Original article

Vascularized fibula with and without extracorporeal radiotherapy for limb salvage surgery in Indian patients[☆] Akshay Tiwari^{a,*}, Sandeep Mehta^b, S.K. Sharma^c, Vijaydeep Chauhan^d, Himanshu Rohela^a, Rajan Arora^e^a Orthopedic Oncology Unit, Department of Surgical Oncology, Rajiv Gandhi Cancer Institute, New Delhi, India^b Plastic and Reconstructive Surgery Unit, Department of Surgical Oncology, BLK Cancer Centre, New Delhi, India¹^c Department of Radiation Oncology, Rajiv Gandhi Cancer Institute, New Delhi, India^d Department of Orthopedics, Ambedkar Hospital, New Delhi, India^e^e Plastic and Reconstructive Surgery unit, Department of Surgical Oncology, Rajiv Gandhi Cancer Institute, New Delhi, India

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ABSTRACT

Background: Reconstruction of segmental bone defects following resection of bone sarcomas is a challenging procedure. Vascularised fibula grafts alone or in combination with extracorporeal radiotherapy and reimplantation of tumor bone have long been established as a method of reconstruction of such defects, with satisfying results. Prompted by paucity of data on Indian patients, we report our experience with vascularised fibula graft for patients undergoing limb salvage surgery for sarcomas of bone.

Material and methods: A total of 25 patients underwent the procedure from December 2008 to December 2014. Femur was the commonest site and osteosarcoma was the commonest diagnosis. Intercalary resection was done in 19 patients and arthrodesis in 6 patients. Vascularised fibula was used in combination with extra corporeally irradiated bone in eight patients, and alone in 17 patients.

Results: All but one limb could be salvaged, and all but three patients had united at final follow up. Combination of extracorporeal radiotherapy and reimplantation with vascularised fibula fared better than vascularised fibula alone in terms of time to union (9.6 months vs 12.2 months) and rate of graft related complications (14.2% vs 62.5%).

Conclusion: Reconstruction with VFG with or without ECRT has a good and predictable functional outcome. Though manageable with active intervention, complications were more commonly seen with vascularised fibula alone than a combination of the two techniques.

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1. Introduction

Reconstruction of segmental bone defects following resection of bone sarcomas is a challenging procedure. While tumor mega prostheses are commonly used for such reconstructions, they have limitations as far as longevity and cost-effectiveness are concerned.¹ Biological methods of reconstruction offer the

advantage of being durable and cost effective.² Vascularised fibula grafts (VFG) have long been established as a method of reconstruction of such defects, with satisfying results.^{3–5} Extracorporeal radiotherapy and re-implantation (ECRT) too is an established method of reconstruction for these large segmental defects, and they may be used either alone or in combination with vascularised fibula graft.^{6–8} A thorough search of literature reveals minimal data on Indian patients undergoing vascularised fibula grafts for extremity sarcomas.⁹ We report our experience with vascularised fibula graft for patients undergoing limb salvage surgery for sarcomas of bone.

2. Material and methods

All patients who underwent reconstruction using VFG (alone or in combination with ECRT) following segmental resection of a bone

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performed between Dec 2008 and Dec 2014 at our institute were included in the present study, to enable all survivors atleast 24 months of follow up available. All patients who had intercalary joint sparing resection with good bone stock in the tumor bearing bone were considered for VFG + ECRT. VFG alone was chosen for patients with predominantly lytic tumor, transarticular resection, and where patients were not willing for reimplantation of tumor bearing bone. Patients undergoing tibialisation of fibula without involvement of plastic/microvascular surgeons were excluded from the study. A total of 25 patients were identified. We recorded patient demographics, treatment details including neoadjuvant and adjuvant treatment, operative details, oncological outcome, time to union, time to optimal function, and complications.

