Total femoral endoprosthetic replacement following excision of bone tumours

We undertook a retrospective review of 33 patients who underwent total femoral endoprosthetic replacement as limb salvage following excision of a malignant bone tumour. In 22 patients this was performed as a primary procedure following total femoral resection for malignant disease. Revision to a total femoral replacement was required in 11 patients following failed segmental endoprosthetic or allograft reconstruction. There were 33 patients with primary malignant tumours, and three had metastatic lesions. The mean age of the patients was 31 years (5 to 68). The mean follow-up was 4.2 years (9 months to 16.4 years). At five years the survival of the implants was 100%, with removal as the endpoint and 56% where the endpoint was another surgical intervention. At five years the patient survival was 32%. Complications included dislocation of the hip in six patients (18%), local recurrence in three (9%), peri-prosthetic fracture in two and infection in one. One patient subsequently developed pulmonary metastases. There were no cases of aseptic loosening or amputation. Four patients required a change of bushings. The mean Musculoskeletal Tumour Society functional outcome score was 67%, the mean Harris Hip Score was 70, and the mean Oxford Knee Score was 34.

Total femoral endoprosthetic replacement can provide good functional outcome without compromising patient survival, and in selected cases provides an effective alternative to amputation.

The femur is the long bone most commonly affected by both primary and secondary malignant lesions. Before the 1980s the primary treatment for such lesions was amputation. However, advances in chemotherapy, imaging, surgical technique and implant design have allowed limb salvage to become the mainstay of surgical management. Although limb salvage is associated with a higher rate of local recurrence compared to amputation, there is no difference in overall patient survival.2,3 Limb salvage has been shown to be more cost-effective than amputation, and can offer improved functional outcome although, with the exception of physical functioning, there is no significant difference in the quality of life.4-6

Following resection of a tumour of the femur, options for reconstruction include the use of autografts,7,8 allografts,9,10 rotation-plasty,11,12 and custom-made or modular endoprostheses.13-15 The incidence of fracture, nonunion and infection make reconstruction with allografts unattractive.9,10 Endoprostheses generally show improved functional outcome and allow patients to weight-bear early. In the skeletally immature patient there is now the option of lengthening using a minimally or non-invasive growing mechanism.14,16-18 Despite the potential complications of endoprosthetic reconstruction, which include infection, aseptic loosening, local recurrence, dislocation, mechanical failure and fracture, either of the prosthesis or of the bone, this procedure remains the main method of limb salvage for malignant bone lesions of the lower limb.

The most radical form of endoprosthetic reconstruction is a total femoral endoprosthetic replacement with excision and replacement of the entire femur and both the hip and knee joints. This procedure may be used as an alternative to disarticulation of the hip following extensive excision of a tumour of the femur, or in cases of aseptic loosening, infection or peri-prosthetic fracture following distal or proximal femoral replacement with associated severe bone loss. It has also been used for limb salvage in patients with non-neoplastic conditions.19 To date, there have been very few studies on the oncological and functional outcome of patients who have undergone this procedure for malignant bone disease. We describe our experience of employing this procedure for
Materials and Methods

Between June 1978 and October 2007, 33 patients underwent a total femoral endoprosthetic replacement at our institution. Of these, 22 had this as a primary limb salvage procedure for malignant disease, and 11 following failure of a proximal or distal femoral replacement or failed allograft reconstruction, all performed originally for a malignant lesion. All the procedures were carried out by the senior surgeons at a single tertiary referral bone tumour unit. Information was collected from the bone tumour database, medical records, imaging studies and individual structured questionnaires from patients. There were 19 males and 14 females, with a mean age of 31 years (5 to 68). Pre-operative staging included plain radiography and MRI of the femur (Fig. 1), CT of the chest and total body scintigraphy. A total of 18 needle biopsies and 15 open biopsies provided the pre-operative histological diagnosis in these patients. Limb salvage with total femoral endoprosthetic replacement was not considered if the tumour had invaded the neurovascular bundle. A total of 30 patients had a primary malignant tumour and three had nearly 30 years, using both a custom-made and a modular total femoral endoprosthetic replacement (Stanmore Implants Worldwide Ltd, Stanmore, United Kingdom).

