Intercalary endoprosthetic reconstruction for diaphyseal bone tumours

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Custom-made intercalary endoprostheses may be used for the reconstruction of diaphyseal defects following the resection of bone tumours. The aim of this study was to determine the survival of intercalary endoprostheses with a lap joint design, and to evaluate the clinical results, complications and functional outcome. We retrospectively reviewed six consecutive patients, three of whom underwent limb salvage with intercalary endoprostheses of the tibia, two of the femur, and one of the humerus. Their mean age was 42 years (28 to 64). The mean follow-up was 21.6 months (9 to 58). The humeral prosthesis required revision at 14 months owing to aseptic loosening. There were no implant-related failures. Musculoskeletal Tumour Society functional outcome scores indicated that patients achieved 90% of premorbid function.

Custom intercalary endoprostheses result in reconstructions comparable with, if not better than, those of allografts. Using this design of implant reduces the incidence of early complications and difficulties experienced with previous versions.

Segmental resection of the diaphysis for primary malignant tumours of bone and for metastatic disease has many advantages, including preservation of the juxta-articular bone and the joint, fewer long-term mechanical problems, and preservation of the epiphysis in children. Advances in MRI, chemotherapy and reconstructive techniques have made more limb salvage procedures possible. Although there appears to be a higher incidence of local recurrence following limb salvage, the overall patient survival is similar for both amputation and limb salvage.1

Reconstruction of segmental skeletal defects from intercalary resection of malignant tumours may be performed using large segmental allografts,2-13 autologous grafts,14-16 bone transport17 and endoprostheses.18,19 Reconstruction with allograft is currently the most frequent type of intercalary reconstruction performed, with a survival rate of 75% to 89% at ten years.2,3,5,6,8,11-13 It allows the restoration of bone stock and soft-tissue reconstruction of ligaments, but the complications significantly outweigh the benefits, especially when used in a systemically compromised host.3,5,7,10 Chemotherapy has an adverse effect on bone healing10 and is associated with high rates of fracture (14.7% to 50.7%),5,7,11,12 nonunion (17.7% to 63.7%),5,6,12,13,20,21 delayed union2 and infection (6% to 30%).7,12,13 There is also the potential for disease transfer from the donor to the patient. Reconstruction with autografts may be achieved using extracorporeal irradiation,15 fibular centralisation,22 free fibular transport,14,16 and hemicortical autografts.23 These reconstructions are plagued with similar complications to allografts, with high rates of nonunion and fracture.14-16

Custom-made intercalary endoprostheses have the advantage of allowing early mobilisation and return to function, and they eliminate complications such as host-donor nonunion and fracture of an allograft.18,19 However, high rates of loosening, wear and breakage have been reported.15 Few studies have been published detailing the results of custom-made intercalary endoprostheses for primary bone tumours.18,19 The purpose of this study was to determine the survival of intercalary endoprostheses, and compare the clinical results, complications and functional outcome with the results of intercalary allografts.

Patients and Methods

We retrospectively reviewed six consecutive patients who had undergone limb salvage for a primary malignant bone tumour or metastatic disease, using intercalary prosthetic reconstruction between July 1988 and July 2005. Patients who had revision of a pre-existing implant performed elsewhere or reconstruc-
tion for non-neoplastic disease were excluded. All the patients had been referred to the senior author (LRM) for further management. There were four men and two women with a mean age of 42 years (28 to 64). The diagnosis included osteogenic sarcoma in two patients, metastatic renal cell carcinoma in two, adamantinoma in one and malignant fibrous histiocytoma of bone in one (Table I).

The primary site of the tumour was the tibia in three patients, the femur in two and the humerus in one. The mean length of bone resected was 12.3 cm (8 to 16). The study design and protocol were approved by the institutional review board.

