Heavy reading in heavy metal
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Chapter 5

Use of internal references for assessing CT density measurements of the pelvis as replacement for use of an external phantom


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ABSTRACT

Purpose
The purpose of this research is to study the use of an internal reference standard for fat- and muscle as a replacement for an external reference standard with a phantom. By using a phantomless internal reference standard, Hounsfield unit (HU) measurements of various tissues can potentially be assessed in patients with a CT scan of the pelvis without an added phantom at time of CT acquisition. This paves the way for development of a tool for quantification of the change in tissue density in one patient over time and between patients. This could make every CT scan made without contrast available for research purposes.

Materials and methods
Fifty patients with unilateral metal-on-metal total hip replacements, scanned together with a calibration reference phantom used in bone mineral density measurements, were included in this study. On computed tomography scans of the pelvis without the use of intravenous iodine contrast, reference values for fat and muscle were measured in the phantom as well as within the patient’s body. The conformity between the references was examined with the intra-class correlation coefficient.

Results
The mean HU (± SD) of reference values for fat for the internal- and phantom references were -91.5 (± 7.0) and -90.9 (± 7.8), respectively. For muscle, the mean HU (± SD) for the internal- and phantom references were 59.2 (± 6.2) and 60.0 (± 7.2), respectively. The intra-class correlation coefficients for fat and muscle were 0.90 and 0.84 respectively and show excellent agreement between the phantom and internal references.

Conclusion
Internal references can be used with similar accuracy as references from an external phantom. There is no need to use an external phantom to assess CT density measurements of body tissue.
INTRODUCTION

Failure of total hip replacement is caused in part by loosening of the cup due to osteolysis.\(^1\,^2\) This complication also plays a role in the biological behavior of metal-on-metal (MoM) total hip replacements.\(^1\,^3\) Acetabular bone stock is an important factor in revision surgery of THA: the preoperative assessment of acetabular bone stock before revision surgery is critical because the amount and location of pelvic osteolysis can determine the type and success of revision surgery. To examine the bone stock in the acetabulum, bone mineral density (BMD) measurements could be performed. The bone density in the acetabulum could serve as a predictor in the behavior of the MoM hip replacements.\(^5\,^7\) Furthermore, adverse soft tissue reactions are observed in THA MoM such as inflammatory capsular reactions resulting in solid, cystic or mixed so-called pseudotumours.\(^8\) At this moment MR seems to be the gold standard as MR is superior in determining soft tissue characteristics. Recently a CT classification of the hip capsule has been described with good association with revision.\(^8\) CT has the added benefit of being able to measure the position of the different components such as anteverision and inclination of cup and stem. CT has the disadvantage of dealing with metal artefacts such as photon starvation, scatter and beam hardening that makes it difficult to assess the hip capsule and its composition. Fatty atrophy of muscle and edema of the soft tissue is not easily assessed at all by means of CT. Metal artefact reduction in CT shows promising results but density measurements in the plane of metal do not seem to be feasible on a 64-slice CT scan; however, various CT innovations such as multislice systems, use of software algorithms to deal with photon starvation and spectral CT for dealing with beam hardening seem to make peri-prosthetic measurements of soft tissue and bone in the future possible.

BMD measurements conducted with dual-energy x-ray absorptiometry (DEXA) are the gold standard in the diagnosis of osteoporosis.\(^9\) Another method of measuring the BMD is the use of volumetric CT image.\(^10\) Recent studies have shown the possibility to assess bone density with the use of CT images.\(^11\,^12\) The direct measured Hounsfield numbers can be used to review bone density because the Hounsfield unit is an index of x-ray attenuation and is, therefore, directly correlated to tissue density.\(^12\) CT for BMD measurements offers some advantages over DEXA: the measurements are volumetric and differentiation between trabecular bone and cortical bone is possible.\(^11\) BMD measurements using CT can be achieved in two different ways: phantom-based and phantomless. In the phantom-based method, calibration is based on an extracorporeal phantom placed under the patient during the CT acquisition. Phantomless BMD (PLBMD) is based on internal patient references obtained from measurements in fat and muscle without the use of a calibration phantom.\(^13\) The calibrations based on internal patient references are needed to account for differences between scans and
The purpose of this study is to examine whether internal references from CT data are consistent with references obtained from a calibration phantom in patients with a metal-on-metal total hip replacement.

