

Change in CT-measured acetabular bone density following total hip arthroplasty: a systematic review and meta-analysis

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Background and purpose — Assessing peri-acetabular bone quality is valuable for optimizing the outcomes of primary total hip arthroplasty (THA) as preservation of good quality bone stock likely affects implant stability. The aim of this study was to perform a meta-analysis of peri-acetabular bone mineral density (BMD) changes over time measured using quantitative computer tomography (CT) and, second, to investigate the influence of age, sex, and fixation on the change in BMD over time.

Methods — A systematic search of Embase, Scopus, Web of Science, and PubMed databases identified 19 studies that measured BMD using CT following THA. The regions of interest (ROI), reporting of BMD results, and scan protocols were extracted. A meta-analysis of BMD was performed on 12 studies that reported measurements immediately postoperatively and at follow-up.

Results — The meta-analysis determined that peri-acetabular BMD around both cemented and uncemented components decreases over time. The amount of BMD loss increased relative to proximity of the acetabular component. There was a greater decrease in cortical BMD over time in females and cancellous BMD for young patients of any sex.

Conclusion — Peri-acetabular BMD decreases at different rates relative to its proximity to the acetabular component. Cancellous BMD decreases more in young patients and cortical bone decreases more in females. Standardized reporting parameters and suggested ROI to measure peri-acetabular BMD are proposed, to enable comparison between implant and patient variables in the future.

Despite the improved results of primary THA involving highly cross-linked polyethylene bearings (1), revision surgery is still required in 5–10% of patients within the first 10 years and revision for loosening/lysis may be challenging (2). Bone quality parameters measured as bone mineral density (BMD) likely affect implant stability. In a recent survey of orthopedic surgeons, 77% stated they would change their implant choice based on osteoporosis, but only 4% of the same surgeons performed formal assessments of bone quality (3).

Peri-prosthetic BMD has commonly been investigated using dual-emission X-ray absorptiometry (DEXA), computerized tomography (CT), or a combination of the 2 imaging methods. Acetabular BMD changes post-THA have not been as extensively studied as femoral due to multiple difficulties, although are known to be reduced post-THA (4–6). Most DEXA studies use the commonly known radiological zones of DeLee and Charnley (7) or the Wilkinson modification into 4 axial regions of interest (ROI) (8). DEXA studies have shown an initial reduction of peri-acetabular BMD, which stabilizes at the level of the implant by early follow-up (5,9,10). This conflicts with CT studies, which have shown progressive BMD reduction particularly in the important retroacetabular zone, which is not visualized by DEXA (11,12). This reduction in BMD over time is due to a combination of factors including the expected BMD reduction with ageing, implant-related stress shielding (13,14), differing vectors of force following implantation (15), and variable patient activity and use of the limb postoperatively (16).

Evaluation of BMD using DEXA has the advantage of a lower patient radiation dose; however, it interprets only a 2D image, is unable to distinguish between cortical and cancellous bone (17), and cannot be used clinically to assess bone stock

or osteolysis. The major limitation of CT is the presence of metal artefact streaking across the peri-acetabular bone, which can make BMD interpretation difficult, particularly in implants of more radio-opaque material such as tantalum and when the scans are performed for alternate pathologies and metal artefact reduction (MAR) software is not utilized. The development of improved MAR CT protocols has significantly improved the ability to assess periprosthetic bone (18,19). With increased ability to assess periacetabular bone quality and frequency of CT imaging there is a significant need for defined, repeatable measurements of CT-measured BMD.

To effectively measure peri-acetabular BMD using CT, the pelvis should be separated into ROIs. Common methods for identifying ROIs in CT include either axial slices of transverse planar CT image moving sequentially distally, circular ROIs centered at the acetabulum (avoiding the metal artefact of the acetabular component), or the use of computer software to split the acetabulum into various volumetric sections. Despite the variation within different methods, the reproducibility of CT-measured BMD has been tested across multiple formats of ROIs including quadrant and axial slice (20–22). Currently, there is no concise summary of CT-measured peri-acetabular BMD changes over time, which makes it difficult to interpret the role of various factors contributing to progressive BMD change.

Our hypothesis was twofold: first, that CT measurements of periprosthetic cancellous and cortical BMD decrease with time and, second, that the rate of decrease would be related to the proximity of the implant due to changes in stress shielding and load.

Therefore, the primary aim was to perform a meta-analysis of peri-acetabular BMD changes over time measured using quantitative CT, and the secondary aim was to investigate the influence of age or sex and fixation on the change in BMD over time.

