Early Results Of The Comparison Of Bone Mineral Density Values Assessed With Digital X-Ray Based Radiogrammetry And Double Energy X-Ray Absoprtiometry On Patients Suffering From Rheumatoid Arthritis

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Abstract

Purpose: To evaluate potential value of computer assisted X-ray based radiogrammetry (DXR) in patients with rheumatoid arthritis.

Patients and Methods: 50 randomly selected patients having rheumatoid arthritis underwent bone mineralization measurements (femoral neck/lumbar spine using DXA and hand using DXR which estimates BMD from radiogrammetrical measurements of middle metacarpal bones. and provides metacarpal and porosity index (MCI; PI).

Results: Pearsons correlation coefficients (BMD-DXR) ranged between r=.56 and .69 (DXA-BMD spine and DXA-BMC femur). MCI DXR reached lower values ranging from .53 to .62 (DXA-BMD spine and femur) all p<.01. PI showed no significant correlations to any DXR/DXA-parameters. DXR-BMD differed depending from the severity of the disease (Steinbroker).

Conclusion: This new radiogrammetry-based system seems to be of promising clinical value with a moderate but significant correlation to DXA-parameters. In patients receiving X-ray of the hand for diagnostic purposes, the new technology is feasible, because for the patient no additional radiation exposure is necessary in order to estimate BMD.

INTRODUCTION

Currently one percent of the European population suffers from rheumatoid arthritis ([1]). As an inflammatory disease rheumatoid arthritis involves several joints as well as synovial sheaths of tendons and bursae; vessels, eyes and other organs may be involved as well. Both, rheumatoid arthritis and its expensive treatment can cause a significant bone loss, i.e. secondary osteoporosis in a high number of patients.

During the treatment of rheumatoid arthritis regularly radiograms of different skeletal parts - including the hands- are necessary to verify the success of the treatment as well as the progress of the disease. For patients with a clinically doubtful or reduced bone density, additional measurements of the bone mineral density (BMD) on either the spine or the femoral neck are required. The increasing value of BMD as a diagnostic parameter can be explained partially by the constant development of more precise, faster and cheaper technologies, which enormously increased availability of these methods in routine clinical settings ([2]).

At the moment the most common bone analysing methods are dual-energy X-ray absorptiometry (DXA), quantitative computed tomography (QCT) and ultrasound. Usually DXA is measured on femoral neck, lumbar spine, forearm and total skeleton, whereas QCT is measured on forearm and lumbar spine. With ultrasound bone mineralization is calculated in an indirect manner via broad-band ultrasound attenuation (BUA) or speed of sound (SOS).

It is common knowledge that also conventional radiographs

can be used to assess the skeletal mineralization status. The inaccuracy of such an assessment is known to be high due to changed conditions for image capture and individual biological variations. Originally proposed by Barnett and Nordin ([3]) and by Virtama and Mahonen ([4]), the use of radiographically-assessed cortical bone thickness as estimation of bone strength became more important during the last decade ([5]). Clinical application of radiogrammetry became more available after refinement, computerization and the use of algorithms for automatic image analysis ([2]). We used the Pronosco X-Posure System (software V.2.), (Pronosco Med Ltd., Denmark) which obtains a BMD estimation through a combined computerized radiogrammetric analysis and textural analysis of the three middle metacarpal bones.

In this study, we wanted to determine the comparability of the DXR-and the DXA system and correlated the parameters provided by both systems. The DXR system (X-posure System) provided three different parameters: the metacarpal cortical index (DXR-MCI) as a radiogrammetric parameter, the porosity index (DXR-PI) as a textural parameter and the BMD as a combination of both (DXR-BMD) by measuring hand X-rays. The DXA system calculated two parameters: the BMD (DXA-BMD) and the bone mineral content (DXA-BMC) by measuring lumbar spine and femoral neck. The study was performed on patients with rheumatoid arthritis who regularly received X-rays of the hand. The aim of the study was, to find out, whether the bone density measurement by radiogrammetry alone might be feasible in patients who are multiple exposed to follow-up X-rays in the course of their disease and who repeatedet achieve bone mineral density calculations due to the illness.

