Megaprosthetic Reconstructions Following Sarcoma Resection

Subjects: Orthopedics

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Megaprostheses have the advantage of a wide availability of different off-the-shelf modular implant systems that allow for individual, exact defect reconstruction, immediate, primary stability and the possibility to start early weight-bearing and functional rehabilitation.

sarcoma megaprosthetic megaprosthesis megaprostheses tumor prostheses

1. Upper Extremity

The most common indications for modular megaprosthetic reconstruction after sarcoma resection involving the upper extremity are proximal humerus resections with or without involvement of the shoulder joint or scapula. In much rarer cases [1][2][3], total humerus resections, distal humerus resections, diaphyseal humerus resections (intercalary megaprosthetic reconstruction) and proximal ulna resection [3] can be addressed. In rare cases custom implants may be used for other forearm tumors [4] or after isolated scapulectomy [5].

1.1. Proximal Humerus Replacement (PHR)

Soft tissue failures (type 1) involving the surrounding tissues leading to dislocation, implant migration or complications regarding implant coverage and wound healing are particularly common in megaprosthetic reconstructions of the shoulder joint, which is best investigated for proximal humerus replacements (PHRs) [6][1][7][8]. The probability of soft tissue failure varies between studies. Henderson et al. [1] in their multi-institutional study including almost 350 prostheses found an overall rate of 4% revisions for soft tissue complications that however represent 25% of all revision of PHR performed; similarly, Bohler et al. [6] found a rate of 12% soft tissue complications that made up 50% of all complications in a study on 48 PHRs from a single center.

Despite these high rates of revision surgery for a soft tissue complication, there is some controversy with regard to when to perform revision surgery for the migrating or subluxated anatomical shoulder hemiprosthesis that is traditionally used. Cannon et al. [9] reported that more than 25% of anatomical hemiprostheses after proximal humerus tumor resection showed signs of proximal migration; however, in their cohort of 83 PHRs none were revised for that reason. Similarly, Nota et al. [10] have investigated the results of 84 proximal humerus megaprostheses and noted subluxation or migration in more than 40% of prostheses, but only performed revision in one case for that reason. Depending on the degree of resection the anatomical PHR hemiprosthesis is usually merely attached using soft tissue fixation to the remaining bone structures. Conservative management was recommendes long as the patient is asymptomatic, unless perforation is imminent. Considering the fair results reported for this approach despite the high prevalence of radiological complications [9][10], aggressive surgical intervention does not seem warranted.

It appears logical that the likelihood for soft tissue failure is increased in resections that are more extensive. In particular, extra-articular shoulder resections involving the scapula (types IV–VI according to Malawer) [8][11] with megaprosthetic PHR have been shown to lead to high rates of prosthetic failure in more than 50% of cases. In particular, soft tissue revisions are common as 25% of patients required unplanned surgery for that indication according to a series of 55 procedures reported by Angelini et al. [8]. However, to the knowledge there are no studies that involve a control group comparing the results of intra- vs. extra-articular shoulder resections and subsequent megaprosthetic reconstruction.

One possible approach to reduce soft tissue complications is the use of synthetic mesh that is sutured on the body of the prosthesis and used to fixate the remaining muscle or capsule on the implant [12][13][14]. In particular, in extra-articular resections a megaprosthesis with a synthetic mesh can be used to attach the arm to the thorax as a "suspensionplasty". While there is currently no robust evidence that this additional foreign material is associated with an increased probability of infection [13], surgeons should be aware of the fact that the increased surface area carries the risk of bacterial adhesion and removal of the mesh may be required in revision surgery in cases of infection. Furthermore, a modified acromion and musculus trapezius transfer in conjunction with megaprosthetic reconstruction has been described although the potential gain in function was limited and the infection rate was high [15].

The functional outcome of PHR greatly depends on the type of resection and prosthetic design used. While for extra-articular resections with suspension of the prosthesis on the remaining thorax or clavicle, hardly any active shoulder motion can be expected, but a functioning elbow and hand can usually be preserved, and intra-articular anatomic prosthesis can preserve some active motion [6][9]. For anatomic shoulder replacements, mean range of motion in abduction and forward flexion is usually limited to around 40–50° [9][16], but depending on the remaining deltoid, rotator cuff and ability to provide soft tissue attachment to the prosthesis, much better results are possible even with anatomic designs [14]. Tang et al. [14] have emphasized the role of soft tissue reconstruction using a synthetic mesh and compared active range of motion as well as Musculo-Skeletal Tumor Society [17] (MSTS) scores in 29 PHRs with or without mesh reconstruction. They found clear improvement of active motion and MSTS score when intra-articular resection had been performed and the deltoid function was intact. The MSTS scores for anatomical PHR have been reported to be between 20–25 points with lifting ability and hand positioning being the limiting factors [6][14]. Additionally to the use of synthetic mesh or during revision surgery, acromion and muscle transfers (modified by Gosheger [18]) can be an option to improve implant coverage and potentially regain function although there are no large-scale, long-term reports on this technique. However, pectoralis major or latissimus flaps might be required for additional implant coverage beyond any functional considerations.

Contrary to the rather limited function of anatomical PHR that was greatly dependent on the remaining soft tissue, reverse shoulder arthroplasty with a PHR has been reported to lead to reproducible, excellent function if the deltoid and axillary nerve can be preserved. Streitbüger et al. [19] reported a mean MSTS of 25 points and reliable restauration of anteversion and abduction to close to 90° if the deltoid can be preserved. Trovarelli et al. [20] even reported an MSTS of 29 points and mean abduction and anteversion of >100°. In the practice, reverse designs were recommended for all patients in whom the deltoid and axillary nerve can be preserved and a glenoid component can be anchored in combination with meticulous soft tissue reconstruction using a trevira synthetic mesh.