Surgical technique. With the patient in the lateral position a longitudinal incision which includes excision of the biopsy track is used. The hip is resected through both anterolateral and posterior approaches. The abductors are detached through their tendinous attachments. The incision extends distally to allow a lateral parapatellar approach to the knee. The tumour is resected according to the principles defined by Enneking, Spanier and Goodman, endeavouring to achieve a satisfactory margin of resection with complete excision of the lesion. A transverse tibial osteotomy is performed 10 mm below the joint line to permit cementing of the tibial component. If the tumour does not extend to the greater trochanter, this structure is removed with the attached abductors and re-attached to the prosthesis with screws and an HA-coated plate. However, it is frequently necessary to include the entire greater trochanter with a layer of soft tissue in order to obtain adequate bone and soft-tissue margins. The remaining abductors are then reconstructed by directly

Fig. 1
Coronal T1-weighted MRI of a 12-year-old patient with a high-grade osteosarcoma of the femur extending from the distal femoral physis to the subtrochanteric region. Axial imaging confirmed that the neurovascular structures were displaced, albeit not encased by tumour.
suturing their tendons to the tensor fascia lata. Occasionally a medial gastrocnemius interposition flap is used to provide soft-tissue cover at the knee if it has also been necessary to resect a portion of the proximal tibia. Intravenous antibiotics are continued for three days after operation. Initially the limb is supported on slings and springs for five days. The patient is then mobilised, bearing weight as tolerated wearing an abduction brace. At six weeks, once active abduction of the hip has been achieved and satisfactory radiographs obtained, the brace is discarded and full weight-bearing is allowed.

### Outcome analysis

The Musculoskeletal Tumour Society Rating Scale (MSTS),\(^{21}\) the Harris Hip score (HHS),\(^{22}\) and the Oxford Knee Score (OKS)\(^{23}\) were used to assess the functional outcome as the procedure replaces both hip and knee joints.

The MSTS is a six-item scale that evaluates mainly clinical measures. Numerical values (0 to 5) are assigned to each of the six categories of pain, function, emotional acceptance, use of supports, walking ability and gait cosmetics, to produce a score ranging from 0 to 30. The HHS evaluates function after THR with the three main categories of pain, function and findings on physical examination, to produce a score out of 100. The OKS is a 12-item questionnaire designed specifically for patients undergoing total knee replacement. Each item has five possible responses and is scored from 0 to 4 to give a cumulative figure of 0 (the worst possible status) to 48 (a normal knee).

The time to failure was defined as the time in years from the date of the original operation to failure. We defined failure of the implant, as described by Meyers et al,\(^{24}\) as the need for any further operation, whatever the cause (re-bushing, revision, excision or local recurrence, dislocation etc); the need for any revision of the prosthesis or part of the prosthesis (e.g. aseptic loosening, fracture of the implant, infection, breakages etc); failure requiring amputation.

### Statistical analysis

Kaplan-Meier survival curves for both implant and patient were used to compare rates of survival (Fig. 4). Survival of the implant was analysed with two endpoints, removal and re-operation. Patients were censored for statistical analysis (observation stopped before the event occurred) if failure had not occurred at the time the patient was last assessed. Patient times of death were also censored at the time of implant failure in cases where the implant failed before death. A p-value of < 0.05 was considered significant.
Results

The mean follow-up was 4.2 years (9 months to 16.4 years) for all the patients, 7.6 years (1 to 16.4) for the 11 who were alive at the time of this review, and 2.6 years (9 months to 13 years) for the 22 who had died. Of the 22 who had died, the cause of death was metastatic disease in 19, neutropenic sepsis in one and unrelated causes in two (Table I). The survival of the implant at five and ten years was 100%, with removal as the endpoint. Where the endpoint was another surgical intervention, survival was 56% at five and 50% at ten years. Survival of the limb was 100%. Patient survival was 32% (9 of 28) at five years, 16% (4 of 25) at ten years and 12% (3 of 25) at 15 years.

Of the 30 patients who had primary malignant tumours of the femur, 19 (63%) had metastases at presentation. Of these, 79% (15 of 19) had metastases in the lung and 26% (5 of 19) in bone. Pulmonary metastases developed post-operatively in one patient who had originally undergone intra-lesional excision of the tumour prior to referral to our institution.

Total femoral endoprosthetic replacement was carried out in 22 patients at the time of primary diagnosis. There were 20 primary tumours, of which 12 were osteosarcomas, three Ewing’s sarcoma, two chondrosarcoma, two malignant fibrous histiocytoma and one multifocal haemangioendothelioma, and two metastases from a renal cell and a breast carcinoma, respectively.