Methods

Search, screening, and selection

A systematic literature review was performed on the January 10, 2022 in accordance with PRISMA standards. A working protocol was made prior to the start of the review (Table 1, see Supplementary data), but not registered. The search was conducted on Scopus, Embase, PubMed, and Web of Science databases using relevant mesh terms where appropriate (Table 2, see Supplementary data). The searches were exported into the Covidence systematic review software (<https://www.covidence.org/>) and blinded review on inclusion was performed by 2 of the authors (TR and SC). The inclusion criterion was any study that used CT to measure peri-acetabular BMD following primary THA. Studies were excluded at the full text level if either the ROI was not defined, BMD was not measured using CT, the CT was performed prior to THA, if the

manuscript was a conference proceeding or in a non-English language, or if the cohort had a significant medical pathology affecting bone quality (metabolic, neoplastic, endocrine, or infectious) making them not representative of a typical arthroplasty cohort.

Data extraction

Data extraction included year of publication, sample size, sex, CT parameters, ROI, and results of density measurements by 1 reviewer (TR). In the event that only a graphical representation of data was available, attempts were made to contact corresponding authors to request full results and in the absence of a response data was extracted with WebPlotDigitizer (<https://automeris.io/WebPlotDigitizer/>) (23). Similarly, when standard deviations (SD) were not reported they were calculated retrospectively from the reported range (24). If SDs were not reported, and a retrograde calculation was not possible, the measurement was allocated a mean SD, which was calculated as a mean of the reported SDs for the other studies in that region of interest (25). If a study had measurements also reported at an early timeframe for the same cohort, they were excluded and only the latest study was included. If percentage change only was reported in the absence of BMD measurements, and a reply was not obtained from the corresponding author, the study was excluded from the meta-analysis. Studies reported BMD in multiple different units, which required conversion to allow meta-analysis. All reported BMD units were converted back to ash density in mg/cm^3 as previously recommended in a review of quantitative CT studies (26). Values are presented as means with 95% confidence intervals (CI).

Analysis

The ROIs were defined as ROI 1–8 starting 40 mm above the acetabular component corresponding to the most proximal axial level reported in the studies (Figure 1). Additionally, the ROIs were split into either cranial (above the level of the acetabular component) or at the level of the acetabular component. At the level of the acetabular component, ROIs were also split into ventral and dorsal. To allow comparison between studies, some assumptions were made regarding the ROIs. If the ROI was not a true axial slice and spanned consecutive axial slices, the midpoint of the ROI was taken. If the study included multiple slices measured for 1 comparison or ROI, the measurement closest to the midpoint of our suggested ROI was used. For example, if there were multiple measurements in region 3 (10–20 mm cranial to the acetabular component), the measurement closest to 15 mm was used. Early follow-up was defined as occurring between 6 and 36 months after THA and late follow-ups were studies with more than 7 years' follow-up.

To simplify the ROIs and allow for a larger comparison of studies for cemented and uncemented components, ROIs were simplified to either cranial to the acetabular component or, at the level of the acetabular component, split into ventral and

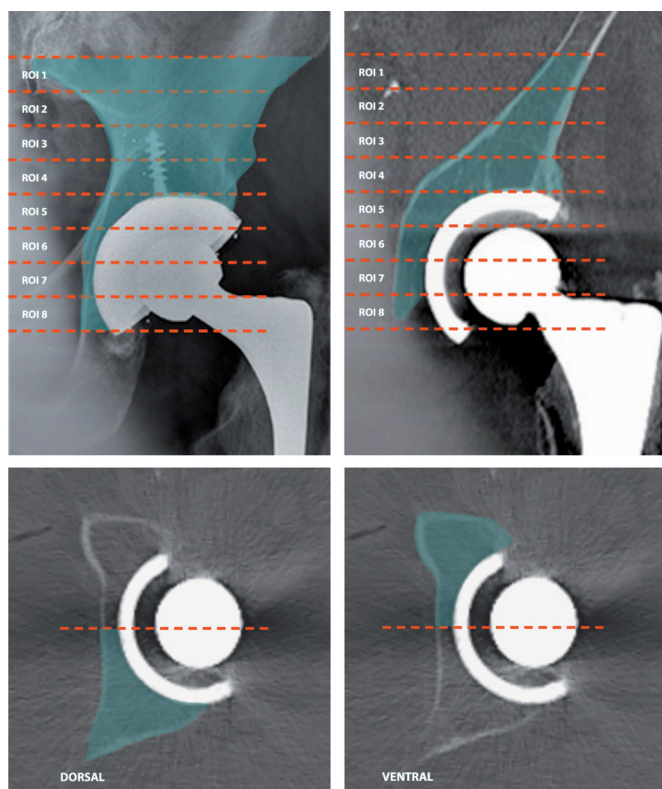


Figure 1. Proposed ROIs 1–8 on a plain radiograph (left) and coronal CT (right) and below the dorsal regions of interest (left) and ventral (right) for ROI 6.

dorsal. Specific comparisons of ROIs 1–8, rather than the 3 groups of cranial, ventral, and dorsal, had insufficient sample sizes from which to draw comparison.

