Osteoporos Int (2000) 11:953–958

Osteoporosis International

Original Article

Metacarpal Morphometry Using a Semi-automated Technique in the Assessment of Osteoporosis and Vertebral Fracture Risk

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Abstract. Metacarpal morphometry represents a potentially cheap and widely available non-invasive assessment of skeletal status. In two cross-sectional studies, we compared the performance characteristics of a semi-automated technique (the Teijin Bonalyzer) with an in-house manual measurement, and with measures of skeletal strength at other sites. The metacarpal cortical index (mCI) was measured on hand radiographs of 178 osteoporotic women using both the Teijin Bonalyzer and a digitizing tablet. Measurements on the latter were consistently lower than with the Bonalyzer except for mCI (0.443 $\pm$ 0.080 vs 0.364 $\pm$ 0.060, $p<0.001$), although correlation coefficients between these two methods were highly significant (r = 0.62–0.83, $p<0.001$). The reproducibility errors of metacarpal bone mineral density (mBMD) were constant (1.1–1.2%) whilst those for mCI showed a marked operator-dependency (2.0–7.9%). In 379 elderly community-dwelling women, Bonalyzer mCI and mBMD showed a significant decline with age (r = -0.30 and -0.27 respectively, $p<0.05$). Both mCI and mBMD correlated significantly with forearm BMD (r = 0.50 and 0.57 respectively, $p<0.001$) and hip BMD (r = 0.48 and 0.53 respectively, $p<0.001$). After adjustment for age and weight, hip BMD demonstrated the best discrimination for prevalent vertebral fractures as judged by the gradient of risk for a 1 SD decrease in measurement (odds ratio (OR) 2.17, 95% CI 1.56–3.01). Similar but smaller gradients of risk were shown by Bonalyzer mCI (OR 1.32, 95% CI 1.00–1.75), mBMD (OR 1.35, 95% CI 1.02–1.78) and forearm BMD (OR 1.39, 95% CI 1.08–1.80). MCI, and in particular mBMD, may be useful assessments of bone mass and fracture risk. In our study, it is comparable to peripheral assessment of skeletal status by forearm densitometry.

Keywords: Bone mineral density; Metacarpal morphometry; Osteoporosis; Semi-automated; Vertebral fracture

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Introduction

Metacarpal morphometry and radiogrammetry for the non-invasive assessment of skeletal status was first described by Barnett et al. [1] in 1960 and remained largely unchanged until the introduction of the 'six metacarpal hand index' by Horsman et al. [2] in 1975. Metacarpal radiogrammetry has had limited use in the evaluation of osteoporosis [3–6] as well as rarer diseases of bone such as osteogenesis imperfecta [7], Klinefelter's syndrome [8] and algodystrophy [9]. Its popularity declined with the development of apparently more sophisticated techniques such as single (SXA) and dual (DXA) energy X-ray absorptiometry [10–13], and more recently ultrasound attenuation and velocity [14–16]. However, the availability of assessments of bone mass and fracture risk remains limited [17], and there is a need for alternative methods of assessing bone strength which incur lower costs and have wider accessibility in the general community.

Metacarpal radiogrammetry has the potential to fulfill these criteria but traditional radiogrammetry has been a

tedious and time-consuming task with the measurement of metacarpal cortical bone widths being undertaken using fine needle callipers and hand radiographs [1,2]. Semi-automated methods have recently been developed to increase the speed of analysis and to allow the combination of traditional metacarpal morphometry with the measurement of cortical bone density [18–20].We have compared one of these new methods (the Teijin Bonalyzer) with measurements determined by our own in-house semi-automated method using a digitizing tablet. We wished to determine whether such measurements were sufficiently reproducible for clinical use, and to examine the relationships with other biological variables including age and bone mineral density (BMD) at other skeletal sites. Finally, we wished to compare the ability of metacarpal measurements and other skeletal assessments to discriminate between women with and without vertebral fracture.

