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Reconstructive techniques in musculoskeletal tumor surgery : management of pelvic and extremity bone tumors

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Chapter 1

General Introduction

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Historical Background & Aim of the Thesis

Primary bone tumors are rare, accounting for only 0.2% of the total human tumor burden¹. In 1879, Samuel Weissel Gross published what was later referred to as the “first comprehensive work on bone sarcoma”^{2, 3}. In this landmark paper, he advocated early amputation for high-grade sarcoma of bone and soft tissues, despite an overall operative mortality of 30%. Amputations at that time were also frequently performed to control local tumor growth, for palliation, because sarcomas often grew to enormous sizes before diagnosis⁴ (figures 1 and 2).



Figure 1: A tumor of the humerus in a 16-year-old woman, four years after onset (from William Gibson, *The Institutes and Practice of Surgery* [Philadelphia: Carey & Lea, 1832], volume 1, facing page 248.)

Amputation long remained the principal treatment for bone sarcoma⁵. In 1940, Dallas Burton Phemister noted that “the proper treatment of bone sarcomas of the limbs without demonstrable metastases in the great majority of cases is amputation”⁶. Despite the aggressive and mutilating surgical approach at that time, the 1938 statistics of the Registry of Bone Sarcoma of the American College of Surgeons showed a mere 13% recurrence-free survival at a minimum follow-up of five years in patients with osteosarcoma⁶.



Figure 2: Specimen of a forequarter amputation carried out by George McClellan in 1838 (from George McClellan, *Principles and Practice of Surgery* [Philadelphia: Grigg & Elliot, 1848], page 412, figure 15).

During the late 19th and early 20th centuries, the first incidental reports on limb-salvaging procedures were published⁷⁻¹⁰. The advent of effective chemotherapeutic agents in the early 1970s caused an increase of five-year survival rates to approximately 55% to 70% for many types of primary sarcoma¹¹⁻¹⁹. Concomitant sophistication of imaging and surgical techniques reduced the need for ablative procedures. Limb-salvage surgery was soon popularized and is now the treatment of choice for over 90% of patients with a primary malignant bone tumor^{5, 20-25} (figure 3).

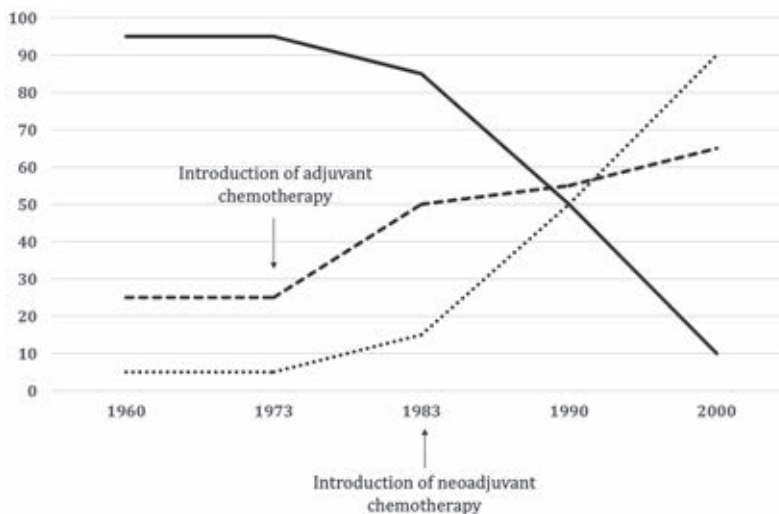


Figure 3: Graph illustrating the trends in the percentages of amputations, limb-salvage procedures, and survival for patients with primary bone sarcomas (solid line, amputations; round dot line, limb salvage procedures; square dot line, survival).

