

Long-term in-vitro precision of direct digital X-ray radiogrammetry

Alvilde Dhainaut · Mari Hoff · Johan Kälvesten ·
Stian Lydersen · Kristina Forslind · Glenn Haugeberg

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Abstract

Objective Digital X-ray radiogrammetry (DXR) calculates peripheral bone mineral density (BMD) from hand radiographs. The short-term precision for direct DXR has been reported to be highly satisfactory. However, long-term precision for this method has not been examined. Thus, the aim of this study was to examine the long-term in-vitro precision for the new direct digital version of DXR.

Materials and methods The in-vitro precision for direct DXR was tested with cadaver phantoms on four different X-ray systems at baseline, 3 months, 6 months, and in one machine also at 12 months. At each time point, 31 measurements were performed.

Results The in-vitro longitudinal precision for the four radiographic systems ranged from 0.22 to 0.43% expressed as coefficient of variation (CV%). The smallest detectable

difference (SDD) ranged from 0.0034 to 0.0054 g/cm².

Conclusions The in vitro long-term precision for direct DXR was comparable to the previous reported short-term in-vitro precision for all tested X-ray systems. These data show that DXR is a stable method for detecting small changes in bone density during 6–12 months of follow-up.

Keywords Digital X-ray radiogrammetry · Precision · Rheumatoid arthritis · Osteoporosis · Bone mineral density

Introduction

Bone densitometry is central for the diagnosis and management of osteoporosis. Several methods for measurement of

A. Dhainaut (✉) · M. Hoff · G. Haugeberg
INM, Rheumatology, Norwegian University of Science and
Technology, MTS, 7489 Trondheim, Norway
e-mail: alvilde.dhainaut@ntnu.no

M. Hoff
e-mail: mari.hoff@ntnu.no

G. Haugeberg
e-mail: glenn.haugeberg@sshf.no

A. Dhainaut · M. Hoff
Department of Rheumatology, St. Olav's Hospital,
Trondheim, Norway

J. Kälvesten
Sectra, Linköping, Sweden
e-mail: johan.kalvesten@sectra.se

S. Lydersen
Unit for Applied Clinical Research,
Department of Cancer Research and Molecular Medicine,
Norwegian University of Science and Technology,
Trondheim, Norway
e-mail: stian.lydersen@ntnu.no

K. Forslind
Section of Rheumatology,
Helsingborgs Lasarett, Helsingborg, Sweden
e-mail: kforslind@hotmail.com

K. Forslind
Section of Rheumatology at the Institution of Clinical Science,
University Hospital, Lund, Sweden

G. Haugeberg
Department of Rheumatology, Sørlandet Hospital,
Kristiansand S, Norway

peripheral bone density have been developed including the digital X-ray radiogrammetry (DXR). DXR calculates BMD at metacarpal hand bones from digital radiographs. DXR-measured bone density has been shown to be a good predictor of fractures [1, 2] and in rheumatoid arthritis (RA) to be a sensitive measure of inflammatory bone involvement [3, 4].

The ability to monitor change is dependent upon the longitudinal reproducibility (precision). The short-term reproducibility for DXR, both in vitro and in vivo has been reported to be in the range 0.14 to 0.30 expressed as coefficient of variation (CV) [5]. For long-term follow-up, uncorrected equipment drift may have a significant impact on the accuracy and precision of the measurements [6]. Long-term precision for the DXR method has previously not been studied. Thus our aim was to explore the long-term in-vitro reproducibility for DXR-hand BMD.

Materials and methods

Direct DXR calculates BMD from digital hand radiographs, which is a further development of DXR [7, 8], a computer version of the traditional radiogrammetry technique [9]. All the digital radiographs were analyzed by the same computer software program, the online service of the manufacturer (DXR-online, Sectra, Linköping, Sweden). To measure online DXR-BMD, the system requires hand radiographs from a digitized X-ray system with known resolution. The computer automatically identifies regions of interest (ROI) around the narrowest part of the second, third, and fourth metacarpal bones on hand radiographs and measures cortical thickness, bone width, and porosity in the region. DXR-BMD is defined as: $c \times VPA_{\text{comb}} \times (1-p)$, where c is a density constant, VPA is volume per unit area, and p is porosity.

