Periprosthetic bone remodelling around a prosthesis for distal femoral tumours

MEASUREMENT BY DUAL-ENERGY X-RAY ABSORPTIOMETRY (DEXA)

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We used dual-energy x-ray absorptiometry (DEXA) to evaluate the extent of periprosthetic bone remodelling around a prosthesis for distal femoral reconstruction, the Kotz modular femoral tibial replacement (KMFTR; Howmedica, Rutherford, New Jersey). A total of 23 patients was entered into the study which had four parts: 1) 17 patients were scanned three times on both the implant and contralateral legs to determine whether the precision of DEXA measurements was adequate to estimate bone loss surrounding the anchorage piece of the KMFTR; 2) in 23 patients the bone mineral density (BMD) in different regions of interest surrounding the diaphyseal anchorage was compared with that of the contralateral femur at the same location to test whether there was consistent evidence of loss of BMD adjacent to the prosthetic stem; 3) in 12 patients sequential studies were performed about one year apart to compare bone loss; and 4) bone loss was compared in ten patients with implants fixed by three screws and in 13 without screws.

The mean coefficients of variation (SD/mean) for the 17 sets of repeated scans ranged from 2.9% to 7.8% at different regions of interest in the KMFTR leg and from 1.4% to 2.5% in the contralateral leg. BMD was decreased in the KMFTR leg relative to the contralateral limb and the percentage of BMD loss in general increased as the region of interest moved distally in the femur. Studies done after one year showed no consistent pattern of progressive bone loss between the two measurements. The ten patients with implants fixed by screws were found to have a mean loss of BMD of 42% in the most distal part of the femur, while the 13 without screw fixation had a mean loss of 11%.

DEXA was shown to have adequate precision to evaluate loss of BMD around the KMFTR. This was evident relative to the contralateral leg in all patients and generally increased in the most distal part of the femur. In general, it stabilised between two measurements taken one year apart and was greater surrounding implants fixed by cross-locking screws.

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Periprosthetic bone remodelling is a frequent complication of implants which have rigid intramedullary stems because of stress shielding. The loss of bone stock may compromise the outcome of total hip replacement (THR) in particular, leading to potential complications such as loosening, fracture, pain and difficulty in performing revision arthroplasty.

A variety of methods has been used to study periprosthetic bone loss in THR including dual-photon analysis, MRI and quantitative CT. The inconsistent effects of the metal implant on all of these imaging techniques have limited their accuracy and reliability in the measurement of bone density. Recently, dual-energy x-ray absorptiometry (DEXA) has been found to give a high level of precision and reliability for measurement of bone density in vivo at the periphery of total hip implants. In our study, DEXA has been used to measure bone loss associated with a prosthesis employed in reconstructing the distal femur after resection of a tumour.

The implant which we studied is the Kotz modular femoral tibial replacement (KMFTR) (Howmedica, Rutherford, New Jersey) which is used primarily for limb-salvage procedures after resection of bone tumours. The KMFTR relies on the non-cemented fixation of a diaphyseal anchorage piece manufactured from cast chrome-cobalt alloy. This has a macrotextured Madreporique surface and is inserted into the distal femoral canal after
appropriate reaming. The KMFTR has a rigid intramedul-
lar stem which may predispose to bone resorption because
of stress shielding.

In our study the KMFTR was designed with lateral and
anterior flanges which fitted along the outside of the femo-
ral cortex. There are perforations in the flanges and in the
core of the diaphyseal anchorage piece which allow inser-
tion of up to six cross-locking screws, three in an antero-
posterior direction and three from lateral to medial.

Using plain radiography to grade the degree of peripros-
thetic bone loss surrounding the diaphyseal anchorage
piece in patients treated with the KMFTR, Capanna et al18
found that the use of three cross-locking screws instead of
six gave sufficient early fixation for initial stability of the
implant, but reduced the extent of stress shielding and bone
loss. They suggested that elimination of fixation of the
screw may further reduce bone loss because of stress
shielding.

Our aim was fourfold: 1) to determine whether the
precision of DEXA would be adequate to estimate the bone
loss surrounding the anchorage piece of the KMFTR; 2) to
compare the bone density surrounding the diaphyseal
anchorage piece with that of the contralateral femur at the
same location in order to evaluate whether there was
consistent loss of bone mineral density (BMD) adjacent to
the prosthetic stem; 3) to compare bone loss in a group of
patients who had sequential studies performed about one
year apart in order to evaluate whether periprosthetic bone
loss increased over time; and 4) to compare the bone loss
surrounding implants fixed by three screws with those
without screws.

