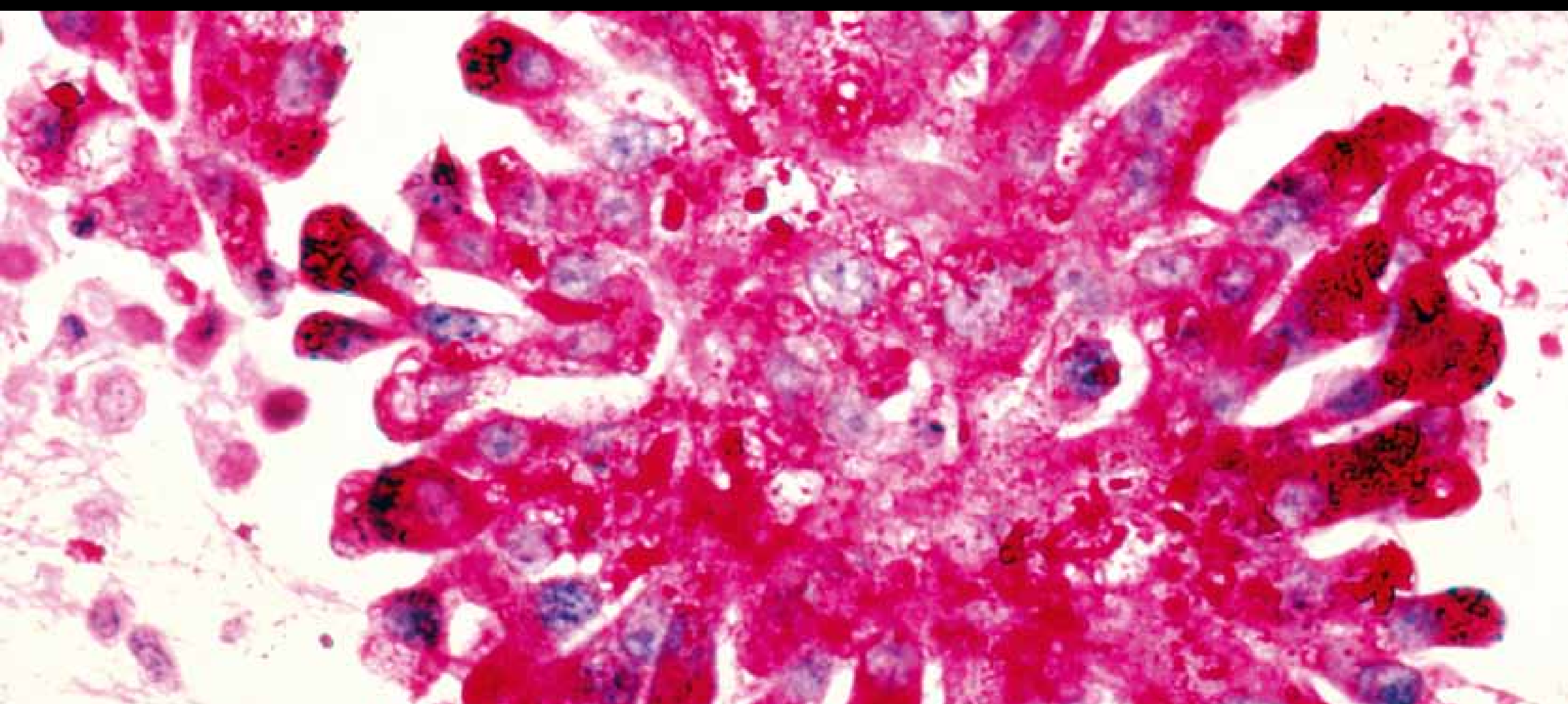
Biological Reconstruction for Sarcoma

Guest Editors: Andreas Leithner, Per-Ulf Tunn, and Pietro Ruggieri



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Editorial Board

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Editorial

Biological Reconstruction for Sarcoma

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Particularly in children and young adults, bone allografts and autografts seem to be a perfect and long-lasting alternative to the use of prostheses after bone resection due to bone or soft tissue sarcomas. However, several topics like osteoarticular massive allografts are still discussed controversially. Might allograft-prosthetic composites reconstructions serve as stable and durable alternatives? Questions like this as well as the long-term results have not been answered sufficiently yet.

In a review, L. A. Holzer and A. Leithner focus on the historical highlights, the present role, and possible future options for biological extremity reconstruction. While hand transplantation is already an option, above-elbow transplantation or limb regeneration might become a topic in the future.

K. Rabitsch et al. report their experience with intercalary reconstructions of the lower limb using a vascularized fibula and an allograft in 12 patients. Although the event-free survival was only 51% at a two-year follow-up full weight bearing was achieved in all cases with all autografts still in place. The authors conclude that this method is a stable and durable reconstruction technique.

M. Niethard et al. illustrate their technique using bilateral vascularized fibular grafts for reconstruction of metadiaphyseal defects of the femur and tibia in 11 patients. Despite a similar complication rate as reported by K. Rabitsch et al., all of the complications were manageable without the loss of the biological reconstruction. The authors also report on the increased risk of fixation failure after radiotherapy.

L. E. Ritacco et al. describe the workflow for structural allograft selection of their renowned three-dimensional virtual bone bank system. Preoperative planning includes a 3D CT-derived bone model to define the exact size and shape in comparison to the planned resection.

F. Traub et al. provide a retrospective analysis of their experience in biological reconstruction following the resection of pelvic tumors. Twenty-seven patients were evaluated for oncological as well as clinical and functional outcome. Hip transposition was used in 16 patients, and autologous nonvascularized fibular grafts were used in five patients. Despite the difficult situation after pelvic resection, MSTS score (mean 16.5) was good or excellent in most of the patients.

The second paper by K. Rabitsch et al. reports on the technique of distal radius osteoarticular allografts, which were used in five patients. With all allografts still in place at a mean follow-up of 32 months the functional results were good or excellent (DASH 8, Mayo wrist 84).

L. A. Aponte-Tinao et al. describe their high level of experience in biological upper extremity reconstruction in 70 patients, including 38 osteoarticular allografts, 24 allograft-prosthetic composites, and eight intercalary allografts. After a mean follow-up of 5 years the authors conclude that intercalary humeral allografts had the best outcome, while the other techniques led to articular deterioration, fracture, and allograft resorption with the need for revision surgeries in 16 patients.

G. L. Farfalli et al. compare 50 nonconstrained knee allograft-prosthetic composites with 36 matched constrained ones. In both groups the authors observed more allograft fractures when the prosthetic stem did not bypass the host-donor osteotomy. However, both groups had good or excellent MSTS functional scores.

These papers represent an exciting and insightful snapshot of the current techniques of biological reconstruction after sarcoma resection. Some sophisticated methods, existing challenges, and possible future topics are highlighted in this special issue, which may inspire the reader and provide a stimulus for the present discussion on limb salvage techniques.

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Andreas Leithner
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Pietro Ruggieri

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Review Article

Biological Extremity Reconstruction after Sarcoma Resection: Past, Present, and Future

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In sarcoma surgery besides a wide local resection, limb salvage became more and more important. Reconstruction of bone and soft tissue defects after sarcoma resection poses a major challenge for surgeons. Nowadays a broad range of reconstructive methods exist to deal with bony defects. Among these are prostheses, bone autografts, or bone allografts. Furthermore a variety of plastic reconstructive techniques exist that allow soft tissue reconstruction or coverage after sarcoma resection. Here we discuss the historical highlights, the present role, and possible future options for biological reconstruction.

1. Introduction

Bone and soft tissue defects after sarcoma resection pose a major challenge for surgeons [1]. While in animal life the regeneration of whole extremities is possible in some species such as starfish [2] or salamanders (Figure 1) [3, 4], in humans surgeons are dependent on advancement and innovations in biological and mechanical reconstruction. In sarcoma surgery besides a wide local resection, limb salvage became more and more important [5]. Mechanical stability and strength and the possibility of reattachment of tendons and ligaments are necessary to achieve motion and good function in reconstructed limbs. Various methods and techniques have been developed and optimized that allow maintaining the function of the extremity. To achieve this, bony defects can now be reconstructed with prostheses, bone autografts, or bone allografts. Furthermore a variety of plastic reconstructive techniques exist that allow soft tissue reconstruction or coverage. Additionally different factors are studied that might promote graft incorporation and bone repair. The aim of this review is to give an overview of historical highlights, the present role of bone grafts, and possible future options for biological reconstruction.

2. Past

The first evidence of human bone allografts in medical literature can be found in a paper published by MacEwen in 1887 [6]. The outcome of this method used in four nononcological cases was published in *Annals of Surgery* in 1909 [7]. One of the first cases which was treated in 1874 was a three-year-old boy with an osteomyelitis of the right humerus. The necrotic bone was removed surgically resulting in a deformed and useless humerus after a fifteen-month of followup. The boy's parents wanted MacEwan to have the boy's arm amputated. MacEwen however performed a bone allograft transplantation to reconstruct the humerus in three stages over a period of five months.

Erich Lexer, a German surgeon, treated septic arthritis and osteomyelitis by the use of long-bone transplants [8]. Lexer used bone allografts from fresh amputated limbs. A success rate of 50% was reported regarding the outcome of normal limb function following half-joint and whole joint osteoarticular transplantations [9].

Often there had been a shortage of bone allografts as grafts were obtained from amputees in most cases [10]. Furthermore there was a lack in the capacities for long-term

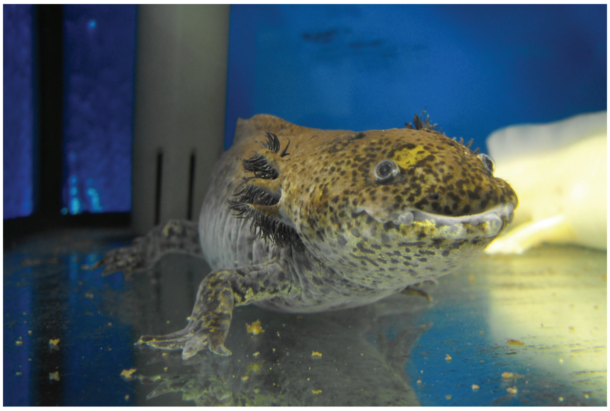


Figure 1: Axolotl or Mexican salamander (*Ambystoma mexicanum*), one of the few species that maintains the ability to regenerate its tail or limbs throughout its life. Karol Głąb/Wikipedia Creative Commons.

storage and preservation [10]. Therefore autografts were preferred in many surgical situations [10]. A few decades later, two events revolutionized the situations for the use of bone allografts: on one hand, the establishment of bone or tissue banks. The first one was the Navy Tissue Bank in Bethesda, Maryland, which was established in 1949 and provided the optimal conditions for storing bone or other tissue and preserve it for a later use [11]. The second event was the invention of the lyophilization (freeze-drying) of bone [12]. As a result the management of bone allografts became more simple. Subsequently the use of bone allograft transplantation gained more and more popularity.

Parrish was the first who used the long-bone transplantation techniques described by Lexer for limb salvage in the proximal femur and distal femur for primary high-grade malignancies in bone [13]. This work was continued by other surgeons including Enneking and Mankin. Enneking et al. showed that a good incorporation of allografts is difficult to achieve due to factors such as infection or fatigue fractures [14]. Mankin et al. showed that about 70% of patients treated with long-bone allografts achieved good clinical results [15]. It was further demonstrated that incorporation of allografts might be negatively influenced by the use of radiation or chemotherapy [16, 17].

In the late 1980s, Capanna et al. introduced an interesting concept of hybrid reconstruction combining allograft shell and free vascularized fibula for large defects after tumor resection. Their hybrid graft offers initial stability and the option of reattachment of tendon and ligaments given by the allograft as well as good biological incorporation due to the vascularized fibula. Additionally soft tissue coverage can be achieved in cases of composite flaps [18].

The first case of limb salvage by the use of a homologous limb transplant can be found in the *legenda aurea* [19]. According to the legend the twin saints Cosmas and Damian performed an amputation in the deacon Justinian due to "cancer" [19]. The importance of this legend, however, results from the subsequent treatment. The leg was reconstructed with a homologous limb transplant. The donor was an Ethiopian who had died some hours before. The legend also provides the outcome of the deacon who was able to walk again and glorify his doctors.

Carl Nicoladoni, an Austrian surgeon, made remarkable contributions to surgery. Among those were the first thumb reconstructions. In 1897, he published three cases of thumb reconstruction using autografts from the chest. Furthermore he proposed the concept of toe-to-thumb transfer for thumb reconstruction in the same paper [20].

The first hand transplantation has been performed in 1964 in Ecuador however unsuccessfully resulting in an amputation. As immunological understanding advanced, the first successful hand transplantation has been performed in the late 1990s. Since then about 70 hand transplantations have been performed worldwide [21].

3. Present

3.1. Bone Banks. The advancements of bone banks are obvious. Meanwhile well-organized bone or tissue banks exist worldwide that provide bone allografts of different size, shape, and quantity to suit the need of surgical reconstruction [22]. This is furthermore reflected by their use in clinical practice. Procedures with allograft increased 14-fold between 1985 and 1996 in the United States of America and account for approximately one third of bone grafts today [23]. Allografts are the most commonly used bone substitutes in Europe [24]. However with the increasing number of bone allografts used there is also an increased demand for supply. Living donors, multiorgan donors, or postmortem donors are the source for bone allografts [24]. Recently a novel concept was introduced. Allografts from a bone bank are scanned using CT and reconstructed three-dimensionally. Preoperatively the most appropriate graft can be selected that matches the host's anatomy and surgical defect best [25].

3.2. Types of Allografts. Various types of bone allografts ranging from small cancellous bone allografts to large vascularized bone grafts are used to reconstruct bony defects [24]. These include the following ones.

Corticocancellous bone allografts are prepared from femoral heads or from long bones of the extremities. These grafts have osteoconductive property only and provide some mechanical support depending on their preparation. Corticocancellous bone allografts are widely used [24].

Demineralized bone matrix is the only bone allograft with osteoinductive capacity. These allografts contain bone morphogenetic proteins and collagen type I which are needed for the osteoinduction to occur. Various types of such allografts are available among them calcium sulphate or porcine collagen enriched demineralized bone matrices. Their use is becoming increasingly popular especially in the treatment of delayed fracture healing or nonunions [24].

Massive structural bone allografts are primarily used for limb salvage procedures in musculoskeletal oncology and pose an option for the anatomical reconstruction of large skeletal defects supporting concomitant surgical interventions such as prosthesis, osteosynthesis, or vascularized bone graft. Among the forms of structural bone allografts there are osteochondral allografts, intercalary allografts, and segmental allografts with arthrodesis or prosthesis or cortical struts. Furthermore osteoarticular allografts are available, for example, for the reconstruction after resection of the proximal humerus or of the distal radius for tumors [26, 27].

3.3. Complications. The most common and devastating complications in bone allograft use are nonunions with an incidence of about 10% to 25% [28, 29], fractures with an incidence of up 20% [30], and infections. High infection rates can be seen in allograft use ranging from about 20% to 70% [31]. The avitality of these grafts is believed as a cause for the high infection rates. High rates of infection are seen in areas that are poorly vascularized such as the pelvis in up to half of the recipients, whereas infection rates in extremities are much lower (5%) [29]. In general, the pelvic region is critical with about half of the reconstructions resulting in failure [29]. Other major complications include degeneration in osteoarticular grafts and epiphyseal slip in younger patients [29].

3.4. Safety Issues. An important issue in bone allograft transplantation is safety concerning disease transmission. Just three years after the first reported cases of AIDS the first HIV-1 transmission in bone occurred in 1984 [32]. Furthermore a few cases of hepatitis C virus infections were reported resulting from the use of bone transplantations [33, 34]. Therefore the safety of bone transplantation gained more attention, and methods of screening donors changed and improved over time. Nowadays more sensitive serologic tests are available for HIV antibodies. HIV antigens and polymerase chain reaction (PCR) are available for screening. Additionally donors' history is checked for risk factors. Furthermore it had been shown that the removal of blood and bone marrow is beneficial and reduces risk of disease transmission [35]. The estimated risk to obtain an allograft from an unrecognized HIV-infected donor is one in 1.6 millions [36].

Another topic that is under discussion currently is the antigenicity of donor material. In general, bone allografts show a low antigenic nature. This fact can be attributed mainly to the preparation and preservation of the allografts. Freeze-dried cortical bone allografts failed to sensitize recipients [37]. Still on the long term, collagen and matrix of allografts can lead to an immune response. Bone graft immunogenicity is mainly attributed to human lymphocyte antigens (HLA) that are controlled by the major histocompatibility complex (MHC) in humans. These antigens are expressed on the cell surface and represent the primary stimulus for transplant tissue rejection when HLA mismatches occur between donors and recipients. Detection of donor-specific anti-HLA antibody formation in a patient receiving bone allografts is an important measure of the clinical immunogenicity of the respective graft material [38]. A chronic type of rejection or an immunologic state of tolerance can occur in bone allograft recipients. Immunologic reaction between host and allograft has an effect on graft incorporation. New bone formation might be reduced and revascularization is delayed or even inhibited [39].

3.5. Types of Autografts. Autogenous bone grafts are used commonly to reconstruct bone voids or to induce bone healing. Cancellous autografts provide good osteoconductive, osteoinductive, and osteogenic characteristics, whereas cortical autografts provide osteoconductive features mainly. The most popular site for autogenous bone grafting is the iliac crest. Alternative sites include the proximal tibia, the distal radius, the distal tibia, and the greater trochanter [40]. Various types of autografts are available as follows.

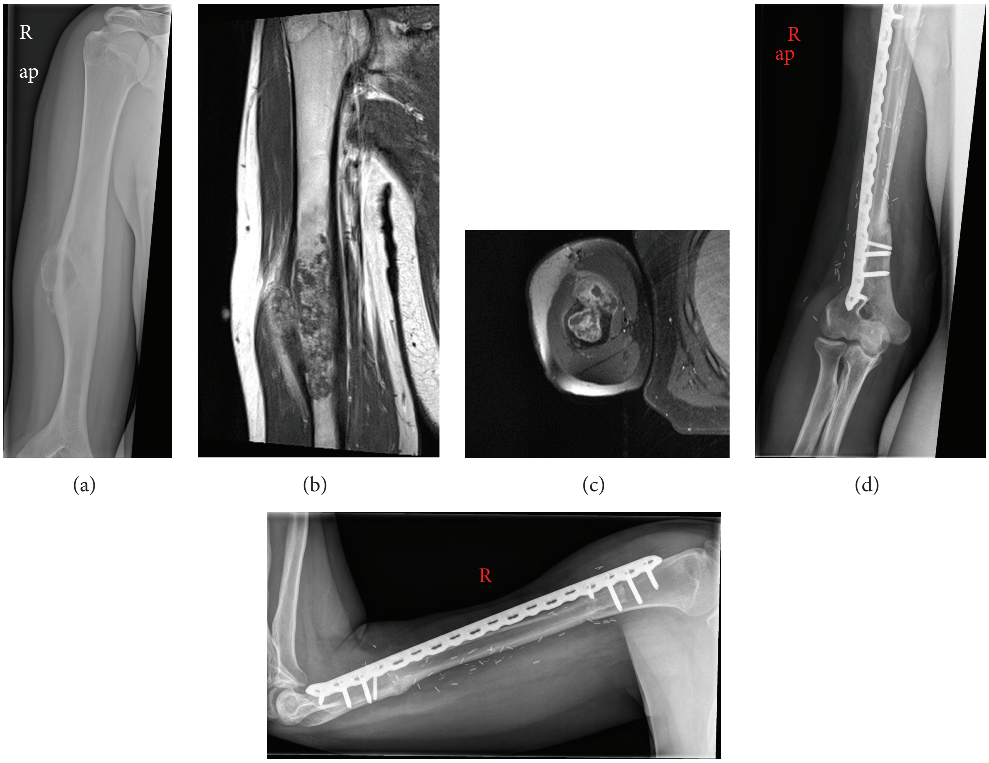
Cortical bone grafts are best suited for structural defects in which immediate mechanical stability is required for healing [40].

Cancellous bone grafts provide a large surface area leading to a high rate of remodeling and incorporation. Their mechanical strength is limited. Therefore cancellous grafts pose an excellent option for arthrodesis and treatment of nonunions [40].

Corticocancellous bone grafts offer the advantages of both cortical and cancellous bone: an osteoconductive, osteoinductive, and osteogenic properties and immediate structural strength [40].

Another option is vascularized bone grafts. These promise the best incorporation and healing due to vascular pedicles. Their use is indicated for large bone defects (>12 cm). The grafts have high osteogenic potential as more than 90% of residual osteocytes survive [40]. Pedicled or free vascularized fibula grafts are among the most commonly used grafts in orthopaedic oncology (Figure 2). They are used in various sites such as humerus, ulna, or radius. Furthermore these grafts pose an option for growth plate reconstruction [29].

3.6. Complications. Nonunions, fractures, and infections are major complications that are seen frequently in bone autograft transplantations. Union rates are seen in 60% to 90% of vascularized and nonvascularized autografts. In nonvascularized grafts union rate is the lowest with about two thirds. Reconstructions in the upper limbs have significantly higher union rates (90%) compared to lower limbs (70%). Increased union rates can be achieved by the use of additional cancellous bone grafting [29]. An average fracture rate of about 7% is reported in bone autografts use. Fracture rate of



(a) (b) (c) (d)

(e)

Figure 2: Chondrosarcoma G2 at the proximal humerus shown in the X-ray (a) and MRI ((b), (c)). Nine-month postoperative X-rays showing the reconstruction after wide resection with an autologous free vascularized fibula graft ((d), (e)).

transplanted fibulae is high with up to 50%. In cases of fibula graft use solely without any allograft, fracture rates are even higher. In the lower extremity rates are lower and seen in up to a fifth of transplant recipients. Generally, longer grafts are more likely to fracture than shorter grafts [29].

Among the minor complications of bone autografts are donor site pain, superficial nerve injury, hematoma formation, seroma formation, and infection. Early donor site pain occurs quite frequently and can be noticed in up to one third of the patients. Furthermore deep hematomas and infections are reported in about 3%. Among the rare major complications are incisional hernias, sacroiliac joint injury, ureteral injury, gait derangement, and donor site fractures [40].

3.7. Plastic Reconstructive Surgery. Soft tissue coverage and reconstruction play an important role in sarcoma surgery as resection often leads to massive soft tissue defects. Standard procedures that are available include skin grafting for superficial defect closure, whereas Vacuum-assisted closure therapy poses an option for temporary defect closure. Since the first microvascular free flaps that were performed in the early 1970s, plastic reconstructive surgery experienced an enormous development. A wide variety of pedicled or free vascularized flaps are available for reconstruction in the whole musculoskeletal system. These include the lateral arm flap, scapula/parascapular flap, radial forearm flap, anterolateral thigh flap, free fibula flap, latissimus dorsi flap, rectus abdominis flap, gracilis flap, free filet flap, the medial femoral condyle periosteal bone flap, or various perforator flaps [41, 42].

