VIA MEDICA

REVIEW ARTICLE

Tomasz Goryń, Bartłomiej Szostakowski, Andrzej Pieńkowski

Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Institute — Oncology Centre, Warsaw, Poland

Advances in bone reconstructions after sarcoma resection

Address for correspondence:
Tomasz Goryń, MD
Klinika Nowotworów Tkanek Miękkich
Kości i Czerniaków
Centrum Onkologii — Instytut
im. Marii Skłodowskiej-Curie
ul. Roentgena 5, 02–781 Warszawa
e-mail: praktyka.goryn@wp.pl

Oncology in Clinical Practice
2018, Vol. 14, No. 6, 331–340
DOI: 10.5603/OCP.2018.0046
Translation: lek. Maciej Kawecki

ISSN 2450–1654

ABSTRACT

Primary malignant bone tumours, or sarcomas, are rare and represent a major diagnostic and therapeutic challenge. According to the EUROCARE database, they do not exceed 0.2% of all malignancies. According to the American Cancer Society, over 40% of primary bone tumours in adults are chondrosarcomas followed by osteosarcoma (28%), chordoma (10%) Ewing sarcoma (8%), malignant histiocytic sarcoma/fibrosarcoma (4%), and the remaining percentages is distributed among several types of rare bone tumours. In children and adolescents (< 20 years), osteosarcoma accounts for 56%, Ewing sarcoma 34% and chondrosarcoma only 6%.

The best treatment results of bone sarcomas are achieved with the use of combined therapy in highly specialised centres. This combined treatment within specialised multidisciplinary teams gives the patient the greatest chance for appropriate management of their disease and increases their chances to be cured and to avoid disability. Limb sparing surgery is currently a standard in surgical treatment of bone sarcomas. This approach helps to obtain a good functional result and limits the patient's disability. The most common methods currently used in sparing surgery include modular oncology endoprostheses (megaprostheses), non invasive growing prostheses used in children, bone auto and allografts, rotationplasties, patient specific surgical implants, arthrodesis of large joints, and in some locations only radical bone resections (shoulder, pelvis). In this short review article we present historical and contemporary methods of surgical treatment of primary bone sarcomas.

Key words: primary bone sarcomas, sparing treatment, megaprosthesis, patient specific surgical implants, custom made implants

Oncol Clin Pract 2018; 14, 6: 331–340

Introduction

Primary malignant tumours of bones, known as sarcomas, are an uncommon entity, problematic to both diagnose and treatment. According to the EUROCARE database, they represent only 0.2% of all cancers [1].

According to the American Cancer Society, chondrosarcomas constitute more than 40% of all primary bone cancers in adults. Other common subtypes are: osteosarcomas (28%), chordomas (10%), Ewing sarcomas (8%), and malignant histiocytic sarcomas/fibrosarcomas (4%). Less frequent sarcomas are mostly limited to a few types of rare bone sarcomas. In children and adolescents (< 20 years-old) 56% of sarcomas are osteosarcomas, 34% are Ewing sarcomas, and only 6% are chondrosarcomas [2].

Due to the low incidence of bone sarcomas, many (even specialised) physicians and general practitioners will not encounter any such case throughout their career. This limited knowledge regarding diagnosis and treatment of bone sarcoma may result in significant delays and errors in the therapeutic process.

Symptoms reported by patients are mostly unspecific. Usually, initial signs of the disease are underestimated by both patient and primary care physician. Depending on the patient's age, they are often mistaken for arthritis or inflammatory changes in older patients, or for injuries and overload changes in younger patients. This may lead to weeks or even months of delay in performing radiological imaging, done only after ineffective conservative treatment.

In early stages, the disease is restricted to bone only, without infiltration of local soft tissues. If the primary radiological imaging is limited only to ultrasonography (USG) or if the initial X-ray is incorrectly interpreted, the patient will receive the wrong treatment, delaying the therapeutic process and only advancing the stage of sarcoma. Such cases might require wider surgical resections, or even amputations as a local treatment, significantly impairing long-term prognosis.

If symptoms, such as joint or bone pains, are present for more than a few weeks, basic radiological imaging, including plain X-rays, are mandatory before initiating any kind of treatment. Any case suspected of bone sarcoma require transferring the patient to a reference centre for further diagnostic/therapeutic procedures.

As well as correct interpretation of radiological images, proper diagnosis and further treatment is based on a histopathological examination of a specimen acquired by a core-needle or open biopsy. The site and method of obtaining the biopsy specimen impact the planning of definitive limb-sparing surgery. If the biopsy is taken from an inappropriate site, further radical resection and subsequent reconstruction with an endoprosthesis might be difficult or even impossible [3].

The best long-term outcomes of bone sarcomas treatment are obtained with a multimodality treatment at highly-specialised centers, which provide the highest chances of cure and disability prevention.

Limb-sparing procedures are the current gold-standard of surgical bone sarcoma treatment. Extremity amputations are accepted only in the presence of a massive soft-tissue, vessel, or nerve infiltration, when patients' performance status is inadequate, or when salvage treatment after inappropriate initial treatment is required. Currently, only about 10% of patients require such procedures.

Long-term outcomes of limb-sparing procedures lead to better overall survival (OS) results when compared to amputations (mostly due to less advanced diseases), especially considering the lesser degree of disability and lower psychological burden associated with limb preservation techniques [4]. Nevertheless, the patient must be informed about specific complications related to implanted endoprosthesis and should receive continuous psycho-oncologic support.