**MATERIALS AND METHODS**

**Patient population and image acquisition**

The pelvic CT scans of 50 patients (21 male, 29 female) from a larger cohort study were prospectively randomly enrolled in this study. Informed consent was obtained. Approval was given by the Medical Ethical Committee under METC number 14.11161. Mean age (± SD) of the reviewed patients was 61.8 years (± 6.4). The minimum and maximum ages were 40 and 72 years respectively.

All patients underwent a unilateral MoM total hip replacement. The replacements were composed of a Bi-Metric porous coated uncemented stem with a metal-on-metal M2a- Magnum femoral head and ReCap acetabular component (Biomet, Warsaw, Indiana, USA). The modular head and acetabular component are high-carbon, as-cast (single heated) components. All CT datasets were obtained with the Philips Brilliance 40-slice CT scanner or the Philips Brilliance 64-slice CT scanner and one patient on 128-slice CT scan. The CT parameters included a slice thickness of 0.9 mm, a tube voltage of 140 kVp, a mean current of 171 mA (range: 97-331) and a matrix size of 512 × 512 for all reviewed CT datasets. CT images were reconstructed with filtered back projection (FBP). During all image acquisitions, a solid phantom was placed underneath the patient at the pelvic level. The phantom consists of five different rods representing the density of, among others, bone and fat.

**HU analysis**

HU analysis was performed in the Philips Extended Brilliance Workspace. Regions-of-interests (ROI) were manually placed with the use of the CT viewer. A slice 1 cm above the metal implant was selected for HU analysis. At this level in the acetabulum, metal artefacts from the MoM prosthesis are not present, which has been researched before\textsuperscript{15} (Supplement: part of the manuscript still in preparation). For each patient, one researcher placed four circular ROIs. In the phantom, the ROIs were placed in the rods with a density comparable with muscle and fat. The internal reference for muscle was placed in the musculus iliopsoas, anterior from the anterior superior iliac spine. The ROI for the internal reference for fat was placed in the dorsal subcutaneous fat, whereas all internal references were placed on the side opposite to the MoM implant. An example is illustrated in Fig. 1. For each ROI, the average HU value was recorded.
Fig. 1. Illustration of ROI placement. Axial view: Four ROIs are placed 1 cm above the metal implant. The average HU values were calculated.

**Statistical analysis**

All statistical analyses were performed with IBM SPSS Statistics, version 22. Association was visualized by scatterplots; explained variance $r^2$ was calculated. Agreement between the phantom and internal references was visualized using Bland Altman plots, and quantified using the intra-class correlation coefficient (ICC). All statistical analyses were performed separately for fat and muscle references.

**RESULTS**

All patients scored a grade 0 or 1 for the Goutallier classification for fatty infiltration of the musculus iliopsoas. The mean ± SD for the average HU values of the internal fat reference is -91.5 ± 7.0 (range: -114.2 to -76.5) and -90.9 ± 7.8 (range: -113.3 to -71.6) for the extracorporal fat reference. For muscle, the mean ± SD or the internal reference is 59.2 ± 6.2 (range: 40.0 - 71.8) and for the extracorporal muscle reference 60.0 ±
7.2 (range: 35.7 - 70.5). Figure 2 shows scatterplots, revealing positive associations between internal references and phantom reference. The explained variance $r^2$ is 0.82 for fat and 0.73 for muscle.

In Fig. 3, the Bland Altman plots are shown for both fat and muscle. A mean bias of -0.59 is found for fat references. The limits of agreement for HU difference range from -7.19 to 6.00. For the muscle references, a mean bias is found of -0.76, while the limits of agreement range from -8.23 to 6.72. The ICC for the fat references is 0.90 and the 95% confidence interval is (0.74, 0.91). For muscle, the ICC is 0.84 with a 95% confidence interval of (0.85, 0.95). Both can be classified as excellent agreement between phantom references and internal references.

Fig. 2. Scatterplots from the phantom and internal references for fat (a) and muscle (b). The HU values for the phantom are plotted against the HU values of the internal references. $R^2$ is the explained variance.

Fig. 3. Bland Altman plots for both fat (a) and muscle (b) references. The difference between phantom and internal references is plotted against the mean of the two references.
DISCUSSION

We have shown that internal soft tissue references have similar accuracy as references obtained from an external phantom in the acetabular roof region in patients with MoM. The ICCs of 0.90 and 0.84 indicate excellent agreement.\textsuperscript{18} The mean bias between the two different references for fat and muscle are −0.59 and −0.76. These findings show that internal references can be used with a similar accuracy as phantom references. We have proven these findings in the acetabular roof region in patients with a metal-on-metal total hip replacement. These results may also be valid in other bone locations in a certain CT scan or in CT scans obtained because of other non-skeletal pathologies.