4. Future

Availability and safety are barriers to the wide use of bone allograft transplantation. However these issues are managed by commercial and noncommercial bone and tissue banks nowadays. So the role of bone allograft transplantation in clinical practice and their outcome will shift into the focus. Minor results and poor function sometimes pose limitations, especially in the use of bone allografts. Furthermore long-term results of transplanted bone allografts show infections, fractures, and nonunions in about 20% of recipients [43]. In general, osteoinduction of allograft is low. Improvement of the incorporation by increasing vascularization, bone remodeling, or osseointegration of bone allograft seems to be one of the major tasks in the future. Various osteoinductive substances have been investigated for bone regeneration [44] that could also improve the incorporation of bone allografts in host tissue.

Several methods (e.g., growth factors, gene therapy) have been studied that might enhance bone regeneration or repair. Their use might be an interesting option for degenerative or traumatic bone defects. However the use of such methods might not be indicated in oncologic patients as they are seen as potential regulators of cancer cell growth and metastasis [45, 46].

Limb lengthening introduced by Ilizarov was a major advancement in orthopaedic practice [47]. Novel techniques were derived using motorized intramedullary nails or magnetically controlled growing rods for osteodistraction. Such nails are available for lengthening of the femur or tibia or correction of spine deformities [48, 49]. Further advancement of such techniques might offer interesting options in the future.

As hand transplantation becomes more frequent, larger transplantations of the upper extremity such as above-elbow arm transplantations are becoming a topic. From the technical point of view such transplantations might be easier to perform as there is just one bone (humerus) and larger vessel compared to further distal sites. However nerve regeneration in larger nerves still poses problems as their structure with multiple fascicles is more complex than that at more peripheral sites [50]. Advancements in this field might revolutionize the management of these procedures [51].

As indicated in the introduction salamanders are one of the rare species that keep the potential to regenerate limbs in case of loss throughout their life by nature. So these animals pose a model to study the process of regeneration. A central role in the regenerative capacity has been attributed to fibroblasts that seem to be primarily responsible for the regeneration of limbs in salamanders. Fibroblasts are also present in human wound healing that lead to a scar formation of injured tissue. Therefore much research is performed to study the signals that allow the tissue regeneration instead of the tissue repair. Further understanding of these physiological processes might pose interesting options for further translational research in humans [52].

Concluding we can say that much advancement has been made in the last century so that today there are many highly potential options for good functional biological reconstruction after sarcoma resection that allow patients to regain a high quality of life.

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Clinical Study

Intercalary Reconstructions with Vascularised Fibula and Allograft after Tumour Resection in the Lower Limb

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Reconstruction with massive bone allograft and autologous vascularised fibula combines the structural strength of the allograft and the advantages of fibula's intrinsic blood supply. We retrospectively analysed the outcome of twelve patients (4 male, 8 female) who received reconstruction with massive bone allograft and autologous vascularised fibula after tumour resection in lower limb. Mean age was 17.8 years (range 11–31 years), with following primaries: Ewing's sarcoma ($n = 6$), osteosarcoma ($n = 4$), liposarcoma grade 2 ($n = 1$), and adamantinoma ($n = 1$). Mean followup was 38.7 months (median 25.7 months; range 2–88 months). Seven tumours were located in the femur and five in the tibia. The mean length of bone defect was 18.7 cm (range 15–25 cm). None of the grafts had to be removed, but there occurred four fractures, four nonunions, and two infections. Two patients developed donor side complication, in form of flexion deformity of the big toe. The event-free survival rate was 51% at two-year followup and 39% at three- and five-year followup. As the complications were manageable, and full weight bearing was achieved in all cases, we consider the combination of massive bone allograft and autologous vascularised fibula a stable and durable reconstruction method of the diaphysis of the lower limbs.

1. Introduction

Limb salvage has become the primary method of bone tumour treatment due to improved therapeutic options, combining polychemotherapy, wide resection, and case-based additional radiation. This led to improved prognosis, with 5-year survival rates up to 85% and 10-year survival rates up to 75% for these patients [1–7]. Advances in diagnostic imaging techniques permit an accurate preoperative determination of the tumour extent [8]. If this tumour extension allows preservation of adjacent joints and intercalary resection, the functional outcome is expected to be superior in intercalary reconstructions, since no joint replacement—neither prosthetic nor allograft—could function better than an intact native joint [9–13]. Intercalary defects can be reconstructed by using massive bone allografts [8, 14–23], vascularised autologous fibula grafts [24–28], the combination of both [27, 29–39], nonvascularised fibula grafts [40, 41], and intercalary prostheses [42–46].

Reconstruction with a massive bone allograft and an autologous vascularised fibula combines the structural strength of the allograft and the advantages of fibula's intrinsic blood supply [30]. To assess the postoperative outcome in our patients, we evaluated durability and complication rates.

2. Material and Methods

We identified twelve patients (4 male, 8 female) who received an autologous vascularised fibula for reconstruction of seven femoral and five tibial defects at the Department of Orthopaedic Surgery, Graz Austria. Patients' medical records were scanned for the following data: age at operation, length of followup, pathology and localisation of the tumour, additive treatment with chemotherapy or radiation, length of bone defect, fixation device, operation time, time to partial weight bearing and time to full weight bearing, complications due to the allograft (infection, fractures, and nonunion) as well as complications due to the tumour (local recurrence, distant metastases, and death of disease), revision procedures, and failure of the reconstruction, defined as removal of the construct for any reason.

Descriptive statistics included means and proportions depending on the type of data. The survival rates of patients as well as of reconstruction were estimated using the Kaplan-Meier method. Log-rank test was used to compare survival curves. Pearson's chi-square test and two-tailed Fisher's exact test were used to analyze correlations.

3. Results

3.1. Patients and Reconstructions. Twelve patients received an autologous vascularised fibula combined with a massive allograft to reconstruct a segmental defect after tumour resection with a mean followup of 38.7 months (median 25.7; range 2–88 months). There were eight female and four male patients with a mean age of 17.8 years (median 14.3 years; range 11–31 years) at time of reconstruction. Seven tumours were located in the femur and five in the tibia. Primary diagnoses included six Ewing's sarcoma, four osteosarcoma, one liposarcoma grade 2 (grading according to the American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC) staging system [47]), and one adamantinoma. Four patients underwent wide resection only; eight patients received additional multimodal treatment including chemotherapy in six patients, chemotherapy and radiation in one patient, and additional radiation only in one patient.

The mean length of bone defect was 18.7 centimetres (median 18.8 cm; range 15–25 cm). The graft-host junctions were augmented with autologous cancellous bone grafts at primary surgery in one patient, while eleven patients had no additional bone grafting. On average the surgical procedure lasted 232 minutes (median 115 minutes; range 86–723 minutes).

3.2. Oncologic Results. At latest followup nine patients were alive without evidence of disease, and none of the twelve patients presented local recurrence. Three patients developed distant metastases in the lung at an average of 10 months after primary surgery—two with Ewing's sarcoma and one with osteosarcoma—and, despite metastasectomy and chemotherapy, died of disease.

The overall survival rate for all patients was 80% after two years and 70% after three and five years (Figure 1).

3.3. Graft Survival and Complications. All patients achieved full weight bearing without support of braces, crutches, or a cane, and none of the grafts had to be removed. Partial weight bearing was allowed at two months after operation on average (median 1.7 months; range 1–4.6 months) and full weight bearing at a mean of 9.4 months after operation (median 7.9 months; range 3.7–27.6 months). The longest period of load relief was 28 months in a patient with nonunion and a fracture.

Six patients had 14 additional surgical interventions due to complications at 10.8 months (mean) after primary surgery on average. The event-free survival rate (Figure 2), with event

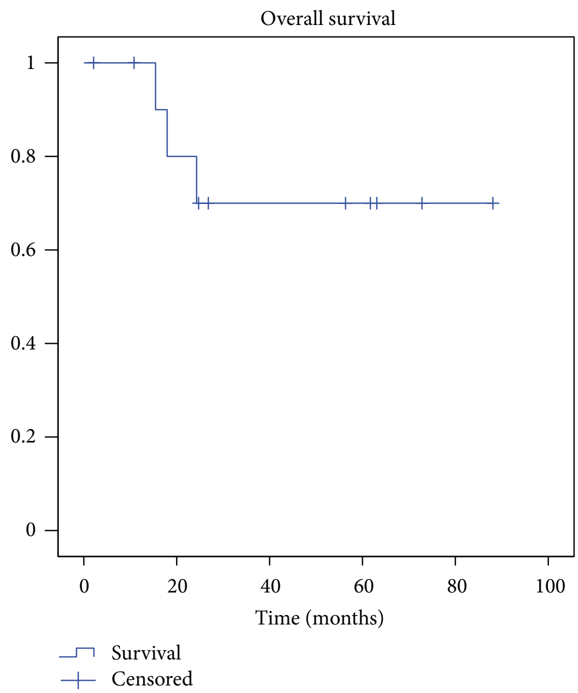

Figure 1: Kaplan-Maier curve for patients' overall survival rate with death of disease as endpoint.

defined as any complication requiring an additional surgical intervention, was 64% after two years and 39% after three and five years.

Seven patients had thirteen local complications at 11 months after primary surgery on average. Four patients, all with femoral reconstructions, sustained graft fracture. Two of them had an adequate trauma: one patient fell because one of his crutches broke in early mobilisation period, and the second patient fell off her bicycle before graft host junctions had totally healed. In the other two patients nonunion or delayed union of the proximal graft-host junction led to wearing of the plate and subsequent plate and graft fracture (Figure 3). All four fractures were successfully treated with open reduction, replacement of internal fixation, and perifractural augmentation with autologous iliac cancellous bone grafts. Four of seven femoral reconstructions fractured, while no tibial reconstruction sustained a fracture ($P = 0.038$). No tendency for higher risk for fracture could be seen anent length of bone defect, time to partial weight bearing, or time to full weight bearing in this analysis (Pearson's chi-square test: $P = 0.544$; $P = 0.819$; $P = 0.477$).

Four patients presented nonunion, two leading to subsequent fracture, as mentioned above. One case of nonunion was successfully treated with ESWT (Extracorporeal Shock Wave Therapy) and one healed without further intervention 18 months after primary surgery (Figure 4).

Wound healing disorders occurred in two patients, both in tibial reconstructions. They both were treated with debridement, vacuum-assisted wound closure (necessary in one patient) and consecutive wound coverage. One of the patients with wound healing disorder developed deep infection which was successfully managed with removal of

Table 1: Comparison of intercalary allograft reconstructions in the lower limb.

Authors	Patients	Fracture	Infection	Nonunion	Grafts failed	Graft survival rate at 5 y/10 y [%]
Zimel et al. [15]	38	1 (2.6%)	7 (18.4%)	6 (15.8%)	15 (39.5%)	70/53
Muscolo et al. [8]	13	3 (23%)	1 (7.8%)	2 (15.4%)	4 (30.8%)	69.2% at 5.25 years
Muscolo et al. [16]	59	4	3 (5%)	9 (15.3%)	9 (15.3%)	79/—
Deijkers et al. [18]	35	12 (34.3%)	3 (8.6%)	10 (28.6%)	6 (17%)	—/79
Chen et al. [14]	13	2 (15.4%)	0	6 (46.2%)	1 (7.7%)	92.3% at 5.5 years

Percentages in brackets.

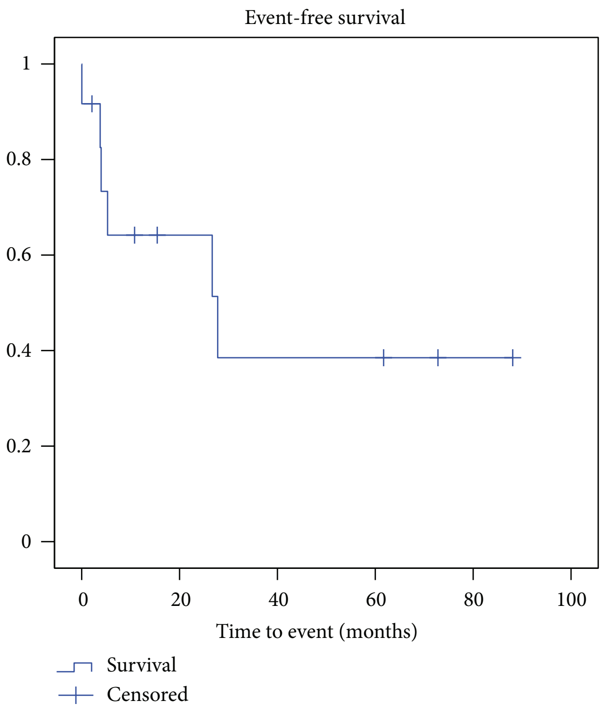

Figure 2: Kaplan-Maier curve for event-free survival, with event defined as any complication requiring additive surgical intervention.

internal device and systemic antibiotics. Another patient also sustained local infection but died due to progressive disease before treatment of infection could be started. Haematoma requiring surgical intervention occurred in one patient.

A trend could be identified that tibial reconstructions favours wound healing disorders, since all occurred in tibial reconstructions ($P = 0.067$).

Two patients had donor side complications, both developed flexion deformity of the big toe.

4. Discussion

Due to more accurate imagine techniques and improved multimodal treatment concepts intercalary resection without compromising safe wide resection margins is possible even if only little juxtaarticular bone is tumour free. In children and adolescent patients preservation of the epiphyseal segment affords further growth. If only a part of the epiphysis is preserved, the risk of varus or valgus deformities rises [9–13].

One popular solution for reconstruction of intercalary defects secondary to tumour resection is the use of massive allografts. Intercalary allografts have a good reputation as better results can be achieved compared to other allograft reconstructions, like osteoarticular allografts or composite allograft reconstructions [9, 17, 48–52]. If there is access to a bone bank, allografts can be obtained—in different sizes and lengths. Massive allografts preserve bone stock, allow adequate attachment of salvaged tendons, and provide initial mechanical strength [14, 16, 17]. After healing, the graft may be progressively incorporated by the host, and it has been demonstrated that intercalary allografts can survive for decades. Ten-year graft survival rates of approximately 80% had been reported (range 53% to 84%) [8, 14–16, 18]. Long-term results of several study groups report a steady state without deterioration of the graft if the allograft endures the first three years, suggesting that it will thereafter remain functional for the duration of patient's life [9, 11, 12, 16, 18, 22, 49–51, 53, 54]. Good functional long-term results are achieved with intercalary allografts, but associated complications as nonunion, fracture, and infection are frequent (Table 1). Up to 70% require additional surgical interventions due to complications, and it has been seen that occurrence of one event of the triad "infection, fracture, and nonunion" compromises the final outcome [17, 48–51, 53, 55, 56]. These problems are the consequence of the graft's avascular status and the incomplete revascularisation and incorporation by the host [9, 30, 32, 36, 57, 58].

To reduce these complications, and improve the outcome, the massive allograft can be combined with an autologous vascularised fibula. The allograft supplies initial mechanical strength, and the fibula provides well-perfused bone and the capability of osteogenesis [9, 13, 30–32, 34, 35]. During the first years the allograft supports the narrow and weak fibula mechanically, but it does not totally shield the fibula from weight bearing. This exposure to weight bearing induces a progressive concentric fibular hypertrophy. Due to this hypertrophy the fibula can compensate weakening of the graft by creeping substitution, the process of vascularisation, resorption and replacement of the graft's scaffolding with new host bone, what leads theoretically to a lower fracture risk [9, 20, 31, 59]. We observed four fractures in twelve patients. Two of them had an adequate trauma causing the fracture,

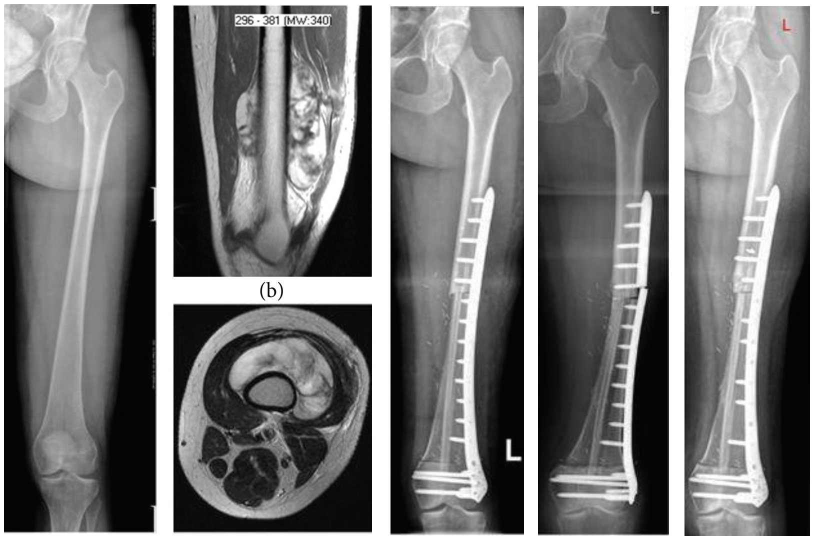

Figure 3: X-ray and MRI imaging in a 31-year-old female patient with Liposarcoma grade 2 of the left femur: before operation (a)-(b), one week after operation (c), plate breakage and fracture 15 months after operation (d), and one month after revision (e).

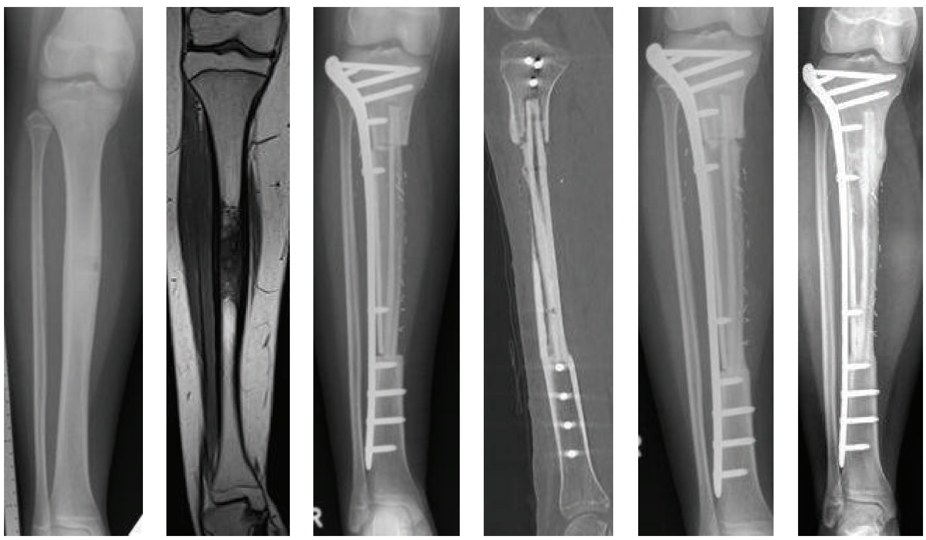

Figure 4: X-ray, CT and MRI imaging in a 14-year-old female patient with Ewing's sarcoma of the right tibia: before operation (a)-(b); three months after operation (c), seven months after operation: no consolidation at the proximal graft host junction (d)-(e); 21 months after operation: fully integrated fibula; and allograft (f).

both in a relatively early mobilisation period, when neither union nor hypertrophy of the fibula was completed. The other two fractures happened subsequently to nonunion, plate wearing, and subsequent plate breakage. The well-perfused fibula is advantageous in the treatment of fractures: all four fractured grafts healed similar to normal bone fractures after open reduction, replacement of internal fixation, and autologous bone grafting. Similar observations concerning fracture healing in combined grafts—unless the anastomosis fails—are reported in the literature (Table 2) [32, 34, 35, 55].

The osteogenic potential of the vascularised fibula does not only improve fracture healing but allows a more rapid and reliable fusion between graft and host, reducing the risk of nonunion. A review of literature reveals lower nonunion rates for combined allograft and vascularised fibula reconstructions (up to 31%) in comparison to allograft alone (nonunion in up to 46%) (Tables 1 and 2) [11, 12, 14, 20, 22, 23, 27, 30–38, 54]. Among our twelve patients, four developed nonunion. One of them has to be seen as a delayed union, since the junction healed without further treatment after 18 months. In one patient, the nonunion was successfully treated with ESWT. Reports about treatment of nonunions in any type of allograft reconstructions with ESWT were not found in the literature, but in this

Table 2: Comparison of intercalary reconstructions with massive allograft and vascularised fibula in the lower limb.

Author	Patients	Complications donor site	Infection	Fracture	Nonunion	Failure	Reconstruction survival
Presented results	12	2 in 2 pat	2 (16.6%)	4 (33.3%)	4 (33.3%)	0	100% at ~3.5 years
Capanna et al. [30]	90	n.s	7 (7.5%)	12 (13.3%)	8 (8.8%)	6 (6.5%)	93.3% at ~9 years
Li et al. [32]	11	10 in 5 pat	0	0	1 (9%)	1 (9%)	90.9% at ~2.8 years
Jager et al. [33]	7	7 in 6 pat	1 (14.28%)	1 (14.28%)	2 (28.5%)	0	100% at ~3.7 years
Li et al. [31]	8	4 in 2 pat	0	0	2 (25%)	1 (12.5%)	87.5% at ~3.2 years
Innocenti et al. [34]	21	5 in 4 pat	1 (4.7%)	6 (28.5%)	2 (9.5%)	4 (19%)	80.9% at 10 years
Abed et al. [35]	25	6 in 5 pat	1 (4%)	9 (36%)	1 (4%)	5 (20%)	79% at 5 years
Moran et al. [36]	7	1 in 1 pat	0	2 (28.6%)	2 (28.5%)	0	100% at ~4.3 years
Bernd et al. [37]	16	1 in 1 pat	2 (12.5%)	1 (6.25%)	5 (31.3%)	1 (6.3%)	93.75% at ~5 years
Hennen et al. [38]	10	0	1 (10%)	0	1 (10%)	2 (20%)	80% at ~2.6 years
Ozaki et al. [39]	12	n.s	0	4 (33%)	n.s	0	100% at ~2.6 years

n.s: not specified; Percentages in brackets.

patient it showed to be a valuable method. In two patients the nonunion or delayed union resulted in plate and graft fracture. Both healed after revision and augmentation with autologous spongiosa, without further delay.