Materials and Methods

Patients

For comparison of the Teijin Bonalyzer and our own in-house semi-automated technique, we used hand radiographs from 178 women with either postmenopausal (137 patients) or secondary (predominantly corticosteroid-induced) osteoporosis (41 patients) at entry to a clinical study of vertebral osteoporosis (mean age 70 years). Osteoporosis was defined as the presence of one or more atraumatic vertebral fractures on lateral spine radiographs as detected by morphometry [21] and/or a spine BMD more than 2.5 SD below the mean BMD in the young, healthy female population. Short-term reproducibility was determined by paired measurements of metacarpal length, cortical and medullary width and mCI in single hand radiographs obtained in these women (see below). In addition, the Bonalyzer allows evaluation of mBMD and the reproducibility for this was also assessed.

Correlation with biological variables and the relationships to vertebral fracture were studied in a separate set of 379 elderly women (aged 75 years or more) recruited at random from the local population in South Yorkshire. The women were studied at entry to a double-masked placebo-controlled trial to determine the efficacy of the bisphosphonate clodronate to reduce bone loss at the hip. Women with concurrent medication or diseases that might influence skeletal metabolism or the interpretation of results were excluded.

In both study populations, standing height was measured using a Harpenden stadiometer. Each individual was weighed and the body mass index computed as weight/height^2. Measurements of skeletal status were obtained as described below. This study had the approval of our local ethics committee and all patients gave informed consent.

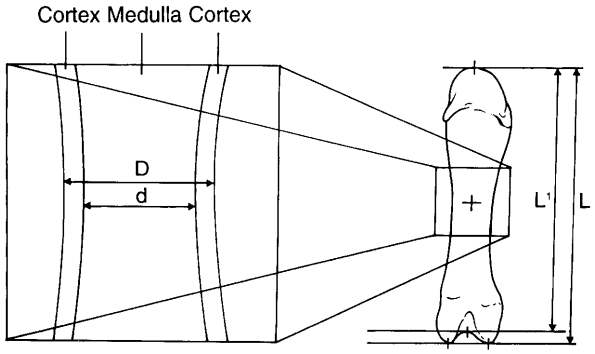

Fig. 1. Metacarpal length (L and L^1), medullary diameter (d), and cortical diameter (D) as measured using the Teijin Bonalyzer and digitizing tablet, respectively.

Metacarpal Bone Mineral Density (mBMD)

Hand radiographs were obtained by placing both hands flat on an X-ray plate. An aluminum step wedge was positioned between the hands at the time of radiography. Measurements of optical density were obtained using the Bonalyzer (supplied by Teijin Corporation, Japan). The equipment combines an image sensor with a microprocessor and automatically corrects for any variation in density between radiographs. This permits a comparison to be made between the optical density of the aluminum step wedge and the region of interest on the hand radiograph. The region of interest was defined as the mid-point of the second metacarpal of the right hand and identified by computer from the placement by the operator of a cursor at each of three points on the second metacarpal (Fig. 1). The points corresponded to the center of the arc of the head of the metacarpal and the lowest point of each of the bony protruberances at its base. The mBMD was then estimated by a fully automated comparison of the optical density of the aluminum step wedge with that of the region of interest.

Metacarpal Cortical Index (mCI)

The metacarpal cortical index (mCI) was derived by two methods. Firstly as part of the automated analysis by the Teijin Bonalyzer the total length of the second metacarpal was recorded (L) and the midpoint determined. The Bonalyzer detects changes in density by comparison with the aluminum step wedge and constructs a cross-sectional density map (Fig. 2). Using this map, the Bonalyzer determines the total width of the second metacarpal (D) at its mid-point and the width of the medullary cavity (d). The periosteal edge is detected as the first point at which the density increases above a threshold white gradient. The interface between cortex and medulla is taken as the maximum peak in density. If there are multiple maximum peaks, the peak nearest the medulla is selected. The mCI was automatically calculated as (D − d)/D.

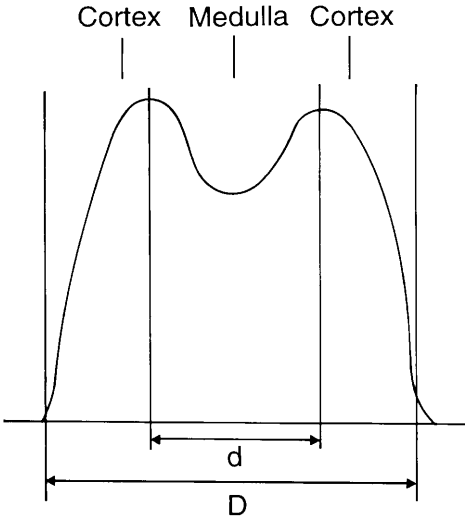

Fig. 2. Metacarpal medullary and cortical diameters (d and D respectively) as measured using the Teijin Bonalyzer. The Bonalyzer differentiates between cortex and medulla on the basis of cross-sectional density at the metacarpal midpoint.