Patients and Methods

Of 64 patients who had been treated for primary malig-
nancy of the distal femur using the KMFTR prosthesis, 23
had at least one DEXA analysis. We excluded patients with
metastatic disease and with local vascular, neurogenic,
mechanical or infectious complications from the study.
Those with fair or poor functional outcome scores as
evaluated by the Musculoskeletal Tumour Society scale20
and those with underlying metabolic bone disease or on
long-term corticosteroids were also excluded. The most
common reason for exclusion was related to the inconveni-
cence of waiting for the investigation to be completed in
patients travelling long distances for follow-up. Before the
final selection of patients for DEXA analysis, plain radio-
graphs were reviewed to ensure that the implant appeared
to be well fixed and patients were excluded if there was
evidence of myositis or formation of callus about the distal
end of the femur. This last exclusion ensured that measure-
ments were obtained from the femur rather than from
adjacent ossification of soft tissue.

There were 12 women and 11 men with a mean age of 38
years (18 to 70). The mean time from surgery to the first
DEXA scan was 31.8 months (8 to 72). The mean length of
resection of the femur was 17 cm (6 to 30). The diagnosis
was osteosarcoma in 12 patients, chondrosarcoma in three,
malignant giant cell tumour in two, spindle-cell sarcoma in
three, malignant fibrous histiocytoma in two and leiomyo-
sarcoma of bone in one. All 18 patients with high-grade
sarcoma of bone had chemotherapy. The same KMFTR
prosthesis was used in all the patients; 21 had diaphyseal
anchorage pieces of 13 mm in diameter and two had
16 mm stems.

We have used the KMFTR since 1989. From 1989 to
1992, all implants were inserted using two or three screws
(Fig. 1). After 1992, most implants were inserted without
cross-locking screws, as long as the implant was rotation-
ally stable after implantation (Fig. 2). Generally, the femur
was reamed 1 mm larger than the diameter of the prosthesis
for implants inserted with or without screws.

Dual-energy x-ray absorptiometry (DEXA). We used the
DPX bone densitometer (Lunar Corporation, Madison,
Wisconsin) to quantify bone loss. This has a constant
potential x-ray source at 76 kVp and a K-edge filter to split
the polynergic x-ray beam into high- and low-energy
components. Each component energy is differentially

Figure 1 – Anteroposterior plain radiograph of a KMFTR
prosthesis inserted using two interlocking screws, one antero-
posterior and one mediolateral, showing marked stress shield-
ing distal to the screw. Figure 2 – Plain radiograph of a
KMFTR prosthesis inserted without interlocking screws.
absorbed by bone and soft tissue and the transmitted radiation is measured using a scintillation counter. After scanning, a computer algorithm calculates bone mineral content (BMC) in grams and BMD as g/cm\(^2\) for various regions of interest (ROI). The radiation dose to the patient is less than 5 mrem per scan.

The software allows measurement of the BMD adjacent to metal implant stems. Regions in which the x-ray beams are attenuated by the metal implant are automatically subtracted from the scan results using the computer algorithm.

All subjects had an anteroposterior DEXA scan on both the leg with the KMFTR implant (KMFTR leg) as well as on the contralateral healthy limb. DEXA was undertaken with the leg in neutral rotation with the toes facing forward within a leg-holding jig.

The values for BMD were calculated at seven designated ROIs (Fig. 3) surrounding the diaphyseal anchorage piece as well as at sites remote from the prosthesis. These were then compared with the corresponding areas in the contralateral normal femur using software which allowed transposition of the image of the prosthesis on to the scan of the normal femur.

**Precision of BMD measurement.** Seventeen patients were scanned three times on the KMFTR leg and the normal leg on the same day. Between scans, they stepped down from the scan table and were then repositioned for the next scan. The precision of these repeated measurements was calculated as the coefficient of variation, by dividing the sd of the multiple measurements by the mean value obtained.

**Comparison of BMD in the KMFTR and contralateral legs.** The scans from all 23 patients were evaluated to determine whether the BMD in each ROI differed from the same region in the contralateral leg and whether bone loss was greatest at the distal end of the femur increasing progressively from the proximal to the distal end of the prosthesis.