The prolonged surgery duration due to the necessary harvesting of the fibula and the vascular anastomosis theoretically may increase the risk of infection, but recorded infection rates are similar to the rates when allograft alone is used [8, 14–23, 27, 29–39]. Infection in combined allograft vascularised fibula reconstructions is a severe complication, but the fibula has the ability to survive infection [30, 34, 35, 60]. In allografts alone a graft failure is seen in 8–40% (Table 1), our results reflect the advantage of a vivid bone in comparison to allograft alone especially in case of infection. In our series of twelve patients, two deep infections occurred. Unfortunately one of them died of progressive tumour disease before infection treatment could be started. In the other case, the graft could be salvaged by infection treatment with systemic antibiotics and removal of affected hardware.

As already mentioned, the vascularised fibula expedites the achievement of a stable graft-host union and consequently leads to a reduction of the time to full unrestricted weight bearing. We allowed partial weight bearing on average 2 months after reconstruction surgery and full weight bearing at 9.4 months postoperatively, earlier than in other reported series, where full weight bearing was allowed at 14 months after operation on average (6–21) [20, 30–34, 36, 37]. To find the right balance between partial weight bearing to minimize the fracture risk and early remobilisation to increase the patient's quality of life is demanding, as literature provides no definite trend. Innocenti et al. [34] and Abed et al. [35], for example, restricted weight bearing the longest in the reviewed literature with 21.6 and 21.4 months to full weight bearing. But even in these collectives observed fracture rates of 28.5% and 36% could be seen.

Limb length discrepancy is recorded as a complication in some reports about allograft reconstructions combined with a vascularised fibula [34–36]. In our series, however, no limb length discrepancy has been seen, but there are some patients with remaining growth, where this could still become a problem. Followup at regular intervals will be performed.

The disadvantages, such as the prolonged surgery time with increased infection risk and the risk of anastomosis' failure by thrombosis among others, have to be kept in mind. In our series two deep infections occurred, but no anastomosis' failure. On the donor side a flexion deformity of the big toe is the most commonly observed complication. We found this complication in two patients. The effects were manageable with physiotherapy and orthotic devices. Other donor side complications recorded in the literature are pain, wound healing disorder, and ankle joint instability, and these were not observed in our patient collective [20, 31, 32, 34, 38].

Complications are quite frequent in this reconstruction type as 50% of our patients needed at least one additional surgical intervention to treat complications, and similar rates are reported in the literature. But despite this frequency, complications are manageable, and only few grafts fail. In our series we found a five-year survival rate of 100%, and in the literature midterm survival rates are also reported ranging between 80% and 100% [30, 32–39]. Capanna et al. [30] reported the series with the longest followup with 93.3% graft survival after 9 years on average, favourably better graft survival in comparison to reconstructions with allograft alone (Tables 1 and 2). Although long-term survival is rarely reported [30, 34], it can be suggested that—similar to single allograft reconstructions—survival rates will not further decline, and the construct becomes a stable and durable system.

Intercalary endoprostheses are a less popular alternative to allograft reconstructions. Published data is rare, and comparison to results with intercalary allograft reconstructions is difficult, as the patients are older in the endoprosthetic series, and also patients with metastatic disease are included [43, 46]. Endoprosthetic reconstruction offers early weight bearing and normal function on one hand, but infection and prosthetic or periprosthetic fracture as well as aseptic loosening and mechanical wear are feared complications on the other hand [9, 42, 43, 45]. Infection and fracture rates are relatively low ranging from 0 to 3.6% and from 0 to 16%, but

Table 3: Comparison of reconstructions with intercalary endoprostheses.

Author	Patients	Survival of implant	Infection (F/T/H)	Prosthetic fracture (F/T/H)	Periprostehtic fracture	Aseptic loosening (F/T/H)
Hanna et al. [42]	28	85% at 5 y and 68% at 10 y	3.6% (1/0/0)	7.1% (2/0/0)	3.60%	3.6% (1/0/0)
Ruggieri et al. [43]	24	n.s	0	4.2% (1/0/0)	0	25% (4/1/1)
Abudu et al. [44]	18	n.s	0	0	0	33% (3/1/2)
Aldlyami et al. [45]	35	63% at 10 y	2.9% (0/1/0)	5.7%	2.90%	20% (5/1/1)
Ahlmann et al. [46]	6	100% at 1 y. 83% at 2 y	0	0	0	16.7% (0/0/1)

n.s: not specified; F: femur; T: tibia; H: humerus.

aseptic loosening is the major problem occurring in up to 33% (Table 3) [42–46].

The major concern in the use of endoprostheses in young patients is their high potential for late failure. While allografts achieve a stable state after the first years, endoprostheses continues to fail [22, 42, 43, 46, 49, 51, 53]. Hanna et al. [42] recorded a five-year survival rate of 85% that declined to 68% at 10 years. Aldlyami et al. [45] published the series with the longest followup and reported a ten-year survival rate of 63%, and the curve is still declining, without achieving a stable plateau. The latter authors even wrote that they do not recommend intercalary endoprostheses in tibial reconstructions except in a palliative situation, but called it an attractive option in femoral defects. But as endoprostheses seem to be inferior to allografts in their durability, they should be used where immediate weight bearing and full function are of greater concern than durability, like in patients with metastatic disease.

In conclusion the presented series indicates that the combination of massive bone allograft and autologous vascularised fibula can achieve a stable and durable reconstruction, despite relatively high complication rates, as the complications are manageable. This reconstruction method is especially beneficial in young patients with primary tumours in contrast to patients with limited life expectancy, as long-term results in the reviewed literature are promising, but further investigations are necessary.

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Clinical Study

Bilateral Fibular Graft: Biological Reconstruction after Resection of Primary Malignant Bone Tumors of the Lower Limb

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This paper deals with bilateral vascularized fibular grafts (BVFG) as a method for reconstruction of metadiaphyseal defects of the femur and tibia in young patients suffering from malignant bone tumors of the lower limb. This reconstructional technique was used in 11 patients undergoing metadiaphyseal resection of lower limb malignant bone tumors. All patients with Ewing's sarcoma and osteosarcoma had multimodal treatment according to the EURO-E.W.I.N.G 99 or COSS-96 protocol. Median FU was 63 months. None of the patients experienced local recurrence during FU. 2 patients died due to distant disease during FU. Full weight- bearing was permitted after a mean of 8 months. The median MSTS score was 87%. Complications occurred in five patients. None of the complications led to failure of the biological reconstruction or to amputation. Biological reconstruction of osseous defects is always desirable when possible and aims at a permanent solution. Good functional and durable results can be obtained by using BVFG for the reconstruction of metadiaphyseal defects of the femur and tibia. Radiotherapy in the multimodal setting increases the risk for graft or fixation failure.

1. Introduction

The prognosis of patients with primary malignant bone tumors has improved within the last 30 years also due to the framework of standard therapy optimization studies (EURO E.W.I.N.G 99, COSS-96). In parallel, the proportion of limb-sparing resection and reconstruction procedures has increased steadily. More than 80% of patients can receive limb-sparing resection [1–4] without having an increased risk of local recurrence. The spectrum of reconstruction possibilities is extensive with options as tumor arthroplasty [3, 5–7], massive allografts [8–13], mantle grafts (massive allograft combined with a vascularized fibular graft [2, 14, 15] or irradiated autograft combined with a vascularized fibular graft [16–18]), and biological methods such as fibular grafts (vascularized/nonvascularized, unilateral/bilateral, "double barrel fibula") [4, 19–28], tibial flake, pelvis flake, and callus distraction [12, 29, 30].

About 65% of primary malignant bone tumors are located in the lower extremities and near to a joint. In German speaking countries arthroplasty is the most common treatment in reconstruction of osseous tumor defects. The 10-year survival rate of endoprothesis is 55%–71% [3, 5–7]. Since it is mostly young patients, revision surgery should be expected in most cases of cured patients. Biological reconstruction techniques should be implemented whenever possible. The goal is a

Table 1: Patient characteristics: tumor resection and reconstruction with a bilateral fibular graft ($n = 11$).

Patient no.	Sex	Age at surgery	Diagnosis	Localisation	Tumor stage	Length of defect (cm)	Radiotherapy	Follow-up
1	w	43	chondrosarcoma	Femur	IIB	16	no	87
2	m	19	Ewing's sarcoma	Femur	IIB	16	no	144
3	w	15	Ewing's sarcoma	Femur	IIB	23	adjuvant	111
4	m	18	Ewing's sarcoma	Tibia	IIB	17	neoadjuvant	35
5	w	12	osteosarcoma	Tibia	IIB	11.5	no	120
6	m	13	Ewing's sarcoma	Femur	IIB	13.5	no	46
7	w	9	Ewing's sarcoma	Tibia	IIB	12	no	66
8	m	12	Ewing's sarcoma	Femur	IIB	16.5	adjuvant	63
9	m	14	Ewing's sarcoma	Tibia	IIB	24.5	no	36
10	w	4	Adamantinoma	Tibia	IIB	8	no	38
11	m	40	Adamantinoma	Tibia	IIB	8	no	12

lasting reintegration and modeling in the area of the graft recipient while keeping functional integrity of the donor site.

The present study presents indication, methods, functional outcome and problems of bilateral fibular grafts for defect reconstruction after resection of primary malignant bone tumors in the long bones of the lower extremity.

2. Materials and Methods

2.1. Patients. Between November 2000 and December 2011, 11 consecutive patients needed a resection of a primary malignant bone tumor of the lower extremity (group of Ewing's sarcoma $n = 7$, osteosarcoma $n = 1$, chondrosarcoma $n = 1$, adamantinoma $n = 2$) and received a defect reconstruction using a bilateral fibular graft. Patients with an Ewing's sarcoma and osteosarcoma were treated according to EURO-E.W.I.N.G.-99 or COSS-96 protocol. Patients included 5 females and 6 males with an age range from 4 to 43 years at the time of surgery (mean age 14 years). All patients presented with tumor stage II B (UICC). Tumors were located in the metadiaphysis of the tibia ($n = 6$) and femur ($n = 5$). The length of the reconstructed defect ranged from 8 to 24,5 cm (median 16 cm). One of the patients underwent neoadjuvant radiotherapy and two other patients received adjuvant radiotherapy as part of the EURO-E.W.I.N.G.-99-protocol (Table 1). The median follow-up was 62 months.

2.2. Reconstructive Methods. Reconstructive approach varied depending on the location. In tibial defects ($n = 6$) the ipsilateral fibula was swivelled into the defect after resection of malignant bone tumor leaving the original blood supply intact. The vessels of the contralateral fibular graft were microscopically anastomosed end-to-side upon the a. and v. tibialis anterior in the majority of cases. The fixation of the fibular grafts was achieved by standard plating (AO) as exemplary shown in Figure 2. In two cases an additional medial gastrocnemius flap was used to cover the ventral side of the fibular graft.

For reconstruction of femoral defects ($n = 5$) two free fibular grafts of the ipsilateral and contralateral sides were used. Both grafts were positioned into the osseous defect and fixed with a condylar plate (AO) followed by microscopically assisted vascular anastomoses. Branches of the profound femoral artery and vein served as donor vessels. The peroneal artery was anastomosed in Y technique at both grafts. Each fibular vein was anastomosed separately for the grafts. One patient needed a custom made condylar plate (length: 43 cm) due to a defect size of 23 cm that had to be reconstructed. No preoperative angiography was performed in any of the patients with normal clinical vascular status. The only postoperative imaging carried out was X-ray.

After a complete ease of the affected limb for 6 weeks weight bearing was initiated with 15 kg starting at the 7th postoperative week. Weight bearing was increased in intervals correlating to the radiological examination outcome. Within the first postoperative year clinical and radiological follow-up was performed in 2- to 3-month intervals.

3. Results

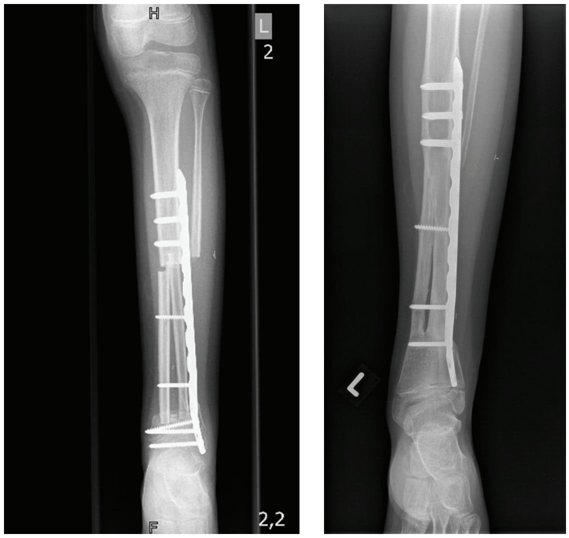
This is a retrospective analysis, based on the clinic's internal bone tumor registry database and the evaluation of the medical records. Two patients died of their disease. The remaining 9 patients are regularly seen for follow-up. Median values were calculated, and the MSTS score was provided [31].

3.1. Oncological Results. In 10 patients, an R0 resection was achieved, and local tumor recurrence did not occur. Resection in patient 11 (adamantinoma) resulted in an R1 resection showing no evidence of disease at follow-up of 12 months.

Patient 6—with Ewing's sarcoma of the proximal femur—developed multiple bone metastasis 18 months after completion of the multimodal treatment. After a second- and later on third-line chemotherapy, the patient died.

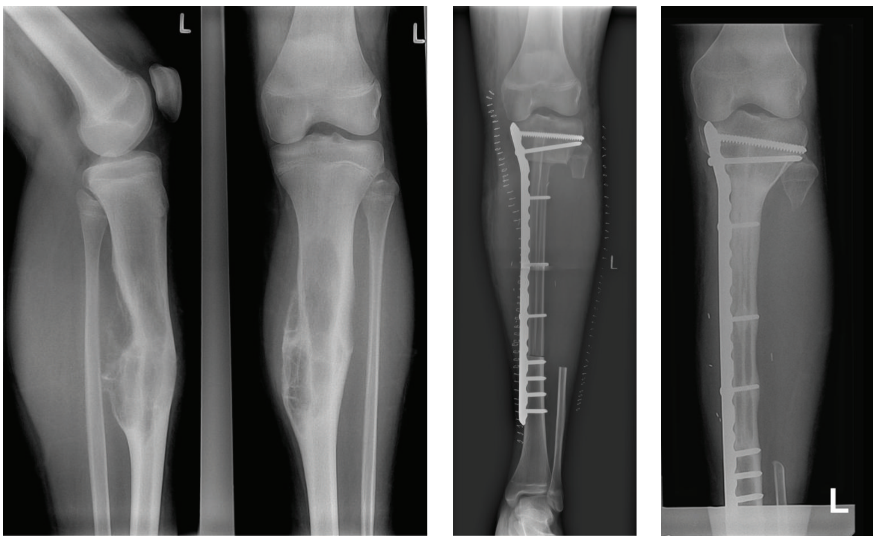
Patient 4—with a Ewing's sarcoma of the tibia—showed multiple bone metastases after 22 months an got a second-line chemotherapy. The patient died.

The remaining nine patients showed no evidence of disease at the end of follow-up (Ewing's sarcoma $n = 5$, osteosarcoma $n = 1$, chondrosarcoma $n = 1$, adamantinoma $n = 2$).



(a) (b)

Figure 1: (Patient no. 7) (a) Radiograph of a 9-year-old girl with Ewing's sarcoma of the distal tibia diaphysis. Defect reconstruction (12 cm) was achieved by using bilateral fibular graft and plate osteosynthesis. Due to the small remaining distal epiphyseal fragment the screws had to be placed in the epiphysis. (b) Radiographic results 29 months after tumor resection giving good evidence of bony healing. The epiphyseal screws have been removed. Nevertheless the ankle shows a mild valgus deformity resulting in an MSTS score of 93%.



(a) (b) (c)

Figure 2: (Patient no. 9) (a) 14-year-old boy with Ewing's sarcoma of the left tibia proximal diaphysis. (b) After completion of neoadjuvant chemotherapy wide resection and reconstruction of the defect (24.5 cm) by a vascularized transposed ipsilateral and contralateral free fibula and medial plate fixation were realised. (c) Radiograph showing osseous integration and hypertrophy of fibular grafts 15 months after operation.

Weight bearing was increased depending on the postoperative radiographic findings in all patients. The full load on the affected limb was released after 4–18 months (median 8 months) (Table 2).

The functional outcome was evaluated using the MSTS score [31] ranging from 60 to 100% with a median of 87%.

3.2. Complications. Four out of eleven patients needed one or more surgical revisions.

Patient 2 suffered from a postoperative arterial bleeding of the vascular anastomosis, which was revised within 10 hours postoperatively. The later healing was uneventful.

Patient 3 suffered from a condylar plate failure at the transition site of fibular graft and proximal femur with delayed bone union 21 months postoperatively. The patient had received adjuvant radiotherapy (regression grade III according to Salzer-Kuntschik). The proximal plate fragment was removed and a reosteosynthesis with a condylar plate and

Table 2: Results after tumor resection and reconstruction with a bilateral fibular graft ($n = 11$).

Patient no.	Resection	Regression grade[a]	Complications	Time until full weight (months)	Outcome	MSTS (1993)
1	R0	*n*	None	8	NED	70%
2	R0	2	Bleeding from anastomosis	5	NED	100%
3	R0	3	Plate failure and delayed union	9	NED	87%
4	R0	1	Fibular graft fracture, conservative treatment	18	DOD	60%
5	R0	3	Infection, and nonunion	8	NED	87%
6	R0	1	None	7	DOD	93%
7	R0	1	None	9	NED	93%
8	R0	4	Plate failure and delayed union	9	NED	80%
9	R0	3	None	13	NED	67%
10	R0	*n*	None	4	NED	87%
11	R1	*n*	None	7	NED	100%

[a]Referred to Salzer-Kuntschik [32]. *n*: not applicable, NED: no evidence of disease, DOD: dead of disease.

autologous cancellous bone graft was performed. Five months postoperatively, full weight bearing was released again. Only 6 months later she suffered a second plate failure resulting in a reosteosynthesis with another condylar plate. Another 6 months later she suffered a third plate failure. The patient was put into an orthesis with tubercular contact and the condylar plate was removed and replaced by a custom made osteosynthesis plate accompanied by autologous cancellous bone graft. There have been no more complications for the following 80 months until today's follow-up.

Patient 4 suffered from a fracture of the fibular graft after reconstruction of the proximal tibia, which healed with conservative treatment in cast immobilization. The patient had received neoadjuvant radiotherapy.

Patient 5 suffered from infection of the osteosynthesis site with synchronous nonunion between the bilateral fibular graft and the distal tibia 3 months postoperatively in relation to adjuvant chemotherapy. The plate was removed followed by surgical debridement and immobilisation in a cast. After healing of the infection adjuvant chemotherapy was continued. Six weeks after the completion of adjuvant chemotherapy the nonunion was resected and an autologous bone graft was performed followed by a lateral reosteosynthesis. Full weight bearing was released 12 weeks postoperatively when complete osseous union was documented by plain X-ray.

Patient 8 suffered from a Ewing's sarcoma of the right femur diaphysis. The biological reconstruction was realised with a bilateral free fibular graft and lateral plate fixation for a defect of 16,5 cm (Figure 3(a)). 15 months after tumor resection a plate fracture occurred at the distal interphase between fibular graft and femur metaphysis combined with a nonunion. The patient had received his neoadjuvant and adjuvant chemotherapy according to EURO-E.W.I.N.G.-99-protocol including adjuvant radiotherapy (Figure 3(b)). The fracture was treated with replating and autogenous bone grafting (Figure 3(c)). 5 months later a second plate fracture occurred on a different level. The fibular grafts themselves showed two fractures on different levels. The bony structures showed signs of demineralization and irregularities due to administered chemo- and radiotherapy (Figure 3(d)). Surgical revision resulted in double plating and autogenous bone grafting. So far there have been no more complications until the last follow-up at 62 months (Figure 3(e)).

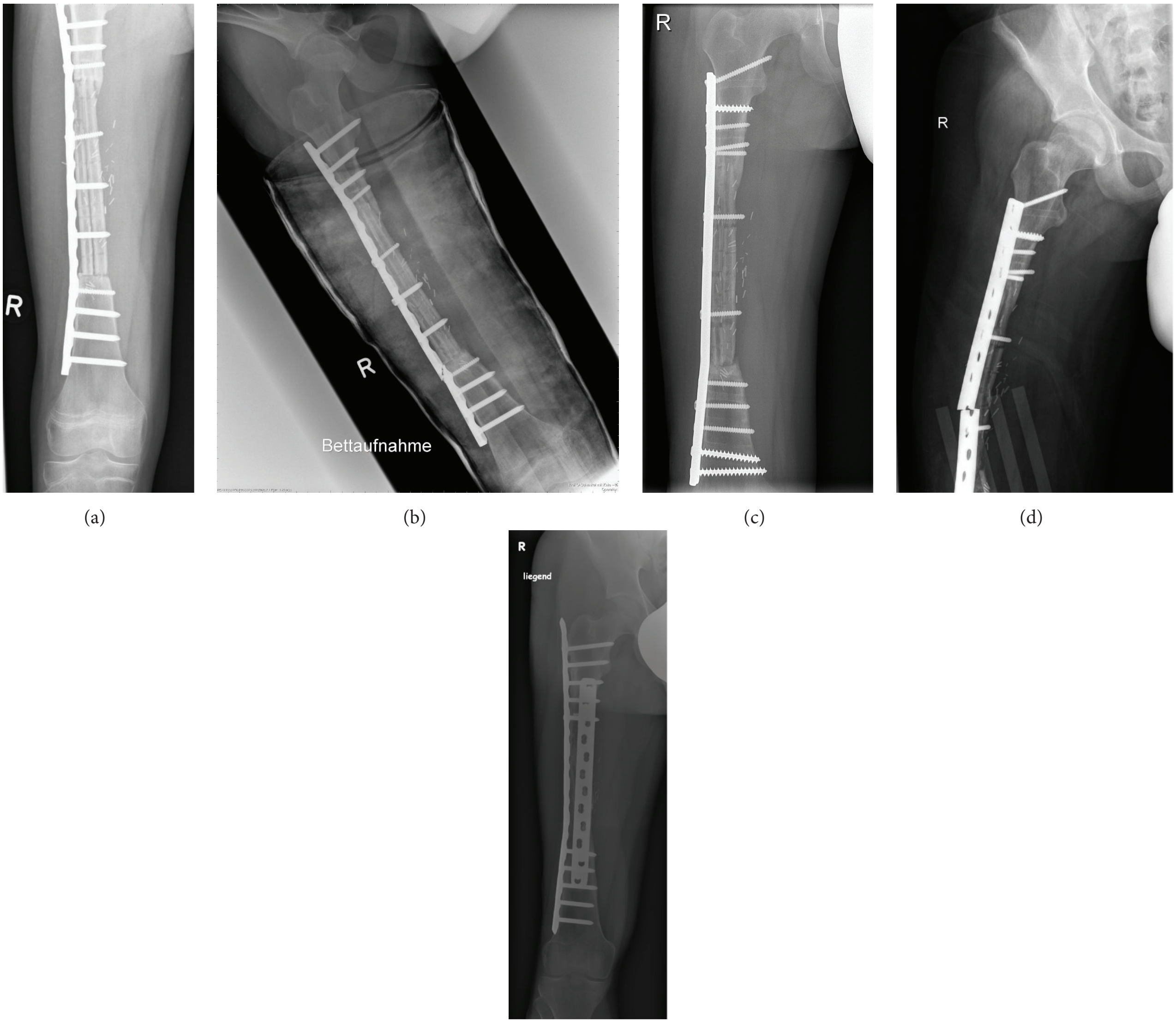
In patient 7 the distal screws for osteosynthesis had to be placed in the epiphysis due to the small remaining distal epiphyseal fragment (Figure 1(a)). The epiphyseal screws were removed 15 months after primary surgery (Figure 1(b)). This was not considered a complication.