If applicable for the type of tumor, patients are first treated with neoadjuvant chemotherapy and/or radiotherapy. The subsequent limb-salvaging surgical procedure consists of three phases: (1) tumor resection, usually with the aim to obtain clear surgical margins, (2) skeletal reconstruction, and (3) soft tissue reconstruction^{25, 26}. The techniques of reconstruction vary and are dictated by surgeon preferences, tumor localization, extent of the defect, and the availability of implants. A large variety of techniques are employed at present, each having its specific advantages and disadvantages; unfortunately, these large reconstructions do not come without complications. Many techniques have not been reviewed properly and therefore, it is difficult to make an evidence-based decision when having to choose the optimal reconstructive technique for the individual patient. Reasons for the paucity of solid evidence include the low incidence of primary musculoskeletal tumors, the heterogeneity in presentation, and significant loss to follow-up due to mortality, as a result of metastases.

The aim of this thesis is to evaluate the outcomes of different reconstructive techniques in treatment of pelvic and extremity bone tumors, to identify risk factors for impaired clinical outcome, and ultimately to improve outcomes for patients with musculoskeletal tumors.

Part I: Management of Pelvic Bone Tumors

Pelvic bone tumors include primary malignancies and metastatic tumors²⁷. The most common primary tumors of pelvic bone are central and peripheral chondrosarcomas, myeloma, Ewing's sarcoma and, to a lesser extent, osteosarcoma^{1, 14, 15, 28-30}. The traditional treatment for malignant tumors of pelvic bone is hindquarter amputation^{21, 31-33}. The term hindquarter amputation (or external hemipelvectomy) is used to designate the complete removal of the lower extremity, the corresponding buttock, and the entire innominate bone in one stage^{34, 35} (figure 4). In 1959, Gordon-Taylor reported on his experiences with hindquarter amputations in a series of 41 patients³⁶. He noted perioperative mortality in 25 patients (61%), and described the procedure as "one of the most colossal mutilations practiced on the human frame".

Internal hemipelvectomy, on the other hand, does not sacrifice the unaffected lower extremity (i.e. the leg on the affected side remains intact, although functionality may be impaired significantly). Internal hemipelvectomies were first performed for treatment of tumors of the ilium and pubis, and were later presented as an alternative treatment for tumors of the (peri-)acetabulum^{37, 38}. In

1978, Enneking and Dunham proposed a classification system for pelvic tumor resections: type 1, involving the iliac wing; type 2, the periacetabular region; type 3, the pubic rami; and type 4, the sacrum (figure 5)^{39,40}. Isolated type 1 or type 3 resections are relatively easy and reconstruction is generally not needed because the acetabulum and weight-bearing axis are preserved³⁸. Type 2 resections however require reconstruction in order to restore force transmission along anatomic axes, and therefore pose unique surgical challenges^{27,41}.



Figure 4: Photograph of specimen immediately after removal by hindquarter amputation (from Gordon Gordon-Taylor and Philip Wiles, Interinnomino-abdominal [hind-quarter] amputation [The British Journal of Surgery: volume XXII – No. 88, 1935]).

Although most patients with a periacetabular bone tumor can at present be treated by internal hemipelvectomy, these procedures are considered some of the most challenging operations in musculoskeletal oncology^{21,41}. First, pelvic neoplasms often grow to immense proportions before diagnosis (figure 6). Second, the pelvic anatomy is complex, and tumors frequently grow close to vital neurovascular structures. As a result, it is often difficult to obtain clear resection margins^{41,42}. Treatment of pelvic metastases is generally less complicated because the procedure is usually intralesional and therefore requires less bone and soft tissue resection³⁸. Third, reconstruction is difficult because of high loading forces, limited bone stock, and large soft-tissue defects⁴³⁻⁴⁶. This reflects an important dilemma in treatment of these tumors: the decision to obtain adequate surgical margins, while salvaging enough bone to preserve longevity and function of the affected limb⁴⁷.

