3D Printing Guide Plate for Accurate Hemicortical Bone Resection in Low-Grade Bone Sarcoma

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Abstract

Background: Surgical resection and reconstruction for low grade bone sarcoma in the metaphysis of the long bone remains challenging. We hypothesize that 3D printing osteotomy guide plate could assist to accurately resect the tumor lesion and save the joint function without higher recurrence rate.

Methods: From January 2017 to August 2019, ten patients with low-grade malignant bone tumor in metaphysis of the limbs were treated with hemicortical resection using 3D printing guide plate and biological reconstruction.

Results: Four patients were paracorticular osteosarcoma, five cases had highly differentiated chondrosarcoma, and one case was a chondromyxoid fibroma. Two of the cases involved the proximal humerus, while eight cases involved the distal femur. There was neither post-operation infection, internal fixation loosening, nor fracture occurrence in any of the patients. The Musculoskeletal Tumor Society score averaged at 27.1, while the International Society of Limb Salvage imaging score examination averaged 87.8%.

Conclusions: Here, we demonstrate that the 3D printing osteotomy guide plate assisted hemicortical bone resection is a beneficial strategy to effectively resect the primary low-grade malignant bone tumors in the metaphysis of long bone and restore excellent joint function.

Introduction

Paracortical osteosarcoma and highly differentiated chondrosarcoma are the most prevalent primary bone tumors\(^1,2\). Conventional segmental bone resection for paracortical osteosarcoma usually results in a large bone defect, requiring a large allograft, bone cement, or metal prosthesis to fill the defect and restore bone stability\(^3\). However, this treatment has potential risks, including high cost, bone nonunion, prosthesis infection and fracture, and unstable joints\(^4\), particularly for bone tumors of adjacent joints, total joint resection, and replacement. This poses serious risks such as loss of joint function and joint infections\(^5-8\). Nevertheless, hemiexcision of the tumor bone with inactivated tumor bone replantation is a valuable surgical procedure for low-grade malignant bone tumors without the medullary cavity or with only one side of the cortical bone.

For safe surgical boundaries, the hemibone resection strategy should retain more normal bone tissue as possible, thus providing favorable conditions for the reconstruction of the bone defects for the rapid postoperative recovery\(^9-11\). With a distinct emphasis on bone tumors of adjacent joints, this can preserve joints and maximize joint function\(^12\). Besides, autologous tumor bone inactivation technology preserves the bone integrity of the patients, kills tumor cells, and reconstructs bone defects. Interestingly, this technology is cheaper compared with the former two and is one of the common surgical strategies for bone defect repair\(^13\). However, based on the uncertainty of the tumor growth site and the irregularity of the
tumor shape, completely removing the tumor and acquiring a reliable, safe resection boundary remains a challenge.\(^{14}\)

Recently, 3D printing technology has been extensively used in the medical field.\(^{15-18}\) For instance, in establishing tumor models \textit{in vitro} to help doctors understand tumor shapes and the adjacent tissues from multiple perspectives, and also identify lesion locations and surgical risks. Additionally, the technology has been applied in 3D printing implants through \textit{in vivo} studies to assist in determining surgical boundaries.\(^{19-21}\) In this respect, currently, there are few studies on the application of a 3D printed osteotomy guide plate for accurate hemiexcision.\(^{22}\) Therefore, in the past three years, we used 3D printed osteotomy guide plate to assist hemibonectomy for low-grade malignant bone tumors of extremities to treat 10 patients through tumor bone resection and routine tumor bone inactivation and replantation for bone defect reconstruction. Consequently, satisfactory short-term efficacy was achieved.

We hypothesized that the adoption of a digital 3D reconstruction technology can help doctors accurately determine the safe boundary of tumor surgery. We also assumed that the corresponding 3D-printed osteotomy guide plate can aid in accurately performing the resection of tumor bone. This will play a crucial role in reducing the recurrence, reconstructing bone defects, and preserving the joint function.

