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ORTHOPAEDIC HERITAGE

Progress in musculoskeletal oncology from 1922 – 2012

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Abstract Since 1922 surgical approaches toward limb salvage in bone and soft tissue tumours have been documented. There is the famous "Umkippplastik" of Sauerbruch, the "Tikhoff-Linberg" inter-scapulo-thoracic resection or in 1943 a metallic tumour prosthesis for the hip joint in the United States (Moore, Bohlman). Since 1960 acrylic prostheses and metallic prosthesis with bone cement have been in use. Cement-free implants and the first modular ceramic prostheses were implanted in the 1970s in Vienna. At the same time successful chemotherapy in bone sarcomas was introduced by Gerald Rosen and Norman Jaffe. This was mainly the decade of custom-made prostheses. In the 1980s modular tumour prostheses with cone connection to be adopted to the needs of the patient were built intra-operatively. Since 1981 biannual international meetings (ISOLS) have pushed forward the field of bone tumour treatment to allow also tumour resection in wide borders for spine and pelvic tumours. New hope for resistant tumours could be monoclonal antibodies or even dendritic cell therapy.

Keywords Malignant bone tumours · Historical overview · Resectional surgery · Tumour prosthesis

Early attempts of limb salvage in bone tumors in the beginning of the 20th century have been, on the one hand, the so-called „Umkippplastik" in lower leg tumors by Ferdinand Sauerbruch in Germany 1922 [1] (Fig. 1) and, on the other hand, in the same year the inter-scapulo-thoracic resection of the shoulder girdle from Tikhov in Tomsk, Russia. A similar work was described by Linberg (Smolensk, Russia) in 1928 [2] with two satisfactory cases. The first striking report on a metal hip joint was in 1943 by Austin Moore and Harald Bohlman [3] (Fig. 2) from the United States with a two-year follow up.

Our reported experience with musculoskeletal oncology dates back to 1962, when the Vienna Bone Tumor Registry was founded. First published in 1968 [4], the Registry has been continuously gathering combined histological and clinical cases in Vienna with a total of 9,256 cases during the last 50 years, with 2,541 of them "primary malignant". The main surgical input in the first ten years was given by Martin Salzer, who created the term "oncological radicality" 1969 [5] and he graded it in „intralesional", "marginal" and „wide in healthy tissues" (Fig. 3).

This was followed by William Ennekings's "Surgical Staging System of Musculoskeletal Sarcoma" in 1980 [6].

In 1964 a distal femur acrylic prosthesis (Fig. 4) was implanted in a giant cell tumor in Vienna. The patient survived with a broken acrylic stem for more than 40 years. In 1968 the first custom-made Vitallium prosthesis for the proximal femur was implanted in a patient with a parosteal osteosarcoma, who is still alive after 46 years without any revision (Fig. 5). In the former USSR the first tumorprosthesis was implanted 1967 by Sivash and Trapeznikov [7] (Fig. 6), who also started in 1974 with a randomized chemotherapy study in osteosarcoma with Adriamycin and had similar results with 40.2 % survival vs 12 % without chemotherapy as Cortes in 1974 [8]. In the United States, Ralph Marcove used total femur and total knee replacement in osteosarcoma cases already in 1974 [9]. John Scales in Stanmore, England was using massive titanium endoprostheses in tumors in 1972 with intramedullary stem fixation with PMMA and was also the first to introduce extending prostheses with a growing mechanism [10]. In Italy, Mario Campanacci published total resection of distal femur or proximal tibia for bone tumors in 1979 [11].

Due to the experience of Norman Jaffe [12] and Gerald Rosen [13], effective chemotherapy has been used since 1975 in Vienna for osteogenic sarcoma patients with high dose

