

Is Navigation-guided En Bloc Resection Advantageous Compared With Intralesional Curettage for Locally Aggressive Bone Tumors?

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Abstract

Background The treatment of locally aggressive bone tumors is a balance between achieving local tumor control and surgical morbidity. Wide resection decreases the likelihood of local recurrence, although wide resection may result in more complications than would happen after curettage. Navigation-assisted surgery may allow more precise resection, perhaps making it possible to expand the procedure's indications and decrease the likelihood of recurrence; however, to our knowledge, comparative studies have not been performed.

Questions/purposes The purpose of this study was to compare curettage plus phenol as a local adjuvant with navigation-guided en bloc resection in terms of (1) local

recurrence; (2) nononcologic complications; and (3) function as measured by revised Musculoskeletal Tumor Society (MSTS) scores.

Methods Patients with a metaphyseal and/or epiphyseal locally aggressive primary bone tumor treated by curettage and adjuvant therapy or en bloc resection assisted by navigation between 2010 and 2014 were considered for this retrospective study. Patients with a histologic diagnosis of a primary aggressive benign bone tumor or low-grade chondrosarcoma were included. During this time period, we treated 45 patients with curettage of whom 43 (95%) were available for followup at a minimum of 24 months (mean, 37 months; range, 24-61 months), and we treated 26 patients with navigation-guided en bloc resection, of whom all (100%) were available for study. During this period, we generally performed curettage with phenol when the lesion was in contact with subchondral bone. We treated tumors that were at least 5 mm from the subchondral bone, such that en bloc resection was considered possible with computer-assisted block resection. There were no differences in terms of age, gender, tumor type, or tumor location between the groups. Outcomes, including allograft healing, nonunion, tumor recurrence, fracture, hardware failure, infection, and revised MSTS score, were recorded. Bone consolidation was defined as complete periosteal and endosteal bridging visible between the allograft-host junctions in at least two different radiographic views and the absence of pain and instability in the union site. All study data were obtained from our longitudinally maintained oncology database.

Results In the curettage group, two patients developed a local recurrence, and no local recurrences were recorded in patients treated with en bloc resection. All patients who underwent navigation-guided resection achieved tumor-free margins. Intraoperative navigation was performed

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Each author certifies that his institution approved or waived approval for the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.

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successfully in all patients and there were no failures in registration. Postoperative complications did not differ between the groups: in patients undergoing curettage, 7% (three of 43) and in patients undergoing navigation, 4% (one of 26) had a complication. There was no difference in functional scores: mean MSTS score for patients undergoing curettage was 28 points (range, 27–30 points) and for patients undergoing navigation, 29 (range, 27–30 points; $p = 0.10$).

Conclusions In this small comparative series, navigation-assisted resection techniques allowed conservative en bloc resection of locally aggressive primary bone tumors with no local recurrence. Nevertheless, with the numbers available, we saw no difference between the groups in terms of local recurrence risk, complications, or function. Until or unless studies demonstrate an advantage to navigation-guided en bloc resection, we cannot recommend wide use of this novel technique because it adds surgical time and expense.

Level of Evidence Level III, therapeutic study.

Introduction

Locally aggressive bone tumors can recur but rarely metastasize [3, 6, 7, 11, 13]. Treatment therefore is a balance between preserving function and avoiding local recurrence, which can result in more surgery. There are two basic approaches to treating benign tumors of bone: curettage or en bloc resection [17]. Wide resection improves local control but increases the risk of complications and morbidity [2, 39]. On the other hand, intralesional resections may result in a higher risk of local recurrence [5, 19, 20].

If en bloc resection could result in a lower risk of recurrence without compromising function, it might offer the advantage of lessening recurrence while preserving function. Navigation allows more precise resections, and so it is tempting to use it to perform resections more often than were previously done using freehand approaches, which are more challenging to perform when a tumor is near the end of the bone [1, 2, 15, 33, 34, 36–39]. However, we do not, in fact, know whether resections will result in a lower likelihood of recurrence, because there are no comparative studies of which we are aware.

