Endoprosthetic replacement for primary tumours around the knee
EXPERIENCE FROM PEKING UNIVERSITY

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In developing countries locally-made low-cost prostheses are mainly used in limb-salvage surgery to alleviate the economic burden.

We retrospectively collected data on 104 patients treated by limb-salvage surgery between July 1997 and July 2005. We used a locally-designed and fabricated stainless-steel endoprosthesis in each case. Oncological and functional outcomes were evaluated at a mean follow-up of 47 months (12 to 118).

A total of 73 patients (70.2%) were free from disease, nine (8.7%) were alive with disease, 19 (18.2%) had died from their disease and three (2.9%) from unrelated causes. According to the Musculoskeletal Tumor Society scoring system, the mean functional score was 76.3% (SD 17.8). The five-year survival for the implant was 70.5%. There were nine cases (8.7%) of infection, seven early and two late, seven (6.7%) of breakage of the prosthesis, three (2.9%) of aseptic loosening and two (1.9%) of failure of the polyethylene bushing. Multivariate analysis showed that a proximal tibial prosthesis and a resection length of 14 cm or more were significant negative prognostic factors.

Our survival rates and Musculoskeletal Tumor Society functional scores are similar to those reported in the literature. Although longer follow-up is needed to confirm our results, we believe that a low-cost custom-made endoprosthesis is a cost-effective and reliable reconstructive option for limb salvage in developing countries.

The knee is a common site for primary malignant tumours. Over the past 25 years, limb salvage has become the preferred method of treatment because of improvements in imaging, chemotherapy, surgical technique and in the design of prostheses.1-5 Limb-salvage techniques now produce rates of recurrence comparable with those of amputation.4 The options available for reconstruction include the use of allografts, segmental endoprostheses, and allograft prosthesis composites. Endoprostheses have the advantage of offering immediate post-operative stability, rapid rehabilitation, and are available off the shelf.6,7 Modular prosthetic systems also offer considerable intra-operative flexibility. The increasing use of endoprostheses in limb-salvage surgery and the need for their long-term survival demand that the factors affecting survival should be well understood. Concern remains about the long-term outcome of prosthetic reconstructions. There has been no reduction in the rate of deep infection in recent years, aseptic loosening remains a major threat3,8 and the high cost of endoprostheses for limb-salvage surgery is a problem in developing countries. Locally-made low-cost prostheses have been used mainly to alleviate the economic burden and have been shown to be effective in India.9

Our primary aim in this study was to determine the short- to medium-term clinical outcome of a locally custom-made rotating-hinge prosthesis. We therefore retrospectively ascertained the clinical outcome and complications by assessing limb and prosthetic survival, the local rate of recurrence, the function score, and the rate of complications. On the basis of the results, we also attempted to identify the factors which were independently associated with the survival of the implant.

Patients and Methods
We retrospectively identified from our tumour registry all the distal femoral and proximal tibial endoprostheses which had been implanted between July 1997 and July 2005. Only patients who had limb-salvage surgery using a locally custom-made endoprosthesis were included. Those who had an imported massive implant or an allograft-prosthesis composite were excluded as were patients with total knee (distal femur and proximal tibia)
Operative technique. An anteromedial approach was used in 75 patients and an anterolateral in 29. The surgical technique involved resection of the tumour and reconstruction of the joint. The complete technique has been described elsewhere.\textsuperscript{12} For distal femoral tumours, the mean resection length was 15.9 cm (9 to 26) and for proximal tibial tumours it was 13.6 cm (10 to 21). Reconstruction of the extensor mechanism was required in all 39 patients with a tibial tumour. However, partial continuity of the extensor mechanism was preserved in 21 (53.8\%) of those patients. In order to maintain part of the extensor mechanism, the insertion of the patellar tendon was elevated subperiosteally from the surface of the tibia in selected cases, and the quadriceps tendon was split coronally into deep and superficial layers. Normally, mobilisation in a cast for four weeks was necessary after extensor reconstruction. Autogenous reconstruction was performed in 35 patients, with the use of a medial gastrocnemius flap to achieve adequate soft-tissue cover. The stem was cemented in 70 patients and cementless in 34. Revision was defined as the need to exchange any part of the implant for breakage, wear, loosening or infection.

Statistical analysis. Descriptive statistics were calculated using means and proportions as appropriate to the type of data. Survival of the prosthesis was calculated using the Kaplan-Meier method. In order to identify factors which affected the survival of the prosthesis both univariate and multivariate (Cox) analysis was carried out. Overall patient and limb survival were also calculated. Statistical analysis was performed using SPSS version 12.0 (SPSS Inc, Chicago, Illinois). A p-value $\leq 0.05$ was considered to be significant.

