Safety of external fixation during post-operative chemotherapy


From Kanazawa University, Kanazawa, Japan

We studied the safety of external fixation during post-operative chemotherapy in 28 patients who had undergone distraction osteogenesis (17, group A) or vascularised fibular grafting (11, group B) after resection of a tumour. Four cycles of multi-agent post-operative chemotherapy were administered over a mean period of 14 weeks (6 to 27). The mean duration of external fixation for all patients was 350 days (91 to 828). In total 204 wires and 240 half pins were used.

During the period of post-operative chemotherapy, 14 patients (11 in group A, 3 in group B) developed wire- and pin-track infection. A total of ten wires (4.9%) and 11 half pins (4.6%) became infected. Seven of the ten infected wires were in peri-articular locations.

External fixation during post-operative chemotherapy was used safely and successfully for fixation of a vascularised fibular graft and distraction osteogenesis in 27 of 28 patients. Post-operative chemotherapy for malignant bone tumours did not adversely affect the ability to achieve union or cause hypertrophy of the vascularised fibular graft and had a minimal effect on distraction osteogenesis. Only one patient developed osteomyelitis which required further surgery.

External fixation is widely used for the treatment of complex fractures, nonunion, malunion, bone lengthening and correction of deformity, as well as in the management of bone tumours.1-3

Recent advances in the diagnosis, management and chemotherapy of tumours have made limb-salvage techniques the standard treatment for many bone tumours, but the results are not always satisfactory.6-8 When choosing which technique to use we should consider the long-term oncological and functional results, the expected survival age of the patient and the early and late complications of the type of reconstruction chosen.9

Distraction osteogenesis (callus distraction) provides a biological method of reconstruction of the bone defect after resection of a tumour and is particularly useful for malignant tumours in young patients with a good long-term prognosis.10,11 Vascularised fibular grafts are associated with rapid incorporation and union, and a low rate of infection, fracture, resorption and nonunion compared with non-vascularised grafts or allografts. They also have the ability to remodel in response to biomechanical loading, but there are limitations to their size and strength.12-14

When external fixation is used in patients with malignant bone tumours during post-operative chemotherapy the main concerns are pin- and wire-track infection, deep soft-tissue infection, osteomyelitis and the negative effects of chemotherapy on bone regeneration and healing.15,16 In this study, we investigated the incidence of infection in two groups of patients who had undergone post-operative chemotherapy. We also evaluated the effect of chemotherapy on the rate of union and the formation of callus.

Patients and Methods

We included 28 patients (20 males, eight females) with bone tumours which had been treated by en bloc resection of the tumour and skeletal reconstruction in this retrospective study with a mean follow-up of seven years (3 to 17). The mean age of the patients at operation was 16.8 years (5 to 46). The histological diagnosis was osteosarcoma in 23, Ewing’s sarcoma in three, peripheral neuro-ectodermal tumour in one and malignant fibrous histiocytoma in one.

The patients were classified into two groups according to the technique of limb-salvage used. In group A distraction osteogenesis was employed in 17 patients, and in group B a vas-
cularised fibular graft was used in 11. External fixation was applied to all the patients either for distraction osteogenesis or to stabilise the vascularised fibular graft. The tibia was involved in 13 patients, the femur in seven, both tibia and femur in seven and the humerus in one. The Ilizarov external fixator (Smith and Nephew plc, Memphis, Tennessee) was used in 15 patients, the Taylor Spatial Frame (Smith and Nephew plc) in two and a variety of unilateral external fixators (Orthofix, (Orthofix Inc., Verona, Italy) Hoffman (Stryker Osteosynthesis, Kiel, Germany) Monotube (Stryker Osteosynthesis), or Fisher (Depuy ACE, Warsaw, Indiana)) in 11.

After resection of the tumour and application of the external fixation, distraction was started seven to 14 days after operation at a rate of 0.25 mm/6 hours or 0.5 mm/12 hours. Antibiotics (penicillins or second generation cephalosporins had been administered as a single intravenous dose before operation and then orally for three to five days after in both groups. After careful attention to the maintenance of aseptic conditions during insertion, care of the wires and half pins was started immediately after operation using 0.05% chlorohexidine gluconate. All the patients (or parents) were taught how to perform pin-site care twice weekly at home after discharge from hospital.

All the patients received post-operative chemotherapy after resection of the tumour and application of the external fixator. A mean of four cycles (2 to 9) of multi-agent chemotherapy including cisplatin, doxorubicin, methotrexate and ifosfamide were administered with a mean duration of 14 weeks (6 to 27). Prophylactic intravenous antibiotics (second generation cephalosporins) were administered for three to five days during each cycle.

We used Paley's classification of pin-track infection as follows: grade I, soft-tissue inflammation; grade 2, soft-tissue infection, and grade 3, bone infection. The development of infection was monitored by clinical observation of any type of discharge, redness or hypertrophic granulation tissue at the wire-skin interface, the development of fever and the leukocyte count. The rates of union, formation of callus and consolidation were followed by radiological examination every week for group A and every two weeks for group B.

