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Reconstruction of Massive Femur Defect with Free Vascularized Fibula Graft Following Tumor Resection

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Abstract. *Background: The reconstruction of femur defects following tumor resection remains a surgical challenge. The clinical outcome of free vascularized fibula graft (FVFG) reconstruction for massive femur defects of more than 10 cm that were secondary to skeletal tumor resection is reported. Patients and Methods: Six patients with a mean of 3.3 years follow-up were reviewed. Five patients received double or folded vascularized fibula grafts and 1 received a single graft. The mean bony defect of the femur was 13 cm and the mean length of grafted fibula was 15 cm. Results: Five patients were free of disease at final follow-up; 10 out of 11 (91%) FVFGSs were transferred successfully. Five patients had a successful outcome with bony union. No stress fractures had occurred up until the final follow-up. All patients except one could walk without a brace after a mean of 9 months post-operatively. Conclusion: Double or folded FVFG is a reliable reconstructive procedure for massive femur defects.*

Recent advances in multimodality treatment with chemotherapy and wide surgical resection margins have improved the prognosis of patients with musculoskeletal sarcoma. Following wide resection of the tumor, several reconstructive procedures have been applied for large bony defects, including mega-prosthesis implantation, as well as allograft and vascularized bone grafts. In view of the long-term viability of spared limbs, the limited durability of prostheses is a major problem. Because of improved long-term survival rates for sarcoma patients, a 10-year lifespan of about 50% for primary prostheses is no longer satisfactory (1).

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The principal disadvantages of intercalary allografts include the high incidence of non-union (17-50%), fracture (17-30%) and infection (10-15%) (2). Allografts are readily available in Europe and Northern America, but are more difficult to obtain in Eastern Asia because of cultural issues.

Our group aimed to achieve biological reconstruction with living bone autografts. Free vascularized fibular graft (FVFG) has become an established procedure for the treatment of massive bone defects (3). Fibula is probably the most suitable donor bone for large defects in long bones because of its length, geometrical shape and mechanical strength. On the other hand, the femur is probably the most difficult bone for reconstruction and limb salvage remains a high-risk endeavor. Some authors hold the view that FVFG to the femur is technically difficult and has a high rate of immediate and late complications (4-7). The recipient bone is located deeper than other long bones and has only one major artery. Internal and external bony fixation is very difficult because of the strong muscle forces across the femur. A femur length discrepancy of more than 2 cm causes gait disturbance. The most important problem is late stress fracture of FVFG due to a low initial mechanical strength.

To our knowledge there have been only a few studies to date describing FVFG for massive bone defects of the femur following tumor resection. In the current study, a series of 6 patients treated for femur reconstruction by FVFG was reviewed. The clinical results and complications are assessed and the hypertrophy and late stress fracture of FVFG are discussed.

Patients and Methods

Patients. Six patients who had undergone a vascularized free fibular transfer procedure for massive femur defect secondary to extensive skeletal tumor resection were reviewed, and their characteristics are summarized in Table I. The four men and two women had a mean age of 31 years (5-55 years) and the mean follow-up period was 3.3 years (1-6 years). Tumor diagnoses were three

Table I. *Patients and reconstruction procedure.*

Case	Age and gender	Diagnosis	Site	Bone defect (cm)	Type of FVFG	Length of FVFG (cm)	Fixation	Follow-up (year)	Prognosis
1	37 M	GCT	Distal	11	Double	14+14	Plate	5	NED
2	48 M	OS	Distal	10	Double	8+12	Plate	6	NED
3	17 M	OS	Distal	13	Double	16+16	Plate	1	DOD
4	5 M	OS	Distal	15	Single	18	Plate	2.5	NED
5	55 M	GCT	Distal	15	Double	18+19	Plate	2	NED
6	23 M	MFH	Mid	12	Folded	11+15	IMR	3	NED

GCT: giant cell tumor, OS: osteosarcoma, MFH: malignant fibrous histiocytoma, IMR: intramedullar rod, NED: no evidence of disease, DOD: dead of disease.