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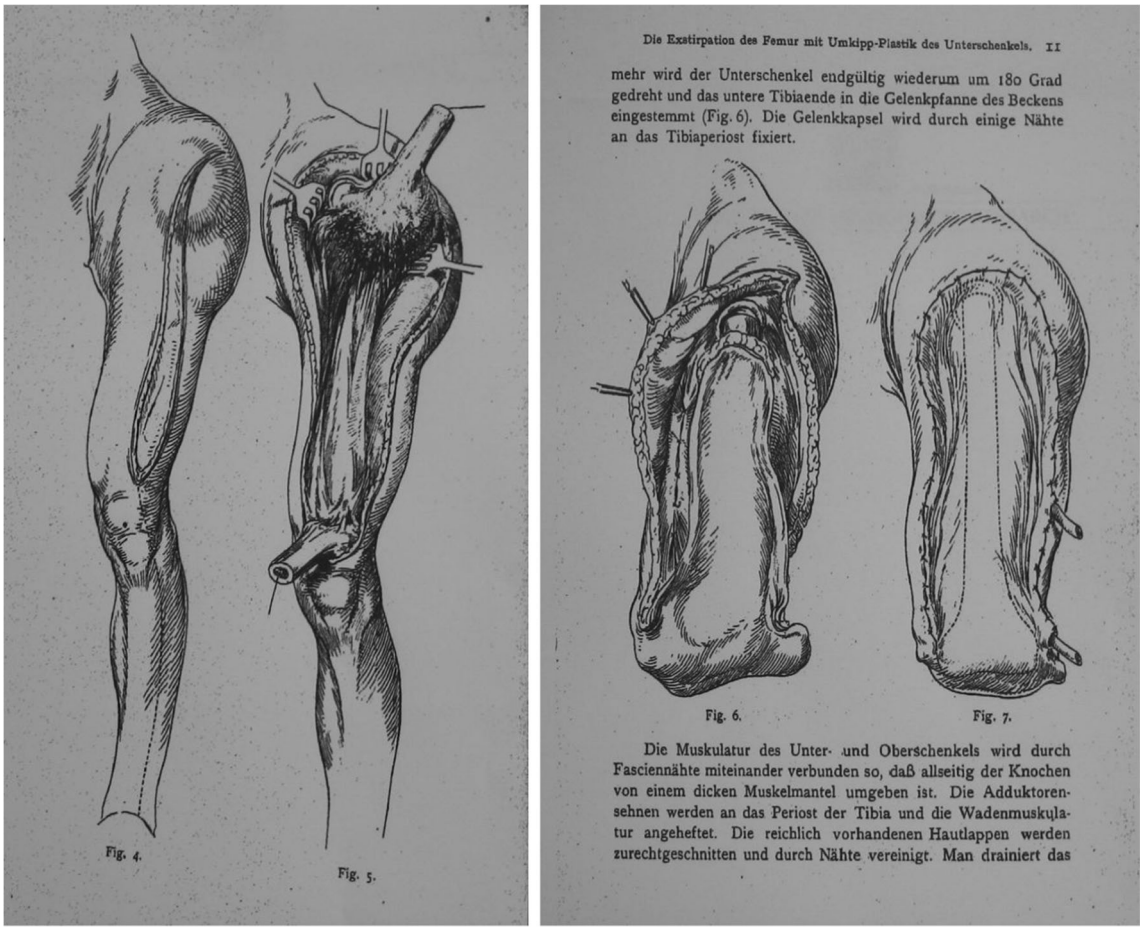
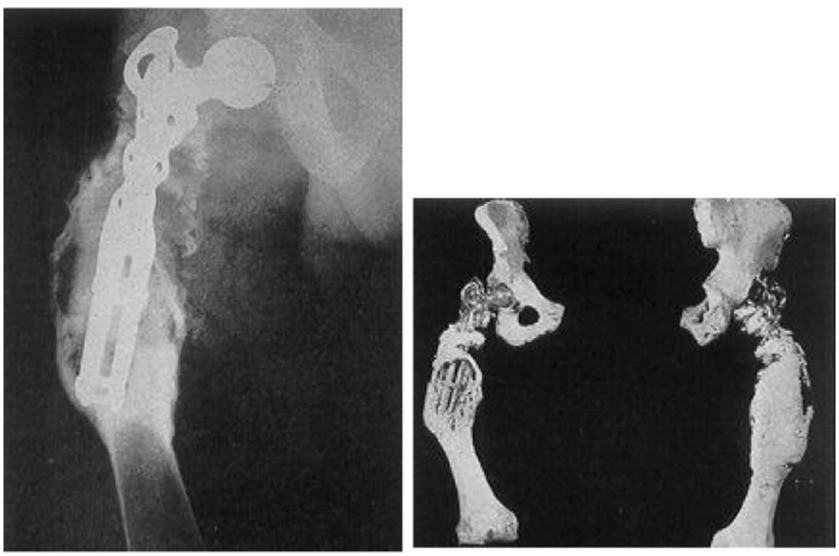


Fig. 1 Umkippplastik [1]

methotrexate [14]. Since then very effective randomized protocols have been used from the Cooperative Osteosarcoma Study COSS [15] and the Cooperative Ewing Sarcoma Study CESS [16], of which the author of this article was the responsible co-worker for the surgical treatment in these protocols for two decades beginning in 1980. With effective chemotherapy the surgical treatment changed over the years, which can be divided into „resection replacement“ by endoprosthesis or bone and into „resection replantation“ after segmental resection of lower and upper limbs. The replantation of the