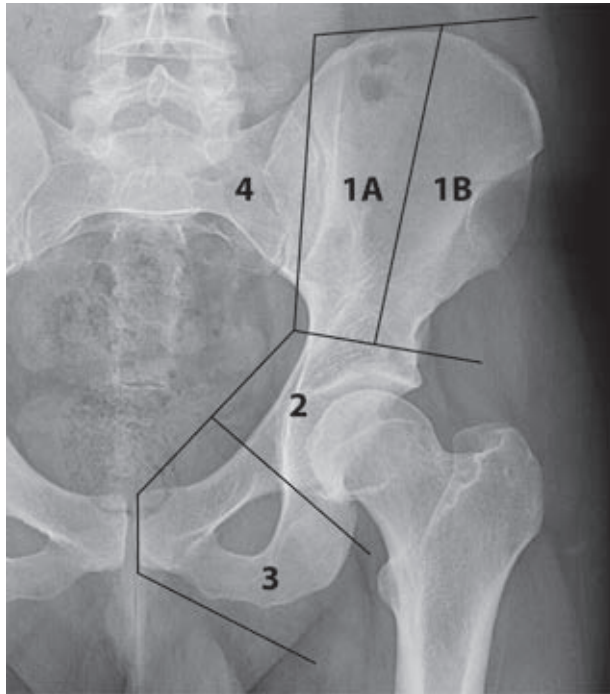


Figure 5: Conventional radiograph of the pelvis showing a modified version of Enneking's classification of pelvic resections. Resections of the ilium are further subdivided into types 1A (those involving the medial part of the ilium) and type 1B (those confined to the lateral portion of the iliac wing). The innermost line depicts the resection plane of a 'conventional' hindquarter amputation.

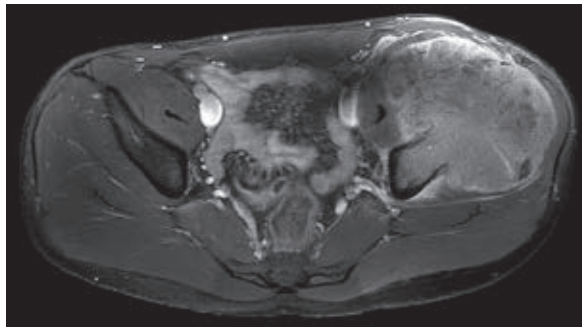


Figure 6: Transverse T1-weighted MR image with SPAIR selective fat suppression, demonstrating a large telangiectatic osteosarcoma originating from the left iliac wing.



The most common primary tumor of the pelvic bones in adults is chondrosarcoma³⁸. Pelvic chondrosarcomas are notorious for the high risk of (late) recurrence⁴⁸. However, specific studies on this tumor type are lacking. Most previous studies focused on outcomes of resection and reconstructive techniques rather than on oncological outcome. However, to choose the optimal treatment and reconstructive technique, and to reduce the rate of unnecessary reoperations, it is important to identify patients with a poor prognosis in an early stage⁴⁹. In chapter 2, we present a multicenter study on primary central chondrosarcoma of the pelvis. With this study, we aimed to gain insight in the outcome of treatment of this specific type of tumor, and to identify risk factors for impaired oncological outcome.

Following a type 2 internal hemipelvectomy, reconstruction can be achieved with metallic implants, biological transplants, or with techniques that utilize a combination of the two. Reconstructions with metallic implants include transposition of the center of the hip joint⁵⁰ and various types of endoprosthetic reconstructions^{41, 51, 52}. Biological techniques include iliofemoral arthrodesis or pseudarthrosis⁵³, pelvic allografts⁵⁴, irradiated autografts (i.e., the resection specimen is irradiated and re-implanted)⁵⁵ and allograft-prosthetic composites⁵⁶. Disadvantages of biological techniques include limited functional outcomes and a considerable risk of infection, nonunion, fracture, and graft resorption^{50, 54-58}.

The majority of surgeons focused on the use of endoprosthetic (metallic) implants during the last decades. Most of the implants that have been used had originally been developed for reconstruction of large acetabular defects in extended revision hip arthroplasty^{41, 51}. The saddle prosthesis (Link, Hamburg, Germany), which was introduced in 1979, was the first implant to be used for pelvic reconstruction in musculoskeletal oncology on a regular basis^{38, 51, 59, 60}. Although favorable short-term results have been published^{38, 61}, long-term clinical outcome and functional results were disappointing⁵¹. Apart from high rates of infection and implant breakage, saddle prostheses were associated with a substantial risk of cranial migration^{51, 62}.

