Osteoporos Int (2000) 11:400–407

Osteoporosis International

Original Article

Detailed Analyses of Periarticular Osteoporosis in Rheumatoid Arthritis

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Abstract. Periarticular osteopenia is the earliest radiographic sign of rheumatoid arthritis (RA). Recent studies using dual-energy X-ray absorptiometry (DXA) have indicated that the loss of periarticular BMD can be quantified by whole-hand bone mineral density (BMD) measurements. The aim of this study was to analyze periarticular BMD in more detail by DXA and quantitative ultrasound (QUS). In a cross-sectional study 23 women aged 30–76 years with early RA, mean disease duration 26 ± 19 months, and 18 men aged 42–69 years, mean disease duration 24 ± 25 months, were examined. All patients received antirheumatic therapy. The reference population consisted of 103 age-matched controls (68 females, 35 males) and young healthy controls. BMD measurements were performed using a DXA Expert XL densitometer (Lunar). BMD of the whole-hand and two subregions was determined: two subchondral regions of interest (S.CH.) were set within the trabecular bone, distal to the proximal interphalangeal joints of digits II and III excluding the dense subchondral bone of the metacarpophalangeal (MCP) joint and two metacarpal regions of interest (MCP) were set including the entire MCP joint of these fingers. QUS measurements at the proximal phalanges of digits II–V were performed using a DBM Sonic (Igea); amplitude-dependent speed of sound (Ad-SoS) was determined. In comparison with whole-hand BMD measurements, bone loss was pronounced in patients with a disease duration of 18–72 months at the subchondral regions of interest in both genders compared with age-matched controls (women: mean BMD loss S.CH. -23%, $p<0.001$, whole-hand -16%, $p<0.001$; men: mean BMD loss S.CH. -19%, $p<0.05$, whole-hand -12%, $p<0.05$). The bone changes were also shown by QUS (women: Ad-SOS values of 1950 ± 90 m/s in RA vs 2137 ± 35 m/s in young healthy controls ($p<0.005$); men AD-SOS 1956 ± 87 m/s in RA vs 2146 ± 41 m/s in young healthy controls ($p<0.05$)). These results show that BMD and Ad-SOS values are significantly lowered in patients with early RA and indicate that periarticular osteoporosis in early RA might possibly be better detected using detailed hand scan analyses.

Keywords: Disease monitoring; Hand bone mineral density; Periarticular osteoporosis; Quantitative ultrasound; Rheumatoid arthritis

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Introduction

Osteoporosis occurs in patients with rheumatoid arthritis (RA) in two forms: periarticular osteoporosis around inflamed joints, which is a characteristic of early disease, and generalized osteopenia/osteoporosis affecting the axial and appendicular bones during the course of rheumatoid disease [1–4]. Recent developments in dual-energy X-ray absorptiometry (DXA) allow the quantification of periarticular bone loss by bone mineral density (BMD) measurements at the hand. Regions of interest (ROIs) can be defined to measure the BMD in periarticular regions due to developments in the software used. This is of particular interest for monitoring diseases such as RA in which local BMD changes take place.

Deodhar et al. [5] showed in 1995 in a cross-sectional study that bone mineral content (BMC) of the hand is reduced in patients with established RA, while Peel et al. [6] showed in 1994 that the BMD changes are more

dramatic at the hand compared with other measurement sites. Furthermore it is known that bone loss at the hand is pronounced during the early course of RA [7,8], despite clinical improvement and sufficient control of inflammation through treatment [5]. It remains to be clarified whether juxta-articular bone loss precedes the development of bone erosions and whether the prevention of periarticular bone loss results in a reduction in bone erosions.

The aim of this cross-sectional study was to examine periarticular BMD in more detail using special hand software (Lunar Expert) and to establish whether the radiologically diagnosed periarticular bone loss (which is called a radiologic early sign of RA) can be quantified and potentially be used for monitoring of the early disease. For this purpose a reference population for BMD measurements at the hand was compiled.

Population and Methods

Reference Population

Hand scans were performed in 119 Caucasian women aged 20–81 years and 91 caucasian men aged 20–86 years (Table 1). The reference population was recruited via posters in the waiting rooms at the hospital and word of mouth recommendation. Health status was assessed using a detailed health questionnaire (data not shown). Women and men with diseases or drugs known to influence bone metabolism were excluded from the reference population. The body mass index (BMI) of all volunteers was between 18 kg/m^2 and 30 kg/m^2.

DXA and quantitative ultrasound (QUS) measurements were performed on the same day. Not all healthy controls received DXA and QUS measurements due to organizational and time problems. A total of 26 men and 46 women received both DXA and QUS measurements at the hand, which included all volunteers receiving a QUS measurement. Of the 210 healthy controls, 103 were age-matched controls (68 women and 35 men).

