



Advances in tumour endoprostheses: a systematic review

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- Tumour endoprostheses have facilitated limb-salvage procedures in primary bone and soft tissue sarcomas, and are increasingly being used in symptomatic metastases of the long bones.
- The objective of the present review was to analyse articles published over the last three years on tumour endoprostheses and to summarize current knowledge on this topic. The NCBI PubMed webpage was used to identify original articles published between January 2015 and April 2018 in journals with an impact factor in the top 25.9% of the respective category (orthopaedics, multidisciplinary sciences).
- The following search-terms were used: tumour endoprosthesis, advances tumour endoprosthesis, tumour megaprosthesis, prosthetic reconstruction AND tumour. We identified 347 original articles, of which 53 complied with the abovementioned criteria.
- Articles were categorized into (1) tumour endoprostheses in the shoulder girdle, (2) tumour endoprostheses in the proximal femur, (3) tumour endoprostheses of the knee region, (4) tumour endoprostheses in the pelvis, (5) (expandable) prostheses in children and (6) long-term results of tumour endoprostheses.
- The topics of interest covered by the selected studies largely matched with the main research questions stated at a consensus meeting, with survival outcome of orthopaedic implants being the most commonly raised research question.
- As many studies reported on the risk of deep infections, research in the future should also focus on potential preventive methods in endoprosthetic tumour reconstruction.

Keywords: advances tumour endoprostheses; bone metastases; bone sarcoma; endoprosthetic reconstruction; outcome; treatment

Cite this article: *EFORT Open Rev* 2019;4:445-459.
DOI: 10.1302/2058-5241.4.180081

Introduction

Endoprosthetic reconstruction in orthopaedic oncology has evolved over the last 30 to 40 years, with novel endoprosthetic systems and solutions developed constantly. Endoprosthetic reconstruction has made limb-salvage surgery possible in many cases, leading to a steady decrease in the rate of amputations.^{1,2} Long-term results of tumour endoprostheses are important to evaluate functional outcome for patients, possible complications and implant survival.

The main objective of the present review was to identify all major studies dealing with endoprosthetic reconstruction in tumour surgery published between January 2015 and 10 June 2018. The specific focus was on long-term results and functional outcome, complications as well as recent advances and novel concepts. Within the last three years, 53 studies have been published in top-ranking journals dealing with tumour endoprostheses in orthopaedic surgery. Most studies came from China ($n = 12$), followed by the United States ($n = 10$) and the United Kingdom ($n = 6$). *International Orthopedics* was the journal with the most publications on the topic 'advances in tumour endoprostheses'.

Materials and methods

All studies published in PubMed between January 2015 and 10 June 2018 were included in the study, after applying the specific search terms listed below. Original articles dealing with tumour endoprostheses published in English in PubMed-indexed journals with an impact factor ranking them in the top 25.9% in the categories multidisciplinary sciences or orthopaedics were considered to be eligible. This number was calculated by dividing the total number of publications in the respective categories through the rank of the journal of interest. Literature research was performed until 10 June 2018.

Search Terms:
 Tumour Endoprosthesis
 Advances Tumour Endoprosthesis
 Prosthetic Reconstruction AND Tumour
 Tumour megaprosthesis

Years:
 2015 - 2018

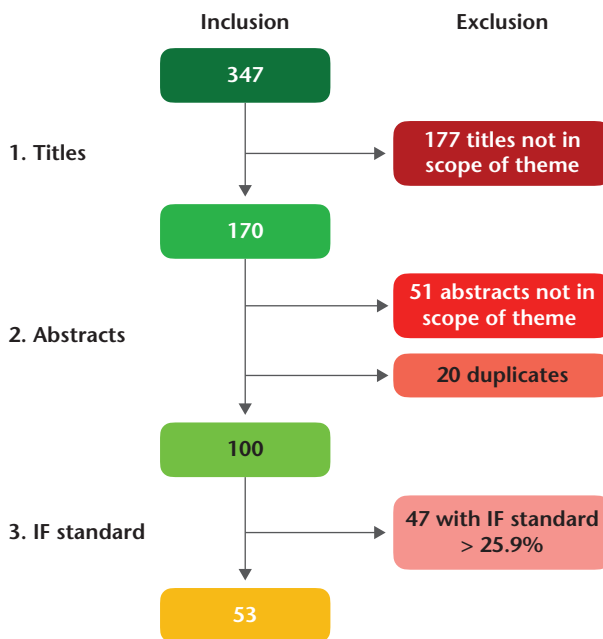


Fig. 1. Flow diagram showing selection of articles

The following search-terms were used to identify studies on advances in tumour endoprostheses: advances tumour endoprostheses, tumour endoprosthesis, tumour megaprosthesis, prosthetic reconstruction AND tumour. Reviews, case reports, duplicates and meta-analyses were excluded manually. Altogether, 347 original studies were identified based on the four abovementioned search terms within the predefined time period. In a first step, 177 articles were excluded from further analyses with study titles not in the scope of the present review, leaving 170 articles potentially eligible. Following the review of the abstract, another 51 articles were excluded due to them not being in the scope of this review and 20 further articles due to duplication. From the remaining 100 articles, 53 had an impact factor ranking them in the top 25.9% either in the category ‘orthopaedics’ or ‘multidisciplinary sciences’ (Fig. 1). All articles with ‘case report’ in the title were excluded in the first step of article selection.

From all articles finally eligible for this study, full-text articles were either downloaded from the respective journal’s website or requested via the author’s own online library. As all necessary information could be extracted from the full-text articles, authors from specific studies were not personally contacted. The majority of the studies were retrospective in design, with only one study with a clear prospective aim.

All articles finally eligible were grouped into six categories: (1) tumour endoprostheses in the shoulder girdle, (2) tumour endoprostheses of the proximal femur, (3) tumour endoprostheses in the knee region, (4) tumour endoprostheses in the pelvis, (5) (expandable)

prostheses in children and (6) long-term results of tumour endoprostheses.

Primary literature research was performed by the first author of the study (MAS), including study selection over the three steps as mentioned above. Those studies finally eligible for the study were reviewed by both the first (MAS) and senior author (AL).

As case reports were excluded from the final analysis, very novel – but to date not well established – reconstructive methods using tumour endoprostheses may not be included in this review. Furthermore, we set the journal’s rating due to the impact factor to < 25.9%, thus potentially excluding studies in small patient cohorts. We only included journals ranking in the top 25.9% of their respective category (this cut-off also includes *International Orthopaedics*) in order to report results of studies with a presumably high impact on readers (see Fig. 2 for the distribution of journals in the respective categories split by impact factor). No additional analyses were performed. The review protocol can be accessed by contacting the corresponding author (MAS).

Results

1) Tumour endoprostheses in the shoulder girdle

Seven studies were identified dealing with tumour endoprostheses around the shoulder girdle (Table 1). In a study by Maclean et al, the outcome of eight patients receiving the Bayle Walker (Stanmore® Implants Worldwide Ltd, Elstree, England, United Kingdom) reversed polarity linked

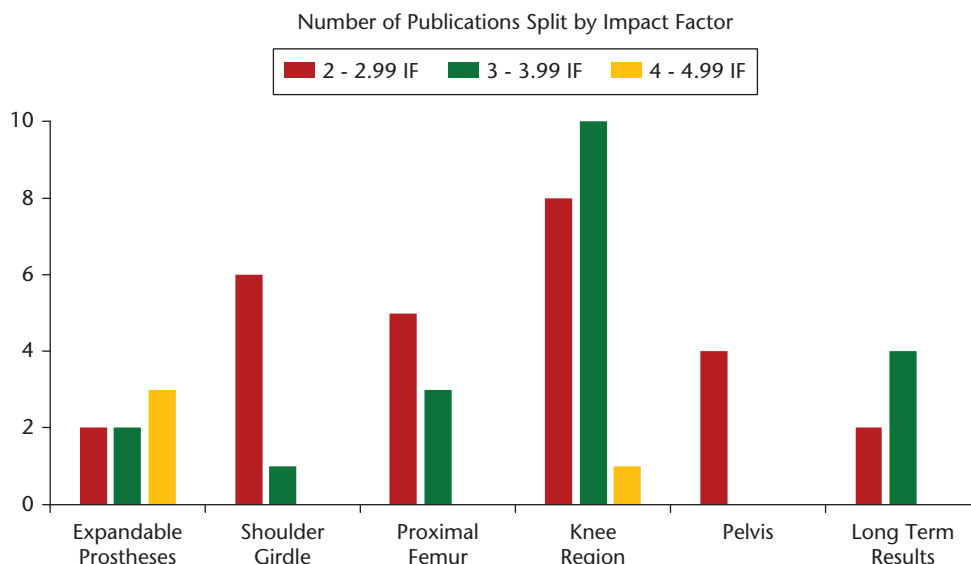


Fig. 2. Number of publications split by impact factor in the respective six categories

