

CLINICAL ARTICLE

Efficacy of a Modified Scoring System to Facilitate Surgical Decision-making for Diaphyseal Malignancies: When is Devitalized Tumor-bearing Autograft of Value?

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Objectives: To evaluate the validity of a modified scoring system (MSS) for inferring the bony quality of tumor-bearing diaphyses and predicting the risk of reconstructive failure after devitalized bone replantation (DBR).

Methods: In this retrospective cohort study, we reviewed the records of 30 patients surgically treated for diaphyseal malignancies between 1996 and 2015. There were 18 male and 12 female subjects; the average age was 34.0 ± 24.5 years (8–82 years). Tumor locations comprised the femur (21), the humerus (4), the tibia (3), the radius (1), and the fibula (1). Histological diagnoses included osteosarcoma (13), metastases (4), Ewing sarcoma (3), chondrosarcoma (3), malignant fibrohistiocytoma (2), periosteal osteosarcoma (1), Langerhans cell sarcoma (1), lymphoma (1), rhabdomyosarcoma (1), and malignant giant cell tumor (1). All primary tumors were rated as stage IIB. Twenty patients underwent DBR. Prosthetic procedures and segmental autografting/allografting were performed in 7 and 3 cases, respectively. MSS (comprising 5 elements: pain, tumor location, bone destruction, localized dimension, and longitudinal dimension) for each patient was calculated in accordance with their preoperative presentations. Outcome measurements included oncological results, outcomes of reconstructions, complications, and functional preservation, presented using the musculoskeletal tumor society (MSTS) scale.

Results: Follow up was available in 29 cases for an average duration of 61.0 ± 49.9 months (12–152 months). Infection occurred in 2 patients (6.9%), primary nonunion in 6 (27.3%), metastases in 9 (31.9%), recurrences in 4 (13.8%), and deaths in 7 (24.1%); 1 subject underwent amputation due to recurrence following endoprosthetic replacement (3.4%). In the DBR group, fractures occurred in 4 cases (21.1%) and nonunion in 5 (25%); internal fixation was related to nonunion (nails, 44.4% vs plates, 9.1%, $P = 0.02$). MSS was associated with fractures of devitalized autografts (11.0 ± 1.2 vs 8.3 ± 1.8 , $P = 0.01$); the system was efficacious in predicting chances of fractures of these grafts ($P = 0.02$). MSS ≥ 10 (with false positive rate $\leq 6.7\%$) suggested increased fracture probability ($\geq 22.7\%$) after DBR; therefore, 10 was considered a cutoff value.

Conclusions: Diaphyseal malignancies with MSS ≥ 10 may contraindicate DBR for increased chances of reconstructive failure. In this situation, alternative procedures are advisable. Further investigations are warranted to assess the efficacy of MSS in implying the validity of DBR for diaphyseal malignancies.

Key words: Bone neoplasms; Diaphyses; Limb salvage; Reconstructive surgical procedures

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Introduction

Advances in neo-chemotherapy, chemotherapy, and surgical techniques have made limb-salvaging surgery (LSS) the mainstay treatment of $\geq 80\%$ of limb malignancies¹. Previous literature has advocated various procedures, including devitalized bone replantation (DBR), autografting, allografting, distraction osteogenesis, and endoprosthetic replacement²⁻¹⁰. Rose *et al.* performed vascularized free-fibula transfer for reconstruction of the humerus; the outcomes suggested that this procedure provides excellent autograft incorporation irrespective of prolonged healing time⁴. Benevenia *et al.* describe the usage of a modular intercalary endoprosthesis as treatment for segmental defects in limbs. At short-term follow up, the implant yielded satisfactory efficacy in terms of oncological and functional results, and the authors recommended cemented fixation for immediate return to weight bearing and improved functional preservation⁸. However, controversy remains regarding the optimal treatment modality. Endoprosthetic procedures are associated with high revision rates (70%) and a lifelong risk of infection (12%), whereas biological reconstructions might be susceptible to complications, including infection, nonunion, fracture and absorption, occurring in up to 43% of cases^{2,8-10}. To date, there has not been a consensus on indications for these limb salvage procedures. A variety of factors, including age, tumor site, tumor size, soft tissue coverage, expected functional preservation, oncological prognosis and surgeons' preference, may exert impacts on the final selection of surgical procedures²⁻¹⁰.

Reconstruction using devitalized tumor-bearing bone (including irradiation, heat ablation, liquid nitrogen, and ethanol) is a valuable procedure. The graft is easy to access, offers perfect anatomic fit, and may allow long-term use if bone union occurs. However, fracture (17%), infection (10%) and nonunion (10%–27%) constitute major complications of this procedure and may impede the usage of this technique¹¹⁻¹⁴. Wu *et al.* reviewed the effectiveness of irradiation-devitalized and autoclaving-devitalized autografts as limb preservation procedures. The complication rate, including infection, fracture and nonunion, was 11%, and was higher than that for prosthetic procedures¹⁵. Pan *et al.* followed up outcomes of 10 re-implanted autoclaved grafts for a mean duration of 35 months; 20% of the patients had reconstructive failure¹⁶. There are two major reasons for high complication rates reported by some authors. First, all methods of tumor sterilization may further deteriorate the skeletal quality of tumor-bearing grafts; this could either affect the mechanical strength of the graft or slow bone incorporation. Clinical observations showed that stress fractures may even occur after bone healing is evident¹¹⁻¹⁴. Second, indications for DBR are unclear in most studies. If bony structure compromise of the tumor graft is too severe, the graft may not be feasible for replantation due to high risk of fractures and remote osteosynthesis. Tumor locations also warrant consideration during surgical planning. Although diaphyseal malignancies account for $<10\%$ of bone tumors,

they are usually larger than metaphyseal lesions and predispose to fractures (29% vs 8%); this implies that the mechanical property of diaphyses may be distinguished from that of periarticular sites^{1,2,17}. Iwata *et al.* conducted a case-control study on clinical features of diaphyseal and metaphyseal osteosarcoma. The authors argued that patients with diaphyseal osteosarcomas had a significantly larger tumor (13.5 cm vs 10 cm) and demonstrated higher pathologic fracture rates (28% vs 12%)¹⁷. Therefore, evaluating the quality of tumor-bearing diaphyses is crucial before implementing DBR; however, to our knowledge, there are no established standards determining what degrees of skeletal destruction may favor or contraindicate DBR^{18,19}. Mirels proposed a scoring system to reflect the bony quality and to predict fracture likelihood of diaphyseal metastases. The system includes pain, location, tumor lesion, and cortical destruction; scores ≥ 9 indicate fracture likelihood $\geq 33\%$ and the need for prophylactic procedures¹⁹. Nevertheless, this system only addresses localized lesions without considering longitudinally extensive neoplasms, which are common among diaphyseal malignancies. It is also unknown whether a system indicating the quality of tumor bones could predict reconstructive failures of DBR².