**Change in BMD with time.** Twelve patients had two scans separated by a period of 10 to 18 months. We tested the change in BMD to determine whether bone loss increased with the service time of the prosthesis. Although bone loss was measured in several ROIs surrounding the prosthesis, it was decided that comparison of bone loss due to stress shielding would be best determined by comparing the BMD in region 1 at the most distal part of the femur. The % BMD loss was calculated as follows:

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\text{% BMD loss} = \frac{[\text{BMD of contralateral leg} - \text{BMD of KMFTR leg}]}{\text{BMD of contralateral leg}}
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This allowed bone loss to be normalised to the density of the contralateral leg thereby decreasing variation in the BMD between individuals. Change in BMD loss was calculated by subtracting the second value from the first. A negative value for change in BMD loss meant that the BMD in ROI 1 actually increased relative to the contralateral leg between the two measurements.

**Comparison of BMD in prostheses inserted with and without screws.** Ten patients with implants fixed by screws (group 1) and 13 without screws (group 2) were scanned. These two groups had a different length of follow-up since the implants fixed by screws were generally used earlier in the overall series than those fixed without screws. Accordingly, when patients had had more than one DEXA scan, the earlier scan results were used for group 1 and the later for group 2. As described above, comparison of bone loss due to stress shielding was performed using the % BMD loss from ROI 1.

**Statistical analysis.** To study precision in the multiple measurements of BMD obtained at the same time of examination, the coefficient of variation was calculated as already described. We used analysis of variance to determine whether the values for BMD for each ROI in the KMFTR leg were different from those in the normal contralateral limb, and a paired \(t\)-test to assess whether there were significant differences between the % BMD loss of two measurements one year apart. Finally, the \(t\)-test statistic was used to compare the % BMD loss surrounding prostheses inserted with or without screws.

**Results**

Review of the clinical outcome of the entire series of 64 patients treated with the KMFTR prosthesis for sarcoma of the distal femur showed that there was no obvious deleterious effect observed in the patients receiving implants inserted without screws. One had required revision for a loose diaphyseal anchorage piece which had originally been fixed by screws. There have been five fractures of the stem in this entire group, three in 11 mm stems and two in...
BMD should be reliably detectable; 15.6% represents two from ROI 1, differences equal to 15.6% of the mean normal contralateral leg (Table I). Using the coefficient of variation to 7.8% in the KMFTR leg and from 1.4% to 2.5% in the variation calculated for the various ROIs ranged from 2.9% been fixed by screws.

a 13 mm stem. All except one occurred in stems which had been fixed by screws.

Precision of BMD measurement. The mean coefficients of variation calculated for the various ROIs ranged from 2.9% to 7.8% in the KMFTR leg and from 1.4% to 2.5% in the contralateral leg (Table I). Using the coefficient of variation from ROI 1, differences equal to 15.6% of the mean normal BMD should be reliably detectable; 15.6% represents two sds from the mean.

Comparison of BMD in the KMFTR and contralateral legs. Using data from all 23 patients, it was evident that the BMD decreased in the KMFTR leg relative to the contralateral leg for each ROI except in the proximal lateral ROI 2 (Table II). In general, the % BMD loss increased as the ROI moved more distally in the femur (Table III).

Change in BMD with time. The mean interval between studies was 13 months (10 to 18). During this time, the % BMD loss in ROI 1 decreased, with the BMD increased relative to the contralateral leg, in seven patients and increased, with the BMD decreased relative to the contralateral leg, in five. The mean change in BMD loss was -7.7%. These results are summarised in Table IV and suggest that there is ongoing change in BMD which may continue for at least one year after insertion of a prosthesis. This change is variable and the data do not suggest progressive loss of BMD after one year.

Comparison of BMD in prostheses inserted with and without screws. In comparing the % BMD loss surrounding prostheses inserted with and without screws, it must be recognised that the two groups do not have a comparable follow-up from the time of implantation because screws were used only in the initial years of our experience with the KMFTR prosthesis. There were no differences in these two groups with respect to the extent of femoral resection; the mean resection was 18.1 cm in the patients fixed by screws compared with 17.5 cm in those without.

Even allowing for the differences in the length of follow-up, there were marked differences in the extent of BMD loss in the two groups (Table V). In ROI 1, the % BMD loss in the group without screws was 11%, compared with 42% in those with screws (p < 0.05). Table V gives the mean BMD loss for all the ROIs.

Discussion

The success of adjuvant chemotherapy in achieving prolonged disease-free survival for patients with high-grade bone sarcoma has increased the necessity for longevity of reconstructive procedures after resection of the tumour. The method of reconstruction most commonly used in the replacement of a distal femoral sarcoma is the cemented femoral prosthesis. It has been shown that the actuarial likelihood of this implant loosening by ten years after insertion is about 30% to 40%. In order to improve this clinical outcome and decrease the likelihood of loosening, uncemented, porous-coated prostheses such as the KMFTR were introduced.