**Materials And Methods**

We retrospectively analyzed the bone tumor patients admitted to Hunan Cancer Hospital from January 2017 to August 2019. This study enrolled 10 patients based on the inclusion criteria. Two of the cases involved the proximal humerus, while eight cases involved the distal femur. There were 5 males and 5 females, and the minimum age of the patients was 10, the maximum 37, and the mean age 21.0 years old (Table 1). The inclusion criteria comprised of: (1) Low-grade malignant bone tumors in the metaphysis of the extremities in the long bone shaft, including paracortical osteosarcoma, highly differentiated chondrosarcoma, and chondromyoid fibroma. (2) The CT and MRI imaging confirmed that only one side of the bone cortex was involved in the tumor-like lesion, and the circumference was less than half. (3) Osteoblastic tumor changes and the tumor did not penetrate through the cortex and extend to the medullary cavity. (4) The tumor was confirmed as a low-grade malignant bone tumor via biopsy pathology. (5) The patients were classified as stage A (seven patients), stage B (three patients) according to Enneking surgical staging system of bone and soft tissue tumors.

On the other hand, the exclusion criteria constituted: (1) Pathological examination, including puncture biopsy that indicated moderate to a high malignant bone tumor. (2) X-ray, CT, and other imaging findings revealed osteolytic bone destruction with or without pathological fracture. (3) Patients that rejected the method of hemiexcision as well as inactivated replantation.

Based on the above criteria, we used the X-ray, thin-layer enhanced three-dimensional CT, and MRI for the examination of the tumor site upon admission. The patients meeting the borderline or the low-grade malignant tumor criteria (Fig. 1, Fig. 3A-C) were informed of the feasibility of this operation based on the
comprehensive assessment of their medical history, clinical signs, and imaging manifestations. After the patients assented to the surgery, we performed three routine laboratory tests, including blood biochemistry, except for the surgical contraindications, and b-ultrasound of the abdomen, and enhanced CT of the lungs to confirm that there was no organic lesion or potential metastasis to other important organs.

Simultaneously, we retrieved the enhanced CT scan data of the bone tumor sites, and used the Mimics software (Materialise’s interactive medical image control system) to extract and reconstruct the 3D CT scan data, to highlight the location, size of the tumor lesions, and print the 3D tumor bone model. Afterward, the doctor determined the safe boundary of tumor resection. For low-grade malignant tumors, 3 cm outside the tumor was generally selected as the safe boundary of resection. We also used the Mimics software to mark the tumor resection scope and the osteotomy model. The osteotomy guide plate was developed to facilitate the determination of the resection boundary and efficacy of accurate osteotomy during the operation (Fig. 2).

During the operation, we adopted general anesthesia and different optimal surgical approaches based on the different tumor sites, so as to completely expose the operative field of tumor bone. The surface of the mass was generally covered with a fibrous capsule. The capsule was not cut directly, while the normal tissue outside the capsule was separated to the cortical surface of the bone. The periosteum stripper stripped the adjacent soft tissue attached to the bone about 3–5 cm up and down, covered the osteotomy guide plate on the surface of the tumor bone, and the pendulum sawing osteotomy removed the whole tumor bone (Fig. 3D). We scraped the visible tumor bone tissue using the curettage and retained the cutting edge for routine disease examination. We treated the remaining bone tissue using hypertonic saline at 70 °C (20%) for 30 min to inactivate the tumor cells in the bone tissue. Subsequently, the inactivated bone tissue was transplanted back to the bone defect site, and the appropriate length of the bone plate was selected to fix the inactivated bone and the adjacent normal bone tissue.

At 3, 6, 12, and 24 months after the operation, we performed regular follow-up for the abdominal B-ultrasound and chest CT to assess whether there was distant metastasis. We adopted the American Society for bone tumors (Musculoskeletal Tumor Society, MSTS) function scoring system to score the limb function after the reconstructive surgery. We also used the international limb-salvage association (International Society of Limb Salvage, ISOLS) imaging scoring system for evaluation of the patients with postoperative radiographic images regarding the bone healing at the cutting surface, the graft bone changes, the stability of the internal fixation, and the joint mobility. Lastly, the percentage evaluation result was obtained by dividing the sum of the integral of each item by the full score.