The measurements of metacarpal and medullary diameter were also undertaken by a manual method whereby the hand radiograph was placed on a rear-illuminated digitizing tablet and two points placed on the second right metacarpal in a similar fashion to that in the Teijin analysis using a cross-wire cursor (Fig. 1). Using the coordinates of these points, the total length (L^1) and the mid-point (M^1) of the metacarpal were determined automatically. The operator then dragged the cursor along the outer (periosteal) and inner (endosteal) edge of the radial and ulnar cortices of the metacarpal (Fig. 1). The coordinates of each cortex edge were determined automatically as the cursor passed the metacarpal mid-point and were used to compute the metacarpal (D^1) and medullary diameters (d^1). These measurements were automatically recorded on a computer database and the mCI was subsequently computed $[(D^1 - d^1)/D^1]$.

Bone Density Measurements

BMD was measured in all patients at the distal and ultradistal radius using single X-ray absorptiometry (DTX-100, Osteometer, CA) and at the nondominant hip (usually the right hip) using dual-energy X-ray absorptiometry (QDR2000plus, Hologic, Bedford, MA). Standardized lateral radiographs of the thoracic and lumbar spine were obtained for vertebral morphometry to determine the presence of vertebral deformities by a technique described previously [21].

Statistics

Three operators (R.C., T.T., L.R.) were used in this study. Inter-observer and intra-observer reproducibility were calculated as the coefficient of variation using the formula for paired observations. For mCI, comparison between values obtained by the Bonalyzer and the manual method were examined using the paired *t*-test. The relationship between each of the measurements obtained by both methods was examined by linear regression.

The subsequent analysis of the relationship with other skeletal measurements and fracture discrimination used only the measurements derived by the Teijin Bonalyzer. The relationships between mBMD and mCI and other variables including age, height, weight, body mass index (BMI) and bone density at other sites were examined using linear regression. Differences between women with and without vertebral fracture were examined by one-way analysis of variance. The gradient of risk for each of the skeletal measurements and prevalent vertebral fractures was compared using the odds ratio for a 1 SD decrease in each of the measurements. The mean and SD were derived from the women without evidence of vertebral fracture and these values were used to convert measured values to SD units in all subjects. The odds ratio was computed as the natural exponent of the coefficient derived using logistic regression analysis to allow adjustment for age and other relevant variables.

Results

Reproducibility and Comparison of mCI between Bonalyzer and Digitizing Tablet

In the 178 women with postmenopausal or secondary osteoporosis, there were systematic differences between the absolute measurements on the Bonalyzer and digitizing tablet (Table 1). The length of the metacarpal was less on the digitizing tablet, reflecting the difference in the point placements at the base of the metacarpal (Fig. 1). In addition, the mean metacarpal diameter and the mean width of the medullary cavity were significantly smaller using the digitizing tablet. The reduction in width of the medullary cavity was more marked, however, leading to a larger mCI using the manual method compared with the Bonalyzer (0.443 ± 0.080 vs 0.363 ± 0.060, $p<0.001$). Correlation coefficients between measurements obtained in the same set of radiographs using the Bonalyzer and the digitizing tablet were compared in those women with established

Table 1. Comparison of the metacarpal cortical index (mCI), cortical width (D), medullary width (d) and length (L) (mean $\pm$ SD) made on the second metacarpal by the Bonalyzer and on the same films using a digitizing tablet

	Bonalyzer (A)	Digitizing tablet (B)	Difference (B − A)
mCI	0.364 ± 0.060	0.443 ± 0.080	0.079 ± 0.054
D (mm)	9.025 ± 0.652	8.520 ± 0.736	-0.505 ± 0.360
d (mm)	5.751 ± 0.746	4.749 ± 0.869	-1.001 ± 0.451
L (mm)	66.595 ± 3.444	63.915 ± 3.371	-2.680 ± 1.080

All differences are highly significant ($p<0.001$).