Capanna et al raised the issue of stress shielding as a potential cause of long-term complications after reconstruction with an uncemented prosthesis. They used a subjective system of radiographic grading to assess bone loss qualitatively at the end of the diaphyseal component. They found bone loss in many of their patients and noted that it seemed to be greater after insertion with six screws rather than with three. Just before the report of Capanna et al we had begun to insert the KMFTR without any screws and our study was designed to determine whether bone loss in the distal femur would be decreased in these patients.
The precision of measurements calculated in the repeated-measures experiments (7.8% coefficient of variation) showed that the difference in bone loss measured in zone 1 in the two groups of patients (11% v 42%) was well within the level of difference that could be reliably detected by DEXA. This coefficient of variation is comparable to the precision obtained with measurements of BMD in the proximal femur of patients with total hip arthroplasty.

The pattern of the bone loss in the femur surrounding the KMFTR prosthesis was also comparable to that observed in total hip arthroplasty. Loss around the KMFTR prosthesis was maximal at the distal end of the femur and progressively decreased towards the proximal end of the stem. Several studies of bone loss adjacent to both cemented and uncemented hip implants have shown that it increases with measurement from the tip of the prosthesis towards the calcar.

One of the critical issues in interpreting measurements of bone loss after insertion of an implant is whether this is continuous or reaches a steady state with time. Our study suggests that bone loss with the KMFTR is not progressive but reaches a plateau. One year after the initial measurement there was no consistent pattern of increased bone loss; more patients had an increased BMD at the second measurement than had decreased density between the two measurements. This plateau in loss of BMD is similar to that found after hip replacement. Cohen and Rushton also reported that loss of BMD at one year did not differ from measurements made at six months after total hip arthroplasty. Marchetti et al. found that proximal femoral bone loss was detectable two months after surgery, had increased by six months and decreased by two years. Kilgus et al. found an association between increased bone loss and time from surgery, although these measurements were not repeated estimates in the same patients.

The suggestion that BMD may increase (i.e., bone loss may decrease) between the measurements made one year apart in our patients may be related to the protocol used in their rehabilitation. We advise against weight-bearing in the first six to eight weeks after implantation of the device with progression to gradual weight-bearing over the next six weeks. This may result in substantial loss of BMD due to disuse at the first DEXA measurement followed by progressive recovery in BMD when the patient has been weight-bearing for more than a year at the second assessment.

Whether the loss of BMD is progressive with time is important in interpreting the observations in patients whose prostheses were fixed with and without screws. The group operated on first who had screw fixation, would be expected to have more loss of BMD than the patients without screw fixation if loss was progressive with time. Measurements made at intervals suggest that a plateau is reached in the loss of BMD whereas the comparison of BMD in patients with prostheses fixed with and without screws suggested a very large increase in loss with screw fixation. These results support the findings of Capanna et al. on bone loss after fixation with six or three screws.

Prevention of bone loss surrounding the distal end of the KMFTR prosthesis is particularly important because of the design of the prosthesis. The most distal holes for cross-screw fixation in the diaphyseal anchorage component are within 1 cm of the end of the bone. If bone loss occurs at the distal end of the femoral shaft, the region at the most distal hole may become less supported by bone and subject to cycling loads which could result in mechanical failure. The KMFTR is potentially at risk for this type of failure since it is a cast, rather than forged, cobalt-chrome prosthesis.

In our patients, five (three 11 mm and two 13 mm) of 64 implants failed through this first screw hole. All except one of the fractured implants had been fixed by screws. Recently, the manufacturer has modified the design to compensate for this risk of fracture by decreasing the number of screw holes from six to three and recessing the first screw hole further from the end of the prosthesis. It seems, however, that even three-screw fixation may increase the extent of loss of BMD.

We have been generally satisfied with the early functional outcome of patients who receive the KMFTR prosthesis. The theoretical advantage of avoiding the osteolysis and loosening found with cemented prostheses makes this implant an attractive option in young patients who, if they survive their disease, will require function for many years. So far, we have seen only one case of loosening with the KMFTR, and bone loss because of stress shielding may be a more significant problem with this implant than loosening. Fixation by screws may increase the extent of the loss of BMD. In view of these results, the manufacturers of this device may reconsider whether screw fixation should be advised for the femoral diaphyseal anchorage piece which is rotationally stable after insertion. It should be recognised that the KMFTR implant was modified (three screw holes instead of six in the diaphyseal anchorage piece) over the course of our study.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References