PATIENTS AND METHODS

50 patients (40 female/10 male) were randomly selected from a data pool of more than 1000 patients treated in the rheumatoid department of our institution.

Inclusion criteria for the study were a) the clinical proven existence of a rheumatoid arthritis on Caucasian patients ([6]) as well as the recommendations of Arnett et al. ([7]) and b) the existence and availability of digitally performed X-rays of the left hand using similar technical parameters and measurement of BMD and BMC on the femoral neck as well as the lumbar spine in an interval of 14 days at most.

Mean age was 59.5 years with a standard deviation of 12.8 years and a range of 18 to 80 years. No traumatic lesions of the examined hands occurred in the patients history. No pre-selection regarding severity of rheumatoid arthritis or steroid therapy was performed. Therefore between patients the duration of treatment varied from 1 month up to 40 years. For each patient a Steinbroker score, as an established assessment of the severity of the disease, was calculated. 8 patients had a score of 1 (mild), 26 had a score of 2 (moderate), 6 score of 3 (severe) and 10 patients a score of 4 (very severe).

The Hologic QDR 4500 (Waltham, Massachussets, USA) DXA-system was used to calculate DXA-BMD and DXA-BMC on the femoral neck as well as the lumbar spine.

The Pronosco X-posure System (Version V.2, Denmark) was used to calculate DXR-BMD, DXR-MCI and DXR- PI based on radiogrammetry which needed digitally acquired X-rays of the left hand. These images were acquired by a Siemens Polydoros SX80 (Germany) with the following parameters: filter 1.0, FFD 1m, aluminium 80, tube voltage 42 kV, exposure 4 mAs, AGFA Scopix Laser 2 B (400).

The digital X-rays were subsequently printed and scanned into the system. The system itself checked the quality of the scanned images and aborted the examination in case of inadequate quality. The involved computer algorithms automatically defined regions of interest (ROI) around the narrowest bone parts of the metacarpals II, III and IV and subsequently found the outer and inner cortical edges of the included cortical bone parts.

There was not only no operator activity required for the location of the ROI, it is even not possible for the operator to modify or influence the size or location of the ROI. The analysed image and the ROI were displayed on the monitor. The mean of the cortical thickness and overall bone cortical thickness of the second, third and fourth metacarpal were estimated. Then, for each bone the cortical volume per area (VPA) was calculated. Based on the mean VPA with a correction for the estimated porosity DXR-BMD was computed. Porosity was derived from the area percentage of local intensity minima found in the cortical part of the bone relative to the entire cortical area. As a separate parameter the DXR-PI was scaled to arbitrary units ranging from 1 to 19. The last parameter, DXR-MCI, expresses the mean cortical thickness normalised with the mean outer bone diameter (width). More detailed physical facts regarding this technology and the used mathematical models are given by

Rosholm et al ([2]).

Due to the retrospective character of the study, there were none additional patient examination or patient contact. Hence, an approval of the local ethical committee was not necessary. For statistical analysis Pearsons correlation coefficients were calculated.

RESULTS

Both, DXR-BMD and DXR-MCI of hands were correlated with DXA-BMD and DXA-BMC of lumbar spine and femoral neck. All correlations were significant (see Table 1). The highest correlation was observed between DXR-BMD and DXA-BMC (r=0.69, p<0.01). DXR-PI did not show any significant correlation to the analysed bone parameter determined by DXA (table 1).

Figure 1

Table 1: Pearson correlation coefficients between bone density parameters measured using DXR and DXA (* p < 0.05, ** p < 0.01). BMD: bone mineral density - MCI: metacarpal cortical index - PI: porosity index - BMC: bone mineral content- FN = femoral neck - LS = lumbar spine.