Table 2. Intra-observer and inter-observer reproducibility errors (CV%) for the Bonalyzer and the digitizing tablet method in assessment of metacarpal cortical index (mCI) and bone mineral density (mBMD), cortical (D) and medullary width (d), and length (L) at the second metacarpal

	Bonalyzer				Digitizing tablet
	Intra-observer 1	Intra-observer 2	Inter-observer 1 vs 3	Inter-observer 2 vs 3	Intra-observer 3
mBMD	1.07	1.18	1.19	0.99	–
mCI	7.92	2.02	8.42	7.21	9.37
D	0.62	0.41	0.51	0.53	4.34
d	4.71	1.16	5.06	4.61	10.36
L	1.04	0.67	0.98	1.07	0.70

osteoporosis. The correlation coefficients were 0.62 for mCI, 0.83 for metacarpal length, 0.75 for medullary width and 0.70 for metacarpal width, and all were highly significant ($p<0.001$).

The measurement of BMD at the mid-point of the second right metacarpal (mBMD) was highly reproducible, with intra-observer and inter-observer coefficients of variation ranging from 0.99% to 1.19% (Table 2). The reproducibility errors of mBMD appear to be constant both within and between operators. In contrast, the reproducibility errors of mCI and the measurements used in its derivation showed a marked operator-dependency. Low reproducibility errors for point placements, as reflected in low errors in metacarpal length, appear to have a marked effect on the mCI as evidenced by the better repeatability of metacarpal length for operator 2.

The reproducibility errors for mCI and metacarpal length derived on the digitizing tablet were comparable with those derived on the Bonalyzer (Table 2). However, the errors for the metacarpal and medullary diameters appear to be greater using the manual method.

Correlation with Biological Variables

The mean age of the 379 elderly women included in the studies of biological correlates and discriminatory value was 80 $\pm$ 4.4 years. Vertebral deformities were detected using vertebral morphometry in 84 (22%) of the women.

In the whole group, both Bonalyzer mBMD and mCI showed a significant decline with age ($r = -0.27$ and -0.30, $p<0.005$) (Table 3). The correlation with age was similar to that observed between age and BMD of the forearm ($r = -0.20$, $p<0.005$) and the hip ($r = -0.27$, $p<0.005$). Body weight correlated positively with mCI ($r = 0.19$, $p<0.005$) and to a similar extent with mBMD ($r = 0.24$), $p<0.005$). Similar associations were observed between body weight and measurements at other skeletal sites, particularly the hip ($r = 0.49$, $p<0.001$). Height was significantly but weakly correlated with several of the measurements including mBMD ($r = 0.21$, $p<0.005$) but not mCI (Table 3).

Table 3. Correlation coefficients for metacarpal bone mineral density (mBMD) and cortical index (mCI), and other skeletal assessments with age, height and weight in an elderly female population. Values in parentheses represent the mean annual percentage change in measurements estimated from the slope of the regression line and the mean population value

	Age (years)	Weight (kg)	Height (cm)
mBMD [Bonalyzer] (g/cm^2)	-0.27** (-1.0%)	0.24**	0.21**
mCI [Bonalyzer]	-0.30** (-1.2%)	0.19**	0.08
Total hip BMD (g/cm^2)	-0.27** (-1.2%)	0.49**	0.24**
Distal forearm BMD (g/cm^2)	-0.20** (-1.1%)	0.28**	0.16**

*$p<0.05$; **$p<0.005$.

Both mBMD and mCI correlated significantly with BMD at the forearm and hip. Correlation coefficients for mBMD and mCI with forearm BMD were 0.57 and 0.50 respectively ($p<0.001$). Similar correlations were observed between mBMD and mCI with total hip BMD ($r = 0.53$ and 0.48 respectively, $p<0.001$).