Nineteen male and six female patients were identified, with a mean age of 22.5 years (range, 8–61 years). All patients were evaluated with preoperative CT scan of chest with whole body bone scan and MRI of the limb with contrast. All patients were non metastatic at presentation. All but one patient were operated for limb salvage surgery for a primary bone sarcoma while the remaining patient was operated for salvage of a failed previous reconstruction with megaprosthesis and was disease free. Sites of surgery included the femur (n=13), tibia (n=5), radius (n=1), humerus (n=3), calcaneum (n=1) and ulna (n=2). Primary histopathological diagnoses included osteosarcoma (n=14), Ewing's sarcoma (n=9), leiomyosarcoma (soft tissue sarcoma involving bone) (n=1) and pleomorphic sarcoma of bone (n=1). Twenty three tumours were high grade and two were low grade (both having low grade osteosarcoma. Of all cases, intercalary resection was done in 19 patients and arthrodesis in 6. Among intercalary resections, ECRT was done in 8 and fibula alone was grafted in 11. Perioperative chemotherapy was received by 23 patients, and radiotherapy was received postoperatively by three patients (one immediate postoperative and two late postoperatively for treatment of local recurrence) We had prior Institutional Review Board approval for this retrospective analysis.

Wide resection of the primary tumour was attempted in all patients. Surgery was done as one stage procedure in all cases. Vascularised fibula was harvested from contralateral limb in most cases. For ECRT, specimen was wrapped in sterile wet clothing after removal of soft tissues and sent for radiotherapy to a dose of 50 Gy as a bolus. The construct usually consisted of double barrel fibula (with maintenance of an intact periosteal sleeve on the concave side of the osteotomy) or single fibula with ECRT for the lower limb, and a single fibula for the upper limb. Osteosynthesis was adapted for individual reconstructions but typically involved plate and screws with or without circlage wiring. The fixation bridged the whole construct in all but three patients. Final follow up was taken as last visit to the outpatient clinic or death of the patient.

Average duration of surgery was 8.2 h and average intra-operative blood loss was 1225 ml. Average duration of hospital stay was 6.7 days. All patients were followed up 3 weeks postoperatively for suture removal and wound inspection, 6 weeks postoperatively, and then every 4–8 weeks until osseous union was deemed adequate. All patients were restricted from weight-bearing in the operated extremity until there was absence of pain and radiological evidence of union. A rehabilitation program of gradually increasing weight bearing was followed over the next

few weeks. Radiographs were obtained at every postoperative visit during this time. Regular local imaging (x ray/CT/MRI) and chest CT were performed to detect any local or distant failure. Osseous union was judged on plain radiographs, and was defined as blurring or absence of osteotomy line, presence of bridging callus, or bony trabeculae crossing the graft –host junction.

Functional result was assessed using the Musculoskeletal Tumour Society score.¹⁰ Surgical outcome was assessed by the time to union using serial Xrays and time to optimal function (defined as the time taken to reach optimal level of function – unrestricted weight bearing for lower limb and unrestricted use of the upper limb). Oncological outcome was assessed by local and distant recurrences.

3. Results

The average follow up was 43 months (range 8–74 months). No patients were lost to follow up. Finally limb salvage could be achieved in all but one patient, who underwent amputation because of persistent infection.

3.1. Oncological outcome

At final follow up, four patients had died of disease (all four developed pulmonary metastases during follow up), one had died of chemotherapy related complications, and one had died of unrelated causes. Two patients had a local recurrence- both in the soft tissues. One patient (pleomorphic sarcoma of bone with VFG alone) was managed by wide excision and post op radiotherapy, while the other (Ewing sarcoma with VFG + ECRT) was managed by definitive RT. Both patients were disease free 48 months and 18 months post operatively.

3.2. Functional outcome

The average MSTS score was 25/30 (19/30 in patients with arthrodesis and 27/30 in those with an intercalary resection). Among the intercalary group, there was no difference in the functional score of patients with VFG as compared to those with VFG + ECRT.