DXR parameters	DXA parameters	Correlation
DXR-BMD	DXA-BMD-FN	0.66**
	DXA-BMD-LS	0.56**
	DXA-BMC-FN	0.69**
	DXA-BMC-LS	0.66**
DXR-MCI	DXA-BMD-FN	0.62**
	DXA-BMD-LS	0.53**
	DXA-BMC-FN	0.55**
	DXA-BMC-LS	0.53**
DXR-PI	DXA-BMD-FN	0.13
	DXA-BMD-LS	0.17
	DXA-BMC-FN	0.16
	DXA-BMC-LS	0.14

The mean DXR-BMD was 0.47 g/cm^2 (SD (standard deviation) = 0.10 g/cm^2), whereas the mean DXA-BMD of the femoral neck was 0.84 g/cm^2 (SD = 0.18 g/cm^2) and 0.88 g/cm^2

(SD=0.18 g/cm^2) for the lumbar spine. The mean DXR-MCI and DXR-PI were 0.35 (SD=0.09) and 4.24 (SD=1.25), respectively. Mean DXR-BMD ranged from 0.55 (SD 0.10) at Steinbroker 1 and 0.38 (SD 0.07) at Steinbroker 4 revealing a significant direct negative correlation (table 2).

Figure 2

Table 2: Relation of severity of rheumatoid arthritis (scores following Steinbroker-criteria) and calculated bone parameters (mean and standard deviation (in brackets))

Steinbroker Score	1	2	3	4
DXR-BMD in g/cm^2 (metacarpals)	0.55 (0.10)	0.48 (0.08)	0.46 (0.12)	0.38 (0.07)
DXR-PI (metacarpals)	3.33 (1.11)	4.28 (1.48)	4.73 (0.69)	4.29 (0.65)
DXR-MCI (metacarpals)	0.42 (0.09)	0.35 (0.07)	0.34 (0.11)	0.29 (0.07)
DXA-BMD in g/cm^2 (FN)	0.87 (0.12)	0.87 (0.17)	0.90 (0.13)	0.70 (0.19)
DXA-BMD in g/cm^2 (LS)	0.95 (0.14)	0.87 (0.17)	0.95 (0.19)	0.83 (0.22)

The correlation of DXR-MCI and DXR-BMD was 0.91, p<0.01. DXR-PI did not reveal a significant correlation to any of both parameters. There was a significant association of severity of radiological signs of rheumatoid arthritis and DXR-BMD, suggesting a decrease of BMD with increasing severity of rheumatoid arthritis. However, when comparing the DXA-parameters regarding the Steinbroker index no such association could be verified:

There is a moderate correlation between age and BMD-DXR, DXR-MCI and DXA-BMD (femoral neck) to age, whereas DXR-PI shows no correlation with age (table 3).

Figure 3

Table 3: Correlation coefficients of bone mineralization parameters and age of the patients (* ≈ p < 0.05, ** ≈ p 0.01).).FN = femoral neck - LS = lumbar spin

Parameters	Correlation with age
DXR-BMD	-0.54**
DXR-MCI	-0.61**
DXR-PI	-0.12
DXA-BMD-FN	-0.37*
DXA-BMD-LS	-0.26
DXA-BMC-FN	-0.29
DXA-BMC-LS	-0.50*

(* p < 0.05, ** p 0.01).).FN = femoral neck - LS = lumbar spine.

Correlation between DXA-values were: BMD-femoral neck: BMD-lumbar spine: r=0.62; BMC-femoral neck/BMC-lumbar spine: 0.61.

Additionally correlation coefficients of BMD calculated using DXR and DXA within each Steinbroker group were calculated reaching values ranging from r=0.64 to r=0.88 (BMC femoral neck), from r=0.42 to r=0.76 (BMC lumbar spine), from r=0.28 to 0.71 (BMD femoral neck) and from 0.39 to 0.66 (BMD lumbar spine). Details are given within table 4.