Wide bone and soft-tissue margins were obtained in 19 patients. Incomplete margins were obtained in three patients, all of whom had been referred to our institution with residual disease following previous surgery. Two had a revision of a failed intramedullary femoral fixation to total femoral endoprosthetic replacement. The other patient had previously undergone an intralesional excision biopsy. Local recurrence was seen in all three of these patients at a mean of 10.3 months (9 to 13). Two subsequently underwent excision of recurrent disease, followed by radiotherapy. The other was managed by radiotherapy alone.
Total femoral endoprosthetic replacement was carried out as a secondary procedure in 11 patients following a failed primary segmental endoprosthetic replacement or allograft reconstruction. Of these, seven were for failed dislocation or required amputation. There were six dislocations of the hip at a mean of 46 months (1 to 147), all in patients who required excision of the abductors at the initial procedure. One was managed by bracing and remained stable after a period of bracing. Of the others, five required open reduction, combined with exchange of the head in three, a Pemberton osteotomy in one, and conversion of a bipolar articulation to a THR in one. The mean time to revision for dislocation was 55 months (2 to 147). Function and stability were restored after these procedures. Patients with a THR were more prone to dislocation (two of six; 33.3%) than those with a bipolar replacement (3 of 16; 18.75%). Peri-prosthetic fractures of the tibia occurred in two patients following falls at a mean of 88.5 months (30 to 147). Both were managed by revision of the tibial component to a longer stemmed cemented implant, with good results. Re-bushing of the primary endoprosthesis was needed in four patients (12%). The mean time from implantation to re-bushing was 132 months (107 to 147).

Of these patients, one also required re-surfacing of the patella for anterior knee pain at 144 months. Another patient with a rotating-hinge knee joint experienced excessive rotatory instability at one month. Open exploration showed that a lateral retinacular contracture was causing the prosthesis to rotate in a clockwise direction when the knee was flexed. A full lateral release allowed the prosthesis to be re-aligned and stability was restored. A sciatic nerve palsy occurred post-operatively in one patient which improved over the following year.

Another had a recurrent deep infection with coagulase-negative staphylococci following failure of a two-stage conversion of an infected distal femoral replacement to a total femoral replacement. This patient was managed with debridement and intravenous antibiotics, followed by long-term suppressive oral antibiotics.

**Functional outcome.** The overall mean MSTS functional outcome score for the 11 patients surviving at the time of this study was 20 (12 to 25). The mean MSTS score for the primary and secondary total femoral replacements was 22 (19 to 25; 73%) and 18 (12 to 25; 60%), respectively (Table III). The mean overall HHS was 70 (51 to 86), indicating a fair result compared to the results for THR. The score for primary total femoral replacements was significantly better (mean 78; 72 to 86) than for secondary procedures (mean 64; 61 to 74) (p = 0.01). The overall mean OKS was 34 (22 to 42), with a mean of 39 (33 to 42) for the primaries and 32 (22 to 40) for the secondaries (p = 0.05). All the patients were able to walk with or without the use of aids, sit in a chair and use public transport. Universally they found difficulty in standing up from a kneeling position.

**Table II.** Mode of failure of the total femoral endoprostheses

<table>
<thead>
<tr>
<th>Mode of failure</th>
<th>Primary TFERs (%)</th>
<th>Secondary TFERs (%)</th>
<th>Total number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instability/dislocation</td>
<td>5 (22.7)</td>
<td>1 (9)</td>
<td>6 (18)</td>
</tr>
<tr>
<td>Local recurrence</td>
<td>3 (13.6)</td>
<td>0 (0)</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Servicing procedures (re-bushing)</td>
<td>2 (9)</td>
<td>2 (18)</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Peri-prosthetic fracture</td>
<td>1 (4.5)</td>
<td>1 (9)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Infection</td>
<td>0 (0)</td>
<td>1 (9)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Aseptic loosening</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Amputation</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other (patella resurfacing, rotational instability)</td>
<td>0 (0)</td>
<td>2 (18)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Total failed prostheses in group</td>
<td>7 (32)</td>
<td>4 (36)</td>
<td>11 (33)</td>
</tr>
</tbody>
</table>

