and right heel in 95 patients (47 male, 48 female; Table 4). QUS parameters showed an excellent correlation between the left and right side for phalangeal SOS (p<0.0001), UBPS (p<0.0001), and calcaneal stiffness (p<0.0001) as tested with Spearman's rank correlation. There were no significant differences for the QUS parameters as measured at the phalanges and calcanei between patients with a normal and those with a low BMD at the vertebral spine or hip.

Mann-Whitney U test revealed no significant difference for the phalangeal ultrasound parameter SOS (2990.9±121.6 vs. 2990.6±161.2 m/s; p=0.80) and UBPS (98.6±43.6 vs. 87.5±38.9; p=0.27) between 28 obese and 69 non-obese patients. Furthermore, Mann–Whitney U test revealed no significant difference for calcaneal stiffness (128.6±21.6 vs. 136.7±24.7; p=0.19) between 27 obese and 68 non-obese patients.

Correlation of DXR and QUS with DXA

The results of Spearman's rank correlation of the different methods are listed in Table 5. There was a significant correlation between the lumbar spine BMD and the mean metacarpal DXR BMD (p<0.0001) and mean metacarpal porosity value (p=0.007) of left and right hand DXR (Table 5). Mann–Whitney U test revealed a significant difference of the mean metacarpal DXR BMD (p=0.01) but not of the mean metacarpal porosity value (p=0.66) of both hands between the groups with normal and low T-scores at the lumbar spine. Additionally, there was a significant correlation between the mean BMD value of left and right hip and the mean value of left and right hand metacarpal DXR BMD (p<0.0001), but not for the porosity index (p=0.11; Table 5). The comparison of DXR BMD values in patients with a normal versus a low T-score in at least one of both hips revealed a significant difference (p<0.0001). This was not the case for the mean metacarpal porosity index (p=0.32). Only the DXR BMD parameter was able to discriminate patients with low BMD T-score at the spine or hips from patients with normal BMD. However, the mean metacarpal DXR BMD value was more suitable to identify female patients (p=0.008) than male patients (p=0.28) with a low BMD at the lumbar spine. In contrast, the mean

Table 3 DXR measurements

Patients n=154		Mean± SD	Range	Correlation between left and right hand	Mean±SD in patients with normal BMD**	Mean±SD in patients with a low BMD**	Mann–Whitney U p-value
*Mean metacarpal BMD	g/cm^2	0.591± 0.079	0.390–0.750	0.95	0.612±0.073	0.573±0.081	p=0.002
*Mean metacarpal porosity	%	4.79± 0.95	2.3–6.8	0.41	4.83±0.89	4.75±1.01	p=0.74

* The arithmetic mean of the metacarpal measurements of the left and right hand is given.
** Patients with a low BMD are those with a T-score value of −1.0 and less, as measured at the lumbar spine or the hip. Patients with normal BMD have T-score values above −1.0.

Table 4 QUS measurements

		Mean± SD	Range	Correlation between left and right side	Mean±SD in patients with normal BMD**	Mean±SD in patients with a low BMD**	Mann–Whitney U p-value
QUS hands (n=97)							
*Mean phalangeal SOS	m/s	1992.6± 100.5	1713.5–2253.0	0.91	1990.9±109.3	1994.3±92.6	p=0.82
*Mean phalangeal UBPS		60.5± 26.6	5.5–100.0	0.89	60.9±28.5	60.1±25.0	p=0.94
QUS heels (n=95)							
*Mean calcaneal stiffness		89.5± 15.7	52–135	0.90	90.3±15.0	88.6±16.2	p=0.65

* The arithmetic mean of phalangeal measurements of both hands and calcaneal measurements of both heels are given.
** Patients with a low BMD are those with a T-score value of −1.0 and less, as measured at the lumbar spine or the hip. Patients with normal BMD have T-score values above −1.0.

metacarpal DXR BMD value was able to identify female and male patients with a low BMD at the hip (female: p<0.0001; male: p=0.008).

No significant difference was found for the mean phalangeal QUS value between patients with lumbar spine osteopenia/ osteoporosis and patients with normal spine BMD (p=0.86). The evaluation of phalangeal QUS revealed that this method was not able to identify patients with a low BMD at the lumbar spine or at the hip level, independent of gender (male: p=0.91 for SOS and p=0.88 for UBPS for hip BMD; p=0.96 for SOS and p=0.73 for UBPS for lumbar spine BMD; female: p=0.92 for SOS and p=0.94 for UBPS for hip BMD, p=0.77 for SOS and p=0.95 for UBPS for lumbar spine BMD).

