We aimed to evaluate the precision and longitudinal sensitivity of measurement of bone mineral density (BMD) in the pelvis and to determine the effect of bone cement on the measurement of BMD in femoral regions of interest (ROI) after total hip arthroplasty (THA).

A series of 29 patients had duplicate dual-energy x-ray absorptiometry (DXA) scans of the hip within 13 months of THA. Pelvic analyses using 3- and 4-ROI models gave a coefficient of variation (CV) of 2.5% to 3.6% and of 2.5% to 4.8%, respectively. Repeat scans in 17 subjects one year later showed a significant change in BMD in three regions using the 4-ROI model, compared with change in only one region with the 3-ROI model (p < 0.05).

Manual exclusion of cement from femoral ROIs increased the net CV from 1.6% to 3.6% (p = 0.001), and decreased the measured BMD by 20% (t = 12.1, p < 0.001). Studies of two cement phantoms in vitro showed a small downward drift in bone cement BMD giving a measurement error of less than 0.03 g/cm²/year associated with inclusion of cement in femoral ROIs.

Changes in pelvic periprosthetic BMD are best detected using a 4-ROI model. Analysis of femoral ROI is more precise without exclusion of cement although an awareness of its effect on the measurement of the BMD is needed.

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contained an area adjacent to the rim of the prosthesis, which is a site of potential increase in BMD, and a medial pelvic area, which has an area of potential decrease in BMD. DXA expresses BMD as the mean mass per unit area for a given ROI. If a ROI contains equal areas of gain and loss of bone, the net detected change in BMD will be zero. Thus, analysis models which include such regions have the potential for poor longitudinal sensitivity to the remodelling process. Korovessis, Piperos and Michael also reported changes in BMD around the acetabular component, applying a non-contiguous model of three ROIs. Their study group, however, contained mixed cemented and uncemented implants, BMD values in the opposite hip were used as a baseline, no details of placement of the ROIs were given, and precision calculations were based on non-operated, normal, control hips.

Many models have been applied to the distribution of periprosthetic DXA ROIs in the femur, but variations in the seven ROIs defined by Gruen, McNiece and Amstutz for describing areas of radiolucency on plain radiographs are the most commonly used. Uncertainty remains as to whether radiopaque PMMA bone cement should be included or excluded from analysis of ROIs when measuring BMD around cemented femoral implants. In cadaver studies cement has been shown to increase artificially the apparent BMD of periprosthetic ROIs in the femur by up to 29% and in clinical studies by 23%, and may lead to masking of true longitudinal changes in the BMD.

During the first weeks after implantation, cement undergoes compositional changes because of the slow completion of polymerisation and the absorption of serum into the cement. These result in an alteration in its physical and mechanical properties. Previous studies including cement in analysis of ROIs have failed to address the question of whether cement itself undergoes longitudinal changes in BMD as a result of the early compositional changes. Such changes could affect the estimates of the baseline BMD and periprosthetic bone remodelling.

Our aim was to develop and validate periprosthetic ROIs in the pelvis based on computer predictions of bone remodelling and to compare their sensitivity with that of a model of three ROIs based on those of DeLee and Charnley, to determine the effect of manual removal of cement on the precision of measurement of periprosthetic BMD in the femur in vivo, and to establish the longitudinal BMD profile of cement in vitro.

Materials and Methods

We recruited into the study 29 patients (17 men and 12 women) with a mean age of 52 years (33 to 67), all of whom had given written, informed consent. The local Ethical Committee approved the study. All had had primary THA (14 left-sided, 15 right-sided) within the previous 13 months for primary or secondary osteoarthritis, and had no current clinical or plain radiological evidence of aseptic loosening. All operations had been performed by the same surgeon using an uncemented, metal-backed pelvic acetabular component (Plasma Cup; B. Braun Ltd, Sheffield, UK), and a cemented, double-tapered, collarless, polished design of femoral prosthesis. Twenty of the femoral prostheses were of the Exeter type (Howmedica Ltd, Staines, UK) and nine were of the TPS type (DePuy International Ltd, Leeds, UK). All femoral prostheses had been introduced using Palacos cement with gentamicin (Schering Plough Ltd, Welwyn Garden City, UK).