1.2. Total Humerus Replacement (THR)

In rare cases of locally advanced tumors, skip metastasis, previous contaminating surgery or failed prior reconstructions, surgeons might use total humerus megaprosthetic replacement (THR) [21][22][23][24] in cases of insufficient bone stock for single joint replacements. There are only very few studies in the literature with Wafa et al. [21] reporting on 34 of such reconstruction, noting a higher failure rate compared to other humeral reconstructions but with good functional long-term outcomes, and concluding that THR is an appropriate extremity salvage treatment as the ten-year implant survival was 90% in their cohort. In particular, soft tissue complications and infection must be considered in THR as it follows the removal of the entire humerus and therefore most muscle attachments of the upper arm. Natarajan et al. [25] noted proximal migration throughout their series of 12 THRs, but only added a synthetic mesh to their reconstructive technique later in the series. Schneider et al. [24] investigated a cohort of 31 THRs performed for bone sarcomas and reported an implant survivorship of 74% after five years with infection and local recurrence being the main reasons for revision surgery. Patients with extra-articular resections were at increased risk for revision in this study.

Long-term functional outcome can be good to excellent [21][24] with an average MSTS of around 25 points and even the more demanding ASES (American Society of Shoulder and Elbow Surgery) score being good, with a median of 83 points [24]. However, considering the small number of patients available there is still uncertainty regarding what determines functional outcomes such as rTSA. Additionally, it is unclear if there is an effect on complication risk depending on adjuvant treatments such as radiation.

1.3. Distal Humerus Replacement (DHR)

The distal humerus is a rare location for bone tumors and therefore there is only limited data on megaprosthetic reconstruction available [1][2][26]. Megaprosthetic reconstruction of the elbow is considered a challenge due to the very limited soft tissue coverage available making the reconstruction prone to complications. Furthermore, functional outcome can be poor if the major nerves in the proximity are damaged during surgery or are resected due to tumor involvement. In recent years two studies have investigated modular megaprosthetic elbow reconstructions with Henrichs et al. [27] report on the outcome of twelve patients treated for malignant and recurrent locally aggressive bone and soft tissue tumors. A total of 25% of their patients underwent amputation for local recurrence and 25% had humeral stem loosening resulting in a revision-free implant survivorship of 64% at five years. Capanna et al. [28] reviewed 31 patients with modular elbow megaprostheses for bone and soft tissue malignancies. They noted a poor overall survival, but very good implant survivorship at five years of 93%. They reported one modular component failure and one infection. As the indications appear to be quite comparable, it is unclear why there are such stark differences in survival. Due to the rarity of studies published and rarity of elbow reconstructions performed using a megaprosthesis, only larger multicenter studies will be able to give a realistic implant survival estimate.

Regarding postoperative function, distal arm function is likely dependent on the ability to preserve the major nerves crossing the elbow region. Furthermore, an active extensor lag was noted in both studies. However, the MSTS scores published were fair in both studies at around 23/30.

2. Lower Extremity

2.1. Proximal Femoral Replacement (PFR)

The proximal femoral replacement (PFR) is one of the most frequently implanted megaendoprostheses and is used not only in tumor surgery but also increasingly in revision arthroplasty [29][30]. In particular, the proximal femur is a common site for bone sarcomas and metastases [31]. Instability (type 1 according to Henderson) is the most common complication after PFR and occurs in up to 1/3 of patients [32][33]. The loss of soft tissues and muscular attachments associated with oncological tumor resection is considered the main contributing factor for instability; however, advanced age, female gender and a primary bone tumor (as opposed to metastatic tumors) are also probably risk factors for dislocation. [32]. Dislocation usually occurs within the first months after surgery. In order to reduce the risk of instability, multiple efforts have been undertaken, with one study group in fact reporting no dislocations after PFR, by reconstructing the hip capsule using a synthetic device in which the abductor muscles and the iliopsoas muscle were reattached [34]. Furthermore, several studies recommend hemiarthroplasty instead of total hip arthroplasty reporting a vastly reduced risk of dislocation of up to 67%. There is a risk of long-term acetabular erosion by performing hemiarthroplasty; however, in these cases conversion to THA still can be performed successfully [32][35][36]. Therefore, a bipolar hemiarthroplasty PFR with meticulous soft tissue combination using a synthetic mesh appears to minimize the risk of instability and should be performed whenever possible [34][32]. It is unclear whether the use of dual-mobility cups, which have been shown to reduce the risk of instability in primary and revision THA, may also justify their routine use in PFR, although some reports with small numbers indicate that they might be an option if bipolar hemiarthroplasty is not possible. However, there are no long-term studies on the use of modern (dual mobility) acetabular components in PFR [37].

Aseptic loosening (Henderson type 2) is also a common failure mode in PFRs and may occur in 0–11% [38]. It is still debated whether cemented or uncemented coated stems provide the best long-term survival. Surgeons need to consider various factors such as the location with respect to the femoral isthmus, patient age, bone quality and associated adjuvant radiation or chemotherapy as they may all impair osseointegration. Generally, with modern implant designs, it appears that a stable long-term stem fixation can be feasible with both modes of fixation; however, porous stem collars or extracortical plates may provide for additional ingrowths and limit the potential impact of stress shielding osteolysis [39].