Before the operation all patients underwent a thorough oncological assessment to determine the extent of local disease and the presence of distant metastases. Staging studies, including plain radiographs and MRI of the limb, CT scans of the chest and total body scintigraphy, were performed prior to biopsy. MRI was performed to define the extent of the lesion, the involvement of the soft tissues, especially the neurovascular bundle, and the level of transection of the bone. Patients with malignant primary bone tumours were staged according to the system adopted by the Musculoskeletal Tumour Society.

All four patients were stage IIB at the time of diagnosis. When indicated, patients received the standard pre-operative chemotherapy regimen in use at the time of treatment. The one patient with malignant fibrous histiocytoma also had neoadjuvant radiation to the tibia. The mean length of follow-up was 21.6 months (9 to 58).

Once the decision had been made to perform intercalary resection and endoprosthetic reconstruction, anteroposterior and lateral radiographs were taken with a size marker placed at the level of the bone to determine magnification, and the level of bone transection marked at between 2 cm and 5 cm from the most proximal and distal extents of the tumour as seen on MRI, with the aim of ideally obtaining a 5 cm margin. If it appeared that less than 5 cm of bone would remain proximally and distally after resection, intercalary resection could not be performed. The shortest length of bone required for fixation of the implant stem is 5 cm; fixation in a shorter segment is hazardous owing to the possibility of early loosening. The marked radiographs were then sent to Stryker (Rutherford, New Jersey) for manufacture of the implant. The titanium intercalary prosthesis used to replace the segmental defect is a four-component bi-stemmed coupled device with a lap joint, a side-to-side mating junction with hemicylindrical cross-sections of equal lengths. With the current design, the two stemmed components are mated to one-half of a lap joint each using a Morse taper design. The lap joint is then assembled and reduced in situ and locked with two set screws (Fig. 1).

All the operations were performed by the senior author (LRM). The biopsy tract was excised as an ellipse and left in continuity with the resected specimen, which was removed en bloc with a wide margin in all cases. After negative margins had been confirmed by intramedullary frozen section, reconstruction was undertaken. The proximal and distal intramedullary canals were reamed to the appropriate size, 2 mm larger than the implant stems. Stems were then secured with a 2 mm mantle of polymethylmethacrylate. Once the cement had fully hardened, each half of the lap joint was placed on to each stem, taking care to achieve the appropriate rotational alignment. The lap joint was then assembled and reduced in situ and locked with two set screws.

![Intra-operative photograph of custom-made intercalary segmental defect replacement system with two-stemmed components that have been mated to one-half of a lap joint each by a Morse taper design. The lap joint has been reduced in situ and locked with two set screws.](image_url)

Table I. Details of six patients with diaphyseal tumours treated with intercalary endoprostheses

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yrs)</th>
<th>Gender</th>
<th>Diagnosis</th>
<th>Stage*</th>
<th>Chemotherapy</th>
<th>Location</th>
<th>Bone resected (cm)</th>
<th>Complications</th>
<th>MSTS†</th>
<th>Follow-up (mths)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58</td>
<td>M</td>
<td>Metastatic renal cell cancer</td>
<td>N/A</td>
<td>Yes</td>
<td>Tibia</td>
<td>12</td>
<td>None</td>
<td>26</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>F</td>
<td>Adamantinoma</td>
<td>IIB</td>
<td>No</td>
<td>Tibia</td>
<td>9</td>
<td>None</td>
<td>28</td>
<td>26</td>
</tr>
<tr>
<td>3</td>
<td>39</td>
<td>M</td>
<td>Malignant fibrous histiocytoma</td>
<td>IIB</td>
<td>Yes</td>
<td>Tibia</td>
<td>13</td>
<td>None</td>
<td>28</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>32</td>
<td>F</td>
<td>Osteogenic sarcoma</td>
<td>IIB</td>
<td>Yes</td>
<td>Femur</td>
<td>16</td>
<td>None</td>
<td>27</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>29</td>
<td>M</td>
<td>Osteogenic sarcoma</td>
<td>IIB</td>
<td>Yes</td>
<td>Femur</td>
<td>16</td>
<td>None</td>
<td>28</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td>64</td>
<td>M</td>
<td>Metastatic renal cell cancer</td>
<td>N/A</td>
<td>Yes</td>
<td>Humerus</td>
<td>8</td>
<td>Aseptic loosening of distal stem at 14 months</td>
<td>25</td>
<td>58</td>
</tr>
</tbody>
</table>