Results

The operative time for this group of patients (10 patients enrolled in this study) was 120–180 min, with an average of 155 min. The volume of blood loss was 200–400 ml, with an average of 290 ml. All the incisions healed at stage I, and no early postoperative complications occurred. All patients received a
complete resection of the bone tumor. In particular, the longest inactivated bone tumor after resection was 11 cm, while the shortest bone tumor was 9 cm, with an average of 10.9 cm. The excised bone accounted for 30% – 40% of the diameter of the diaphysis, with an average of 34%. Notably, postoperative pathological analysis revealed 1 case of chondromyoid fibroma, 4 cases of paracortical osteosarcoma, 1 case of osteochondroma with local sarcoma, and 4 cases of highly differentiated chondrosarcoma (Table 1).

Additionally, no residual tumor at the postoperative incision edge was noted in any patient based on the pathological examination. However, a postoperative superficial infection was observed in 1 case (Case 4), who recovered after anti-infection and superficial debridement treatment, and thus the internal fixation was not removed. Overall, the pain score at 3 months after surgery was 1–4 points, averaging 2.2 points. All patients were followed up after surgery for 9–45 months, and the median follow-up time was 20.9 months. Thereafter, X-ray re-examination results demonstrated that none of the patients developed loosening and fracture of the internal fixation. However, 4 cases exhibited inactivated graft bone and autograft bone union (25–45 months after surgery), 2 cases developed bone resorption at the broken end, 2 cases developed osteoporosis, and 2 cases showed no significant change in X-ray manifestation.

Furthermore, two patients with humerus tumors were started on shoulder joint function exercise 1 month after forearm sling fixation. On the other hand, 8 patients with a femoral tumor walked with crutches after surgery. Remarkably, the X-ray examination for the first time 3 months post-surgery showed no abnormalities in the bone graft and internal fixation. These patients started to walk with full weight without crutches. During the last follow-up, all patients exhibited satisfactory limb function and good joint activity. One case (case 2) was found that the re-implanted bone graft reached union with the host bone 3 years after primary surgery and the internal fixation was successfully removed. The joint function of the knee remained excellent (Fig. 4). The MSTS score averaged at 27.1, while the ISOLS imaging score examination averaged 87.8%. Of note, there was no postoperative recurrence, internal fixation loosening and fracture, bone mass displacement, and metastasis in all patients (Table 2).

Discussion

Currently, it is challenging to surgically repair bone defects caused by bone tumors. Several methods are used to treat such defects, such as artificial bone\textsuperscript{24}, allograft bone\textsuperscript{12}, bone cement\textsuperscript{4}, autograft bone\textsuperscript{11, 25}, bone transport\textsuperscript{26} and tumor bone inactivation and replantation\textsuperscript{27}. Although artificial bones can repair the defect area, the mechanical stability of such bones is poor, and autogenous bones do not heal effectively. In addition, allograft bone faces challenges including rejection, broken bone resorption, nonunion, fracture, and infection. On the other hand, autologous bone overcomes these challenges, but the supply is limited, causing a secondary trauma and bone defect to the patient. Moreover, bone transport provides good repair of large bone defects as it exploits the healing ability of the body. Thus it’s widely adopted in bioremediation. However, this approach is time-consuming, and also difficult to take care of the external fixator. Additionally, its efficacy is limited by infection, pain, and psychological problems.
Inactivation of bone tumors and replantation is an effective method used to treat low grade nonosteolytic malignant bone tumors. The primary benefit of this technique is that scaffolds for bone tumors have no tumorigenic activity, kill tumor cells through high-temperature heating, retains the appearance and mechanical support of the residual bone, and do not cause exclusion compared with allogeneic bone. It is also much cheaper than the allogeneic bone. Elsewhere, various methods have been noted to inactivate tumors including high-temperature water bath inactivation, \textit{in vitro} irradiation inactivation\textsuperscript{27, 28}, liquid nitrogen inactivation\textsuperscript{29}, and pasteurization inactivation\textsuperscript{10, 30}. Studies have enumerated that pasteurization has therapeutic effects as a biologic reconstructive option. In the study, 80\% of the patients survived over 20 years and 62\% of the patients had no complications, but it is not ideal for the long term\textsuperscript{30}. However, hypothermia inactivation of the bone tumor using hyperosmotic saline is an effective approach to inactivate tumor cells. This method retains the activity of collagen fibrin and protein effectively which may be associated with hyperosmotic saline used as the protein stabilizer\textsuperscript{31}. Therefore, inactivated bone tumor allow integration of grafted bone and autogenous bone, and retains the shape and mechanical strength of the original bone defect. Furthermore, it is a relatively inexpensive treatment method, making it a common method in clinical practice. Despite these benefits, large segments of autogenous bone are inactivated, the bone loses its biological activity, and cannot participate in the metabolism of normal bone tissue or integrate with autogenous bone tissue. Hence, for long-term applications, continuous auxiliary internal fixation is needed to maintain mechanical stability.