There were no signs of donor site morbidity (e.g., Peroneal nerve Paloy, deformity of the tibia, ankle instability). None of the complications resulted in a loss of the affected extremity.

4. Discussion

Tumor arthroplasty will remain the most common reconstructive method of near-joint defects caused by resection of primary malignant bone tumors. 5- and 10-year survival rates of arthroplasty are 67%–87% and 55%–71%, respectively [3, 5–7]. Advantages of tumor arthroplasty are the primary stability and good functionality of the limb. Since the majority of the patients are young, revision surgery is undesirable but may be an unavoidable consequence if there is no evidence of disease. In particular infections, aseptic loosening, wear of the joint components and stress fractures are causes for revision surgery. Each intervention increases the risk for a new complication that in the worst case may result in the loss of the affected extremity.

Massive allografts have similarly high rates of complications including mainly nonunion and infection [8–11]. Mantle grafts (as described in the Capanna's method [33]) represent a fusion between biological and allograft reconstruction. Particularly for the reconstruction of long bone metaphyseal defects an "allograft-mantled" unilateral vascularized fibular graft can enable a high primary stability and in addition promote the bony consolidation of the fibula in the recipient area. Therefore mantle grafts are frequently used in the lower extremity [34–36] but require a bone bank for matching allografts. Postoperative complications include fractures,



(a) (b) (c) (d)

(e)

Figure 3: (Patient no. 8) (a) 12-year-old boy with Ewing's sarcoma of the right femur diaphysis. Radiograph showing the reconstructive result with a bilateral free fibular graft and lateral plate fixation for a defect of 16,5 cm. (b) 15 months after tumor resection plate failure occurred at the distal interphase between fibular graft and femur metaphysis showing an osseous nonunion. The patient had received his neoadjuvant and adjuvant chemotherapy according to EURO-E.W.I.N.G.-99-protocol including adjuvant radiotherapy. (c) The fracture was treated with replating and autogenous bone grafting. (d) 5 months later a second plate fracture occurred in the middle of the fibular grafts. The fibular grafts themselves showed two fractures on different levels. The bony structures show signs of demineralization and irregularities due to administered chemo- and radiotherapy. (e) Surgical revision resulting in double plate osteosynthesis and autogenous bone grafting. So far there have been no more complications until the last follow-up at 62 months.

nonunions, and infections [2, 13–15, 36, 37]. Current available data show that mantle grafts provide a higher primary stability compared to bilateral fibular grafts [14, 15].

The advantage of bilateral fibular grafts in long bone metadiaphyseal defect reconstruction of the lower extremity is the autologous transplant which provides excellent chances for remodeling at the recipient's site [21, 23, 25, 28, 38–40]. Particularly reconstruction of femoral defects shows good results with less complications (infections, nonunions) in both procedures compared to the reconstruction of tibial defects. However, the currently available data does not answer the question which reconstruction method (mantle graft versus bilateral fibular graft) provides better results in the long-term survey.

4.1. Stability and Weight Bearing. Biological reconstructions of osseous defects claim to be a permanent solution. Unilateral vascularized and nonvascularized fibulas are used for various reconstructions of the upper and lower extremities. The advantage of vascularized grafts was clearly demonstrated based on animal studies and in clinical trials [4, 27, 39]. From a functional perspective the aim of reconstruction of the lower limb should be to allow early weigth bearing. In the immediate postoperative course a long time of none or partial weight-bearing of the affected limb has to be accepted. This unavoidable restriction can lead to complications such as muscular insufficiency, demineralization of the original bone and graft and pathological fractures [26, 37, 41]. The fibula as an unilateral transplant can only partially provide primary stability in reconstruction of long lower limb bone defects. Weight bearing can sometimes not be permitted for a long time until a hypertrophy of the unilateral fibular graft has taken place [14, 21, 42]. The younger the patient is, the earlier the bone remodelling is expected to take place. Therefore an ipsilateral fibula only as "fibula per tibia" for reconstruction in young patients with malignant tibial bone tumors is adequate since hypertrophy of the fibular graft is expected [21].

Besides the mantle graft which represents a combination of an autologous fibular graft and an allograft the primary stability can be reached and even improved without allogenic transplants by a bilateral fibular graft (fibula per tibia plus free fibular graft of the contralateral side for tibial defects or bilateral free fibular graft for femoral defects). The aim is to reduce time until recovery. This reconstruction method is more complex regarding its surgical technique compared to tumor arthroplasty or unilateral fibular graft and has been repeatedly described in detail [4, 20, 25, 27, 28]. The ipsilateral fibula is positioned into the tibial defect and only the vessels of the contralateral fibula have to be anastomosed in microsurgical technique. For femoral defect reconstruction a bilateral free fibular graft can increase the primary stability and the increase of weight bearing can be accelerated. Osteosynthesis ensures primary stability during exercise. Considering the fact that most patients receive postoperative chemotherapy during treatment optimization studies (in the group of Ewing's sarcoma sometimes additional radiotherapy) an internal fixation (plating, Kirschner wires, etc.) is preferred to an external fixator. The aim is to reduce the risk of infection during times of pancytopenia [12]. Another reason for internal fixation is that generally a removal of the osteosynthesis is not required. Weight bearing is increased individually according to osseous integration of the fibular graft into the bone.

In our group of patients full weight-bearing of the affected limb was allowed after a median of 8 months corresponding to the results of Tomita et al. [28] and El-Gammal et al. [22, 23].

4.2. Postoperative Imaging. Plain radiographs in two planes are adequate for postoperative imaging. To the authors' opinion a general implementation of postoperative angiography or scintigraphy is not justified since it will not have surgical consequences in an asymptomatic patient (e.g., angiographically undetectable vascular anastomosis).

4.3. Limitations. A limitation of the bilateral fibular graft on one hand is the tumor location and on the other its expansion. Bilateral fibular grafts are favorable if the tumor is located meta- or diaphyseally in the long bones of the lower limb. Due to the rare occurrence of malignant bone tumors requiring diaphyseal resection the case number is low.

Tumor arthroplasty or allografts remain the reconstruction mode of choice if the epiphysis reveals tumor infiltration and neither a wide resection of the primary tumor nor a sufficient fixation of the interposition can be realized although there have been efforts even to implement biological reconstruction methods for osteoarticular defects [43].

Complications in the postoperative course after biological reconstruction cannot be avoided. They include in particular fractures of the fibular graft, non-union, and infection and are almost exclusively temporary [14, 24, 26, 41]. The causes of complications are versatile. Osseous integration of the graft during systemic chemotherapy is often delayed so that an increase in weight bearing must usually be performed over several months. In an asymptomatic patient this can lead to an unintended early increased weight bearing, which may result in a failure of fixation as seen in two of our patients.

In the group of Ewing's sarcomas often a neo- or adjuvant radiotherapy is indicated according to therapy optimisation studies and depending on the response rate to systemic chemotherapy. Those cases are predestined for a delayed union or pathological fractures, due to the well-known side effect of radiation therapy in musculoskeletal oncology [44]. In our group of patients all three patients (100%) who had received radiotherapy suffered either a fracture of the fibular grafts (patient 5) or a fatigue fixation failure combined with a delayed union (patient 3 and 8).

Infections are expected much less frequently in biological reconstructions than during the implantation of mega prosthesis. The cause of infection in biological reconstructions is either inadequate soft tissue coverage or osseous nonunion. Infection occurred in one of our patients who had received reconstruction of a proximal tibial defect (patient 7). Infection occurred despite a medial gastrocnemius flap and an additional fasciocutaneous flap and was accompanied by synchronous nonunion which was cured surgically.

Reported results in the literature are similar, while they are limited by low case numbers [23, 25, 26, 37, 41, 42]. There are only few reports on donor site morbidity [34]. Our patients did not suffer any. This corresponds to observations of Zaretski et al. [37].

5. Conclusions

In summary the biological reconstruction of metadiaphyseal defects of the long bones of the lower extremity with a bilateral fibular graft is a highly demanding surgical procedure aiming at limb salvage. Despite a high primary complication rate [1, 38, 42] resulting in secondary revisions, after managing complications and completion of osseous integration of the fibular grafts a permanent reconstruction can be assumed, making this procedure clearly superior to tumor arthroplasty. The authors therefore ask to consider biological reconstruction techniques as an adequate surgical option.

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Research Article

Three-Dimensional Virtual Bone Bank System Workflow for Structural Bone Allograft Selection: A Technical Report

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Structural bone allograft has been used in bone defect reconstruction during the last fifty years with acceptable results. However, allograft selection methods were based on 2-dimensional templates using X-rays. Thanks to preoperative planning platforms, three-dimensional (3D) CT-derived bone models were used to define size and shape comparison between host and donor. The purpose of this study was to describe the workflow of this virtual technique in order to explain how to choose the best allograft using a virtual bone bank system. We measured all bones in a 3D virtual environment determining the best match. The use of a virtual bone bank system has allowed optimizing the allograft selection in a bone bank, providing more information to the surgeons before surgery. In conclusion, 3D preoperative planning in a virtual environment for allograft selection is an important and helpful tool in order to achieve a good match between host and donor.

1. Introduction

The uses of bone allograft after bone tumor resection have been described with acceptable results in osteoarticular, transepiphyseal, and intercalary reconstructions [1–4].

Selection of the closest anatomical match between the host and the donor is crucial in order to obtain adequate joint stability, alignment, appropriate wound closure, and minor degenerative changes of the articular surface in osteoarticular allograft.

Since 1950, bone allograft selection according to size and shape for limb reconstruction was made by comparing X-ray images between donors and patient [5]. This method had inaccuracies between the X-ray magnification scale and real bone, altering the final selection [6]. In the 1970s, CT scanner allowed to refine these inaccuracies taking into account one image slice in two dimensions [7]. The previous two decades have seen an increase in the use of virtual scenarios and informatics developments for preoperative planning [8–10]. Three-dimensional patient-specific anatomical models can be constructed from medical image data.

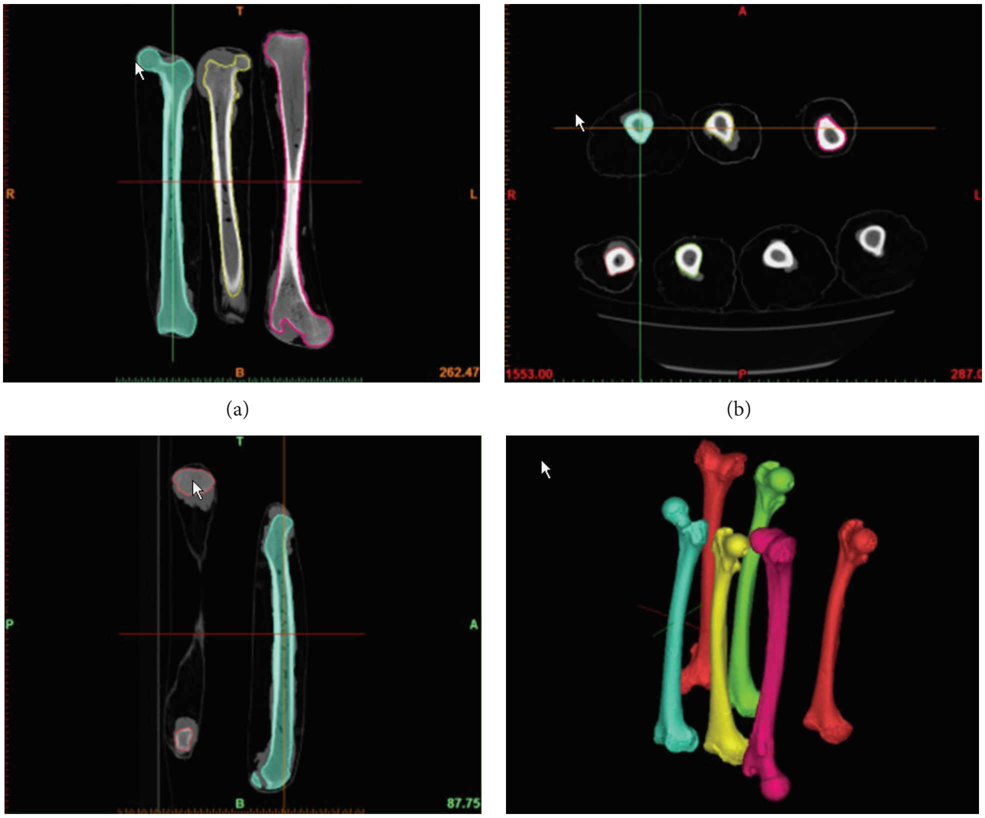
We described a virtual technique capable of selecting a suitable allograft according to size and shape through a three-dimensional virtual model.

The aim of this paper was to describe the workflow of this technique in different cases in order to explain how to choose the best allograft using a virtual bone bank system.

2. Material and Methods

Three-dimensional (3D) virtual bone models from host and donor were obtained following these steps: *image acquisition*, *image segmentation,* and *3D bone reconstruction*, described in detail below.

Once this workflow was completely defined, we were capable of measuring each bone in a virtual environment and establishing 3D comparisons between host and donor to determine the best match.



(a) (b) (c) (d)

Figure 1: (a)–(c) Image segmentation. (d) Bone allograft was 3D reconstructed.

All images were acquired using a CT scanner (Mutislice 64, Aquilion, Toshiba Medical Systems, Otawara, Japan). Magnified slices with 0.5 mm thickness were obtained using a soft tissue standard filter, a matrix of 512×512 pixels, and stored in Digital Imaging and Communication in Medicine (*DICOM*) format.

In order to establish comparable measurements, image acquisition protocols should be equal in host and donor. Image magnification process is an important step to obtain images in high definition. Thus, we suggest magnifying the image as much as possible.

Image segmentation is a process which consists in changing the representation of a DICOM image into an image that is easier to analyze. We used a specialized software for the segmentation tasks (Mimics software, Leuven, Belgium). Through this process, an operator assigns a color to every pixel in an image such that pixels with the same intensity define a separate structure: for example, cortical and trabecular bone. In our case, the bone after the segmentation process was isolated from the other tissues and structures such as muscle, fat, skin, ice, and metal table of CT scanner (Figure 1).

The result of image segmentation is a set of segments or a set of contours extracted from the image that collectively cover the entire 3D bone model. Each of the pixels in a region is similar according to intensity. The resulting contours after image segmentation were used to create 3D reconstructions with the help of interpolation algorithms. In this manner, a three-dimensional bone model was created (Figure 1). The segmentation process of a whole large bone takes a mean of 10 hours.

Take into account that the "contrast" in the CT for image segmentation is the calcium density. In oncologic patients, pain and lack of mobility lead to low calcium density. In consequence, the cortical and trabecular bones are replaced by the tumor action, erasing the anatomical shape and recognizable landmarks. In this way, 3D tumoral bone models appear to be incomplete.

Hereby, exploiting the symmetry of the human body [11, 12], we create a 3D mirror model from the patient's healthy side.

In order to select the best size, six anatomical landmarks were defined determining three principal measures from the 3D mirror model: A is transepicondylar, B is medial anterior-posterior condyle, and C is lateral anterior-posterior condyle (Figure 2). Once the whole bank was measured we created a table with all the ABC extents. First we search, as a screening step, ABC donors closest to ABC host. Next, in order to compare and select the best shape, 3D mirror model is overlapped with the available donors. Before comparing 3D shapes, all 3D bones were positioned in the same coordinate system. This process is called 3D registration.

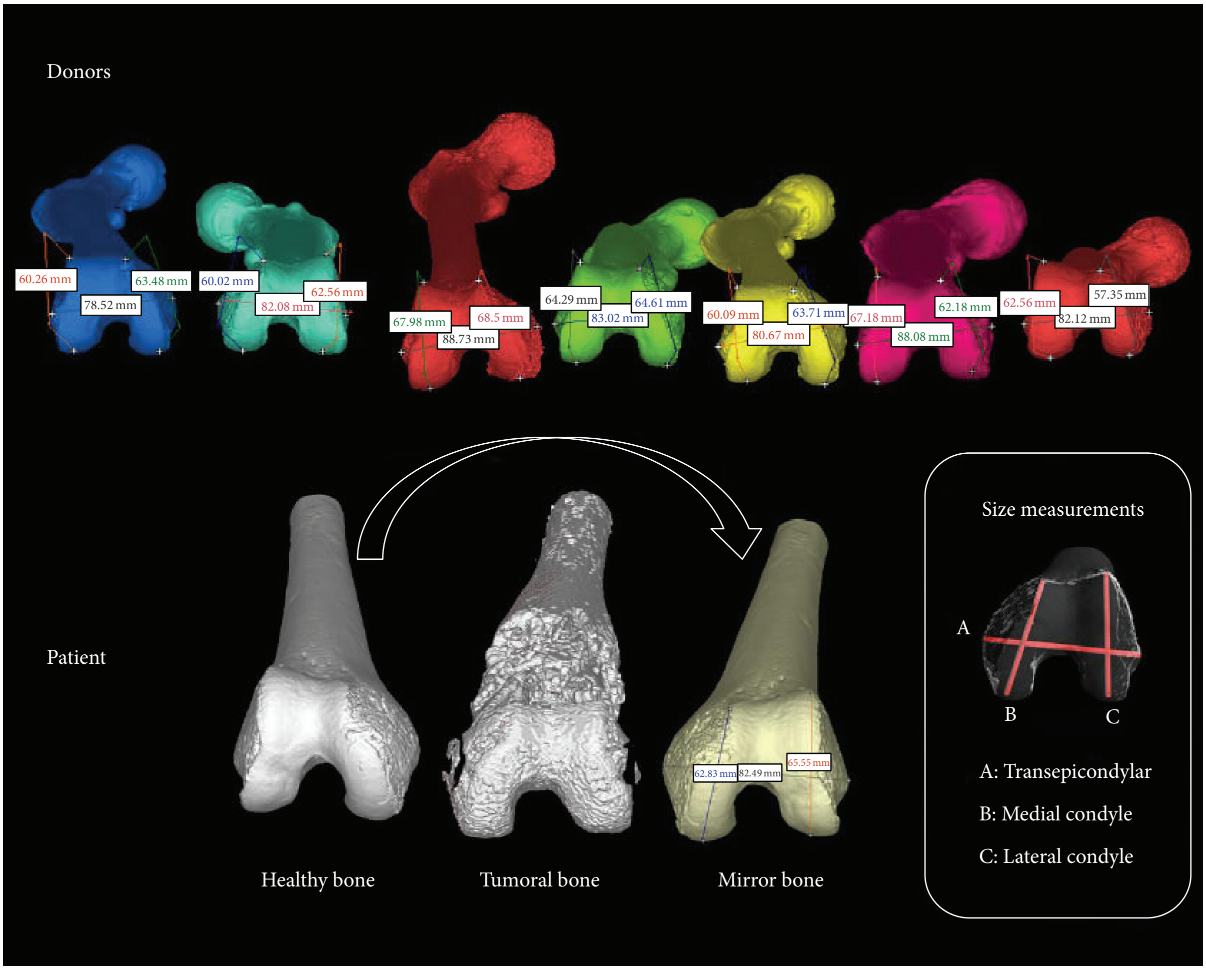


FIGURE 2: Donors were measured using ABC measurements. The healthy bone of the patient was mirrored and then measured with ABC measures in order to compare the best match according to the sizes.

Using a point cloud model of surfaces, it was possible to obtain a numeric value (a mean) that reflects the goodness of the match [12].

Distances between host and donor were illustrated in a colorimetric mapping.

This tool allowed us to determine which is the most similar area with a color scale (Figure 3).

Since it is not an easy task to determine natural landmarks in transepiphyseal and diaphyseal allografts, only it is possible to determine a match by overlapping the host with available donors (Figure 4).

3. Discussion

Paul et al. in their study [11] explored the use of 2-dimensional template comparison for allograft matching. However, the cited study also describes a 3D registration method and states that the 2-dimensional template comparison is ineffective.

The correspondence between the 3D models and the real bone depends heavily on CT scanner, segmentation, and interpolation software [11].

Published studies on three-dimensional preoperative planning using virtual environments for allograft selection have reported benefits in pelvis and femur [11–14]. The use of this technology allowed optimizing the allograft selection in a bone bank, providing three-dimensional visual information to the surgeon before surgery is executed.

As well, if the host has to be compared against multiple available donors, the process would be very time consuming if it were to be performed manually [14]. Actually, the algorithms described in the cited articles were capable of automatically choosing the best allograft according to the size and shape criteria. We also have already published acceptable results applying an automatic method to select the best match [15, 16].

Although we know that anatomical matching is only one of multiple factors that could affect the outcome of an allograft reconstruction, poor matching between host and donor can alter joint kinematics and load distribution, leading to bone resorption and joint degeneration [17, 18]. Pathological studies showed that allografts retrieved from patients with a nonsimilar joint had earlier and more advanced degenerative

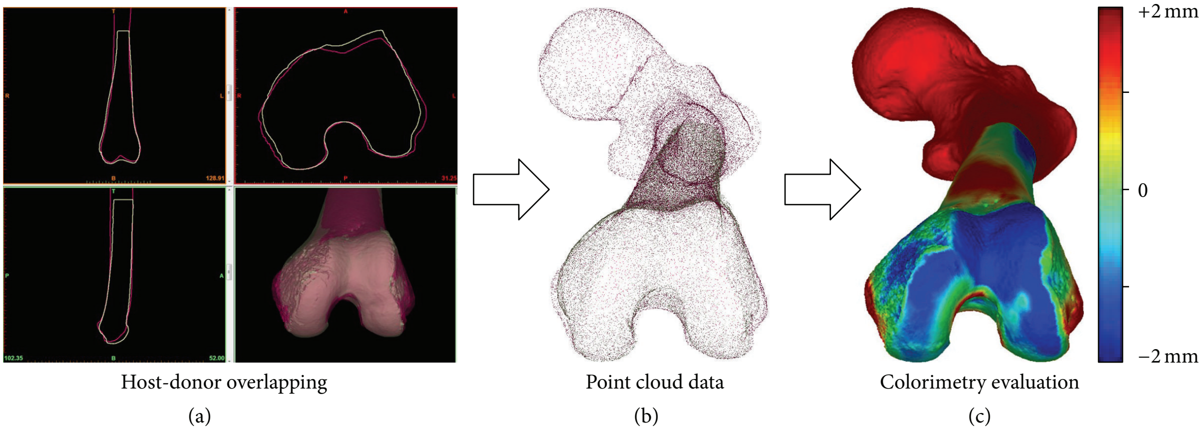


Figure 3: (a) Host and donor were overlapped in a virtual platform in order to compare the best match according to the shapes. (b) 3D models were exported to point cloud data. (c) A colorimetry evaluation was applied comparing host and donor surfaces.