The long-term in-vitro precision for direct DXR was tested on four different X-ray systems from different manufacturers located at three different centers (Kristiansand and Trondheim in Norway and Helsingborg in Sweden). We used three different cadaver forearm phantoms for the in-vitro precision test, one at each center. For all four X-ray systems the phantom hand DXR-BMD was measured 31 times with repositioning of the phantom between each radiograph. This procedure was performed at baseline, 3 months, 6 months, and in Kristiansand also after 12 months. The following X-ray systems (computed radiography (CR)/ digital radiography (DR); film focus distance (FFD); tube voltage; exposure dose) were tested: in Kristiansand Fuji FCR XG1 (Fujifilm Corporation, Tokyo; Japan) (CR, 100 cm; 50 kV; 5 mAs), in Trondheim Agfa ADC Compact plus (Agfa-Gevart N.V., Mortsel, Belgium) (CR, 100 cm; 50 kV; 5 mAs) and in Helsingborg we tested both the Fuji FCR Profect (Fujifilm Corporation, Tokyo; Japan) (CR, 100 cm, 40 kV; 8 mAs) and

Sectra MicroDose D40 (Sectra, Linköping, Sweden) (DR, 66 cm built-in; 35 kV; 10 mAs) (Table 1).

The X-ray systems were in clinical use at the different hospitals with their own maintenance and quality assurance (QA) procedures. The X-ray tube of the Sectra MicroDose was changed between baseline and 3 months.

Statistics

Precision measures were estimated separately for each of the four X-ray systems. At each time point j we measured the short-term precision in terms of the standard deviation $SD = \sqrt{\sum_{i=1}^{n_j} (x_{ij} - \bar{x}_{.j})^2 / (n_j - 1)}$, and the coefficient of variation $CV\%_{\text{shortterm}} = (SD/\bar{x}_{.j}) \times 100$. To estimate the long-term precision, we used an extension of the traditional Bland–Altman method, a one-way ANOVA random effects model, $x_{ij} = \mu + A_j + \varepsilon_{ij}$ where the two last terms have standard deviations σ_A and σ_ε , and represent between follow-up and within follow-up variation, respectively. This gives $CV\%_{\text{longterm}} = \sqrt{\sigma_A^2 + \sigma_\varepsilon^2} / \bar{x}_{\text{total}}$. The smallest detectable difference (SDD) was identified using the Bland–Altman 95% limits of agreement method [10] with $SD_{\text{diff}} = \sqrt{2\sigma_A^2 + 2\sigma_\varepsilon^2}$. Since this is a phantom measurement, no true change is expected, thus d is expected to be 0 and $SDD = 1.96SD_{\text{diff}}$.

Statistical analyses were performed with SPSS version 15 (SPSS Inc., Chicago, IL, USA) and Excel (Microsoft Office, Microsoft Corporation, Redmond, WA, USA).

Results

The mean BMD values for the tested phantoms and the in-vitro precision data ($CV\%_{\text{short term}}$, SD, $CV\%_{\text{long term}}$ and SDD) for the four X-ray systems are shown in Table 1.

The $CV\%_{\text{long term}}$ ranged from 0.22 to 0.43%. The precision data for Fuji FCR XG1 system in Kristiansand remained stable also over the 12-month period: $CV\%$ 0.35 and SDD 0.0046 g/cm² both after 6 months and 12 months. Among the four systems, those systems with higher resolution resulted in better long-term precision expressed as lower $CV\%$ (Table 1 and Fig. 1).

Discussion

Using a cadaver study, we have shown that DXR is robust and stable for measurements of BMD over a follow-up time of 6 and 12 months. The in-vitro precision ($CV\%$) over 6 months for the four systems ranged from 0.22 to 0.43%, and for one system, no difference in the long-term precision data was found between 6 months and 12 months.