Results
For all patients the mean time of external fixation was 350 days (91 to 82), 352 days (109 to 731) in group A and 348 days (91 to 828) in group B. The mean length of distraction in group A was 9.3 cm (3 to 17) and the mean external fixation index was 37.9 days/cm (27.0 to 63.5).

Fever was observed in 12 patients. Eight patients from group A and four from group B had high fever a mean of 2.3 times (1 to 5) during chemotherapy. The causes were bone-marrow suppression in eight, a common cold in two, infection of the catheter for intravenous hyperalimentation in one and pin-track infection in one. All were treated by intravenous administration of antibiotics. The mean minimal white blood cell count after each cycle of chemotherapy was 1676/mm³ (210 to 4800). Granulocyte colony-stimulating factor was administered to 15 patients.

During the post-operative chemotherapeutic period, 14 patients (11 in group A, 3 in group B) developed wire- and pin-track infection. Ten of 204 wires (4.9%) and 11 of 240 half pins (4.6%) became infected. Seven of the ten infected wires were in peri-articular locations and seven of the 11 infected half pins had threads outside the skin.

According to Paley's classification, 52.4% (11 of 21) of the pin-track infections were soft-tissue inflammations (grade 1) and 38.1% (8 of 21) soft-tissue infections (grade 2) which responded to local care of the pin-site and antibiotics. Three patients (27%) in group B had only grade-1 soft-tissue inflammation. In group A, a marked discharge was observed in six patients (35%); all responded well to irrigation and intravenous antibiotics. One patient developed a deep infection with purulent discharge immediately after definitive surgery, but responded to irrigation and intravenous antibiotics. Deep infection occurred in one patient who had a purulent discharge from a peri-articular wire and osteomyelitis (Staphylococcus aureus) was established six months after the completion of chemotherapy. This patient was successfully treated by resection of the infected focus followed by shortening of the infected site and a separate diaphyseal distraction procedure.

We used the classification system of Catagni et al18 for the radiological evaluation of the formation of callus in group A. A total of 12 patients were judged to be normotrophic and five hypotrophic with multiple radiolucencies in the regenerated bone. Of the latter five patients, in two we stopped distraction for one week, then restarted it at a rate 0.25 mm/12 hours for one week, 0.25 mm/8 hours for another week and 0.25 mm/6 hours thereafter when the radiological appearance of the regenerated bone had improved. In the third patient it was only necessary to slow the distraction rate to 0.25 mm/8 hours for two weeks and the radiological appearance of the new callus improved. Two patients required iliac-bone grafting at the regeneration site because of poor formation of callus (Fig. 1). Bone grafting from the iliac crest was performed at the docking site in all patients after completion of distraction. However, in four patients, a second bone graft at the docking site was necessary for delayed union.

In the vascularised fibular graft group (group B), the fibula was inserted as a single strut in all patients and a variety of external fixators were used for stabilisation of the graft (Orthofix in seven patients, Ilizarov in two, Fischer in one and Monotube in one). Arthrodesis of the knee was performed in nine patients, reconstruction of the humeral diaphysis in one and pelvic reconstruction in one. Although all the grafts had united within a mean of 3.8 months (3 to 7) after transfer, the period of external fixation was extended with the intention of inducing hypertrophic change and preventing fracture. Considerable hypertrophic change in the graft (≥ 30% of the original fibular diameter).
occurred in all patients (Fig. 2). There were no deep soft-tissue or bony infections in this group.

We used the evaluation systems of Berrey et al.\textsuperscript{19} and Mankin, Doppelt and Tomford\textsuperscript{20} for assessment of vascularised fibular grafts, which grades the outcome as follows: 1) excellent, no evidence of disease, normal function of the grafted part with minimal limitations in normal activities; 2) good, no evidence of disease, restricted function of the limb but no need for a brace or a support in order to return to most daily activities and; 3) fair, no recurrence of the tumour, but the presence of a functional deficit which requires the use of a brace or other support. The outcome was judged to be a failure if the limb had to be amputated because of recurrence of the tumour, fracture or removal of the graft or deep infection. According to this classification, excellent results were achieved in two patients and good results in nine.

Discussion
Reconstruction of the defect after resection of a tumour is now considered to be the standard treatment for bone tumours rather than amputation. Distraction osteogenesis or vascularised fibular grafting supported by external fixation are useful techniques especially in young patients.

We investigated the risk of infection and osteomyelitis with the use of external fixation during the post-operative period of chemotherapy and the effect of chemotherapy on bone healing and the rate of union. Our protocol for care of the pin-site began on the first day of surgery with a single dose of prophylactic intravenous antibiotic followed by oral antibiotics for three to five days and local care with 0.05% chlorhexidine gluconate twice weekly. This regime became a daily routine in the patients who developed pin-track infection or showed signs of inflammation at the site of the pin-skin interface. The overall incidence of pin-track infection in our series was 4.7% (47.7% of infections involved wires and 52.3% involved half pins). The incidence of wire infections was 4.9% and of half-pin infections 4.6%.