3.3. Union rates and complications

Three patients had infection- two (one each with VFG and VFG + ECRT) had early post-operative infection (limb salvaged in one patient with VFG and amputated in the other patient with VFG + ECRT) and the third had late infection after one year of surgery (VFG alone). Of all patients, two could not be assessed for union/function because of the follow up being interrupted by severe infection (managed by amputation) in one and chemotherapy related death in the other. The outcome of remaining 23 patients is shown in [Tables 1 and 2](#).

At final follow up, all patients with ECRT+VFG had united ([Fig. 1](#)), while among the VFG alone group, all but three patients had united. One patient was awaiting union after repeat surgery, while two patients with tumors in ulna refused proposed surgery (one had a non-union at osteotomy site and the other had an un-

Table 1
Outcome in VFG and VFG + ECRT groups.

Type of Reconstruction	Resection length (cm)	Time to union (months)	Time to optimal function (months)	Duration of surgery (hours)	Blood loss (ml)
VFG	15.8	12.2	15.4	7.9 h	1203
ECRT + VFG	16.8	9.6	12.07	9 h	1275

Table 2

Complications (barring infection/local recurrence).

	Non union	Graft fracture	Repeat surgery	Percentage of complication/re-surgery
VFG	7	3	6 ^a	62.5%/37.5%
VFG+ ECRT	1	None	1 ^b	14.2%/14.2%

^a Debridement for infection followed by bone grafting in one, re-fixation with bone grafting in six; Surgery was proposed in eight patients- two patients with non-union/graft fracture ulna refused surgery), two patients with implant failure and non-union were managed conservatively with plaster immobilisation.

^b One patient with non-union healed after percutaneous bone marrow injection.

Fig. 1. (a) Osteosarcoma femur. (b) Postoperative xray after reconstruction with VFG + ECRT. (c) No sign of union one year post op. (d) United after percutaneous bone marrow injection.

united fractured graft). The rate of complication (apart from infection and oncological complications) was 62.5% (Fig. 2) (10 complications in 16 patients) in the VFG group and 14.2% (one complication in 7 patients) in the VFG + ECRT group. Two patients with non-union with implant failure could be managed conservatively with immobilisation in cast for three months (Fig. 3). Among the patients with non-union/implant failure with graft fracture, three had a non-bridging fixation, one had a history of fall, and two had post-operative radiotherapy.

4. Discussion

Reconstruction of segmental bone defects is an important component of limb salvage surgery for bone tumors. While prostheses offer a viable option with predictable results, it has its own limitations in terms of cost, longevity and function.¹ On the

other hand, biological reconstruction in the form of allografts has been seen to have disadvantages like fracture, osteoarthritis, infection, and requirement of a cadaveric bone bank.^{11,12} A vascularised fibula autograft is a very good alternative which is biological, and has the advantage of being a durable reconstruction option. Use of a VFG has been well described for reconstruction of segmental defects of long bones, with good outcomes.^{3,4,7,8} A growing vascular proximal fibula has the advantage of restoring some of limb length discrepancy in upper limbs in young children, as is well described and was achieved in one of our patients.¹³ However, a vascularised fibula too has the disadvantages of requiring availability of technical expertise and of providing a suboptimal bone stock in the early post-operative period, before it hypertrophies.

The use of a single barrel VFG in the weight bearing bones is associated with a higher rate of late fractures/non unions, and

Fig. 2. (a) Pleomorphic sarcoma femur. (b) Post op x ray showing reconstruction with folded double barrel vascular fibula. (c) 6 months post op. (d) One year post op x-ray showing spontaneous resorption of graft. (e) Consolidation of graft 3 months after cancellous bone grafting.

many workers have recommended the use of VFG either as double barrel or in combination with an allograft/treated tumor bone.¹⁴ Hence, in the absence of an availability of a bone bank, we have used either a double barrel VFG or, wherever feasible- extracorporeally irradiated tumour bone. The technique of a composite of an allograft with a vascularised fibula described by Capanna was developed with the aim to achieve a high rate of union and a graft that is both strong and eventually vascularised.²