In the quest for a successful implant for pelvic reconstruction, many designers have come up with a stemmed acetabular device. These often show similarities to the Ring prosthesis, which was introduced in 1968. He presented a device that consisted of a cup with a long, threaded stem, designed for reconstruction of acetabular defects⁶³ (figure 7). Ring described that “weight is transferred from the sacrum to the articular facet of the ilium, and thence through a thick bar of bone which extends down to the upper part of the acetabulum”.



Figure 7: Drawings of the surgical procedure of reconstructing an acetabular defect with the “Ring prosthesis”. First, a cannulated drill prepares the track for the prosthesis. Next, the cup is countersunk by using a conical reamer, and the implant is inserted (from P.A. Ring, Complete replacement arthroplasty of the hip by the ring prosthesis [Journal of Bone & Joint Surgery, British Volume: volume 50 – Issue 4, 720-731]).

The pedestal cup endoprosthesis (Schoellner cup; Zimmer, Freiburg, Germany) is one of the implant designs that follow this principle. In chapter 3, we evaluate clinical outcome of periacetabular reconstruction with the pedestal cup endoprosthesis in treatment of periacetabular tumors. Experiences with this implant in both revision hip arthroplasty and orthopaedic oncology had previously been described⁶⁴⁻⁶⁶. We were the first to report on its use in a consecutive series of patients with a pelvic malignancy⁴¹.

Based on experiences with the pedestal cup endoprosthesis, the LUMiC prosthesis (implantcast GmbH, Buxtehude, Germany) was designed. Chapter 4 evaluates the short-term clinical results of periacetabular reconstruction with this novel device, and describes results from a retrospective multicenter study⁵².

Part II: Management of Extremity Bone Tumors

In the history of orthopaedic surgery, there has always been a strong desire for successful reconstruction of diseased, deformed, or disabled limbs. This dream was presumably first described in the “Miracle of the Black Leg”, in the third century AD⁶⁷. In this folktale, the Saints Cosmas and Damian successfully amputated a cancerous lower limb of a church retainer, and replaced it with the leg of a Moor who had died that morning (figure 8). Over the centuries that followed, many authors reported on their attempts to successfully reconstruct a diseased (segment of) bone with an allograft – a transplant from a genetically non-identical donor of the same species. The first successful bone allograft transplantation is generally ascribed to Macewen, who reconstructed part of the humerus in a 3-year-old boy who had osteomyelitis with bone segments obtained from a rachitic patient⁶⁸.



Figure 8: Painting of the "Miracle of the Black Leg" by Pedro de Berregete in the 15th century AD. The Saints removed the right leg of a church retainer, which was affected by a tumor, and replaced it with the leg of a Moor who had died that morning⁶⁷.

Various case reports were published in the years that followed. However, it was not before the early 1970s that the first series on patients with allograft reconstructions for bone tumors were published by groups led by Volkov (Moscow, Russia), Parrish (Houston, United States) and Ottolenghi (Buenos Aires, Argentina)⁶⁹⁻⁷². Many advances in the field of allotransplantation had been made in the years before. These included techniques to freeze allografts following procurement and to thaw them during tumor resection, and resulted in an enormous decrease in the risk of allograft rejection⁶⁷. The progress in the use of bone allograft can in part be attributed to efforts of the United States Navy, which became interested in preservation of human bone following the Second World War. Also, it has been claimed that the US navy founded the first 'bone bank'⁶⁷.