Table 1. Characteristics of rheumatoid arthritis (RA) patients versus age-matched healthy persons

	RA	Reference group
Women		
n	23	68
Age (years)	54 ± 13	52 ± 8
Height (cm)	163 ± 5	165 ± 6
Weight (kg)	67 ± 14	63 ± 8
BMI (kg/cm^2)	25 ± 5	23 ± 3
Men		
n	18	35
Age (years)	56 ± 8	57 ± 9
Height (cm)	177 ± 9	175 ± 6
Weight (kg)	83 ± 10	79 ± 12
BMI (kg/cm^2)	27 ± 3	26 ± 3

BMI, body mass index.

Rheumatoid Arthritis Population

Twenty-three women aged 30–76 years with early RA (diagnosed according to the criteria of the American College of Rheumatology) with a disease duration of 2–48 months and 18 men aged 42–69 years with a disease duration of 1–69 months were scanned and underwent QUS measurements at both hands (Table 1). All patients received antirheumatic therapy including corticosteroids and DMARDs and their BMI was between 18 kg/m^2 and 30 kg/m^2. Patients with a Larsen score >2 were excluded from the study population. All patients had hand radiographs which showed in all cases periarticular osteoporosis (Larsen score <2 [9]) but no erosions or joint destruction.

Methods

(i) DXA Measurements of the Hand

Hand measurements were performed using the DXA Expert XL densitometer (Lunar, Madison, WI). The software (version 1.63) offers a new mode for hand measurements (134 kV, 1 mA). The hands are positioned on top of the Lunar forearm positioner according to the Lunar manual. BMD of the entire hand was analyzed by the Lunar software. Contours were manually corrected due to contour finding problems with the software. Additional 'in-fillings' were sometimes needed. To determine early BMD changes in juxta-articular bone of rheumatoid patients, two different kinds of rectangular ROI were set in the region of the proximal part of the proximal phalanges of digits II and III of both hands (Fig. 1):

Subchondral ROI (S.CH.): The ROI was set distal to the joint, excluding the dense subchondral bone of the metacarpal joint. It was positioned within the trabecular bone of the phalanx. The ROI's height corresponded to 20% of the phalanges' lengths in men, and in women to 30% of the phalanges' lengths; the width corresponded to the bone diameter (Fig. 1a).

Metacarpal ROI (MCP): The ROI included the entire metacarpal joint. The middle line of the ROI was positioned at the joint, the ROI's height corresponding to 75% of the phalanges' lengths (Fig. 1b).

All hand BMD scan analyses were done by the same operator. All ROIs were set manually; some 'in-fillings' were needed.

Image resolution was determined by a line-pair phantom. The surface dose was measured with an ionization chamber (PTW-Nomex) on the Expert.

(ii) Quantitative Ultrasound Measurements at the Proximal Phalanges of the Hand

The device used for the determination of ultrasound velocity measured at the proximal phalanges of the hand was the DBM Sonic 1200 (Igea, Carpi, Italy). It consists