Fig. 2 A metal hip joint [3]



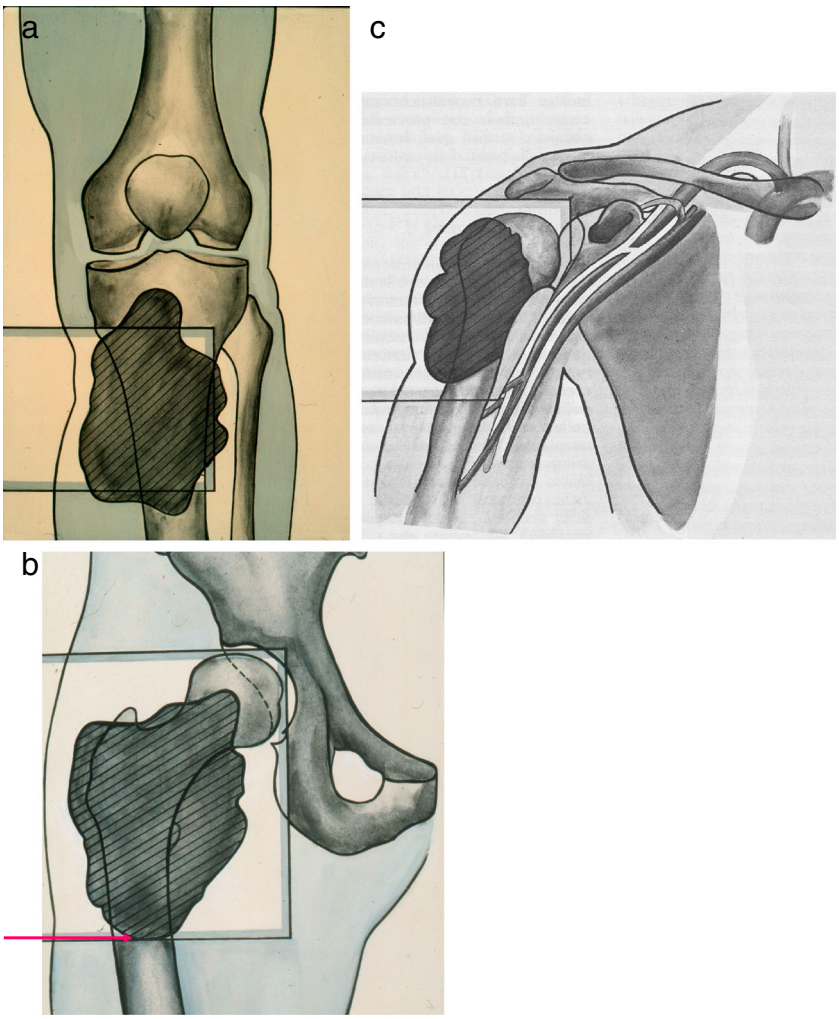


Fig. 3 **a** Intralesional. **b** Marginal. **c** Wide

remaining extremity in the lower extremity was performed as rotationsplasty [17] (Fig. 7). From 1974 until 1986 rotationsplasty of childhood osteosarcoma of the distal part of the femur was used very frequently. Seventy cases were reported in 1989 [18], of which 44 patients were with a stage 2B lesion osteosarcoma and could be followed and their data analysed for survival statistics. These patients had a 58 % rate of disease-free survival.

In the upper extremity, „resection replantation" for primary malignant tumors of the elbow or shoulder was documented in 1995 [19] (Fig. 8) with 12 cases between 1987 and 1992 of which five patients have no evidence of disease at the time of publication. No patient had a local recurrence.

In the case when limb salvage procedure was possible, modular prostheses were used from the beginning. This started in 1972 with humerus modular ceramic prosthesis by Martin Salzer [20] (Fig. 9). We have 27-year results of these three-part ceramic modular humerus prostheses. Before effective chemotherapy, 13 of 16 patients died, nine had complications requiring revision and no amputations were necessary.

Due to the experience with this ceramic prosthesis, the Howmedica humerus modular replacement system (HHMRS) from Vitallium was constructed, which is even now in use and has been since 1989 [21]. A replacement of the proximal or total humerus was combined with a variety of fixation methods of the humerus head to the shoulder (fascia lata stripes, pectoralis major transposition or LARS augmentation). According to the experience with 120 cases of malignant tumors of the humerus from 1989 to 2002 there were only five amputations (4.2 %).