Figure 4: (a) Bone allograft was selected according to the shapes comparison between host and donor. The original tumor diagnosis was a chondrosarcoma. (b) Allograft was selected and tumor was resected. (c) Allograft was fixed in the patient through a plate and screws. (d) and (e) Postoperative X-rays.

changes in the articular cartilage than did allografts retrieved from patients with a stable joint [17, 19].

4. Conclusion

We consider that a three-dimensional preoperative planning in a virtual environment for allograft selection is an important and helpful tool in order to achieve a good match between host and donor. Currently, we are following these patients to assess their limb function at several postoperative intervals.

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Clinical Study

Biological Reconstruction Following the Resection of Malignant Bone Tumors of the Pelvis

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Background. Surgical treatment of malignant pelvic bone tumors can be very challenging. The objective of this retrospective study was to evaluate the oncological as well as the clinical and functional outcome after limb salvage surgery and biological reconstruction. *Methods*. The files of 27 patients with malignant pelvic bone tumors, who underwent surgical resection at our department between 2000 and 2011, were retrospectively analyzed (9 Ewing's sarcoma, 8 chondrosarcoma, 4 osteosarcoma, 1 synovial sarcoma, 1 malignant fibrous histiocytoma, and 4 carcinoma metastases). *Results*. After internal hemipelvectomy reconstruction was performed by hip transposition ($n = 16$), using autologous nonvascularised fibular graft ($n = 5$) or autologous iliac crest bone graft ($n = 2$). In one patient a proximal femor prothetis and in three patients a total hip prosthesis was implanted at the time of resection. The median follow-up was 33 months. Two- and five-year disease-specific survival rates of all patients were 86.1% and 57.7%, respectively. The mean functional MSTS score was 16.5 (~55%) for all patients. *Conclusion*. On the basis of the oncological as well as the clinical and functional outcome, biological reconstruction after internal hemipelvectomy seems to be a reliable technique for treating patients with a malignant pelvic bone tumor.

1. Introduction

Chondrosarcomas, Ewing's sarcomas, and osteosarcomas are the most common primary bone sarcomas of the pelvis and account for 5% to 10% of all malignant bone tumors.[1, 2]. The prognosis and survival of patients with bone sarcomas in this location are much less favorable than for patients with tumors of the extremities. Additionally the pelvis is the second most common site of bone metastases after the spine.

The treatment of malignant bone tumors involving the pelvis is a great challenge to the orthopaedic surgeon in terms of local control owing to the complexity of pelvic anatomy, which increases the difficulty of resection and reconstruction. First attempts to excise malignant bone tumors of the pelvis were reported by Enneking in 1966 [3] and Steel in 1978 [4]. Resection of the tumor can be performed either by internal or external hemipelvectomy. Pelvic resections have been classified by the Musculoskeletal Tumor Society into 4 resection types: type I (iliac), type II (periacetabular), type III (os pubis, ischii), and type IV (sacrum) [5–8]; see also Figure 1.

Because of the improvements in imaging modalities and in multimodal treatment plans, leading to a prolonged patient survival, limb sparing procedures are usually the treatment of choice, especially considering the low patient acceptance of hindquarter amputation.

The reconstruction procedures after internal hemipelvectomy include endoprosthetic replacement [9] and biological reconstruction using autografts or allografts [10–12] as well as hip transposition [13].

The aim of this report was to evaluate patients with malignant tumors of the pelvis after biological reconstruction with regard to oncological, clinical, and functional outcomes.

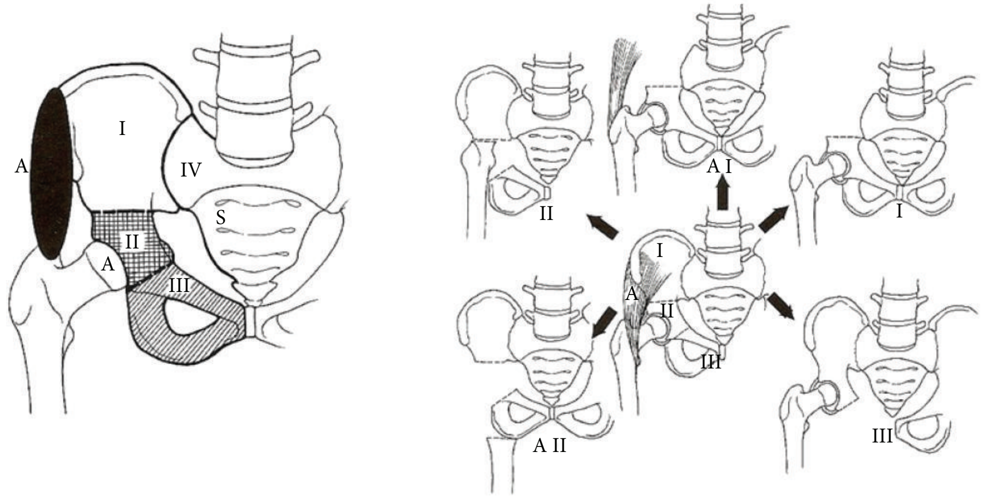


Figure 1: A Classification of pelvic resection [5].

2. Material and Methods

The medical files of 27 patients with a malignant pelvic bone tumor surgically treated at our institution between 2000 and 2012 were retrospectively analyzed. All patients had signed a consent form at hospital admission, allowing the use of anonymized information for research purposes.

There were 12 female and 15 male patients with an average age of 44.6 years (range 10–77 years) at the time of the first surgical intervention. According to the histological report, the primary tumor was recorded as Ewing's sarcoma in 9 patients, chondrosarcoma in 8, osteosarcoma in 4, synovial sarcoma, and malignant fibrous histiocytoma of the bone in one patient each, respectively. Four patients presented with solitary metastases to the pelvis from renal cell carcinoma in two cases, thyroid cancer in one and invasive ductal carcinoma of the breast in another patient. Tumor volume was assessed by the pathologist during examination of the surgical specimen or in the Ewing's sarcoma by the radiologist before neoadjuvant treatment was started. The average tumor volume was 451 cm^3 (214–2200 cm^3).

All patients diagnosed with an osteo- or Ewing's sarcoma received neoadjuvant chemotherapy as determined by the appropriate protocols. One patient with a Ewing's sarcoma received a combination of radiation and chemotherapy prior to surgery.

Sixteen patients had a hip transposition after a resection involving the acetabulum. This procedure was first described by Gebert et al. [13], the procedure involved moving the femoral head proximally to the lateral side of the sacrum or the underside of the resected ilium after resection of the acetabulum (Figure 3). The joint capsule was reconstructed with use of a polyethylene terephthalate mesh tube (Implantcast, Buxtehude, Germany), which was fixed to the pelvis with transosseous sutures and formed a pouch for the femoral head. Soft tissues were reattached to the tube. Five patients had a P1 resection and pelvic reconstruction stabilized with an autologous nonvascularized fibular graft, and in two patients an autologous iliac crest bone graft was used for the pelvic reconstruction after P1 resection (Figure 2). In one patient an endoprosthetic replacement of the hip was already done before the diagnosis of the pelvic tumor, and in three patients the resection of the femoral head was required to achieve wide surgical margins. In these three cases a femoral respectively a total hip prosthesis was implanted at the time of resection.

Surgical margins were divided into intralesional, marginal, wide, and radical, according to the classification of Enneking et al. [14]. The Musculoskeletal Tumor Society (MSTS) scoring system for the lower limb was employed to assess the functional outcome [15].

A major complication was defined as one that necessitated additional surgical intervention. A minor complication was defined as one that necessitated nonoperative management.

Survival analysis was performed using the Kaplan-Meier method. Disease-specific survival was calculated from the date of diagnosis (biopsy) until death related to disease or treatment and event-free survival from the date of tumor resection until disease recurrence or death (Figure 5).

3. Results

The characteristics of the patients are summarized in Table 1. The average blood loss was 2050 mL (range 900 mL–3100 mL). Bed rest was normally seven days. In eight patients it was extended to 10–14 days. Patients stayed in the hospital an average of 27.7 days after surgery (range 15–69 days). At the time of discharge all patients were able to walk using crutches or a walking frame.

At the time of the last follow-up 15 patients were alive with no evidence of disease, 5 patients were alive with disease, and 7 patients had died from disease. The median follow-up was 33 months. Two- and five-year disease-specific survival rates of all patients were 86.1% and 57.7%, respectively. Surgical margins were classified as wide in 20 patients. In

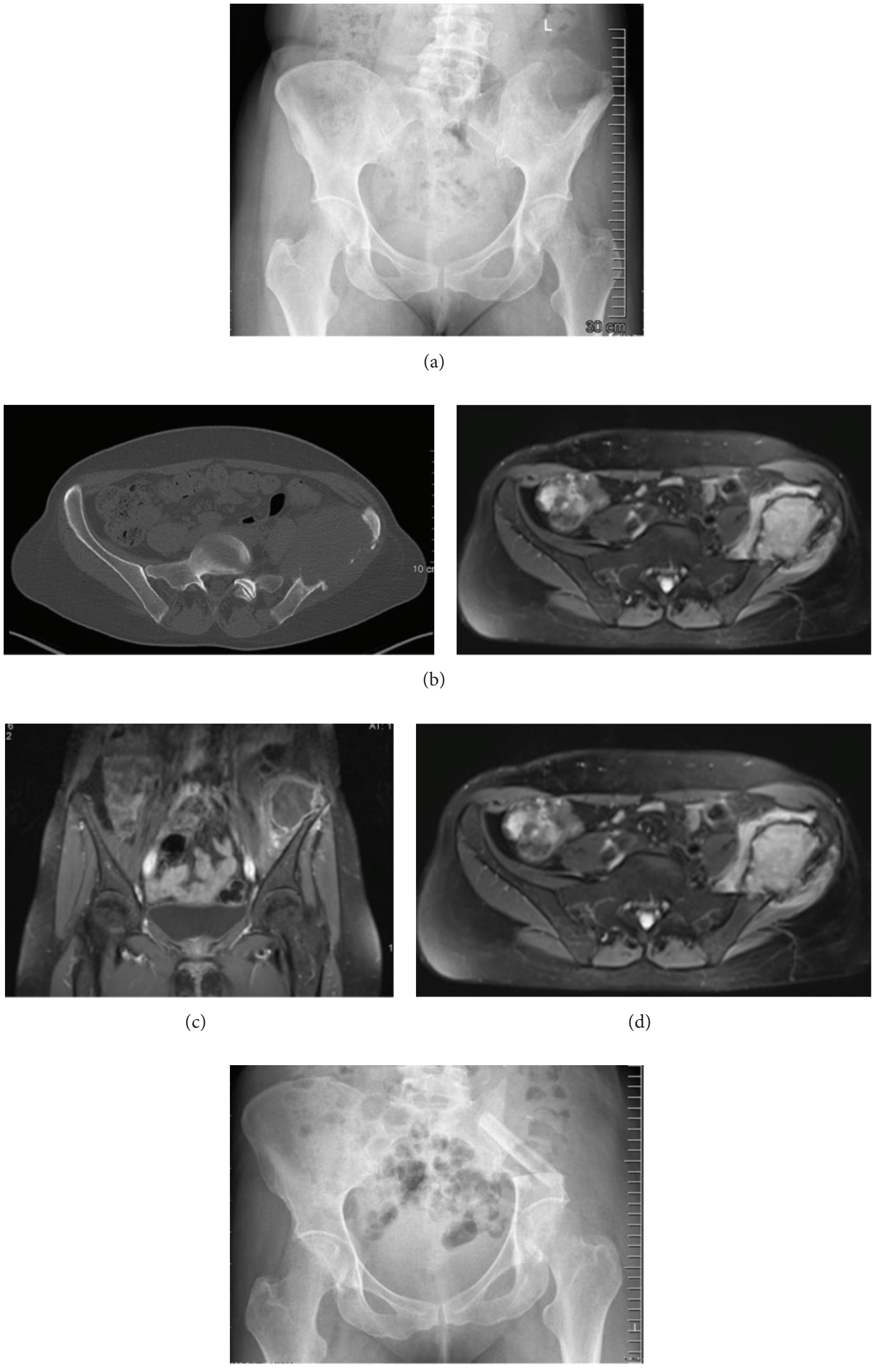
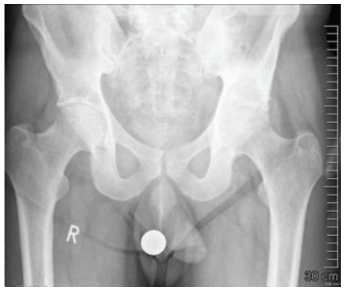


Figure 2: (a) Anteroposterior radiograph of the pelvis, showing a large osteolytic lesion of the left iliac bone (synovial sarcoma). (b) CT scan of the same patient showing the size of the tumor. Notably is the lack of matrix or calcification inside the tumor. (c) and (d) MRI scan of the same patient showing the intra- and extrapelvine size. (e) Postoperative X-ray after P1 resection and pelvic reconstruction stabilised with an autologous nonvascularised fibular graft.



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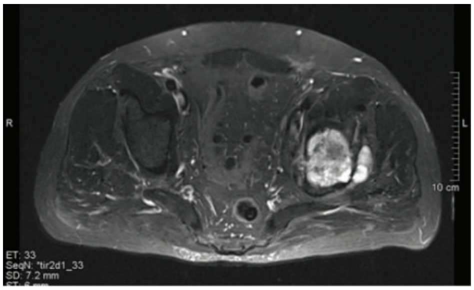
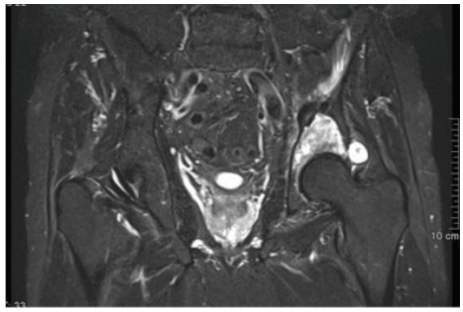
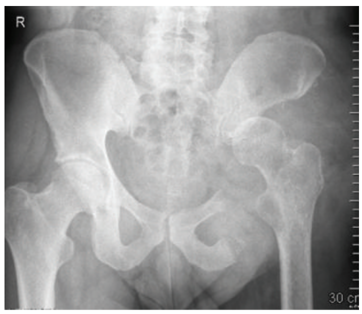




(b) (c)



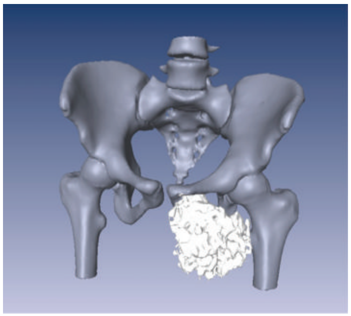
(d)

Figure 3: (a) Anteroposterior radiograph of the pelvis, showing a periacetabular chondrosarcoma on the left. (b) and (c) MRI of the pelvis, showing the destruction of the cortical bone and extraosseous tumor expansion. Notably is that the hip joint is not infiltrated. (d) Anteroposterior radiograph after P2 resection and hip transposition.

four patients marginal resection were achieved, and three patients had an intralesional resection. Two patients experienced a local relapse (one osteosarcoma and one Ewing's sarcoma), although the surgical margins were wide. Both patients received a second-line chemotherapy and palliative irradiation in the further course of the disease. The two patients died of isease 29 respectively 51 month after primary diagnosis. Five patients with a primary bone tumor and one patient with metastatic renal cell carcinoma died from metastatic disease without local recurrence after an average of 32 month after diagnosis of the pelvic tumor.

The mean functional MSTS score was 16.5 (~55%) for all patients. Three patients were able to walk without any support (Figure 4), two had a transposition after P2-3 resection, and the other patient had a P1 resection and was reconstructed with an autologous iliac crest bone graft. All the other patients need at least one cane for longer distances. The MSTS score in the subgroups after resection and biological reconstruction was after P1 resection 16,9 (10–26), after P1-2 resection 16 (14–18) and after P1-3 resp. P2-3 resection 17,4 (9–30). The MSTS score in the patient with the P1+4 resection was 18, and in the patient after P2-4 resection was 20.

There were nine complications which required an operative intervention. Four patients developed a superficial postoperative wound infections involving the skin. All healed after revision surgery. In one patient a previously implanted Hickman line had to be changed short time after the surgery, because of sepsis. In two patients the endoprosthesis had to be removed because of dislocation and septic loosening. In one patient with a fibular autograft after P1 resection there was an osteomyelitis of the bone graft, and a sequestrum had to be removed. Shortly after this procedure a postoperative pseudarthrosis was observed, but causing no problems. And in one patient a paresis of the leg developed directly after the surgery, because the sciatic nerve had to be resected.



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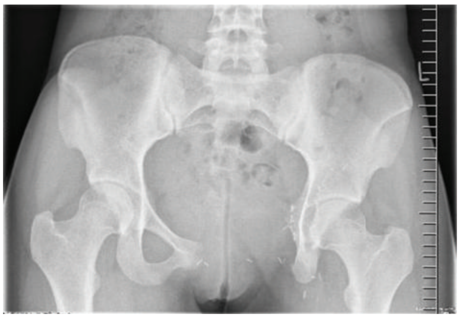

(b)

Figure 4: (a) CT reconstruction of the pelvis of a 15-year-old girl with a chondrosarcoma of the left os pubis and os ischii. (b) Anteroposterior radiograph after P3 resection.

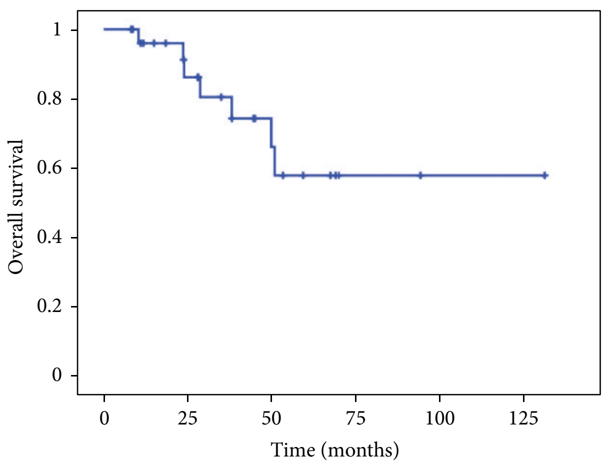

Figure 5: Kaplan-Meier plot showing the overall survival of all patients.

Table 1

	n
Patients	27
Female 12, male 15	
Age	44.6 (10,3–77,2)
Diagnosis	
Ewing's sarcoma	9
Chondrosarcoma	8
Osteosarcoma	4
Synovial sarcoma	1
Malignant fibrous histiocytoma	1
Metastasis-renal cell carcinoma	2
Metastasis-invasive ductal carcinoma of the breast	1
Metastasis-thyroid cancer	1
Tumor stage (Enneking)	
Ib	1
IIa	2
IIb	20
IV (metastasis)	4
Grading (for primary tumors)	
G1	1
G2	5
G3	17
Neoadjuvant therapy	
Polychemotherapy	15
Radiotherapy + polychemotherapy	1
Adjuvant therapy	
Polychemotherapy	8
Radiotherapy	3
Radiotherapy + polychemotherapy	4
Resection type (according to Enneking)	
P1	6
P1-2	3
P1-3	5
P2-3	11
P2-4	1
P1+4	1
Regression after neoadjuvant treatment available for 4 osteosarcoma and 7 Ewing's sarcomas according to Salzer-Kuntschik	
Grade 1	2
Grade 3	3
Grade 4	4
Grade 5	2
Surgical margins	
Wide	20
Marginal	4
Intralesional	3
Oncological outcome	
No evidence of disease (NED)	15
Alive with disease (AWD)	5
Died of disease (DOD)	7

4. Discussion

In the operative treatment of malignant tumors in the pelvis, limb-salvage surgery, combined with chemo- or radiotherapy, showed similar survival, recurrence, and complication rates as well as an improvement in the quality of life of the patients when compared to hindquarter amputation [16, 17]. The overall survival of patients with a pelvic sarcoma is often far worse than for those with one in an extremity [18, 19]. This poor prognosis may be partially attributable to the fact that pelvic sarcomas are often diagnosed in an advanced stage, when the tumor is more likely to be large in size [2, 17]. As studies have shown that limb-salvage techniques and the amputation show no difference in terms of the survival rate of patients with malignant bone tumors, the limb-salvage techniques are now being frequently used even for cases of advanced tumors. Tumor size and localization are the determining factors when it comes to decide which reconstruction technique is employed following limb sparing surgery. The bony defect in type I resections can be reconstructed with autograft fibula, cortical or pelvic allograft, or bone cement. The advantages of replacing the resected bone are pelvic stability and maintenance of limb length. No formal reconstruction is required for type III resections [16]. The hip transposition technique involves refixation of the inferior part of the acetabulum to the preserved bone into an artificial capsule that is attached to the intact proximal bone (ilium or sacrum).

In our series, acceptable functional results, with an average MSTS score of 16 could be achieved after a median of 33 months prospective followup examination. Thus our results are comparable to the findings in the literature [9, 10, 20]. Compared with MSTS scores after hemipelvic endoprosthesis reconstruction our results are equal [9, 21]. Because of the fact that hemipelvic megaprosthetic replacement is associated with a high complication rate and the fixation of the megaprosthesis in the pelvic bone as well as loosening of the prosthesis are still major problems, we recommend the biological reconstruction using hip transposition [13] or reconstruction of the pelvic stability by bone autografts [10].