The patients had duplicate DXA scans of the hemipelvis and ipsilateral proximal femur on the same day after repositioning. The scans were performed with the patient lying supine on the scanner with the legs in extension and the foot of the operated side held in a neutral position using the Hologic ‘metal removal hip’ positioning device. Seventeen patients (11 men, 6 women) returned 13 months later for a further DXA scan of the pelvis. All studies were carried out using the same Hologic QDR 4500A fan-beam densitometer (Hologic Inc, Waltham, Massachusetts).

Scan acquisition. Scans were performed using the ‘metal removal hip’ scanning mode which has a higher resolution than the standard mode, giving a point resolution of 0.06 mm and a line spacing of 0.11 mm.

Pelvic scan acquisition was begun 2 cm below the lower border of the inferior pubic ramus, using a field width of 15 cm. The scans were centred so that the acetabular component lay in the centre of the field. Acquisition was continued proximally to 2 cm above the lower limit of the ipsilateral sacroiliac joint (Fig. 1). Femoral scan acquisition was started approximately 2.5 cm distal to the tip of the femoral prosthesis, with the longitudinal axis of the shaft of the prosthesis vertical and occupying the centre of the scan field. The scan was continued proximally until 2 cm above the tip of the greater trochanter (Fig. 2).

Scan analysis. The duplicate pelvic and femoral scans were analysed independently by a single observer (JMW) using Hologic metal removal software. Two different ROI models were applied to the pelvic analyses. In the first method a three-region model was used based on the lines of demarcation which DeLee and Charnley used for describing areas of visible osteolysis around the circumference of the acetabular component on plain radiographs. The central limit of each region was created by bisecting the centre of the component with a horizontal and a vertical line. The superior and inferior borders of the regions were then defined by horizontal lines placed 30 pixel lines superiorly and inferiorly to the upper and lower limits of the component, respectively. The medial and lateral boundaries were defined by vertical lines placed 15 pixels outside their respective limits (Fig. 1).

In the second method a four-region model was applied. In this model we aimed to create simple rectangular ROIs which contained only areas of predicted bone loss or bone gain. The medial and lateral borders of the regions were created by two vertical lines; one projected along the
medial border of the obturator foramen, and the other along the lateral border of the femoral prosthesis. The superior limit of region 1 was defined by a horizontal line lying 30 pixels superiorly from a horizontal line touching the top border of the cup, which defined its lower limit. Region 2 extended from here to a horizontal line bisecting the centre of the cup, and region 3 extended from there to the lower border of the cup. Region 4 extended from the line marking the lower border of the cup to a further line lying 30 pixels below that (Fig. 1). For both ROI models the analysis software was modified to increase the threshold for exclusion of metal since the preset threshold was insufficient to distinguish between the thick bone of the pelvis and the metal of the cup.

The femoral ROIs were defined by dividing the proximal femur into seven Gruen ROIs according to guidelines in the Hologic user manual (Fig. 2). Two methods were used to analyse the femoral scans. In the first the defaults for metal exclusion of the Hologic software were used, and for the second all visible cement was manually excluded from the scan field using the software ‘paint’ facility, but leaving the position of the ROIs unchanged from the first analysis set.

The results were expressed as area (cm$^2$), bone mineral content (BMC(g)), and BMD (g/cm$^2$) for each analysis ROI. The term net ROI defines a global region of interest encompassing all of the individual ROIs for a particular analysis. To assess the effect of time after operation on the precision of BMD measurement, patients were divided into two groups, namely, those who had their scan within six months of THA (n = 16) and those who were scanned seven or more months after THA (n = 13). The short-term in vivo precision of the BMD was calculated for each of the methods and expressed as the coefficient of variation (CV) according to the formula:

$$CV\% = 100 \times \frac{\delta}{\mu}$$

for each ROI, where $\delta$ represents the standard deviation of the differences between the paired BMD measurements, and $\mu$ is the overall mean of all the BMD measurements for that ROI. The least significant change (LSC) at $p = 0.05$ was calculated as $CV\% \times 2.8$. The mean change in BMD ($\Delta\%$) was expressed as follows:

$$\frac{(\text{BMD}_1 - \text{BMD}_2) \times 2}{\text{BMD}_1 + \text{BMD}_2}$$

The longitudinal sensitivity (LS) was expressed as modulus ($\Delta\%/CV\%$) $\times$ 100.