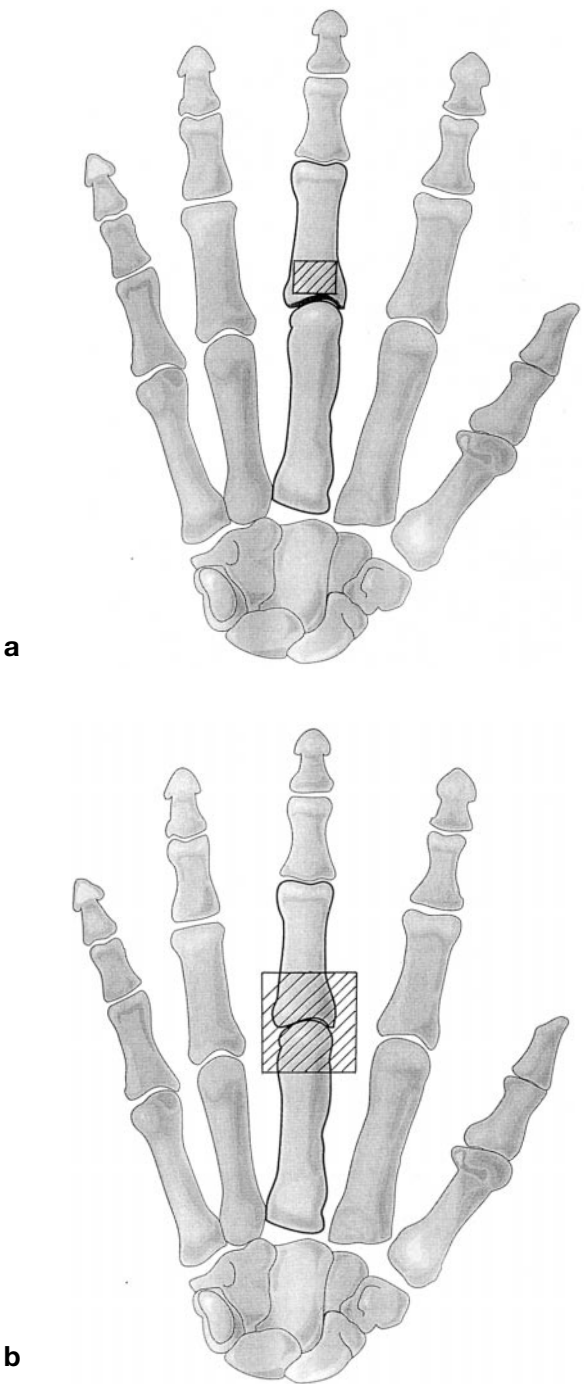

Fig. 1. a Subchondral region of interest (ROI); **b** metacarpal ROI.

of two 12 mm diameter zirconate-titanate crystals embedded in 16 mm diameter probes which are mounted on a caliper. A 1.25 MHz pulse ultrasound signal is generated, the attenuated ultrasound signal being shown on a screen as well as the results of the amplitude-dependent speed of sound (Fig. 2). The device calculates the velocity by taking into account a predetermined minimum amplitude value (2 mV) which has to be

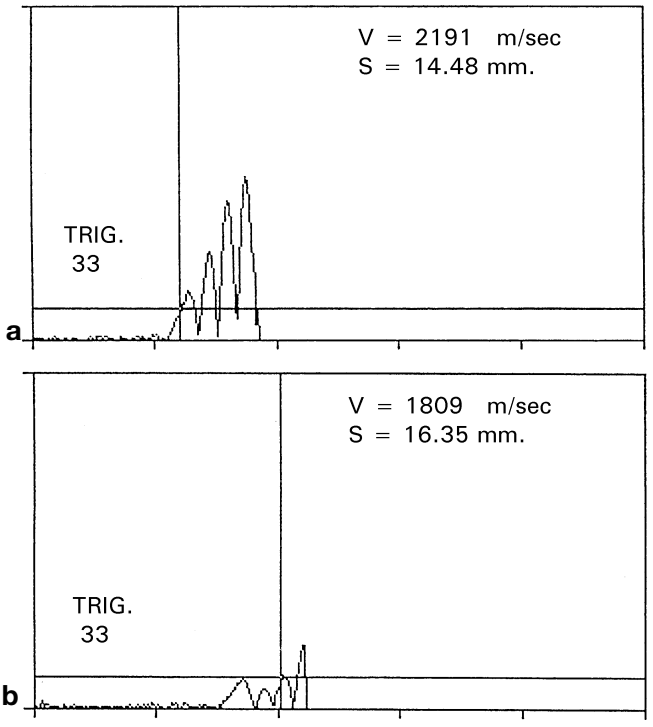

Fig. 2 Amplitude-dependent speed of sound (Ad-SOS) characteristicts in **a** a healthy person and **b** an RA patients.

reached by the signal. Therefore the velocity measured is amplitude-dependent and is called the amplitude-dependent speed of sound (Ad-SOS). To limit the influence of surrounding soft tissue each measurement starts with the determination of the speed of sound through soft tissue at the interdigital region. These measurements are performed between thumb and index finger, as this site is considered to be representative for soft tissue velocity of the hand. The measured value is taken into account to calculate a correction factor that

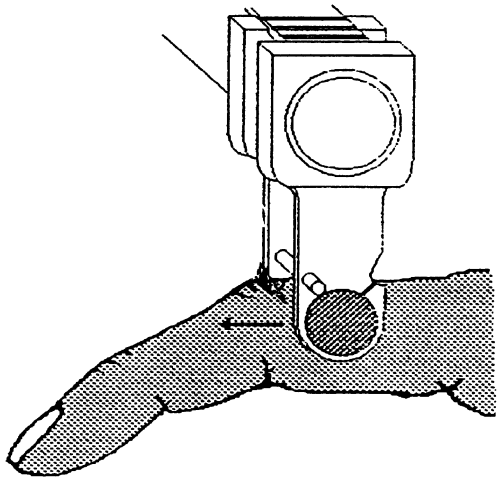

Fig. 3. QUS measurement site.

will be automatically applied by the system to the following speed of sound results through the whole phalanx (for measurement site see Fig. 3).