Together with proximal humerus resections, there were 34 elbow prostheses (Fig. 10) in malignant tumors (19 of them metastases) and three giant cell tumors (a total of 37). Twenty-four died after 13 months (one to 44), and 13 were with no evidence of disease after 54 months (three to 218). Only nine complications were observed with six infections (two amputations), two wound healing disturbances and one aseptic loosening. Clinical performance of the elbow function was as good as in conventional elbow prostheses in degenerative disease [22].

Fig. 4 Acrylic prosthesis

The first custom-made knee prosthesis for tumors was implanted in 1975 in Vienna followed by a total of 15 cases between 1976 and 1982 with different types of cementless stem fixation with two plates and a fixed hinge [23] (Fig. 11). The 25-year results showed two wound healing disturbances, two fractures or fissures, one contracture, one ligament rupture and five infections. Prostheses complications were loosening in seven, breakage of the screws or prosthesis in four, instability in two and bushing debris in one. Surgery complications included ten changes of prosthesis and one amputation due to a severe infection after radiation therapy before surgery. During the production of these custom-made prostheses the design changed due to experience, and the final design led to a modular system in 1982 which was published as the Kotz modular femur tibia reconstruction system (KMFTR) in 1986 [24] (Fig. 12) with a tapered cone coupling to connect prostheses parts together. Twenty-six major parts of this system gave the possibility of replacing the bones of the lower extremity from the head of the femur to the distal third of the tibia. The first consecutive 100 cases were published in 2001 with ten-year results [25]. In 35 patients non-prostheses-related complications had been seen. Major prostheses-related complications were observed in 19 patients with 11 aseptic loosening, four septic loosening and four implant fractures. Minor prostheses-related complications were bushing failure in 41. At present we oversee 88 cases with 20-year results: dead of disease in 53 (60.2 %), soft tissue reconstruction in 16, allograft augmentation in 12 and patella revisions in four. Only one patient was amputated (1.1 %).

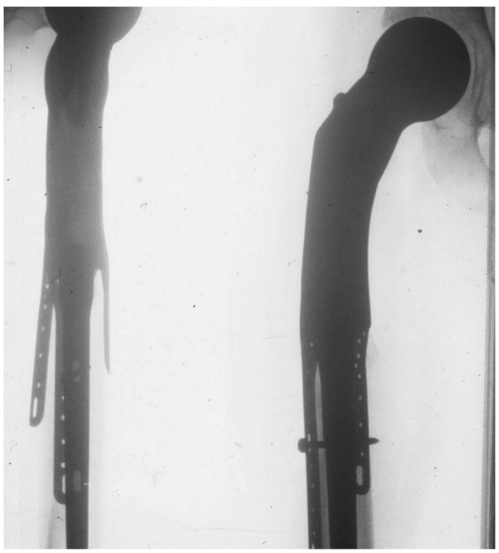


Fig. 5 Custom-made Howmedica

The ten-year survival rate of KMFTR prostheses is 70 %, the 20-year survival rate is 40 %, and the limb salvage survival rate remains at 98.9 %. In regards to these complications examinations were carried out together with Mario Campanacci, Rodolfo Capanna and Pietro Ruggieri [26] and the system was changed in 1988. We included porous coating on the prosthesis surface in order to give extra cortical bone bridging and changed from a stem with two plates and six screws to a stem with one plate and three screws in order to reduce stress shielding. The axis was also improved by omitting the plastic shoulders, as they led to instability. By changing to the Howmedica Modular Resection System (HMRS), together with Mario Campanacci, it was important that there was compatibility with the former KMFTR system. The ten-year results with the new system in 198 cases showed a survival of 98 patients (51.9 %) with non prosthesis related complications in 41.8 %, with 37.5 % prostheses changes and 16.4 % bushing changes. Only three cases had to be amputated (1.6 %).

If one compares the ten-years results of the forerunner KMFTR system with the subsequent HMRS there is a dramatic reduction in bushing changes from 41 % to only 16.4 %. Prosthesis changes were marginally higher from 30 to 37.5 %. It was possible to maintain the extremities in nearly all the cases with 1 % amputations with the first system and 1.6 % with the second system. In 1996 a rotating hinge knee was added to the modular system as a further improvement to the prosthesis (Fig. 13) regarding the axis and an improvement in the function of knee motion. This could be used optionally for the distal or total femur. Due to the clinical success of the rotating hinge a new Global Modular Replacement System (GMRS) was put on the market in 2002 after co-operation of