The purpose of this study was to compare curettage plus phenol as a local adjuvant with navigation-guided en bloc resection in terms of (1) local recurrence; (2) nononcologic complications; and (3) function as measured by revised Musculoskeletal Tumor Society (MSTS) scores.

Patients and Methods

A retrospective analysis from the longitudinally maintained oncology database of our institution was done for

all patients with metaphyseal and/or epiphyseal local aggressive primary bone tumors treated by curettage and adjuvant therapy or en bloc resection assisted by navigation between May 2010 and May 2014. During this time period, we treated 45 patients with curettage of whom 43 (95%) were available for followup at a minimum of 24 months (mean, 37 months; range, 24–61 months), and we treated 26 patients with navigation-guided en bloc resection, of whom all (100%) were available for study. No patients who had a recurrence before 2 years were excluded. The general indications for those types of resections and reconstructions were a locally aggressive primary bone tumor causing bone destruction and with the potential for further growth if not treated. The indication for navigation-guided en bloc resection was when resection could be performed with safe margins without compromising the articular surface. If this could not be achieved, intralesional curettage was done. Patients who matched the inclusion criteria (histologic diagnosis of a primary benign bone tumor or low-grade chondrosarcoma) treated initially at our institution were included for analysis. For low-grade chondrosarcoma classification, the World Health Organization criteria were used in which Grade 1 chondrosarcomas are defined as moderately cellular neoplasms with hyperchromatic plump nuclei of uniform size. No enchondromas were included in this series [7].

A total of 43 patients were included in the intralesional resection group and 26 patients in the en bloc resection group. Mean followup was 37 months (SD 11.14; range, 24–61 months) for patients treated with curettage and 37 months (SD 9.78; range, 24–56 months) for patients treated with en bloc resection and computer-assisted tumor surgery (Table 1). Six of the patients undergoing curettage and none of the patients undergoing navigated resection were lost to followup.

All patients were studied with preoperative radiographs (AP and lateral views), MR images, and CT scans and were examined by a multidisciplinary oncology team. CT chest scans were done for all the patients with chondrosarcoma and giant cell tumors to exclude lung metastasis. None of the patients included in this analysis had systemic disease. A preoperative core needle biopsy was done in all patients and diagnosis was confirmed by histology and classified according to Enneking score [12] (Table 1). The following variables were compared: (1) occurrence of local recurrence; (2) nononcologic complications; and (3) functional outcomes.

Curettage was done in all patients through a full bony window, extended 1 cm proximal and 1 cm distal from the lesion, to achieve maximal visualization of the cavity. A high-speed burr was used to extend the curettage and phenol was applied as local adjuvant therapy in all patients. The bone defect was filled with a combination of fragmented and structural bone allograft [5].

For patients treated with en bloc resection assisted by navigation, CT scans and MR images were fused to

Table 1. Demographic characteristics of the 69 patients of the series

| Demographic | Group 1 | Group 2 | p value |
|-------------------------------------|---|--|---------|
| Total | 43 | 26 | - |
| Gender | Female: 22 Male: 21 | Female: 16 Male: 10 | 0.12 |
| Age (years) | 33 (range, 14-62) | 34 (range, 16-71) | 0.69 |
| Type of tumors | ABC: 3 Chondrosarcoma Grade 1: 14 Chondroblastoma: 8 Osteoblastoma: 3 GCT: 15 | ABC: 2 Chondrosarcoma Grade 1: 14 Chondroblastoma: 2 Fibroma chondromyxoid: 3 Osteoblastoma: 4 GCT: 1 | |
| Tumor grade Enneking classification | Grade 1: 0 Grade 2: 28 Grade 3: 15 | Grade 1: 0 Grade 2: 23 Grade 3: 3 | |
| Followup (months) | 37 (range, 24-61) | 37 (range, 24-56) | 0.8 |

ABC = aneurysmal bone cyst; GCT = giant cell tumor of bone.