The purposes of the present study include: (i) to adapt the scoring system depicted by Mirels to diaphyseal malignancies to better demonstrate the clinical features of tumors arising from this location; (ii) to describe the outcomes and effectiveness of various limb salvage procedures for diaphyseal malignancies at mid-term follow up; and (iii) to analyze the effectiveness of the modified scoring system (MSS) in predicting chances of fractures of replanted devitalized autografts in the diaphyses, thereby providing deeper insights into selection of reconstructive procedures for diaphyseal malignancies.

Patients and Methods

Clinical Data

In this retrospective cohort study, we reviewed the records of 30 patients with diaphyseal malignancies treated in our institute from December 1996 to December 2015. There were 18 male subjects. The average age was 34.0 ± 24.5 years (range, 8–82 years). Tumor locations included the femur (21), the humerus (4), the tibia (3), the radius (1), and the fibula (1). Diagnoses were osteosarcoma (13), metastases (4), Ewing sarcoma (3), chondrosarcoma (3), malignant fibrohistiocytoma (2), periosteal osteosarcoma (1), Langerhans cell sarcoma (1), lymphoma (1), rhabdomyosarcoma (1), and malignant giant cell tumor (1). All diagnoses were determined based on histologic findings. Six patients (19.4%) had pathologic fractures. Three of them had undergone unplanned surgeries in other institutes. The current study was approved by the Ethical Committee of the General Hospital of Jinan Military Commanding Region and every patient or parent provided written informed consent. The methods described were performed in line with relevant guidelines and regulations.

All operations were performed by the same team of surgeons with adequate clinical experience in surgical oncology. Inclusion criteria for the present study were as follows: (i) primary bone malignancies and metastatic diseases of the extremities determined by histologic findings; (ii) diaphyseal tumors at least 5 cm from the lesion center to either epiphyses; (iii) LSS being performed with use of the devitalized tumor-bearing bone and other reconstruction constructs; and (iv) adequate outcome measures including functionality, complications, and revision surgeries being recorded with a follow up of at least 12 months. Exclusion criteria were as follows: (i) benign and borderline tumors determined by histologic examination; (ii) tumors arising from the metaphyseal locations and the epiphyses, and those located in the axial sites; (iii) tumors requiring amputation or no reconstruction construct being used; and (iv) lack of outcome measures with the follow-up duration less than 12 months.

The paper has been approved by the Ethics Committee of the General Hospital of Jinan Military Commanding Region, and all patients provided written informed consent.

Preoperative Evaluation of Tumor Bone Quality

The MSS includes pain, location, tumor lesion, localized erosion, and longitudinal destruction (Table 1). In T1-weighted magnetic resonance images, the ratio of tumor longitudinal

dimension to the total shaft length reflects longitudinal destruction. The total score measures 15; higher values indicate poorer skeletal quality of tumor bones.

Surgical Techniques

Resection of the Tumor

All the operations were performed by a senior orthopaedic surgeon. The patient was placed in a supine position on the operating table. The skin incision, including an elliptical removal of the biopsy puncture point, was marked. After prepping and draping, the skin and superficial layer were incised, followed by wide resection of the tumor as per standards described by Enneking²⁰. The tumor was excised with a soft tissue cuff and osteotomy was performed at least 2 cm from the end of the lesion, as indicated by the preoperative sagittal T1-weighted MRI. Cancellous bone from the adjacent intramedullary canal was curetted and sent for frozen section to confirm a negative margin.

Reconstructive Procedures

A wide variety of techniques were performed to reconstruct the bone defect. All cases with metastases underwent endoprosthetic reconstruction due to compromised prognosis. Tumors invading an extensive range of the shaft also required prosthetic replacement. Those cases exhibiting good prognosis and showing favorable bone stock underwent biologic reconstructions. The procedures included DBR (20), segmental prosthetic replacement (4, metastases), non-vascularized fibula autografting (2, radius), total femur replacement (2), segmental allografting (1, femur), and arthroplasty (1). Except for 1 patient exhibiting a distal radius tumor, all biological reconstructions were joint-sparing. For DBR, two techniques were used to devitalize the tumor bone, including soaking the resected bone in ethanol (18) and *in-situ* microwave ablation (2) (Fig. 1)^{12,14}. The former intervention comprised tumor excision, bone denuding, tumor curettage, drilling and preparation for internal fixation, soaking in 95% ethanol (30 min), and replantation¹⁴. Microwave ablation offers *in vivo* devitalization, with core temperatures being 108°C (30 min) and that of normal tissue ≤40°C, followed by tumor curettage and fixation¹². We also used polymethylmethacrylate (PMMA) cement and bone grafting accordingly for structural augmentation and facilitation of osteosynthesis. Internal fixation for devitalized grafts included the plate (11) and the nail (9). A modular segmental prosthesis was used to fill the bone defect in the diaphysis. The two pegs of the prosthesis were inserted into the proximal and distal intramedullary canals and were fixed with the use of PMMA cement. For tumors with a wide range of erosion, total femur replacement and arthroplasty were performed. The fibula autograft was used for the distal radius with fixation of a plate. The segmental allograft was used to fill the diaphyseal defect, with fixation using a plate.