Results
At the time of the final follow-up at a mean of 47 months (12 to 118), 73 patients (70.2\%) were alive and free from disease. Nine patients (8.7\%) were alive with disease and 22 had died from the disease. Of the 22 deaths (6 proximal tibial, 16 distal femoral), 19 (18.5\%) were due to local recurrence or metastatic disease involving at least the lungs, and three (3\%) due to other causes. The survival rate of the 75 patients with a stage-IIIB sarcoma was 65.8\% at five years. Five of the six patients with a stage-III sarcoma died after surgery. One of the three patients with a stage-IIB sarcoma died seven months after operation. No patients with a stage-I A or stage-IIIA sarcoma died during the follow-up period. There was local recurrence in nine patients (8.7\%), six of whom required amputation and one revision to a total femoral prosthesis. The remaining two patients underwent successful local tumour resection. There were six recurrences (9.2\%) after resection of a distal femoral tumour, in three of which a pathological fracture had been present pre-operatively. Of the three patients (7.7\%) who developed a recurrence in the proximal tibia, one required a posterior resection of tibial vessels and reconstruction during the initial procedure because of vascular involvement by the soft-tissue tumour mass. Metastasis occurred in 13 patients (12.5\%) at a mean of 20 months post-operatively.
Functional evaluation of the 73 surviving patients who were free from local recurrence or metastatic disease was made according to the MSTS functional assessment system (Table II). The mean functional score was 76.3% (SD 17.8); 77.0% (SD 17.7) for the distal femoral replacement and 75.1% (SD 18.2) for the proximal tibial replacement. Active extension varied greatly depending on the status of the reconstruction of the extensor mechanism.

The three- and five-year survival for all implants was 79% and 71% with a mean survival of 42 months (6 to 118). The rate of limb preservation was 93% at three years and 90% at five and ten years after primary implantation (Fig. 2). Univariate analysis showed that the proximal tibial prosthesis did not survive as well as the distal femoral prosthesis (p = 0.0276; Fig. 3). With the numbers available, we could not detect a significant association between survival of the prosthesis and age (p = 0.514), gender (p = 0.993), the method of fixation of the stem (cemented or uncemented; p = 0.421) or a resection length of 14 cm or more (p = 0.0681). Multivariate analysis showed that the significant negative prognostic factors were a proximal tibial prosthesis (p = 0.029) and resection of 14 cm or more (p = 0.045). The two factors were combined to compare the difference in survival between a tibial prosthesis with a resection length of more than 14 cm and a femoral prosthesis with a resection length of less than 14 cm. There was a significant difference between the two (p = 0.004; Fig. 4).

Deep peri-prosthetic infection was the most common complication and occurred in seven of the 104 patients (6.7%). The mean time to the diagnosis of infection was 13 months (7 to 108). Five cases were diagnosed within one year of the initial operation. Two patients developed late infection more than one year post-operatively, at 31 and 108 months. All seven patients with a peri-prosthetic infection underwent removal of the prosthesis and implantation of an antibiotic spacer, followed by staged re-implantation of the prosthesis. Five infections ultimately resolved. However, one patient, infected with "Enterococcus faecalis,"
required an amputation because of recurrent symptomatic infection, as did another in whom recurrent infection was caused by *Staphylococcus aureus*. Another two patients had deep soft-tissue abscesses which did not involve the prosthesis and were managed successfully by irrigation and debridement.

Fracture of the stem of the prosthesis occurred in seven patients (6.7%) and also influenced outcome. Six were cemented stems and one was uncemented. Two fractures occurred at the junction of the distal femoral prosthesis and the base of the diaphyseal stem. Five stem fractures (all distal femoral) occurred proximal to the start of the intramedullary portion of the stem. All the patients underwent successful revision to a larger cemented stem. The metal bushing component functioned as an extension-stop mechanism and fractured in three patients (2.9%). This was a failure in design which has been rectified.

Further complications included aseptic loosening of the stem in three patients (2.9%), two of whom required revision. Of the three stems, two had been cemented and one uncemented. Two patients (1.9%) presented clinically with an unstable knee due to failure of the polyethylene bushes. These were replaced after 35 and 52 months, respectively.

**Discussion**

Our primary aim was to evaluate the functional outcome, complications and the short- to medium-term survival of locally custom-made implants for reconstruction of defects in the distal femur and proximal tibia after limb-salvage surgery.

The limitations of our study were lack of a group of patients with different implants for comparison, and the short follow-up. The body mass index and other factors such as the use of neoadjuvant treatment may also have affected the validity and reproducibility of these results. In addition, the radiographs taken at follow-up were not specifically aimed at identifying discrete or subclinical loosening of the implant. Despite this, our three- and five-year survival rate and the incidence of failure of the implant were consistent with other published series and represent valid findings. Furthermore, it is a relatively large series with intermediate follow-up.

There were nine cases of local recurrence (8.7%). This falls within the previously-reported local recurrence rate of between 4% and 9%. The promotion of limb-salvage surgery as a safe alternative to amputation is based on recurrence rates close to those found after amputation. In 2005, Torbert et al reported a local recurrence...
rate of 6.8% in 74 patients with primary malignant bone tumours treated by limb salvage with endoprosthetic replacement. From our experience and from the results of other studies these rates are similar to those found in patients treated by amputation. Although it may result in revision or amputation, local recurrence reflects the adequacy of the surgical margin and aggressiveness of the tumour rather than the quality of the implant.