determine bone cortex and intra- and extraosseous soft tissue tumor extension to program a virtual osteotomy [32, 34] (Fig. 1). Using a three-dimensional (3-D) virtual platform, (MIMICS® software; Materialise, Leuven, Belgium), preoperative osteotomy planning was defined according to tumor biologic activity, growth potential, and location [31, 32]. Once the 3-D preoperative planning was obtained in a computer-aided design format for both tumor resection and allograft reconstruction, 3-D models were converted to CT data sets in Digital Imaging and Communications in Medicine format and imported to the navigator (3D Ortho Map navigation software, Version 1.0; Stryker Navigator, Freiburg, Germany) [32]. Multiplanar osteotomy was planned and performed in all patients treated with en bloc resection assisted with navigation. During the surgical procedure, after exposure, surgeons (GLF, LAA-T) placed an infrared tracking device in uncompromised bone and established correspondence between the 3-D images and the patient bone with visible anatomic points [1]. After that, surface mapping of the bone was done to reduce any mismatch between the 3-D image and the true bone (Fig. 2). When the surgeons were confident with the accuracy of the registration (< 2 mm), the osteotomies were marked with a surgical pen using a navigated pointer [1, 2]. Finally, the osteotomies were performed with a freehand saw following the previous mark (Fig. 2). We did not record the time needed for the registration and planning of these navigated resections.

In the group of patients treated with navigation, after macroscopically and microscopically review by a musculoskeletal tumor specialized pathologist (PR), all margins were classified as being free of tumor. Intraoperative navigation was performed successfully in all patients and there was no failure in registration. Registration error, which represents the degree of mismatch between the patient's anatomy and the virtual preoperative images, was a mean error of 0.57 mm (range, 0.3-0.7 mm).

After tumor resection, the surgical specimen was macroscopically and microscopically reviewed by a musculoskeletal tumor-specialized pathologist (PR) to confirm diagnosis and

tumor margins after en bloc resection. Reconstruction was done with bone grafting from fresh deep-frozen allografts in all patients.

No patient in the series received postoperative adjuvant therapy. Antibiotics were given intravenously according to the usual prophylactic protocol, and no routine anticoagulation therapy was used. The rehabilitation protocol was standardized according to the specific anatomic area and was the same in both groups. Plain radiographs and physical examination were performed at each followup. Outcomes, including allograft healing, nonunion, tumor recurrence, fracture, hardware failure, and infection, were recorded. Bone consolidation was defined as complete periosteal and endosteal bridging visible between the allograft-host junctions in at least two different radiographic views and the absence of pain and instability in the union site. The revised system established by the MSTs was chosen to assess functional outcome by the orthopaedic oncology team involved in the care of the patients (GLF, LAA-T, JIA) through our longitudinally maintained institutional database [13].

Statistical analysis was performed using the R programming language [27]. The variables were analyzed using Fisher's exact test and Wilcoxon rank test with continuity correction. A value of $p < 0.05$ was considered significant [27].

Results

Five percent (two of 43) of the patients treated with curettage and local adjuvant therapy developed a local recurrence. The primary diagnoses of these patients were giant cell tumor Campanacci Grade II and aneurysmal bone cyst. None (zero of 26) of the patients treated with en bloc resection developed a local recurrence in the followup period. With the numbers available, no difference in recurrence was seen between patients treated with curettage and those treated with en bloc resection assisted with navigation ($p = 0.52$). We did not