The indications for pelvic reconstruction include young patients, resection of weight-bearing or -moving elements (such as the hip joint), primary sarcomas, and solitary pelvic bone metastasis in patients with "favorable" cancers such as thyroid, renal, and breast cancer with long life expectancies [22]. From the oncological point of view the outcome of the patients with a primary pelvic tumor should be differentiated from that of patients with a metastasis. In our study the survival did not differ significantly. The rate of metastasis in our study is similar to the one reported by other authors, potentially reflecting more biological aspect of the disease than the operative approach [2, 10, 23]. When the lesion is small but causes destruction of the hip joint, a hip replacement can be performed. However, implant stability may be impaired by the cancer and/or any postoperative chemotherapy or radiation therapy. When cancer has destroyed the acetabulum to the extent that it is no longer a contained defect, more extensive surgical procedures are necessary. In these cases, en bloc resection of the diseased bone is performed, using the same surgical principles to achieve tumor-free margins of resection as for primary bone tumors, and perform hemipelvectomy [23, 24]. Although these procedures are associated with increased morbidity and mortality rates that require longer hospitalization and rehabilitation [21, 25], we consider this approach for appropriate when locally advanced disease precludes internal stabilization. Limited data are available regarding the survival of patients with solitary pelvic metastases [24, 25]. Patients with solitary pelvic metastases seem to have favorable survival times, thus we think this may justify consideration of a radical surgical approach. However, it is not proven that major surgeries are related with an improved survival compared to curettage in patients with pelvic metastases [26].

5. Conclusion

The use of limb-salvage pelvic resections has increased with the advances in imaging and surgical techniques and instrumentation. However, pelvic surgery for malignant bone tumors remains challenging because of the complex anatomy and the extent of tumor growth.

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Research Article

Reconstruction of the Distal Radius following Tumour Resection Using an Osteoarticular Allograft

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Reconstruction of the distal radius following tumour resection is challenging and various techniques are recorded. We retrospectively analysed the outcome of five patients (one male and four females) after reconstruction of the distal radius with osteoarticular allograft, following tumour resection. Mean followup was 32 months (range, 4–121). In three of the five patients the dominant limb was affected. Mean bone resection length was 6.5 centimetres (range, 5–11.5). Two grafts developed nonunion, both successfully treated with autologous bone grafting. No infection, graft fracture, or failure occurred. Mean flexion/extension was 38/60 degrees and mean pronation/supination was 77/77 degrees. The mean Mayo wrist score was 84 and the mean DASH score was 8, both representing a good functional result. Therefore we state the notion that osteoarticular allograft reconstruction of distal radius provides good to excellent functional results.

1. Introduction

Although the distal radius is an untypical location for primary bone malignancies, about 10 percent of all giant cell tumour (GCT) affects this part of the skeleton. It represents the third most common location after the distal part of the femur and the proximal part of the tibia [1–4].

In recurrent or local aggressive cases of GCT as well as in malignant lesions, resection and subsequent reconstruction of the distal radius is indicated [2–4]. Reconstruction is challenging due to the high functional demands on the hand. Common reconstruction techniques include arthrodesis with different autografts [1, 5–9], prosthetic replacement [10–13], ulnar translocation [5, 14], arthroplasty using (vascularised [8, 15] or nonvascularised [5, 16–18]) autologous fibula graft, or osteoarticular allograft reconstructions (Figure 1) [5, 16, 17, 19–25].

Functional outcome as well as durability is of high importance, as affected patients are generally young with high functional demand due to their long life expectancy. Therefore, we reviewed our experience in osteoarticular allografts to assess durability, complication rates, and functional outcome of this reconstruction method.

2. Material and Methods

We started with searching our database for patients who received an osteoarticular allograft for reconstruction of the distal radius after tumour resection and determined age at operation, followup, resection length, complications, and revision procedures from those patients' records. General operation procedure included first, preparation and resection of the tumour including osteotomy in respect of compartmental structures. Second, preparation of the allograft and fixation of the plate on the allograft is required before; third, the plate-allograft unit is implanted and fixated to the host radius. Finally the capsule, ligaments, and eventually resected tendons are reconstructed by end to end anastomoses of the relevant anatomical structures of allograft and host.

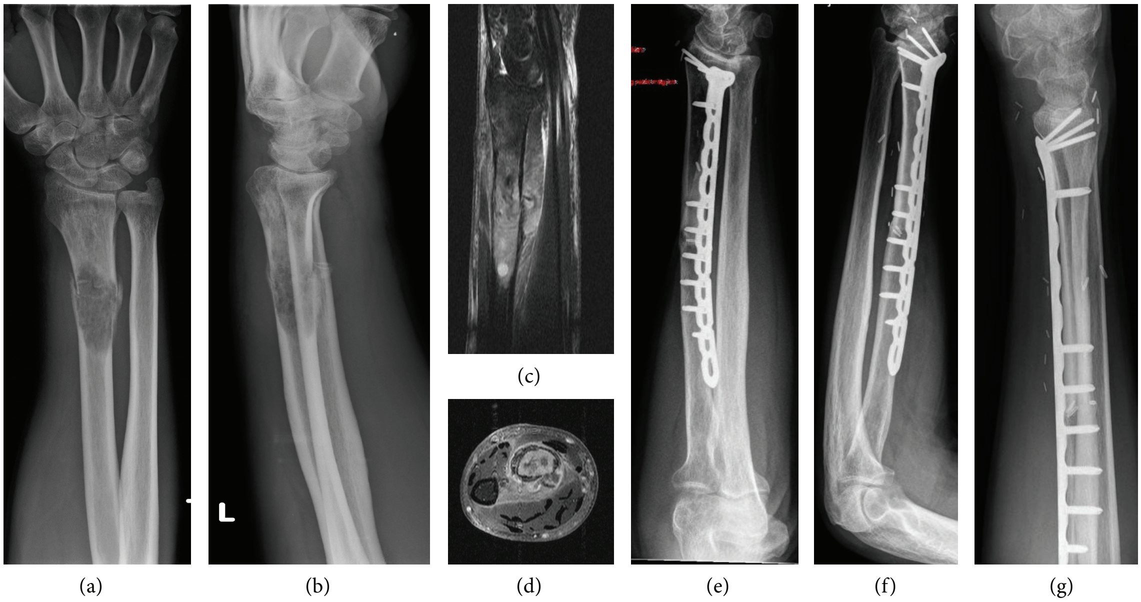

Figure 1: (a–g). Preoperative X-ray (a-b) and MRI (c-d) of a 64-year-old patient with osteosarcoma of the left distal radius; X-ray 22 months after replacement with allograft (e–g).

Mayo wrist score and DASH score were used to evaluate functional outcome. The Mayo wrist score is an objective evaluation of function by comparing range of motion with the healthy side and examining grip strength and pain. A maximum score of 100 points is attainable and results are classified as excellent (91–100), good (80–90), fair (65–79), and poor (below 65). The DASH score measures general function in daily life by 30 items scored from 1 to 5, with 1 standing for no disability and 5 for maximum disability. The end score is converted to a scale from 0 to 100 where 0 implies no disability and 100 maximum disability.

Statistical analysis was done by using descriptive methods, as means and proportions, appropriate to the type of data.

3. Results

From 2000 to 2011 five patients, one male and four females, with a mean age of 42 years (range, 22–64) received an osteoarticular allograft reconstruction of the distal radius. Four reconstructions followed en bloc resection of a giant cell tumour and one was done after wide resection of an osteosarcoma (Figures 1 and 2).

In three of the five patients the dominant limb was affected. Mean bone resection length was 6.5 centimetres (range, 5–11.5) and mean followup was 32 months (range, 4–121). Two patients developed nonunion at the allograft-host junction, which was successfully treated with autologous bone grafting. No infections, fractures, or fixation failures occurred.

Two patients with giant cell tumour were primarily treated with curettage and polymethylmethacrylate filling, but they experienced local recurrence. Therefore en bloc resection and subsequent reconstruction with an osteoarticular allograft was performed.

The mean flexion/extension was 38/60 degrees and the mean pronation/supination was 77/77 degrees. The mean Mayo wrist score was 84 and the mean DASH score was 8, both representing a good functional result (**Figure 3**).

At followup none of the patients expressed pain and everyone could return to prior work.

4. Discussion

In a recently published clinical trial phase II, Denosumab, a RANK ligand inhibitor, achieved excellent results in treatment of GCT of the bone. In this study Denosumab significantly reduced or eliminated RANK-positive tumour giant cells and also reduced the relative content of proliferative, densely cellular tumour stromal cells, replacing them with nonproliferative, differentiated, and densely woven new bone. Denosumab continues to be studied as a potential treatment for GCTB [26].

At time of operation of our four patients with GCT, alternatives like Denosumab were not available. Because of tumour extension including cortical breakthrough and relatively high recurrence rates at this location, en bloc resection was the method of choice [2–4].

A skeletal defect of the distal part of the radius following tumour resection is challenging. Reconstruction as well as functional restoration is required. In patients who need a strong and stable wrist to deal with high loads, for example, manual workers, arthrodesis is the method of choice. Arthrodesis provides stability at the expense of wrist motion, which further might cause some impairment in daily life activities. Nevertheless, good postoperative results are

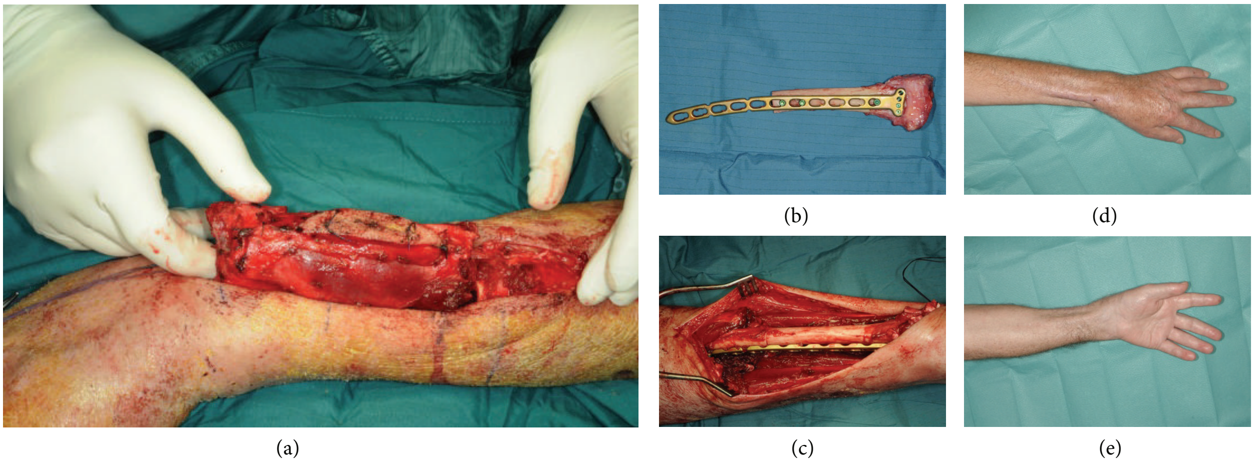

FIGURE 2: Allograft implantation in the left distal radius after resection of an osteosarcoma in a 64-year-old patient (a–c) and postoperative functional result 7 months after operation (d-e).

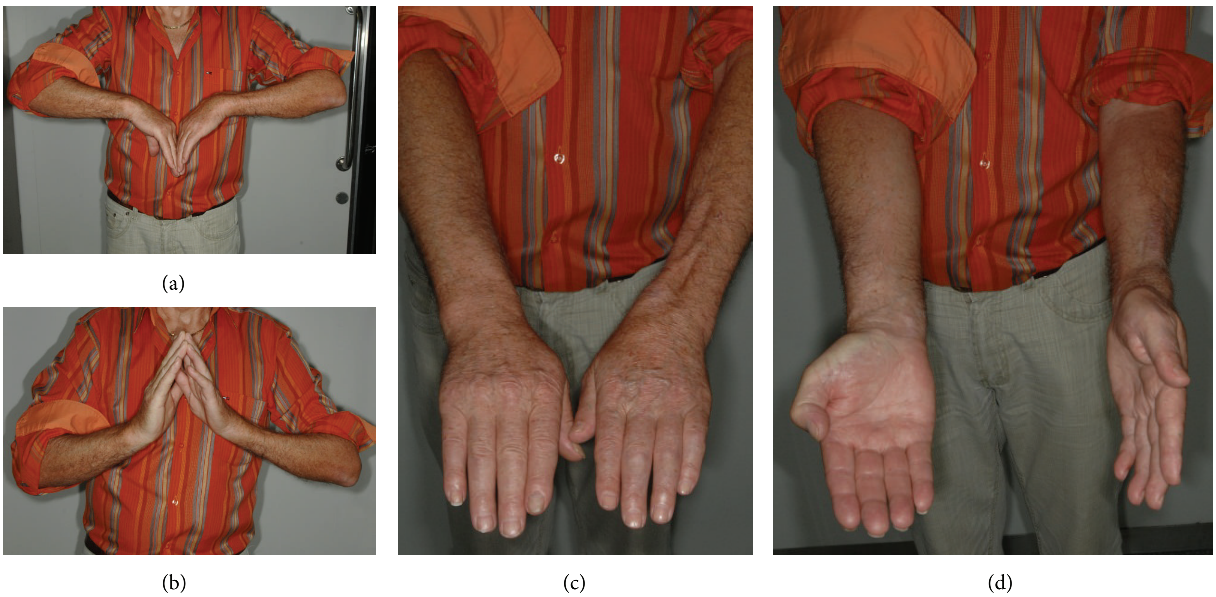

FIGURE 3: (a–d). Postoperative functional result 18 months after allograft implantation in the left distal radius after resection of an osteosarcoma in a 64-year-old patient.

reported in the literature with satisfying wrist function with little to no restrains [1, 5–9].

In order to preserve some wrist motion partial arthrodesis, with graft fixation only to the scapholunate portion of the carpal row, can be performed. This method provides a stable and pain-free wrist with sufficient range of motion for daily life activities [27, 28], wherefore it is recommended by Muramatsu et al. [27], especially for young patients.

In attempt to preserve full wrist function the proximal fibula (vascularised or nonvascularised) is sometimes used for arthroplasty due to its similarity in shape and size to the distal radius. Additionally, in children the vascularised fibula provides the possibility of epiphyseal transfer and further longitudinal growth, avoiding radial club hand development. Fibula arthroplasty achieves good to excellent functional results with satisfying range of motion, but instability and degenerative change of carpofibular joint are frequently observed. Despite these complications, in most cases only minimum pain and little limitation in daily living are observed [5, 8, 15–18, 28–30]. The low level of pain is suspected to be a result of denervation of wrist joint during surgery. First, articular degeneration seemed to result from a lack of viability in nonvascularised fibula grafts. Vascularised fibula grafts, however, provide viable articular cartilage, but nevertheless, this cannot prevent joint degeneration due to the relatively incongruence of fibulocarpal articular surfaces [5, 8, 15–18, 28–30].

Osteoarticular allografts, however, offer best anatomical match with the first carpal row and avoid donor side morbidity. Further, the operation time is shorter in comparison

Table 1: Osteoarticular allograft reconstructions at distal radius: comparison of results.

	Patients	Followup (months)	Nonunion	Infection	Fracture	Instability	Failed	Survival	Flex/ext [°]	Pron/sup [°]
Presented results	5	32 (3,7; 121)	2 (40%)	0	0	0	0	100% at 3 years	38/60	77/76,7
Scoccianti et al. [19]	17	58,9 (28; 119)	2 (11,8%)	0	2 (11,8%)	4 (23,5%)	1	94,1% at 4,9 years	56/58	80/84
Szabo et al. [20]	9	100 (39; 219)	0	1 (11%)	1 (11%)	0	0	100% at 3,5 years	26/52	80/67
Bianchi et al. [21]	12	52 (26; 145)	1 (8,3%)	0	0	7 (58,3%)	1	91,7% at 4,3 years	51/37	n.s.
Kocher et al. [22]	24	130,8 (25; 268)	0	0	6 (25%)	0	8	66% at 10,9 years	36/21	72/58
Asavamongkolkul et al. [17]*	8	52,7 (41,5; 90,9)	2 (25%)	0	1 (12,5%)	0	1	87,5% at 4,4 years	35/40	50/70
Vander Griend and Funderburk [5]*	1	36	0	0	1	1	1		n.s.	n.s.
Gitelis et al. [23]*	4	80,5 (43; 105)	0	0	0	1 (25%)	0	100% at 5 years	39/51	n.s.
Harness and Mankin [24]*	15	228	2 (13,3%)	0	n.s.	2 (13,3%)	4	73,3 at 19 years	n.s.	n.s.
van Isacker et al. [25]*	2	149.5	0	0	0	0	1	50% at 12,5 years	n.s.	n.s.

Range and percentages in brackets.
* Also other reconstruction methods than osteoarticular allografts had been used in these series.
n.s.: not specified.

with autografts. Good to excellent functional outcome can be achieved; nevertheless complications are still common. In contrast to allograft reconstructions at other locations, infection is rare in osteoarticular reconstructions of distal radius [5, 16, 17, 19–25]. Only Szabo et al. [20] observed one minor infection (Table 1) [17, 19–22, 24, 25], whilst the incidence of fractures and nonunion reaches up to 25% for both [17, 19–22, 24, 25].

In our patients all grafts were fixed with a long bridging plate and no patient suffered from an allograft fracture. Therefore, we assume that a long bridging plate presents a supportive tool to prevent fractures [16].

The relatively avascular host bed at the wrist probably favours nonunion. Two of our five patients (40%) developed nonunion, but they could be successfully treated with additional autologous bone grafting. As a possible cause we identified the use of below elbow casts for postoperative immobilisation and changed this regime to above elbow casts for the last two patients for six weeks.

The most frequent complications observed in arthroplasties with osteoarticular allografts are joint instability and articular degeneration [16, 17, 19–25]. None of the five patients in our series developed any form of instability, but recorded incidences in the literature are quite high. Cheng et al. [16] even found in all of their four study patients a translocation of the graft. In most cases only mild instability occurs without disabling patients in their working or daily life activities. Failure due to instability is rare, but instability accelerates degeneration of articular surface. Szabo et al. [20] additionally performed the Sauve-Kapandji procedure in their osteoarticular allograft reconstructions to prevent instability and found no form of joint instability at a medium followup of 8.3 years.

Degenerative changes of articular cartilage were observed in nearly all cases, but most patients reported none to only mild pain or disability and only few had to be revised due to arthritic disorders [16, 17, 19–25]. We found degenerative changes in all five patients but all were asymptomatic.

The long-term outcome and survival rates of osteoarticular allografts for distal radius still have to be studied. Our paper, as well as other studies, with short to medium followup, recorded low failure rates. Kocher et al. [22] presented the study with the longest followup of 10.9 years. They reported an average reconstruction failure of 33% after 8.1 years mean followup. This might indicate that osteoarticular allografts deteriorate with time. Long-term observations are needed to assess the real durability of this reconstruction type.

Reconstruction of the distal part of radius with prostheses as a contingent alternative to bone grafts is scarcely reported and the early attempts with them were not encouraging [10, 11]. Hatano et al. [12] reported about two reconstructions with ceramic prosthesis over ten years. Both developed radial deviation and radiolucent lines but had no clinical symptoms and achieved acceptable range of motion and function of wrist and hand. Because of radial deviation and slight instability, the author would not recommend prosthetic reconstruction in cases with more extensive soft tissue involvement to prevent subluxation and dislocation. Natarajan et al. [13] used a new designed bipolar hinge custom prosthesis in 24 patients and achieved satisfactory functional outcome and a 10-year prosthetic survival of 87.5%. Further investigations are necessary to obtain more information for considering a prosthetic reconstruction as an acceptable alternative to bone grafts.

In conclusion, although there are some problems with joint degeneration and instability, the complication rate of osteoarticular allografts is relatively low and this reconstruction method of the distal radius provides good to excellent outcome in terms of function, durability, and avoidance of donor side morbidity.

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Clinical Study

Allograft Reconstruction for the Treatment of Musculoskeletal Tumors of the Upper Extremity

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In comparison with the lower extremity, there is relatively paucity literature reporting survival and clinical results of allograft reconstructions after excision of a bone tumor of the upper extremity. We analyze the survival of allograft reconstructions in the upper extremity and analyze the final functional score according to anatomical site and type of reconstruction. A consecutive series of 70 allograft reconstruction in the upper limb with a mean followup of 5 years was analyzed, 38 osteoarticular allografts, 24 allograft-prosthetic composites, and 8 intercalary allografts. Kaplan-Meier survival analysis of the allografts was performed, with implant revision for any cause and amputation used as the end points. The function evaluation was performed using MSTS functional score. Sixteen patients (23%) had revision surgery for 5 factures, 2 infections, 5 allograft resorptions, and 2 local recurrences. Allograft survival at five years was 79% and 69% at ten years. In the group of patients treated with an osteoarticular allograft the articular surface survival was 90% at five years and 54% at ten years. The limb salvage rate was 98% at five and 10 years. We conclude that articular deterioration and fracture were the most frequent mode of failure in proximal humeral osteoarticular reconstructions and allograft resorption in elbow reconstructions. The best functional score was observed in the intercalary humeral allograft.

1. Introduction

Excisions of a bone tumor in the upper extremity may result in a large residual osseous defect and the loss of periarticular soft-tissue stabilizers of the shoulder [1–10], elbow [11, 12], or wrist [13–15] with potentially deleterious effects on both function and viability of the limb. For these locations, there are different reconstructions options including prosthetic devices [3, 5–7], biological constructs either with autografts [5, 6] or allografts [1–15], or the combination of allograft with prosthesis [7–11].

Reconstruction with a massive allograft is preferred in our service due to the possibility of obtaining supporting mechanical loads and the ability to attach host ligaments and muscles to the grafts.

The purpose of this study was to investigate the survival of allograft reconstructions in the medium to long term, to determine factors associated with their failure, and to analyze the final functional score compared to the anatomical site and the type of the reconstruction.

2. Patients and Methods

From January 1990 to December 2008, we performed a consecutive series of 72 patients with a musculoskeletal tumor from the upper limb who underwent reconstruction with a massive allograft. Two patients were excluded due to a lack of adequate followup data, leaving 70 cases for analysis.

Of the 70 reconstructions, 38 were osteoarticular allografts, 23 were allograft-prosthetic composites (APC), and 9 were humeral intercalary allografts. Of the 38 osteoarticular reconstructions, 21 were of the proximal humerus (Figure 1), 16 were of the distal radius (Figure 4), and one of the distal humerus. Of the 23 allograft-prosthetic composites, 16 were proximal humeral reconstructions (Figure 2), and 7 were elbow reconstructions (Figure 3).

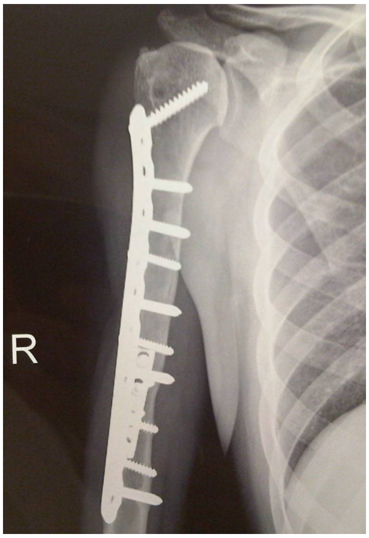

Figure 1: Anteroposterior radiograph of an osteoarticular allograft of the proximal humerus after 5 years of reconstruction.