Around the same time, other groups experimented with major prosthetic reconstruction for large osseous defects, including those caused by tumor resections^{22,73}. The first known report on metallic hip replacement was published in 1942 by Austin T. Moore and Harold R. Bohlmann who replaced the proximal half of the femur in a patient with a recurrent giant cell tumor of bone with a vitallium endoprosthesis (figure 9)⁷⁴. In 1949, in the United Kingdom, the first large

endoprosthetic reconstruction was performed for a tumor of the distal femur, using an implant designed by professor Scales and manufactured by Stanmore (Stanmore Implants Worldwide, Elstree, United Kingdom)⁷⁵. Endoprostheses at that time were custom-made, based on calculations made from radiographs of the affected bone(s), and it generally took six to eight weeks before the final endoprosthesis was ready for implantation (figure 10)^{22,74,75}.



Figure 9: Reconstruction of the proximal femur with a "metal hip joint", performed in 1942 by Moore and Bohlmann⁷⁴.

To ensure ready availability of endoprostheses and to allow for intraoperative flexibility, Kotz from Vienna (Austria) introduced the concept of a modular implant for reconstruction of large osseous defects in 1975. Professor Kotz later developed an entire modular implant system for reconstruction of various tumor sites, the Kotz Modular Femur and Tibia Reconstruction (KMFTR) system, which relied on uncemented stem fixation with two additional plates, and had a fixed hinge for reconstructions around the knee⁷⁶. Despite several changes in endoprosthetic design over the years that followed, the basic idea behind the modern modular endoprosthetic systems is still comparable with the KMFTR system⁷³.

A few years later, Kotz and Salzer published on their early experiences with rotationplasty as an alternative method of reconstruction for patients with a tumor of the distal femur⁷⁷. With this technique, that had earlier been described by Borggreve⁷⁸ and Van Nes⁷⁹ for treatment of femoral deformities, the ankle acts as a knee following resection of the knee and 180° rotation of the remaining lower limb⁸⁰. Although patients have to use an external prosthesis and the cosmetic

consequences are considerable, this technique allows patients to participate in unrestricted physical activity and may yield functional results that are comparable to endoprosthetic reconstructions. Moreover, these procedures are often definitive; the need for further surgical intervention is rare⁸⁰⁻⁸³. As opposed to limb-salvaging techniques, it may also be used in case the vessels are involved in the tumor.



Figure 10: Unassembled parts of the Kutz Modular Femur and Tibia Reconstruction System⁷⁶.

To understand and compare the various techniques used for reconstruction of osseous defects in the extremities, it is important to distinguish between joint replacements and intercalary (joint-preserving) reconstructions. Primary extremity bone tumors preferentially affect the meta-epiphyseal regions of the distal femur, proximal tibia, proximal humerus and proximal femur. Due to aggressive biological behavior, periarticular structures are frequently involved in the tumorous process, and partial or complete removal of the adjacent joint is commonly indicated^{1,14,28,84}. Reconstruction can then be performed using an endoprosthesis⁸⁵, an osteoarticular allograft⁸⁶, or a combination of an allograft and a metallic implant – an allograft-prosthetic composite (APC)⁸⁷. In other cases, however, it may be possible to salvage the joint and to perform an intercalary (segmental) resection. Several techniques have been described for reconstruction of segmental intercalary osseous defects, including allografts⁸⁸, vascularized fibular autografts⁸⁹, a combination of the two – the “Capanna technique”⁹⁰, extracorporeally irradiated autografts⁹¹, segmental (metallic) prostheses⁹², or bone transport with the Ilizarov technique⁹³.

Traditionally, massive allograft implantation was the most common technique for reconstruction of intercalary defects⁹⁴. Ready availability of well-procured and

well-preserved human grafts in the Netherlands was ensured by The Leiden Bone Bank Foundation, which was founded in 1988⁹⁵. In chapter 5, we evaluate the results of intercalary allograft reconstructions in treatment of primary bone tumors from the four appointed centers for orthopaedic oncology in the Netherlands⁸⁴.