Table II. *Clinical outcomes and complications.*

Case	Survival of graft	Vascular complication	Union proximal	Union distal	Hypertrophy proximal (%) inlay/onlay	Hypertrophy middle	Hypertrophy distal	FWB	MTS
1	Yes	No	5	7	54/20	17/0	27/8	10	80
2	Yes	V.T.	7	8.5	20/8	15/4	15/8	10	85
3	Yes	V.T.	6.5	6.5	0/0	0/0	0/0	-	-
4	Yes	No	3	NU	113	89	89	7	73
5	only 1	A.T.	5	9	0/15	0/10	0/20	9	70
6	Yes	No	6	8	50/8	42/0	31/13	7	85

FWB: full weight-bearing, MTS: muscoloskeletar tumor society, V.T.: venous thrombus, A.T.: artelial thrombus, NU: not united.

osteosarcomas, two giant cell tumors and one malignant fibrous histiocytoma. The bone tumor site was the distal third or supracondyle in five patients and the mid-shaft in one patient. Two patients underwent pre-operative neoadjuvant chemotherapy using methotrexate, doxorubicin and cisplatinum.

Surgical procedures. Skeletal fixation of the femur was performed with a plate and screws in five patients, in which the bone tumor was located in the distal third and with an intramedullary rod in the remaining patient with a mid-shaft tumor. Double or folded (twin-barreled) FVFGs (8) were transferred in five patients and a single FVFG was used in one patient. In cases with double or folded fibula grafting, one was placed as an in-lay (intramedullar) graft and the other was used as an on-lay graft. The mean length of bone defect was 13 cm (range 11-15 cm) and the mean length of FVFG was 15 cm (8-19 cm). In 8 out of the 11 FVFGs, the donor peroneal artery was anastomosed to the branch of the femoral artery by the end-to-end technique and in three it was by the end-to-side anastomosed directly to the femoral artery. The peroneal veins were anastomosed to the vanae comitantes of the recipient artery and/or the saphenous vein by end-to-end anastomosis technique.

Evaluation. Graft survival was evaluated by a peroneal skin flap in five patients and by bone scintigram in one (case 6). Bony union and hypertrophic changes of FVFG and the occurrence of stress fractures were confirmed by plain radiographs obtained monthly for one year after surgery. Functional recovery was evaluated at final follow-up using the system proposed by the Musculoskeletal Tumor Society (MTS) (9).

Results

The clinical outcomes and complications per case are summarized in Table II.

Oncological outcome. There was no local recurrence of malignant bone tumor, but one patient died with multiple lung metastases. The remaining five patients showed no evidence of disease at the final follow-up.

Graft survival. Three FVFGs (27%) had vascular complications as detected by monitoring of the skin flap and required re-exploration within 5 days of the initial operation. Venous thrombosis was found in two of these cases and an arterial thrombosis in the other. Two flaps survived following thrombectomy. In total, 10 out of the 11 (91%) FVFGs were successfully transferred. Vascular complications were not correlated with pre-operative chemotherapy or type of anastomosis. There were no complications from infection or wounds at either of the recipient or donor sites.

Rate of bony union. In the case of double FVFGs, bony union was considered complete when one fibula and femur were united. Eleven out of twelve (92%) junctions between femur and fibula were united following the vascularized fibular transfer. One patient had a residual non-union of the distal bony junction because the distal end of the femur had

Figure 1. *Radiograph of Case 1 at 3 years. A 37-year-old woman with a giant cell tumor of the distal femur. An 11-cm femur defect was reconstructed with 14-cm double FVFGs. The inlay fibula graft showed marked hypertrophy, whereas the onlay graft showed only mild hypertrophy. Bony union was achieved within 7 months post-operatively. Full weight bearing was permitted 10 months and no stress fractures occurred thereafter.*

Figure 2. *Radiograph of Case 5 at 2 years. A 55-year-old woman with a giant cell tumor of the distal femur. A 15-cm femur defect was reconstructed with 18+19 cm double FVFGs. The inlay fibula graft did not survive due to vascular complication and showed no hypertrophy. Full weight bearing was permitted 9 months after operation and no stress fractures occurred.*

been devitalized by a high dose of intra-operative irradiation (Case 4). Although the exact time to bony union was difficult to diagnose using only plain radiographs, three of the femurs at the proximal junction were united by five months and an additional three by seven months. More than 6 months were necessary at the distal junction. Bony union appeared to be earlier and stronger at the proximal compared to the distal junction.