A risk of bias assessment was performed by 1 reviewer using a modified version of the Newcastle–Ottawa scale. A modification of the scale was made to tailor it to the standards of CT density studies (Table 3, see Supplementary data).

The meta-analysis and forest plots were produced using the Cochrane review Review Manager (RevMan) software (<https://training.cochrane.org/online-learning/core-software/revman>) with a generic inverse variance approach using a random effects model for mean differences. Additionally the open source OpenMeta[Analyst] software (<http://www.cebm.brown.edu/openmeta/>) was used to calculate mean BMD of the sample groups.

The amount of statistical heterogeneity was assessed through inspection of the forest plots, χ^2 and the I^2 statistics (25). The I^2 statistic estimates how much of the total variability in the effect size estimates is due to heterogeneity among the true effects (25). In the presence of heterogeneity, and if the data allowed, we performed a random-effects meta-regression on predefined factors (study-level covariates: age, percentage women, ROI, follow-up duration, and fixation). All analyses were performed using the metafor package in R statistics (R Foundation for Statistical Computing, Vienna, Austria) (27).

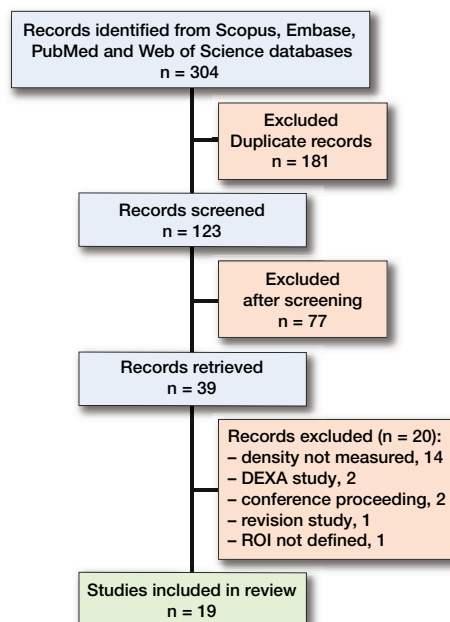


Figure 2. Prisma chart of Covidence review process.