Figure 4

Table 4: Relation of BMD calculated using DXR to bone mineralization parameters using DXA within the Steinbroker scores

Steinbroker Score	1	2	3	4
DXA-BMD FN	0.68	0.71	0.28	0.58
DXA-BMD LS	0.39	0.64	0.66	0.55
DXA-BMC FN	0.88	0.70	0.73	0.64
DXA-BMC LS	0.55	0.76	0.42	0.70

DISCUSSION

TECHNICAL ASPECTS

Previously reported results of radiogrammetric methods for the evaluation of BMD vary significantly depending on the technique of measurement. To determine the BMD most of these studies focus either on the combined cortical thickness, on the metacarpal index or on the inner diameter of the medullar space .

The clinical use of the different methods has been impeded by the acceptance of DXA-BMD as the golden standard. However, it has been demonstrated, that cortical thickness is a predictive factor of fracture rate ([5], [10]). A moderate association of cortical thickness and calculated bone density of the forearm was shown in a couple of studies with correlation coefficients ranging from 0.50 to 0.65 using single photon absorptiometry (SPA) and conventional radiography ([7], [11]).

The DXR technology used in this study is based on a physical model of the bone (mainly cylindrical and elliptical model) as suggested by Lazenby ([12]). BMD is estimated from geometrical measurements of the cortical thickness and the width of the bone, which are automatically conducted in a single anterior-posterior image of the hand.

Following the suggestions of Meema et al. ([13]) and Bloom ([14]), more than one bone is analysed (metacarpalia 2-4) and the results are averaged to improve precision and accuracy. Compared to conventional radiogrammetry, the computer based radiogrammetry implements a larger number of measuring points along the bone (118 points per centimetre). The measurement area (ROI) is fixed by the system in a predefined not observer dependent manner.

In contrast to radioabsorptiometry, a standardized exposure is not necessary for the DXR-technique. DXR calculates BMD using the cortical thickness of the metacarpals II-IV. It has been recently reported, that the precision error of the DXR-method is low and seems to be at least equivalent with peripheral DXA ([2]).

CLINICAL ASPECTS

As results of our study it could be demonstrated that the DXR-technique for bone density determination can be used on conventional X-rays of the hand. Therefore additional X-ray application to patients suffering from rheumatoid arthritis to determine the degree of bone mineralisation may be reducible in the future. Nonetheless, it should be emphasized that the new method is not evaluated in general and the X-ray exposure rate of DXA is rather low.

It should be noted, that bone mineral density might be over- or underestimated depending on the technical parameters used (such as film-focus-distance, tube voltage, film-object-distance). Although DXR-BMD is remarkably insensitive to almost all capture conditions ([15]), a technical study reported, that the tube voltage of 44 kV (as used in this study) causes a mean difference on a bone model (performed on 50 kV) of 3.6 mg/cm^2 ([16]).

Due to these differences, the method seems to be more suited for follow-up-examinations using the same technical parameters. Normative data should only be used, if the X-ray images used for calculation were acquired with similar technical parameters. Another potential limitation seems to be the peripheral location of measurement. Deviations from the skeletal status at axial measurement sites are likely. Moreover theoretically there are at least some advantages of DXR over DXA. Compared to densitometric technologies, digital X-rays reach a higher spatial resolution; consequently the separation of cortical and trabecular regions is more precise. There is no significant influence of beam hardening and soft tissue thickness to radiogrammetry ([17]). Additionally there is no limit in size and weight for the DXR-method in contrast to DXA-methods, which might lead to applications ([18]) especially in the diagnosis of osteoporosis. Although it would be of major interest to calculate T-scores and to correlate these T-score to those given from DXA calculations this is up to now not possible due to the fact, that the available German normative values only address female data ([19]).