The analysis of QUS of the heels using the Mann–Whitney U test also revealed no significant difference between the mean stiffness value of the patients with a low and a normal T-score at the lumbar spine (p=0.62) or hips (p=0.61). The mean stiffness value of heel QUS measurements was not able to identify those patients with a low BMD at the lumbar spine and hips in the male patients (p=0.46 for hip BMD, p=0.43 for lumbar spine BMD) and in the female patients (p=0.22 for hip BMD, p=0.91 for lumbar spine BMD).

Table 5 Spearman's rank correlation of methods

	Mean metacarpal DXR, BMD correlation, p-value	Mean metacarpal DXR, porosity correlation, p-value	Mean phalangeal QUS, SOS correlation, p-value	Mean phalangeal QUS, UBPS correlation, p-value	Mean calcaneal QUS, stiffness correlation, p-value	Lumbar spine BMD correlation, p-value
Mean metacarpal DXR, porosity	0.22, 0.007 *					
Mean phalangeal QUS, SOS	−0.02, 0.85	0.11, 0.28				
Mean phalangeal QUS, UBPS	0.02, 0.85	0.12, 0.25	−0.82, <0.0001 *			
Mean calcaneal QUS, stiffness	0.01, 0.97	0.04, 0.69	0.52, <0.0001 *	0.54, <0.0001 *		
Lumbar spine BMD	0.38, <0.0001 **	0.10, 0.24	−0.04, 0.72	−0.01, 0.93	0.03, 0.97	
Mean hip BMD	0.66, <0.0001 **	0.13, 0.11	0.01, 0.96	0.09, 0.42	0.08, 0.47	0.65, <0.0001 *

Spearman's rank correlations and p-values are given for the measurements.
* A significant relationship was found for the ultrasound measurements at the different sites and for the measurements of BMD and porosity at the metacarpals and BMD measurements at the hips and lumbar spine, respectively.
** The correlation of DXR based metacarpal BMD and DXA based BMD of the hip or spine is highly significant.

Performance of the measurement methods

The ability of DXR and QUS measurements to predict a low BMD at the vertebral spine or hip was additionally evaluated using the T-score values of the DXR and QUS measurements. The sensitivity and specificity for the mean DXR T-score of ≤−1.0 as measured with DXR of both hands to identify a hip BMD of ≤−1.0 was 70% (male 60%, female 74%) and 71% (male77%, female 65%). For the identification of a low BMD at the lumbar spine the sensitivity and specificity was 43% and 68%, only, for male and female patients together. In contrast, the sensitivity and specificity for the mean T-score of ≤−1.0 as measured with QUS of both heels to identify a hip BMD of ≤−1.0 was 47% and 55% calculated for both genders together. For the identification of a low BMD at the lumbar spine the sensitivity and specificity was 45% and 56% for male and female patients together. The sensitivity and specificity for the mean T-score of ≤−1.0 as measured with QUS of both hands to identify a hip BMD of ≤−1.0 was 70% and 26% calculated for both genders together. For the identification of a low BMD at the lumbar spine the sensitivity and specificity was 79% and 34%.

In combination with T-score values of ≤−1.0 of the DXR and QUS devices to identify patients with a low BMD as defined by DXA, the DXR method had the best predictive power to indicate osteopenia or osteoporosis at the hip in both male and female patients. The area under the curve was 0.82 (95% CI: 0.74–0.90) for all patients. In Fig. 1 the ROC curves of male and female patients are shown. The area under the curve for female patients was 0.83 (95% CI: 0.74–0.93) and for male patients 0.77 (95% CI: 0.60–0.93). However, DXR was less suitable for predicting a low BMD at the vertebral column with an area under the curve of 0.64 (95% CI: 0.55–0.73) for male and female patients together. In contrast, the predictive power of QUS measured at the heels was insufficient to identify patients with a low BMD at a hip with an area under the curve of 0.46 (95% CI: 0.31–0.61), as well as patients with a lumbar spine T-score of ≤−1.0 with an area under the curve of 0.51 (95% CI: 0.38–0.63). The predictive power of QUS measured at the phalanges was also insufficient to identify patients with a low BMD at a hip with an area under the curve of 0.53 (95% CI: 0.38–0.67), as well as patients with a T-score of ≤−1.0 at the lumbar spine with an area under the curve of 0.44 (95% CI: 0.33–0.56), as calculated for male and female patients together.