Table 1. Tumour endoprostheses in the shoulder girdle

Publication	Results
Maclelan S et al. <i>J Shoulder Elbow Surg</i> 2017 ³	<ul style="list-style-type: none"> – eight patients treated with the Bayley Walker (Stanmore implants Worldwide Ltd, Elstree, England, UK) reversed polarity, linked shoulder replacement – reason for reconstruction was chondrosarcoma in four, metastatic disease in two, Ewing sarcoma and osteomyelitis in one each – Trevira tube used in half of patients – mean follow-up of 4.1 years, survivorship of 100% – neuropathic pain in one patient postoperatively, no local recurrences
Min L et al. <i>Int Orthop</i> 2017 ⁸	<ul style="list-style-type: none"> – 15 patients with scapular hemiarthroplasty following total scapulectomy retrospectively included (2011–2014) – six chondrosarcomas, four osteosarcomas, two Ewing sarcomas, two myelomas, one malignant fibrous histiocytoma (MFH) – average follow-up of 3.4 years, with no infection, dislocation, pressure ulcer, wound healing problems or mechanical failures – three deaths due to lung metastases, no local recurrence – average range of motion (ROM): shoulder abduction 45.3°, forward flexion 65.7° – patients with rotator cuff reconstruction had better postoperative hand positioning, lifting ability, Musculoskeletal Tumour Society (MSTS) score and abduction functions than patients without rotator cuff reconstruction
Schmolders J et al. <i>Int Orthop</i> 2017 ⁴	<ul style="list-style-type: none"> – 30 patients treated with MUTARS (implantcast GmbH, Buxtehude, Germany) for intra-articular resection of proximal humerus, of whom 15 additionally received a Trevira tube – reconstruction for (semi-)malign tumours (n = 9) and metastases (n = 21) – mean follow-up of 2.2 years, with 96% limb survival after this time period – six complications in total (20%), of which three were subluxations of the prosthesis, one local recurrence, one radial palsy, one periprosthetic joint infection (<i>staph. epidermidis</i>; this patient had a Trevira tube), two periprosthetic fractures – mean Enneking score of 20 points – no difference in ROM between Trevira and non-Trevira treatment group
Wang B et al. <i>Int Orthop</i> 2015 ⁵	<ul style="list-style-type: none"> – 18 patients treated with endoprosthesis polypropylene (PPP) mesh composite after bone tumour resection of the proximal humerus included – pre- and postoperative pain scores (VAS) analysed, with most patients experiencing some pain alleviation two weeks after surgery – mean follow-up of 4.7 years, with a mean MSTS score of 66.7% at last follow-up – ROM was 36° for abduction and 39° for shoulder flexion – three complications altogether (16.7%), with one anterior subluxation
Fujibuchi T et al. <i>J Shoulder Elbow Surg</i> 2015 ⁷	<ul style="list-style-type: none"> – nine patients with proximal humeral endoprosthesis suspended by polypropylene (PPP) mesh in bone compared with 12 patients treated with PPP only attached to soft tissues – four of 12 patients with conventional method showed shoulder instability (33.3%), compared with none of the patients with bone-suspended method – shoulder flexion was better in the bone-suspended PPP-mesh method, whilst shoulder abduction was similar in both groups
Meijer ST et al. <i>J Shoulder Elbow Surg</i> 2017 ⁹	<ul style="list-style-type: none"> – 150 patients reviewed for infection rate treated with allograft prosthetic composites (n = 20), endoprostheses (n = 85) or osteoarticular allografts (n = 45) – altogether, 19 patients developed an infection (12%) – allografts were not associated with a higher infection rate (11% in osteoarticular allografts, 14% in endoprostheses, 10% in allograft prosthetic composites)
Tang X et al. <i>Clin Orthop Relat Res</i> 2015 ⁶	<ul style="list-style-type: none"> – 29 patients with intra-articular resections of proximal humerus reconstructed with endoprostheses and a follow-up > two years – synthetic mesh used in half of patients (n = 14), soft tissue reconstruction without mesh in the other half of patients (n = 15) – mean MSTS significantly better for patients in the mesh group (80.0% vs. 66.7%) – forward flexion, external rotation and abduction likewise significantly better in the mesh group as compared with conventional soft tissue reconstruction group

shoulder endoprosthesis was analysed.³ In half of patients, a Trevira® tube was used to potentially enhance shoulder stability.³ The mean Musculoskeletal Tumour Society (MSTS) score in this patient cohort was 60.0%.³ This is comparable to a mean MSTS score of 66.7% reported by Schmolders et al in a study including 30 patients receiving a MUTARS® anatomical prosthesis (implantcast GmbH, Buxtehude, Germany) for intra-articular resections of the proximal humerus.⁴ In this cohort, again half of patients received a Trevira® tube.⁴ Of note, the authors discovered no difference between the Trevira® and non-Trevira® groups with regard to range of motion (ROM), being on average 38° flexion, 35° abduction and 15° external rotation.⁴ This is comparable to the 36° abduction and 39° shoulder flexion as reported by Wang et al in a cohort of 18 patients treated with endoprosthesis (LDK, Co., Ltd, Haidian, Beijing, China) polypropylene mesh composite (PROLENE® light mesh, Ethicon) after bone tumour resection of the proximal humerus.⁵ In that study, a mean MSTS score of 66.7% at last follow-up was reported.⁵ In a similar study by Tang et al, mesh-suspended proximal humeral endoprostheses (LARS (Laboratoire d'Application et de Recherche Scientifique, Arc-sur-Tille, France) wrapped around the shaft of the endoprosthesis; $n = 14$) for malignant tumours were compared with proximal humeral endoprostheses with soft tissue reconstruction only ($n = 15$).⁶ Of note, a significantly better MSTS score was observed in patients with mesh reconstruction than in the soft tissue reconstruction only group (80.0% vs. 66.7%; $p = 0.001$).⁶ Moreover, none of the patients in the mesh group showed proximal migration of the prosthesis, compared with five of 15 patients without mesh reconstruction (33.3%; $p = 0.042$).⁶ This number is similar to the 33.3% of shoulder instability observed by Fujibuchi et al, although these patients had received a proximal humeral endoprosthesis wrapped in PMKM (Marlex mesh or Bard mesh, Warwick, RI, USA) fixed to soft tissues (4/12).⁷ On the other hand, the same mesh fixed to bone resulted in less shoulder instability (0/9) and better shoulder flexion (65° vs. 35° in the soft tissue suspension group; no p -value provided by authors).⁷

In another study by Min et al, the functional outcome of patients with scapular hemiarthroplasty following total scapulectomy for tumours was investigated.⁸ The ROM, with average shoulder abduction of 45.3° and flexion of 65.7°, was relatively better than in the abovementioned studies on proximal humeral resections followed by endoprosthetic reconstruction.⁸ Moreover, rotator-cuff reconstruction was associated with a better postoperative function and improved MSTS score.⁸

Regarding complications of proximal humeral endoprostheses in tumour surgery, Schmolders et al observed six complications in 30 patients (20.0%) treated with a MUTARS® endoprosthesis, of which one was related to

deep infection (3.3%).⁴ This is less than the 12.0% infection rate reported by Meijer et al in a large study on 150 patients with proximal humeral reconstruction for tumours.⁹ In their study, osteoarticular allografts ($n = 45$) were not associated with a higher infection rate (11%) in comparison to endoprostheses ($n = 85$; 14% infection rate) or allograft prosthetic composites ($n = 20$; 10% infection rate).⁹

To summarize, MSTS scores in tumour endoprostheses of the shoulder girdle range between 60.0% and 80.0%, depending on the type of reconstruction. A shoulder flexion up to 65° has been reported in one study where a synthetic mesh was fixed to the bone, thus improving shoulder stability.