In the case of a bone tumor adjacent to a joint, excision of large segments of the joint requires extensive joint reconstruction, resulting in reduced joint function and a similar risk of infection to other internal plants. Therefore, it is recommended that large active bone tissue should be retained as much as possible to maintain bone biomechanics, metabolism and prevent infections and preserve the integrity and function of adjacent joints. However, despite its limited indications, hemiarticular resection followed by inactivation and replantation is recognized and applied by many scholars\textsuperscript{9–11, 29}. Campanacci was the first to report the application of hemiectomy in bone tumor surgery\textsuperscript{32}. Also, some scholars have used hemiexcision for the surgical treatment of high-grade osteosarcoma. It has been noted that it is suitable for eccentric bone tumors, but its long-term effects remain elusive\textsuperscript{29}. In particular, hemiexcision is more predominantly used for low-grade malignant tumors\textsuperscript{10, 12, 33–35}. The benefits of hemiexcision include; tumor resection can be expanded, preserves the stability and integrity of adjacent joints, and enhances the residual normal bone mechanics using autologous or allogeneic bone grafting, matches the size of the original bone defect accurately, and has no risk of disease transmission. Of note, the initial safety margin of tumor resection is crucial to the treatment effect. Factors such as tumor location, shape, and size pose challenges to the effective application of hemibone resection. Due to the irregular shape of the tumor, and the restriction of the surgical field of view, surgeons may have to make certain plan changes during the osteotomy procedure. This may lead to the unsafe tumor resection border and the recurrence of residual tumor. For malignant bone tumors at the distal end of the posterior femur, it is difficult to preserve blood vessels as well as joint function\textsuperscript{35}.
In the past, no method was available to make three-dimensional measurements on the tumor before surgical resection. However, computer technology has enabled this measurement to be made, thus achieving a higher matching degree between the tumor defect removed and the bone graft reconstructed\textsuperscript{22}. Another method used to accurately remove a tumor from bone is the surgical navigation robot, but this tool is expensive and not readily available in ordinary hospitals. Recently, 3D digital reconstruction and 3D printing of osteotomy guide plate technology have improved osteotomy for hemibonectomy of bone tumors. The 3D reconstruction of the bone tumor is achieved using a three-dimensional CT scan which transmits the data into a 3D reconstruction software to establish a 3-dimensional model. This technique reveals the tumor after printing, thus allowing doctors to make a plan for the resection border. The corresponding resection guide plate can be fabricated according to the plan\textsuperscript{22}. Theoretically, the safe boundary of osteotomy for this method is more reliable, and the chances of postoperative recurrence are lower. Moreover, with the assistance of the osteotomy guide plate, the time needed for osteotomy localization is relatively shorter, which reduces the operation time and in turn decreases blood loss, thus making it more effective in the rehabilitation of patients. Using the osteotomy guide plate, most of the bone tumor can be removed as a whole, rather than unplanned lumps. After inactivation treatment, the original shape of most of the bone tumor is maintained which creates a very high matching degree with the bone defect site. This ensures good fixation of bone blocks and also shortens the operation time. Overall, this method results in good postoperative recovery and functional recovery.