Fig. 6 Shivas K and Trapeznikov N prostheses

the author (RK) with Jeff Eckhart, Martin Malawer and Mario Mercuri [27] (Fig. 14). It is a combination of the international HMRS and the American MRS, both manufactured by Howmedica, uniting the best attributes of both systems to create a global system. Intensive work was especially given to the cementless stem implantation. In cooperation with Bologna due to experimental examinations on bones of corpses in the laboratory of the University Clinic of Orthopedics in Vienna, a cementless forged titanium stem was developed and rotation stability was achieved by proximally arranged fins. This system, which is only equipped with the rotating hinge, was increasingly used also in large resections, for which only a rigid axis had been available before. In all the rotating hinge tumor prostheses used from 1996 to 2002, a total of 48 cases, no bushing change was necessary, which is a substantial improvement. In a retrospective review of 2,174 cases in 2011 of Henderson et al. [28] significant differences were detected when polyaxial and uniaxial joints were compared. Also since 2002 there has been no stem loosening or fracture in the new cementless GMRS stem.

Fig. 7 Knee rotation plasty

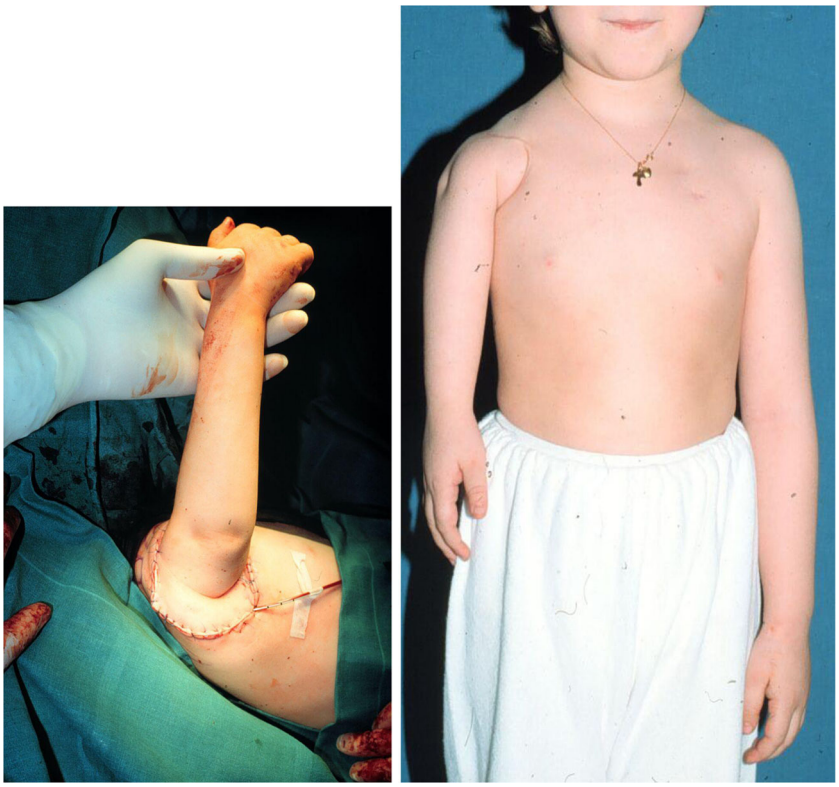


Fig. 8 Resection replantation

From 1975 to 2003 resection reconstructions with biological transplants were carried out in 195 patients in Vienna, whereby in 126 autologous transplants 23 vascularized and 94 free transplants were used, and in 69 homologous transplants 16 osteoarticular grafts and 53 strut grafts were implanted. Survival in this group was much higher (68.8 %) as these tumors were mostly smaller and good resection was possible with local relapses in only 6.3 %. This could be proven on the example of parosteal osteosarcoma [29].

Since 1982 pelvic resections have been carried out in selected cases instead of a hemipelvectomy, for example, in 35 patients from 1985–2000 who had mainly a diagnosis of chondrosarcoma [30] with the main location being the ileum. There were 11 type I, II or IV resections according to Enneking, ten type II and III resections, six type I, II and III resections, four type II resections, two type I and II, and two type I, II and III resections. In 32 patients the resections were wide, two were marginal and one intralesional. Of the various reconstruction possibilities the most common one was custom-made pelvis prostheses in 25 patients. Only two patients had a local relapse, 14 patients were without evidence of disease after an average of 54 months, 12 were DOD after an average of 23 months, six patients were DOOD whereby three had an infection and three had a perioperative complication, and three patients were living with their disease. The high