2) Tumour endoprostheses in the proximal femur

Eight studies dealing with tumour endoprostheses of the proximal femur could be included in our review (Table 2). The largest study was performed by Henderson et al, comprising 527 patients with proximal femoral arthroplasty for primary bone tumours (benign and malignant) as well as metastases.¹⁰ The authors observed postoperative instability in 20 patients (4.0%), developing after a mean of 35 days.¹⁰ Of note, no capsular repair was not associated with a reduced rate of instability, whilst advanced age, female gender and primary bone tumours were risk factors for instability.¹⁰ The only protective factor against hip instability was a posterolateral approach.¹⁰ Moreover, the authors concluded that a posterolateral approach, together with application of a synthetic device for reconstruction of the soft tissues and a hemiarthroplasty should be best chosen to reduce instability.¹⁰ Corresponding to this, Du et al investigated hip instability in 58 patients with total femoral replacement for sarcoma.¹¹ In 12 patients, a LARS artificial ligament was additionally wrapped spirally around the proximal end of the prosthesis, resulting in a significantly lower hip dislocation rate as compared with conventional soft tissue reconstruction.¹¹ Moreover, the infection rates were comparable between LARS-augmented prostheses and conventional reconstruction (8.3% vs. 10.9%; $p = 0.529$).¹¹ These infection rates are less than the 20.0% observed by Gorter et al in 10 patients treated with push-through total femoral endoprostheses.¹² However, this system allows preservation of parts of the femur as well as its muscle attachments, thus potentially resulting in a better postoperative function.¹² Interestingly, though, a mean MSTS score of 64.0% was achieved in their cohort, in comparison to 72.3% in the group by Du et al, where additional reconstruction with a LARS band significantly increased the postoperative MSTS score from 70.4% to 80.0%.^{11,12} Moreover, the authors observed that simple re-attachment of the gluteus maximus to the LARS band does not improve active ROM, whilst re-attachment of other external rotators (i.e.

Table 2. Tumour endoprostheses in the proximal femur

Publication	Results
Li D et al. <i>Int Orthop</i> 2018 ¹³	<ul style="list-style-type: none"> – extra-articular resection of osteosarcoma ($n = 7$), chondrosarcoma ($n = 7$), undifferentiated pleomorphic sarcoma (UPS; $n = 3$) and malignant peripheral nerve sheath tumour (MPNST; $n = 1$) in hip/proximal femur – pelvic defect reconstructed by modular hemipelvic endoprosthesis, proximal femur reconstructed by using custom-made or modular prox. femoral endoprosthesis – one patient died perioperatively, the other 17 patients were followed-up for 35 months (mean), with 10 patients having no evidence of disease (NED), and 7 patients having died of disease (DOD) – disease-free survival (DFS) and overall-survival (OS) for all patients were 50% each – no difference in outcome between patients treated primarily at tumour centre and those with relapse ($p = 0.287$) – average Musculoskeletal Tumour Society (MSTS)-score of 93, with patients in whom the ilium had been resected having a lower MSTS score ($p = 0.024$)
Stevenson JD et al. <i>Bone Joint J</i> 2018 ¹⁷	<ul style="list-style-type: none"> – proximal femoral replacement without acetabular resurfacing reviewed in 100 patients treated between 2003 and 2013 – 74 procedures for metastases, 20 for primary bone tumours and six for myeloma – acetabular resurfacing graded according to Baker (0 = normal, 3 = protrusio acetabuli) – unipolar in 64 patients, bipolar in 36 – follow-up > one year in 49 patients (mean: 3.6 years), of whom six had Grade 1 acetabular wear and two Grade 2 acetabular wear; the others had normal acetabular wear – femoral reconstruction without acetabular resurfacing seems justified in the short term
Houdek MT et al. <i>J Arthroplasty</i> 2017 ¹⁵	<ul style="list-style-type: none"> – hemiarthroplasty in 199 patients with pathological femoral fractures between 1992 and 2014, mean follow-up of four years – conversion to total hip arthroplasty in two patients (1%) – complications in 12% of patients ($n = 24$), most commonly thrombosis or pulmonary artery embolism (PAE)
Henderson ER et al. <i>Bone Joint J</i> 2017 ¹⁰	<ul style="list-style-type: none"> – 527 patients reviewed, treated with proximal femoral arthroplasty for tumours (209 metastatic disease, 106 chondrosarcoma, 52 osteosarcoma, 38 Ewing sarcoma, 122 others) – instability of the hip in 20 patients (4%), developing after a mean of 35 days – capsular repair not associated with reduced rate of instability – in multivariate analysis, age > 60 years, female gender, a malignant primary bone tumour and benign conditions were associated with higher rate of postoperative instability – posterolateral approach protective against instability – no difference whether hemiarthroplasty, total hip (un)-constrained was used for reconstruction regarding development of instability
Gorter J et al. <i>Int Orthop</i> 2017 ¹²	<ul style="list-style-type: none"> – oncological resections or complications of segmental femoral prostheses can result in severe femoral bone loss – a push-through total femoral endoprosthesis (PTTF) can be used to preserve parts of the femur and its muscle attachments – 10 patients treated between 2005 and 2014 with a PTTF retrospectively included – mean follow up of 5.3 years, with an implant, limb and prosthesis survival of 90%, 100% and 80%, respectively – four failures occurred (two infections, two mechanical failures) --> one amputation for infected prosthesis
Du Z et al. <i>J Arthroplasty</i> 2018 ¹¹	<ul style="list-style-type: none"> – 58 patients treated with total femoral replacement for primary bone or soft tissue sarcoma – artificial ligament (LARS; Laboratoire d'Application et de Recherche Scientifique, Arc-sur-Tille, France) was wrapped spirally around the proximal site of the total femur in 12 patients – hip dislocation rate lower in patients with LARS-augmentation and active range of motion (ROM) as well as limb function better in this cohort – infection rates similar (1/12 for LARS, 5/46 for conventional total femur)
Hobusch GM et al. <i>Clin Orthop Relat Res</i> 2017 ¹⁴	<ul style="list-style-type: none"> – 16 patients with proximal femoral reconstructions for bone sarcoma and a minimum follow-up of five years – preoperatively, 14 patients were able to do sports, as compared to 11 patients at last follow-up – preoperative University of California at Los Angeles (UCLA) and modified Weighted Activity Score levels dropped from 9 and 6 to 6 and 3 at last follow-up
Drexler M et al. <i>Bone Joint J</i> 2015 ¹⁶	<ul style="list-style-type: none"> – 65 patients treated with bipolar proximal femoral endoprostheses for tumours (most commonly osteosarcoma, $n = 20$) – mean follow-up of 9.1 years, after which degenerative changes in the acetabulum were seen in three patients (4.6%), heterotopic ossifications in 17 (26%) and prosthetic head protrusion in nine patients (13.8%) – revision became necessary in eight patients (8.3%), in whom three prostheses were converted to total hip arthroplasty

gemellus, obturator, piriformis, quadratus femoris) may improve external rotation. Of note, Li et al observed a mean MSTS score of 93.0% for patients treated with hemipelvic and proximal femoral endoprostheses, although significantly more structures had to be sacrificed in their procedures.¹³

With regard to postoperative function, Hobusch et al investigated the functional outcome of 16 patients with proximal femoral reconstructions for bone sarcomas and a minimum follow-up of five years.¹⁴ Prior to surgery, 14 of 16 patients (87.5%) were able to do sports. At the mean latest follow-up of 18 years (range 5–27 years), 11 of these patients had resumed sporting activities (68.8%).¹⁴

Another question that arises when dealing with proximal femoral endoprostheses is the durability of hemiarthroplasty in view of chondro-osseous wear-off. With regard to this, Houdek et al investigated the outcome of

hemiarthroplasty for pathological femoral fractures in 199 patients.¹⁵ After a mean follow-up of four years, two patients required conversion to a total hip arthroplasty (1.0%).¹⁵ Reasons for conversion may be prosthetic head protrusion, as observed by Drexler et al in nine out of 65 patients (13.8%) treated with bipolar proximal femoral endoprostheses for tumours.¹⁶ In their cohort, three prostheses had to be converted to total hip replacement after a mean follow-up of 9.1 years (range: 2.0 to 11.8 years; 4.6%).¹⁶ Interestingly, according to Stevenson et al, only eight out of 49 patients treated with unipolar ($n = 64$) and bipolar ($n = 36$) endoprostheses without acetabular resurfacing showed acetabular wear after a minimum follow-up of one year, not exceeding Baker Grade 2.¹⁷

In tumours involving the hip joint, extra-articular resection may become necessary, as described by Li et al in a study involving 18 patients.¹³ Modular hemipelvic

prostheses and custom-made or modular proximal femoral endoprostheses were used for reconstruction.¹³

Conclusively, the better the stability of a proximal femoral implant, the better the postoperative functional outcome can be expected. Moreover, bipolar reconstruction is justified in tumour patients, as acetabular wear can be expected to be minimal.

