LIMB CONSERVATION IN PRIMARY BONE TUMOURS
BY RESECTION, EXTRACORPOREAL IRRADIATION AND
RE-IMPLANTATION

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En-bloc resection, extracorporeal irradiation and re-implantation of the irradiated bone have been used to treat 15 patients suffering from primary malignant tumours of bone or cartilage and two with benign lesions. This treatment is an alternative to replacement by prosthesis or allograft bridging techniques. After a mean follow-up of over five years results are encouraging, despite some complications and the relatively long period before weight-bearing is allowed.

The treatment and prognosis of osteosarcomata and other primary bone tumours have changed dramatically since adjuvant chemotherapy began to be used in the early 1970s (Merle d’Aubigné and Dejouany 1958; Jaffe 1972; Rosen et al. 1974). Radical ablative surgery has been largely abandoned in favour of limb salvage by procedures consisting of en bloc resection of the tumour and reconstruction with a prosthesis, an allograft or a bridging technique, as introduced by Juvara (1921) and popularised by Merle d’Aubigné and Campanacci (Merle d’Aubigné, Méary and Thomine 1966; Marcove 1978; Campanacci and Costa 1979; Marcove 1981; Mankin et al. 1982).

We have opted for a fourth alternative, namely the en bloc resection of the tumour, and its extracorporeal irradiation followed by re-implantation. This technique has several theoretical advantages. It preserves the mobility of a joint, as compared with the Merle d’Aubigné technique. It avoids the problem of early and late loosening or breakage of a massive prosthesis and it also obviates some of the problems of allografting, such as the organisation of a bone bank and the rejection of a graft. Moreover, it can be plausibly suggested that the dead tumour cells may stimulate the body’s own immunological system.

MATERIAL AND METHODS
We have treated 22 patients by en bloc resection, extracorporeal irradiation and re-implantation of the irradiated bone. We now report our first 17 cases, with a median follow-up in surviving patients of more than five years.

Details of the cases are given in Table I. In all, five men and five women (age 12 to 56 years) presented with osteosarcoma, and one patient each with fibrosarcoma, chondrosarcoma, intraosseous liposarcoma, malignant fibrous histiocytoma, Ewing’s sarcoma, and recurrent chondroblastoma. One patient had a large osteochondroma of the ilium. Pre-operative investigations included standard and chest radiography, routine laboratory tests, technetium whole body scans, arteriography and computerised axial tomography.

The procedure is carried out in three stages during one operative session: resection, extracorporeal irradiation and re-implantation. A biopsy was performed previously only when there was serious doubt as to the malignant nature of the condition. In all other cases definitive surgery was done primarily, in order to minimise the possibility of local recurrence. For patients with osteosarcoma it was preceded by chemotherapy (Rosen et al. 1975).