TABLE 1 Modified scoring system (MSS) indicating quality of tumor bones

Subject	Values
Location	
Upper limb	1
Lower limb	2
Peritrochanter	3
Lesion	
Osteolytic	1
Mixed	2
Osteogenic	3
Pain*	
Light	1
Moderate	2
Severe	3
Cross-sectional extension [†]	
<1/3 circumference	1
1/3–2/3 circumference	2
>2/3 circumference	3
Longitudinal extension [‡]	
<1/3 shaft length	1
1/3–2/3 shaft length	2
>2/3 shaft length	3

* Severity of pain is determined by visual analog scale (VAS); 0–3 denotes light pain, 4–6 moderate, 7–10 severe. [†] Cross-sectional extension is demonstrated through T1-weighted axial scan by ratio of tumor extension to circumference of shaft. [‡] Longitudinal extension is measured through T1-weighted sagittal scan by the ratio of tumor extension to total length of shaft. Total score measures 15; higher values indicate inferior bone quality.

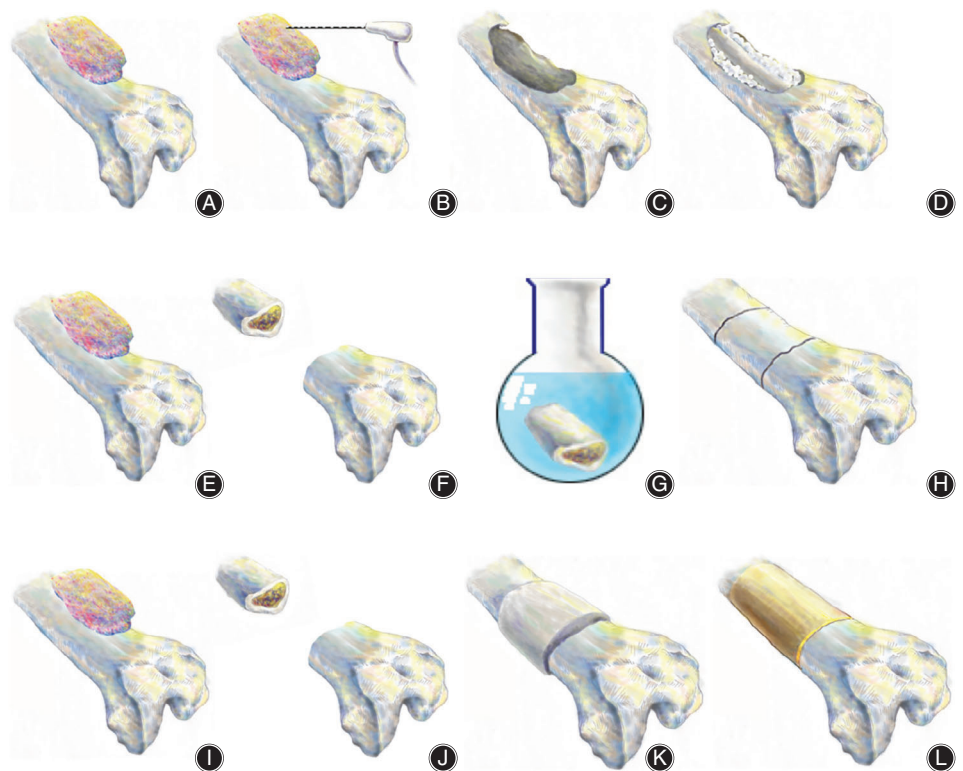


Fig. 1 Flowchart of the surgical procedures. (A–D) The *in-situ* microwave ablation procedures. After inactivation the tumor is thoroughly curetted, followed by structural and cancellous grafting. (E–H) The tumor bone is harvested and soaked in 95% alcohol. After inactivation the graft is re-implanted to reconstruct the bone defect. (I–K) The tumor bone is replaced by the allograft. (L) The endoprosthesis is used to fill the bone defect.

Follow up and Outcome Evaluation

For patients having biological reconstructions, operated limbs were positioned in braces and functional exercises started when wounds healed. Partial weight-bearing ambulation was not allowed until imaging evidence and physical examination demonstrated bony union. Outpatient visits were conducted once every 3 months for the first 2 years, every 4 months in the third year, every 6 months in the fourth to fifth year, and annually afterwards. Outcome measures included the following: (i) physical examination was conducted by a clinician in the surgery team, and the gait, appearance, muscle strength, range of motion of the joints, and limb length were recorded; (ii) pulmonary CT was performed to detect metastasis; (iii) and imaging of the surgical site was performed to reveal bone healing, local complications, and recurrences. The limb function was evaluated by a clinician in the surgery team with use of the musculoskeletal tumor society (MSTS) scale. The system assigns values of 0–5 for six categories: pain, overall function, acceptance, braces, and walking and gait in lower extremities (hand positioning, dexterity, and lifting ability in upper extremities)²¹.

Statistical Analysis

We applied SPSS software 13.0 (SPSS, Chicago, IL, USA) for statistical analyses. Fisher's exact test was used for categorical variables, whereas analysis of variance (ANOVA) was used for continuous variables. We utilized the receiver operating characteristic curve (ROC) to exploit the efficacy

of MSS. Binary logistic regression revealed the relative chance of fractures for MSS and identified the cutoff score. All values were presented as mean \pm SD; *P*-values < 0.05 were considered significant.

Results

General Results

At the end of the follow up, 1 case was lost and all primary tumors were rated as stage IIB according to the Enneking surgical staging system¹⁸. The mean follow-up duration was 61.0 ± 49.9 months (range, 12–156 months). There were 7 deaths, 9 cases of metastasis, and 4 cases of recurrences (3 located in periphery soft tissue following DBR, with 1 in bone adjacent to endoprosthesis). One case underwent amputation for recurrence following endoprosthetic replacement.