As is expected, we have seen an earlier union and return to full weight bearing in patients who had an augmentation with ECRT and re-implantation of tumor bone. We believe the combination of good vascularity at the osteotomy combined with large surface area of bone contact is responsible for earlier union in the ECRT + VFG group. Besides, the excellent bone stock in ECRT + VFG group gives the confidence of an earlier commencement of full weight bearing. Similar results have been reported with the use of vascularised fibula grafts combined with ECRT and re-implantation previously.^{7,8} Most of our patients received chemotherapy, and union was seen only between 6 months to 20 months post operatively; an observation made by others too.⁴ Hence, we follow a policy of beginning weight bearing only after union is evident, and then a program of gradually increasing weight bearing over next few weeks.

Besides earlier rehabilitation, the overall complication rate (graft fracture/non-union) was also much lower in the VFG+ ECRT group than in the VFG alone group. Absence of graft fracture in the ECRT group reflects the robust bone stock provided by the radiated

bone, which prevents fracture as well as implant failure. Our findings agree with Hilven et al. who had reported fracture in 15% patients undergoing VFG alone.⁴ Similarly, non-union too was rare to be seen in VFG + ECRT group, which was much lower than VFG alone patients in our and others' series, as well as in ECRT alone patients in other series.⁶

The fixation of small fragments in reconstruction for bone sarcomas has been a matter of much discussion. It is well established that fixation of such grafts should preferably be done by heavy locking plates bridging across the graft, spanning from one host bone to the other.^{4,15} It is significant that all three patients in our series who had a non-bridging fixation had a failure of the reconstruction by either graft fracture or non-union. As an inlay graft is desirable for earlier hypertrophy of vascularised fibula,¹⁶ intramedullary nails were not used in any of our patients because they prevent an intramedullary placement of the grafts. Hence, we too recommend fixation by locking plates which are heavy and which bridge the grafts.¹⁷ In two of our patients, non-union with implant failure could be managed with plaster immobilisation that resulted in quick union, a distinct advantage of the graft being vascular.

We have reported, to the best of our knowledge, the largest number of Indian patients undergoing vascularised fibula graft reconstruction for an extremity sarcoma of bone. However, it is a retrospective study with a short to medium term follow up. In the long term, there might be more patients with reconstruction related problems. Besides, a longer follow up is required for

Fig. 3. (a) Osteosarcoma distal radius with distal ulna involvement. (b) Intra operative picture- osteocutaneous flap. (c) Plaster immobilisation for implant failure. (d) Complete healing with angulation at osteotomy site, good post op function.

analysing the outcome of the two techniques in the long term, as reported by other workers too.^{3,5}

5. Conclusion

Reconstruction with VFG with or without ECRT has a good and predictable functional outcome. Although there is a significant incidence of early complications, aggressive management enables optimal outcome in the majority of patients. Though complications can be managed by timely and active intervention in the majority, their incidence should be expected to be significantly higher with VFG alone, and all endeavours should be made to combine VFG with extracorporeally treated bone or allografts.

Author contributions

AkshayTiwari: Conception and design, analysis and interpretation of data, drafting the article and revising it critically for important intellectual content.

Sandeep Mehta:Acquisition of data, analysis and interpretation of data, revising it critically for important intellectual content.

S K Sharma: Acquisition of data, analysis and interpretation of data, drafting the article or revising it critically for important intellectual content.

VijaydeepChauhan: Conception and design, Acquisition of data, drafting the article.

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Conflict of interest

None to declare. The present manuscript has been read and approved by all the authors. The manuscript represents honest work done at Rajiv Gandhi Cancer Institute. None of the present work has been part of any previous publication.