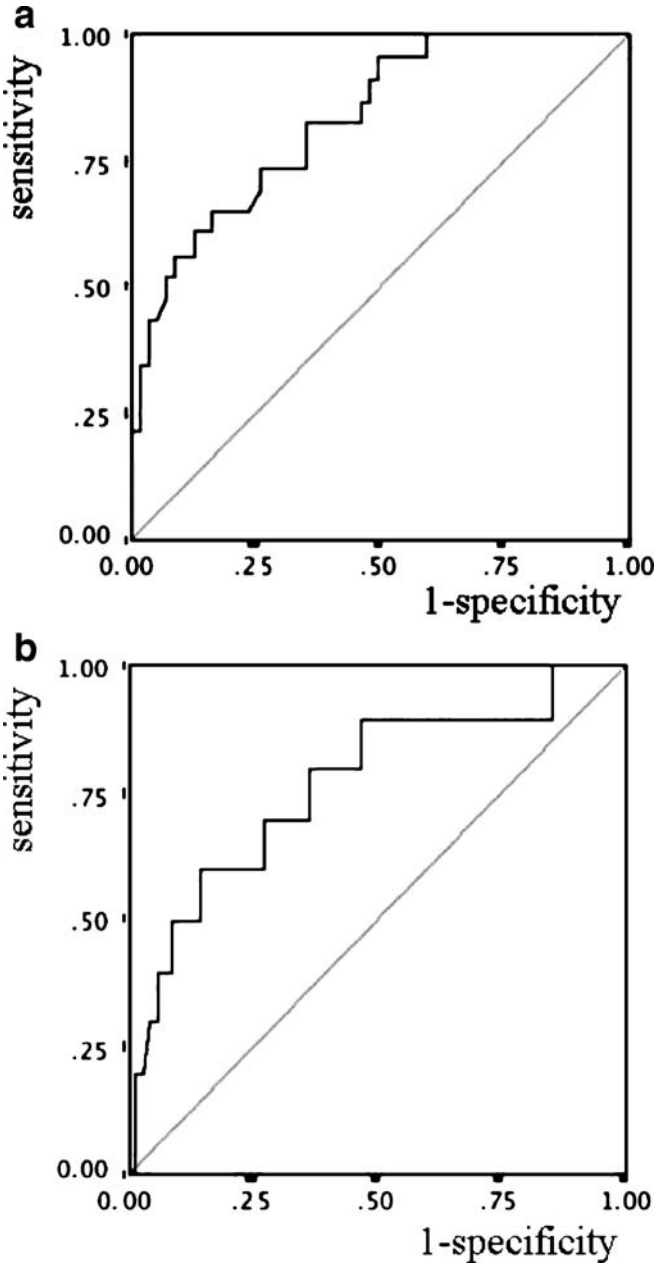

Fig. 1 **a** and **b** ROC curve of female (1A) and male (1B) patients for the ability of a low mean DXR T-score (≤−1.0) to identify osteopenia or osteoporosis at a hip. The area under the curve was 0.83 for female and 0.77 for male patients

Discussion

In this study, DXR of the metacarpals was able to identify male and female patients with a low hip BMD corresponding to a T-score ≤−1.0 as measured with DXA. In contrast, neither phalangeal QUS of both hands nor calcanei was able to identify OA patients with osteopenia or osteoporosis at the lumbar spine or hips. The use of QUS and DXR for screening purposes has already been evaluated by several groups [32–35]. According to the official positions of the ISCD, DXA measurements are useful in women 65 years of age and older, in men 70 years of age and older, and in patients with an underlying disease, condition or medication associated with low bone mass or bone loss [36]. Therefore, DXA cannot be recommended as a screening tool in patients such as those examined in our

study. Since OA is common in the elderly and is known to have an influence on BMD, the possible use of new screening techniques has also to be evaluated in OA patients [16]. Screening of patients with DXR could be a simple and accessible method to identify patients in high-risk groups for osteoporosis. The possibility to identify patients who are likely to have a low T-score at the lumbar spine and hips is interesting in regard to future clinical application. In our male and female knee OA patients, the DXR technique was able to identify patients with a low hip BMD with an acceptable sensitivity and specificity, although the prevalence of osteopenia and osteoporosis is rather low in OA patients. On the other hand, the test performance was insufficient for the identification of a low BMD at the lumbar spine and only the DXR BMD parameter was able to discriminate these patients, while the porosity index was not. Because it is common to acquire hand radiographs in patients with OA to assess involvement of finger joints, DXR may become a cost efficient screening method in OA patients.