Among patients with osteosarcoma (13, 44.8%), all cases had neo-adjuvant chemotherapy and postoperative chemotherapy, as described in the literature¹⁸. Recurrence occurred in 1 subject (7.7%), metastasis in 2 (15.4%), and death in 2 (15.4%). Among 4 cases with metastases (13.8%), no recurrence occurred, while death occurred in 3 subjects (75.0%). One recurrence occurred in patients with Ewing's sarcoma (1/3, 33.3%), metastasis occurred in 2 patients (66.7%) and death in 2 patients (66.7%), respectively. All cases had neo-adjuvant chemotherapy and chemotherapy as described in the literature¹⁸. There was no recurrence, metastasis, and death in subjects with chondrosarcoma (3). One case with malignant fibrohistiocytoma (50%) had



Fig. 2 Tibial osteosarcoma (modified score system, MSS = 6) treated with devitalized bone replantation (DBR). A 14-year old male patient presented with osteogenic lesion in his left tibia. (A, B) Preoperative X-ray films showing an osteogenic lesion. (C) Re-implanted devitalized graft (ethanol sterilization) stabilized using a plate. (D, E) Diaphyseal union occurred 12 months after the procedure. (E, F) He had well preserved limb function 24 months after the operation.

recurrence and 1 had metastasis (50%), while no death occurred. One subject with Langerhans cell sarcoma had recurrence.

Clinical Outcomes

The DBR procedures related to lower MSS (8.9 ± 2.0 vs, 11.6 ± 1.0 , $P < 0.01$, Fig. 2, Table 2). In the DBR group, patients had equivalent MSTs with other cases ($80.4 \pm 23.0\%$ vs $76.5 \pm 23.0\%$, $P = 0.67$, ANOVA) at equivalent follow up (60.1 ± 46.5 vs 63.2 ± 58.0 , $P = 0.88$, ANOVA). Nailing correlated to higher MSS than plating (10.3 ± 0.9 vs 7.9 ± 2.1 , $P = 0.01$, ANOVA, Table 3). This technique was associated with more primary nonunion

(44.4% vs 9.1%, $P = 0.02$, ANOVA) and a tendency towards more frequent fractures (37.5% vs 9.1% , Fig. 3).

In the DBR group, fractures occurred in 4 cases (21.1%) exhibiting higher preoperative MSS (11.0 ± 1.2 vs 8.3 ± 1.8 , $P = 0.01$, ANOVA). ROC revealed that MSS was powerful in predicting fractures ($P = 0.02$) and its area under the curve outweighed that of the previous system (0.90 vs 0.86), indicating that MSS may yield superior performance in diaphyseal malignancies (Fig. 4). Binary logistic regression demonstrated the MSS of 10 suggested 22.7% probability of fractures, with the false positive rate being 6.7%, while score of 11 indicated likelihood of 62.1%, with the false positive rate being 0; 10 was also the point from which fractures occurred (Table 4). Therefore, we considered 10 as the cutoff value (Fig. 5).

TABLE 2 Analysis of factors associated with devitalized bone replantation (DBR)

Variable	DBR	Other procedures	P-value
Age (years)	27.5 ± 20.2	49.8 ± 27.4	0.02^\dagger
Male (n, %)	10, 52.6	7, 70.0	0.45*
Mirels' score	7.8 ± 2.0	10.2 ± 1.0	$<0.01^\dagger$
Modified score	8.9 ± 2.0	11.6 ± 1.0	$<0.01^\dagger$
Operative time (min)	184.5 ± 35.2	159.5 ± 52.1	0.14^\dagger
Blood loss (mL)	600.0 ± 498.6	735.0 ± 625.4	0.50^\dagger
Blood transfusion (n, %)	10, 66.7	5, 33.3	0.89*
Infection (n, %)	1, 5.3	1, 10.0	$>0.99^*$
Complication (n, %)	5, 26.3	1, 10.0	0.58*
Recurrence (n, %)	2, 10.5	2, 20.0	0.59*
Metastases (n, %)	5, 26.3	4, 40.0	0.68*
Death (n, %)	5, 26.3	2, 20.0	0.54*
MSTS (%)	80.4 ± 23.0	76.5 ± 23.0	0.67^\dagger
Follow-up (months)	60.1 ± 46.5	63.2 ± 58.0	0.88^\dagger

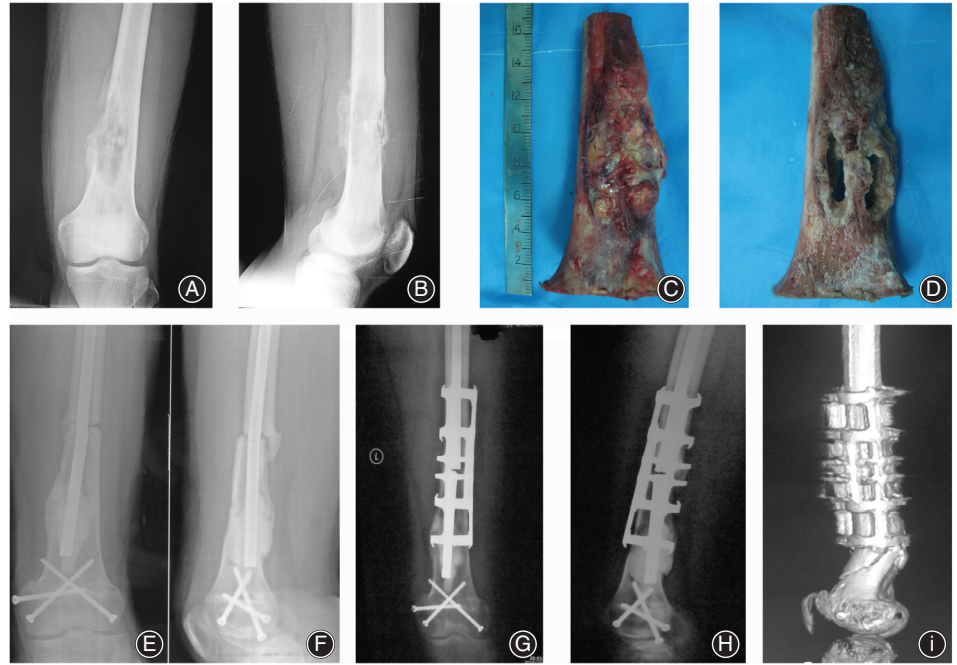
* Denotes Fisher's exact test. † Denotes analysis of variance.

