Effect of a Cast on Short-Term Reproducibility and Bone Parameters Obtained from HR-pQCT Measurements at the Distal End of the Radius

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Abstract: BACKGROUND High-resolution peripheral quantitative computed tomography (HR-pQCT) is a promising tool to assess the fracture-healing process at the microscale in vivo. Since casts are often used during fracture treatment, they might affect the assessment of bone density, microarchitectural, and biomechanical parameters and the short-term reproducibility of those parameters, e.g., as a result of beam-hardening. The aim of this study was to assess the effect of a plaster-of-Paris and/or fiberglass cast on bone parameters and on the short-term reproducibility of the HR-pQCT measurements of those parameters. METHODS The effects of a cast on HR-pQCT-derived bone parameters were evaluated by comparing HR-pQCT scans of fifteen human cadaveric distal radial specimens from one male and fourteen female donors (median age, eighty-four years [range, sixty-two to ninety years] at the time of death) in three conditions: with a plaster-of-Paris cast, with a fiberglass cast, or without a cast. Short-term reproducibility was assessed using duplicate scans of the distal end of the radius in sixteen healthy volunteers without a fracture (nine men and seven women with a median age of twenty-six years; range, twenty-two to thirty-nine years) while wearing and not wearing a fiberglass cast. RESULTS Compared with measurements made with no cast, the plaster-of-Paris cast introduced a systematic error in the bone parameters ranging from -2.6% in trabecular separation to -9.8% in cortical thickness. Bone parameters were affected only marginally by fiberglass, with errors between -0.6% and -1.6% in trabecular separation and cortical thickness, respectively. Short-term reproducibility with a fiberglass cast was similar to that with no cast: approximately 1% for bone density parameters, 4% to 5% for microarchitectural parameters, and 3% to 4% for biomechanical parameters. CONCLUSIONS A plaster-of-Paris cast has a considerable effect on HR-pQCT measurements. A fiberglass cast only marginally affects the bone parameters, and the short-term reproducibility of HR-pQCT measurements in patients with a fiberglass cast is comparable with that in patients without a cast. In studies on fracture-healing using HR-pQCT, a fiberglass cast is desirable if immobilization is indicated. The use of a plaster-of-Paris cast should be avoided if possible; however, if not avoidable, corrections after the scan are desirable to adjust for the error introduced in the bone parameters.

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Background: High-resolution peripheral quantitative computed tomography (HR-pQCT) is a promising tool to assess the fracture-healing process at the microscale in vivo. Since casts are often used during fracture treatment, they might affect the assessment of bone density, microarchitectural, and biomechanical parameters and the short-term reproducibility of those parameters, e.g., as a result of beam-hardening. The aim of this study was to assess the effect of a plaster-of-Paris and/or fiberglass cast on bone parameters and on the short-term reproducibility of the HR-pQCT measurements of those parameters.

Methods: The effects of a cast on HR-pQCT-derived bone parameters were evaluated by comparing HR-pQCT scans of fifteen human cadaveric distal radial specimens from one male and fourteen female donors (median age, eighty-four years [range, sixty-two to ninety years] at the time of death) in three conditions: with a plaster-of-Paris cast, with a fiberglass cast, or without a cast. Short-term reproducibility was assessed using duplicate scans of the distal end of the radius in sixteen healthy volunteers without a fracture (nine men and seven women with a median age of twenty-six years; range, twenty-two to thirty-nine years) while wearing and not wearing a fiberglass cast.

Results: Compared with measurements made with no cast, the plaster-of-Paris cast introduced a systematic error in the bone parameters ranging from $-2.6\%$ in trabecular separation to $-9.8\%$ in cortical thickness. Bone parameters were affected only marginally by fiberglass, with errors between $-0.6\%$ and $-1.6\%$ in trabecular separation and cortical thickness, respectively. Short-term reproducibility with a fiberglass cast was similar to that with no cast: approximately $1\%$ for bone density parameters, $4\%$ to $5\%$ for microarchitectural parameters, and $3\%$ to $4\%$ for biomechanical parameters.