QUS measurements were performed at digits II–V on both hands. QUS and DXA measurements were performed on the same day.

Statistics

To assess the short-term precision in vivo (expressed as the root mean square coefficient of variation, CV%), the BMD of the entire hand and of the ROIs were measured in 5 healthy volunteers with 5 repeated measurements in one day. Also QUS measurements were performed in 5 volunteers 5 times. For QUS measurements the precision was calculated for the mean value of the measured Ad-SOS of digits II–V.

Simple regression analyses were performed proving the age dependency of the measured parameters at the hand and proving the dependency of hand BMD parameters on disease duration.

Independent sample tests were performed proving the significance of the differences of mean values calculated for measurement results in RA patients and age-matched healthy controls or young healthy controls. As there is evidence that BMD loss in RA takes place in the first years of the disease, the analyses were performed in two subgroups of RA patients: patients with a disease duration of less than 18 months and patients with a disease duration of between 18 and 72 months.

T-scores were calculated for QUS results as follows: *T*-score = (individual data-mean 25–35 sex-matched controls)/standard deviation 25–35 sex-matched controls. As not all volunteers received QUS and DXA measurements at the hand, the *T*-scores were calculated with partially different controls.

Results

Short-term precision in vivo expressed as the root mean square coefficient of variation (CV according to [10]) was 0.9% for BMD measurements of the whole-hand, 2.7% for measurements of the subchondral ROIs of digits II+III, 3.2% for the metacarpal ROIs of digits II+III and 5% for QUS measurements at the proximal phalanges (mean of digits II–V). In RA patients the CV for subregional analyses of DXA hand scans was 3.9–4.2%. The image resolution of the densitometer screen was between 0.6 and 0.8 lines/mm. The surface dose of hand measurements using the DXA Lunar Expert XL (134 kVp, 1 mA) was 130 μGy.

Table 2 shows BMD data of the reference population. Mean values of measured BMD for the whole-hand and the different ROIs at digit II (i.e., Index) and digit III (i.e., Middle) for healthy men and women are given for each decade.

A moderate correlation between BMD (g/cm^2) of the whole-hand and AD-SOS (in m/s) at the fingers (mean value of the measurements of digits II–V) could be shown. Linear regression analyses showed for females a correlation coefficient of $r = 0.54$ ($p < 0.01$). Furthermore there was a weak correlation of whole-hand BMD with age in women; in men no age dependency of BMD of the hand could be shown (Fig. 4).

There was a difference in BMD in RA patients when comparing the right and the left hand which did not reach statistical significance. However, this difference was pronounced in the subchondral and metacarpal ROIs (in females: 32% of whole-hand BMD, 50% of subchondral ROI and 55% of metacarpal ROI; in males: 52% of whole-hand BMD, 62% of subchondral ROI and 52% of metacarpal ROI showed more than 10% difference comparing BMD values of the right and the left hand). Given this difference in BMD of the hands in RA patients all following analyses were performed only at the hands with the lower BMD. Also the QUS results

Table 2. Reference data for BMD measurements at the whole hand and the different subregions at digits II and III for healthy men and women

Decade (years)	*n*	BMD hand (g/cm^2)	SD	S.CH. index (g/cm^2)	SD	S.CH. middle (g/cm^2)	SD	MCP index (g/cm^2)	SD	MCP middle (g/cm^2)	SD
Women											
20-29	24	0.383	0.03	0.263	0.04	0.264	0.03	0.337	0.03	0.333	0.03
30–39	26	0.392	0.03	0.268	0.04	0.266	0.04	0.345	0.04	0.346	0.04
40–49	26	0.396	0.03	0.266	0.03	0.263	0.03	0.354	0.03	0.351	0.03
50–59	22	0.403	0.04	0.267	0.03	0.271	0.03	0.356	0.04	0.359	0.04
60–69	9	0.341	0.05	0.237	0.04	0.229	0.04	0.305	0.04	0.300	0.04
70–79	6	0.334	0.05	0.233	0.05	0.220	0.04	0.292	0.04	0.289	0.05
Men											
20–29	22	0.420	0.05	0.279	0.04	0.282	0.04	0.358	0.04	0.355	0.04
30–39	23	0.441	0.04	0.298	0.03	0.305	0.03	0.380	0.04	0.374	0.04
40–49	18	0.450	0.05	0.309	0.04	0.314	0.03	0.396	0.04	0.392	0.05
50–59	15	0.425	0.05	0.281	0.04	0.275	0.05	0.374	0.04	0.363	0.05
60–69	8	0.404	0.07	0.260	0.04	0.260	0.05	0.354	0.06	0.343	0.07
70–79	3	0.407	0.07	0.259	0.05	0.244	0.05	0.336	0.06	0.320	0.05

All values are given as mean BMD in g/cm^2 ± standard deviation (SD).
S.CH., subchondral region of interest; MCP, metacarpophalangeal region of interest.