During rheumatoid arthritis there is an early decrease of hand BMD linked to inflammation of joints and thus, density behaviour of this site may be different than the one of spine and hip. This aspect is reflected by a higher relative decrease of BMD using DXR-method compared to DXA-calculations

of lumbar spine and femoral neck.

The potential influence of swollen joints, and finger deformities on precision was not investigated in this study, should be judged, however low, because the system only calculates BMD when recognising the cortical structures in a predefined ROI. Therefore swollen soft tissues and deformities of the phalanges are not taken into calculation by the system.

ASPECTS OF THE PARAMETERS

Some studies report a significant correlation of DXR-calculations and DXA-calculations both determined on the forearm ([8]). Correlation of DXR-BMD to DXA-parameters were 0.9 (with DXA on the wrist) and 0.61 (with DXA on the hip) ([8]). In a couple of studies correlations of peripheral and central techniques were found similar to those obtained in this study ([20]). These reported values implement, that about 40% of the variability of one technique can be explained by the other. Consequently one measurement does not warrant speculation about the data level of the other and the DXR calculation does not measure the extent of demineralisation of the whole skeleton and will not replace such measurements. In our study an association of BMD calculated by DXR with radiological signs of severity of rheumatoid arthritis could be verified, whereas this association was not significant when using DXA-methods on lumbar spine or femoral neck.

In order to judge the achieved correlations correctly, it should be addressed that correlation using the same technology DXA on two different bones (lumbar spine and femoral neck) is rather low (0.61 and 0.62, respectively). Publications support this dependence of bone density on measured site and the association to the used technology ([21]).

Additionally is has to be mentioned, that the study was performed retrospectively on a limited number of patients. Further extended studies should implement a higher number of patients using a longitudinal study design in order to verify our results.

DXR may be of clinical use when performed in follow-up examinations for the assessment of the clinical benefit and early side effects of the treatment of rheumatoid arthritis. Our initial data suggest that DXR calculates periarticular demineralisation as well as cortical demineralisation which is also associated with rheumatoid arthritis whereas DXA calculates the central bone mineral density loss. Our study hints that the progress of the rheumatoid arthritis of the hand itself is quantifiable by calculating the sum of periarticular cortical demineralisation associated with steroid induced bone loss. This option of DXR might be clinically useful in the early detection of periarticular demineralisation, which is often described as an early sign of a clinical manifestation of rheumatoid arthritis.

The expected association of BMD-DXR to age should be taken into account when using the values in follow up examinations.

Due to the calculation process of both, metacarpal index as well as bone mineral density, a high correlation of DXR-MCI and DXR-BMD was to be expected. Differences between both parameters are explainable by the correction algorithm for porosity which is implemented in the DXR-BMD calculation. The correlation of MCI of the forearm determined by DXR to DXA of the forearm was reported to be 0.51 ([22]). The estimation of MCI might be of clinical relevance in patients suffering from renal failure, after oophorectomy, after gastrectomy, in hyperthyreosis, and in some cases of malnutrition, as suggested by Nordin more than 20 years ago ([23]).

Porosity is the fraction of cortical bone that is not occupied by compact bone ([2]). Intracortical porosity seems to increase with age ([24]). In our study it was not possible to demonstrate any significant correlation nor association of porosity (DXR-PI) to bone mineralization, age and severity of disease.

SUMMARY

The use of X-ray densitometry (DXR) in patients suffering from rheumatoid arthritis seems feasible and shows for parameters with a similar rationale (BMD and MCI) promising correlations to DXA, the golden standard method at present. The use of DXR might reduce the X-ray exposure for these patient group especially in follow-up examinations. Digital X-ray based radiogrammetry will not replace calculation of BMD on the lumbar spine but might be used as an extension and potential method of quantification of cortical bone loss of the hand as a parameter of the progression of rheumatoid arthritis Constancy for the acquisition parameters and hence similar quality of X-ray images are, however, essential to get valuable information.

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