A common approach to reduce the risk of infection is the use of coated implants. Currently, the most investigated coating is silver that has been applied by several manufacturers and has been shown to reduce the infection risk and the invasiveness of potential revision procedures (18.2% vs. 4.5%; $p = 0.222$), concluding that silver coating can reduce infection rates, without systemic side effects [40]. However, there are no randomized trials available and future studies should try to include other potential approaches such as the use of local or systemic antibiotics [29][41].

Despite these complications, numerous authors describe very promising limb salvage rates in oncologic patients, with values reported between 92% and 100% [34][29][35][36]. The survival rate of PFR at 5 years is reported to be between 55% and 90.7% [42][43][44][45][46], between 55 and 86% at 10 years [47][46][48] and 56% at 20 years [49].

2.2. Distal Femoral Replacement (DFR)

The distal femur is a frequent location for primary bone malignancies. At present, a limb-salvaging surgical approach can be chosen for most tumors and the use of a megaprosthetic distal femoral replacement (DFR) is a common reconstruction [50]. Nevertheless, the long-term failure rates of DFR are still quite high, although survival and common failure modes vary throughout different investigations.

The probability of a soft tissue complication (type I) after DFR was significantly higher for oncological indications than for revision arthroplasty (13.3% vs. 3.3%) [51]; these findings were associated with the considerably greater soft tissue trauma in the context of tumor resection, although adjuvant therapy certainly also played a role. However, soft tissue failure, i.e., tendon rupture, was less common, probably because patients are young and did not have previous surgical trauma.

According to Pala et al., soft tissue failure occurred in 7% of DFRs with a mean of one year, mostly involving superficial wound infections, hematomas or wound dehiscence [52]. These findings were confirmed, which reported a mean soft tissue failure rate of 8.9% with a mean follow-up of 80 months in oncological indications [53]. Interestingly it was reported on a higher type I complication rate in DFR, compared to PTR, which are often associated with a higher rate of complications.

The dynamic compression fixation was presented as an option to reduce osteolysis in the implantation of shorter stems and thus enable increased osseointegration, but aseptic loosening also occurred in 9.7% of cases, including periprosthetic fractures due to aseptic loosening in a study group of 82 patients [39]. However, inconsistent results can be found in the literature. The cementless stems are considered to have a better survival due to osseointegration, but the cemented stems show better stress-shielding properties [54]. Further long-term studies on the best stem fixation are certainly required in this context, especially for homogeneous study groups.

Infection (type IV) is described in many studies as the most common problem after DFR, and always represents a serious complication, resulting in necessary amputation in 4.5% of patients [55]. Nonetheless, being the most common complication (8.5%), the infection rate in oncologic patients was significantly higher, compared with revision arthroplasty patients (11.4% vs. 4.1%), which is related to chemotherapy and the subsequent immunosuppression as well as the significantly higher intraoperative trauma due to the resection of bone and soft tissues in the primary surgery. Henderson et al. similarly reported the risk of infection of DFR as 8.3% [1] and Mavrogenis et al. as 8.2% [56]. Likewise, the overall infection rate of DFR in tumor cases was indicated by Haijie et al. to be 8.5%, with significantly higher incidence of infection in cementless implants, compared to cemented (9.0% vs. 5.8%; $p = 0.003$) and rotating-hinge prosthesis in comparison to fixed-hinge implants (10.2% vs. 4.4%; $p \leq 0.001$) [53]. However, resection height also appears to have a significant impact on postoperative infection risk, with the extraarticular resection in the distal femur being associated with a 6.2-fold increased risk of infection compared with intraarticular resection ($p = 0.004$) [34].

2.3. Proximal Tibial Replacement (PTR)

Although 15% of all osteosarcomas are found in the proximal tibia, surgical treatment continues to present difficulties to the surgeon [57], particularly soft tissue coverage can be an issue. Numerous studies have reported the failure rate in the proximal tibia to be the highest in the entire lower extremity [52][58][59], with some reporting it as high as 56% [60]. Pala et al. reported an overall failure rate of 36.7% in their collective in PTR, and again the largest group (13.3%) consisted of soft tissue problems, followed by infections as the second most common complication with 11.6% [52]. Mavrogenis also reported an overall complication rate of 25%, albeit infection (12%) was the most common, followed by aseptic loosening (6%) [61].

Soft tissue failures (type I) are common in PTR and were reported to be as common as 13.3% [52]. This is firstly related to the difficult soft-tissue coverage in the proximal tibial region and secondly due to the need to reconstruct the extensor mechanism as it is essential for knee functionality [43]. During resection of the proximal tibia, the extensor mechanism must be detached and adequately readapted to the megaendoprosthesis. To complicate matters, even without the need for tumor resection there are few soft tissue reserves, one the proximal tibia and the anterior tibial edge [57][62][63]. In particular, the risk of postoperative wound healing problems was significantly increased in patients with a high BMI or after previous radiotherapy [62]. Unfortunately, however, it is precisely these postoperative wound-healing disorders that pose a great risk of developing a periprosthetic infection in the further course; in some studies, 35–44% of patients with a postoperative wound-healing disorder developed a periprosthetic infection in the area of the proximal tibia in the subsequent period [60][62]. Thus, it is considered a high priority to provide adequate soft tissue coverage after the implantation of a PTR [62] and for this reason, some surgeons recommend the routine use of a gastrocnemius muscle flap [64][57][62][65]. According to a study by Hardes et al. ($n = 98$), soft-tissue failures occurred in 17.3% of patients after implantation of a proximal tibia due to oncologic diagnoses [63], while other studies report a tissue failure rate of 10% [60]. In contrast, however, a recent review consisting of 15 studies reported only 5.1% soft tissue failures in PTR, highly significantly lower even than in DFR (8.9%; $p = 0.001$) [53]. Thus, the literature remains highly discordant here as well and there is definitely a need for more extensive research in this field.