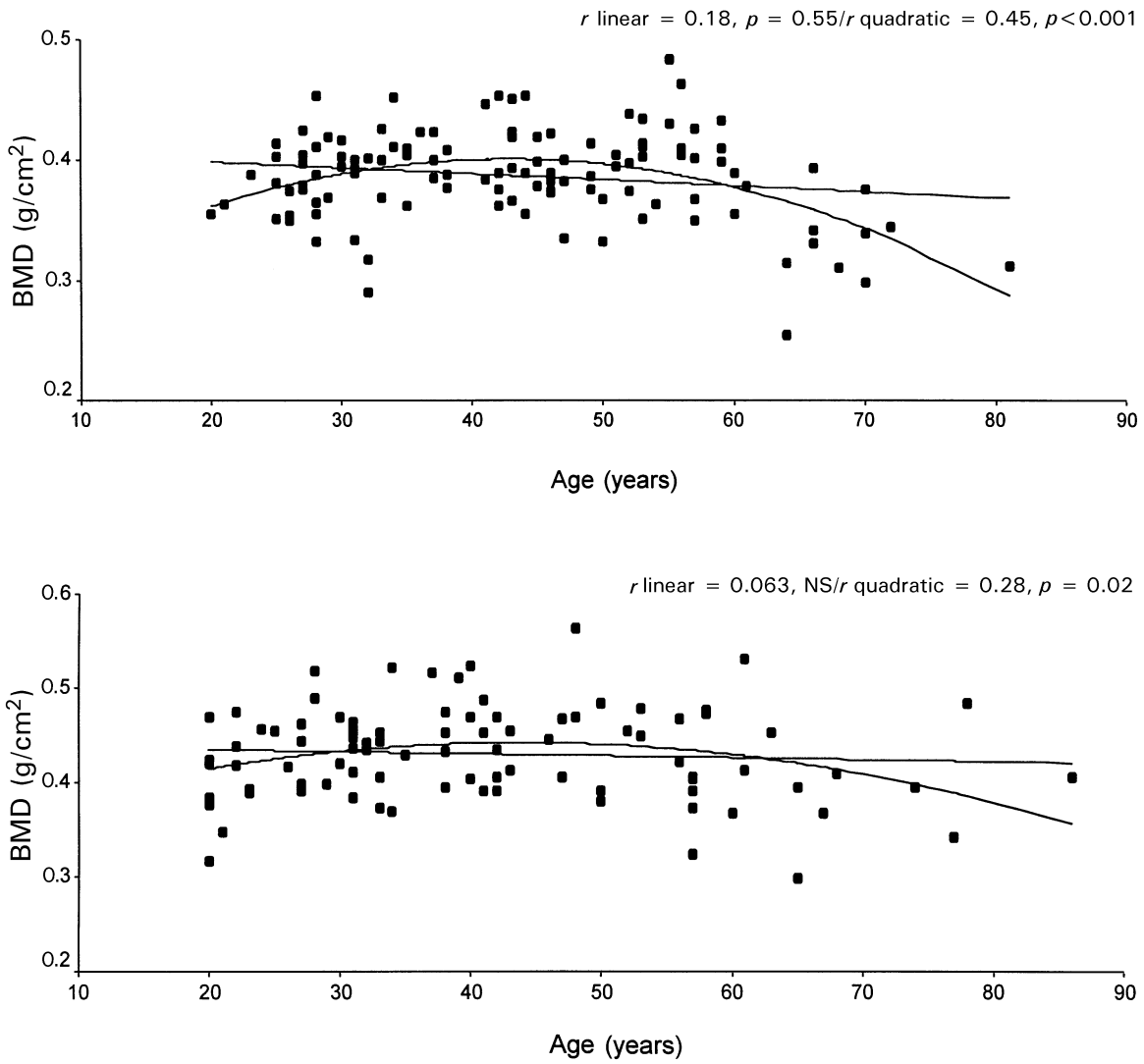

Fig. 4. Correlation of whole-hand BMD with age in a reference population of **a** women and **b** men.

of the hand with the lower BMD were analyzed. Only the correlation between disease duration and BMD of the hand was performed on the results of both hands.