* according to the Musculoskeletal grading system
† MSTS, Musculoskeletal Tumour Society score
situ; two set screws were placed through the implant to lock the joint in place. All three patients with intercalary tibial resections required muscle flaps for soft-tissue cover of the implant, including two local rotational flaps and one latissimus free muscle transfer (Fig. 2). All the wounds were then closed in the usual manner and a suction drain inserted. The patients received antibiotics until the drain was removed once the output had decreased to < 50 ml/day, and were discharged from hospital when medically stable.

Immediately after operation the patients were allowed to bear full weight and mobilise as tolerated without the use of a brace or cast. Routine follow-up was undertaken every three months for the first two years after surgery, every six months between two and five years after treatment, and annually for 10 years thereafter.

Failure was defined as revision of any or all components of the implant, removal of the implant, or amputation of the limb. The patients’ records were reviewed for the onset of complications and causes of failure leading to revision,
including infection, recurrent tumour, aseptic loosening, fatigue failure and peri-prosthetic fracture. The findings were compared to historical controls from the existing literature.

The functional outcome was assessed for all surviving patients using the revised Musculoskeletal Tumour Society functional rating system. This uses a 30-point scale to weight equally each of six parameters, comprising pain, functional limitation, walking distance, use of a support, emotional acceptance and gait. Patients completed a questionnaire, either by telephone or at their latest review. The questionnaire was administered by an investigator (ERA) who was not involved in the care of the patient.

Statistical analysis was performed using the Kaplan-Meier method to generate survival curves, with corresponding 95% confidence intervals (CI) for implant and patient survival using the GraphPad Prism software (GraphPad Software Inc., San Diego, California). The date of implantation of the initial prosthesis was the start of the curve and the end-point was defined as the need for revision, removal of the implant or amputation.

**Results**

The patient with the intercalary implant of the humerus underwent revision for aseptic loosening of the distal stem 14 months after the operation. Revision of the stem was carried out and the patient has since remained asymptomatic, with no evidence of loosening 44 months after the second procedure. The remaining five patients had no clinical or radiological evidence of loosening. The overall survival of the intercalary implants based on the Kaplan-Meier estimates was 100% (95% CI 0.239 to 1.571) at one year and 83% (95% CI 0.348 to 2.125) at two years. The longest surviving implant has remained in place for 44 months. There were no infections, local recurrences, wound complications, peri-prosthetic fractures or failures of the implants.

The mean follow-up was 21.6 months (9 to 58) at which time all the patients were alive and well. The mean Musculoskeletal Tumour Society functional outcome score was 27 (25 to 28), indicating 90% normal function. The patient with the lowest score had undergone early revision of the humeral stem. His functional deficits were related mainly to weakness as a result of his condition as a whole. The functional outcome for reconstructions of the lower limb was excellent. No patient required assistive devices for walking. All were satisfied with the outcome and stated that they would have the same procedure again under similar circumstances.