Previous studies have reported that fractures, infections and incomplete resection contributes to the development complications of hemiexcision. Specifically, fracture is one of the leading cause (10\%-18\%)\textsuperscript{12,36}. In 2014, some scholars used computer-assisted surgery to design an allograft bone graft to repair the bone defect of hemibonectomy. They noted that the method achieved resection and reconstruction precisely with less time-consuming and also reduced the incidence of fracture\textsuperscript{22}. Therefore, 3D printed osteotomy guide plate can be used to perform accurate osteotomy based on the preoperative surgical plan, without any intraoperative or postoperative fractures. Herein, the inactivated bone tissue transplanted back into the patient perfectly matched with the original bone defect, shortening the time taken to reconstruct the bone defect and adjust the bone mass. Besides, our short-term postoperative follow-up results enumerated no recurrence in all 10 patients. This implies good patient selection and safe tumor resection boundary. We also achieved accurate R0 resection and successful reconstruction even for adjacent joint lesions, and this perhaps may have contributed to the highly preserved joint function. Functional scores of the affected limbs after surgery were above 24 points in all patients, while patient satisfaction was very high. This finding is consistent with the recent reports by Japanese scholars\textsuperscript{37} and also exceeds scores reported in a review by Dutch scholars\textsuperscript{9}. Therefore, this surgical approach is effective for the removal of bone tumors and bone reconstruction. High short-term efficacy following inactivation and replantation of hemibone resection for highly malignant bone tumors has been reported\textsuperscript{29}. This indicates that it is possible to achieve an effective safe boundary for tumor control. However, the long-term efficacy of our method should be investigated further to confirm these intriguing findings, especially in follow-up studies.
In summary, digital three-dimensional reconstruction is a valuable technique for formulating osteotomy boundary and osteotomy guide plate assisted osteotomy, which makes hemibone resection more convenient, faster, and reduces the risk of postoperative complications, and lowers the recurrence rate. Furthermore, the method used herein is cheap, reliable, and results in quick recovery. Notably, this is important for reserving the joint function regarding the tumor adjacent to the joint. Despite these benefits, we acknowledge that hemiexcision has its inherent limitations. Among them is the risk of postoperative recurrence and insecure surgical boundaries. The follow-up period for patients in this study is relatively short, and thus a longer follow-up duration is needed to test the long-term effect of this surgical method. Also, the current digital three-dimensional reconstruction does not accurately identify the tumor tissue, making it difficult to achieve intelligent grasp recognition. Therefore, manual intervention is required to determine the tumor boundary. We believe that with the further advancements in imaging, digital technology, and artificial intelligence, these problems will be gradually solved, and hemibonectomy will yield better therapeutic effects.

Conclusions

The 3D printing guiding plate offered a useful approach for completely resecting low malignant metaphyseal bone tumor. The joint function is excellent and recurrence rate is low for short term follow up. The technic saves time and decreases bleeding during the operation. The cost of this technic is affordable and worthy to be applied to this kind of disease.

Declarations

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Availability of data and materials

All the data and material are available from the corresponding author upon reasonable request.

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Contributions

Dr. Hongwei Wu wrote the manuscript and Dr. Xian’an Li conceived the study and revised the manuscript. Other authors contributed to the data analysis, manuscript editing, article revision, and data supplement. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

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Ethics declarations

Ethics approval and consent to participate

The ethics approval was not applicable in this study. Written informed consent participation was required from all patients before the start of therapy.

Consent for publication

Written informed consent was required from patients in Case 2 and Case 9 for publication in this manuscript respectively. Copies of the written consent are available for review by the Editor-in-Chief of the journal.

Competing interests

The authors declare no conflicts of interest.