The mean BMD values of RA patients were compared with those of the age-matched reference group (Table 1). The percentage difference in BMD for the entire hand as well as for the subregions were calculated. RA patients were compared with a healthy age-matched reference population (Table 3). BMD was most markedly reduced after a disease duration of 18–72 months. BMD loss was pronounced at the periarticular ROIs in both genders (women: S.CH. index and middle −23%, MCP index and middle −18%; men: S.CH. index and middle −19%, MCP index −16% and MCP middle −14%) in comparison with BMD loss at the whole hand (women: −16%; men: −12%). Additionally correlations between disease duration and BMD of both hands and the subregions were performed (Table 4). In women there was a stronger correlation between disease duration and BMD and BMD in the subchondral regions than between disease duration and whole-hand BMD; in men the correlation did not reach statistical significance.

QUS Results

Amplitude-dependent speed of sound (Ad-SOS) was measured at digits II–V at the distal metaphyses of the proximal phalanges of both hands. The mean value of these four measurements was taken into account. RA patients were compared with a young and healthy reference population aged 25–35 years. In both genders there was a significant Ad-SOS loss in patients with RA. In females the Ad-SOS loss was even pronounced in those patients with a longer disease duration (Ad-SOS: women <18 months, 2029 ± 84 m/s; women 18–72 months, 1950 ± 90 m/s; healthy women, 2137 ± 35 m/s).

Table 3. BMD values of RA patients of different disease duration compared with an age-matched healthy population

	Reference population	Disease duration <18 months (6 ± 5)	*T*-score (in SD)	Disease duration 18–69 months (38 ± 13)	*T*-score (in SD)	ΔBMD	ΔBMD**
Men							
Hand	0.42 ± 0.06	0.43 ± 0.06	–0.23	0.37 ± 0.07	–1.63	+2%	–12%‡
S.CH index	0.27 ± 0.04	0.27 ± 0.04	–0.79	0.22 ± 0.05	–2.30	0%†	–19%‡
S.CH middle	0.27 ± 0.05	0.27 ± 0.05	–0.81	0.22 ± 0.07	–2.20	0%†	–19%‡
MCP index	0.37 ± 0.05	0.36 ± 0.05	–0.88	0.31 ± 0.06	–1.70	–3%†	–16%‡
MCP middle	0.36 ± 0.06	0.35 ± 0.05	–0.88	0.31 ± 0.07	–1.75	–3%†	–14%‡
Women							
Hand	0.38 ± 0.03	0.38 ± 0.07	–0.66	0.32 ± 0.07	–2.40	0%	–16%‡
S.CH index	0.26 ± 0.04	0.23 ± 0.06	–1.20	0.20 ± 0.05	–1.90	–12%†	–23%‡
S.CH middle	0.26 ± 0.04	0.23 ± 0.05	–1.20	0.20 ± 0.06	–1.90	–12%†	–23%‡
MCP index	0.34 ± 0.04	0.33 ± 0.08	–0.60	0.28 ± 0.06	–1.70	–3%†	–18%‡
MCP middle	0.34 ± 0.04	0.33 ± 0.08	–0.86	0.28 ± 0.07	–2.20	–3%†	–18%‡

Difference is shown in % change: Δ BMD, = difference in BMD comparing healthy controls and RA patients with a mean disease duration <18 months; Δ BMD**, difference of BMD comparing healthy and RA with a mean disease duration of 18–69 months. *T*-scores are shown for the different disease durations.
BMD is given as mean values ± standard deviation (SD); disease duration is given as mean ± SD in months, S.CH., subchondral ROI; MCP, metacarpal ROI; †$p<0.05$, ‡$p<0.001$ compared to age matched controls; *T*-scores in standard deviation (SD).

Table 4. Correlation of BMD of the whole hand and different subregions with disease duration in women and men (all values are given as *r*)

	Women		Men	
	r	*p*	*r*	*p*
Hand	0.31	0.18	0.32	NS
S.CH. index	0.39	0.005	0.30	NS
S.CH. middle	0.42	0.002	0.29	NS
MCP index	0.26	0.052	0.26	NS
MCP middle	0.30	NS	0.25	NS

Table 5. Ad-SOS in women and men with RA of different disease duration compared with a young healthy reference population aged 25–35 years

	Healthy	RA	RA
Disease duration (months):		<18	18–69
Mean age (years):		54 ± 8	57 ± 14
Women			
Ad-SOS (m/s)	2137	2029*	1950*
SD	35	84	90
T-score		–3.1	–5.4
% difference		–5%	–9%
Men			
Ad-SOS (m/s)	2146	1966*	1956*
SD	41	96	87
T-score		–4.4	–4.6
% difference		–9%	–9%

T-score given in standard deviation (SD), % differences, difference in mean Ad-SOS of RA in comparison with the healthy reference population expressed as a percent change; *$p<0.05$ in comparison with the reference population.