Conclusions: A plaster-of-Paris cast has a considerable effect on HR-pQCT measurements. A fiberglass cast only marginally affects the bone parameters, and the short-term reproducibility of HR-pQCT measurements in patients with a fiberglass cast is comparable with that in patients without a cast. In studies on fracture-healing using HR-pQCT, a fiberglass cast is desirable if immobilization is indicated. The use of a plaster-of-Paris cast should be avoided if possible; however, if not avoidable, corrections after the scan are desirable to adjust for the error introduced in the bone parameters.

Level of Evidence: Diagnostic Level III. See Instructions for Authors for a complete description of levels of evidence.

Distal radial fractures are among the most common types of fractures. Women are particularly vulnerable, with a lifetime risk of a distal radial fracture reported to range between $13\%$ and $21\%$ at fifty years of age. In closed, non-displaced, or reduced stable fractures, cast immobilization is the most common treatment. At routine follow-up of five to six

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of stable distal radial fractures can be obtained using HR-pQCT that detailed information about changes in bone density, microprocess at the microscale in vivo. In a recent study, we demonstrated that HR-pQCT is a promising tool to assess the fracture-healing process and of bone strength recovery than is possible using only radiographs. Thus, it may be warranted to have a more detailed evaluation of the fracture-healing process and of bone strength recovery than is possible using only radiographs.

For osteoporotic patients, clinicians may question whether this standard fracture treatment is optimal for an individual patient. The influences on the healing process due to osteoporosis or medication suggest that the treatment of osteoporotic fractures may benefit from patient-specific adjustments, as it may take longer before an osteoporotic fracture can be fully loaded. Thus, it may be warranted to have a more detailed evaluation of the fracture-healing process and of bone strength recovery than is possible using only radiographs.

High-resolution peripheral quantitative computed tomography (HR-pQCT) is a promising tool to assess the fracture-healing process at the microscale in vivo. In a recent study, we demonstrated that detailed information about changes in bone density, microarchitecture, and bone biomechanical properties during the healing of stable distal radial fractures can be obtained using HR-pQCT. Because that study was the first in which HR-pQCT was used to monitor fracture-healing, the accuracy (i.e., closeness to the true value) of the obtained bone parameters and the short-term reproducibility (the ability to reproduce similar results, given no real biological change) of the measurements are two important considerations that need to be addressed.

For standard HR-pQCT measurements, the accuracy and reproducibility of the bone density, microarchitectural, and biomechanical parameters have been tested and validated extensively. When fracture-healing of the distal end of the radius is studied, however, the wrist is usually immobilized with a forearm-based cast. Hence, HR-pQCT measurements of the distal end of the radius are performed with a cast; therefore, the cast may adversely influence the obtained bone parameters and the reproducibility of those measurements. First, a cast absorbs some radiation, which could lead to unwanted effects such as beam-hardening and increased noise. Thus, for common cast materials,
the results might be affected because of these potential deteriorating effects on image quality. Second, the presence of a cast precludes the use of the standard holder and thus requires a nonstandard cylindrical holder to fixate the forearm immobilized in a cast. In that situation, the cast rather than the forearm is fixated, leaving room for potential movement of the forearm within the cast. This seemingly less strict fixation could in turn affect the reproducibility of the measurements.

The purpose of the present study, therefore, was to quantify the extent to which a cast would affect (1) the bone density, microarchitectural, and biomechanical parameters obtained from HR-pQCT measurements, and (2) the short-term reproducibility of those measurements.

Materials and Methods

Material and Subjects

To measure the effect of a cast on bone parameters obtained from HR-pQCT measurements, fifteen human cadaveric radii (from one male and fourteen female donors with a median age of eighty-four years [range, sixty-two to ninety years] at the time of death) were imaged by HR-pQCT in three conditions: without a cast (control), with a 4-mm-thick plaster-of-Paris cast, and with a fiberglass cast (Fig. 1). The radii were obtained from the Department of Anatomy and Embryology of the University of Amsterdam and were preserved in formalin. The history of the donors was unknown, and no selection criteria were applied.