Gordon et al.\textsuperscript{21} used a daily shower for pin-site care with no physical cleansing in children, but those with inflamed or infected pin-sites were treated with oral antibiotics for ten days. The incidence of infection in their series was 4.0%. All infections were grade 1 (85%) or grade 2 (15%). None of the children developed deep infection. The rate of infection was the same with either half pins or wires, but infection in the diaphyseal area was much less common than in the peri-articular region.
In the study of Catagni et al.\textsuperscript{18} which compared rates of infection between wires and half pins, the incidence of wire infections was 4.73\% and that of half pins 3.11\%. This study also showed that there was no significant difference between half pins with threads outside the skin and those with threads entirely beneath the skin. Their care of the pin-site was similar to ours. In our series part of the pin threads was outside the skin in seven of the 11 infected half pins.

Hutson and Zych\textsuperscript{22} studied the incidence of infection in peri-articular fractures with external fixators. Their care of the pin-site included daily cleaning with water and soap, removal of crusts, application of antimicrobial ointment and the use of frame covers. They reported a high incidence of infection with peri-articular wires (13\%). Deep infections occurred in 4\% and septic arthritis in 2\%. In the series of Catagni et al\textsuperscript{18} and Gordon et al\textsuperscript{21} all the infections were grade 1 or grade 2. There were no grade-3 cases. In our series, one patient developed osteomyelitis (Paley grade-3 infection) which required treatment by resection and distraction osteogenesis. Another patient with deep soft-tissue infection was treated by irrigation and intravenous antibiotics. Both patients were in the distraction osteogenesis group and both infections involved peri-articular pins. Hypermobility of the interface between the skin and the peri-articular wires or pins can promote a profuse discharge and an increased risk of infection.

Cañadell et al\textsuperscript{23} studied the effect of chemotherapy on bone transport and recommended this method of reconstruction after resection of a tumour only in very young patients, suggesting that chemotherapy has an adverse effect on bone consolidation. However, Kapukaya et al\textsuperscript{6} found that there were no significant adverse effects of chemotherapy on callus distraction and reported seven excellent and good, two fair and no poor results in their clinical study. Tsuchiya et al\textsuperscript{11} described the results of distraction osteogenesis in a series of 19 patients treated for tumour. Although seven of these patients received chemotherapy post-operatively, there was no significant difference in the duration of fixation or rates of healing when these patients were compared with those who did not receive chemotherapy after surgery. Subasi et al\textsuperscript{24} investigated the effect of chemotherapy on callus distraction in rabbits and found that they had no significant effect on distraction osteogenesis. Jarka et al\textsuperscript{16} studied the effect of methotrexate on distraction osteogenesis in rats radiologically, chemically and histologically. They concluded that chemotherapy did not have a serious adverse effect on distraction osteogenesis. In another animal study on the effect of chemotherapy on callus distraction in goats, Gravel, Le and Chapman\textsuperscript{25} found that there was no significant difference in the radiological, histological and mechanical parameters measured in animals which had received chemotherapy and those which had not. They concluded that the effects of chemotherapy on bone metabolism were minimal or only transient. However, we would recommend the use of iliac-bone graft to the docking site or regeneration site when union is judged to be delayed.

The use of vascularised fibular graft to reconstruct the bone defect after resection of a sarcoma with external fixation to stabilise the graft was described by El-Gammal et al\textsuperscript{12} to maximise hypertrophy of the graft and to avoid the stress-shielding effect of internal fixation. Good results have been reported following the use of non-vascularised fibular grafts.\textsuperscript{26}

Shea et al\textsuperscript{27} studied the use of a vascularised fibular graft after the resection of bone tumours and found that there was no significant difference in bone healing and incorporation of the graft between patients who received chemotherapy and those who did not. Union of the graft was evaluated radiologically and delayed union was defined as the absence of the formation of bone between the vascularised free fibular graft and host bone, after an arbitrarily selected interval of four to five months. In our series, all grafts had united and no additional grafting was needed. The low incidence of wire- or pin-track infections in group B was probably because the wires and pins had been placed in immobile skin areas.

We conclude that external fixation during post-operative chemotherapy is successful for fixation of a vascularised fibular graft and in distraction osteogenesis in patients. Post-operative chemotherapy for malignant bone tumours did not adversely affect the union or hypertrophy of the vascularised fibular graft and there were minimal effects on distraction osteogenesis. The incidence of wire- or pin-track infection is probably related to the duration of external fixation and myocutaneous movement around the wires or pins. When infection occurred, it was controllable in most patients by local antiseptic care and the intravenous administration of antibiotics.

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