The MSTS functional scores in our study were also similar to those in previous reports. The inferior functional outcome for patients with a proximal tibial endoprosthesis was directly related to the disruption of the extensor mechanism. The decreased range of movement in the knee could also be related to the prolonged period of immobilisation of the knee after surgery. Reconstruction by re-attachment of the remnant of the patellar tendon directly to the prosthesis may decrease knee flexion because of the need for prolonged immobilisation. Malawer and McHale described a method of reconstruction of the extensor mechanism using a medial gastrocnemius flap. An excellent to good functional outcome was achieved in 71% (5 of 7) patients. Partial continuity of the extensor mechanism was preserved by a subperiosteal approach, thereby minimising the disruption in selected cases. No local recurrence had developed in the 21 patients who showed a tendency towards better function. This low rate of local recurrence also attests to the safety of limb salvage for sarcoma of the proximal tibia.

The five-year survival of endoprostheses after resection of malignant tumours of the knee is reported to range between 79% and 93%,7,8,12,14-23-25 The five-year survival of 71% in our series is clearly less favourable. However, direct comparison of survival results in our series to those of other published reports is difficult because of the heterogeneity of the series, particularly with respect to patient population and the implant used. We found that the anatomical location of an implant had a direct effect on survival of the prosthesis. The five-year survival rates for distal femoral prostheses have been reported to be between 88% and 93%, whereas those for proximal tibial implants were only 58% to 86%,8,12,26 The five-year survival of the distal femoral and proximal tibial endoprostheses in our study were 80.6% and 54.3%, respectively (p < 0.05). These findings were consistent with the results reported by Biau et al.1 We hypothesised that the length of bone resected may be related to early failure of the prosthesis. We found that prostheses failed earlier if 14 cm or more of the affected bone were resected (Fig. 4).

The risk of stem fracture in our series of 6.7% was higher than the 3% to 5% risk reported elsewhere.19,26-28 Each of the seven stem fractures in our series occurred early and contributed to the decreased five-year survival. The high rate of stem fracture in our study is due to the narrow diameter of the stem and the lack of an anatomical curve. Kawai et al19 reported a significantly lower survival rate for straight stems than for curved. Fracture of the metal bushing component was attributed to the peak stress caused by loss of extension control, which can also cause aseptic loosening.26,29

Peri-prosthetic infection occurred in seven patients (6.7%), two of whom ultimately underwent amputation. Infection is especially problematic in the proximal tibia because of the difficulty in achieving good soft-tissue cover. Although most (35 of 39) of our patients had a muscle flap as part of their reconstruction, the infection rate was still higher than that typical of other sites in the femur.7,16,30 Although our rate of infection was high it remains comparable with that of other published reports which range from 5% to 15%,1,8,24,28 Neutropenia from chemotherapy and poor soft tissues were thought to have contributed to deep infection in the seven early infections in our study. Malawer and Chou proposed the administration of long-term suppressive antibiotics during chemotherapy to decrease the risk of infection, but this approach remains controversial. Whether the surface finish of the endoprosthesis has a role in the infection process remains to be seen. We did, however, find black staining of the peri-prosthetic pseudocapsule at revision. Sharma et al21 routinely used antibiotic-loaded cement for endoprosthetic replacement to reduce the risk of infection. Two-stage revision is more effective at controlling infection in these circumstances. A one-stage procedure is not successful because in most of the infections the endoprosthesis will have loosened or infection will have spread along the cement-bone interface. It is essential to remove the implant and all remaining bone cement.31

Only three patients (2.9%) in our study developed aseptic loosening. This is lower than the 5% to 20% reported in the literature in which it was the principal cause of failure.6,25,30 This reduction can be attributed to improvements in cementing technique, prosthetic design and manufacture. We used a third-generation cementing technique in our series.8,32 The use of extramedullary porous ingrowth surfaces on more recent implants encourages the ingrowth of bone and soft tissue, thereby increasing load-sharing with the stem.33 Others have found that a high body-weight and high level of activity accentuated the rate of aseptic loosening.1 The low rate of aseptic loosening in our study, however, must also take into account the fact that many patients died within five years of the initial procedure,1 with longer follow-up, the rate of aseptic loosening may have increased but in our study the implant was durable enough to outlive most patients.

In summary, the oncological results were encouraging. The three- and five-year rates of survival of the implant which we used were 80.6% and 54.3%. The mean MSTS score was 76%. The primary cause of failure was infection. The anatomical location and resection length were independent predictors of failure of the implant. The distal femoral prosthesis gave better results than the proximal tibial prosthesis. Overall, our endoprosthetic survival rate and
functional score were similar to those reported in the literature. Although long-term follow-up is needed to confirm our results, we believe that in developing countries a low-cost custom-made endoprosthesis is a reliable reconstructive option after limb-salvage surgery.

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References