This could not significantly be shown for men (Ad-SOS: men <18 months, 1966 ± 96m/s; men 18–72 months, 1956 ± 87 m/s; healthy men, 2146 ± 41 m/s) (Table 5).

Discussion

The data from this cross-sectional study indicate that detailed analyses of BMD hand scans allow the quantification of periarticular bone loss in both genders. Thus the subjective impression of a radiological diagnosis of periarticular osteoporosis can be specifically quantified. The degree of periarticular bone loss was pronounced in the subchondral subregions in both genders, indicating that the monitoring of patients with RA by quantifying subchondral bone loss might be superior to quantification of whole-hand bone loss, which is currently the standard examination in patients with RA. This is the first time that data have been presented on juxta-articular osteopenia at phalangeal joints of the hand in RA measured with DXA. Furthermore this paper shows normative data for hand BMD measurements.

The degree of BMD loss at the hand in early disease duration in the current cross-sectional study is comparable to that found in the studies of Deodhar et al. [5]. However, the degree of bone loss in the subregions is higher in comparison with whole-hand BMD loss in this cross-sectional study. Whether this is relevant to functional outcome or development of bone erosions in RA needs to be clarified. Furthermore it needs to be clarified in a longitudinal study whether bone loss in the subregional regions is large enough to exceed the least significant change taking the greater precision error of the subregional analyses into account. A prospective study is already in progress in our department proving the value of BMD measurements at the periarticular regions at the hand in disease monitoring and predictability of future disease activity.

Although the difference of hand BMD was seen in 32-55% of RA patients when comparing BMD measurements of the right and the left hand, this did not reach statistical significance. This might imply that hand BMD

and also BMD of the periarticular regions reflect a combined result of generalized BMD loss plus a local effect of the underlying disease. From the clinical point of view, hand BMD measurements should therefore always be performed at both hands to avoid misleading interpretation of measurement results.

The precision data of about 3% in the subregions in healthy controls indicates that the analyses of periarticular bone loss using DXA is a sufficient method for determining BMD changes in RA patients. Comparable results of in vivo precision could be shown for RA patients for DXA and QUS measurements (CV% for subregional analyses 3.9–4.2%). It should be mentioned that due to the small areas of the subregions and problems in contour finding there is an operator dependency especially concerning the analyses of the subregions. As the image resolution is not good enough to replace radiographs by DXA scans, morphology must still be analyzed with conventional radiographs.

Quantitative Ultrasound at the Proximal Phalanges of the Hand

It is demonstrated that amplitude-dependent speed of sound through the proximal phalanges significantly decreased in patients with early RA, possibly due to changes in cortical and trabecular structure (periarticular osteoporosis). As SOS characterizes bone as a constant of the material through which the signal is conducted, changes in SOS allow the presumption that the material has changed. It could be suggested that SOS changes in RA signify changes towards, for example, regional osteomalacia.

Unfortunately, due to the small number of age- and sex-matched controls, QUS results were compared with reference data obtained in young and healthy controls aged 25–35 years. It must be pointed out that the calculation of *T*-scores is not yet a validated method for ultrasound data. Still, in the study under way the QUS data will be compared with an age-matched reference population, proving in a larger population whether the Ad-SOS loss is due only to age-related changes or, as stated, is disease-related. In a previous study it was shown that there is a strong age dependency of Ad-SOS [11].

The analyses on RA patients with different disease durations showed different results in the two genders. For QUS data in men no dependency of AD-SOS results on disease duration could be shown. This is surprising as the bone loss quantified by DXA significantly differed in these two subgroups and showed a dependency on disease duration. It should therefore be clarified in prospective studies whether these differences between QUS and DXA measurement results in men and women are sex-specific in patients with RA or whether the two different techniques reflect different bone entities. This again would stress that QUS and DXA quantify partially different bone ‘qualities’ and not BMD exclusively. In this context the documented moderate correlation between BMD and QUS measurements could be seen which confirms existing cross-sectional data [11,12].

Studies in pigs have demonstrated that SOS values at the phalanges are dependent on structural characteristics of the bone which partially reflect cortical bone [13]. In general, for SOS measurements through bone a linear dependency of velocity on the apparent density of the bone [14] and a dependency on the elasticity modulus [15] were detected. Furthermore velocity appeared to be a predictor of bone strength in vitro [16].