The structural failure rate was higher, particularly due to the necessary replacement of bushings, which were required in 8.6% to 19% of the patients, after a median of 69 months [53][64][60] with this explained by the increased torsional and shear forces that occur with the bushings. The risk is significantly higher with fixed-hinge implants than with rotating-hinge prostheses [53].

Secondary amputation had to be performed in 8.2% of patients, and the survival rate of the PTR was reported at 94.9% after one year, 90.5% at two, 79.2% at five and 74.5% at ten years [63]. These data are similar to that a survival rate at five years of 75%. However, after five years there was a significant decrease in survival from 60% at 10 years, 55.3% at 15 years and only 25.1% at 20 years [53]. Comparing the survival of megaprostheses at different sites of the lower extremity, a reduced survival of the PTR was shown in contrast to the femoral implants, which was also explained by the problems in soft tissue coverage [60].

2.4. Total Femoral Replacement (TFR)

TFR is an option in locally advanced tumors or in the context of prior contaminating surgery, skip lesions or in pathological fractures if the entire femur needs to be resected. Furthermore, it can be used in megaprosthetic revision surgery if severe bone loss is present, and salvage of the hip or knee joint is considered impossible. However, the expected risk of complications and revision surgeries is high. Nonetheless, considering that for many patients with extensive tumors amputation as a hip disarticulation must be considered alternatively, TFR is a reasonable option for a limb-saving approach.

Due to the extent of soft tissue dissection and loss of muscle attachments, soft tissue failures (Henderson type 1), including hip instability, are common. Toepfer et al. reported soft tissue failure in six of nine cases (67%) in the oncology group, of which dislocation occurred in three patients (30%) [45]. Sevelda et al. found a soft tissue failure following tumor resection in 13 patients (38%), including 8 patients with at least one dislocation (23.5%) [66]. Although soft tissue failures were less frequent in a study by Medellin, dislocation still occurred in 10% of their patients [50]. Considering the retrospective nature of the aforementioned studies and the small numbers gathered over long periods of time, one potential reason for hip instability is the type of acetabular reconstruction. In the dual mobility cup group, no dislocation occurred, but in contrast, cemented acetabular cups had the highest dislocation rate (26%), followed by bipolar heads with a dislocation rate of 14%. In conclusion, it was recommend the use of dual mobility cups in combination with TFR.

While the rate of structural failures is not considered high despite the size of the reconstruction, [1], there still is the risk of bushing wear at the knee joint. Toepfer et al. reported bushing failure in 2 of 22 patients (9%), although they were able to perform uncomplicated bushing exchange [45]. Medellin et al. found structural failure in seven patients (8.6%), with complications occurring less frequently in TFRs with rotating hinge knees than in those with fixed hinge knees [50].

Infection is a devastating complication after TFR and accounts for 42.9% of all complications in TFRs [1]. In the retrospective study by Medellin, postoperative infection occurred in 18.5% of 81 patients and there was a threefold risk for infection if TFR was performed as a revision case (8% vs. 25%; $p = 0.001$) [50] With the numbers available, silver coating did not reduce the risk for infection (17% vs. 19%; $p = 0.869$) and 9% of patients still underwent hip disarticulation to eradicate the infection. However, as there are different types of silver coating, future studies should be performed as silver has been shown to reduce the infection risk in other high-risk situations. Additionally, the surgical and antibiotic treatment of infected megaprostheses is debated; therefore, future studies must consider multiple aspects such as microbiology in treating these patients.

2.5. Combined Distal Femoral and Proximal Tibial Replacement (CFTR)

Although the most common locations of sarcomas are in the distal femur and proximal tibia [67], there is little data on the combination of these two megaprosthesis types [68]. However, according to Henderson, this combination had the highest failure rate and poorest survival of all tumor prostheses [1]. Sevelda et al. followed up 39 of these prosthesis combinations, with 37 patients operated on for sarcoma and 2 for metastases [68]. Overall revision-free survival was 3.7 years, but with a significant difference (p = 0.02) between primary surgeries (6.1 years) and revision surgeries (1.2 years). The most common types of implant failure were infections (16/39) and soft tissue failures (12/39). Of the 16 infections, 8 were cured, but 5 patients developed chronic infection and 3 patients required amputation. In the soft tissue group, eight patients developed extensor mechanism insufficiency. The use of synthetic devices to bridge or reinforce ligamentous structures, especially to reattach the extensor mechanism in the knee, is discussed controversially. Reconstruction with a synthetic device has a trend toward inferior survival and the use of the gastrocnemius muscle flap may be the more successful method. This is currently discussed controversially in other studies; some report an increased risk of amputation after combining a synthetic device and a tumor prosthesis in the knee joint [69], but others find no increased infection rates with this combination in the proximal tibia [70]. The third most common failure type was structural failure (9/39), including five prosthesis fractures. It was explained this fact by the large leverage effect of this type of prosthesis. Nevertheless, aseptic loosening occurred in only one case. In terms of functional outcome, the mean MSTS scores were better with primary implantation, compared to the use of the CFTR as a revision implant (83% vs. 70%; p = 0.041). Based on the 94% limb survival rate, the use of this prosthesis were recommended, despite the frequent need for revision surgery, especially in early years.