TABLE 3 Analysis of factors associated with fixation construct in devitalized bone replantation

Variable	Nailing	Plating	P-value
Age (years)	19.9 ± 8.7	33.1 ± 24.5	0.17^\dagger
Male (n, %)	5, 62.5	5, 45.5	0.65*
Mirels' score	9.1 ± 1.0	6.8 ± 1.9	0.01^\dagger
Modified score	10.3 ± 0.9	7.9 ± 2.1	0.01^\dagger
Operative time (min)	180.0 ± 29.4	187.7 ± 39.9	0.65^\dagger
Blood loss (mL)	687.5 ± 543.6	536.4 ± 338.4	0.47^\dagger
Blood transfusion (n, %)	6, 75.0	4, 36.4	0.17*
Infection (n, %)	0, 0	1, 9.1	$>0.99^*$
Fracture (n, %)	3, 37.5	1, 9.1	0.26*
Recurrence (n, %)	2, 25.0	0, 0	0.16*
Metastases (n, %)	4, 50.0	1, 9.1	0.11*
Death (n, %)	4, 50.0	1, 9.1	0.11*
MSTS (%)	82.1 ± 9.9	86.7 ± 13.8	0.44^\dagger
Follow-up (months)	62.0 ± 52.3	58.7 ± 44.4	0.89^\dagger

* Denotes Fisher's exact test. † Denotes analysis of variance.

Fig. 3 Diaphyseal lymphoma (modified score system, MSS = 10) treated with devitalized bone replantation (DBR). A 23-year old male patient presented with lymphoma in his left femoral diaphysis. (A, B) Preoperative X-ray films demonstrating a mixed lesion. (C, D) The resected specimen before and after soaking in ethanol intraoperatively with the joint being spared; (E, F) Postoperative bending and breakage of intramedullary nail while bony union was not detected at the diaphyseal site at 8 months. (G, H) The patient had revision surgery with a bracing fixator. (I) Nonunion and fracture of the graft at 36 months; he received bone grafting and plating and recovered.



Complication Evaluations

Infection occurred in 2 patients, 1 having total femur replacement which recovered after debridement and vacuum

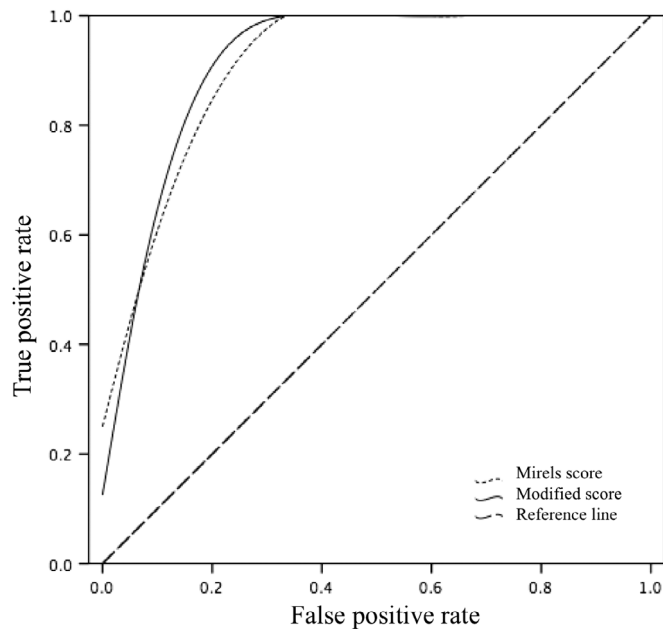


Fig. 4 Validity of the modified scoring system (modified score system, MSS) in predicting reconstructive failures of devitalized autografts. The receiver operating characteristic curve (ROC) demonstrates the feasibility of Mirels' score (dotted line) and MSS (solid line) in predicting reconstructive failures of devitalized autografts. MSS was effective ($P = 0.02$) and exhibited superior performance with regard to the area under the curve (0.90 vs 0.86).

drainage; the other undergoing DBR had fixation removal and PMMA spacer implantation. In the DBR group, 4 patients had fractures (1 at 12 months after microwave ablation; 3 at 6, 8, and 24 months after ethanol devitalization). Because 1 subject exhibited infection, the graft was replaced with a PMMA spacer; the other 3 cases had bone grafting and internal fixation. Six patients had primary nonunion (1 after allografting and 5 following DBR). Four of them underwent bone grafting and internal fixation and union occurred in all. One had obvious limb discrepancy and knee ankylosis after DBR. Distraction osteogenesis and joint lysis were performed at 7 and 9 years. All patients

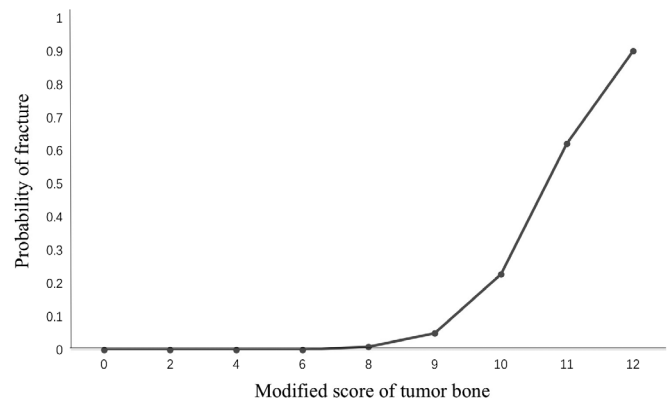


Fig. 5 Relationship between the modified scoring system (MSS) and the probability of fractures of devitalized autografts. Relevant chance of fractures for each MSS value is demonstrated in devitalized autografts. Fractures occurring from MSS 10 suggests 22.7% chance of fractures. Higher MSS values implied dramatically increased risk of fractures.