Reconstructions after resection of sarcomas are a difficult challenge, even to experienced surgeons. Post-surgical bone detriment is usually accompanied by a significant loss of surrounding soft-tissues, conditioned by the necessity of achieving a proper surgical margin. An additional factor that increases risk of complications is pre- and post-operative systemic treatment, bringing an additional burden to the patient's organism and greatly impacting regenerative processes after surgery [5, 6]. Before the introduction of adjuvant systemic treatment, bone sarcomas were lethal in more than 80% of patients, and as a result of poor prognosis the surgical treatment was limited mostly to simple amputations [7, 8]. With improved prognosis and overall survival, post-treatment quality of life gained significant value. As a result, surgical procedures aimed at preserving limb functionality, limiting disability, and improving patients' quality-of-life were introduced.

Currently, limb-sparing procedures using bone implants or biological reconstructions are a standard of bone sarcoma treatment. The most common methods of reconstruction use either modular or custom-made prostheses. However, some cases require other methods, such as vascularised bone grafts or tumour resections only in feasible situations.

History of bone reconstructions in musculoskeletal system oncology

Use of implants as part of the reconstruction after bone sarcoma resection is not new. In 1896 Kronecher described the replacement of fibula affected by tumour with a prosthesis from ivory. Unfortunately, apart from a short description published in the doctoral thesis of Marcel Beaume in 1927, no detailed knowledge regarding the patient's fate is available [9].

Since the 1940s, multiple attempts to reconstruct osseous defects with metal implants as part of tumour treatment have been undertaken. Austin T. Moore, inventor of the most popular hemi-hip prosthesis used until today after hip fracture, is considered as a pioneer of reconstruction with megaprosthesis. In 1940 Austin T. Moore and Harold R. Bohlman, who originated usage of Vitallium alloy (cobalt-chromium-molybdenum), created a customised implant to reconstruct the proximal part of the femur for patients with hip fractures resulting from giant cell tumours of bone (GCTB). This procedure was the first of its kind, in which the whole proximal part of femur was replaced. The calculations necessary to develop the implant were drawn from the results of X-rays and led to the creation of wax models. The models were used to form a mould, which was used to produce 12-inch (30.5-cm) Vitallium implant that replaced the proximal extremity of the femur [10].

In 1952 in the Royal National Orthopaedic Hospital Sir Herbert Seddon implanted the first megaprosthesis of distal part of femur with simultaneous replacement of a knee — postsurgical fixed prosthesis of distal femur extremity and proximal tibia extremity — in a cancer-free patient suffering from bone echinococcosis. A similar type of prosthesis was used in 1954 in an 18-year-old patient with GCTB of distal femur extremity — the surgery was done by a team under the lead of Harold Jackson-Burrows and Prof John T. Scales [11, 12], and it took a whole day. As no intramedullary fixation nor bone cement was known at that time, the prosthesis was settled with cortical screws, inserted through holes in flange plates that were an integral part of the prosthesis. After the procedure the patient returned to normal functioning and was under routine orthopaedic supervision. In subsequent years she gave birth to several children and was able to walk them to school on a daily basis, covering a distance of approximately eight miles (~13 km) on foot.

Prof Rainer Kotz, a European pioneer of oncological reconstructions, introduced modular prostheses in the early 1980s. Upon a standard set of ready elements (modules), an appropriate length of prosthesis can be obtained to compensate for specific bone loss. The introduction of this kind of prosthesis accelerated further development of oncological bone surgery, expanding options of bone reconstructions compared to custom made prostheses. This pioneering idea is the basis of modern reconstructions, and modularity is commonly used by companies producing oncological implants for bone reconstructions [13, 14].

The first international symposium regarding limb-sparing techniques in surgical oncology of the musculoskeletal system took place in 1981 in Rochester. This incentive to spread modern knowledge about the treatment of primary bone tumours came from the Mayo Clinic team, partially due to a rising number of patients who required secondary procedures as a result of inappropriate primary treatment of bone and soft tissues sarcomas. During the first meetings, which took place in the 1980s, physicians and scientists from the whole world focused on technologies of fixating prostheses in bones, reconstructive techniques used after resections in the pelvic area, novel technologies in modular and custom-made prostheses, and the impact of chemotherapy on limb-sparing techniques and on adjuvant effects of proper cementing. The meeting constituted a solid basis for further advancements in limb-sparing surgery of musculoskeletal tumours [15].

Modern surgical and reconstructive procedures

Currently — just as in the past — the basic goal of surgical procedure is to achieve full resection of a tumour with a sufficient fragment of unaffected bone, allowing surgical margins within normal tissues (R0 resection). At the stage of surgery planning, it is essential to determine whether radical resection is obtainable. If there is no possibility of achieving adequate surgical margin and R0 resection, limb-sparing procedures or even whole surgical treatment should be abandoned. R2 resections (without macroscopic radicality) result in a significant deterioration of patients' prognosis, usually leading to a substantial disability, and therefore should be avoided. Radical resections require wide excision within normal tissues, with at least 2 cm of healthy bone margin recommended.

Maintaining a functional effect after resection and reconstruction is nearly as important as achieving R0 surgical margins. An adequately functioning limb should: provide proper structural support and prehensile capabilities, maintain both deep and superficial sensations, yield muscular system granting efficient limb mobility, and have sufficient cover with soft tissues of the reconstructed fragment.