References

1. Henderson, E.R.; Groundland, J.S.; Pala, E.; Dennis, J.A.; Wooten, R.; Cheong, D.; Windhager, R.; Kotz, R.I.; Mercuri, M.; Funovics, P.T.; et al. Failure mode classification for tumor endoprostheses: Retrospective review of five institutions and a literature review. J. Bone Jt. Surg. Am. 2011, 93, 418–429.
2. Below, C. Dahlins Bone Tumors: General Aspects and Data on 11087 Cases, 5th ed.; Lippincott-Raven: Philadelphia, PA, USA, 1996.
3. Creighton, J.J., Jr.; Peimer, C.A.; Mindell, E.R.; Boone, D.C.; Karakousis, C.P.; Douglass, H.O. Primary malignant tumors of the upper extremity: Retrospective analysis of one hundred twenty-six cases. J. Hand Surg. Am. 1985, 10, 805–814.

4. Ackmann, T.; Klingebiel, S.; Gosheger, G.; Rachbauer, A.; Theil, C.; Andreou, D. Reconstruction of Total Bone Defects following Resection of Malignant Tumors of the Upper Extremity with 3D Printed Prostheses: Presentation of Two Patients with a Follow-Up of Three Years. Case Rep. Orthop. 2020, 2020, 8822466.
5. Grossi, S.; D'Arienzo, A.; Sacchetti, F.; Ceccoli, M.; Cosseddu, F.; Neri, E.; Colangeli, S.; Parchi, P.D.; Andreani, L.; Capanna, R. One-Step Reconstruction with Custom-made 3D-printed Scapular Prosthesis after Partial or Total Scapulectomy. Surg. Technol. Int. 2020, 36, 341–346.
6. Bohler, C.; Bronimann, S.; Kaider, A.; Puchner, S.E.; Sigmund, I.K.; Windhager, R.; Funovics, P.T. Surgical and Functional Outcome after Endoprosthetic Reconstruction in Patients with Osteosarcoma of the Humerus. Sci. Rep. 2018, 8, 16148.
7. Dubina, A.; Shiu, B.; Gilotra, M.; Hasan, S.A.; Lerman, D.; Ng, V.Y. What is the Optimal Reconstruction Option after the Resection of Proximal Humeral Tumors? A Systematic Review. Open Orthop. J. 2017, 11, 203–211.
8. Angelini, A.; Mavrogenis, A.F.; Trovarelli, G.; Pala, E.; Arbelaez, P.; Casanova, J.; Berizzi, A.; Ruggieri, P. Extra-articular shoulder resections: Outcomes of 54 patients. J. Shoulder Elbow Surg. 2017, 26, e337–e345.
9. Cannon, C.P.; Paraliticci, G.U.; Lin, P.P.; Lewis, V.O.; Yasko, A.W. Functional outcome following endoprosthetic reconstruction of the proximal humerus. J. Shoulder Elbow Surg. 2009, 18, 705–710.
10. Nota, S.; Teunis, T.; Kortlever, J.; Ferrone, M.; Ready, J.; Gebhardt, M.; Raskin, K.; Hornicek, F.; Schwab, J.; Lozano Calderon, S. Functional Outcomes and Complications After Oncologic Reconstruction of the Proximal Humerus. J. Am. Acad. Orthop. Surg. 2018, 26, 403–409.
11. Malawer, M.M.; Meller, I.; Dunham, W.K. A new surgical classification system for shoulder-girdle resections. Analysis of 38 patients. Clin. Orthop. Relat. Res. 1991, 267, 33–44.
12. Gosheger, G.; Hillmann, A.; Lindner, N.; Rodl, R.; Hoffmann, C.; Burger, H.; Winkelmann, W. Soft tissue reconstruction of megaprostheses using a trevira tube. Clin. Orthop. Relat. Res. 2001, 393, 264–271.
13. Schmolders, J.; Koob, S.; Schepers, P.; Kehrer, M.; Frey, S.P.; Wirtz, D.C.; Pennekamp, P.H.; Strauss, A.C. Silver-coated endoprosthetic replacement of the proximal humerus in case of tumour-is there an increased risk of periprosthetic infection by using a trevira tube? Int. Orthop. 2017, 41, 423–428.
14. Tang, X.; Guo, W.; Yang, R.; Tang, S.; Ji, T. Synthetic mesh improves shoulder function after intraarticular resection and prosthetic replacement of proximal humerus. Clin. Orthop. Relat. Res. 2015, 473, 1464–1471.