3) Tumour endoprostheses in the knee region

Nineteen articles were identified dealing with tumour endoprostheses around the distal femur and proximal tibia (Table 3). The largest study identified was that of Pala et al, including 687 distal femoral modular tumour endoprostheses implanted between 1983 and 2010.¹⁸ Of these, the majority were fixed hinge ($n = 491$), whilst 196 implants were rotating hinge.¹⁸ Altogether, 27.0% of patients ($n = 185$) developed complications, with no difference between the rotating hinge and fixed hinge systems.¹⁸ However, all component breakages occurred in prostheses with a rotating hinge system, whilst there was no difference in rate of aseptic loosening (5.9% vs. 2%; $p = 0.55$) or infection (8.9% vs. 6.6%, $p = 0.237$) between fixed-hinge vs. rotating-hinge.¹⁸ Of note, patients with a rotating hinge system had a significantly better mean MSTS score (82.7% compared with 76.3%).¹⁸ This MSTS score is comparable to the 76.3% reported by Zhang et al in a study investigating the outcome of 108 patients with endoprosthetic rotating hinge knee replacement for osteosarcoma.¹⁹ Implant failures occurred in 21 patients (19.4%) after a mean follow-up of 4.4 years, most commonly due to infection.¹⁹ Of note, though, an overall incidence rate of complications of 41.7% was observed in the entire cohort, including peroneal nerve palsy, local recurrences, periprosthetic fracture, joint instability, wound healing disorders, aseptic loosening, mechanical dysfunction, prosthetic infection and breakage of the prosthesis.¹⁹ Moreover, the authors observed a slightly better functional outcome in patients with tumours located in the distal femur in comparison to the proximal tibia, which could be partly related to the fact that proximal tibial resection often necessitates reconstruction of the extensor mechanism, thus influencing postoperative function.¹⁹ These results are contradictory to the observations made by Pala et al in a study on 247 rotating-hinge GMRS knee prostheses (Stryker Inc., Rutherford, NJ, USA) implanted for bone tumours, where there was no difference in MSTS score between distal femoral and proximal tibial tumours (mean MSTS score 84.0%).²⁰ An even better MSTS score was reported by Wang et al in a study on 41 patients reconstructed with allograft-prosthesis composites and rotating-hinge knee prostheses for tumours, being 93.4% on average.²¹

The overall failure rate of the GMRS prosthesis as evaluated by Pala et al was 29.1% (72/247), with infections

being most common ($n = 23$), followed by soft tissue failure ($n = 21$).²⁰ These rates are comparable with those reported by Bus et al in a study on 101 patients with 110 reconstructions with a MUTARS® implant of the distal femur or proximal tibia for malignancy.²² Of 63 complications observed (57.3%), 14 were due to infection and 15 due to structural failure.²² Also in the cohort of Holm et al, most complications observed in this study on 50 patients with megaprostheses of the knee joint and total femur were due to deep infection ($n = 19$).²³ Additionally, in the cohort by Harges et al, the most common complication in 98 patients treated with a MUTARS® endoprosthesis of the proximal tibia was due to infection ($n = 15$).²⁴ Moreover, eight of these patients ultimately required an amputation.²⁴

Twenty-seven stem fractures (12.2%) were reported by Hauer et al in a study involving 221 patients treated with the Kotz Modular Femoral Tibial Reconstruction System (KMFTR®; Stryker Inc., Rutherford, NJ, USA).²⁵ Notably, stem fractures were associated with a significantly smaller stem diameter and a significantly longer extramedullary component.²⁵ Therefore, augmented systems with osteoarticular allografts may be used, as described by Qu et al in a study on 29 patients treated with cortical strut bone grafts combined with long-stem endoprosthetic reconstruction in the knee joint.²⁶ In their study, bone healing was observed in 23 of 29 patients reconstructed with cortical strut allografts in addition to tumour endoprostheses after a mean of 3.9 years.²⁶

In patients receiving endoprostheses or osteoarticular allografts in the proximal tibia, mean MSTS scores of 88.6% and 91.7% were observed by Albergo et al.²⁷ Interestingly, failure rates were higher in the osteoarticular allograft group as compared with the group of patients reconstructed with endoprostheses (18.0% vs. 27.0% at five years). Moreover, mechanical failure was the most common reason for revision in patients with endoprostheses, whilst infections were the main cause in the osteoarticular allograft group.²⁷

Regarding periprosthetic joint infections, the use of silver-coated implants in order to minimize infection risk is of interest. In the study by Harges et al, the infection rate was lower in 56 silver-coated implants of the proximal tibia in comparison to 42 titanium-based implants in the same body region after a median follow-up of 8.2 years (8.9% vs. 16.7%).²⁸ Additionally, only one patient in the silver-coated implant group had to undergo an amputation, as compared with three patients in the titanium-based group.²⁸

With regard to osseointegration of tumour endoprostheses, Liang et al compared the functional and oncological outcomes of 62 cases with uncemented tibial fixation and 58 cases with cemented tibial fixation in distal femoral replacement for bone tumours.²⁹ Osseointegration was observed in 64.3% of patients with an uncemented