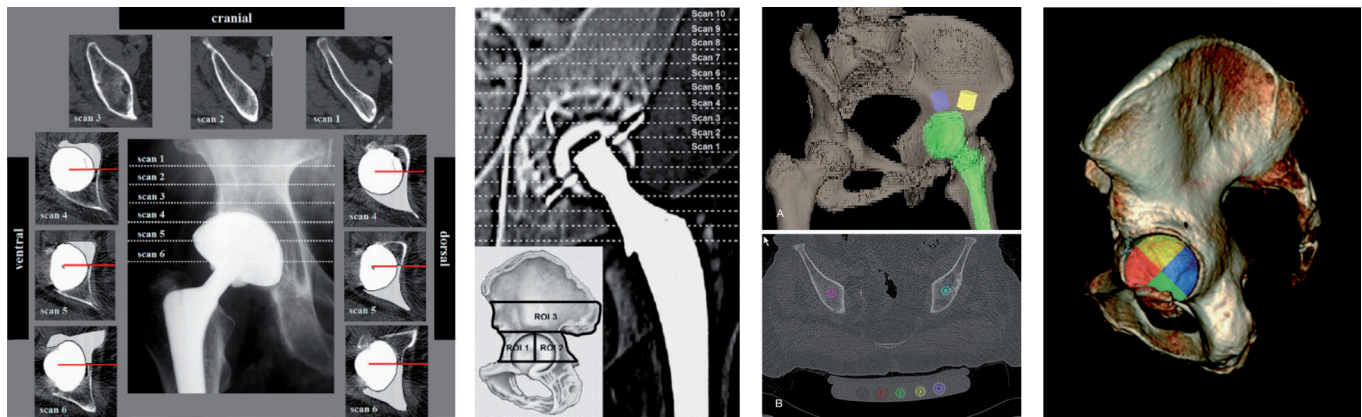
Results

Data collection

123 studies were screened for eligibility. Of those, 39 required full text assessment. 19 studies fulfilled the requirement of CT-measured peri-acetabular BMD after THA and were included in the systematic review (Figure 2). The characteristics of the studies including implant details, age, sex, and scan protocol are displayed in Table 4, see Supplementary data). Of those, 12 included BMD measurements at 2 time points after THA and were included in the meta-analysis investigating change in BMD over time. In addition, 13 studies had measurements at 1 timeframe and were included in the meta-analysis of mean peri-acetabular BMD, noting that duplicate cohorts from the same study group were not included at multiple time points. The remaining 6 studies did not report actual BMD values or did not separate their ROI to allow comparison. Table 5, see Supplementary data) depicts the extraction of data and conversions made for the 13 studies, which had measures available for meta-analysis at 1 or more timepoints (4,11,12,20,22,28-38). The results of the modified Newcastle–Ottawa bias assessment (Table 6, see Supplementary data) showed fair quality, with all but 1 study (39) having a rating of ≥ 4 (Table 6, see Supplementary data). All studies used a similar kVp with 140 kVp being the most frequently reported, but there were variations in ROI used (Figure 3) and reporting of statistical parameters.

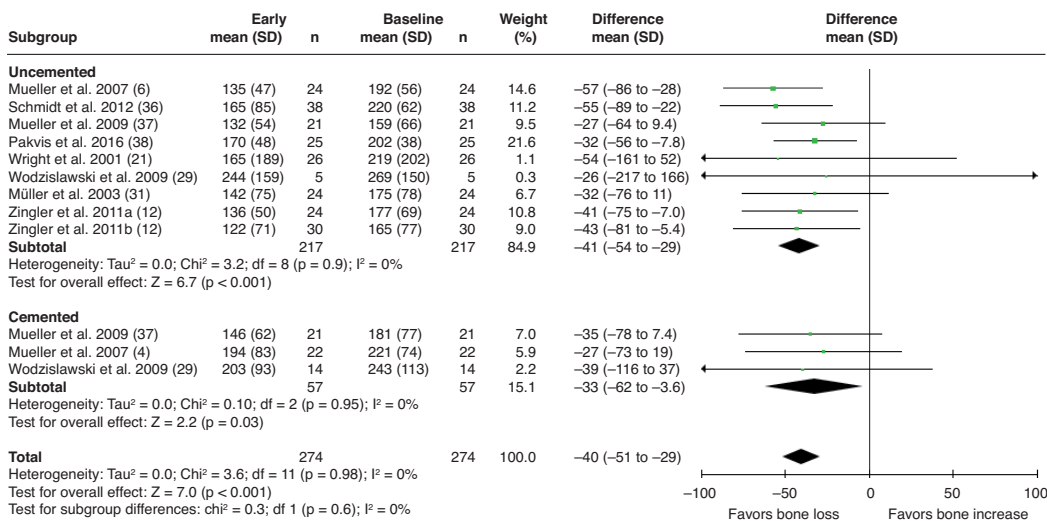
Comparison of peri-acetabular BMD change between cemented and uncemented component fixation

The meta-analysis depicts a significant change in cancellous bone density for cemented and uncemented acetabular



Mueller et al. 2007 (4) Mueller et al. 2009 (37) Mueller et al. 2009 (37) Mussmann et al. 2018 (20)

Figure 3. Examples of different regions of interest used in previous CT studies of peri-acetabular BMD following THA.



components cranial to the level of the cup (BMD -40 mg/cm³ [CI -51 to -29], Figure 4a). This significant change is also seen for ventral cancellous bone density (Figure 4b). The heterogeneity of the results increased dorsal to the component and there are no significant changes in BMD dorsally for cemented components (Figure 4c).