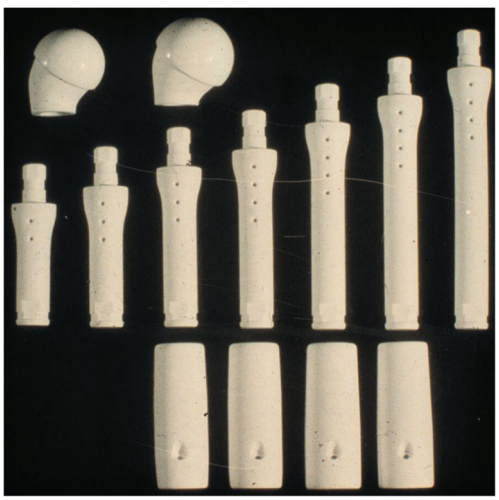


Fig. 9 Modular ceramic prosthesis

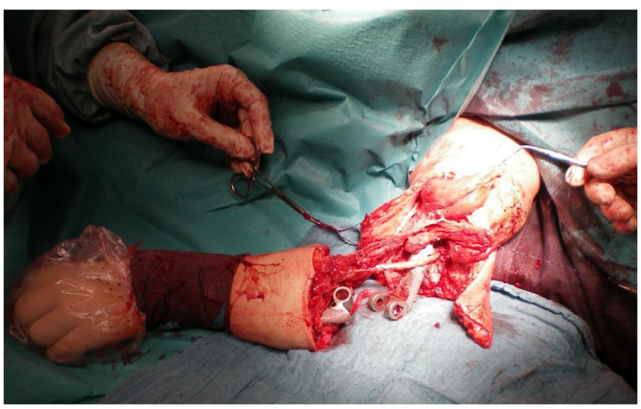


Fig. 10 Elbow tumor prosthesis

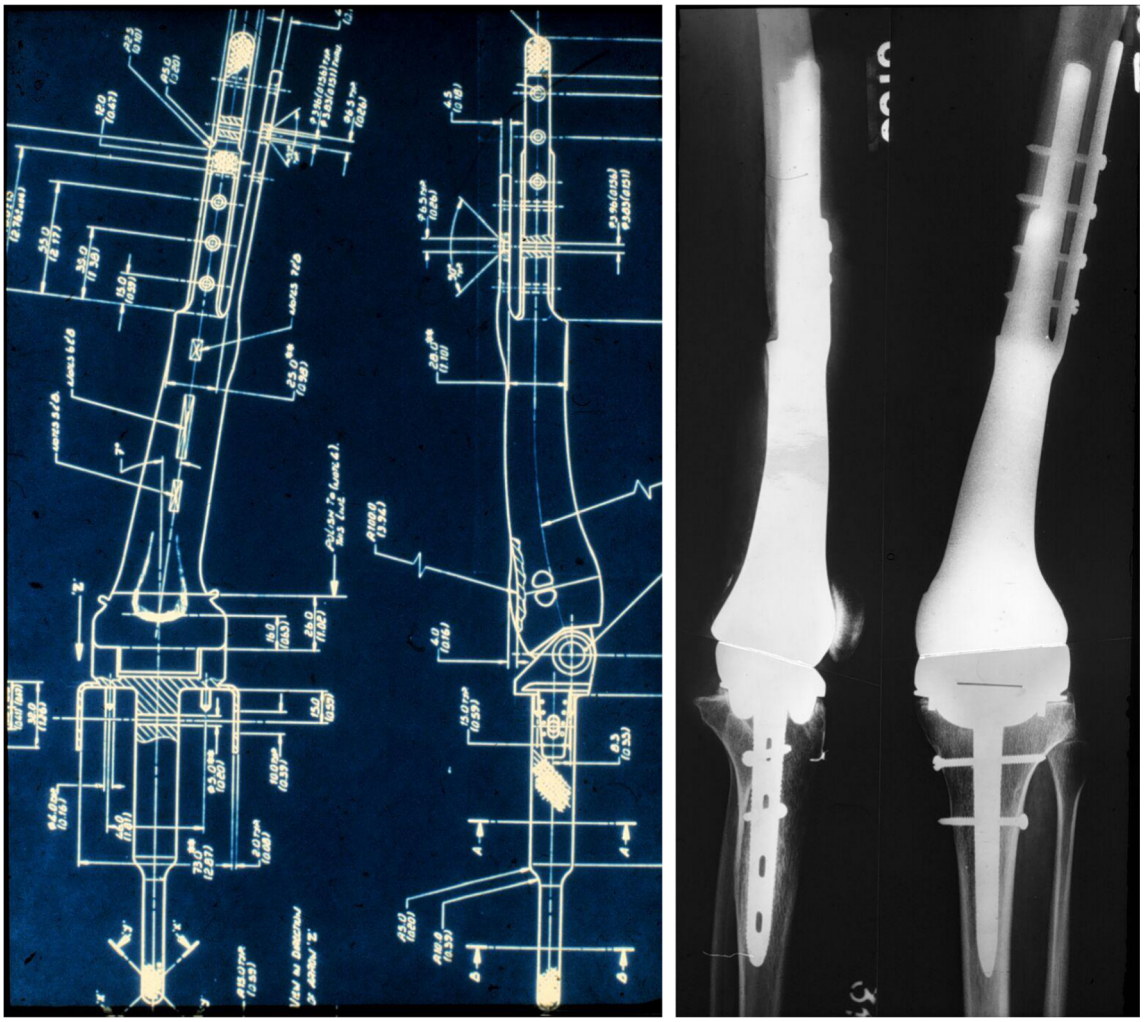


Fig. 11 Custom-made distal femur prosthesis

number of 76 complications was due to 29 wound healing disturbances and 12 cases of infection. The patients had 68 re-operations, of which 44 were necrosectomies. Only in four cases a secondary hemipelvectomy was necessary. After analysing these cases in 2000 the reconstruction was changed to the so-called „stemmed socket“ in cases when preserving of a part of the ileum was possible oncologically. These cases had significantly less complications.

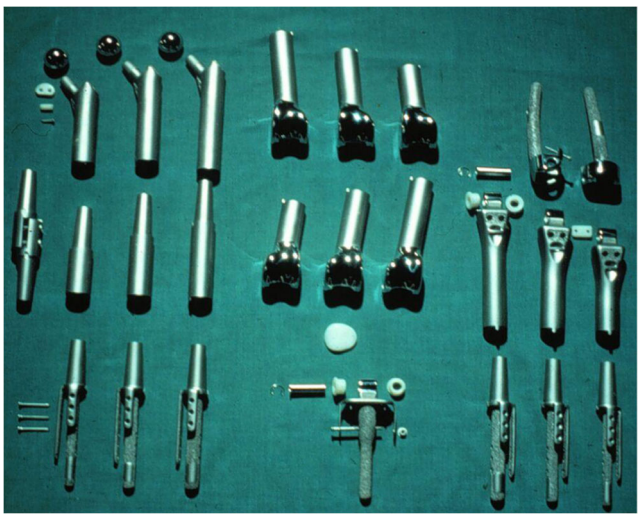


Fig. 12 Kotz femur tibia reconstruction (KMFTR) system

In the Vienna Bone Tumor Registry there are also records of seven cases of “total vertebrectomies” (modification according to Tomita [31]) whereby four patients survived with no evidence of disease.