Table 3. Tumour endoprostheses of the knee region

Publication	Results
Hardes J et al. <i>Int Orthop</i> 2018 ²⁴	<ul style="list-style-type: none"> – 98 patients undergoing reconstruction with MUTARS (implantcast GmbH, Buxtehude, Germany) endoprostheses following intra-articular resection of proximal tibia – median age 18 years, median follow-up 98 months – five- and ten-year implant survival rates of 90.5% and 74.5% – cumulative incidence of implant failure 29% at five years, with infections being most frequent reason for secondary amputation
Pesenti S et al. <i>Int Orthop</i> 2018 ³²	<ul style="list-style-type: none"> – 15 patients (mean age of 25.2 years) included – nine patients underwent surgery with allograft and sparing of epiphysis – six patients received a megaprosthesis – decreased knee flexion in loading response phase in both groups upon gait analysis – no difference in gait pattern between treatment groups, using Gait Deviation Index and Gillette Gait Index
Hardes J et al. <i>J Arthroplasty</i> 2017 ²⁸	<ul style="list-style-type: none"> – 98 patients treated with MUTARS endoprostheses (silver-coated $n = 56$; titanium $n = 42$) retrospectively analysed for infections – Infection rate lower in silver than titanium group (8.9% vs. 16.7%), as was implant survival (90% vs. 84%) – secondary amputation necessary in 14.3% of silver-coated implants, compared with 37.5% of titanium implants
Etchebehere M et al. <i>J Bone Joint Surg Am</i> 2016 ³¹	<ul style="list-style-type: none"> – 48 patients with and 60 without patellar resurfacing following resection of femoral tumour with endoprosthetic reconstruction – mean age 33.9 years, mean follow-up of 4.5 years – no difference in anterior knee pain or Musculoskeletal Tumour Society (MSTS) score between both groups – complication rates comparable between the two groups – resurfacing group significantly more often showed peripatellar calcifications
Zimel MN et al. <i>Clin Orthop Relat Res</i> 2016 ³⁵	<ul style="list-style-type: none"> – 27 patients (mean age 30 years) undergoing revision surgery for failed distal femoral prosthesis using the Compress Compliant Pre-stress (CPS; Zimmer Biomet, Warsaw, IN, USA) implant – cumulative incidence for mechanical failure was 11%, occurring after a median of five months – incidence of remaining failures was 18%, most commonly due to deep infections – median MSTS score of 27 (after a minimum of two years of follow up or until implant removal)
Holm CE et al. <i>Int Orthop</i> 2018 ²³	<ul style="list-style-type: none"> – megaprostheses of distal femur ($n = 29$), proximal femur ($n = 9$), proximal tibia ($n = 9$) and total femur ($n = 3$) – three years from primary surgery to first revision, in 27 patients altogether (54%)– deep infection as main cause for revision ($n = 19$), 78 revision surgeries in total – implant revision-free survival at five and ten years: 43% and 24% – finally amputation in six patients (12%) – overall survival at five and ten years: 89% and 83% (with 30 osteosarcomas, nine chondrosarcomas, 6 giant cell tumours, four Ewing sarcomas and one angiosarcoma of bone) – 22 of 50 patients died during follow-up (44%; causes not explored)
Hauer TM et al. <i>J Arthroplasty</i> 2018 ²⁵	<ul style="list-style-type: none"> – 221 patients treated with the Kotz Modular Femoral Tibial Reconstruction System (KMFTR, Stryker Inc. Rutherford, NJ, USA) reviewed for implant fracture (112 distal femur, 53 proximal tibia, 40 proximal femur, 13 total femur, three distal femur + proximal tibia) – system failure in 27 patients (12%), most commonly in the distal femur ($n = 21$) – mean time to fracture of system: seven years – in patients with stem fracture, the stem diameter was significantly smaller (12 vs. 14 mm, $p = 0.001$), and with a significantly longer extramedullary component (18 vs 15 cm, $p = 0.04$)
Goulding KA et al. <i>Clin Orthop Relat Res</i> 2017 ³⁶	<ul style="list-style-type: none"> – compressive osseointegration endoprostheses (Compliant Prestress Device (Zimmer Biomet, Warsaw, IN; USA)); coupled with various modular prostheses to replace segmental humeral bone loss) used in nine patients who underwent 13 endoprosthetic replacements – two for proximal humerus, two for humeral diaphysis, seven for distal humerus, two for proximal ulna – minimum follow-up of two years in 12 implants, of which six required revision – the compressive osseointegration endoprosthesis allows reconstruction of difficult revisions or sarcoma resections in the upper extremity – however, complications frequently occur
Albergo JJ et al. <i>Clin Orthop Relat Res</i> 2017 ²⁷	<ul style="list-style-type: none"> – 133 patients treated between 1990 and 2012 at two tumour centres with proximal tibial resections for primary bone tumours were included – reconstruction either with osteoarticular allograft ($n = 45$) or endoprosthesis ($n = 88$) – mean follow-up of 9.5 years for endoprostheses and 7.4 years for osteoarticular allografts – implant failure for endoprosthetic reconstruction was 18% at five years, compared with 27% for osteoarticular allografts – 51 endoprostheses failed (58%, most commonly mechanical failure), in comparison to 19 osteoarticular allografts (42%, most frequently infection)
Bus MP et al. <i>Clin Orthop Relat Res</i> 2017 ²²	<ul style="list-style-type: none"> – inclusion of 101 patients with a total of 110 reconstructions (after exclusion of four cases lost to follow-up) – median follow-up of 8.9 years – most common diagnosis osteosarcoma ($n = 56$) – altogether, 63 complications were observed – Hydroxile apatite (HA) coated uncemented implants with lower risk for loosening – infections occurred in 14 reconstructions and structural complications in 15 reconstructions – at last follow-up, 90 patients (89%) had a MUTARS in situ (although some had been salvaged after complication)
Etchebehere M et al. <i>J Arthroplasty</i> 2016 ³⁰	<ul style="list-style-type: none"> – distal femoral replacement in 108 patients with malignant ($n = 81$), benign ($n = 11$), metastatic ($n = 15$) and non-tumoral ($n = 1$) lesions – patellar height was calculated with Insall-Salvati ratio (ISR) and Insall-Salvati patellar tendon insertion ratio (PTR) directly postoperatively and at last follow-up – average follow-up of 4.5 years – patellar height was not associated with range of motion (ROM), anterior knee pain or extension lag, but generally decreased significantly after distal femoral resection (from 1.45 to 1.4 for the PTR)
Barut N et al. <i>Int Orthop</i> 2015 ³⁴	<ul style="list-style-type: none"> – 17 patients with 18 periprosthetic fractures following implantation of a tumour endoprosthesis in hip or knee were included – 12 fractures occurred after femoral resection (67%) and six following tibial resection – most common fracture type was located in the femoral or tibial shaft – most patients underwent surgery for periprosthetic fracture ($n = 16$), with only one patient receiving another implant – overall probability of failure following periprosthetic fracture for any reason was 27% at five and 55% at ten years
Qu H et al. <i>Bone Joint J</i> 2015 ²⁶	<ul style="list-style-type: none"> – 29 patients included, treated with cortical strut bone graft combined with long-stem endoprosthetic reconstruction (cemented) – bone healing in 23 patients (86%) after a mean of 3.9 years – mean MSTS score was 85% (57 to 97) and five-year implant survival 81% – ten complications observed (four non-unions, two aseptic loosening, two infections, one haematoma, one patellar dislocation)

(continued)

Table 3. (Continued)

Publication	Results
Lang NW et al. <i>Clin Orthop Relat Res</i> 2015 ³³	<ul style="list-style-type: none"> – 27 patients treated for osteosarcoma around the knee with modular endoprosthetic reconstruction between 1995 and 2005 (out of 120) – distal femur in 16 and proximal tibia in 11 – prior to implantation and at last follow-up, 24 (89%) and 24 (89%) of patients were able to perform sports, with the rate increasing over the years (from 33% over 74% to 89%) – higher sport activity levels prior to surgery were associated with higher sport activity levels at last follow-up – although 14 patients underwent revision surgery, they had no influence on sport activity levels
Liang H et al. <i>Int Orthop</i> 2018 ²⁹	<ul style="list-style-type: none"> – comparison between 62 cases with uncemented tibial fixation and 58 cases with cemented tibial fixation in distal femoral replacement – operation time shortened by 26 minutes when uncemented method used – no disadvantage in oncological and prosthetic outcomes for uncemented system – uncemented systems rather helped to preserve anterior cortical thickness during follow-up – osseointegration observed in 64.3% of cases ($n = 36$) with uncemented system
Zhang C et al. <i>Int Orthop</i> 2018 ¹⁹	<ul style="list-style-type: none"> – 108 patients treated with endoprosthetic knee replacements for osteosarcoma (between 2006 and 2013), located either in the distal femur ($n = 72$) or proximal tibia (36) – at last follow-up, 33 patients were dead of disease (DOD) and 10 patients have had local recurrence, with five-year overall-survival (OS) of 71% – 45 patients developed a total of 51 complications, resulting in five-year implant survival rates of 77.7% – 21 implant failures occurred, most commonly due to infection (5/21) – mean MSTS score at last follow-up was 76.3% – implant survival, functional outcome and complication rates were slightly better for prostheses with tumours located in the distal femur as compared to proximal tibia
Pala E et al. <i>Int Orthop</i> 2016 ¹⁸	<ul style="list-style-type: none"> – between 1983 and 2010, 687 distal femoral tumour modular prostheses were implanted (491 fixed hinge, 196 rotating hinge) – failure occurred in 27% of patients ($n = 185$) – 10- and 20-year failure rates were 70% and 50%, with no difference between fixed and rotating-hinge systems – all component breakages occurred in the rotating-hinge system – no difference in rate of aseptic loosening or infection was identified between the two systems – patients with rotating-hinge systems had significantly better MSTS score (82.7% vs. 76.3%)
Wang CS et al. <i>J Arthroplasty</i> 2015 ²¹	<ul style="list-style-type: none"> – 41 patients with high-grade malignant bone tumours around the knee receiving a bone prosthesis composite and rotating-hinge knee prosthesis – nine tumours in the proximal tibia, 32 tumours in the distal femur – mean follow-up of 4.5 years, with mean ROM in the knee of 125° – five complications observed (11%), including two local recurrences, one periprosthetic fracture and two non-unions – mean MSTS score at last follow-up was 93.4%
Pala E et al. <i>Clin Orthop Relat Res</i> 2015 ²⁰	<ul style="list-style-type: none"> – 247 rotating-hinge GMRS knee prostheses (Stryker Inc., Rutherford, NJ, USA) implanted for malignant and aggressive benign bone tumours, of whom 175 were primary implants – of the 175 patients with primary implants, 117 patients had no evidence of disease (NED) at latest follow-up, 26 had NED after having had a recurrence, eight were alive with disease (AWD) and 24 DOD – overall failure rate of the GMRS megaprosthesis was 29.1% (72/247) – infections were most common (9.3%; 23/247), followed by soft tissue failure (8.5%; 21/247) – overall implant survival rate of 70% at four and 58% at eight years – mean MSTS score of 84% at last follow-up, with no difference regarding site (proximal tibia vs. distal femur)

system. Moreover, the surgical time was reduced by 26 minutes on average when implanting an uncemented system, prompting the conclusion that in tumour patients with a poor general condition uncemented systems are likewise suitable with the advantage of shortened surgery time.²⁹ There was no difference in revision rates between cemented and uncemented systems (9.6% vs. 5.4%, $p = 0.399$).