Thus, without additional radiation more information from every CT scan made in the radiology department can potentially be extracted. This study is part of a larger research in our institute to study the biological behavior of MoM total hip replacements. An extensive database was set up with patients who underwent MoM total hip replacement; therefore, a relatively large patient group could be used in this study. All patients were reviewed for muscle inhomogeneities and all patients met criteria for Goutallier 0 and occasionally 1 for muscle fatty degeneration.\textsuperscript{16,17}

In the literature, acetabular bone-density measurements have been previously described.\textsuperscript{6,19} Zijlstra et al.\textsuperscript{19} conducted DEXA measurements in all four regions according to Wilkinson.\textsuperscript{6} In this study, acetabular bone density was not significantly decreased in any of the regions. In this study, DEXA measurements in combination with metal exclusion software were used. These results were compared with MoP (metal-on-polyethylene) bearings, which showed decreased bone density in three-quarters of the regions. This study shows the clinical utility of BMD measurements in THA follow-up. When standard follow-up CT scans can be used to measure BMD, additional DEXA measurements will be redundant. PLBMD measurements in the thoracic and lumbar vertebrae, using internal references for calibration, have already been described.\textsuperscript{13,20-22} These studies appear to show a patient-friendly method of measuring bone density with a lower dose, a better resolution and less artefacts. There are multiple advantages when using PLBMD compared to phantom-based BMD measurements: the internal references are close to the bone of interest, which makes the measurement less prone to imaging artefacts. Besides, every CT scan can be used for PLBMD measurements. There may also be some disadvantages to the use of PLBMD:\textsuperscript{13} inhomogeneities in the internal muscle or fat references as well as variation in vasculature can influence the accuracy of the internal calibration measure. Use of BMD values has multiple advantages over the use of Hounsfield units, whose values are dependent on a number of factors, including radiation dose, patient constitution and artefacts. For this reason, for example in CT PLBMD measurements, the internal HU references are used to correct the bone density. Because the BMD is a corrected, calibrated measure, tissue density measurements
can be compared in a patient over time or between patients regardless of the afore-
mentioned factors and without a phantom and with- out an extra scan, thus without 
extra radiation.

However, some conditions have to be met for the implementation of PLBMD mea-
surements of the periprosthetic hip in current practice, such as dealing sufficiently with 
metal artefacts in affected regions of interest and the need of a clinical reference list 
regarding attenuation of bone in an age- and sex-adjusted score, analogue to the T- and 
Z-score in DEXA. The PLBMD method applied in bone stock measurements of the ac-
etabular roof could potentially be used in cross-sectional studies as well as follow-up 
 studies for patient who undergo total hip replacements if certain conditions are met. 
Pre-operative CT scans and follow-up CT scans can thus potentially be used without 
adjustments in scan protocol to study the progress of the acetabular roof bone density 
without an additional DEXA scan. A weakness of our study is that these measurements 
can only be done in region 1, according to Wilkinson et al. due to the metal artefacts 
present in the other regions. Investigations using metal artefact reduction for orthope-
dic implants (O-MAR) show only the region above the metal implant is unaffected by 
metal artefacts (Supplement: part of the manuscript still in preparation).

Currently in 9.6 % of patients with a MoM THA, revision is needed. Clinical relevance 
for being able to measure BMD, in addition to subjective visual interpretation, of the ac-
etabular roof might be of interest for the orthopedic surgeon in charge of revision who 
likes to be informed beforehand whether or not he needs to harvest bone in the case of 
cup revision. Secondly, it could be of interest to have a simple tool that is able to study 
the bone density reaction when future newly developed implants are being placed in 
patients when particle disease and bone loss is associated with failure of the implant. The results from this study give a basis to investigate the use of PLBMD measurements 
in the acetabular roof in patients with a metal-on-metal total hip replacement. This 
phantomless method has the potential to increase the applicability in today’s clinical 
practice. Ultimately all CT scans could be used to measure and follow-up bone density.

**CONCLUSION**

This study shows that internal references of fat and muscle are of similar accuracy as 
compared to references obtained from an extra-corporal phantom at the level of the ac-
etabular roof in patients with a one-sided MoM THA. The intra-class correlation coef-
ficient shows excellent agreement between the two different references. Thus, there 
is no need to use an external phantom to quantify CT density measurements of body 
tissue.
REFERENCES


**SUPPLEMENT**

**CONFLICTS OF INTEREST**

Dirk Mueller and Julien Milles are employees of Philips Healthcare.