**Discussion**

The improved life expectancy of patients with malignant tumours of bone has led to an increased emphasis on limb salvage and maximisation of function. The optimal method of reconstruction after resection of diaphyseal tumours remains a subject of debate. Important considerations to take into account when performing reconstruction after intercalary resection of a tumour include the morbidity of the procedure, the incidence of complications, the functional demands of the patient and the durability of the reconstruction. The large size of the skeletal defects that require reconstruction limits the options available. Vascularised and non-vascularised autogenous grafts are associated with morbidity at the donor site and are not appropriate for large defects. Autoclaved or irradiated autografts are often used as an alternative to allografts but are associated with a high rate of nonunion, fracture and infection. Distraction osteogenesis has proved useful in the treatment of post-traumatic defects in bone, but its use in patients undergoing treatment for malignant bone tumours is limited by the adjuvant treatments being given and the long period of treatment. The most commonly used technique is allograft reconstruction, but custom-made endoprostheses are now being used more frequently. Intercalary reconstruction with large-segment allografts has the advantage of allowing for reconstruction of ligaments to the implant and accurate matching of the graft to the defect. The disadvantages include the potential for disease transfer, the long period of immobilisation required for bony union, and a high incidence of nonunion, infection and fracture. Custom-made endoprostheses allow an early return to function and immediate weight-bearing, without the complications seen with allografts.

The frequency of nonunion after massive allograft reconstruction has been recorded as between 17.7% and 63.7%. An association between the immunosuppressive effects of adjuvant chemotherapy and non-union of the allograft-host junction has been suggested. A reduction in bone remodelling and vascular invasion of the graft, resulting in delayed osteointegration, may result from chemotherapy. Fracture of the graft has been reported to occur in 14.7% to 50.7% of cases, and has been suggested to result from the use of dead bone, which remains structurally weak and never incorporates fully into the host. Reconstruction with endoprostheses avoids these problems and avoids the long period of immobilisation and partial weight-bearing after allograft reconstruction, with immediate return to function for patients who may have a limited life expectancy.

A previous study evaluating 18 intercalary endoprostheses performed for malignant tumours of the humerus, femur and tibia found that four patients (22%) required revision for loosening. Both patients who had a humeral reconstruction experienced early loosening by 18 months, but none developed wear or breakage of the implant at a mean follow-up of 65 months. Another study, of 34 patients evaluating the use of a modular intercalary humeral replacement system of a different design from that used in the current study reported failure of the implant in six (17.6%), usually due to disengagement or instability of the components of the male-female junction. The only failure in our series was in the one patient who had a humeral reconstruction, who successfully underwent revision and remains asymptomatic.
It may be that the increased rotational stresses in the upper extremity lead to a higher rate of failure with humeral reconstructions.

We have experienced no failures attributable to the design of the implant. Prior to the development of the lap joint design, the initial implant consisted of a two-component bi-stemmed conically-coupled joint locked with two set screws. Only a limited range of diameters and lengths of stem was available, resulting in implants that were often undersized. In these implants, the most common reason for failure was dis-engagement or instability of the conically-coupled joint which occurred as early as one month after initial implantation. In these implants, the most common reason for failure was dis-engagement or instability of the conically-coupled joint which occurred as early as one month after initial implantation. We did not encounter these problems with our custom-made implants.

Many patients develop a bone bridge linking the proximal and distal bone fragments, essentially encasing the implant with heterotopic bone. This was previously noted along the medial aspect of femoral intercalary reconstructions. It is unclear why this develops, but it may be of benefit in preventing or limiting aseptic loosening. It is possible that the bone bridge shields the prosthesis from stress and thereby prolongs its survival. The current intercalary implant is smooth, without coating, but in future it may be beneficial to coat it with a porous coat or hydroxyapatite to further stimulate bone production.

The functional outcome in this series was excellent, with patients regaining a mean of 90% of their premorbid function. This is in contrast to outcomes noted after allograft reconstruction, ranging between 80% and 90% of normal function, but with many studies finding only 40% to 50% of their patients having excellent results.

Intercalary resection and reconstruction is of benefit to patients with diaphyseal tumours as adjacent joint function is preserved. The results of endoprosthetic replacement are comparable with, if not better than, those of large-segmental allografts. In the lower limb the clinical and functional outcomes appear excellent, while in the upper limb the high rotational stresses may lead to early loosening. Using this design of implant reduces the incidence of early complications and the difficulties experienced with previous versions.

References