Another interesting finding regarding the postoperative function of tumour endoprostheses around the knee joint was reported by Etchebehere et al in a study involving 108 patients with distal femoral endoprosthetic replacement for tumoural ($n = 107$) and non-tumoural reasons ($n = 1$).³⁰ They investigated the relative patellar height by applying the Insall-Salvati ratio (ISR) as well as the Insall-Salvati patellar tendon insertion ratio (PTR) directly postoperatively and at last follow-up.³⁰ Of note, the patellar height was not associated with ROM, anterior knee pain or extension lag, but generally decreased significantly after the operation (from 1.45 to 1.4 for the PTR (ratio of two lines drawn on lateral radiographic images of the knee)).³⁰

Regarding patellar resurfacing, Etchebehere et al analysed the outcomes of 48 patients receiving tumour endoprostheses of the distal femur or proximal tibia with patellar resurfacing and 60 patients without patellar resurfacing.³¹ There was no difference in anterior knee pain between the groups.³¹ Moreover, anterior knee pain did not significantly alter extensor lag, range of motion, reoperation or complication rates.³¹ Although complications in general were similar between the resurfaced and non-resurfaced groups, peripatellar calcifications were more frequently seen in the resurfaced group.³¹ Nevertheless, mean MSTS scores of 81% and 71% were observed for the non-patellar resurfacing and patellar resurfacing-groups respectively, which was not statistically significant ($p = 0.30$).³¹ Consequently, the decision in favour of or against patellar resurfacing should be made individually in each case.

Another interesting study investigated the postoperative mobility in patients receiving allografts ($n = 15$) or megaprostheses ($n = 6$) for malignant tumours of the knee region.³² An allograft augmented with a fibula graft was implanted in cases where more than 2 cm above the knee joint could be

Table 4. Tumour endoprostheses in the pelvis

Liang H et al. <i>Bone Joint J</i> 2017 ³⁸	– 35 patients treated with 3D-printed pelvic endoprostheses between 2013 and 2015 (three iliac prostheses, 12 standard hemipelvic prostheses, 20 screw-rod connected hemipelvic prostheses) – lesions were Type I in three, Type II+III in 12, Type I+II in five, Type I+II+III in two, Type I+II+IV in 10 and Type I-IV in three – implants used for osteosarcoma ($n = 11$), chondrosarcoma ($n = 9$), Ewing sarcoma ($n = 6$) and others ($n = 9$) – wide margins in 15 patients (42.9%), marginal in 14 (40%) and intralesional in six (17.1%) – after a mean follow-up of 1.7 years, 25 patients had no evidence of disease (NED), 5 were alive with disease (AWD) and five patients were dead of disease (DOD) – mean MSTS-score of 63.7%, and generally lower for patients with screw-rod connected prosthetic reconstruction – complications developed in nine patients (seven with delayed wound healing requiring debridement, two with hip dislocation)
Wang B et al. <i>Int Orthop</i> 2015 ³⁹	– six patients included treated for a malignant pelvic tumour involving regions I/II/IV with a hemipelvic prosthesis (LDK, Co. Ltd., Haidian, Beijing, China) – mean postoperative MSTS score was 53.9% – stress tests were performed at a force of 400 N when sitting and standing on two feet – in normal pelvis, stress distribution was around acetabulum, arcuate line, SI joint and sacral midline in both positions – in the reconstructed pelvis, stress distribution was mainly concentrated on the connecting rods of the acetabular component and the proximal segment of the pedicle rods – generally higher peak stresses in reconstructed pelvis as compared to normal pelvis
Issa SP et al. <i>Int Orthop</i> 2018 ³⁷	– Integra® (Lépine, Genay, France) ice-cream-cone prosthesis used in 24 patients with periacetabular malignant tumours (Type II or Type II+III resections) – after a mean follow-up of 4.1 years, patient survival was 88% (of whom 15 had NED) – mean MSTS score was 72% at last follow-up – in 14 patients, at least one complication developed, with four infections, four dislocations and two mechanical failures – five-year implant survival was 75%
Wang B et al. <i>Int Orthop</i> 2018 ⁴⁰	– 11 patients with periacetabular malignant bone tumours treated by personalized 3D-printed hemipelvic prosthesis – average follow-up of 1.3 years – hip dislocation observed in two patients and delayed wound healing in one – pre- vs. postoperative visual analogue scale (VAS) score was 4.5 vs. 1.8 – mean Musculoskeletal Tumour Society (MSTS) score at last follow-up was 64%

kept. According to Pesenti et al, there was no difference in gait pattern between the groups, albeit in the megaprosthesis group, a decreased knee flexion during the load and stance phase was observed.³² Moreover, the Gait Deviation Index (GDI), was significantly lower in both groups as compared to a control group.³² Therefore, sparing of the epiphysis may not significantly increase the functional outcome in patients with tumours around the knee joint.

With regard to functional outcomes, Lang et al investigated the postoperative ability of patients to perform sports following reconstruction with modular tumour endoprostheses around the knee joint.³³ Prior to implantation, 24 of 27 (89.0%) patients were able to do sports, as were 24 patients at last follow-up (89.0%). Importantly, the rate of sporting activity increased steadily over the years, from 33.0% over 74.0% to the abovementioned 89.0% at an average follow-up of 11 years.³³ Even revision surgeries that became necessary in 14 patients had no influence on the patients' activity levels.³³

One study elaborating the outcome of tumour patients with periprosthetic fractures was performed by Barut et al.³⁴ They investigated 17 patients with 18 periprosthetic fractures following endoprosthetic replacement for tumours around the knee joint.³⁴ Sixteen of these patients underwent surgery, with only one requiring another implant. Overall probability of failure following periprosthetic fracture for any reason was 55.0% at 10 years.³⁴

Another problem in reconstruction with (tumour) megaprostheses is the huge bone loss in case of failed treatment, limiting further reconstructions. With regard to this, Zimel et al have discovered low rates of mechanical failure in 27 patients treated with the Compress®

Compliant Prestress Device (Zimmer Biomet, Warsaw, IN, USA) for failed reconstruction of the distal femur for tumoural ($n = 26$) and non-tumoural ($n = 1$) indications.³⁵ The cumulative incidence of mechanical failure was 11% at five years and did not increase thereafter. A median MSTS score of 90.0% was reported, which is surprisingly high.³⁵ Noteworthy, the Compress® Compliant Prestress Device requires few bone contacts in the shaft, but has a shallow learning curve.

Contrary to this, Goulding et al have investigated the outcome of a compressive osseointegration endoprosthesis (Compress® Compliant Prestress Device; Zimmer Biomet, Warsaw, IN, USA) coupled with modular prostheses in nine patients with a total of 13 endoprosthetic replacements and discovered a high complication rate.³⁶ The revision rate of 50% in 12 implants with a follow-up > 24 months was relatively high.³⁶

4) Tumour endoprostheses in the pelvis

Four studies were focused on tumour endoprostheses and prosthetic reconstruction in the pelvis (Table 4). Two of these described the results of 3D-printed pelvic endoprostheses for large bone defects following wide tumour resection, whilst the third investigated the outcome with the Integra® ice-cream cone prosthesis (Lépine, Genay, France) and the fourth study reported the results on a custom-designed hemipelvic prosthesis.