We aimed at a wide resection (Enneking 1983), but in some cases we were limited to a marginal excision by anatomical and functional features. The excised speci-
<table>
<thead>
<tr>
<th>Case number</th>
<th>Age (years)</th>
<th>Diagnosis</th>
<th>Site</th>
<th>Surgical stage*</th>
<th>Chemotherapy</th>
<th>Follow-up (years)</th>
<th>Complications</th>
<th>Oncological result</th>
<th>Orthopaedic result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>Fibrosarcoma</td>
<td>Proximal humerus</td>
<td>G1, T2, M0 (I, B)</td>
<td>-</td>
<td>1</td>
<td>Death from side effects of chemotherapy</td>
<td>NED at post mortem</td>
<td>No pain Abduction 100°</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>Osteogenic sarcoma</td>
<td>Distal femur</td>
<td>II B</td>
<td>Vincristine Methotrexate† Doxorubicin Cyclophosphamide</td>
<td>1</td>
<td>Death from lung infection</td>
<td>Distant metastasis No local recurrence</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>Intra-ossseous liposarcoma</td>
<td>Radius</td>
<td>II B</td>
<td>Vincristine Doxorubicin Cyclophosphamide</td>
<td>3</td>
<td>-</td>
<td>Death by distant metastasis No local recurrence</td>
<td>Normal mobility and function of the elbow and wrist</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>Osteogenic sarcoma</td>
<td>Distal femur</td>
<td>II B</td>
<td>Vincristine Methotrexate† Doxorubicin Cyclophosphamide</td>
<td>8</td>
<td>Bone resorption and refraction, grafted</td>
<td>NED</td>
<td>No pain Flexion 70° Walks without support</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>Osteogenic sarcoma</td>
<td>Distal femur</td>
<td>II B</td>
<td>Vincristine Methotrexate† Doxorubicin Cyclophosphamide</td>
<td>9</td>
<td>Epiphysiolysis Bone necrosis Pseudarthrosis at tumour site</td>
<td>NED</td>
<td>No pain Severe joint laxity Orthosis</td>
</tr>
<tr>
<td>6</td>
<td>25</td>
<td>Chondrosarcoma</td>
<td>Medial femoral condyle</td>
<td>II B</td>
<td>-</td>
<td>6</td>
<td>-</td>
<td>NED</td>
<td>No pain Normal function Sport</td>
</tr>
<tr>
<td>7</td>
<td>15</td>
<td>Osteogenic sarcoma</td>
<td>Distal femur</td>
<td>II B</td>
<td>Vincristine Methotrexate† Doxorubicin Cyclophosphamide</td>
<td>5</td>
<td>Local recurrence Hip disarticulation</td>
<td>NED</td>
<td>Prosthesis</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
<td>Ewing’s sarcoma</td>
<td>Distal femur</td>
<td>II B</td>
<td>-</td>
<td>2.5</td>
<td>No local problems</td>
<td>Death from distant metastasis</td>
<td>No pain Rigid ankle Walks without support</td>
</tr>
<tr>
<td>9</td>
<td>15</td>
<td>Osteogenic sarcoma</td>
<td>Distal femur</td>
<td>II B</td>
<td>-</td>
<td>8</td>
<td>Necrosis of femoral condyles</td>
<td>NED</td>
<td>No pain Flexion 70° Severe joint laxity Walks without support</td>
</tr>
<tr>
<td>10</td>
<td>15</td>
<td>Osteogenic sarcoma</td>
<td>Proximal tibia</td>
<td>II B</td>
<td>Vincristine Methotrexate† Doxorubicin Cyclophosphamide (also total lung irradiation)</td>
<td>0.5</td>
<td>Death from lung fibrosis and heart failure</td>
<td>No local recurrence or distant metastasis at post mortem</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>16</td>
<td>Osteogenic sarcoma</td>
<td>Proximal tibia</td>
<td>II B</td>
<td>Vincristine Methotrexate† Doxorubicin Cyclophosphamide</td>
<td>2</td>
<td>Osteomyelitis necessitating above-knee amputation</td>
<td>No local recurrence Death from distant metastasis</td>
<td>Above-knee prosthesis</td>
</tr>
<tr>
<td>12</td>
<td>45</td>
<td>Osteogenic sarcoma</td>
<td>Distal femur</td>
<td>III B</td>
<td>Vincristine Methotrexate† Doxorubicin Cyclophosphamide</td>
<td>1</td>
<td>Local recurrence Hip disarticulation</td>
<td>Death from distant metastasis</td>
<td>-</td>
</tr>
<tr>
<td>13</td>
<td>51</td>
<td>Malignant fibrous histiocytoma</td>
<td>Radius</td>
<td>II B</td>
<td>Cyclophosphamide Vincristine Doxorubicin DTIC</td>
<td>3</td>
<td>Osteomyelitis</td>
<td>NED</td>
<td>Wrist arthrodesis Limited finger function Normal sensation “Helper” hand</td>
</tr>
<tr>
<td>14</td>
<td>16</td>
<td>Recurrent chondroblastoma</td>
<td>Proximal lateral tibial epiphysis</td>
<td>I A</td>
<td>-</td>
<td>4</td>
<td>Moderate valgus deformity Osteotomy</td>
<td>NED</td>
<td>No pain Flexion 130° Sport</td>
</tr>
<tr>
<td>15</td>
<td>18</td>
<td>Large osteochondroma</td>
<td>Blade of ilium</td>
<td>I A</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td>NED</td>
<td>Normal function Ballet dancer</td>
</tr>
<tr>
<td>16</td>
<td>16</td>
<td>Osteogenic sarcoma</td>
<td>Distal tibia</td>
<td>II B</td>
<td>Vincristine Methotrexate† Doxorubicin Cis-platinum</td>
<td>3</td>
<td>Skin necrosis Lung metastases</td>
<td>NED at one year after lung resections</td>
<td>No pain Rigid ankle Walks without support</td>
</tr>
<tr>
<td>17</td>
<td>17</td>
<td>Osteogenic sarcoma</td>
<td>Proximal femur</td>
<td>II B</td>
<td>Methotrexate† Doxorubicin Cis-platinum</td>
<td>2.5</td>
<td>Open reduction of dislocation Aseptic necrosis THR</td>
<td>NED</td>
<td>No pain Walks without support indoors; cane outdoors</td>
</tr>
</tbody>
</table>

men including the tumour-bearing bone and its surrounding tissues was initially sent to our department of radiotherapy for irradiation, but we now use the linear accelerator at the nearby Institute of Nuclear Physics of Ghent University. The specimen is routinely given a dose of at least 30,000 rads. Transport and irradiation takes about one hour, during which time the remaining bone is prepared for repair, such as intramedullary nailing.