The methods currently most often used in limb-sparing procedures include: modular endoprostheses dedicated to oncology (megaprostheses); expandable endoprostheses used in children; bone auto- and allografts; rotationplasty; arthrodesis of large joints; and in some locations (shoulder or pelvis) radical bone resection without reconstruction might be a feasible option.

With all the modern advancements in endoprosthesis development, especially the introduction of 3D printing, personalised implants (custom made) are more accessible. The application of new technologies allows reconstructions after more extensive resections of bones and joints. Unfortunately, the complex spectrum of technological nuances in implant production also has a negative effect. Incorrect qualifications due to the application of custom-made implants is becoming more common. Surgeons, tempted by the possibility of using 3D printing to create implants capable of reconstructing any bone detriment, often forget the basic rule of surgical oncology, i.e. obtaining a radical resection. Preserving limb functionality, albeit undoubtedly important, is not the primary goal of treatment.

Planning of a limb-sparing surgical procedure, with the exception of tumours involving pelvic structures, requires inclusion of patients' biological age and perspectives on rehabilitation. These procedures, with a extremly high risk of complications, require significant engagement of the patient, physician, and physical therapist in the postoperative period. Without the patient's cooperation and without proper rehabilitation, outcomes of surgical treatment remain unsatisfactory.

Tumour resection with a proper margin usually requires resection of the nearest joint. This kind of vast resection is a real challenge to reconstructive surgeons, especially considering the necessity of obtaining durable restitution of limb function.

Due to the extensity of resections, patients' performance status, sarcoma biology, and neoadjuvant treatment with chemotherapy, surgical treatment of osteosarcoma and Ewing sarcoma is associated with an increased risk of failure and significant complications. Many patients undergoing this treatment require reoperations, mostly as a result of complications or unfavourable disease course. The commonest indications for subsequent surgical treatment are: periprosthetic infections; aseptic or septic implant loosening; mechanical damage to the elements of the endoprosthesis; and local or distal sarcoma recurrences.

As important as the surgical treatment is the appropriate rehabilitation after reconstructive procedures, which supports patients in reaching adequate performance and functional status. However, functional outcomes after vast resections and reconstructions in oncology are generally inferior to those obtained after reconstructions due to arthritis.

The most important part of bone reconstructive procedures is precise preoperative planning, which facilitates avoidance of unplanned events during surgery and allows achievement of optimal reconstructive outcomes. An elementary condition required for the reconstruction, besides profound anatomical knowledge of involved site, is access to appropriate instrumentation, with a full availability of implants. A *sine qua non* condition of a responsibly planned reconstruction is proper preoperative radiographic imaging that includes plain radiography, magnetic resonance imaging (MRI), and computed tomography (CT).

Reflecting the most common localisations of bone sarcomas, the most common reconstructions involve the femur, with both its proximal and distal extremities, and proximal extremities of the tibia and humerus.

The common application of modular prostheses (post-resection megaprostheses) as a standard in bone and joint reconstructions after resections of sarcomas simplified and shortened the duration of reconstructive procedures. Simplicity of instrumentation and flexibility in the choice of implant length assure high quality of reconstructions and improve postoperative functional outcomes.

The introduction of titanium as a basic reconstructing material, implementation of hydroxyapatite to hasten endoprosthesis oosteointegration, and modern modifications of implants, such as addition of positive silver ions on the surface to lower infection risk in the post-operative period and during prosthesis osteointegration, all lead to improved quality of reconstructions and prolonged implant survival without a negative impact on functional outcomes.

One of the major problems in the treatment of bone sarcomas in children was growth of the skeletal system with the patients' age. Due to extensive postoperative bone decrement and further growth of the patient, usage of standard prostheses was limited by the necessity of subsequent reoperations. Some patients, who underwent standard prostheses implantation in early childhood, required several operational revisions with implantations of larger prostheses until the end of skeletal growth. The answer to this issue was the introduction of expandable endoprostheses. After initial technical difficulties, a new type of expandable endoprosthesis was introduced, with expansion done through a small transdermal incision with a dedicated chuck key. Further technological advancements led to the development of endoprostheses expanded completely noninvasively [16–18].

Figures 1–9 show examples of bone and joint reconstructions in the most common localisations of osteosarcoma, Ewing sarcoma, chondrosarcoma, and GCTB. Reconstructions in less common localisations, requiring dedicated endoprostheses, are also presented.