In the Integra® ice-cream cone study by Issa et al, 24 patients with periacetabular malignant tumours – necessitating Type II ± Type III resections – were followed-up for a mean of 4.1 years.³⁷ Mean MSTS score was 72.0% at last follow-up.³⁷ However, complications were observed in 14

patients (58.3%), with infections being most common ($n = 4$).³⁷ In comparison to periacetabular resections, the mean MSTS scores for hemipelvic resections were relatively lower in the other studies, ranging from 53.9% to 64.0%.^{38,39} The largest of the three studies by Liang et al investigating the outcome after hemipelvic resection involved 35 patients reconstructed with 3D-printed pelvic endoprostheses.³⁸ Nine patients (25.7%) developed complications (seven wound healing deficits, two hip dislocations), albeit no deep infection was observed, after a median of 20.5 months.³⁸ In another study by Wang et al, the outcomes of 11 patients receiving personalized 3D-printed hemipelvic endoprostheses were investigated.³⁹ Comparable to the study by Liang et al, one patient presented with delayed wound healing and two patients had hip dislocation.⁴⁰ The mean MSTS score at last follow-up was 64.0%, which is comparable with the 53.9% observed by Wang et al in six patients receiving hemipelvic prostheses for bone tumours.³⁹ The authors did not only investigate the subjective outcome, but also performed stress tests with patients sitting or standing on two feet.³⁹ Whilst stress distribution in the normal pelvis was mainly located around the acetabulum, arcuate line, sacroiliac joint and sacral midline both when sitting or standing, the stress distribution moved to the connecting rods of the acetabular component and the proximal segment of the pedicle rods in patients with reconstructions.³⁹ This highlights that peak stresses are generally higher in the reconstructed pelvis, which should be considered in the development of new implants.

5) (Expandable) prostheses in children

Seven original articles were identified dealing with expandable tumour endoprostheses in young patients (Table 5). Gilg et al investigated 51 custom-made growing prostheses (Juvenile Tumour System, Stanmore® Implants Worldwide Ltd, Elstree, England, UK) used for reconstruction of primary bone sarcoma of the femur and proximal tibia in 50 children between 2003 and 2014.⁴¹ Three- and five-year revision-free survival were 81.7% and 61.6%, with deep infections (Henderson Type IV) being most common ($n = 10$).⁴¹ In another study by Arteau et al, distal femoral growing prostheses in 23 children were investigated (Repiphysis® (Wright Medical Technology Inc., Arlington, TN, USA)) in 14 patients, custom Biomet® prosthesis (Zimmer Biomet, Warsaw, IN, USA) in eight, Juvenile Tumour System (Stanmore® Implants Worldwide Ltd, Elstree, England, UK) in one patient), with specific focus on leg-length discrepancy.⁴² In 65% of patients, the proximal tibial epiphysis – although intact except for the insertion point of the tibial stem – grew less over time than the contralateral epiphysis.⁴² Interestingly, in one patient an overgrowth of the proximal physis was observed.⁴² Corresponding to this, Cipriano et al reported

the outcomes of the Repiphysis® (Wright Medical Technology Inc., Arlington, TN, USA) expandable prosthesis in 10 young patients with osteosarcoma.⁴³ Altogether, they observed 37 implant-related complications (amounting to an average of 3.7 complications per patient), requiring 15 revision surgeries.⁴³ Slightly fewer complications were reported by Schinhan et al on the identical system, with a mean of 2.6 complications per patient.⁴⁴ Each patient in this cohort underwent a mean of 4.4 lengthening procedures (invasive, minimally invasive and non-invasive) with an average limb elongation of 70.8 mm.⁴⁴ This is more than the 42.7 mm reported by Gilg et al and the 39 mm observed in the study by Staals et al.^{41,45}

Interestingly, mean MSTS scores of 88.3% and 87.8% were observed in the study by Gilg et al and Schinhan et al,^{41,44} compared to 64.0% and 67% reported by Staals et al and Cipriano et al.^{43,45} In the latter three studies, the Repiphysis® system was used, where no clear tendency towards a poorer outcome can be observed.

Additionally, Torner et al reported on a mean lengthening of 36.4 mm in seven patients receiving a MUTARS® Xpand Growing Prosthesis (implantcast GmbH, Buxtehude, Germany) in the distal femur ($n = 6$) and proximal femur ($n = 1$), and a mean MSTS score of 87.7%.⁴⁶ Notably, none of the patients in this cohort developed any local recurrence and one deep infection was treated by arthroscopy and antibiotics.⁴⁶ On the other hand, seven out of 50 patients (14.0%) in the cohort by Gilg et al finally underwent amputation due to infection ($n = 4$) or local recurrence ($n = 3$).⁴¹ A lower rate was observed by both Arteau et al, with two out of 23 patients undergoing amputation for local recurrence (8.7%),⁴² and Schinhan et al, with 2 out of 71 patients (2.8%) undergoing amputation, again due to local recurrences.⁴⁴

Another technique that may be used in reconstruction of large bone defects, especially in children, are resurfaced allograft-prosthetic composites, as described in the study by Campanacci et al including 19 young patients treated with this method for bone tumours of the proximal tibia.⁴⁷ The mean implant survival was 68 months, with major complications including six allograft fractures, two non-unions and one infection.⁴⁷ The most common complication was leg-length discrepancy that could be lowered to a mean of 1.9 cm at latest follow-up following contralateral epiphysiodesis. The mean MSTS score was 73.3% in this cohort.⁴⁷

6) Long-term results of tumour endoprostheses

Altogether, six articles published between 2015 and 2018 meeting the abovementioned criteria were dealing with the long-term outcome of tumour endoprostheses in primary and metastatic bone disease as well as soft tissue sarcomas (Table 6). Regarding very long-term complications, Grimer et al observed in their cohort of 230 patients treated