Relationship to Vertebral Fracture Risk

Women with vertebral deformity were significantly older than those without deformity (81.1 $\pm$ 5.0 vs 79.7 $\pm$ 4.2 years, $p<0.011$). They were also shorter (153.3 $\pm$ 6.4 vs 155.2 $\pm$ 6.0 cm, $p<0.014$) and weighed less (60.0 $\pm$ 11.0 vs 64.5 $\pm$ 11.3 kg, $p<0.001$). Mean values for mBMD and mCI were significantly lower in the women with vertebral deformity compared with those without deformity (mBMD 2.05 $\pm$ 0.33 vs 2.20 $\pm$ 0.35, $p<0.001$; mCI 0.346 $\pm$ 0.055 vs 0.369 $\pm$ 0.061, $p<0.003$) (Table 4). Mesurements of BMD at the forearm and hip were also significantly lower in the patients with deformity (Table 4).

All measurements showed a significant gradient of risk for prevalent vertebral fracture. The odds ratio (OR) ranged from 1.50 (95% CI 1.15–1.95) for mCI to 2.25 (95% CI 1.68–3.01) for total hip BMD (Table 5). Following adjustment for age and weight for the whole population of 379 women, total hip BMD remained the

Table 4. Characteristics of elderly women with and without vertebral deformity on lateral spine radiographs (mean $\pm$ SD). Metacarpal bone mineral density (mBMD) and cortical index (mCI) are assessed on the Bonalyzer

	Vertebral deformity (n = 84)	Without vertebral deformity (n = 295)	p value
Age (years)	81.1 $\pm$ 5.0	79.7 $\pm$ 4.2	0.011
Height (cm)	153.3 $\pm$ 6.4	155.2 $\pm$ 6.0	0.014
Weight (kg)	60.0 $\pm$ 11.0	64.5 $\pm$ 11.3	0.001
mBMD [Bonalyzer] (g/cm^2)	2.05 $\pm$ 0.33	2.20 $\pm$ 0.35	0.001
mCI [Bonalyzer]	0.346 $\pm$ 0.055	0.369 $\pm$ 0.061	0.003
Total hip BMD (g/cm^2)	0.629 $\pm$ 0.132	0.734 $\pm$ 0.130	<0.001
Forearm BMD (g/cm^2)	0.292 $\pm$ 0.079	0.328 $\pm$ 0.076	<0.001

Table 5. Gradient of risk (expressed as an odds ratio with 95% confidence intervals) for the increase in risk of vertebral deformity for a 1 SD decrease in each of the measurements. Metacarpal bone mineral density (mBMD) and cortical index (mCI) are assessed on the Bonalyzer

	Odds ratio[a]	95% CI[a]	Odds ratio[b]	95% CI[b]
Total hip BMD (g/cm^2)	2.25	1.68–3.01	2.17	1.56–3.01
Forearm BMD (g/cm^2)	1.53	1.20–1.95	1.39	1.08–1.80
mBMD [Bonalyzer] (g/cm^2)	1.53	1.18–1.99	1.35	1.02–1.78
mCI [Bonalyzer]	1.50	1.15–1.95	1.32	1.00–1.75

[a] Unadjusted for age and weight.
[b] Adjusted for age and weight.

best discriminator amongst the methods used, with an OR of 2.17 (95% CI 1.56–3.01). The adjusted OR for Bonalyzer mBMD was 1.35 (95% CI 1.02–1.78) whilst mCI retained borderline significance (OR 1.32, 95% CI 1.00–1.75). Both these measurements were comparable to forearm BMD (OR 1.39, 95% CI 1.08–1.80).

Discussion

In this study we have assessed the performance characteristics of a semi-automated method (Teijin Bonalyzer) to evaluate mCI and mBMD. The results suggest that metacarpal assessments, particularly mBMD, have comparable performance to other peripheral assessments of bone strength.

mCI has been demonstrated in several studies to be associated with bone mass at other skeletal sites and fracture risk [4,22,23]. Measurement of mCI by the Bonalyzer and our in-house system shows similar errors of reproducibility. As expected from the differing point placements between the two methods, there is a systematic difference in metacarpal length. However, whilst this difference in length may contribute to the systematic differences in medullary and metacarpal diameter, its magnitude (approximately 1.3 mm between the two midpoint estimates) is probably too small to account for all the differences in mCI. As described above, the Bonalyzer differentiates between soft tissue, cortex and medulla using thresholds and peaks in density. Our observations suggest that there are systematic differences in the abilities of the Bonalyzer and the human eye to detect these interfaces. The differences between the Bonalyzer mCI and the manual measurements were greatest for the medullary width, leading to significantly smaller values for mCI on the Bonalyzer. This may relate to the fact that the Bonalyzer selects the maximum cortical peak to determine the limits of the medulla while the manual operator selects the visually detected edge between cortex and medulla. The difficulty in identifying the relatively indistinct endosteal margin (compared with the sharp change in density at the periosteal margin) is reflected by the reproducibility errors, which are greatest for medullary width in both techniques.