Graft hypertrophy. Hypertrophy of the fibular graft was assessed by the modified method of DeBoer (10) at the levels of proximal, middle and distal thirds.

Excluding the three FVFGs that involved non-weight bearing (Case 3) and a failed vascularized graft (Case 5) (Figure 2), the remaining intercalary grafts showed varying degrees of hypertrophy at final follow-up. Hypertrophy was most marked in the proximal third of the FVFG, with a mean DeBoer index of 36% (range 8-113%) compared to 22% (0-42) in the middle third and 26% (8-31%) in the distal third. In three cases with double or folded grafts (Cases 1, 2 and 6) (Figures 1, 3), hypertrophic changes occurred predominantly in the inlay graft compared to the onlay graft. The mean DeBoer index for the inlay FVFG was 30% (15-54%) and for the onlay FVFG was 11% (0-20%). Late stress fracture did not occur once weight bearing was permitted.

Functional outcome. With the exception of Case 3, the time required for patients to walk without braces was a mean of 9 months (range 7-10 months). In these five cases, the MTS score was classified as good and the mean score was 79 points (range 70-85 points). No patient reported serious functional impairment of the donor limb.

Discussion

Massive femur defects resulting from bone tumors present a major challenge because of limitations with the available reconstructive methods. Although the role of FVFG for

Figure 3. *Radiograph of Case 6 at 3 years. A 23-year-old man with a malignant fibrous histiocytoma of the femur shaft. A 12-cm femur defect was reconstructed by 11+15-cm folded FVFG. The inlay fibula graft showed marked hypertrophy. Bony union was achieved within 6 months and full weight bearing was permitted after 7 months. No stress fractures occurred thereafter.*

difficult long bone defects has been well recognized, there are problems with femur reconstruction that are specific to this bone.

Operative complications of FVFG for femur reconstruction. The first problem is the technically demanding nature of this procedure. The femur is located deeper than other long bones and has few main vessels suitable for microsurgical anastomosis. Monitoring of graft vascularity is troublesome because the peroneal flap used for this purpose sometimes fails to reach the skin surface. In our experience, the final survival rate of FVFG was favorable at 91% (10/11 fibulas) but three cases had vascular complications (two venous and one arterial thrombosis). Few papers have clearly provided demonstration of graft survival. Yajima *et al.* (5) reported that femur reconstruction using FVFG was successful in 19 out of 20 patients (95%), and that vascular complication of the monitoring peroneal flap occurred in 5 cases (three overstretched flaps and two thromboses). We propose that an important factor for graft survival is not the mode of anastomosis, but rather the selection of recipient vessels. Pre-operative planning is easier in tumor cases compared to traumatic cases because any scar formation at the site of vascular anastomosis is usually minimal. Careful pre-operative selection of recipient vessels and post-operative observation of the monitoring flap are essential, as is the immediate re-exploration of cases showing complication.

Acceptable rate of bony union between FVFG and femur. The second problem with massive femur defects is the rate of bony union between FVFG and femur. Union rates of more than 80% have been reported after successful transfer. Jupiter *et al.* (6) were the first to report reconstruction of femur defects with FVFG. Primary bony union was achieved with single FVFG in five out of seven patients with post-traumatic infection or non-union. Wood *et al.* (4) reported the largest series (n=35) of femur reconstruction with FVFG. Overall, 69% of patients were healed with single FVFG and 83% following additional operations. These authors recommended using FVFG for the reconstruction of massive femur defects greater than 10 cm. Hou *et al.* (9) reviewed five cases with infection and non-union of the femur. They used folded FVFG for relatively short defects (6-10 cm) after debridement and all fractures healed within 6-12 months accompanied by hypertrophy of FVFG. Yajima *et al.* (5) also demonstrated a high rate of bony union (95%) at an average time of 6.4 months after surgery. Hsu *et al.* (11) reported that overall bony union with FVFG reconstruction was achieved in 90% of the cases after an average post-operative period of 7.6 months.