Whether QUS at the proximal phalanges is more sensitive to changes in bone during the course of therapy and duration of disease in RA compared with DXA measurements has to be clarified with a prospectively designed study which is already in progress. Further studies comparing techniques for noninvasive assessment of the skeleton should prove whether early RA may serve as an in vivo model for the examination of structural changes of bone and its relationship to BMD and QUS measurements.

In conclusion, this cross-sectional study demonstrates that BMD and QUS measurements at the proximal phalanges show significantly lower values in patients with early RA. Given the early bone loss in patients with RA, which is known as juxta-articular osteoporosis, regions of interest set in these areas might serve for the quantification of periarticular bone loss. As methods using radiographs should not be unnecessarily repeated, the maximum information should be achieved from one examination. This examination should include the subregion analyses of DXA scans of the hands.

QUS possibly gives information on structural changes in bone affected by RA. Larger studies should compare measurements in RA patients with those in age- and sex-matched controls. Prospective studies should prove whether the analyses of periarticular ROIs are superior to whole-hand BMD scans in the monitoring of antirheumatic therapy and the prediction of future disease activity, and whether the combination of QUS and DXA measurements might lead to a more comprehensive bone assessment in RA.

References

1. Gough AKS, Lilley J, Eyre S, Holder RL, Emery P. Generalised bone loss in patients with early rheumatoid arthritis. Lancet 1994;344:23–7.
2. Sambrook PN, Eisman JA, Champion GD, Yeates MG, Pocock NA. Determinants of axial bone loss in rheumatoid arthritis. Arthritis Rheum 1987;30:721–8.
3. Shenstone BD, Mahmoud A, Woodward R, Elvins D, Palmer R, Ring EF, et al. Longitudinal bone mineral density changes in early rheumatoid arthritis. Br J Rheumatol 1994;33:541–5.
4. Hansen M, Florescu A, Stoltenberg M, Pødienphant J, Pedersen-Zbinden B, Hørslev-Petersen K, et al. Bone loss in rheumatoid arthritis. Scand J Rheumatol 1996;25:367–76.
5. Deodhar AA, Brabyn J, Jones PW, Davis MJ, Woolf AD. Longitudinal study of hand bone densitometry in rheumatoid arthritis. Arthritis Rheum 1995;38:1204–10.

6. Peel NFA, Spittlehouse AJ, Bax DE, Eastell R. Bone mineral density of the hand in rheumatoid arthritis. Arthritis Rheum 1994;37:983–91.
7. Hill CL, Cleland LG, Schultz C, Chatterton BE, Pile KD. Measurement of hand bone mineral density in early rheumatoid arthritis using dual-X-ray absorptiometry (DEXA). Arthritis Rheum 1997;9(Suppl):S324.
8. Green MJ, Proudman S, Stewart S, Wakefield RJ, McGonagle D, Smith MA, et al. Serial hand bone densitometry with Lunar-XL densitometer in the assessment of patients with very early inflammatory arthritis. Arthritis Rheum 1997;9(Suppl):S292.
9. Rau R, Wassenberg S, Herborn G, Stucki G, Gebler A. A new method of scoring radiographic change in rheumatoid arthritis. J Rheumatol 1998;25:2094–107.
10. Glüer C-C, Blake G, Lu Y, Blunt BA Jergas M, Genant HK. Accurate assessment of precision errors: how to measure the reproducibility of bone densitometry techniques. Osteoporos Int 1995;5:262–70.
11. Alenfeld FE, Wüster C, Beck C, Pereira-Lima JFS, Fritz T, Meeder P-J, Ziegler R. Ultrasound measurements at the proximal phalanges in healthy and patients with hip fractures. Osteoporos Int 1998;8:393–8.
12. Sili-Scavalli A, Marini M, Spadaro A, Messineo D, Cremona A, Sensi F, et al. Ultrasound transmission velocity of the proximal phalanxes of the non-dominant hand in the study of osteoporosis. Clin Rheumatol 1997;16:396–403.
13. Cadossi R, Cane V. Pathways of transmission of ultrasound energy through the distal metaphysis of the second phalanx of pigs: an in vitro study. Osteoporos Int 1996;6:196–206.
14. Tavakoli MB, Evans JA. Dependence of the velocity and attenuation of ultrasound in bone on the mineral content. Phys Med Biol 1991;36:1529–37.
15. Ahsman RB, Rho JY, Turner CH. Anatomical variation of orthotropic elastic moduli of the proximal human tibia. J Biomech 1989;22:859–900.
16. Turner CH, Eich M. Ultrasonic velocity as a predictor of strength in bovine cancellous bone. Calcif Tissue Int 1991;49:116–9.

Received for publication 2 February 1999
Accepted in revised form 25 October 1999