To compare the short-term reproducibility of HR-pQCT measurements without and with a cast, sixteen healthy individuals (nine men and seven women with a median age of 25.5 years; range, twenty-two to thirty-nine years) without a fracture underwent four separate HR-pQCT scans of the distal end of the radius on the dominant side within four hours: two consecutive HR-pQCT scans without a cast and two consecutive HR-pQCT scans with a fiberglass cast. The forearm of each participant was completely repositioned between each scan. The casts were applied by a professional cast technician. Because the standard positioning holder that is supplied by the manufacturer could not fit the forearm with a cast, we used a newly designed cylindrical holder for all measurements, i.e., the CT Carpal X1 (Pearltec). This holder, which was also used in our earlier studies, consists of a cylindrical carbon fiber tube and an inflatable bag with soft liner on the inside (Fig. 2), allowing firm fixation of the forearm.

This feasibility study was performed within the framework of a larger fracture-healing study approved by our institutional medical ethics committee (registration number NTR3821). All participants were informed and gave written permission for the scans.

Scanning by HR-pQCT

All radii were imaged by HR-pQCT (XtremeCT; Scanco Medical) at clinical in vivo settings recommended by the manufacturer (peak voltage of 60 kVp, tube current of 900 μA, and 100 ms integration time). A scout view was made...
before each measurement to determine the region of interest. The distal end of the radius proximally from the subchondral plate was chosen as the region of interest because this is the region where a fracture of the radius typically occurs. In the cadaveric radii, the region of interest started just below the subchondral plate (Fig. 3). In the healthy individuals, the region of interest started at an offset of 5 mm from the distal edge of the lunate bone (Fig. 3). Because some distal radial fractures might not be fully covered by one standard stack of 110 slices, the scan length was set to 18.04 mm for all measurements. With an isotropic voxel size of 82 μm, each measurement resulted in 220 parallel CT slices. The total effective radiation dose received per individual was 24 μSv.

After scanning, all HR-pQCT images were checked by one operator (JJA, d.J.) for motion-induced image artifacts and were quality-graded as described by Pialat et al.13. This grading system consists of five grades (ranging from 1, indicating no motion artifacts, to 5, indicating extreme motion artifacts), where grades 1, 2, and 3 are considered to be of sufficient quality because of cortical continuity13.

Evaluation of Bone Density and Microarchitecture
The HR-pQCT images were evaluated using the standard patient evaluation protocol that was provided by the manufacturer and that has been described previously in detail14–16. The following bone density parameters were calculated from the images: total, trabecular, and cortical volumetric bone mineral density (BMD). Also bone volume to total volume (BV/TV) was calculated for the trabecular region. The microarchitectural parameters that were calculated in the trabecular region were the trabecular number, thickness, and separation. For the cortical region, the cortical thickness was obtained.

Micro-Finite Element Analysis
Micro-finite element models were created directly from the segmented HR-pQCT images, similar to earlier studies17–19. In short, each voxel that represents bone tissue was converted into a brick element of the same size, thus creating a representative micro-finite element model of the microarchitecture of the bone. Equal properties were assigned to every element: a Young modulus of 10 GPa and a Poisson ratio of 0.3. By applying a “high-friction” compression test in the axial direction as described by Pistoia et al.17, compression stiffness and estimated ultimate failure load were determined.

Statistical Analysis
Deviation in the bone parameters obtained from the HR-pQCT scans made with the plaster-of-Paris and fiberglass cast was reported as the root-mean-square coefficient of variation (RMS-CV) as described by Glüer et al.19. Wilcoxon signed-rank testing was used to test whether there was a difference in short-term reproducibility of the bone parameters between the conditions with and without a cast.

A significance level of 0.05 was used for all tests. All statistical analyses were performed with SPSS Statistics for Windows (version 20.0; IBM).

Results
Errors in Bone Parameters
The mean bone density, microarchitectural, and biomechanical parameters (and standard deviation) of the cadaveric radii measured without a cast (control), with a 4-mm plaster-of-Paris cast, and with a fiberglass cast are presented in Table I. All bone parameters were affected by the presence of a cast (the F-ratio for all bone parameters was significant; p < 0.001).

The magnitude of the errors in the measurements with a fiberglass cast ranged from 0.6% to 1.6%. The errors in the bone density and biomechanical parameters ranged between −0.9% and −1.1%, indicating a slight underestimation of the (cast-immobilized) bone density. Trabecular thickness and cortical thickness were also underestimated by −1.5% and −1.6%, respectively. Trabecular number was overestimated by 0.7%, and trabecular separation was underestimated by −0.6%.