* TFERs, total femoral endoprosthetic replacements

**Table III.** Mean functional outcome scores in the primary and secondary total femoral endoprosthetic replacements (TFERs)

<table>
<thead>
<tr>
<th>Scoring system*</th>
<th>Combined mean score (n = 11)</th>
<th>Primary TFERs mean score (n = 4)</th>
<th>Secondary TFERs mean score (n = 7)</th>
<th>p-value difference between primary and secondary group (Mann-Whitney U test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSTS (% score)</td>
<td>67</td>
<td>73</td>
<td>60</td>
<td>0.07</td>
</tr>
<tr>
<td>HHS (max. score = 100)</td>
<td>70</td>
<td>78</td>
<td>64</td>
<td>0.01</td>
</tr>
<tr>
<td>OKS (max. score = 48)</td>
<td>34</td>
<td>39</td>
<td>32</td>
<td>0.05</td>
</tr>
</tbody>
</table>

* MSTS, musculoskeletal tumour society; HHS, Harris hip score; OKS, Oxford knee score
Discussion

The femur is the most common site for primary and secondary malignant bone tumours of the appendicular skeleton. Limb salvage has replaced amputation as the optimum treatment for these lesions, largely owing to improvements in chemotherapy which have made this possible without adversely affecting survival.2,3,25-27 Limb salvage is more cost effective than amputation and is usually preferred by the patient as it can provide improved functional outcome, although there is no significant difference in the quality of life.4,6 The indications for complete excision of the femur in the treatment of primary tumours are rare, but this radical procedure may be necessary with skip metastases or with extensive diaphyseal involvement making endoprosthetic fixation to the remaining bone difficult after excision of the tumour. The other main indications are recurrence or infection after segmental endoprosthetic limb-salvage procedures.

There have been few survival studies on total femoral replacements in malignancy. There are a number of small series documenting a high incidence of both oncological and prosthesis-related complications. Ahlmann et al16 followed up seven patients and found 100% survival of the implant at ten years. Ward et al19 retrospectively reviewed 21 patients with a mean follow-up of 31 months (1 to 125). They used both fixed-length custom implants and modular prostheses (Howmedica, Rutherford, New Jersey, and Link America, Denville, New Jersey). Of the procedures, 12 were performed following resection of a tumour. Complications in patients with a tumour included two dislocations, one rotational subluxation, two deep infections and two local recurrences. Disarticulation for deep infection and recurrence was required in two patients, and two died within two months of the initial operation. The functional results were reported retroactively as good in seven, fair in nine and poor in three.

Morris et al28 reviewed seven patients who had a total resection of the femur with replacement by the Kotz Modular Femur-Tibia Reconstruction system (Howmedica Osteonics). Only three of these operations were for primary malignant tumours; four were salvage procedures after failed limb-sparing surgery. The authors described excellent or good clinical and radiological results, although the follow-up was limited to an average of 23 months. Disarticulation of the hip was required in one patient 15 days post-operatively for ischaemia of the lower limb. A change of bushings was needed in one, and there was one periprosthetic fracture. These authors highlighted the benefit of modularity, a bipolar head and soft-tissue preservation in reducing the rate of dislocation. Both series looked at malignant and non-malignant conditions, and neither study analysed survival of the patients or prostheses.

In common with reports of segmental endoprosthetic reconstruction of the proximal femur, the main cause of failure of the total femoral replacements was instability of the hip. In our series, 18% (6 of 33 patients) dislocated at a mean time of 46 months, with five requiring a revision procedure. Factors that influence dislocation include resection of the joint capsule, the technique of attachment of the abductors to the endoprosthetic, acetabular resurfacing, patient age, the size of the head and the use of a bipolar head rather than a THR. Bickels et al30 found only one dislocation in 57 patients who had a bipolar or unipolar reconstruction of the proximal femur with acetabular preservation, capsular repair and abductor reconstruction to the endoprosthesis. In proximal femoral replacements, patients with a THR have been shown to be more prone to dislocation than those with bipolar replacements.16 The high rate of dislocation in our study reflects the nature of the primary pathology and the subsequent inability to preserve the capsule and the abductors. Instability of the hip in children undergoing total femoral replacement remains a particularly difficult problem. Dislocation occurred in one child immediately following lengthening of a non-invasive ‘grower’ endoprosthesis. Stability was achieved by performing a Pemberton iliac osteotomy and cautious subsequent lengthenings. In our series, patients who had THR were more prone to dislocation (two of eight) than those who had bipolar replacements (4 of 25). Primary total femoral replacements were more prone to dislocation (5 of 22) than secondary procedures (1 of 11), and those who dislocated had required abductor sacrifice to achieve adequate margins. Consequently, we now prefer to use large-diameter metal-on-metal articulations in adults undergoing total femoral replacement. We have observed no functional difference between patients undergoing the procedure with custom-made implants compared to those with modular prostheses. We currently prefer to use a modular prosthesis in adults because of advantages in intra-operative flexibility, cost and manufacturing time compared to custom-made implants. In children and adults with significant shortening due to fracture or previous surgery, non-invasive growing prostheses are used.