TABLE 4 Modified scores and relevant chance of fractures in devitalized grafts

Subject	Modified scores					
	6	8	9	10	11	12
Fracture	0	0	0	2	0	2
Non-fracture	5	1	4	4	0	0
True positive rate (%)	100	100	100	50.0	50.0	0.0
False positive rate (%)	66.7	60.0	33.3	6.7	0.0	0.0
Probability of fracture (%)	0.0	0.1	5.0	22.7	62.1	90.1

Binary regression analysis reveals the relevant likelihood of fracture for each score. Fracture started from a score of 10. It is associated with a 22.7% chance of fracture and a 6.7% false positive rate. Higher values show a sharp increase in fracture incidence.

exhibiting pathologic fractures underwent endoprosthetic reconstruction (Fig. 6).

Discussion

Efficacy of Devitalized Bone Replantation for Diaphyseal Malignancies

To date, there is no well-established procedure for diaphyseal malignancies due to their rarity. Endoprosthetic reconstruction has been advocated because it offers instant stability and fast functional restoration⁸. However, prolonged life expectancies of patients result in increased revision risk (70%) of this procedure^{22,23}. Henderson *et al.* found that implant failures occurred in 25% of prostheses and reoperations can present a tremendous challenge to surgeons^{24,25}. Bone grafting is also a valuable procedure, but allografting requires a bone bank. Disease transmission, immunologic rejection, and

nonunion (43%) are also issues of concern. Autografts may provide effective alternatives, but they are not suitable for large defects and exhibit high complication rates in diaphyses (60%)³⁻⁵.

Although DBR requires a prolonged bone healing process (metaphyses, ≥ 7 months; diaphyses, ≥ 11 months)^{11,13,26}, this procedure still provides the following benefits: (i) long-term use of the graft; (ii) lower revision difficulty; (iii) perfect anatomic fit; and (iv) potential tumor-specific immunologic activation^{26,27}. Whether DBR could completely eradicate tumor cells has been questioned in previous literature; however, laboratory and clinical research have validated the efficacy of the procedures used in the current study^{12,14,28-30}. We also found no difference in oncologic outcomes between DBR and other procedures (Table 2). Recurrences occurred in soft tissues but not the grafts or recipient-graft junctions; this is consistent with previous

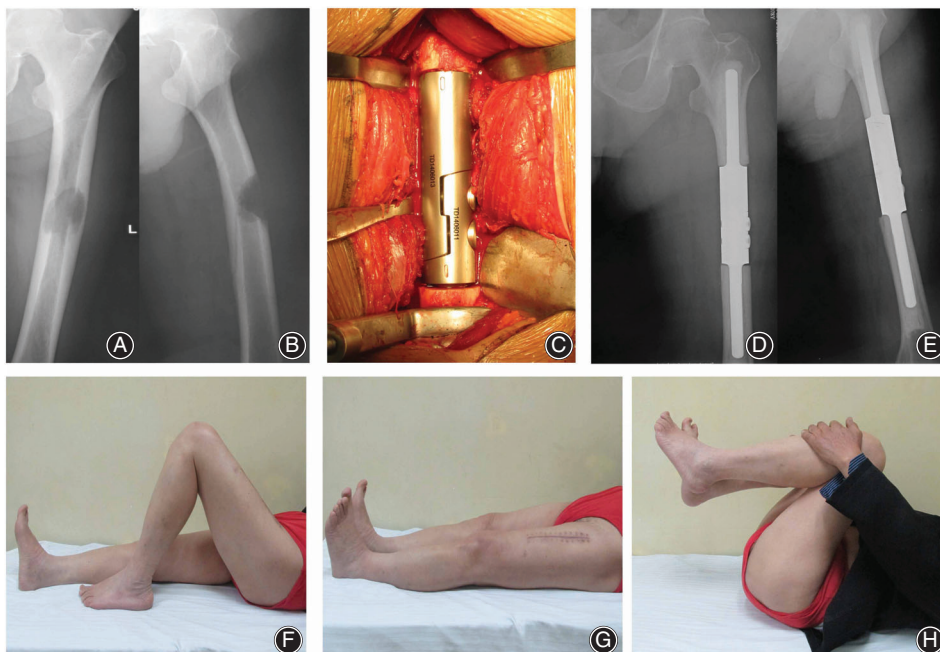


Fig. 6 Femur metastasis (modified score system, MSS = 12) treated with intercalary segmental endoprosthesis. A 78-year old male patient had metastases in his left femur, (A, B) Preoperative radiographs demonstrating an osteolytic lesion located in the diaphysis. (C) Intraoperative fixation of a modular segmental endoprosthesis after wide resection of the tumor. (D, E) Postoperative radiographs of the implant. (F-H) The patient's limb function was well preserved at 12 months postoperatively.

reports^{14,26}. Diaphyseal tumors enable surgeons to preserve the joint when performing biological reconstruction, so limb function is acceptable (77%)³¹. In the DBR group, patients had equivalent MSTs to other cases ($80.4\% \pm 23.0\%$ vs $76.5\% \pm 23.0\%$, $P = 0.67$, ANOVA). High complication rates following DBR (33%) were reported in the literature¹³. In the present study, we found that the complication rate was acceptable and comparable with that of other procedures (26.3% vs 10.0% , $P = 0.58$, ANOVA). Our findings (although underpowered by restricted sample size and study limitations) suggest that DBR is safe and efficacious as a treatment of diaphyseal malignancies.