15. Ahrens, H.; Theil, C.; Gosheger, G.; Rodl, R.; Deventer, N.; Rickert, C.; Ackmann, T.; Schwarze, J.; Klingebiel, S.; Schneider, K.N. The Bateman-Type Soft Tissue Reconstruction around Proximal or Total Humeral Megaprostheses in Patients with Primary Malignant Bone Tumors-Functional Outcome and Endoprosthetic Complications. Cancers 2021, 13, 3971.
16. Funovics, P.T.; Dominkus, M. Modular tumor prostheses of the humerus. Orthopade 2010, 39, 968–979.
17. Enneking, W.F.; Dunham, W.; Gebhardt, M.C.; Malawar, M.; Pritchard, D.J. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. Clin. Orthop. Relat. Res. 1993, 241–246.
18. Gosheger, G.; Hardes, J.; Ahrens, H.; Gebert, C.; Winkelmann, W. Endoprosthetic replacement of the humerus combined with trapezius and latissimus dorsi transfer: A report of three patients. Arch. Orthop. Trauma Surg. 2005, 125, 62–65.
19. Streitbuerger, A.; Henrichs, M.; Gosheger, G.; Ahrens, H.; Nottrott, M.; Guder, W.; Dieckmann, R.; Hardes, J. Improvement of the shoulder function after large segment resection of the proximal humerus with the use of an inverse tumour prosthesis. Int. Orthop. 2015, 39, 355–361.
20. Trovarelli, G.; Cappellari, A.; Angelini, A.; Pala, E.; Ruggieri, P. What Is the Survival and Function of Modular Reverse Total Shoulder Prostheses in Patients Undergoing Tumor Resections in Whom an Innervated Deltoid Muscle Can Be Preserved? Clin. Orthop. Relat. Res. 2019, 477, 2495–2507.
21. Wafa, H.; Reddy, K.; Grimer, R.; Abudu, A.; Jeys, L.; Carter, S.; Tillman, R. Does total humeral endoprosthetic replacement provide reliable reconstruction with preservation of a useful extremity? Clin. Orthop. Relat. Res. 2015, 473, 917–925.
22. Puri, A.; Gulia, A. The results of total humeral replacement following excision for primary bone tumour. J. Bone Jt. Surg. Br. 2012, 94, 1277–1281.
23. Kotwal, S.; Moon, B.; Lin, P.; Satcher, R., Jr.; Lewis, V. Total Humeral Endoprosthetic Replacement following Excision of Malignant Bone Tumors. Sarcoma 2016, 2016, 6318060.
24. Schneider, K.N.; Broking, J.N.; Gosheger, G.; Lubben, T.; Hardes, J.; Schorn, D.; Smolle, M.A.; Theil, C.; Andreou, D. What Is the Implant Survivorship and Functional Outcome After Total Humeral Replacement in Patients with Primary Bone Tumors? Clin. Orthop. Relat. Res. 2021, 479, 1754–1764.
25. Natarajan, M.; Sameer, M.; Kunal, D.; Balasubramanian, N. Custom-made endoprosthetic total humerus reconstruction for musculoskeletal tumours. Int. Orthop. 2012, 36, 125–129.
26. Hennessy, D.W.; Raskin, K.A.; Schwab, J.H.; Lozano-Calderon, S.A. Endoprosthetic Reconstruction of the Upper Extremity in Oncologic Surgery. J. Am. Acad. Orthop. Surg. 2020, 28, e319–e327.

27. Henrichs, M.P.; Liem, D.; Gosheger, G.; Streitbuerger, A.; Nottrott, M.; Andreou, D.; Hardes, J. Megaprosthetic replacement of the distal humerus: Still a challenge in limb salvage. J. Shoulder Elbow Surg. 2019, 28, 908–914.
28. Capanna, R.; Muratori, F.; Campo, F.R.; D’Arienzo, A.; Frenos, F.; Beltrami, G.; Scoccianti, G.; Cuomo, P.; Piccioli, A.; Muller, D.A. Modular megaprosthesis reconstruction for oncological and non-oncological resection of the elbow joint. Injury 2016, 47 (Suppl. S4), S78–S83.
29. Funovics, P.T.; Hipfl, C.; Hofstaetter, J.G.; Puchner, S.; Kotz, R.I.; Dominkus, M. Management of septic complications following modular endoprosthetic reconstruction of the proximal femur. Int. Orthop. 2011, 35, 1437–1444.
30. Hardes, J.; Budny, T.; Hauschild, G.; Balke, M.; Streitburger, A.; Dieckmann, R.; Gosheger, G.; Ahrens, H. Proximal femur replacement in revision arthroplasty. Z. Orthop. Unfall. 2009, 147, 694–699.
31. Calabro, T.; Van Rooyen, R.; Piraino, I.; Pala, E.; Trovarelli, G.; Panagopoulos, G.N.; Megaloikonomos, P.D.; Angelini, A.; Mavrogenis, A.F.; Ruggieri, P. Reconstruction of the proximal femur with a modular resection prosthesis. Eur. J. Orthop. Surg. Traumatol. 2016, 26, 415–421.
32. Henderson, E.R.; Keeney, B.J.; Pala, E.; Funovics, P.T.; Eward, W.C.; Groundland, J.S.; Ehrlichman, L.K.; Puchner, S.S.; Brigman, B.E.; Ready, J.E.; et al. The stability of the hip after the use of a proximal femoral endoprosthesis for oncological indications: Analysis of variables relating to the patient and the surgical technique. Bone Jt. J. 2017, 99-B, 531–537.
33. Puchner, S.E.; Funovics, P.T.; Hipfl, C.; Dominkus, M.; Windhager, R.; Hofstaetter, J.G. Incidence and management of hip dislocation in tumour patients with a modular prosthesis of the proximal femur. Int. Orthop. 2014, 38, 1677–1684.
34. Gosheger, G.; Gebert, C.; Ahrens, H.; Streitbuerger, A.; Winkelmann, W.; Hardes, J. Endoprosthetic reconstruction in 250 patients with sarcoma. Clin. Orthop. Relat. Res. 2006, 450, 164–171.
35. Menendez, L.R.; Ahlmann, E.R.; Kermani, C.; Gotha, H. Endoprosthetic reconstruction for neoplasms of the proximal femur. Clin. Orthop. Relat. Res. 2006, 450, 46–51.
36. Ruggieri, P.; Bosco, G.; Pala, E.; Errani, C.; Mercuri, M. Local recurrence, survival and function after total femur resection and megaprosthetic reconstruction for bone sarcomas. Clin. Orthop. Relat. Res. 2010, 468, 2860–2866.
37. Lex, J.R.; Evans, S.; Parry, M.C.; Jeys, L.; Stevenson, J.D. Acetabular complications are the most common cause for revision surgery following proximal femoral endoprosthetic replacement: What is the best bearing option in the primary and revision setting? Bone Jt. J. 2021, 103, 1633–1640.
38. Janssen, S.J.; Langerhuizen, D.W.G.; Schwab, J.H.; Bramer, J.A.M. Outcome after reconstruction of proximal femoral tumors: A systematic review. J. Surg. Oncol. 2019, 119, 120–129.