We observed no local recurrence in any patient treated exclusively at our institution. However, local recurrence was seen in 9% of all patients (3 of 33) at a mean of 10.3 months. This rate is similar to previous reports of recurrence of sarcomas,13,16,30 and similar to those found in patients with osteosarcoma treated by amputation.31 Ward et al32 showed that factors associated with recurrence include the margin of resection, a poor response to chemotherapy, intravascular extension of the tumour, and situations where local spread of tumour may occur. All the patients who developed recurrence in our series had previously had operations on the affected limb that would have caused local seeding of sarcoma cells within the surgical field. None of our patients who had a percutaneous needle biopsy followed by resection of the tumour and total femoral replacement developed recurrence. None required a disarticulation of the hip. This compares favourably with other forms of endoprosthetic reconstruction for lower limb malignancy. Amputation rates of 10.7% for distal femoral,24 17.5% for proximal tibial33 and 13% for
proximal femoral replacements\textsuperscript{13} have been recorded. The 100\% limb survival in this series probably reflects the relatively low rates of local recurrence and infection with reduced patient survival.

Infection is a major problem in surgery for orthopaedic malignancy and appears to be related to the difficulties of achieving adequate soft-tissue cover, together with the requirement for immunosuppressive chemo- and radiotherapy.\textsuperscript{34} In our series one patient developed infection after staged revision of an infected distal femoral replacement.\textsuperscript{13,35,36}

Aseptic loosening is a common complication of endoprosthetic reconstruction which can necessitate amputation. Rates of 5\% to 35\% have been observed for distal femoral replacements.\textsuperscript{14,24} Loosening is usually observed around the femoral component, but is seen less often when hydroxyapatite collars or conical fluted stems are used.\textsuperscript{24,37} In our series, no patients developed aseptic loosening at the acetabulum or the tibia.

Survival of 32\% at five years and 16\% at ten years puts these patients in a poor prognostic group. A large tumour, the presence of metastases and delays in diagnosis are adverse prognostic factors for survival in primary bone sarcoma.\textsuperscript{38,39} The patients in our study had large tumours and 67\% had metastases at presentation, reflecting the aggressive and advanced stage of disease. Of the 30 patients with primary tumours, 15 had metastases in the lung and five had skeletal metastases at presentation. Our survival rate is comparable to that in other studies of metastatic osteosarcoma, in which long-term survival is possible for only 10\% to 30\% with isolated pulmonary metastatic disease if they are able to undergo resection of all metastases or achieve a complete response to chemotherapy.\textsuperscript{40} The prognosis is worse when bone metastases are present.\textsuperscript{41} In Ewing's sarcoma long-term cure has been reported in up to 20\% of patients who present with metastatic disease.\textsuperscript{42} This figure has failed to improve even with more intensive chemotherapy regimens using additional agents.\textsuperscript{38}

Although survival was poor, the functional outcome was good. All the patients preferred the limb salvage option. The mean MSTS score was 20, with satisfactory hip and knee function. However, function might not have been as good had all patients survived for ten years. Function after primary total femoral replacement was better than after a secondary procedure. Radiotherapy to the soft tissues for recurrence and multiple operative procedures may have contributed to the reduced function seen in the secondary total femoral replacements.

The overriding principles when managing patients with limb salvage are that survival should not be compromised, that patients are able to resume near-normal function as soon as possible, and the prostheses must demonstrate good long-term survival. Even though the complication rate is high, we believe that this study supports the continued use of total femoral endoprosthetic replacement in patients with malignant bone tumours, as survival does not appear to be compromised, the functional outcome is good, and patients can bear weight early with an implant that does not require removal.

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References