Efficacy of Modified Scoring System in Predicting the Likelihood of Reconstructive Failure of Devitalized Bone Replantation

The quality of sterilized autografts is compromised by tumor invasion and devitalization. Moreover, diaphyseal locations are prone to fractures (46%) and delayed union (>11 months). Therefore, treatment of diaphyseal malignancies using DBR may theoretically be susceptible to reconstructive failures, and the bony quality of tumor bones needs to be scrutinized². Some authors argue that only lesions exhibiting osteoblastic changes are candidates for DBR; however, lytic and mixed tumors do not necessarily have catastrophic impacts on mechanical strengths of the tumor grafts. More indices such as lesion number, tumor size, and site should be taken into consideration¹³. The system proposed by Mirels facilitates treatment of diaphyseal metastases, but it does not include longitudinal tumor occupancy and may not precisely indicate the mechanical strength of diaphyseal grafts^{2,19}. The current study demonstrates that MSS may yield favorable performance in predicting reconstructive failures of replanted tumor-bearing autografts; cases exhibiting $MSS \geq 10$ are exposed to $\geq 22.7\%$ likelihood of fractures, although several procedures including bone grafting and cement may augment the rigidity of devitalized grafts. Skeletal quality of tumor bones remains a key factor. If it is severely disrupted, procedures other than DBR may be advisable²⁶. This is the first study looking at the correlation between quantitative assessment of tumor bone quality and outcomes of DBR in diaphyses, MSS may provide insights into surgical selection for diaphyseal malignancies, and further long-term studies of larger sample size are warranted to verify the potency of MSS.

Optimal Fixation Construct for Devitalized Autografts

Intramedullary nails and plates are 2 main fixators used in DBR; however, the optimal fixation construct remains to be

elucidated. Nails are placed coaxially with the shaft, and biomechanical research suggests that the procedure exhibits superior axial and bending stiffness, whereas plating allows for anatomic reduction and has greater torsional tolerance^{32–35}. Several meta-analyses have reported inconsistent findings for outcomes of the two procedures. Plating correlates with reduced risk of malalignment (8.7% vs 24.9%) and fewer shoulder problems, whereas it had equivalent performance with nailing in terms of bony union and wound complications^{32–35}. In femur shafts, due to the off-axis loading, plating is theoretically prone to bending or breakage, whereas nailing is mechanically advantageous and may result in longer fatigue life³⁵.

Unfortunately, reports looking at fixation constructs for devitalized grafts are lacking. We infer that internal fixation in DBR may be special, because devitalized grafts have inferior bony quality. The ability of osteointegration is compromised, and this may simulate osteoporotic bones with poor blood supply. Therefore, nailing may predispose to loss of fixation as the nail can toggle in the wide cavity, such as metaphyseal fragments and locations with skeletal defects, resulting in cut-out of locking screws easier than plating³⁶. Although it has been shown that adding the fixed-angle property to interlocking screws leads to longer fatigue life of nails, the torsional stability is still inferior to plating³⁵. There is also a potential risk of tumor contamination into the healthy medullary cavity as the nail is placed^{1,37}. This study shows that nailing correlates to more nonunions and a tendency towards more reconstructive failures. Although the evidence level was underpowered by the sample size, our findings still indicate that fixation constructs may exert impacts on outcomes of DBR. Combined use of plates and nails may offer a satisfactory solution. Biomechanical studies show that usage of both modalities yields more axial and torsional stability with longer fatigue life; this has also been verified in clinical studies^{38,39}.

Limitations of the Study

This study is subject to the limitations of a single-center study. Due to the rarity of diaphyseal malignancies, the sample size is restricted. There was heterogeneity with regard to diagnoses, tumor locations, and treatment modalities.

Conclusions

This preliminary study suggests that MSS may be effective in predicting the likelihood of fractures of devitalized autografts. $MSS \geq 10$ may contraindicate DBR, and in such situations other procedures are advisable. Further studies are warranted to verify the strength of MSS.

References

1. Sim FH, Frassica FJ, Unni KK. Osteosarcoma of the diaphysis of long bones: clinicopathologic features and treatment of 51 cases. *Orthopedics*, 1995, 18: 19–23.
2. Kong CB, Kim MS, Lee SY, et al. Prognostic effect of diaphyseal location in osteosarcoma: a cohort case-control study at a single institute. *Ann Surg Oncol*, 2009, 16: 3094–3100.
3. Schuh R, Panotopoulos J, Puchner SE, et al. Vascularised or non-vascularised autologous fibular grafting for the reconstruction of a diaphyseal bone defect after resection of a musculoskeletal tumour. *Bone Joint J*, 2014, 96: 1258–1263.
4. Rose PS, Shin AY, Bishop AT, Moran SL, Sim FH. Vascularized free fibula transfer for oncologic reconstruction of the humerus. *Clin Orthop Relat Res*, 2005, 438: 80–84.