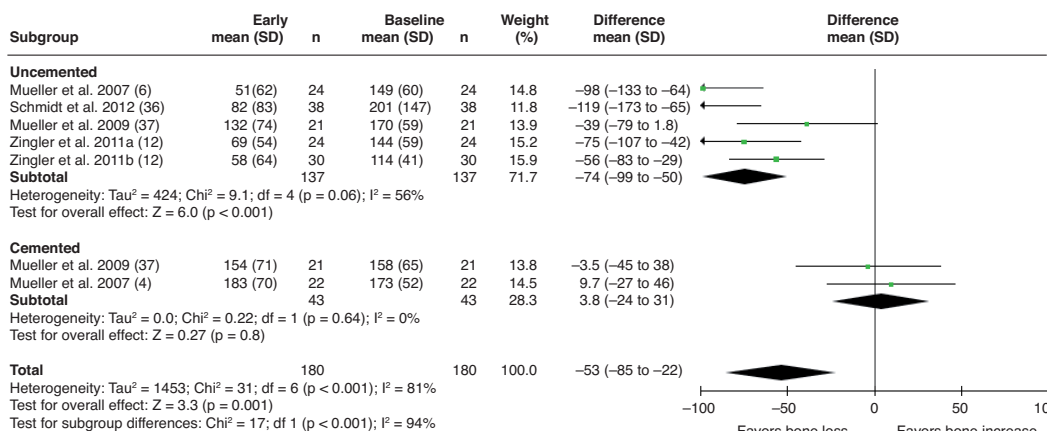
Mean BMD at baseline and early follow up

The meta-analysis of mean BMD at both baseline and early follow-up of cancellous bone shows the least density at baseline and short-term follow-up dorsal to the acetabular component; conversely, the bone cranial to the acetabular component is of greatest density at both early timepoints (Table 7).

Mean BMD at late follow-up

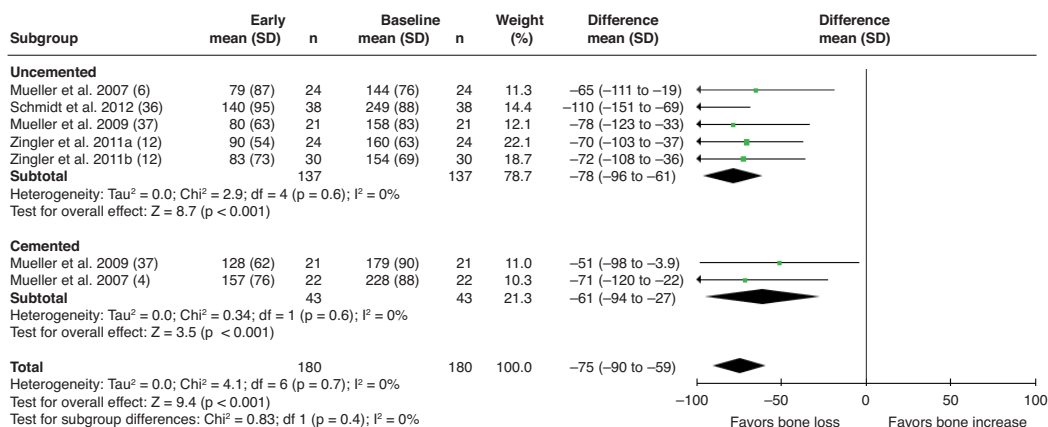
In the meta-analysis, there was a trend of increased bone loss at late follow-up in all ROIs (Figure 4d). Interestingly and potentially skewing results, in

a. Cancellous bone cranial to the level of the acetabulum component for uncemented and cemented components.

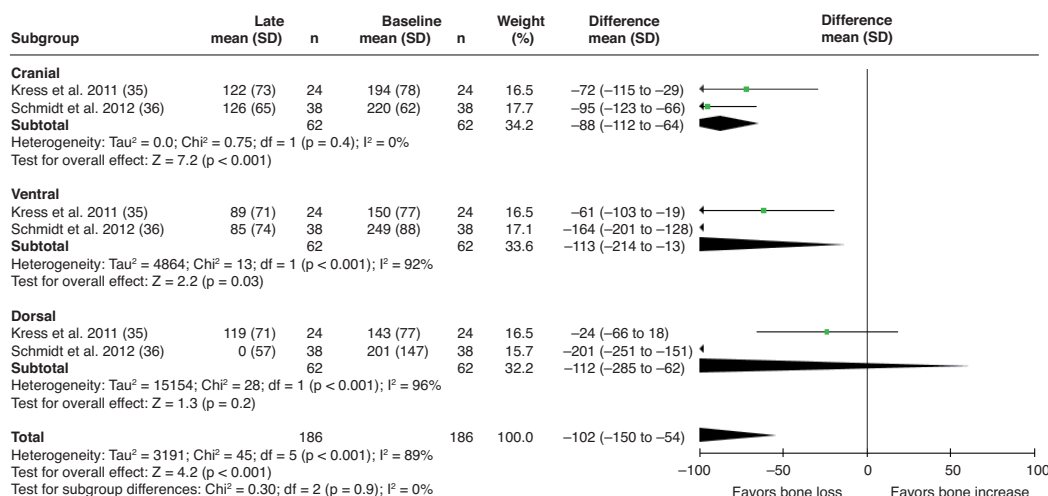


b. Early follow-up of cancellous bone dorsal to the acetabulum component for uncemented and cemented components.