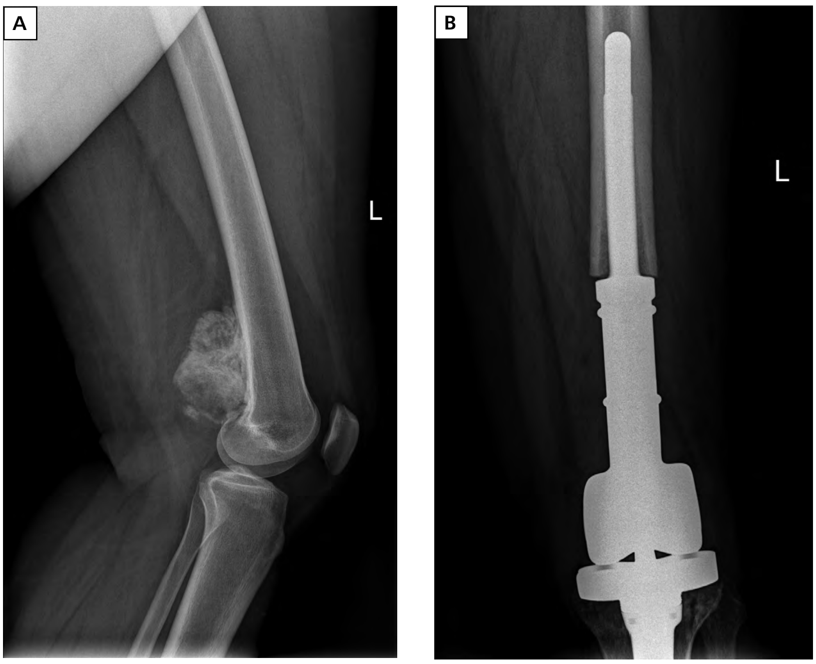

Figure 1. Chondrosarcoma located in the distal extremity of left femur: **A.** Preoperative imaging; **B.** Postoperative imaging

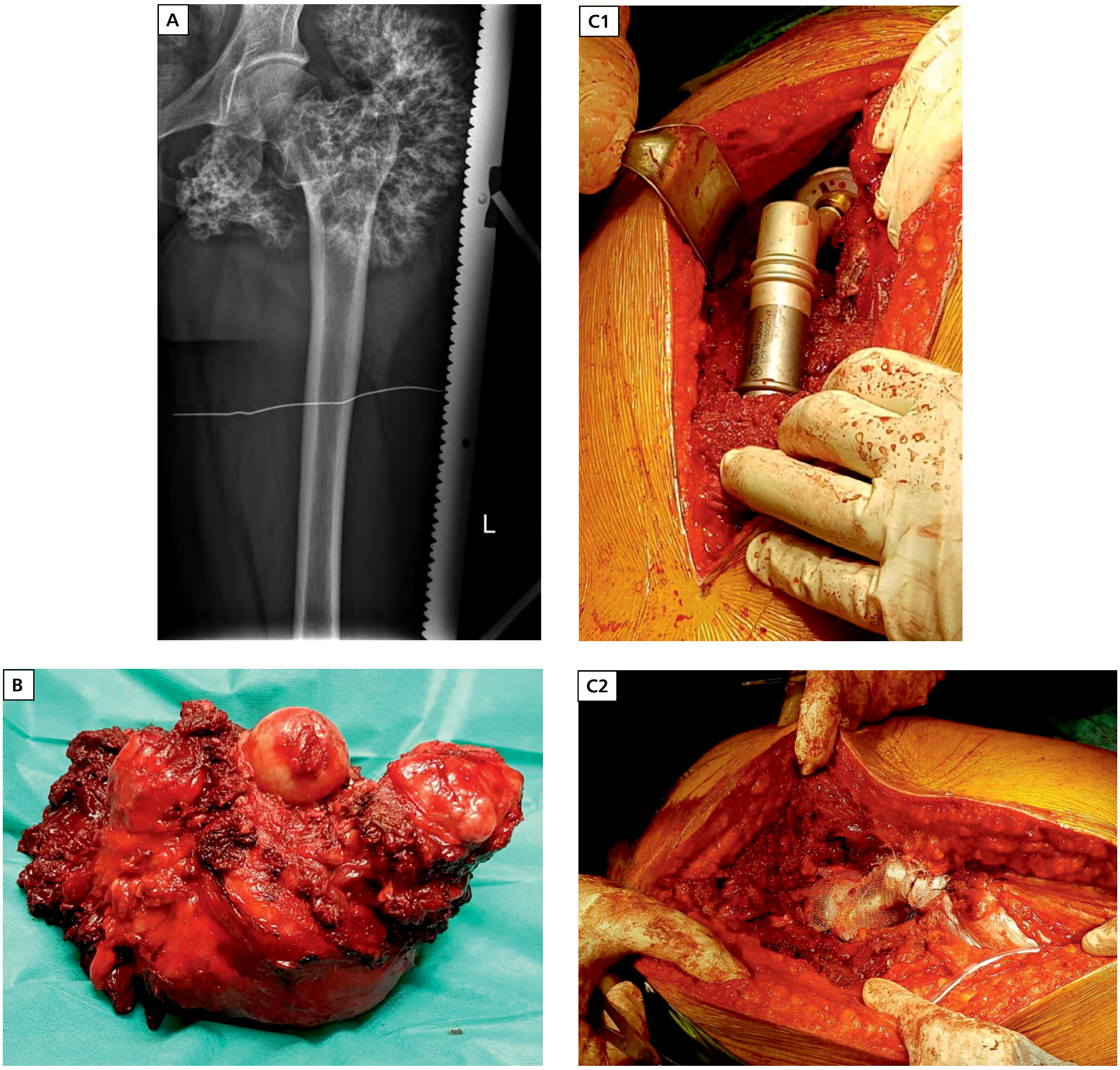

Figure 2. Extensive chondrosarcoma located in the proximal extremity of femur: **A.** Preoperative imaging; **B.** Picture of resected specimen; **C1**, **C2**, **C3.** Postoperative imaging