5. Deijkers RL, Bloem RM, Kroon HM, Lent JB, Taminiau AH. Epidiaphyseal versus other intercalary allografts for tumors of the lower limb. *Clin Orthop Relat Res*, 2005, 439: 151–160.
6. Muscolo DL, Ayerza MA, Aponte-Tinao L, Ranalletta M, Abalo E. Intercalary femur and tibia segmental allografts provide an acceptable alternative in reconstructing tumor resections. *Clin Orthop Relat Res*, 2004, 426: 97–102.
7. Dormans JP, Ofluoglu O, Erol B, Moroz L, report DRSC. Reconstruction of an intercalary defect with bone transport after resection of Ewing's sarcoma. *Clin Orthop Relat Res*, 2005, 434: 258–264.
8. Benevenia J, Kirchner R, Patterson F, *et al*. Outcomes of a modular intercalary endoprosthesis as treatment for segmental defects of the femur, tibia, and humerus. *Clin Orthop Relat Res*, 2016, 474: 539–548.
9. McGrath A, Sewell MD, Hanna SA, Pollock RC, Briggs TW. Custom endoprosthetic reconstruction for malignant bone disease in the humeral diaphysis. *Acta Orthop Belg*, 2011, 77: 171–179.
10. Piccioli A, Rossi B, Scaramuzza L, Spinelli MS, Yang Z, Maccauro G. Intramedullary nailing for treatment of pathologic femoral fractures due to metastases. *Injury*, 2014, 45: 412–417.
11. Hong AM, Millington S, Ahern V, *et al*. Limb preservation surgery with extracorporeal irradiation in the management of malignant bone tumor: the oncological outcomes of 101 patients. *Ann Oncol*, 2013, 24: 2676–2680.
12. Li J, Guo Z, Wang Z, Fan H, Fu J. Does microwave ablation of the tumor edge allow for joint-sparing surgery in patients with osteosarcoma of the proximal tibia? *Clin Orthop Relat Res*, 2015, 473: 3204–3211.
13. Tsuchiya H, Nishida H, Srisawat P, *et al*. Pedicle frozen autograft reconstruction in malignant bone tumors. *J Orthop Sci*, 2010, 15: 340–349.
14. Yu XC, Xu SF, Xu M, Liu XP, Song RX, Fu ZH. Alcohol-inactivated autograft replantation with joint preservation in the management of osteosarcoma of the distal femur: a preliminary study. *Oncol Res Treat*, 2014, 37: 554–560.
15. Wu X, Cai ZD, Chen ZR, Yao Z, Zhang G. A preliminary evaluation of limb salvage surgery for osteosarcoma around knee joint. *PLoS One*, 2012, 7: e33492.
16. Pan KL, Chan WH, Ong GB, Premseenthil S, Zulkarnaen M, Norlida D. Limb salvage in osteosarcoma using autoclaved tumor-bearing bone. *World J Surg Oncol*, 2012, 10: 105.
17. Iwata S, Nakamura T, Gaston CL, *et al*. Diaphyseal osteosarcomas have distinct clinical features from metaphyseal osteosarcomas. *Eur J Surg Oncol*, 2014, 40: 1095–1100.
18. Chen Y, Yu XC, Xu SF, Xu M, Song RX. Impacts of tumor location, nature and bone destruction of extremity osteosarcoma on selection of limb salvage operative procedure. *Orthop Surg*, 2016, 8: 139–149.
19. Mirels H. Metastatic disease in long bones. A proposed scoring system for diagnosing impending pathologic fractures. *Clin Orthop Relat Res*, 1989, 415: 256–264.
20. Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma. *Clin Orthop Relat Res*, 1980, 415: 106–120.
21. 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.
22. Janssen SJ, Teunis T, Hornicek FJ, Bramer JA, Schwab JH. Outcome of operative treatment of metastatic fractures of the humerus: a systematic review of twenty three clinical studies. *Int Orthop*, 2015, 39: 735–746.
23. Wang CS, Yin QH, Liao JS, Lou JH, Chen KM. Primary diaphyseal osteosarcoma in long bones: imaging features and tumor characteristics. *Eur J Radiol*, 2012, 81: 3397–3403.
24. Henderson ER, Groundland JS, Pala E, *et al*. Failure mode classification for tumor endoprostheses: retrospective review of five institutions and a literature review. *J Bone Joint Surg Am*, 2011, 93: 418–429.
25. Damron TA, Leerapun T, Hugate RR, Shives TC, Sim FH. Does the second-generation intercalary humeral spacer improve on the first? *Clin Orthop Relat Res*, 2008, 466: 1309–1317.
26. Kunz P, Bernd L. Methods of biological reconstruction for bone sarcoma: indications and limits. *Recent Results Cancer Res*, 2009, 179: 113–140.
27. Nishida H, Yamamoto N, Tanzawa Y, Tsuchiya H. Cryoimmunology for malignant bone and soft-tissue tumors. *Int J Clin Oncol*, 2011, 16: 109–117.
28. Singh VA, Nagalingam J, Saad M, Pailoor J. Which is the best method of sterilization of tumour bone for reimplantation? A biomechanical and histopathological study. *Biomed Eng*, 2010, 9: 48.
29. Yasin NF, Ajit Singh V, Saad M, Omar E. Which is the best method of sterilization for recycled bone autograft in limb salvage surgery: a radiological, biomechanical and histopathological study in rabbit. *BMC Cancer*, 2015, 15: 289.
30. Han K, Dang P, Bian N, *et al*. Is limb salvage with microwave-induced hyperthermia better than amputation for osteosarcoma of the distal tibia? *Clin Orthop Relat Res*, 2017, 475: 1668–1677.
31. Ortiz-Cruz E, Gebhardt MC, Jennings LC, Springfield DS, Mankin HJ. The results of transplantation of intercalary allografts after resection of tumors. A long-term follow-up study. *J Bone Joint Surg Am*, 1997, 79: 97–106.
32. Kwok CS, Crossman PT, Loizou CL. Plate versus nail for distal tibial fractures: a systematic review and meta-analysis. *J Orthop Trauma*, 2014, 28: 542–548.
33. Lee SM, Oh CW, Oh JK, *et al*. Biomechanical analysis of operative methods in the treatment of extra-articular fracture of the proximal tibia. *Clin Orthop Surg*, 2014, 6: 312–317.
34. Zhao JG, Wang J, Wang C, Kan SL. Intramedullary nail versus plate fixation for humeral shaft fractures: a systematic review of overlapping meta-analyses. *Medicine (Baltimore)*, 2015, 94: e599.
35. Pekmezci M, McDonald E, Buckley J, Kandemir U. Retrograde intramedullary nails with distal screws locked to the nail have higher fatigue strength than locking plates in the treatment of supracondylar femoral fractures: a cadaver-based laboratory investigation. *Bone Joint J*, 2014, 96: 114–121.
36. Schutz M, Muller M, Krettek C, *et al*. Minimally invasive fracture stabilization of distal femoral fractures with the LISS: a prospective multicenter study. Results of a clinical study with special emphasis on difficult cases. *Injury*, 2001, 32: 48–54.
37. Bong MR, Egol KA, Koval KJ, *et al*. Comparison of the LISS and a retrograde-inserted supracondylar intramedullary nail for fixation of a periprosthetic distal femur fracture proximal to a total knee arthroplasty. *J Arthroplasty*, 2002, 17: 876–881.
38. Said GZ, Said HG, el-Sharkawi MM. Failed intramedullary nailing of femur: open reduction and plate augmentation with the nail in situ. *Int Orthop*, 2011, 35: 1089–1092.
39. Basci O, Karakasli A, Kumtepe E, Guran O, Havitcioglu H. Combination of anatomical locking plate and retrograde intramedullary nail in distal femoral fractures: comparison of mechanical stability. *Eklemler Hastalik Cerrahisi*, 2015, 26: 21–26.