39. Healey, J.H.; Morris, C.D.; Athanasian, E.A.; Boland, P.J. Compress knee arthroplasty has 80% 10-year survivorship and novel forms of bone failure. Clin. Orthop. Relat. Res. 2013, 471, 774–783.

40. Streitbuerger, A.; Henrichs, M.P.; Hauschild, G.; Nottrott, M.; Guder, W.; Hardes, J. Silver-coated megaprostheses in the proximal femur in patients with sarcoma. Eur. J. Orthop. Surg. Traumatol. 2019, 29, 79–85.

41. Jeys, L.M.; Grimer, R.J.; Carter, S.R.; Tillman, R.M. Risk of amputation following limb salvage surgery with endoprosthetic replacement, in a consecutive series of 1261 patients. Int. Orthop. 2003, 27, 160–163.

42. Chandrasekar, C.R.; Grimer, R.J.; Carter, S.R.; Tillman, R.M.; Abudu, A.; Buckley, L. Modular endoprosthetic replacement for tumours of the proximal femur. J. Bone Jt. Surg. Br. 2009, 91, 108–112.

43. Goryn, T.; Pienkowski, A.; Szostakowski, B.; Zdzienicki, M.; Lugowska, I.; Rutkowski, P. Functional outcome of surgical treatment of adults with extremity osteosarcoma after megaprosthetic reconstruction-single-center experience. J. Orthop. Surg. Res. 2019, 14, 346.

44. Sambri, A.; Zucchini, R.; Giannini, C.; Zamparini, E.; Viale, P.; Donati, D.M.; De Paolis, M. Silver-coated (PorAg((R))) endoprosthesis can be protective against reinfection in the treatment of tumor prostheses infection. Eur. J. Orthop. Surg. Traumatol. 2020, 30, 1345–1353.

45. Toepfer, A.; Harrasser, N.; Petzschner, I.; Pohlig, F.; Lenze, U.; Gerdesmeyer, L.; von Eisenhart-Rothe, R.; Muhlhofer, H.; Suren, C. Is total femoral replacement for non-oncologic and oncologic indications a safe procedure in limb preservation surgery? A single center experience of 22 cases. Eur. J. Med. Res. 2018, 23, 5.

46. Zehr, R.J.; Enneking, W.F.; Scarborough, M.T. Allograft-prosthesis composite versus megaprosthesis in proximal femoral reconstruction. Clin. Orthop. Relat. Res. 1996, 322, 207–223.

47. Houdek, M.T.; Wagner, E.R.; Wilke, B.K.; Wyles, C.C.; Taunton, M.J.; Sim, F.H. Long term outcomes of cemented endoprosthetic reconstruction for periarticular tumors of the distal femur. Knee 2016, 23, 167–172.

48. Farid, Y.; Lin, P.P.; Lewis, V.O.; Yasko, A.W. Endoprosthetic and allograft-prosthetic composite reconstruction of the proximal femur for bone neoplasms. Clin. Orthop. Relat. Res. 2006, 442, 223–229.

49. Bernthal, N.M.; Schwartz, A.J.; Oakes, D.A.; Kabo, J.M.; Eckardt, J.J. How long do endoprosthetic reconstructions for proximal femoral tumors last? Clin. Orthop. Relat. Res. 2010, 468, 2867–2874.

50. Medellin, M.R.; Fujiwara, T.; Clark, R.; Stevenson, J.D.; Parry, M.; Jeys, L. Mechanisms of failure and survival of total femoral endoprosthetic replacements. Bone Jt. J. 2019, 101, 522–528.

51. Toepfer, A.; Harrasser, N.; Schwarz, P.R.; Pohlig, F.; Lenze, U.; Muhlhofer, H.M.L.; Gerdesmeyer, L.; von Eisenhart-Rothe, R.; Suren, C. Distal femoral replacement with the MML system: A single center experience with an average follow-up of 86 months. BMC Musculoskelet. Disord. 2017, 18, 206.

52. Pala, E.; Trovarelli, G.; Calabro, T.; Angelini, A.; Abati, C.N.; Ruggieri, P. Survival of modern knee tumor megaprostheses: Failures, functional results, and a comparative statistical analysis. Clin. Orthop. Relat. Res. 2015, 473, 891–899.