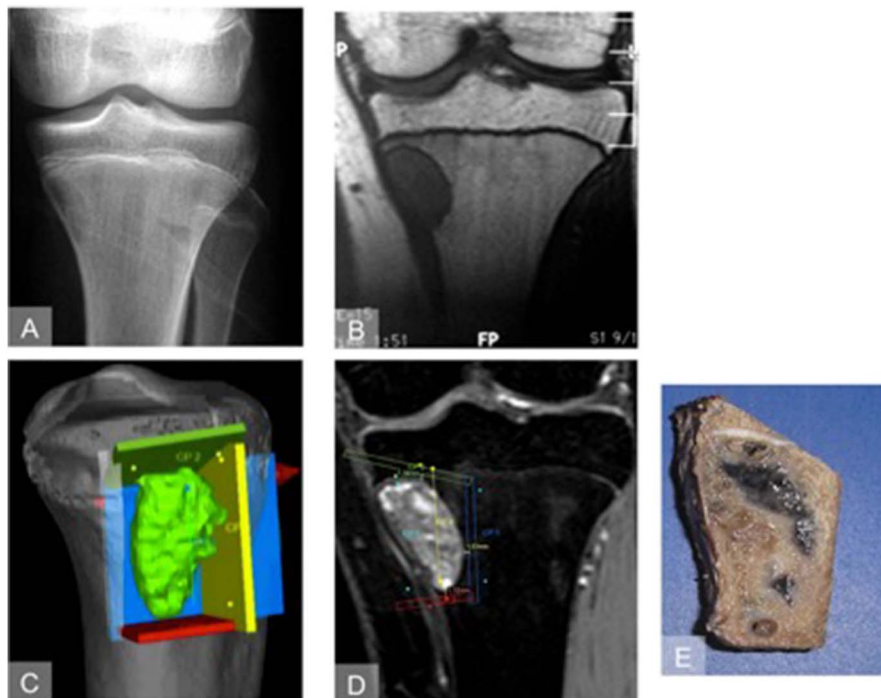


Fig. 1 A-E A 16-year-old boy had an aneurysmal bone cyst located in the proximal tibia. **(A)** Pre-operative AP radiographs of the proximal tibia show bone tumor extension. **(B)** Coronal MRI shows the extension of the tumor without compromise of the epiphysis. **(C)** This image shows the 3-D virtual surgical planning with fused MR and CT images with the preoperative cuts planned. **(D)** Coronal MRI shows the osteotomies that were planned in the 3-D model. **(E)** This is a macroscopic histologic specimen after resection showing adequate margins.

calculate odds ratios because the patients treated with navigation-guided resection had no local recurrences.

Surgical complications occurred in 7% (three of 43) of the patients treated with curettage and included proximal femur bone collapse associated with growing physal injury, reabsorption of the morsellized allograft, and a stiff knee. The complication rate for patients treated with en bloc resection assisted by navigation was 4.5% (one of 23) and was recorded as an incomplete fracture resulting from a fall from the patient's own height treated with a new osteosynthesis achieving solid consolidation after 3 months without additional complications at last followup (46 months after the second surgery). In all the other patients, no infection or hardware failure occurred and all allografts healed before 1-year followup. With the numbers available, no difference in surgical complications was seen between patients treated with curettage and those treated with en bloc resection assisted with navigation ($p = 0.93$; odds ratio, 1.87; 95% confidence interval [CI], 0.18-19). We want to highlight that with 80% power at $p < 0.05$ with the numbers of patients we had available ($n = 69$), the size effect of our research was 0.34 with an odds ratio of 4.6.

With the numbers available, there was no difference between patients treated with curettage and those treated with en bloc resection in terms of the mean 29 ± 1.4

MSTS score (28.8 ± 1.5 versus 29.3 ± 1 , mean difference 0.3; 95% CI, 0.06-1.15 points; $p = 0.1$).

Discussion

Before the 1980s, the surgical treatment of locally aggressive osseous tumors was mainly block resection (oncologic resection). This type of surgery allowed for local control of the disease, but it generated permanent functional problems resulting from the large loss of osteoarticular tissue. Later, with the advances in the diagnosis and treatment, the vast majority of these tumors began to be treated with intralesional resections (curettage) [5, 6, 11, 26]. This type of conservative resection leaves a more functional limb but at the same time has a higher likelihood of local recurrence [19-23]. Wide resection improves local control but may increase the risk of complications and morbidity [2, 17]. If it were possible to perform more precise en bloc resection with navigation, it might have the benefit of a lower risk of recurrence without compromising function. Navigation allows more precise resections and so it is tempting to use it to perform en bloc resections with more precision than can be done using freehand approaches. Resections done freehand,