Figure 4. Forest plots meta-analysis of cortical and cancellous bone. Note all eligible studies included for each subgroup. Those not estimable have been omitted.



c. Early follow-up of cancellous bone ventral to the acetabulum component for uncemented and cemented components.



d. Long term follow-up of cancellous bone cranial, ventral, and dorsal to the acetabulum component.

Figure 4 continued

Table 7. Mean cancellous bone mineral density at baseline, early, and late follow-up of uncemented components. Values are mean (standard error; SE) [95% confidence interval; CI] in mg/cm³

ROI	Cancellous bone mineral density mean (SD) [CI]
At baseline	
Cranial	189 (8.0) [173–205]
Dorsal	152 (14) [125–178]
Ventral	173 (19) [135–211]
Early follow-up	
Cranial	145 (6.8) [132–158]
Dorsal	77 (12) [53–101]
Ventral	94 (11) [73–114]
Late follow-up	
Cranial	124 (8.6) [107–141]
Dorsal	59 (60) [0–176]
Ventral	87 (9.3) [68–105]

the study by Kress et al., the most central region dorsal to the component (ROI 5) shows bone loss down to 0 for cancellous bone (35).

BMD changes of cortical and cancellous bone at early follow-up
Cancellous bone

Mean patient age, follow-up duration after THA, ROIs used, and component fixation were effect modifiers on mean cancellous bone loss. For every year increase in mean age, the mean bone loss decreased by 1.6 mg/cm³ (CI 0.7–2.6, Figure 5a). For every month follow-up the mean bone loss increased by 1.8 mg/cm³ (CI 0.4–3.2, Figure 5b). For every unit increase in ROI the bone loss increased by 5.9 mg/cm³ (CI 1.0–11, Figure 5c). For uncemented implants the mean bone loss was 65 mg/cm³ (CI 57–73) and for cemented implants it was 24 mg/cm³ (CI 10–38). Patient sex was not an effect modifier.

Cortical bone

The ROI used, percentage women, and acetabular component fixation were effect modifiers on mean cortical bone loss. For every unit increase in ROI the bone loss increased by 14 mg/cm³ (CI 7.2–21, Figure 6a). For every 10% women in a study, the mean bone loss increased by 8.8 mg/cm³ (CI 2.3–15, Figure 6b). For uncemented implants the mean bone loss was 65 mg/cm³ (CI 51–80) and for cemented implants it was 35 mg/cm³ (CI 12–57). Mean patient age and follow-up after THA were not effect modifiers.

Discussion

This is the first systematic review and meta-analysis performed on CT studies of peri-acetabular BMD following THA. With the increasing clinical use of CTs, and the large improvements in MAR, the authors postulate that measurements of peri-acetabular BMD will be used more frequently. Knowledge

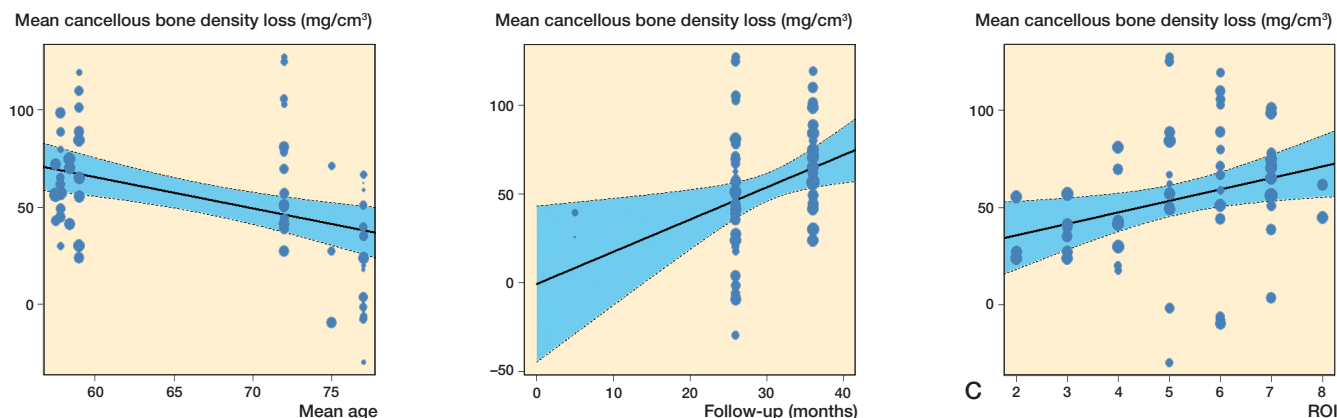


Figure 5. Changes in cancellous bone. A. Bone loss relative to age at early follow-up. B. Bone loss relative to time at early follow-up. C. Bone loss relative to region of interest.