Orthopaedic surgeons later postulated that bone tumors with limited osseous and intramedullary involvement may be adequately treated by hemicortical (hemicylindrical) resection, leaving part of the cortical bone intact^{96,97}. Hemicortical defects may be reconstructed using allografts⁹⁶, autografts⁹⁸, or autologous iliac crest grafts⁹⁹. Although autografts have favorable biological properties, allografts were the preferred technique in the Netherlands, because they allow for reconstruction of larger defects. Moreover, they avoid donor site morbidity, which occurs in approximately 10% of patients and includes prolonged pain complaints, large hematomas, unsightly scars, and sensory loss¹⁰⁰. In 2002, investigators from our center reported on the results of 22 hemicortical allograft reconstructions in treatment of low-grade malignant bone tumors⁹⁶. The authors reported excellent results, with none of their patients experiencing local tumor relapse, fracture, or infection. Later, others reported comparable results, but all described small case series and most lacked long-term follow-up^{97-99, 101-103}. In chapter 6, we present the results of a nationwide retrospective study on complications and oncological outcome after hemicortical resection of primary tumors of the musculoskeletal system¹⁰⁴.

In the early 1990s, allografts were also commonly used for (partial) joint replacement following tumor resection¹⁰⁵⁻¹⁰⁷. It soon appeared that specific problems of joint reconstruction with allografts were the high risks of joint instability, cartilage degeneration, and subchondral collapse¹⁰⁸⁻¹¹⁰. However, large studies focusing on the long-term outcomes of these osteoarticular allografts were lacking. In chapter 7, we evaluate our own experiences with osteoarticular allograft reconstructions, and present a systematic review of the literature, in an attempt to quantify the risk of complications after osteoarticular allograft reconstruction.

One of the major complications of allograft reconstructions is nonunion of allograft-host junctions^{111,112}. Treatment of nonunion is often problematic because one side of the junction is comprised of nonvascular bone¹¹¹. Nonunion is assumed to result from a complex interplay between biological and mechanical factors¹¹¹. The influence of many factors, including the use of adjuvant chemotherapy, osteosynthesis type and location of the junction, has been thoroughly evaluated^{84, 88, 111, 113}. On the other hand, it has been stated that construct stability and contact

between host bone and the graft – presumably in combination with compression at the junction – are the principal determinants of union¹¹⁴. However, the influence of contact at the allograft-host junction had never been evaluated properly. In chapter 8, we present a study on the influence of contact between the allograft and host bone in intercalary reconstructions of the femur and tibia.

During the early 1990s, endoprosthetic implants rapidly refined with respect to modularity and thus possibilities to reconstruct resected bone, consequently these implants popularised^{84, 112, 115-117}. Endoprostheses have the advantage of providing a relatively easy and quick reconstructive technique which allows for early postoperative mobilisation and weight bearing²². Pioneering centers mainly used custom-made endoprosthetic devices during the 1970s and 1980s. An inherent but important disadvantage of custom-made implants is the lack of intraoperative flexibility (i.e. modularity)¹¹⁸. MUTARS® (implantcast, Buxtehude, Germany) was one of the first modular implant systems that were specifically designed for reconstruction after tumor resection or extended revision arthroplasty. As opposed to custom-made implants, modular endoprostheses allow for intraoperative adjustment, for example when greater resection is needed than was anticipated¹¹⁸. Moreover, modular implants are available off-the-shelf and are generally less expensive than custom-made implants^{118, 119}. Key features of the MUTARS® system include its uncemented, hexagonal-shaped stem, saw teeth at the junctions of stems and extension pieces to allow rotational adjustment, and the attachment tube for soft-tissue reconstruction^{120, 121}. Encouraging results of its use in orthopaedic oncology and revision arthroplasty surgery were documented^{120, 122, 123}. However, studies focusing on the long-term results of MUTARS® reconstructions around the knee were lacking, while studies on other endoprosthetic systems demonstrated that late complications are of frequent occurrence^{115, 116}. In chapter 9, we present a study on distal femoral and proximal tibial replacements from two Dutch tertiary referral centers¹²¹.

Finally, in chapters 10, 11, and 12, we present a general summary, general discussion, and summary in Dutch.

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