For the plaster-of-Paris cast measurements, the errors were larger for all bone parameters, ranging in magnitude from 2.6% to 9.8%. Again, an underestimation was found for bone density, thickness, and biomechanical parameters, whereas there was an overestimation for trabecular number. For the bone density parameters, the errors ranged from −3.4% to −5.3%. For trabecular thickness and cortical thickness, the errors were −6.5% and −9.8%, and the errors in compression stiffness and estimated ultimate failure load were −7.5% and −6.6%. The error in trabecular number was 3.0%. The smallest error in the plaster cast measurements was −2.6% for trabecular separation.

Short-Term Reproducibility
Characteristics of the healthy individuals and the bone parameters measured at the distal end of the radius without a cast are...
listed in Table II. From the sixty-four initial measurements, seven (11%), six done without a cast and one with a cast, were insufficient image quality because of motion artifacts. From the thirty-two measurements without a cast, eleven scans were grade 1; nine scans, grade 2; six scans, grade 3; five scans, grade 4; and one scan was grade 5. The grade-5 scan contained a large amount of extreme motion artifacts because the participant tried to remove his forearm from the positioning holder during scanning. Therefore, this scan was excluded from short-term reproducibility calculation. From the thirty-two measurements with a cast, eight scans were grade 1; thirteen scans, grade 2; ten scans, grade 3; and one scan, grade 4.

RMS-CVs for the short-term reproducibility without wearing a cast were found to be generally between 0.6% and 4.0% (Table III). Whereas CVs of density parameters varied between 1.1% (total BMD) and 0.6% (cortical BMD), the CVs for structural parameters were higher: 1.7% for cortical thickness and between 3.5% (trabecular thickness) and 4.0% (trabecular separation) for the trabecular structural indices. The biomechanical parameters of compression stiffness and estimated ultimate failure load showed CVs of 3.3% and 3.7%, respectively. Short-term reproducibility was not significantly different with a fiberglass cast for any of the bone parameters, except for cortical thickness. In general, the CVs for the bone density parameters were slightly lower when a fiberglass cast was worn (0.5% to 0.7%) than when one was not worn (0.6% to 1.1%). Except for cortical thickness, the CVs for the bone macroarchitectural and biomechanical parameters were slightly higher when a fiberglass cast was worn (3.7% to 5.3%) than when one was not worn (3.3% to 4.0%). However, these differences did not reach significance (Table III).

Only the CV of cortical thickness was significantly lower when a fiberglass cast was worn (p = 0.028).

**Discussion**

The present study evaluated the effect of a cast on bone density, microarchitectural, and biomechanical parameters obtained from HR-pQCT measurements at the distal end of the radius, and the short-term reproducibility of those parameters.

**Errors in Bone Parameters**

The results suggest that both types of casts introduced systematic errors in the bone parameters. However, the differences when a fiberglass cast was worn and when no cast was worn were very small (approximately 1%). Although significant, these differences may not be clinically relevant, in particular when the reproducibility error and the fact that changes during fracture-healing are generally in the range of 10% to 20% are considered.

The use of plaster of Paris, on the other hand, can considerably bias measurement results. Compared with scanning without a cast, many parameters for measurements with such a cast deviated by 5% to almost 10%. Admittedly, such a bias might be acceptable in follow-up studies that aim at quantifying changes in parameters over time. Additionally, depending on whether a plaster-of-Paris cast is in place or removed, it presumably would be possible to correct the calculated bone parameters according to the percentages presented in Table I. However, these values were obtained in cadaveric radii, with low bone density (because of old age), that were not scanned at the standard region. Also, we did not vary the thickness of the plaster-of-Paris cast. Since the thickness of plaster-of-Paris casts might differ between patients, the errors in the bone parameters caused by the plaster-of-Paris casts might vary as well. Hence, the percentages in the present report are not immediately applicable to the general patient population in the clinical setting and should at least be adjusted proportionally to the thickness of the casts used on patients.