There are also records of two cases of hemicorporectomies in Vienna (unpublished). The first case in 1974 died peri-operatively after 48 hours. The second patient in 2004, who also had a giant pelvic chrondrosarcoma, was amputated between the 4th and 5th lumbar vertebrae (Fig. 15), survived for 14 days due to the interdisciplinary co-operation of the neurosurgeons, vascular surgeons, plastic surgeons and abdominal surgeons and died due to nonoperative complications in intensive care.

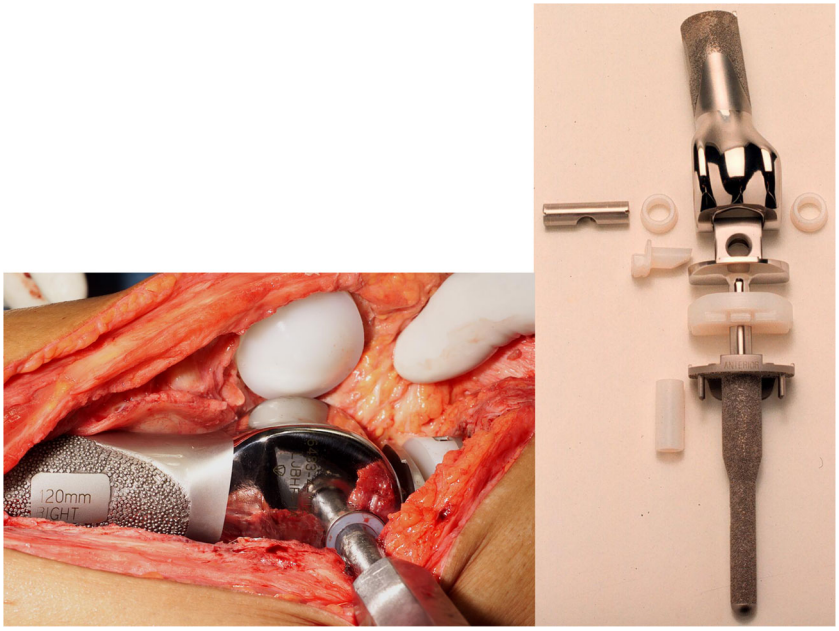


Fig. 13 "Rotating Hinge" Knee since 1996

From 1986 to 2002, 68 children with malignant bone tumors in the lower extremity were treated with growing prostheses [32]. Fifty-four of them suffered from osteosarcomas and 14 from Ewing's tumors. Fifteen of the whole group died of metastases (22 %), two had amputations due to complications (e.g. irradiation) and one was due to a local recurrence. We have no information from two patients. Out of the remaining 48 patients 28 children reached skeletal maturity.