Table 1 Long-term in-vitro cadaver phantom precision for the direct DXR-BMD tested in four different X-ray systems over a period of 6 months for all equipments and for Fuji FCR XG1 (Kristiansand) also tested at 12 months

X-ray equipment centre	Resolution mm/pixel	CV% “short time”, 0 months, 3 months, 6 months	Mean BMD value (g/cm ²)			SD		CV% “long-term”	SDD (g/cm ²)
			0 month 6 month	3 month	total	Between follow-up σ_A	Within follow-up σ_ε		
Fuji FCR XG1 Kristiansand	0.100	0.22	0.471		0.471	0.0009	0.0013	0.35	0.0046
		0.39	0.469						
		0.24	0.471						
		0.21*	0.469*	0.470*	0.0010*	0.0013*	0.35*		
Agfa ADC compact plus Trondheim	0.114	0.44	0.455		0.455	0.0007	0.0018	0.43	0.0054
		0.39	0.455						
		0.38	0.455						
Fuji FCR profect Helsingborg	0.050	0.14	0.546		0.547**	0.0008	0.0009	0.22	0.0034
		0.17	0.547						
		0.17	0.547						
Sectra MicroDose Helsingborg	0.049	0.11	0.544		0.545**	0.0011	0.0006	0.24	0.0036
		0.12	0.546						
		0.10	0.545						

* Data from 12 months

**The same phantom was used for both equipments

SD = standard error; CV% = coefficient of variation; SDD = “Smallest detectable difference”