**PMMA cement phantoms.** Two identical phantoms were created using six types of cement from three manufacturers (CMW 1 Original and CMW 2000 Gentamicin, DePuy International Ltd; Palacos R and Palacos R with gentamicin, Schering Plough Ltd; and Simplex-P and Antibiotic Simplex, Howmedica Ltd). Each phantom consisted of six strips of freshly-prepared cement 50 $\times$ 10 $\times$ 5 mm in dimension mounted on a stainless-steel bar to simulate an implant-cement construct. Two cement strips from each manufacturer were included on each phantom, one representing the antibiotic-impregnated and one the non-antibiotic-impregnated form of their product. The phantoms were immersed in separate isotonic saline water baths at a constant 37°C to simulate a physiological environment and scanned regularly over a ten-month period with the Hologic...
QDR 4500A densitometer. Scan acquisition and analysis were performed using metal exclusion software. The longitudinal BMD equivalent for each type of cement at each time point was calculated as the mean value of the paired samples from the duplicate water baths.

F-tests, Student’s *t*-tests and linear regression analyses were carried out using Statgraphics for Windows version 4 (Manugistics Inc, Chertsey, UK). The level of significance was taken as *p* < 0.05.

**Results**

The precision of the net BMD of the 3-ROI analysis model was not significantly different from that of the 4-ROI model (*F* = 1.24, *p* > 0.05). The latter gave a greater variation in precision for individual regions of interest, ranging from 2.5% to 4.8% compared with 2.5% to 3.6% for the 3-ROI model (Table I). The 4-ROI model, however, had better LS% than the 3-ROI model. Three of the four ROIs had an LS% of greater than 100% compared with only one with an LS% greater than 50% in the 3-ROI model. Three of the four ROIs showed a significant change in BMD at 13 months compared with change in only one region in the 3-ROI model.

Gender appeared to influence the precision of BMD measurements for the 3-ROI model (male CV = 2.7%, female CV = 1.1%), but this result is of doubtful significance since the male population net BMD included two outliers from the normal distribution for this analysis. No significant differences in precision were found for the type or side of implant or time since operation for either analysis method.

Inclusion of cement in the femoral periprosthetic ROIs gave a measured net BMD 20% greater than that for the cement removal analysis (paired *t*-test, *t* = 15.1, *p* < 0.001). Exclusion of cement from the analysis regions led to a significant increase in the variance of the net BMD (*F* = 3.64, *p* = 0.001), with coefficients of variation approximately double those without manual removal of cement in all ROIs (Table II). Exclusion of cement also gave rise to differences in the precision of the net BMD in men and women (*F* = 0.29, *p* = 0.03), corresponding to CV values of 2.5% and 4.7%, respectively. No significant differences in precision were found for the type or side of implant, or time since operation for either method of analysis. Men had a net region of interest of larger area than women for both the pelvic and femoral analysis methods (*t* = 4.4, *p* < 0.001), and higher BMC (*t* = 2.3, *p* = 0.03), but did not have a significantly higher BMD.

All manufacturers’ cement showed a negative slope for BMD over the 290-day study period ranging from -0.000005 to -0.000008 g/cm²/day. The slopes of the regression lines for Simplex P, antibiotic-loaded Simplex, and antibiotic-loaded CMW were significant (Fig. 3). The maximum gradient for the slope of these regression lines, however, was small equating to an equivalent error in BMD measurement by including cement in the analysis of -0.000008 g/cm²/day.

**Discussion**

The poor sensitivity of plain radiography has led to DXA becoming the method of choice for the quantification of loss of femoral periprosthetic bone after THA. We have found that pelvic periprosthetic BMD may be measured with a similar level of precision to that which can be achieved for the femur. Differences in pelvic shape between men and women, and lack of ability to stabilise externally the position of the pelvis on the scanning table, did not appear to have a significant effect on the precision achieved. We also found the level of precision to be independent of the time since operation and the side of implant.