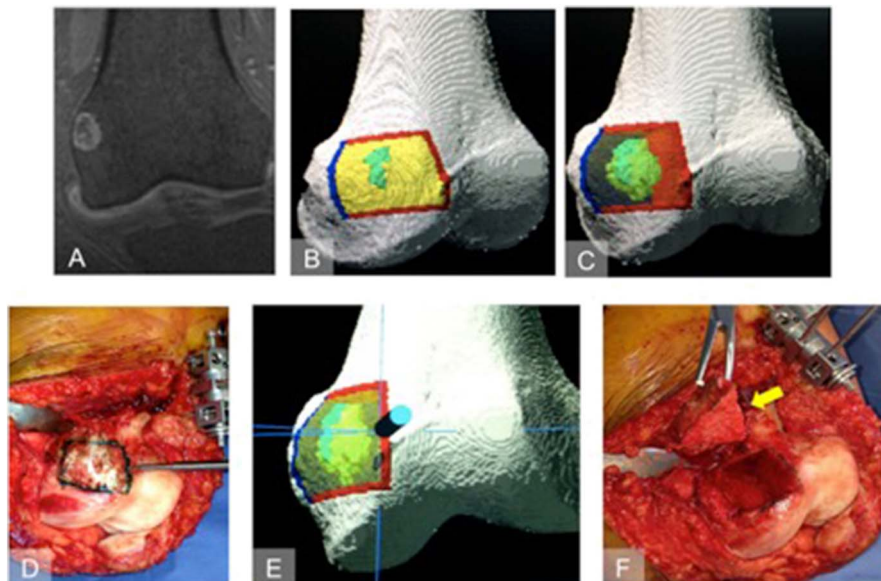


Fig. 2 A-F A 43-year-old woman presented with a low-grade chondrosarcoma of the distal femur. (A) Coronal MRI of the distal femur shows the tumor extension. (B) This image shows the 3-D virtual surgical model based on fused MR and CT images showing the lines where the osteotomies should be made. (C) This image shows the 3-D virtual surgical model showing the osteotomies in full extension. (D) An intraoperative photograph shows the mark on the bone surface according to the preoperative plan. (E) An intraoperative photograph shows how the surgeon evaluates the correct orientation of one of the osteotomies with a navigated pointer. (F) An intraoperative photograph shows the macroscopic specimen resection (yellow arrow) at the time of resection, after the osteotomies were completed.

even with the use of fluoroscopy, are challenging to perform when tumors are located very close to an articular surface [2, 9, 10, 18, 34]. However, we do not, in fact, know whether it will result in a lower likelihood of recurrence, because there are no comparative studies of which we are aware. Curettage continues to be the main treatment method for local aggressive tumors. However, in some metaphyseal or epiphyseal tumors, it might be possible to perform a resection giving a free margin without injuring the articular surface or violating the tumor capsule and with potentially a low complication rate.

Our study has certain limitations. First, we recognize the retrospective design and the lack of randomization of this study, which makes selection bias a prominent issue here. Specifically, the fact that indications differed between the procedures implied that those patients (and their tumors) were not necessarily comparable. This leaves open the possibility that the effects attributed to the treatments (or the lack of differences) could, in fact, have been a function of differences in tumor type or location. We attempted to mitigate this by defining and applying clear and consistent indications. Despite that, we recognize that the heterogeneity of the diagnoses and stages of the tumors are likely not equal in the two groups. For instance, there were more giant cell tumors of bone in the curettage group and one of the two recurrences was a giant cell tumor. Third, the

group has some inherent heterogeneity in terms of diagnosis, the amount of soft tissue resection, extent of internal fixation, and extent of resection, which could affect the incidence of failures, complications, and functional outcomes. We do not have a group of patients who had resection without navigation. An ideal study would also have a third group comprised of patients who had resection without the assistance of navigation to be able to judge the value of adding additional expense and operative time to the procedure. In addition, it is likely we were underpowered to detect a difference on our endpoints between groups. Even so, studies like ours in which there was no difference are important to publish for consideration in future systematic reviews.