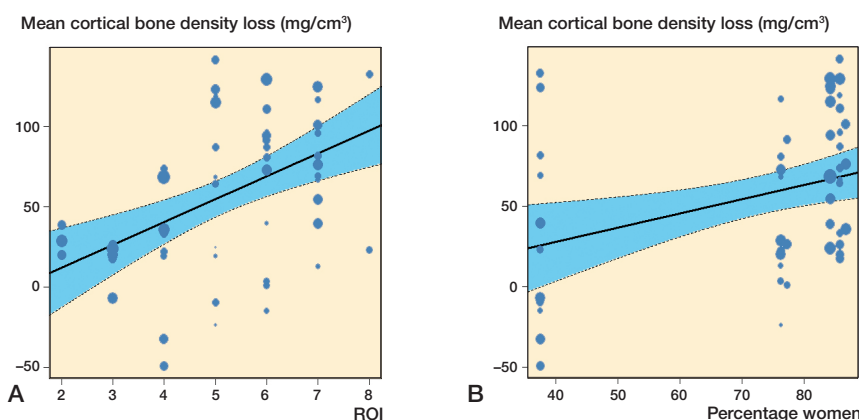


Figure 6. Changes in cortical bone. A. Bone loss relative to region of interest. B. Bone loss relative to sex by percentage of women.

Table 8. Recommendations to improve the reporting of CT studies of peri-acetabular BMD

Standard of reporting	Explanation
Prosthetic components	Details of femoral, acetabular, and liner components used
Sample size	No. of participants
Age	Mean and range
Sex	Proportion
CT scanner type	Manufacturer and type
CT parameters	kVp and mAs
Defined ROI	Recommend axial slices starting 40 mm above cup. Split into ventral and dorsal as desired
Results	Density results for each ROI in mg/cm ³ ± desired unit choice of phantom
Standard deviation	Standard deviation of each ROI in mg/cm ³ to allow for comparison

of the peri-acetabular BMD is important clinically for planning revision THA and in research when investigating implant and patient variables that may influence change in BMD over time. For example, improved reporting of mean BMD may be used for finite element analysis of loading patterns following THA. This implicates a necessity for standardization of mea-

suring changes in peri-acetabular BMD. The authors propose improved standardized reporting of CT-measured BMD following THA by including CT parameters, implant specifications, patient characteristics, follow-up time points, and using standardized ROIs in analysis (Table 8).

Future CT studies of peri-acetabular BMD that use more consistent ROIs will allow investigations of correlation with early component stability and long-term loosening (40). The question is posed as to whether acetabular component migration is the due progressive loading of the component and the component migration towards the path of least resistance or reduced BMD. Additionally, a standardized way of measuring BMD in the peri-acetabular region allows direct comparison of implant variables that are proposed to result in increased or decreased BMD in the periacetabular region. We acknowledge that whilst adoption of our recommendations in Table 8 would be of benefit, future CT scanning protocols are expected to improve with additional MAR techniques.

Our meta-analysis demonstrates that the peri-acetabular cortical and cancellous BMD decreases significantly following THA. The differentiation in rate of cortical compared with cancellous bone moving distally from ROIs 1–8 is proposed to be

due to a shift in the load to cortical bone at the level of the component. The causation of BMD loss following THA is likely multifactorial but driven largely by changes in stress loading of the bone due to implantation of the acetabular component (13). It has been observed in the native acetabulum that bone remodeling is influenced by muscle-force-induced bone stress

(41). The implant orientation is known to change loading of the acetabulum following THA (15). Additional factors leading to decreased BMD include changes in postoperative use of the limb, age-related bone loss, and increasing comorbidities of the ageing patient. A comparison with the contralateral native acetabulum and loading changes was performed in 2 of the reviewed studies showing increased bone loss relative to the native side (38). Pakvis et al. particularly noted increased periacetabular cancellous bone loss with preservation of cranial and cortical bone (38). Bone loss relative to the contralateral side further contributes to the proposed mechanism of bone loss due to stress shielding and changes in postoperative limb use rather than ageing and development of comorbidities of the host.