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# Tables

**Table 1 Clinical characteristics in patients who received hemicortical resection and reconstruction**

| No | Age/Gender | Diagnosis | Site | Resected bone(cm) | % of cortical circumstance | Fixation |
|----|-------------|-----------|------|--------------------|---------------------------|---------|
| 1  | 11/F        | PO        | Femur| 11                 | 40                        | P+S     |
| 2  | 10/F        | CM        | Femur| 13                 | 30                        | P+S     |
| 3  | 37/M        | CS        | Femur| 9                  | 40                        | P+S     |
| 4  | 16/F        | PO        | Humerus| 10               | 40                       | P+S     |
| 5  | 17/M        | PO        | Femur| 11                 | 35                        | P+S     |
| 6  | 25/M        | CS        | Humerus| 10               | 30                        | P+S     |
| 7  | 33/F        | CS        | Femur| 10                 | 30                        | P+S     |
| 8  | 10/M        | PO        | Femur| 12                 | 35                        | P+S     |
| 9  | 19/F        | CS        | Femur| 13                 | 30                        | P+S     |
| 10 | 32/M        | CS        | Femur| 10                 | 30                        | P+S     |

Note: CM: Cartilaginous Myxofibroma; PO: Paracortical Osteosarcoma; CS: Chondrosarcoma; P+S: Plate and Screw.

**Table 2 Clinical outcome of 10 patients with hemicortical resection and reconstruction**
| No. | Age/Gender | Complications/ Fixation failure | Pain score | FWB months | Follow-up months | MSTS Score | ISOLS Score | Recurrence/ Metastasis |
|-----|------------|---------------------------------|------------|------------|------------------|------------|-------------|------------------------|
| 1   | 11/F       | Incision exudation/N            | 4          | 3          | 10               | 27         | 83          | N/N                    |
| 2   | 10/F       | None/N                          | 1          | 3          | 45               | 28         | 88          | N/N                    |
| 3   | 37/M       | Wound effusion/N                | 4          | 3          | 9                | 26         | 78          | N/N                    |
| 4   | 16/F       | Superficial infection/N         | 2          | 0          | 23               | 29         | 89          | N/N                    |
| 5   | 17/M       | None/N                          | 1          | 3          | 29               | 27         | 91          | N/N                    |
| 6   | 25/M       | None/N                          | 3          | 0          | 20               | 25         | 90          | N/N                    |
| 7   | 33/F       | None/N                          | 2          | 3          | 10               | 29         | 93          | N/N                    |
| 8   | 10/M       | Incision exudation/N            | 3          | 3          | 25               | 26         | 88          | N/N                    |
| 9   | 19/F       | Wound effusion/N                | 1          | 3          | 12               | 24         | 84          | N/N                    |
| 10  | 32/M       | None/N                          | 1          | 3          | 26               | 29         | 94          | N/N                    |

Note: FWB: Full weight-bearing; MSTS: Musculoskeletal Tumor Society; ISOLS: International Society of Limb Salvage; N: Negative.
Figure 1

Case 9: Nineteen years old female patient with chondrosarcoma. A and B: X-ray indicated large osteogenic bone lesion at the posterior femur of the left leg. C: MRI enhanced scan showing the lesion was closely adjacent to the popliteal vessels. D: Cross section of CT scan demonstrated that lesion was close next to the vessels.
Figure 2

Case 9: Operation procedure for resection of the tumor. A: 3D printing guide plate in both medial and lateral side. B: 3D printing model for the tumor and the planned resection boundary. C and D: 3D printing guide plate guiding the resection in both medial and lateral side. E: The resected bone lesion and corresponding printing model. F: The inactivation bone was re-implanted orthotopically.

Figure 3

Case 2: Ten years old female patient with cartilaginous myxofibroma. A and B: X ray indicated large osteolytic bone lesion at the distal femur of the right leg. C: CT scan images of the lesion showing that osteolytic lesion locates at the metaphyseal site and lateral side of the distal femur. D: Photos taken during the operation showing that the lesion was resected completely and the lesion was removed from the residual bone graft.
Figure 4

Case 2: X ray three years post primary operation and joint function evaluation. A and B: X ray before the internal fixation was removed. C and D: X ray after the internal fixation was removed showing union in the graft. E: Images showing that the joint function was excellent for both stretch and flex movement.