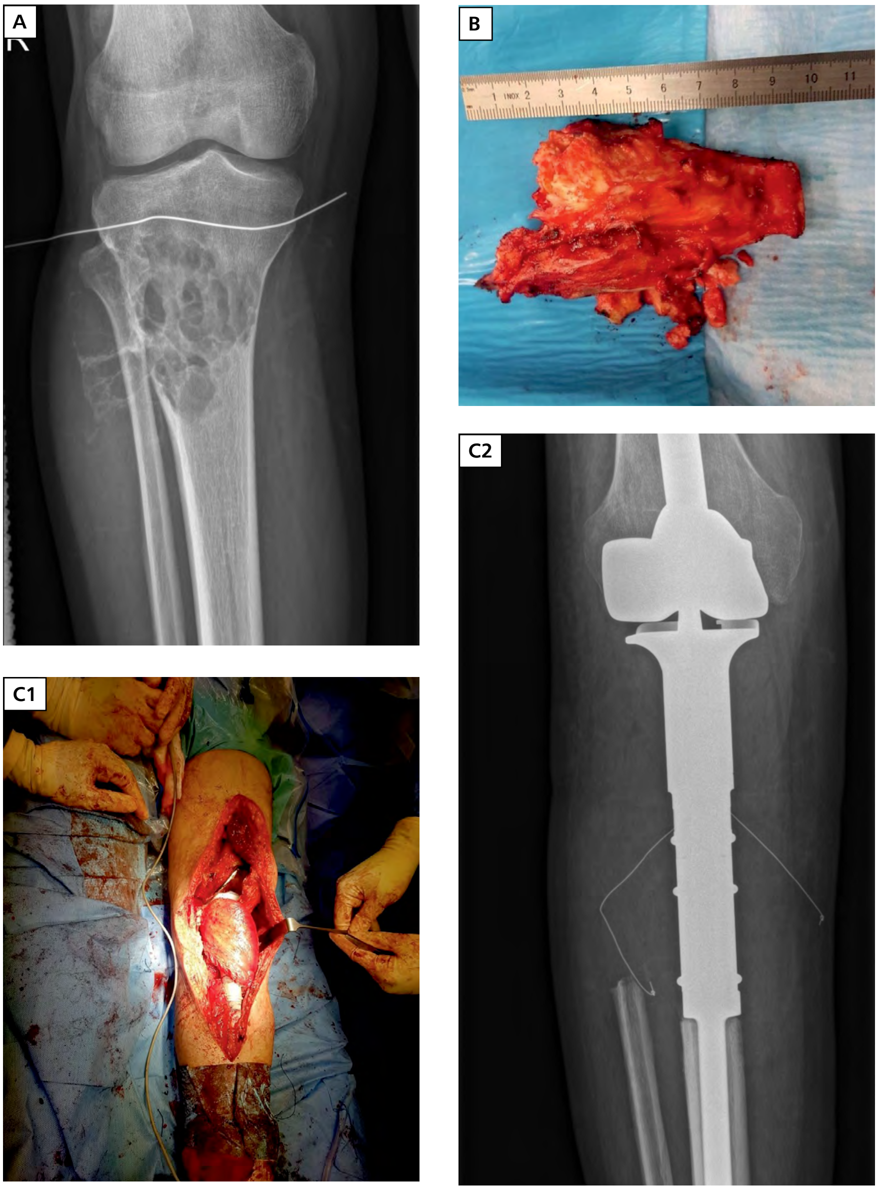

Figure 3. Giant-cell tumour of bone (GCTB) located in the proximal extremity of tibia: **A.** Preoperative imaging; **B.** Picture of resected specimen; **C1, C2.** Postoperative imaging