Our meta-analysis found an early increased amount of cancellous bone loss for younger patients undergoing THA. This is likely due to younger patients having a higher initial BMD and when the loading pattern in the pelvis changes postoperatively they subsequently have a larger amount of bone loss possible. There is no known link between osteolysis and bone density changes and these are thought to be separate entities. Density changes occur due to aforementioned factors such as stress shielding and load changes, whereas osteolysis occurs due to macrophages in response to the innate immune system releasing cytokines and reactive oxygen species in response to particle debris (42). Whilst separate entities, there is certainly crossover in the arthroplasty revision setting when surgeons are treating patients with a combination of osteolysis and poor BMD.

This systematic review identified the varying ROIs that have been used in clinical CT studies to date, which limits the ability to compare studies. It is also acknowledged that our review is limited by the inconsistent reporting by other studies, the conversions of units made, and the limited number of studies published in this field, particularly long-term follow-up studies. There was insufficient data to draw comparisons between different implants and liner types. Regarding measurements in close proximity to the acetabular component for cemented components, due to the irregularity of the interface it is possible a portion of the density measurements included cement (20). Of significance also is that CT density measurements of the periacetabular region are not yet validated. This would require an *ex vivo* cadaveric or retrieval study with elimination of metal artefacts and calibration against known density phantom measurements and is identified as an area of future work.

The ideal classification system of ROIs must be easily used by a clinician on simple radiological software assessing a patient in a busy outpatient department, as well as adequately characterizing the changes in peri-acetabular BMD. A simplified system would split the pelvis into zones of axial slices progressing towards the top of the acetabular component as several studies have done at varying intervals (11,31,38). However, a quadrant system is appealing, given the potential advantages of planning surgical fixation when the acetabu-

lar socket is split into quadrants and any screw augments are aimed towards the posterior superior zone or “safe zone.” The limitation of using quadrant ROIs is that large amounts of bone at varying distances proximal or distal to the acetabular component are pooled together. Given that distance relative to the acetabular component has been shown to be clearly related to BMD, we recommend that future investigators refer to any new description of ROI as relative to the most proximal point of the acetabular component as a subtype within that region, similar to the methods used by Barbu-McInnes et al. (39). Like the methods of the most prolific research group in this area led by Mueller and Schmidt, the regions should be split into axial slices differentiating cancellous and cortical bone (33,37). The regions would be split into 8 10-mm axial ROIs with region 1 starting 40 mm above the acetabular component and continuing 10 mm distally (Figure 1). Region 2 involves bone 30–20 mm above the component and so on until region 8 pertains to –30 to –40 mm below the top of the acetabular component. In addition, the axial ROIs 5–8 at the level of the acetabular component should be split into subgroups dorsal and ventral.

Uncemented and cemented fixation were postulated to create a difference in periacetabular BMD changes due to a difference in the potential loading of the bone and stress shielding. As outlined by Mueller et al. and others, historical finite element analysis studies predicted cemented components would transfer load to the cranial and medial or dorsal portions of periacetabular zone (4,43–45). Within our meta-analysis, cemented components had no change in cancellous bone dorsally but did have slightly smaller bone loss cranially compared with uncemented components (4,29,37). However, when corrected for age, the differences between fixation types for cancellous bone loss were not significant. The reduction in BMD for dorsal regions of cemented components at late follow-up was only noted in 1 study and more studies of cemented components at late follow-up are required. The region dorsal to the component records bone loss down to 0 for cancellous bone in ROI 5 in the Kress et al. study (35) which is thought to be an anomaly rather than taken as. It is worth noting the proximity of ROI 5 to the acetabular component and the large amount of artefact dorsally, which may have hampered measurements in this region (43). The reduction of cancellous bone density cranial to the acetabular component at late follow-up is thought to be of real significance and mean bone loss of 88 mg/cm³ compared with 41 mg/cm³ at early follow-up represents a decrease in the rate of bone loss and likely correlates with a plateau in the effect of the loading of the periacetabular region.

Conclusion

This review of CT studies identified the varying methods of measuring, stratifying, and reporting peri-acetabular BMD following primary THA. Young patients had greater cancellous bone loss and female patients were found to have greater

loss of cortical bone at short-term follow-up. We recommend that future studies should report BMD in 8 ROIs relative to the top of the acetabular component and include patient, implant, and scanning details.

Supplementary data

Tables 1–6 and completed disclosure forms for this article following the ICMJE template are available on the article page, doi: 10.2340/17453674.2023.11635

TR, BS, RN, and SC contributed to study design, data extraction, analysis, and manuscript production. ZM and BP performed data analysis, data extraction, and manuscript production.

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