Figure 2: Anteroposterior radiograph of an APC of the proximal humerus showing adequate union of the junction.

Figure 3: Anteroposterior radiograph of an APC of the elbow after resection of the proximal ulna.

Figure 4: Anteroposterior radiograph 16 years after distal radius osteoarticular reconstruction. Although degenerative changes are evident, the patient is asymptomatic with excellent function.

Demographic data, diagnosis, site of the neoplasm, operations performed, surgical complications, outcomes after surgery, date of last followup evaluation, and local recurrence were reviewed for all patients.

There were 38 men and 32 women in the study group. The mean age at presentation was 32 years (range 4–71 years). The most common indication for reconstruction was chondrosarcoma in 18 patients, followed by osteosarcoma in 15, giant cell tumors in 15, metastasis in 6, Ewing sarcoma in 5, chondroblastoma in 2, and others types of tumors in the remaining 9 patients. The mean duration of followup was 5 years for patients who survived the original disease (range 1–20 years).

Postoperatively, patients were seen at 1 week, 2 weeks, 1 month, 2 months, 3 months, and then every 3 months thereafter until 2 years, after which we met annually. Beginning 1 month after the operation, we obtained plain radiographs at every visit. We performed functional evaluation using the revised 30-point functional classification system established by the MSTS [16], which assessed pain, function, emotional acceptance, hand positioning, dexterity, and lifting ability. Each variable was assessed on a 5-point scale. Function was compared according the anatomical site and the type of reconstruction performed. Surgical complications were defined according to the Clavien-Dindo classification [17] that separates complications in five grades: Grade I, any deviation from the normal postoperative course without the need for pharmacologic treatment or surgical, endoscopic, and radiographic interventions, with acceptable therapeutic regimens including drugs, such as antiemetics, antipyretics,

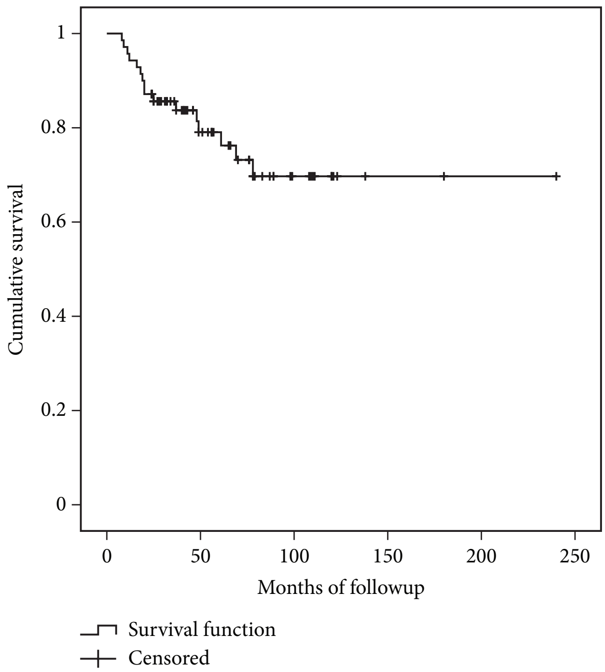

Figure 5: Allograft survival.

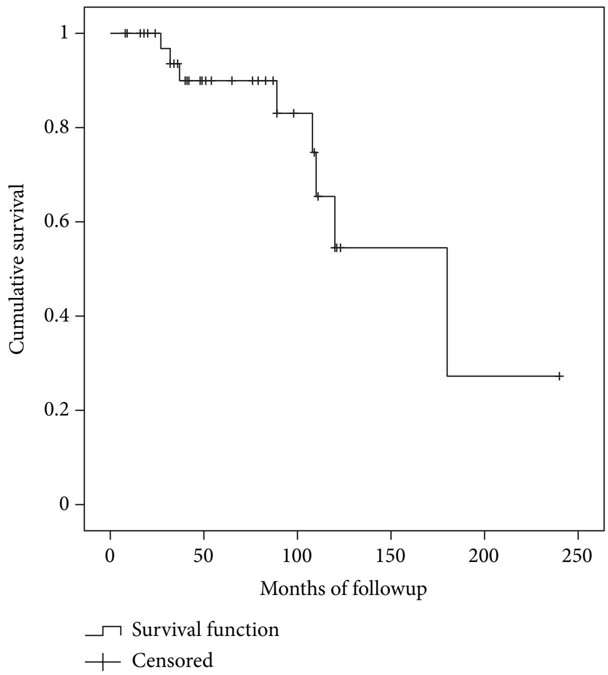

Figure 6: Articular surface survival.

analgesics, diuretics, electrolytes, and physiotherapy; Grade II, complication requiring pharmacologic treatment with drugs other than those allowed for Grade I complications; Grade III, complication requiring surgical, endoscopic, or radiographic intervention; Grade IV, life-threatening complication; and Grade V, death of a patient. We analyzed only Grades III, IV, and V complications in this series.

We considered an allograft to have failed when it was removed through either a revision procedure or an amputation, and in osteoarticular reconstructions, we considered a joint to have failed when the allograft was not removed, but symptomatic degeneration of the joint was present at the last followup.

The rates of survival of the allograft, the limb, and the joint surface were estimated with the use of the Kaplan-Meier method, starting on the date of the operation and ending on the date of removal, amputation, or the latest followup. Cox regression analysis was done to determine whether age, gender, diagnosis, type, and site of the reconstructions were independent prognostic factors. The log-rank test was used to compare the survivorship curves. A P value of <0.05 was considered to be significant.

3. Results

Allograft survival (Figure 5) at five years was 79% (CI95%: 68%–90%) and 69% (CI95%: 55%–83%) at ten years for failure from any cause as the end point (Figure 1). The limb survival rate was 98% at five and 10 years (CI95%: 94%–100%).

We identified 22 patients with complications requiring a second surgery (32%), including 7 local recurrences, two deep infections, 5 fractures, 5 resorptions, and 3 nonunions. However, only in 16 patients (23%) the allograft was removed (4 local recurrences, 5 resorptions, 2 infections, and 5 fractures) (Table 1). In 6 patients the allograft was not removed (3 local recurrences in soft tissue and the 3 nonunions).

Seven patients had local recurrences. Three recurrences were in the soft tissue and were resected with wide margins; in these three cases the reconstructions were not revised, so the allograft reconstruction was not affected. In four patients the allograft was compromised by the local recurrence. In these four cases the graft was removed with the local recurrence and only two of them were reconstructed. One was reconstructed with a new allograft (distal radius) and the other with a proximal humerus endoprosthesis. The remaining two patients were treated with a resection arthroplasty and with an amputation (both of them located in the humerus).

Two patients had an acute deep infection, in which the allograft was removed, and a temporary cement spacer with antibiotics was implanted. After 6 weeks of intravenous antibiotics and another 6 weeks of oral antibiotics, we reimplanted another allograft in one patient (wrist arthrodesis), and the other patient was reconstructed with proximal humeral prosthesis.

Five patients suffer an allograft fracture, and all occurred in proximal humeral osteoarticular reconstructions. All patients required a second operation, including a second allograft reconstruction with an APC in 3 patients, a second osteoarticular allograft in one, and a cement spacer in the remaining patient.

Five patients had allograft resorptions, all of them occurred after an elbow reconstruction (four APCs and one osteoarticular allograft). Of the failed elbow reconstructions,

Table 1: Allograft complications according the different types of reconstructions.

Reconstruction	Local recurrence	Infection	Fracture	Resorption	Nonunion	Total (%)
PHOA	2	—	5	—	—	33%
PHAPC	1	1	—	—	2	25%
HIA	1	—	—	—	—	11%
ER	1	—	—	5	—	75%
DROA	2	1	—	—	1	25%

PHOA: proximal humerus osteoarticular allograft; PHAPC: proximal humerus allograft prosthetic composite, HIA: humeral intercalary allograft; ER: elbow reconstructions; DROA: distal radius osteoarticular allograft.

Table 2: Mean MSTS functional results comparison of different types of reconstructions.

Reconstruction	Pain	Function	Emotional acceptance	Hand positioning	Dexterity	Lifting ability	Total
PHOA	4	3	4	3	5	4	23
PHAPC	4	4	5	3	5	4	25
HIA	5	5	5	5	5	5	30
ER	3	4	4	4	5	4	24
DROA	4	4	5	5	5	5	28

PHOA: proximal humerus osteoarticular allograft; PHAPC: proximal humerus allograft prosthetic composite, HIA: humeral intercalary allograft; ER: elbow reconstructions; DROA: distal radius osteoarticular allograft.

two were converted to an elbow endoprosthesis, two had a resection arthroplasty, and one had a cement spacer.

The three patients who underwent nonunion were treated with autologous bone graft and a new plate, without revision of the reconstruction.

The articular surface survival (Figure 6) of the group of patients treated with an osteoarticular allograft was 90% (CI95%: 79%–100%) at five years and 54% (CI95%: 39%–69%) at ten years (Figure 2). All symptomatic articular deteriorations occurred in the proximal humeral reconstructions, and none of them required revision because of this event.

The only independent prognostic factors that were found to be significant on Cox regression analysis, with revision for any cause as the end point, were the gender of the patient (more frequent in males: $P = 0.02$).

For the patients who retained the reconstruction (54 cases), the mean MSTS functional score at last followup was 26 of 30 (83%, range 18–30). The best mean functional score was observed in the intercalary humeral allograft group. (mean 30: 100%). The worst functional score was observed in proximal humeral osteoarticular allograft group (23 points, range 18–26), and this lower score was mainly related with patients who had a significant articular deterioration (Table 2).

4. Discussion

In comparison with the lower extremity, there is relatively paucity literature reporting survival and clinical results of allograft reconstructions after excision of a bone tumor of the upper extremity. We include in this report all reconstructions done in the upper extremity done in our unit.

There are some limitations to this study. This is a retrospective study with a relatively low number of patients and followup. In addition, there are many variables related to the anatomic location of the reconstructions. Despite these limitations, we believe that this series is one of the largest series reported in the literature, and our results may provide some trends in the treatment of massive bone defects in the upper limb.

Regarding anatomical site, most publications are related to the proximal humerus. Osteoarticular allografts are used less frequently than in the lower extremity, but there are reports regarding this type of reconstruction in the proximal humerus. Although some authors reported satisfactory results with osteoarticular allografts of the proximal humerus [1] and survival rates of 78% at five years [2], recent reports suggest that better or at least similar results are obtained with allograft prosthesis composite and endoprosthesis reconstructions regarding reconstruction survival and complications [3–8]. Peabody [4] report that due to functional limitations as well as an extremely high rate of complications, they do not use osteoarticular allografts to replace the proximal aspect of the humerus. However, in a recent report [7] that analyzed 38 reconstructions of the proximal humerus the endoprosthetic group presented the smallest complication rate of 21%, compared to 40% in the allograft prosthesis composite and 62% in the osteoarticular allograft group. However, in another report that analyzed 45 patients [5] reconstructed after tumor resection of the proximal humerus they found that all limb-salvage procedures for the proximal humerus were satisfactory for long-term survival, but none of the 26 disease-free surviving patients was able to abduct their shoulder more than 90°, and only five could achieve active abduction of more than 30°. The survival rate was 83% for endoprosthesis, 79% in clavicula prohumero, and 75% in osteoarticular allograft [5].

Reconstructions with APC in the proximal humerus avoid problems of endoprosthesis or osteoarticular allografts used alone [8–10]. In our series the higher amount of fractures occurred at shoulder reconstructions with osteoarticular allografts, and these complications could be avoided with an APC. In recent reports [8, 10] there are not differences regarding complications or survival with other methods.

Although, reports on elbow reconstructions [11, 12] showed satisfactory functional outcome and survival, both reports included trauma and tumor patients. In our series, we found high complication rate (75%) and a mean functional score of 24 points. Five of seven patients' present allograft resorption, and this complication was noted in previous report [12].

All distal radius reconstructions in this series were osteoarticular allografts. In our series we found low complication rate (19%) and high functional score (28 points). Similar results are found in the literature [13–15]; however, all series include a high percent of patients with benign tumors (GCT). This could lead to less damage of soft-tissue structures and better survival of the patient and reconstruction. Although degenerative changes are reported [14], these are usually asymptomatic (Figure 4).

The lower complication rate and the best mean functional score were observed in the intercalary humerus allograft group. Van Isacker et al. [18] report in a series of forearm allograft similar results, they found that intercalary allograft had fewer complications than osteoarticular allografts, and they had a better functional MSTS score.

5. Summary

This study showed that allograft reconstruction after a tumor resection of the upper limb may be durable, with a 69% survival rate at ten years. Despite the 32% incidence of complications, only 16 patients (23%) required an allograft removal and were considered as failures. We conclude that articular deterioration and fracture were the most frequent mode of failure in shoulder reconstructions and allograft resorption in elbow reconstructions. The humeral intercalary allografts had the lesser complication rate and the best functional score.

Conflict of Interests

Each author certifies that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interests in connection with the submitted paper.

Disclosure

Each author certifies that his institution has approved the reporting of this study, and that all investigations were conducted in conformity with ethical principles of research.

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Clinical Study

Comparison between Constrained and Semiconstrained Knee Allograft-Prosthesis Composite Reconstructions

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Allograft-prosthesis composite (APC) can restore capsular and ligamentous tissues of the knee sacrificed in a tumor extirpation. We asked if performing APC would restore knee stability and allow the use of nonconstrained arthroplasty while preventing aseptic loosening. We retrospectively compared 50 knee APCs performed with non-constrained revision knee prosthesis (Group 1) with 36 matched APCs performed with a constrained prosthesis (Group 2). In Group 1, the survival rate was 69% at five and 62% at ten years. Sixteen reconstructions were removed due to complications: eight deep infections, three fractures, two instabilities, one aseptic loosening, one local recurrence, and one nonunion. In Group 2, the survival rate was 80% at five and 53% at ten years. Nine reconstructions were removed: 3 due to deep infections, 3 to fractures, and 3 to aseptic loosening. In both groups, we observed more allograft fractures when the prosthetic stem does not bypass the host-donor osteotomy ($P > 0.05$). Both groups had mainly good or excellent MSTS functional results. Survival rate and functional scores and aseptic loosening were similar in both groups. A rotating-hinge APC is recommended when host-donor soft tissue reconstruction fails to restore knee instability. The use of a short prosthetic stem has a statistical relationship with APC fractures.

1. Introduction

The potential benefits of allograft-prosthesis composite (APC) include restoration of bone stock, possible reattachment of tendons to the graft, and improved longevity through load-sharing properties of the allograft [1–3]. The ongoing challenge is choosing the most appropriate implant for this type of reconstruction. Constrained implants provide the needed stability for arthroplasty in the presence of a deficient soft-tissue envelope. However there is a requisite transmission of grater forces to the fixation interfaces, which may lead to premature aseptic loosening [4, 5]. A posterior-stabilized or semiconstrained revision knee arthroplasty is usually contraindicated in knees with severe metaphyseal bone loss and instability [3, 6, 7]. Nevertheless, when the less constrained device is combined with a massive allograft stabilizing soft tissue elements may be sufficient [8–10]. If stability is not maintained, problems of edge loading, aseptic loosening, and fracture may ensue. Each type of articulation has theoretic advantages and disadvantages.

The type of arthroplasty device to be used is determined by how much stability is lost from the tumor resection [8–10]. If a significant amount of the collateral ligaments is taken with the tumor, a constrained articulation, such as a rotating hinge, may be indicated. Nevertheless, if a minimum amount of soft tissue must be sacrificed or soft tissue reconstruction restores stability, a less constrained device, such as a constrained condylar knee, may potentially be chosen. Only small series of patients who have undergone these procedures have been reported [8–13], and the competing techniques have not been compared.

Given the lack of outcome data of using these kinds of reconstructions, we compared the experiences of similar patient populations at two orthopedic oncology centers utilizing either a constrained or nonconstrained prosthesis in patients treated with knee APC. We therefore determined (1) the overall APC survival and (2) the differences in survival between constrained and nonconstrained APCs, (1) to identify and compare complications associated with failure in each different group and (2) and to assess functional results.

2. Materials and Methods

Between January 1989 and August 2008, we retrospectively reviewed 93 consecutive cases collected from two different Orthopaedic Oncology Services' databases. A minimum followup time of 2 years was required for inclusion, unless failure occurred earlier. We excluded 7 patients. Five of them died of disease before 2 years of followup and the remaining 2 cases were lost before 2 years of followup. The duration of followup was calculated from the surgery to the date that the patient was last seen (for asymptomatic patients) or the date of death, amputation, or revision surgery. This left 86 patients in the study.

Patients were divided into two groups: those who received a nonconstrained APC (Group 1: 50 patients) and those who received a constrained APC (Group 2: 36 patients).

In Group 1 (nonconstrained APC), the reconstruction was indicated for a revision of another reconstruction in 26 cases, tumor resection in 22 cases, and traumatic bone loss in 2. Twenty-eight were distal femur and 22 proximal tibia APC reconstructions. Most of the distal femoral APCs were indicated for a fracture of osteoarticular allografts or when femoral attachments of the cruciate ligaments were involved by the tumor. Proximal tibia APCs were indicated mainly for extensor mechanism reconstruction in skeletally mature patients, when tibial attachment of the cruciate ligaments was involved by the tumor, and for resurfacing of a failed osteoarticular allograft. Thirteen patients in this group received chemotherapy. The average followup in Group 1 was 69 months (range, 8 to 141 months). Demographics data are shown in Table 1.

Surgical technique for Group 1 (Figures 1 and 2): through an extended anterior-medial approach, the tumor resection or the extraction of the previous reconstruction was made, preserving as much as possible the patient's soft tissue insertions. No extra-articular resection was performed in this group. All prostheses utilized in this group were nonconstrained modular revision prostheses. For APC fixations, different techniques were performed. In 23 patients the reconstruction consisted in prosthesis cementation in the allograft and implanted without cement in the residual tibial or femoral diaphysis without an osteosynthesis plate. In 27 patients a compression plate was placed to improve contact and stability at the host donor osteotomy. However, in 11 of 27 patients, a short stem that did not bypass the host-donor osteotomy was utilized, so fixation was only with the osteosynthesis plate. The corresponding component was cemented into the host bone on the opposite side of the joint. The prostheses utilized in this group were Coordinate Revision Knee System (DePuy, Warsaw, IN) in 11 cases, Scorpio TS Revision Implant (Stryker Orthopaedics, Mahwah, NJ) in 12, Sigma PFC Revision Implant (DePuy, Warsaw, IN) in 6, Next Gen LCCK Revision Implant (Zimmer, Warsaw, IN) in 6, Continuum Knee System (CKS) in 4 (Stratec Medical, Oberdorf, Switzerland), and Genesis II Implant (Smith & Nephew, Memphis, TN) in 11.

Nonirradiated fresh-frozen allografts were used as previously described [15]. After the assembling of the allograft-prosthesis composites and the receiver, the host posterior capsule and the collateral ligaments were sutured to corresponding ligaments of the graft. In seven patients the medial collateral ligament was too short to be reattached, and in 2 patients the lateral collateral ligament also was too short to be reattached to the corresponding structure. In those patients almost the entire medial and lateral ligaments were replaced with the ligament provided by the allograft. In all the proximal tibial reconstructions, the extensor mechanism then was reconstructed to the corresponding tissue of the allograft using a previously described technique [16].

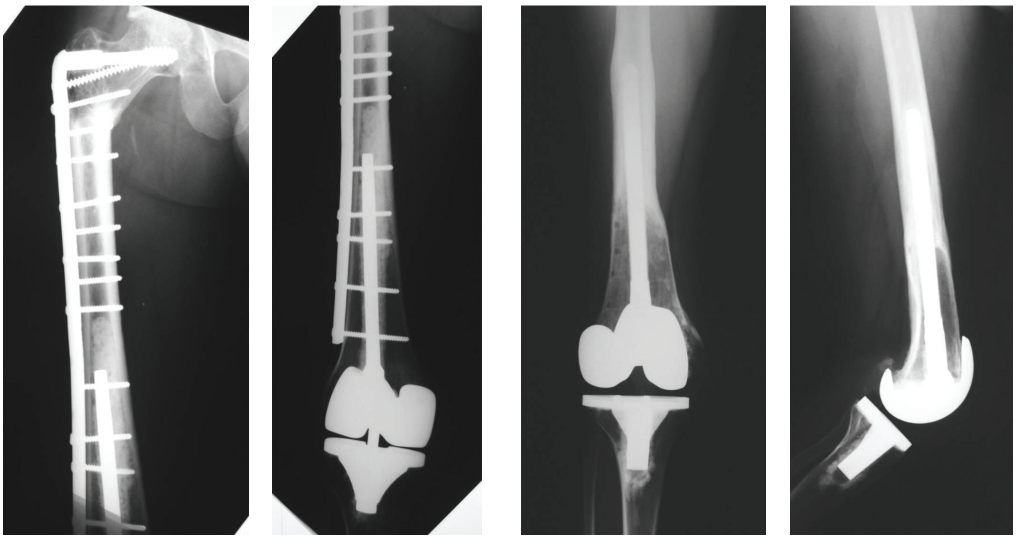
In Group 2 (constrained APC), the reconstruction was indicated for a revision of tumor endoprosthesis in 14 patients, revision of an osteoarticular allograft in three, and tumor resection in 19 cases. Most distal femoral APCs were indicated when the proximal femur was too narrow or short to receive an intramedullary stem. Proximal tibia APCs were indicated mainly in skeletally mature patients for extensor mechanism reconstruction. Fifteen patients received chemotherapy in this group. Nineteen were proximal tibia and 17 distal femoral APC reconstructions. The average followup in Group 2 was 75 months (range, 7 to 197 months). Demographics data are shown in Table 1.

Surgical technique for Group 2 (Figure 3): through an extended anterior-medial or anterior-lateral approach, the tumor resection or extraction of the previous reconstruction was made. An extra-articular resection was performed in four patients and intra-articular resection in 32. The standard technique of reconstruction with the composite prosthesis involves the use of a rotating hinge revision modular prosthesis cemented in the allograft and implanted in the residual tibial or femoral diaphysis with cement in 22 cases or without cement in 14 cases. The standard technique of reconstruction with the composite prosthesis involves the use of a rotating hinge revision modular prosthesis (Finn Knee prostheses; Biomet, Warsaw, IN) cemented in the allograft and implanted in the residual tibial or femoral diaphysis with cement in 24 cases or without cement in 12 cases. Of this series of 36 patients, only two patients received another type of hinge prosthesis. One had a custom-made Lane-Burstein (Biomet, Warsaw, IN) prosthesis and the other a Guepar prosthesis (Wright Medical, Arlington, TN). Three cases of this group had a short stem that did not bypass the host-donor osteotomy, so dynamic compression plates stabilized the graft-host junction.