The overall union rate of 91% achieved in the current study compares favorably to other reports and supports the use of FVFG as a stable procedure for femur reconstruction. The single FVFG with failed bony union was a 5-year-old boy with osteosarcoma. The affected distal femur had been devitalized by a single, high dose of irradiation and was then re-implanted into the original site. This suggests that primary bony union is difficult to achieve in devitalized bone even with successful FVFG transplant.

Preventing late stress fracture of FVFG. The third problem encountered in femur reconstruction with FVFG is late stress fracture. The fibula normally contributes only 1/7 to 1/10 of the total weight bearing. Its anatomic configuration, therefore, cannot be compared with the femur in terms of size or biomechanical strength. Late stress fracture is probably prevented by hypertrophic changes in the FVFG. Little is known, however, about the relationship between stress fractures and FVFG hypertrophy in femur reconstructions. In the study by Wood (4), late stress fractures occurred in two patients and other authors have also reported a rate of approximately 10% (7-16%) for late stress fractures of grafted fibula (5, 6). We previously reported stress fracture of FVFG in cases with post-traumatic non-union of the femur (12). The main reason for late fracture was misalignment of FVFG of more than 15 degrees from the anatomical direction of the femur. In an attempt to minimize the risk of graft fracture, we have taken careful note of the following three points: double FVFG, rigid internal fixation and proper alignment of inlay FVFG.

To raise the primary mechanical strength of fibula grafts, we attempted double or folded vascularized fibula grafts for massive femur defects. The first FVFG was fixed as an inlay graft that worked mainly to support weight-bearing, while the second was an onlay graft that provided additional support. As an alternative method, Chang *et al.* (13) used combined vascularized fibula graft and allograft to reconstruct massive diaphyseal bone defects after tumor resection. This combination could prevent the non-union of allografts and is recommended where allografts are available.

We believe that a key factor in preventing stress fracture is to hold the femur in anatomical alignment using a strong fixation device. All patients in the current study except one could walk without long leg braces at final follow-up, but this took 9 months on average after fibula graft. Yajima *et al.* (5) recommend telescoping external fixators to gradually stress the fibula graft. Although we have no experience with external fixators, rigid internal fixation using an intermedullar interlocking rod or supracondyler plate may also help to prevent stress fractures and allow early weight-bearing of affected limbs.

One of the major advantages of using a living fibula transfer is its ability to hypertrophy (10). Although the causes of satisfactory hypertrophy are not completely understood, the high incidence of graft hypertrophy observed here was probably related to the mechanical stimulation provided by weight-bearing. Interestingly, the intercalary inlay graft in this series showed marked hypertrophy compared to the non-weight-bearing onlay fibula. These results demonstrate that hypertrophy of the fibula graft is associated with mechanical stimulation from weight bearing. The inlay FVFG should be placed in the correct anatomical alignment following proper fixation of the femur.

Alternative techniques. We cannot conclude that FVFG is the best option for femur reconstruction, because we have no direct experience with alternative treatments. Tsuchiya *et al.* (14) used the distraction osteogenesis technique for limb salvage following skeletal tumor resection. Their results suggest that this technique may provide sufficient biomechanical strength and durability and is especially beneficial in growing children. Araki *et al.* (15) and Kubo *et al.* (16) used extracorporeally-irradiated autograft and demonstrated good clinical results. This technique can be combined with FVFG to raise the mechanical strength. However, the results from our series demonstrate that FVFG is a reliable and safe procedure for femur reconstruction. There were complications involving post-operative embolism or delayed weight bearing, but these were mostly resolved without influencing the final outcome.

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