The principle was the implantation of a modular prosthesis with manual growing modules in 24 and automatic modules in four. Ten were male, 18 female, six of them had Ewing's tumors and 22 osteosarcomas. The average age was 10.7 years (6.6–16.1). Seventeen had a distal femur, five a total femur, eight a proximal tibia and one a proximal femur replacement.

All reported cases had nearly the identical leg length at skeletal maturity. Complications of the prostheses were loosening in 12, bushing change in six, screw or prosthesis breakage in six, malfunction of the elongation mechanism in three and others in three (30 in 28=1.1/case). Other non-prosthesis-related complications were infection in 17, skin necrosis in 12, haematoma in ten, restriction of motion in ten, nerve lesion in

Fig. 14 GMRS - Global Modular Replacement System (Kotz R, Mercuri M, Malawer M, Eckhardt J) since 2002

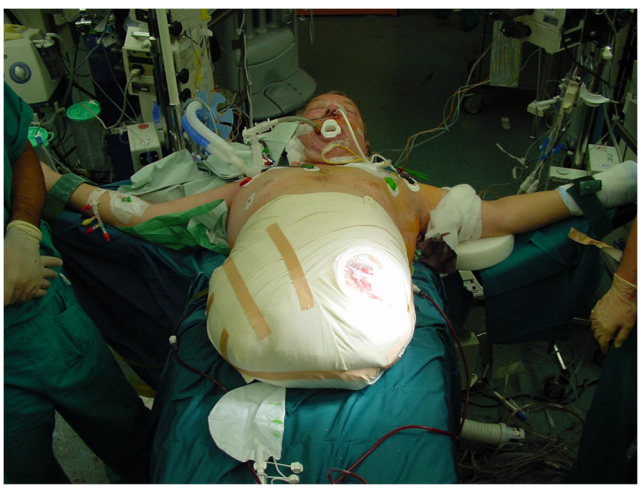


Fig. 15 Hemicorporectomie (between L4 and L5)

four, instability in four, stress shielding in three, fractures in three, and thrombosis in two (65 in 28=2.3/case). In most cases of major complications they could be solved surgically and the MSTS scores at the end of growing were identical to them who received tumor prostheses as adults.

Automatic modules were only used in distal femur locations (Fig. 15). To compare manual with automatic module applications we chose four pairs with equal age, growing capacity and distal femur location in order to allow comparability.

Module	Ø age	Number of surgeries	Millimetre lengthening	Surgery/cm
Manual	9.1	7.5	80	0.9
Automatic	8.9	4.0	62	0.6

With the first generation of automatic growing modules there was a significant reduction of operations/cm elongation. There will be further improvement in the second generation of automatic growing prostheses, which we used in 2000–2009 [33].

Additional to the improvement of surgical procedures, chemotherapy was improved also by stepwise changes of the COSS [34] and CESS [35] protocols. Though the prognosis reached 70 % survival there were resistant cases that developed metastases mainly in the lung and bones. Salvage chemotherapy protocols usually could not improve the situation satisfactorily. This was the impact for further experiments with biologic methods.

Coley's Toxins [36] inspired us in 1972 to start experimental immunological studies together with the Cancer Institute [37]. Due to the striking effect of chemotherapy in 1974 we changed our research strategy totally to chemotherapy. Only after the newly developed dendritic cell therapy by Ralph Steinmann in 1973, which started in 1995 with the first sensational success of the clinical application [38], together with the Children Cancer Center in Vienna [39] we initiated a phase 1 trial with 15 cases with a dendritic cell therapy. Two cases with local relapses and multiple metastases had a striking success and were with NED for more than three years (unpublished data).

Conclusion

Though oncologic surgery in orthopedics in the last five decades was characterized by a high number of different varieties of complications, with which the surgeon had to deal, in recent years improvement could be observed. The prosthetic devices have been improved substantially, and complications with chemotherapy or infections could be diminished within the last five decades. A new hope for relapsing cases will be molecular biological treatment.

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