Computed finite-element analysis of redistribution of stress around femoral implants predicts the observed changes in BMD measured by DXA well. When designing our 4-ROI pelvic model we aimed to map areas of decrease and increase in BMD predicted by finite-element analysis into different DXA analysis regions. The theoretical lack of sensitivity of ROIs modelled on the DeLee and Charnley

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**Table I.** Precision of pelvic periprosthetic measurements of BMD (mean ± sd) using 3- and 4-ROI analysis models (see text)

<table>
<thead>
<tr>
<th>ROI</th>
<th>Area (cm²)</th>
<th>BMC (g)</th>
<th>BMD (g/cm²)</th>
<th>CV% (n = 29)</th>
<th>LSC% (n = 29)</th>
<th>Δ% (n = 17)</th>
<th>LS% (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net</td>
<td>20.60 ± 0.91</td>
<td>23.22 ± 0.83</td>
<td>1.13 ± 0.03</td>
<td>2.14</td>
<td>5.99</td>
<td>1.05</td>
<td>49</td>
</tr>
<tr>
<td>1</td>
<td>3.88 ± 0.35</td>
<td>5.37 ± 0.47</td>
<td>1.40 ± 0.05</td>
<td>2.53</td>
<td>7.09</td>
<td>3.73*</td>
<td>147</td>
</tr>
<tr>
<td>2</td>
<td>7.19 ± 0.72</td>
<td>8.57 ± 1.39</td>
<td>1.24 ± 0.06</td>
<td>3.21</td>
<td>8.98</td>
<td>-1.05</td>
<td>33</td>
</tr>
<tr>
<td>3</td>
<td>9.81 ± 0.79</td>
<td>9.38 ± 0.60</td>
<td>0.96 ± 0.05</td>
<td>3.56</td>
<td>9.96</td>
<td>1.74</td>
<td>49</td>
</tr>
<tr>
<td>Net</td>
<td>22.13 ± 0.90</td>
<td>24.10 ± 0.93</td>
<td>1.09 ± 0.03</td>
<td>1.98</td>
<td>5.55</td>
<td>0.19</td>
<td>10</td>
</tr>
<tr>
<td>1</td>
<td>7.82 ± 0.55</td>
<td>10.70 ± 0.79</td>
<td>1.38 ± 0.05</td>
<td>2.52</td>
<td>7.06</td>
<td>2.52†</td>
<td>127</td>
</tr>
<tr>
<td>2</td>
<td>3.30 ± 0.23</td>
<td>3.48 ± 0.25</td>
<td>1.08 ± 0.07</td>
<td>4.79</td>
<td>13.40</td>
<td>-2.74</td>
<td>57</td>
</tr>
<tr>
<td>3</td>
<td>4.98 ± 0.60</td>
<td>4.95 ± 0.50</td>
<td>1.00 ± 0.05</td>
<td>3.82</td>
<td>10.70</td>
<td>-4.72*</td>
<td>123</td>
</tr>
<tr>
<td>4</td>
<td>6.93 ± 0.51</td>
<td>5.94 ± 0.43</td>
<td>0.86 ± 0.04</td>
<td>3.25</td>
<td>9.10</td>
<td>3.79†</td>
<td>117</td>
</tr>
</tbody>
</table>

*p* paired *t*-test *p* < 0.05  
† paired *t*-test *p* < 0.01
radiological regions was borne out in our longitudinal pelvic BMD results. The net change in BMD for both pelvic models was not significant over the period of study, because some regions around the prostheses were undergoing bone loss and others bone gain. Significant regional changes in BMD were detected in regions 1, 3 and 4 using the 4-ROI model, but only in region 1 using the 3-ROI model (Table I). The 4-ROI model also reflected the increase in BMD adjacent to the prosthetic rim and the decrease in the central pelvic zones predicted by the computer simulations of Levenston et al.\textsuperscript{11} Thus, the 4-ROI model provided greater sensitivity to local longitudinal changes in BMD than the 3-ROI version despite greater inter-regional variation in precision.

Analysis of pelvic periprosthetic BMD did present some technical problems. We found that often the thicker bone of the pelvis caused the metal exclusion algorithm to mistake some bone areas for metal and exclude them. We initially corrected this problem manually by painting back in these areas using the software paint facility, but this led to poor precision in some regions.\textsuperscript{25} We overcame the problem by increasing the metal exclusion threshold on our analysis software, requiring less manual painting, and resulting in improved precision.

When analysing the femoral periprosthetic DXA scans for this study we used the interpretation of the Gruen regions as defined by the Hologic user manual. Our precision results were similar to those reported from other centres for cemented implants without manual removal of cement,\textsuperscript{2,26,27} and were independent of gender, type and side of implant, and time since operation.