A limitation of our data is that there were not enough patients for a subgroup comparison of patients with osteopenia and osteoporosis. 52% of the patients had a T-score indicating osteopenia at the lumbar spine or hip and 13% of all patients had osteoporosis. We pooled these patients and compared the patients with a normal T-score with those having a low T-score of ≤ -1.0 corresponding to osteopenia or osteoporosis. Furthermore, the number of subjects undergoing the three different techniques greatly varied and, therefore, an analysis of further subgroups such as male and female patients with osteopenia or osteoporosis would have been less meaningful.

The results of this study are in line with previous observations suggesting that osteoporosis is a rather uncommon finding in OA patients [18]. The DXA Z-score of our study patients, i.e., the comparison to age and gender matched controls, indicated a tendency to a relatively higher BMD at the lumbar spine and both hips. The slightly higher Z-score probably reflects the effect of the patients' weight on structural bone properties and not a direct influence of OA on the bone structure. Many patients in this study had a high BMI and it is well known that OA patients are often obese. The separate analysis of patients with a BMI of ≥ 30 kg/m^2 revealed that the total lumbar and mean hip BMD as measured with DXA was significantly higher in obese patients than in patients with a BMI of less than 30 kg/m^2 (normal weight and overweight patients). In contrast, there was no difference for the DXR parameters metacarpal BMD and porosity between obese and non-obese patients. Additionally, there was no difference for phalangeal SOS and UBPS measurements as well as for calcaneal stiffness for these two patient subgroups. This finding is explained by an influence of obesity on the technical performance of DXA BMD measurement, leading to overestimation of BMD values. It has previously been shown that in contrast to the DXA method, there is no influence of body size and weight on the results of DXR-BMD measurements [36].

In accordance to the official positions of the International Society for Clinical Densitometry, we used the femur BMD value with the lower total femur BMD to define the presence of osteopenia or osteoporosis at the hip level for the statistical evaluation [37]. In contrast, we used the mean values of the DXR and QUS measurements, obtained at both hands and heels, and not the lowest value of just one side. Often the measurements are only acquired on the non-dominant hand or heel. In a previous work, it has been suggested to measure both calcanei and to use the lower of both measured values in routine clinical practice [38]. Furthermore, it has been recommended to acquire ultrasound measurements at other sites, such as the forearm on both sides [39]. In our study, we used the mean values of QUS and DXR measurements of both hands and the mean values for the calcaneal QUS as it may be difficult to choose the non-dominant hand or leg in patients with knee OA. The use of walking sticks, altered loading and weight-bearing may influence bone properties at the so-called non-dominant side. We decided to use the mean values in order to avoid overestimation of the incidence of pathologically low values.

To further evaluate the performance of the DXR device and QUS devices, we used the T-score values. For these devices the use of T-score values has not been validated for their clinical significance. In contrast, the T-score values used for BMD results, as based on DXA, express important clinical information in terms of increased fracture risk. It might be argued that a T-score value, when used for DXR, is meaningless, as its clinical role has not been defined. Therefore, we suggest performing studies to appraise the use of T-score values in DXR and QUS based techniques and to better define the clinically relevant thresholds.

In this cross-sectional study we did not assess the influence of OA in our patients on fracture incidence. We assessed a group of rather young patients with a mean age of approximately 63 years and, therefore, with a low probability of fracture. It is well known that calcaneal QUS is almost as predictive for fracture as hip DXA, but at this stage, it is not clear if DXR or QUS of the phalanges are reliable screening tools to predict fracture risk. Therefore, studies should further assess the clinical role of hand measurements using DXR and QUS and evaluate the relationship between knee OA and fracture risk.

The results of this study suggest that DXR of hand radiographs, which are often acquired in patients with knee OA, have the potential to identify male and female patients with a low hip BMD corresponding to a T-score ≤ -1.0 as measured by DXA. In contrast, QUS measurements of the heels and fingers acquired in this population, with a low

prevalence of osteopenia or osteoporosis, were not suitable to identify patients who possibly should undergo DXA.

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