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References

1. Grimer RJ, Aydin BK, Wafa H, et al. Very long-term outcomes after endoprosthetic replacement for malignant tumours of bone. *Bone Joint J.* 2016;98-B(June (6)):857–864.
2. Capanna R, Campanacci DA, Belot N, et al. A new reconstructive technique for intercalary defects of long bones: the association of massive allograft with vascularized fibular autograft. Long-term results and comparison with alternative techniques. *Orthop Clin North Am.* 2007;38:51–60.
3. Hariri A, Mascard E, Atlan F, et al. Free vascularised fibular graft for reconstruction of defects of the lower limb after resection of tumour. *J Bone Joint Surg Br.* 2010;92(November (11)):1574–1579.
4. Hilven PH, Bayliss L, Cosker T, et al. The vascularised fibular graft for limb salvage after bone tumour surgery: a multicentre study. *Bone Joint J.* 2015;97-B (June (6)):853–861.
5. Houdek MT, Wagner ER, Bishop AT, et al. Complications and long-term outcomes of free fibula reconstruction following resection of a malignant tumor in the extremities. *Plast Reconstr Surg.* 2017;139(February (2)):510e–519e.
6. Puri A, Gulia A, Jambhekar N, Laskar S. The outcome of the treatment of diaphyseal primary bone sarcoma by resection, irradiation and re-implantation of the host bone: extracorporeal irradiation as an option for reconstruction in diaphyseal bone sarcomas. *J Bone Joint Surg Br.* 2012;94(July (7)):982–988.
7. Krieg AH, Davidson AW, Stalley PD. Intercalary femoral reconstruction with extracorporeal irradiated autogenous bone graft in limb-salvage surgery. *J Bone Joint Surg Br.* 2007;89:366–371.
8. Muramatsu K, Ihara K, Hashimoto T, Seto S, Taguchi T. Combined use of free vascularised bone graft and extracorporeally-irradiated autograft for the reconstruction of massive bone defects after resection of malignant tumour. *J Plast Reconstr Aesthet Surg.* 2007;60(9)1013–1018 Epub 2007 May 11.
9. Parag S1, Yogesh P2, Rathod J2, Nikhil P1, Amit J2. Limb salvage with microvascular free fibula following primary bone sarcoma resection. *Indian J Plast Surg.* 2016;49(September-December (3)):370–377.
10. Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. *Clin Orthop Relat Res.* 1993;286:241–246.
11. Muscolo DL, Ayerza MA, Aponte-Tinao L, Farfalli G. Allograft reconstruction after sarcoma resection in children younger than 10 years old. *Clin Orthop Relat Res.* 2008;466:1856–1862.
12. Hornicek FJ, Gebhardt MC, Tomford WW. Factors affecting nonunion of the allograft-host junction. *Clin Orthop Relat Res.* 2001;8:7–98.
13. Manfrini M, Tiwari A, Ham J, Colangeli M, Mercuri M. Evolution of surgical treatment for sarcomas of proximal humerus in children: retrospective review at a single institute over 30 years. *J Pediatr Orthop.* 2011;31(January-February (1)):56–64.
14. Tanaka K1, Maehara H, Kanaya F. Vascularized fibular graft for bone defects after wide resection of musculoskeletal tumors. *J Orthop Sci.* 2012;17(March (2)):156–162.
15. Agarwal M, Puri A, Gulia A, Reddy K. Joint-sparing or physeal-sparing diaphyseal resections: the challenge of holding small fragments. *Clin Orthop Relat Res.* 2010;468(November (11)):2924–2932.
16. Muramatsu K1, Ihara K, Shigetomi M, Kawai S. Femoral reconstruction by single, folded or double free vascularised fibular grafts. *Br J Plast Surg.* 2004;57 (September (6)):550–555.
17. Umer M1, Abbas K, Khan S, Rashid HU. Locking compression plate in musculoskeletal oncology 'a friend in need'. *Clin Orthop Surg.* 2013;5 (December (4)):321–326.