Except for the joint capsule, the soft tissues and the bulk of the tumour are removed from the heavily irradiated resection specimen, but part of the tumour is always left in place, so that some dead tumour cells are available to help stimulate the patients' immunological system, if indeed this is relevant. At the epiphyseal and metaphyseal parts of the specimen, some cancellous bone is removed and a 0.5 cm slit is made in the diaphysis. The defects so produced are filled with autologous grafts from the iliac crest. Fixation is then achieved by means of an intramedullary rod or nail combined with a plate and screws. Only rarely did we use plate and screw fixation alone.

Postoperatively, immobilisation in plaster or an orthosis is continued until there is radiographic evidence of bony union. For a tumour in the lower limb, weight-bearing is prohibited for approximately one year because of the time needed for the vascularisation and remodelling of a massive autograft. This will depend on the size and anatomical location of the graft, but will be at least six months, and may never be complete. Samples of bone taken at reoperation, one year or more later, show that there is partial replacement by new bone and fresh fibrous tissue but that a framework of dead bone is also present.

ILLUSTRATIVE CASES
More details are given in Table I.

Case 9 (Figs 1 to 4). A 15-year-old girl with an osteogenic sarcoma of the distal femur was treated by resection, extracorporeal irradiation and re-implantation. After eight years the oncological result is excellent with no evidence of disease. The functional result is good, with no pain, but with some laxity of the knee and a reduced range of flexion. She walks without support, but uses a cane for longer walks and shopping.

Case 6 (Figs 5 to 8). A woman aged 20 years presented with a recurrence of a low-grade chondrosarcoma of the medial femoral condyle. The condyle and part of the medial metaphysis were resected en bloc, the specimen was irradiated with 30,000 rads, and the cancellous bone of the specimen was curedt and replaced by autologous cancellous grafts from the iliac crest. The specimen was then re-implanted. Six years after operation there is no evidence of disease, and the patient enjoys sport including skiing.

Case 16 (Figs 9 to 11). A girl of 15 years presented with an osteogenic tumour of the distal tibia. A marginal resection was performed with re-implantation after irradiation with 30,000 rads. One year after the procedure the local result was satisfactory: she was able to walk without support, had no pain and a functional ankle joint, but there remained a small skin defect without evidence of infection. Before plastic surgery could be performed, two lung metastases were discovered; these were removed by thoracotomy and local resection. One year after thoracotomy, there is no evidence of disease, but the patient has refused plastic repair for the moment. Her function, however, remains excellent.

Fig. 1
Fig. 2
Fig. 3
Fig. 4

Case 9. Figure 1 Pre-operative radiograph showing an osteogenic sarcoma of the distal femur. Figure 2. At operation the irradiated re-implanted distal femur shows the slit in the diaphysis which will be filled with autogenous bone graft. Figures 3 and 4 Radiographs three years after operation. These are unchanged after eight years. Function is good.
RESULTS

We have evaluated results both from a specific oncological point of view and from an orthopaedic view of function (Table I). Two patients died early from the side-effects of treatment.

Oncological results. Ten patients survive with no evidence of disease. In five patients generalised metastatic disease resulted in death, three from osteosarcoma, one from Ewing’s sarcoma and one from intraosseous liposarcoma. Local recurrence of tumour was seen in two cases: one after marginal resection in a patient with telangiectatic osteosarcoma, and one in a patient with a very large osteosarcoma involving the distal femoral metaphysis. This site had been punctured several times for suspected synovitis and the tumour had continued to grow rapidly despite pre-operative chemotherapy with high-dose methotrexate and doxorubicin. In both cases disarticulation of the hip was performed. One patient died of metastatic disease, the other is disease-free five years later.

Orthopaedic results. In the assessment of the orthopaedic results, we have considered the ultimate function, the complications, and the patients’ opinions regarding the end result. As regards the functional results we used the

Case 6. Figure 5 – Chondrosarcoma of the medial condyle of the femur. Figure 6 – Radiograph five years after treatment. Figures 7 and 8 – The appearance and the excellent functional result.

Case 16. Figure 9 – Specimen of distal tibia and fibula resected for osteogenic sarcoma. Figure 10 – The irradiated specimen during re-implantation. Figure 11 – Radiographs taken two years after operation.
criteria set out in Table II. In the 12 patients surviving long enough to make assessment possible, there were 10 good and two fair results. Three patients could not be evaluated for orthopaedic function because of early death and two had early amputation because of infection. This, and other complications are considered below.

*Deep infection* was seen in two cases: an above-knee amputation was required in one, three months after the resection; the second patient, who had a malignant fibrous histiocytoma of the radius, required a secondary partial resection of the radius, with centralisation of the carpal bones on the ulna.