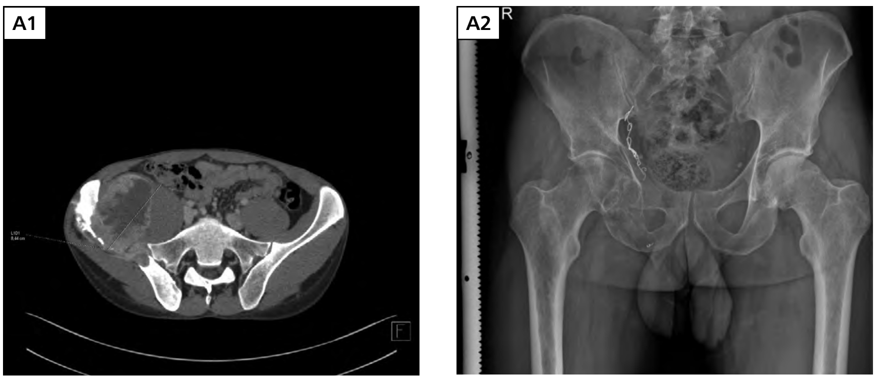

Figure 4. Osteosarcoma of the ilium: **A1, A2.** Preoperative imaging

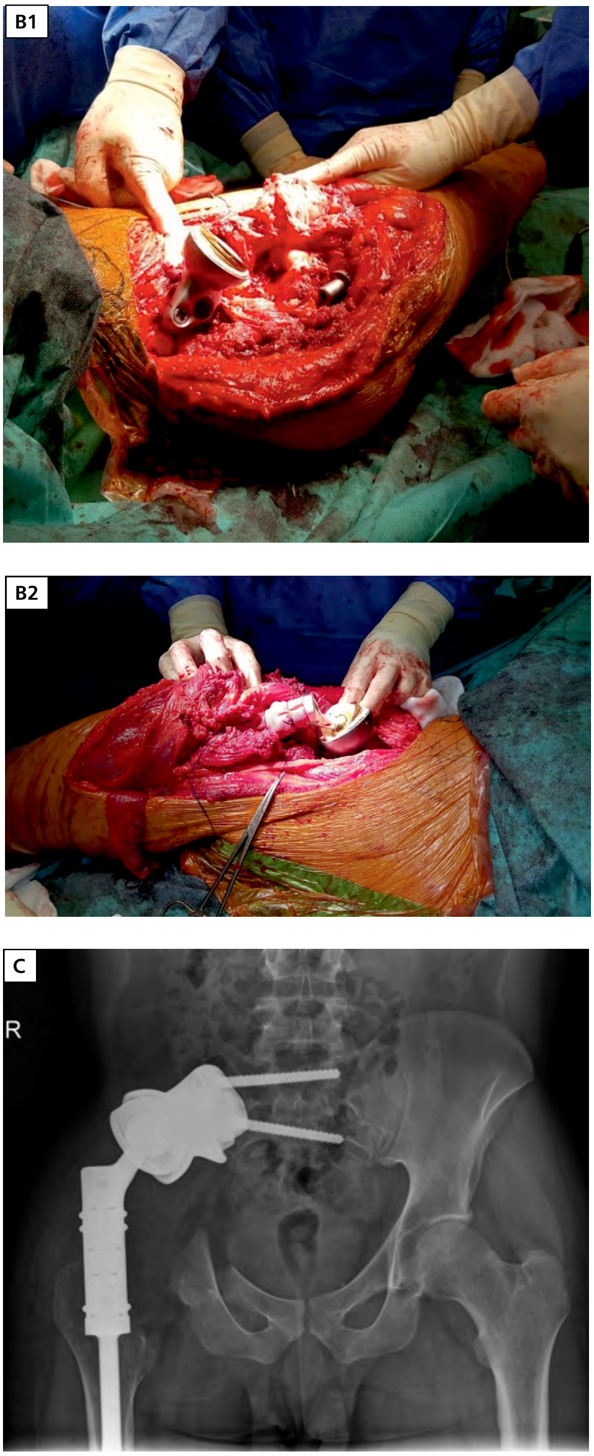

Figure 4. (cont.). Osteosarcoma of the ilium: **B1**, **B2.** Picture of resected specimen; **C.** Postoperative imaging

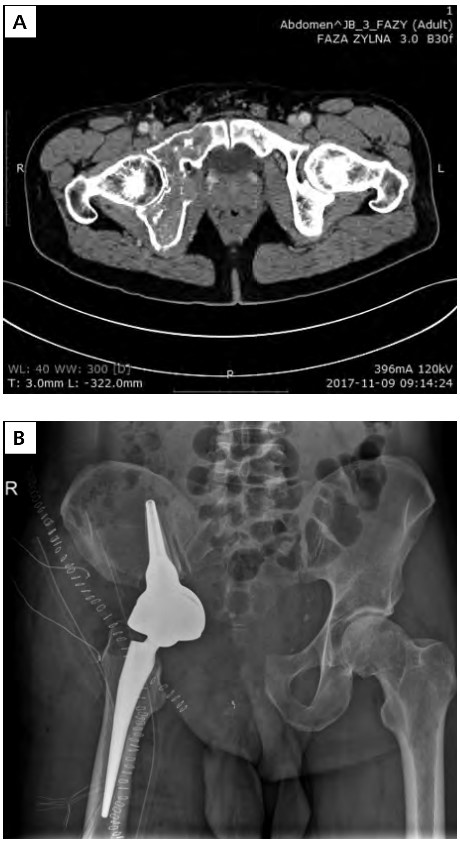

Figure 5. Chondroblastoma of the ilium: **A.** Preoperative imaging; **B.** Postoperative imaging

Figure 6. Giant-cell tumour of bone (GCTB) of the radius: **A.** Preoperative imaging; **B.** Postoperative imaging

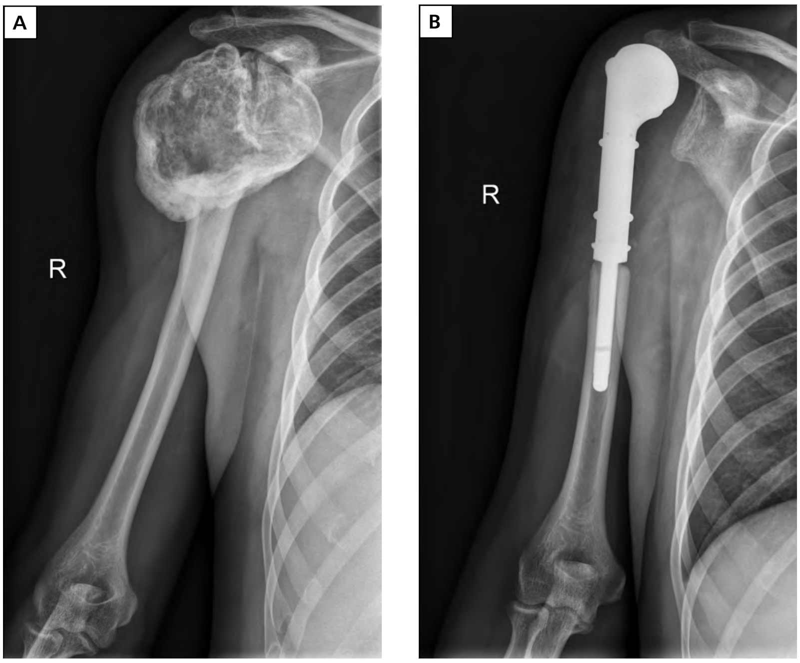

Figure 7. Osteosarcoma of the right humerus: **A.** Preoperative imaging; **B.** Postoperative imaging