With the numbers available, we saw no difference between the groups in terms of local recurrence risk. Until or unless an improvement in this or some other important endpoint is demonstrated favoring navigation-guided en bloc resection, we cannot recommend wide use of this novel technique because it adds surgical time and expense. From a local recurrence point of view, it is logical to think that resection would be associated with a lower rate of recurrence than curettage, but with the limited number of patients we had, we cannot document a difference in this regard. It appears that properly done, both approaches are reliable for treatment of benign tumors [28-30]. Wide

excision is the accepted and recommended treatment for intermediate and high-grade chondrosarcomas of long bone [14, 16, 24]. However, appropriate low-grade chondrosarcoma treatment generates uncertainty regarding the best treatment among clinicians and disagreement in the literature [8, 33]. Although low-grade chondrosarcomas rarely metastasize, they may recur if inadequate surgery is performed [24, 33]. Advocates of intralesional resection support that it preserves the adjacent bone and joint surfaces; however, it is a dilemma to determine which intra-medullary low-grade chondrosarcomas can be treated with this technique [24]. Furthermore, intralesional curettage may leave behind microscopic tumor, which is a source of recurrence [2]. Wide excisions have the advantage of low local recurrence rates, but there has been concern regarding the related complications [4]. The use of navigation for the treatment of benign and low-grade malignant bone tumors has been described in the last years [2, 15]. Gerbers et al. [15] described in a series of 43 low-grade chondrosarcoma treated with curettage with navigation assistance a local recurrence and another case of remaining residual tumor. In addition, in other series in which low-grade chondrosarcomas were treated with en bloc resection under navigation assistance, no local recurrences were observed [15]. We also believe that when indicating curettage, it does not make sense to have computer assistance, because there is no real benefit with respect to local recurrences. Although curettage and bone grafting with or without adjuvant therapy is also the accepted method for management of aneurysmal bone cyst, en bloc resection has been associated with the lowest recurrence rate, but again at the cost of reconstruction problems and of possible complications that the benign nature of aneurysmal bone cyst cannot justify [23, 25, 31]. Analogous scenarios are seen with the treatment of most locally aggressive bone tumors. Osteoblastomas may be treated with intralesional curettage effectively in many patients; however, because the recurrence rate is relatively high, when possible en bloc resection is the preferred method for definitive management [22]. Chondroblastoma and chondromyxoid fibroma may also be treated with curettage and bone grafting, but wide resection or en bloc excision has been reported to be the best method to avoid recurrence [20, 28, 35]. For giant cell tumor of bone, the accepted approach of treatment is intralesional curettage with or without adjuvant therapy, leaving en bloc resection as an alternative in recalcitrant or recurrent cases and aggressive Stage 3 tumors [5, 19, 30].

With regard to the nononcologic complications described in our series, we observed three complications in the patients who underwent curettage (growing physal injury, joint stiffness, and graft reabsorption). In the group of patients treated with en bloc resection, only one complication was reported. In general, with intralesional curettage for aggressive benign tumors, the principal goal is

to extend the zone of curettage 1 cm beyond the lesion in all directions to be sure that a complete lesion is achieved. This treatment is less precise than en bloc resection guided by navigation and, in particular, for metaphyseal tumor in skeletally immature children, this could increase the risk of physal injury causing growth disturbance. Previous publications demonstrate that patients treated with curettage had more local recurrences but fewer orthopaedic complications compared with those treated with extensive resections [15, 17]. We suggest that in certain cases in which navigation-guided resections can be performed on metaphyseal tumors, we can preserve the joint with extralesional resection [2, 4]. This way we could lower the index of local recurrences without increasing the index of orthopaedic complications.

Both groups analyzed had excellent postoperative function without significant differences in the MSTS functional score. There is evidence that en bloc resections generate worse functional results than in patients treated with curettage [17]. Possibly these good functional results observed in both groups are a consequence of the two techniques of tumor resection used, are conservative, and preserve the adjacent joint.

In this small comparative series, navigation-assisted resection techniques allowed conservative en bloc resection of locally aggressive primary bone tumors with no local recurrence. Nevertheless, with the numbers available, we saw no difference between the groups in terms of local recurrence risk, complications, or function. We believe that in selected situations, the use of navigation may be useful compared with curettage or resection without navigation. However, until or unless studies demonstrate an advantage to navigation-guided en bloc resection, we cannot recommend wide use of this novel technique because it adds surgical time and expense.

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