The reproducibility errors are comparable for mCI using either method, and comparable to those in the literature [1,24–26]. In contrast, mBMD is more reproducible than mCI, possibly due to lower operator-dependency than mCI. However, simple comparisons of reproducibility errors may be misleading. For example a measurement may be highly reproducible but show a very small variation within the population. In such a circumstance, the ability to stratify an individual within the population would be limited, as would the ability to detect change over time. From Table 4, it can be seen that the population standard deviation, expressed as a percentage of the mean population value, is comparable for both mCI (15.9%) and mBMD (16.1%) in women without fracture. The ratio between the population SD and the reproducibility error is greater for mBMD (14.5 and 13.3 for operator 1 and 2 respectively) than for mCI (2.0 and 8.0 for operator 1 and 2 respectively). The larger ratio, comparable but not identical to the standardized coefficient of variation [27], suggests that mBMD may prove a more useful measure to stratify individuals within the population than mCI. Furthermore, analysis of the change in mBMD and mCI with age gives an annual decrease of approximately 1% for both, as shown in Table 3. The higher reproducibility errors for mCI suggest that an individual would need to be followed for 5–22 years to detect a significant change in mCI. The comparable figure for mBMD is approximately 3 years. These observations suggest that mBMD may be a more useful clinical tool, but either measure may be too inaccurate in assessing bone loss over time.

In the evaluation of BMD and vertebral fracture risk, total hip BMD remained the best predictor after adjustment for age and weight. It is well established that absorptiometry at the forearm correlates significantly with absorptiometry at the hip [28,39] but the correlation is not close enough to be predictive. More importantly, longitudinal studies show that forearm BMD is a significant predictor of fracture risk [30]. Our study confirms the significant correlation between metacarpal assessments and BMD at both local (forearm) and distant sites [26], suggesting that the metacarpal assessments, and mBMD in particular, are comparable to the more established assessment of forearm BMD. The relatively low odds ratios derived for metacarpal and forearm measurements in our study (1.3–1.4) suggest that these measurements would be of little use when used in isolation for the management of osteoporosis. It is likely that they should be used in combination with other BMD-independent risk factors to identify patients at high risk of fracture. Prospective studies of fracture risk are required in combination with assessment of the long-term reproducibility of the technique in separate radiographs from the same patient.

The equipment of hip densitometry is expensive, bulky and infrequently found outside specialized centers [17], whereas metacarpal morphometry is potentially

available to any institution with access to conventional radiographic equipment. The Bonalyzer is not commercially available outside Japan, but it is likely that the purchase costs of comparable equipment would be similar to or less than either ultrasound or forearm densitometry. Although there is the cost of a hand radiograph to consider, the point placement is straightforward and rapid (approximately 2 min), so that it may be performed by the radiographer, obviating the need for a specially trained operator. The operating costs are therefore likely to compare favorably with other techniques.

We conclude that metacarpal cortical index, and in particular metacarpal BMD, may be useful assessments of bone mass and fracture risk. In our study it performs less well than hip BMD, but is comparable to another peripheral assessment of skeleton. Furthermore, the automated analysis is both reproducible and highly applicable. Although metacarpal morphometry may have a role as a screening tool in osteoporosis [4,31], its precise role as a management tool requires prospective evaluation.

Acknowledgements. Many thanks to Linda Reaney (L.R.) at the WHO Collaborating Centre for Metabolic Bone Diseases, University of Sheffield Medical School, and Pat Elliot in Medical Illustration, Royal Hallamshire Hospital, Sheffield. This study received a grant from Teijin Corporation, Japan.

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Received for publication 22 February 2000
Accepted in revised form 6 June 2000