53. Haijie, L.; Dasen, L.; Tao, J.; Yi, Y.; Xiaodong, T.; Wei, G. Implant Survival and Complication Profiles of Endoprostheses for Treating Tumor Around the Knee in Adults: A Systematic Review of the Literature Over the Past 30 Years. J. Arthroplasty 2018, 33, 1275–1287.e3.

54. Ozger, H.; Alpan, B.; Salduz, A.; Gurkan, V.; Sungur, M.; Valiyev, N.; Eralp, L. Mid-term implant survival, functional and radiological results and mechanical complications of mega-prosthetic reconstruction around the knee with the PENTA(R) system. Arch. Orthop. Trauma. Surg. 2021.

55. Myers, G.J.; Abudu, A.T.; Carter, S.R.; Tillman, R.M.; Grimer, R.J. Endoprosthetic replacement of the distal femur for bone tumours: Long-term results. J. Bone Jt. Surg. Br. 2007, 89, 521–526.

56. Mavrogenis, A.F.; Pala, E.; Angelini, A.; Calabro, T.; Romagnoli, C.; Romantini, M.; Drago, G.; Ruggieri, P. Infected Prostheses after Lower-Extremity Bone Tumor Resection: Clinical Outcomes of 100 Patients. Surg. Infect. 2015, 16, 267–275.

57. Grimer, R.J.; Carter, S.R.; Tillman, R.M.; Sneath, R.S.; Walker, P.S.; Unwin, P.S.; Shewell, P.C. Endoprosthetic replacement of the proximal tibia. J. Bone Jt. Surg. Br. 1999, 81, 488–494.

58. Bickels, J.; Wittig, J.C.; Kollender, Y.; Neff, R.S.; Kellar-Graney, K.; Meller, I.; Malawer, M.M. Reconstruction of the extensor mechanism after proximal tibia endoprosthetic replacement. J. Arthroplasty 2001, 16, 856–862.

59. Horowitz, S.M.; Lane, J.M.; Otis, J.C.; Healey, J.H. Prosthetic arthroplasty of the knee after resection of a sarcoma in the proximal end of the tibia. A report of sixteen cases. J. Bone Jt. Surg. Am. 1991, 73, 286–293.

60. Puchner, S.E.; Kutscha-Lissberg, P.; Kaider, A.; Panotopoulos, J.; Puchner, R.; Bohler, C.; Hobusch, G.; Windhager, R.; Funovics, P.T. Outcome after Reconstruction of the Proximal Tibia—Complications and Competing Risk Analysis. PLoS ONE 2015, 10, e0135736.

61. Mavrogenis, A.F.; Pala, E.; Angelini, A.; Ferraro, A.; Ruggieri, P. Proximal tibial resections and reconstructions: Clinical outcome of 225 patients. J. Surg. Oncol. 2013, 107, 335–342.

62. Hardes, J.; Henrichs, M.P.; Gosheger, G.; Guder, W.; Nottrott, M.; Andreou, D.; Bormann, E.; Eveslage, M.; Hauschild, G.; Streitburger, A. Tumour endoprosthesis replacement in the proximal tibia after intra-articular knee resection in patients with sarcoma and recurrent giant cell tumour. Int. Orthop. 2018, 42, 2475–2481.

63. Hardes, J.; Henrichs, M.P.; Hauschild, G.; Nottrott, M.; Guder, W.; Streitbuerger, A. Silver-Coated Megaprosthesis of the Proximal Tibia in Patients With Sarcoma. J. Arthroplasty 2017, 32, 2208–2213.

64. Myers, G.J.; Abudu, A.T.; Carter, S.R.; Tillman, R.M.; Grimer, R.J. The long-term results of endoprosthetic replacement of the proximal tibia for bone tumours. J. Bone Jt. Surg. Br. 2007, 89, 1632–1637.

65. Schwartz, A.J.; Kabo, J.M.; Eilber, F.C.; Eilber, F.R.; Eckardt, J.J. Cemented endoprosthetic reconstruction of the proximal tibia: How long do they last? Clin. Orthop. Relat. Res. 2010, 468, 2875–2884.

66. Sevelda, F.; Schuh, R.; Hofstaetter, J.G.; Schinhan, M.; Windhager, R.; Funovics, P.T. Total Femur Replacement After Tumor Resection: Limb Salvage Usually Achieved but Complications and Failures are Common. Clin. Orthop. Relat. Res. 2015, 473, 2079–2087.

67. Carter, S.R.; Grimer, R.J.; Sneath, R.S. A review of 13-years experience of osteosarcoma. Clin. Orthop. Relat. Res. 1991, 270, 45–51.

68. Sevelda, F.; Waldstein, W.; Panotopoulos, J.; Stihsen, C.; Kaider, A.; Funovics, P.T.; Windhager, R. Survival, failure modes and function of combined distal femur and proximal tibia reconstruction following tumor resection. Eur. J. Surg. Oncol. 2017, 43, 416–422.

69. Hardes, J.; Henrichs, M.P.; Gosheger, G.; Gebert, C.; Holl, S.; Dieckmann, R.; Hauschild, G.; Streitburger, A. Endoprosthetic replacement after extra-articular resection of bone and soft-tissue tumours around the knee. Bone Jt. J. 2013, 95-B, 1425–1431.

70. Cho, W.H.; Song, W.S.; Jeon, D.G.; Kong, C.B.; Kim, J.I.; Lee, S.Y. Cause of infection in proximal tibial endoprosthetic reconstructions. Arch. Orthop. Trauma Surg. 2012, 132, 163–169.