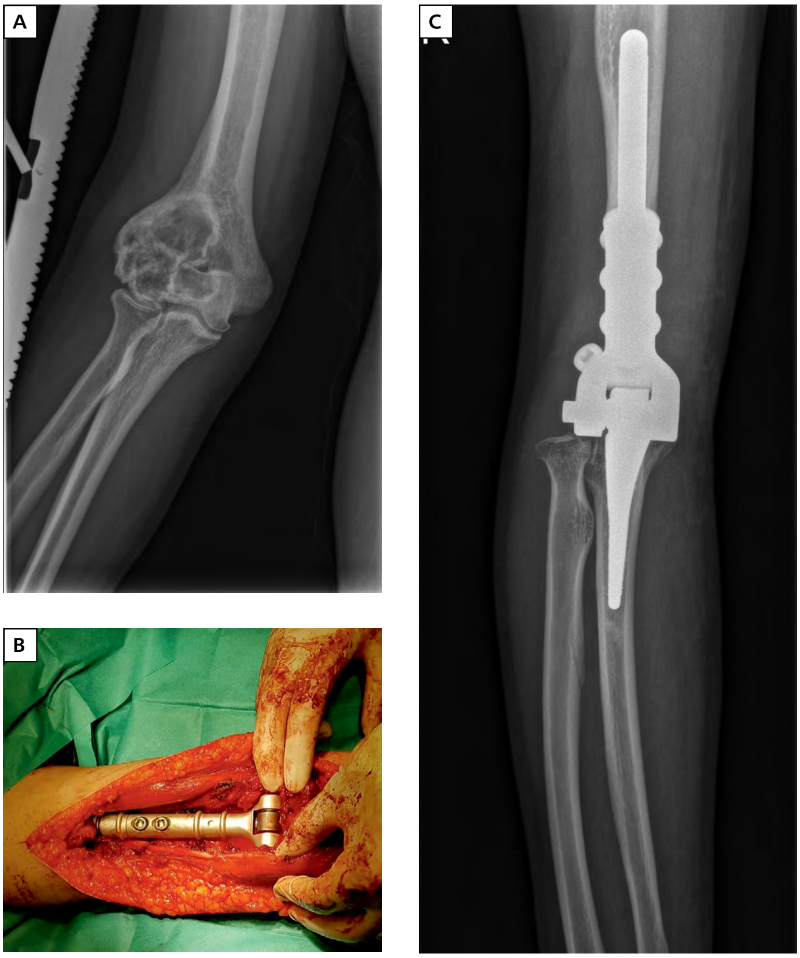

Figure 8. Ewing sarcoma located in the distal extremity of left humerus: **A.** Preoperative imaging; **B.** Picture of resected specimen; **C.** Postoperative imaging