Manual removal of cement gave rise to poorer precision, which in some ROIs led to a least significant change of a similar order of magnitude to the amount of bone loss which might be expected longitudinally. Thus, the precision of measurements using manual removal of cement may be of use in population studies but of limited value in the monitoring of individuals. The main reason for this poor precision lies in the difficulty of consistently removing the same amount of cement from baseline and subsequent analyses. Good cementing technique at THA necessitates extensive penetration of cement into the interstices of the surrounding bone. The line of demarcation between cement and bone is therefore an indistinct one. Attempts to completely exclude cement manually or by using an automated step-off from the margin of the prosthesis are therefore unreliable.

Inclusion of radiopaque cement in the analysis of femoral ROIs gave a net value for BMD which was 20% higher than that with exclusion of cement, a figure similar to the findings of other in vivo\textsuperscript{2} and ex vivo studies.\textsuperscript{16} The increase in BMD is partly accounted for by the cement itself, but also includes a component caused by the inclusion of an additional envelope of periprosthetic bone, such

### Table II. Precision of proximal femoral periprosthetic measurement (mean ± SD) of BMD before and after manual exclusion of cement (see text)

<table>
<thead>
<tr>
<th>ROI Area (cm(^2))</th>
<th>BMC (g)</th>
<th>BMD (g/cm(^2))</th>
<th>CV%</th>
<th>LSC%</th>
</tr>
</thead>
<tbody>
<tr>
<td>38.98 ± 0.98</td>
<td>3.03 ± 0.51</td>
<td>1.0 ± 0.04</td>
<td>2.81</td>
<td>7.88</td>
</tr>
<tr>
<td>1 11.95 ± 0.32</td>
<td>11.37 ± 0.74</td>
<td>0.0 ± 0.05</td>
<td>4.47</td>
<td>12.52</td>
</tr>
<tr>
<td>2 4.40 ± 0.41</td>
<td>3.89 ± 1.01</td>
<td>1.87 ± 0.09</td>
<td>3.29</td>
<td>9.20</td>
</tr>
<tr>
<td>3 4.22 ± 0.37</td>
<td>8.23 ± 0.90</td>
<td>1.92 ± 0.10</td>
<td>3.58</td>
<td>10.02</td>
</tr>
<tr>
<td>4 5.67 ± 0.24</td>
<td>12.79 ± 0.41</td>
<td>2.25 ± 0.05</td>
<td>1.54</td>
<td>4.32</td>
</tr>
<tr>
<td>5 3.98 ± 0.28</td>
<td>7.71 ± 0.41</td>
<td>1.94 ± 0.08</td>
<td>2.83</td>
<td>7.93</td>
</tr>
<tr>
<td>6 4.54 ± 0.27</td>
<td>6.45 ± 0.43</td>
<td>1.39 ± 0.05</td>
<td>2.64</td>
<td>7.40</td>
</tr>
<tr>
<td>7 4.89 ± 0.35</td>
<td>6.17 ± 0.38</td>
<td>1.72 ± 0.04</td>
<td>2.35</td>
<td>6.57</td>
</tr>
</tbody>
</table>

* data for exclusion of cement are shown in italics

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![Graph showing changes in BMD equivalent for PMMA samples in vitro. The suffix 'A' indicates antibiotic-impregnated types of cement (a: linear regression \( r^2 = 0.49 \), slope = 0.00008 g/cm\(^2\)/day, \( p < 0.001 \); b: linear regression \( r^2 = 0.39 \), slope = 0.00006 g/cm\(^2\)/day, \( p < 0.001 \); c: linear regression \( r^2 = 0.38 \), slope = 0.00007 g/cm\(^2\)/day, \( p < 0.001 \).](image)
that the contribution of cement to the measured BMD is less than 20%.

Compositional changes which occur in cement after implantation may give rise to changes in measured BMD. The rate of change which we observed, however, was very small and of limited clinical importance when compared with changes seen in periprosthetic bone after THA.

In summary, precise measurements of BMD may be made around both prosthetic components after THA with a level sufficient to detect changes in individuals in prospective series. Pelvic periprosthetic BMD is best measured using a 4-ROI analysis model, but modifications to software are necessary to achieve good precision. Cemented femoral periprosthetic BMD is most precisely measured without exclusion of cement, although an awareness of underestimation of a true change in BMD and small changes due to inclusion of cement should be appreciated in prospective series.

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