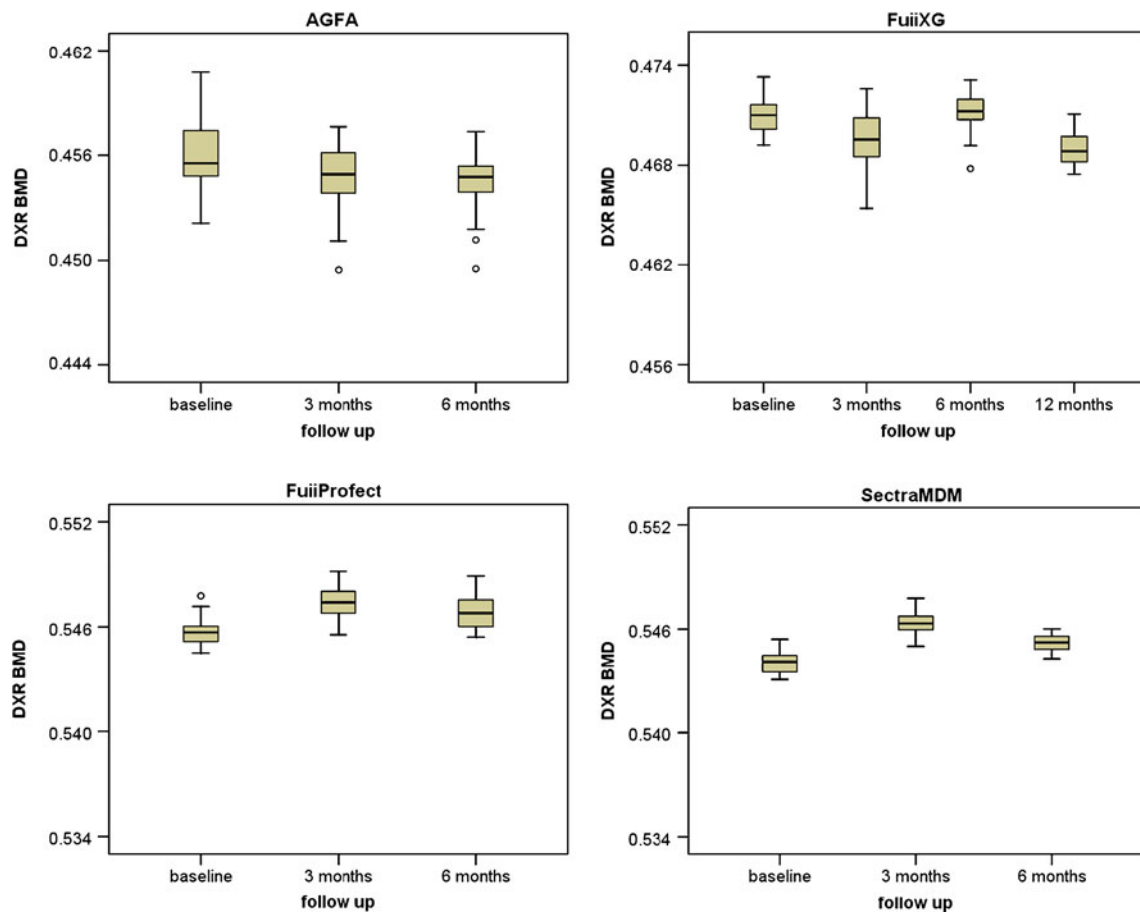


Fig. 1 Cadaver phantom bone mineral density (BMD) values in four tested X-ray systems. Measurements at baseline, 3 months, and 6 months and for FujiXG (Kristiansand) also at 12 months (box-and-

whisker plot: the marked *line* shows the median, and the bottom and top of the box show the lower and upper quartiles. *Circles* represent single observations outside the range of the whiskers

Annual loss of DXR-BMD for RA patients has been reported to range from 1.7% [4] to 10% in patients with early RA [11]. Thus, the ability to detect small changes using DXR based on the good precision reported here means that a significant loss can be detected within a short interval in RA patients with high disease activity. This may be of clinical importance, as changes in DXR-BMD have been shown to be strongly associated with markers of disease activity, disease severeness, and to future radiographic joint damage [4, 12–16]. While CV% is calculated using the mean BMD, SDD gives an absolute estimation of the random measurement error, which in our study was low and ranged from 0.0034 to 0.0054 g/cm².

As the cadaver phantoms are fragile and cannot be sent by mail, we were not able to test all cadaver phantoms on all four X-ray machines, which is a limitation of our study. However, this most likely only had a minor influence on the results. The BMD level for all three cadaver phantoms were in the middle range of BMD values seen in adult individuals. Theoretically, more cadaver phantoms with a broad range of BMD should have been tested. For dual-energy X-ray (DXA), precision has been reported to be better for higher BMD levels than for lower BMD levels [17]. In a recently published short-term study, no major differences in the DXR BMD precision were found between high and low bone density [5]. Thus, the precision for the DXR method seems to be less influenced by the BMD level than DXA. In this same study, we reported that different X-ray systems measured different values for the DXR-BMD on the same phantom [5]. Although these differences are small, they may have a significant influence on individual bone density follow-up results. Thus, in follow-up of a patient, the same X-ray system should be applied to achieve the most reliable results.

For logistic reasons, we performed cluster measurements at the different time points instead of daily measurements, which is a limitation of our study. Everyday measure of the phantom would have made it easier to observe if the measured values were drifting as a trend over time or more a stepwise shift after, e.g., change of the X-ray tube. However, as depicted in Fig. 1, we found only minor variations for the mean DXR-BMD values between the various time points. Further for FujiXG1, we found no difference in CV% or SDD between 6 and 12 months.

In previous DXR studies calculating bone density on conventional hand X-rays, the precision did not seem to be significantly influenced either by film brand, film focus distance, or exposure level, but tube voltage may have an influence [18, 19]. For the Sectra MicroDose X-ray machine, the tube was changed between 0 and 3 months, however, the voltage was 35 kV at all time points. This change of X-ray tube did not appear to influence the reproducibility of the BMD measurements (Fig. 1).

We conclude that in vitro long-term precision for direct DXR is comparable to previously reported short-term in-vitro precision data. The DXR method may thus be a potential important research and clinical tool for follow-up of changes in hand bone density, in particular for assessment of patients with osteoporosis and RA.

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