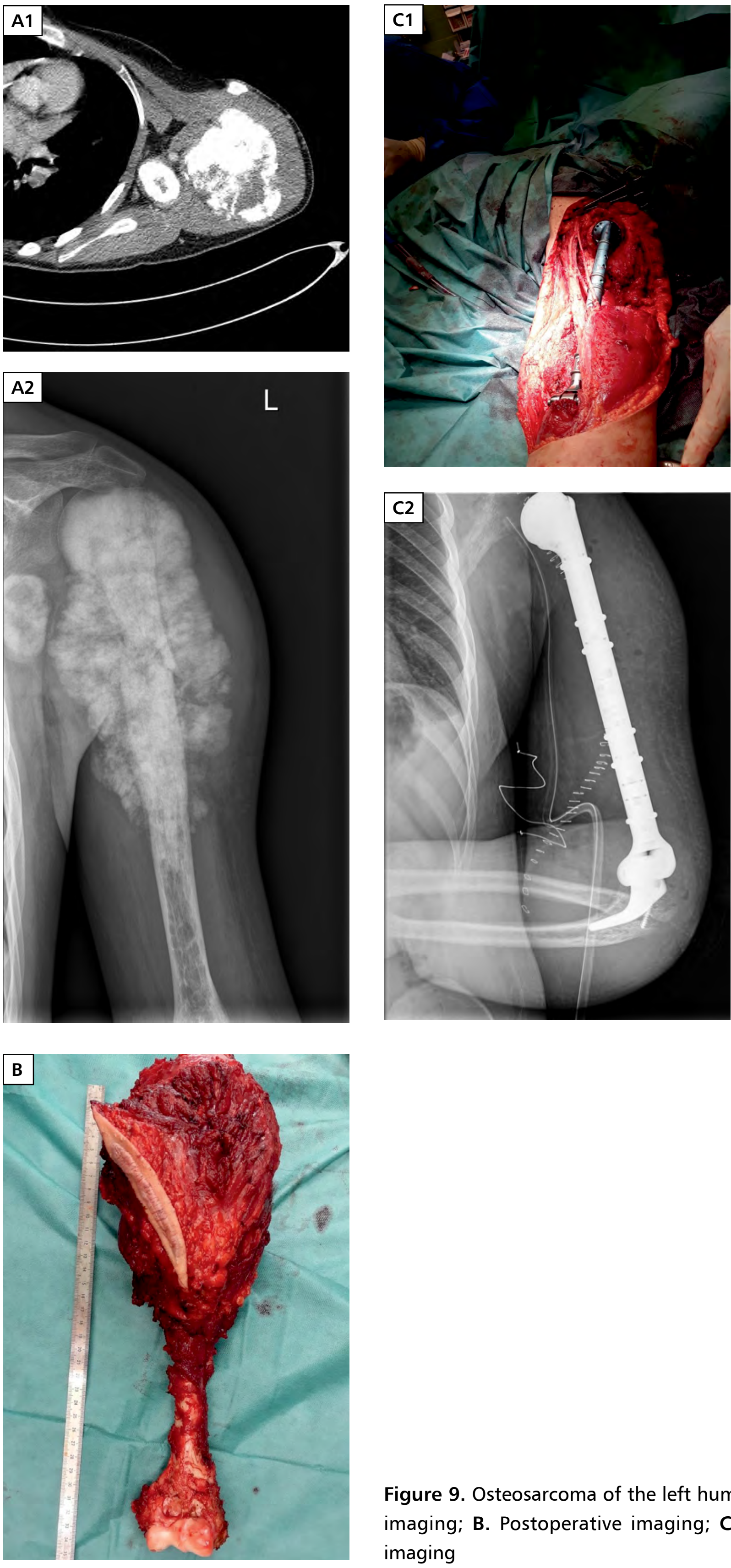

Figure 9. Osteosarcoma of the left humerus: **A.** Preoperative imaging; **B.** Postoperative imaging; **C1**, **C2.** Postoperative imaging

References

1. Stiller CA, Craft AW, Corazziari I, et al. EUROCARE Working Group. Survival of children with bone sarcoma in Europe since 1978: results from the EUROCARE study. Eur J Cancer. 2001; 37(6): 760–766, indexed in Pubmed: 11311651.
2. https://www.cancer.org/cancer/bone-cancer/about/key-statistics.
3. .08.2018.
4. Smolle M, Tunn PU, Goldenitsch E, et al. The Prognostic Impact of Unplanned Excisions in a Cohort of 728 Soft Tissue Sarcoma Patients: A Multicentre Study. Annals of Surgical Oncology. 2017; 24(6): 1596–1605, doi: 10.1245/s10434-017-5776-8.
5. Han G, Bi WZ, Xu M, et al. Amputation Versus Limb-Salvage Surgery in Patients with Osteosarcoma: A Meta-analysis. World J Surg. 2016; 40(8): 2016–2027, doi: 10.1007/s00268-016-3500-7, indexed in Pubmed: 27116252.
6. Janíček P, Pink, T. Influence of chemotherapy on deep infections of megaprostheses. 1998; 71: 379–384.
7. Payne WG, Naidu DK, Wheeler CK, et al. Wound healing in patients with cancer. Eplasty. 2008; 8: e9, indexed in Pubmed: 18264518.
8. Link MP, Goorin AM, Miser AW, et al. The effect of adjuvant chemotherapy on relapse-free survival in patients with osteosarcoma of the extremity. N Engl J Med. 1986; 314(25): 1600–1606, doi: 10.1056/NEJM198606193142502, indexed in Pubmed: 3520317.
9. Taylor W, Ivins J, Pritchard D, et al. Trends and Variability in Survival Among Patients With Osteosarcoma: A 7-Year Update. Mayo Clinic Proceedings. 1985; 60(2): 91–104, doi: 10.1016/s0025-6196(12)60293-6.
10. Beaume, Marcel. Prothèse En Ivoire Pour Réparer Les Pertes De Substance Des Os. Paris: M Vigné, 1927 Print.
11. Hernigou P, Quiennec S, Guissou I. Hip hemiarthroplasty: from Venable and Bohlman to Moore and Thompson. Int Orthop. 2014; 38(3): 655–661, doi: 10.1007/s00264-013-2153-5, indexed in Pubmed: 24170131.
12. Chillag KJ. Giants of Orthopaedic Surgery: Austin T. Moore MD. Clin Orthop Relat Res. 2016; 474(12): 2606–2610, doi: 10.1007/s11999016-5116-5, indexed in Pubmed: 27752987.
13. Burrows H, Wilson JN, Scales JT. Excision of tumours of humerus and femur, with restoration by internal prostheses. The Journal of Bone and Joint Surgery. British volume. 1975; 57-B(2): 148–159, doi:
14. .1302/0301-620x.57b2.148.
15. The step into the unknown. The incredible story of one of limb salvage surgery's longest surviving patients. Stanmore Implants Issue 1 September; 2015.
16. Coombs R, Gristina A, Hungerford D. Joint replacement: state of the art. St. Louis: Mosby Year Book 1990.
17. Enneking W. Limb salvage in musculoskeletal oncology. New York: Churchill Livingstone. 1987; pp xv, xvi, xxxi.
18. Benevenia J, Patterson F, Beebe K, et al. Results of 20 consecutive patients treated with the Repiphysis expandable prosthesis for primary malignant bone. Springerplus. 2015; 4: 793, doi: 10.1186/s40064-0151582-6, indexed in Pubmed: 26702382.
19. Kenan S, Lewis MM. Limb salvage in pediatric surgery. The use of the expandable prosthesis. Orthop Clin North Am. 1991; 22(1): 121–131.
20. Nystrom LM, Morcuende JA. Expanding endoprosthesis for pediatric musculoskeletal malignancy: current concepts and results. Iowa Orthop J. 2010; 30: 141–149, indexed in Pubmed: 21045986.