The difference between the effect caused by a fiberglass cast and a plaster-of-Paris cast can be explained by the different material properties of the two casts (see Appendix). At the standard settings of the XtremeCT, plaster of Paris absorbs more lower-energy photons than fiberglass does\(^4\), resulting in underestimation of the bone density and increased beam-hardening artifacts and noise (Fig. 1). These effects were confirmed by phantom artifacts.
measurements with and without a plaster-of-Paris cast (results not shown). Due to the beam-hardening effect and the increased noise, segmentation of the trabecular structure apparently results in a three-dimensional model with more, but thinner, trabeculae and a lower estimated bone stiffness and strength.

Short-Term Reproducibility
We found that when HR-pQCT and the nonstandard cylindrical holder (without a cast) were used, bone density parameters could be assessed with high precision (RMS-CVs of 0.6% to 1.1%) and microarchitecture and biomechanical parameters, with good precision (RMS-CVs of 1.7% to 4.0%). Similar values when the standard holder and no cast were used have been reported in the literature. Surprisingly, short-term reproducibility improved slightly when the wrist was immobilized by a cast. Presumably, the cast leads to a better fixation of the forearm in the cylindrical holder, resulting in fewer motion artifacts.

It should be noted that the reproducibility measured in the present study was obtained from HR-pQCT measurements that require twice as much scanning time because of the increased scan length compared with standard HR-pQCT measurements, i.e., 5.6 minutes and 18 mm versus 2.8 minutes and 9 mm, respectively. With longer scan times, the chance of motion-induced artifacts increases, and an increased scan time in principle could negatively affect the reproducibility. However, the increased scan time in our study did not decrease the short-term reproducibility of the measurements. A possible explanation is that the cylindrical holder with its inflatable bag better fixed the forearm than the standard holder used in other studies.

For the clinical application of HR-pQCT to monitor fracture-healing, it is important to know the precision of the HR-pQCT measurements (with a cast), since this determines the change in bone parameters that can be considered significant (expressed as the least significant change). Given the measured short-term reproducibility in this study and a statistical confidence level of 95%, the least significant change for the bone density parameters was approximately 2%. The least significant change was 14% for the microarchitectural parameters and 11% for the biomechanical parameters. When these least significant change values were compared with the changes that we found in our previously reported study on fracture-healing, we noticed that the observed changes in bone parameters were well above these least significant changes. For example, the cortical and trabecular bone density changed –4.1% and 20%, respectively, at six to eight weeks after the fracture. For the structural parameters, trabecular thickness changed by 30% at twelve weeks after the fracture, and at the same time, biomechanical parameters increased by 31%. Hence, the precision of HR-pQCT measurements with a cast is good enough to reliably detect changes in bone parameters typically occurring during the fracture-healing process.

Limitations
Reproducibility of a measurement is ideally assessed in a group of subjects similar to the group in which the measurement will be performed—in this instance, osteoporotic women over fifty years old with a distal radial fracture. As mentioned before, we used healthy individuals between twenty-two and thirty-nine years old. Nevertheless, recent data have indicated that differences in reproducibility between age groups are small and that reproducibility does not necessarily decrease with age.

Another limitation is the modest number of individuals in the reproducibility group, and hence, the large confidence intervals of the RMS-CV. In addition, the reproducibility study was performed with a fiberglass cast only and not a plaster-of-Paris cast. However, it seems unlikely that motion artifacts, which are the major source of reproducibility errors, would differ between the two cast materials.

Last, the cadaveric radii were scanned without soft tissue surrounding the bone and in the absence of the ulna. Although we used a repeated-measures design, this extra tissue would have absorbed some of the radiation and the results might be different in intact forearms.

Overview
In conclusion, bone parameters obtained from HR-pQCT measurements at the distal end of the radius, and the short-term reproducibility of these measurements, are only marginally affected by a fiberglass cast. However, a considerable bias in the measurement results is to be expected when a plaster-of-Paris cast is used so corrections ideally should be made after scanning. On the basis of these results, we recommend immobilization with a fiberglass cast if possible when monitoring distal radial fracture-healing with HR-pQCT. Furthermore, we advocate that the cast be worn during all follow-up measurements to maintain the same scanning conditions.

Appendix
An explanation for the different magnitude of errors in bone parameters introduced by the fiberglass cast and the plaster-of-Paris cast is available with the online version of this article as a data supplement at jbjs.org.
References