*Pseudarthrosis* at the tumour site and limb shortening occurred in one patient with osteosarcoma of the distal femur, who was operated on at the age of 12 years. Nine years after the initial procedure, the patient declined any further surgery such as grafting of the pseudarthrosis, limb lengthening or amputation.

*Aseptic necrosis* was seen in two cases. One patient had necrosis of the femoral head following extracorporeal irradiation of the proximal third of the femur and, one year later, had a standard total hip replacement with an excellent result. The other patient, with osteosarcoma of the distal femur, had bone necrosis and loss of substance developed in the metaphysis and epiphysis which required internal fixation and grafting. The final outcome was satisfactory.

*Partial skin necrosis* was seen in two cases. In one patient there was also deep infection which resulted in amputation. In the other case, a patient with osteosarcoma of the distal tibia, the skin eventually healed.

*Instability of the knee* was always seen when either the distal femur or the proximal tibia had been resected and replaced. However, this instability was well tolerated by the patients and did not seem to interfere with normal daily activities.

Two deaths were due to adjuvant chemotherapy. One patient died from lung fibrosis after combined chemotherapy (high-dose methotrexate, doxorubicin, vincristine and cyclophosphamide) associated with prophylactic whole lung irradiation with 1000 rads before surgery. Another patient died shortly after having received cyclophosphamide, having left hospital against medical advice. A direct relationship between chemotherapy and death was assumed but not proven.

**DISCUSSION**

The results and complications seen in our series are characteristic of this type of pathology and surgery. Oncological assessment is difficult because of the variety of our cases. However, our survival rate for osteosarcoma is similar to those recorded in the recent literature, and provides no strong case for this type of surgery.

Local tumour recurrence needs consideration, since this may not have occurred with more radical surgery such as disarticulation or amputation. In our series local recurrence did not affect the ultimate course of the disease; one patient died of pre-existent metastatic disease, the other showed no evidence of disease five years after disarticulation at the hip. This is not to say that local recurrence may not lead to a spread of the disease, but that the risk of local recurrence is inherent in this type of surgery, where a sensible compromise is required between reduced but still acceptable function after resection and as wide a resection as possible (Marcove 1978, 1981). In our experience, the risk of local recurrence can be minimised by careful pre-operative planning and staging of the disease by imaging techniques as well as the mandatory use of intensive chemotherapy.

**Table II. Criteria used to classify the functional results**

<table>
<thead>
<tr>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Useful position and range of movement at any joint involved</td>
<td>Fails to meet above-mentioned criteria but the patient is pleased</td>
<td>Patient would have been better off with an external prosthesis after a radical resection</td>
</tr>
<tr>
<td>No problems with activities of daily living</td>
<td>Acceptable cosmetic appearance</td>
<td>No need for external support during walking</td>
</tr>
<tr>
<td>Acceptable cosmetic appearance</td>
<td>No need for external support during walking</td>
<td>Patient would have been better off with an external prosthesis after a radical resection</td>
</tr>
</tbody>
</table>

From an orthopaedic viewpoint, there are significant complications, which include skin necrosis, infection, and partial resorption of the massive, dead autograft. However, these are no worse than those produced by allografting (Dick, Malinin and Mnaymneh 1985), while function was largely satisfactory in most cases. It is not clear how much the chemotherapy contributed to these complications.

In our series, solid union between the remaining bone and the re-implanted specimen was recorded in every single case, while pain was absent and remained so. There was a marked discrepancy between the clinical and the radiographic findings, which sometimes showed a grotesque image produced by necrosis and remodelling. In the majority of cases, the end result has been a functional and cosmetically acceptable limb. The period of morbidity is relatively long for the lower limbs, full weight-bearing being allowed only after 12 months. However, this restriction is during the period when morbidity due to chemotherapy is already considerable; the return to near-normal gait coincides with general reintegration into social life.

The results obtained at 12 to 18 months after the operation have proved to be durable for the five to eight years of medium-term follow-up; this is promising in comparison with massive arthroplasty, after which loosening and material breakage become more likely in the longer term. We believe that this technique will
prove to be at least equal, and possibly superior to prosthetic replacement. Its possible advantages will need to be substantiated by more experience.

Conclusions
1. Resection, extracorporeal irradiation and re-implantation may provide a rewarding alternative to allografting or prosthetic replacement for primary tumours of bone.
2. The number of complications in our series did not exceed that of replacement by allograft.
3. The functional outcome after one to two years was maintained in the medium term.
4. There was no problem with pain, but radiographic appearances tended to be deceptively poor.
5. Instability of the knee was observed in some cases, but was well tolerated by the patient.

REFERENCES


Juvara E. Procédé de résection de la partie supérieure du tibia avec substitution, à la partie enlevée d'une greffe prélevée sur le fémur. Presse Méd 1921;29:241-3.