Fresh-frozen nonirradiated allografts were used, and bacteriological and viral studies were performed in accordance with the recommendations of the American Association of Tissue Banks and the tests available at the time. Eleven patients were reconstructed with a telescope allograft technique [17].

Table 1: Differences between groups of APC knee replacements.

	Group 1 (nonconstrained APC)	Group 2 (constrained APC)
Number	50 patients	36 patients
Diagnostic (n)	Revision, osteoarticular allograft (20) Revision, knee prosthesis (6) Osteogenic sarcoma (8) Chondrosarcoma (7) Leiomyosarcoma (2) Fibrosarcoma (2) Giant cell tumor (2) Desmoplastic fibroma (1) Traumatic bone loss (2)	Revision, tumor endoprosthesis (14) Osteogenic sarcoma (11) Revision, osteoarticular allograft (3) Chondrosarcoma (3) Lymphoma (2) Soft tissue sarcoma (1) Malignant fibrohistiocytoma (1) Giant cell tumor (1)
Followup	69 months (range, 8–141 months)	75 months (range, 7–197 months)
Age	35 years old (range, 15–80)	35 years old (range, 8–84)
Sex	22 females; 28 males	18 females; 18 males
Location (n)	Distal femur (28) Proximal tibia (22)	Distal femur (17) Proximal tibia (19)



(a) (b)

Figure 1: Reconstructions performed for distal femur in Group 1. (a) Distal femoral APC with a short stem. (b) Distal femoral APC with a long stem.

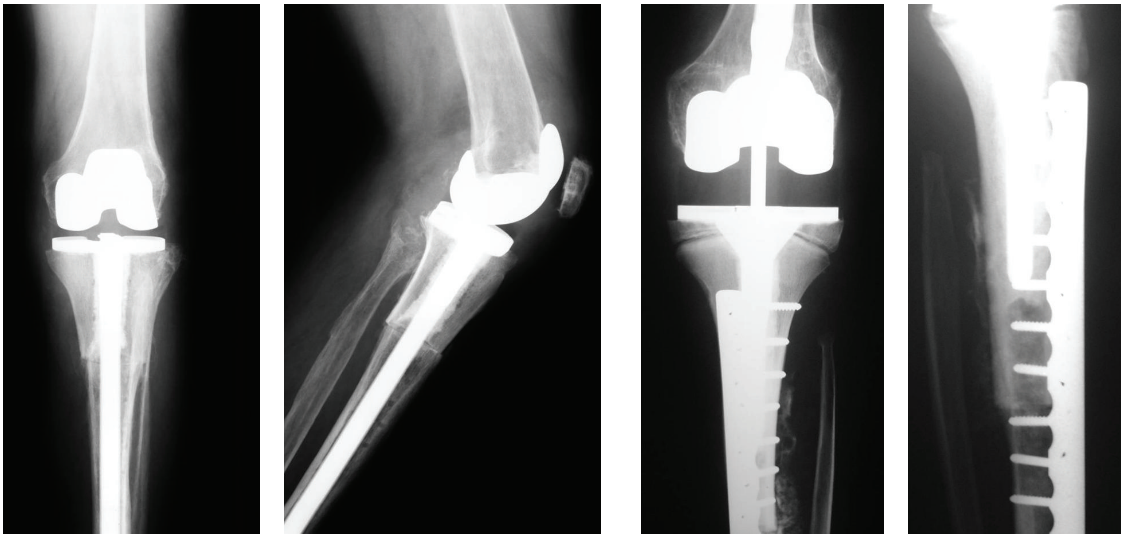
After the assembling of the allograft-prosthesis composites and the host, the capsule and the collateral ligaments were sutured when possible.

In all the proximal tibial reconstructions, the patellar tendon was repaired by direct suture overlapping the autologous proximal part onto the distal one provided by the graft, and a medial gastrocnemius rotation flap was performed in 16 of the 19 tibial reconstructions.

The functional evaluation was performed in both groups using the revised 30-point functional classification system established by the Musculoskeletal Tumor Society [18].

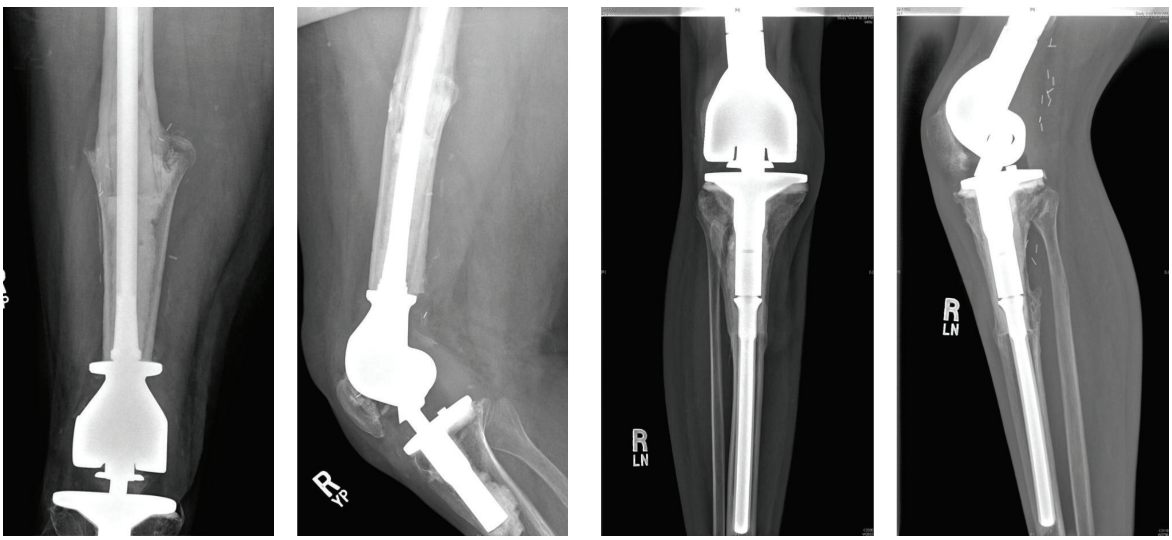
Surgical complications were defined according to the Clavien-Dindo classification [19] that separates complications in five grades: Grade I, any deviation from the normal postoperative course without the need for pharmacologic treatment or surgical, endoscopic, and radiographic interventions, with acceptable therapeutic regimens including drugs, such as antiemetics, antipyretics, analgesics, diuretics, and electrolytes, and physiotherapy; Grade II, complication requiring pharmacologic treatment with drugs other than those allowed for Grade I complications; Grade III, complication requiring surgical, endoscopic, or radiographic intervention; Grade IV, life-threatening complication; and Grade V, death of a patient. We analyzed only Grades III, IV, and V complications in this series.

2.1. Statistical Analysis. Survival of the different APCs was calculated using the Kaplan-Meier method. Differences in survival between groups were assessed with the log-rank test. To identify factors that affected the survival of the reconstructions a univariate analysis was carried out. A P value ≤ 0.05 was considered significant. We used SPSS 17.0 for Windows (Chicago, IL) for statistical analyses.



(a) (b)

Figure 2: Reconstructions performed for proximal tibia in Group 1. (a) Proximal tibia APC with a long stem. (b) Proximal tibia APC with a short stem.



(a) (b)

Figure 3: Standard reconstructions for Group 2. (a) Distal femoral APC. (b) Proximal tibia APC.

3. Results

The overall APC survival was 70% at five years (SE 5.4%) and 61% (SE 7,8%) at 10 years. The mean APC duration was 140 months for all patients (SE 9.7, 95% confidence interval, 121 to 159 months). Distal femur APCs survival was 73% at five years (SE 6.8%) and 48% at ten years (SE 12.2%). The mean APC duration was 97 months for this location (SE 7.6, 95% confidence interval, 81 to 112 months). Proximal tibial APCs survival was 75% at five years (SE 7.3%) and ten years. The mean APC duration was 156 months for this location (SE 11.8, 95% confidence interval, 133 to 180 months) (Figures 4 and 5).

In Group 1 (nonconstrained APC), the survival rate was 69% at five years (SE 6.7%) and 62% at ten years (SE 8.9%). The mean APC duration was 104 months for all patients (SE 7,5, 95% confidence interval, 89 to 119 months) (Figure 6). In this group, four patients had a minor medial instability and four had major instability. Three of the minor ligament instability needed no external support, and the remaining patient used a cane. Two patients had a major medial instability, and they were revised with hinge prosthesis. The other two major instabilities refused second surgery and used an external brace. Thus the allograft ligamentous reconstructions restored stability in 42 of 50 patients.

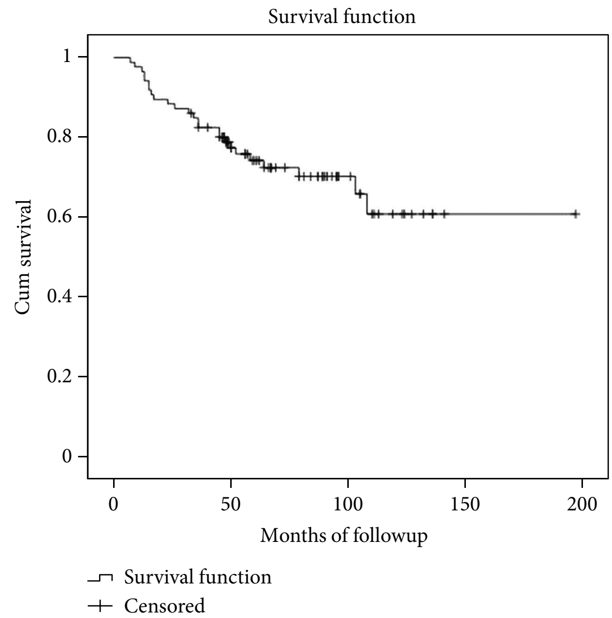


Figure 4: Kaplan-Meier curve showing the overall APC survival.

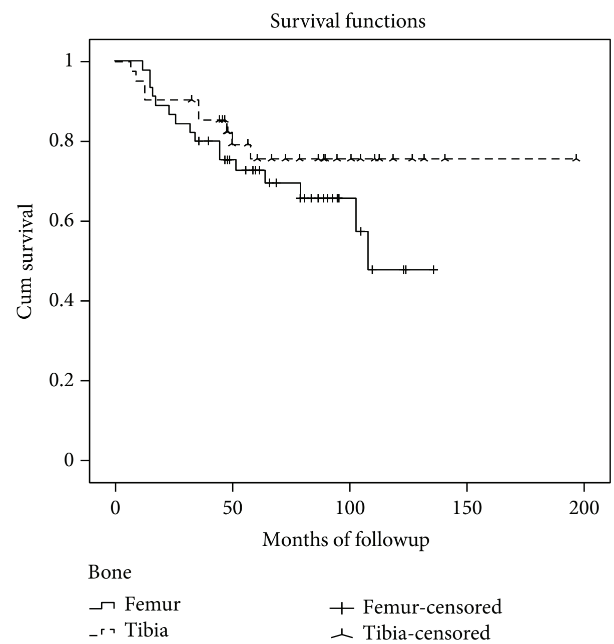


Figure 5: Kaplan-Meier curve showing the differences in APC survivorship according to the affected bone.

Sixteen reconstructions were removed due to major complications: eight deep infections, three fractures, two instabilities, one aseptic loosening, one local recurrence, and one nonunion.

Of the 8 patients with a deep infection, four were proximal tibia reconstructions and four distal femoral APCs. In two patients, amputations were required due to a persistent infection. The remaining six patients with an infected allograft were treated with resection of the allografts-prosthesis and

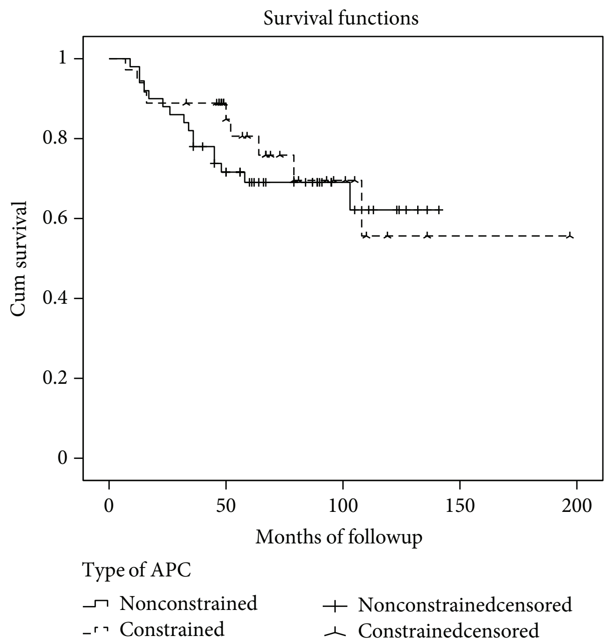


Figure 6: Kaplan-Meier curve showing the differences in APC survivorship between hinged and nonhinged knee replacements.

maintenance of limb length with an antibiotic-impregnated polymethylmethacrylate spacer. Antibiotics that were appropriate for the microorganisms that recovered from the site of the infected allograft prosthesis were administered for one to three months. After the infection was under control, a second limb-salvage procedure was performed in six patients. These included three knee endoprostheses, one new hinged APC, and two knee arthrodeses.

The APC was removed in three patients with a fracture, endoprostheses applied in two patients, and a new APC placed in the remaining patient. Two allograft fractures were in distal femoral and one in proximal tibial APC. All fractures-occurred in patients with a short stem (Table 3).

Both patients with a nonunion and with aseptic loosening were treated with a distal femoral endoprosthesis. The patient with a local recurrence was treated with an amputation.

Three other APC complications did not require removal of the allograft prosthesis including two peroneal nerve palsy (both after proximal tibial reconstruction) and one nonunion in a distal femoral reconstruction (treated with a new osteosynthesis and with autologous bone grafts).

Two patients died from tumor-related causes without APC failure after a two-year radiographic and functional followup was done.

For the patients who retained the APC (34 cases), the mean MSTS functional score at last followup was 25 of 30 (83.3%, range 10–30). For distal femoral APCs the mean score was 25 (83.3%, range 10–30) and 24.6 (82%, range 13–30) for proximal tibial APCs. Physical examination revealed that the arc of active motion of the knee averaged 94.4° (range, 45° to 120°). The mean extensor lag was 3.5° (range, 0° to 20°) (Table 4).

Table 2: Comparison of the results between groups.

	Group 1 (nonconstrained APC)	Group 2 (constrained APC)
Survival rate at 5–10 years	69%–62%	80%–53%
Failures	16 cases	9 cases
Cause of revision (*n*)	Deep infection (8) APC fracture (3) Instability (2) Nonunion (1) Aseptic loosening (1) Local recurrence (1)	Aseptic loosening (3) APC fracture (3) Deep infection (3)
Instability	8 cases	No cases

Table 3: Features of patients with fractures.

	Group 1 (nonconstrained APC)	Group 2 (constrained APC)
Fractures (*n*)	3	3
Stem	3 short stems	2 short stems,1 long stem
Prosthesis*	1 Coor, 1 PFC, 1 SN	1 Guepar, 1 LB (ls), 1 Finn
Plate fixation	All cases	2 cases (Guepar and Finn)
Stem fixation	None	1 case (LB ls)

Coor: Coordinate prosthesis; PFC: Johnson & Johnson prosthesis; SN: Smith & Nephew prosthesis; LB (ls): Lane-Burstein long stem.

Table 4: Comparison of mean functional scores between groups (Musculoskeletal Tumor Society).

Measure	Group 1 (nonconstrained APC)	Group 2 (constrained APC)
Pain	4.5	4.5
Function	3.8	3.7
Acceptance	4.4	4.5
Supports	4	4.1
Walking	4.3	4.4
Gait	3.9	3.9
Total score	25 (83.3%)	25.3 (84.3%)
Range of motion	94° (45° to 120°)	90° (25° to 120°)
Extensor lag	3.5° (0° to 20°)	8° (0° to 70°)

In Group 2 (constrained APC), the survival rate was 80% at five years (SE 7,3%) and 53% at ten years (14,7%). The mean APC duration was 138 months for all patients (SE 17, 95% confidence interval, 105 to 171) (Figure 6). There were 12 complications among 36 patients of which 9 were major requiring removal of the APC and 3 were minor and could be solved while retaining APC. Nine reconstructions were removed: 3 due to deep infections, 3 to fractures, and 3 to aseptic loosening.

Of the three patients with deep infection, all were distal femoral APCs. One of them had a previous reconstructive surgery. One of these patients was treated with resection of the APC and maintenance of limb length with an antibiotic-impregnated polymethylmethacrylate spacer. Several spacer exchanges were necessary to control the infection. Antibiotics appropriate for the microorganisms that recovered from the site of the infected APC were administered for several months. After the infection was under control, a total femur replacement was performed. In the remaining two patients an amputation was indicated due to persistent infection.

APC complications did not require us to remove the allograft prosthesis: one with polyethylene failure, one with superficial infection, and one with secondary reinforcement of the patellar tendon.

Of the three patients with fractures, in two, the APC was removed and a new APC applied, and in the remaining patient, an endoprosthesis was placed. Two allograft fractures were in distal femoral and one in proximal tibia APC. Two of them happened in patients with a short stem. The femoral fractures occurred in APCs performed with the Guepar and with the Lane-Burstein prostheses. The tibial fracture was in short-stem APC performed with Finn Knee prosthesis (Table 4).

The three patients with aseptic loosening were revised with a new APC in two patients and with a distal femoral endoprosthesis in one. In two patients, the failure occurred after five years of followup, and in the remaining one loosening happened at 19 months. All patients with aseptic loosening were distal femoral APC.

Five patients died from tumor-related causes without APC failure after a two-year radiographic and functional followup could be carried out.

The patients who retained the APC (27 cases), the mean MSTS functional score at last followup was 25.3 of 30 (84.3%, range 13–30). For distal femoral APCs the mean score was 26 (86.6%, range 21–29) and 24.9 (83%, range 13–30) for proximal tibial APCs. Physical examination revealed that the arc of active motion of the knee averaged 90° (range, 25° to 120°). The mean extensor lag was 8° (range, 0° to 70°). Two patients with extra-articular resection at the primary surgery showed the worst extension lag (50° and 70°) (Table 4). No patient had clinical instability.

Comparison of the two groups revealed that no statistical difference was observed in survival rates, functional scores, or number of complications and the incidence of aseptic loosening (Table 2). Group 1 showed a statistical relationship with residual knee instability ($P = 0.034$). In both groups, the use of a short prosthetic stem has a statistical relationship with APC fractures ($P = 0.0001$).

4. Discussion

Allograft-prosthetic composite combines a metallic implant with a large fragment allograft to reconstruct bone and joint deficiency [8, 12, 13]. This procedure has several potential advantages. By combining a metallic implant with an allograft, the surgeon has the option of replacing as many bones as necessary. In addition, by resurfacing the bone with an implant, allograft cartilage degeneration is not a problem.

The composite allograft also affords the opportunity for soft tissue attachment, thus making joint stability and functional recovery potentially greater [2, 13, 20].

We acknowledge some limitations of this study. This is a retrospective study with a relatively small number of patients with intermediate average followup, and thus it had limited ability to detect potential long-term differences between the groups, including survival and rates of individual complications. Given the relative rarity of this reconstructive problem and the unique surgical treatment for each individual, it would be difficult to obtain a longer series for more robust results. However, to our knowledge, this is the largest comparative study of alternative methods of knee APCs. Despite these limitations we could see some meaningful trends.

The overall APC survival was 70% at five years (SE 5.4%) and 61% (SE 7,8%) at 10 years. Distal femur APCs survival was 73% at five years (SE 6.8%) and 48% at ten years (SE 12.2%). Proximal tibial APCs survival was 75% at five years (SE 7.3%) and ten years. These survival rates are similar to those of other reconstructive techniques such as endoprosthesis or knee osteoarticular allograft [13, 14, 21–25]. Previous reports showed a worse survival rate in proximal tibial compared to distal femur reconstructions [11, 14, 21, 22, 24, 26]; nevertheless in this series, proximal tibial had a slightly better performance than distal femur APC reconstructions. No difference was observed in survival rates between both groups at five years.

In Group 1, infection was the main cause of failure. As reported in the literature, infection rate could be related to multifactorial causes. Common factors associated with infection in similar reconstructions include an extensive soft tissue dissection, compromised vascular supply, proximal tibial location, the immunosuppressive effect of chemotherapy, a long operating time, blood transfusion, and obesity [27]. However, the rates were not higher than those reported by other groups with just an osteoarticular allograft or endoprosthetic alone over the same time period [24, 26, 28, 29].

Aseptic loosening was observed in both groups, but was more frequent in the hinged APCs (3 cases: 8% versus 1 case: 2%), but these differences were not statistically significant. These failures may be related to the stress concentration at the stem-bone junction of hinged implants [4, 22, 23]. The use of a rotating-hinge mechanism may decrease torque transmitted to the implant interfaces [4, 6] but the forces still exceed those of a nonhinged prosthesis.

Instability was observed in nonhinged APCs. Of the six patients with instability, four of them had a minor medial instability and two patients had a major medial instability with indicatioan for revision surgery. In situations like extra-articular resections or massive resections of host ligaments, rotation hinged APCs can provide initial stability [10]; therefore nonhinged APCs should be avoided.

Several factors may have played a role in occurrence of allograft fracture: irradiation of the allografts [30], perforation of the cortex [31], and nonunion [32]. We found that utilization of a short stem was a risk factor for allograft failures in both groups even when an external plate was placed for APC fixation. Proximal tibia and distal femur allografts are very wide with a thin cortex at the metaphyseal level. Therefore, stress forces localized at the tip of the stem could fracture the APC even when an external plate is placed to support the allograft. Also, in Group 2, two of the fractures occurred in the more constrained prosthesis (Guepar and Lane-Burstein), and the only long-stem fracture was with the Lane-Burstein APC (Table 4).

The MSTS functional scores in our study were similar to similar reconstructive option [4, 8, 13, 14, 21–23].

In this study, survival rate and functional scores were similar in both groups. Aseptic loosening may have been lower in APC performed with a nonhinged prosthesis, but rotating-hinge APC is recommended when host-donor soft tissues reconstruction is insufficient to reestablish stability. The use of a short prosthetic stem that does not bypass the host-donor osteotomy has a statistical relationship with APC fractures.

Conflict of Interests

Each author certifies that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, and so forth) that might pose a conflict of interests in connection with the submitted paper. Each author certifies that his institution has approved the reporting of this study and that all investigations were conducted in conformity with ethical principles of research.

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