Table 5. (Expandable) prostheses in children

Publication	Results
Torner F et al. <i>Int Orthop</i> 2016 ⁴⁶	<ul style="list-style-type: none"> – seven paediatric patients (mean age 9.8 years) included, undergoing surgery for femoral tumours using an uncemented non-invasive growing prosthesis – mean follow-up of 65.3 months – mean bone resection length 18 cm (distal femur) and 24 cm (proximal femur) – Musculoskeletal Tumour Society (MSTS) score at a mean of 26.3 after rehabilitation – 36.4 mm as mean lengthening distance – two implant related complications
Gilg MM et al. <i>Bone Joint J</i> 2016 ⁴¹	<ul style="list-style-type: none"> – 50 children receiving 51 growing prostheses between 2003 and 2014 – most common location was distal femur ($n = 40$), followed by proximal tibia ($n = 6$), total femur ($n = 4$) and proximal femur ($n = 1$) – reason for reconstruction was osteosarcoma in 47 patients (92.2%) and Ewing sarcoma in four (7.8%) – three- and five-year overall survival (OS) of 84% and 70%, respectively and revision-free three- and five-year survival 81.7% and 61.6% – deep infections developed in 10 patients (19.6%), followed by failure of lengthening mechanism in five (9.8%) – local recurrences occurred in five patients (9.8%) – at last follow-up (mean time of 5.3 years), 34 patients had no evidence of disease (NED), 13 had died of disease (DOD) and 3 were alive with disease (AWD) – 53 additional operations were performed, of which seven were amputations (three for local recurrence, four for infection) – revision surgery less often in distal femoral replacement compared to other sites (see above) – neither age nor implant of the prosthesis before 2009 were risk factors for OS or implant-survival
Arteau A et al. <i>J Bone Joint Surg Am</i> 2015 ⁴²	<ul style="list-style-type: none"> – 23 children treated between 1994 and 2012 with an expandable distal femoral endoprosthesis were included – the proximal tibial physis was intact in all patients following surgery (except for the insertion point of the tibial stem) – in 65% of patients ($n = 15$), the proximal tibia had grown less than the contralateral limb – in five of these patients, the discrepancy stabilized while it worsened in ten patients – in one patient, overgrowth of the proximal tibia was observed – in seven patients, no discrepancy developed – more than 2 cm discrepancy at last follow-up was found in five patients (22%) and three of these later on underwent contralateral epiphysiodesis
Schinhand M et al. <i>J Bone Joint Surg Am</i> 2015 ⁴⁴	<ul style="list-style-type: none"> – 71 children treated with extendible prosthesis and a follow up > 2 years were analysed – at last follow-up, 12 patients were DOD (16.9%) – mean MSTS score was 87.8% – 184 complications in 58 patients were observed, most commonly related to soft tissues (Henderson Type I), requiring 2.5 re-operations per patient on average – on average, each patient received 4.4 lengthening procedures for a limb elongation of 70.8 mm
Cipriano CA et al. <i>Clin Orthop Relat Res</i> 2015 ⁴³	<ul style="list-style-type: none"> – repiphysis expandable prosthesis for distal femoral osteosarcoma used in ten children with a mean follow-up of six years – average MSTS score was 67% – 37 implant-related complications, necessitating 15 revision surgeries (of which six were for aseptic loosening) – a median of two lengthenings performed in each patient – all patients showed metadiaphyseal compromise surrounding the prosthesis stem, complicating potential future treatment with standard stem prostheses
Staals EL et al. <i>Clin Orthop Relat Res</i> 2015 ⁴⁵	<ul style="list-style-type: none"> – 15 children treated with the repiphysis expandable prosthesis after resection for malignant bone tumours (14 osteosarcomas, one Ewing sarcoma) – five patients died with the prosthesis in situ or underwent amputation before five years of follow-up leaving ten long-term survivors – of the ten long-term survivors, nine underwent revision of the implant for mechanical failure (eight implant breakages and one stem loosening) and five of these required segmental bone grafts during revision – mean MSTS score of 64% prior to revision surgery and at final follow-up 81% – an average lengthening of 39 mm was achieved – at last follow-up, six patients had another type of growing prosthesis in situ and three patients and adult-type megaprosthesis
Campanacci L et al. <i>J Bone Joint Surg Am</i> 2015 ⁴⁷	<ul style="list-style-type: none"> – 19 children with a resurfaced allograft-prosthetic composite for proximal tibial bone sarcoma included (18 osteosarcomas, three Ewing sarcomas, one giant cell tumour) – mean follow-up of 6.5 years – mean implant survival of 68 months, with major complications including one infection, two non-unions, and six allograft fractures – contralateral epiphysiodesis left a mean leg-length discrepancy of 1.9 cm – 13 patients had retained original construct at last follow-up, with a mean MSTS of 73.3% and range of motion (ROM) > 90° knee flexion in eight patients (62%)

with growing ($n = 46$) and non-growing ($n = 184$) tumour endoprostheses in the knee joint, hip, humerus and pelvis 2.7 further operations on average (equivalent to 610 additional surgeries), most commonly aseptic loosening ($n = 112$), re-bushing ($n = 40$) and deep infection ($n = 25$) after a mean follow-up of 29.4 years.⁴⁸ On the other hand, Capanna et al observed in their cohort of 200 patients treated with the Megasystem C (Waldemar LINK® GmbH & Co. KG, Hamburg, Germany) for tumours of the hip and knee 71 failures in 58 implants, most commonly due to mechanical reasons (59.2% of all failures, including aseptic loosening, soft tissue failure and structural failure).⁴⁹

In order to minimize the risk of implant fractures, extra-cortical plates may be used for augmentation of short-stemmed endoprostheses, as described in the study by Stevenson et al.⁵⁰ In their cohort of 37 patients reconstructed with tumour endoprostheses augmented by extra-cortical plates for large resections exceeding > 70.0% of the bone's original length, there was no difference in implant survival when compared to standard stemmed controls at any site (humerus, hip and knee).⁵⁰

Another important topic regarding long-term outcome of tumour endoprostheses is the postoperative mobility of patients. In the study by Bernthal et al, the postoperative

Table 6. Long-term results of tumour endoprostheses

Publication	Results
Bernthal NM et al. <i>Clin Orthop Relat Res</i> 2015 ⁵¹	<ul style="list-style-type: none"> – 69 patients undergoing endoprosthetic reconstruction for bone sarcoma of lower extremity – 24 patients (eight proximal tibial, nine distal femoral, seven proximal femoral implants) underwent gait analysis at a mean of 13.2 years postoperatively – median O₂-consumption comparable to control group, as was walking speed – reduced knee extension/flexion strength in patients with proximal tibial replacement compared to other sites
Stevenson JD et al. <i>Bone Joint J</i> 2017 ⁵⁰	<ul style="list-style-type: none"> – short-stemmed endoprostheses may be augmented by extra-cortical plates to minimize risk of aseptic loosening – 37 patients with limb salvage for primary bone neoplasm between 1998 and 2013 (nine proximal humerus, nine proximal femur, 13 distal femur, six proximal tibia) – 25 revision procedures (68%) and 12 primary surgeries (32%) – amount of resected bone was > 70% of its length and statistically greater than the standard control group at each site involved (matched controls) – mean stem length in proximal humerus 33 mm and 79 mm in the lower limb (all Stanmore custom-made implants, Stanmore Implants Worldwide Ltd, Elstree, England, United Kingdom) – no difference in implant survival between short-stemmed endoprostheses and standard-stemmed controls at any site – none of the implants with extra-cortical plate suffered loosening, in comparison to three out of ten without osseointegration (30%)
Grimer RJ et al. <i>Bone Joint J</i> 2016 ⁴⁸	<ul style="list-style-type: none"> – 230 patients with a mean follow-up of 29.4 years were included, treated with endoprosthetic replacement for malignant bone tumours – most common diagnosis was osteosarcoma ($n = 132$), followed by Ewing sarcoma ($n = 31$), chondrosarcoma ($n = 24$), spindle cell sarcoma ($n = 19$) and giant cell tumour ($n = 18$) – most common site was distal femur in 102 patients – each patient underwent, on average, 2.7 operations following primary surgery – infections were associated with a higher rate of re-operation – the highest risk for infection was in the proximal tibia and generally developed earlier after any revision surgery
Benevenia J et al. <i>Clin Orthop Relat Res</i> 2016 ⁵³	<ul style="list-style-type: none"> – 41 patients treated with 44 intracalarey implants between 2008 and 2013 (21 femur, 18 humerus, five tibia) – majority had metastatic lesions ($n = 33$; 80%) – average follow-up of 1.2 years, with 14 patients dead of disease (DOD) – 13 complications altogether, most commonly structural failures ($n = 6$, 14%; Henderson Type III) – most complications occurred in the femur ($n = 12$), whilst in tibia and humerus no complications developed – mean Musculoskeletal Tumour Society (MSTS) score of 77%, with cemented implants having a higher score
Wang B et al. <i>Clin Orthop Relat Res</i> 2016 ⁵²	<ul style="list-style-type: none"> – ten patients treated with unipolar prosthesis after resection of Grade III giant cell tumours in the distal radius – six out of ten patients developed complications, including one aseptic loosening and two wrist subluxations – in two patients, pain associated with the implant was present at last follow-up
Capanna R et al. <i>Clin Orthop Relat Res</i> 2015 ⁴⁹	<ul style="list-style-type: none"> – 200 patients with minimum follow-up of two years included, treated with Megasystem C megaprosthesis for tumours of hip or knee (most commonly osteosarcoma, in 58 cases) – proximal femur in 69, distal femur in 87, proximal tibia in 32 and total knee in 12 patients – 71 failures in 58 implants were observed (29%), with mechanical failures being most common (59.2% of all failures) – the anatomical site had no influence on occurrence or type of complications – overall incidence of infection was 9.5%

mobility of 24 patients treated with tumour endoprostheses in the hip ($n = 7$) and knee ($n = 17$) was analysed using gait analysis and O₂-consumption.⁵¹ According to their results, the median O₂-consumption was not significantly different in the tumour prosthesis group as compared with healthy controls.⁵¹ Interestingly, patients with proximal tibial replacements had reduced knee extension (reduced by 84%) and flexion strength (reduced by 35%) in comparison to patients in the other reconstruction groups, which is comparable to the results of the study by Pesenti et al.³²

Very few studies were discovered in the present review dealing with smaller joints such as the ankle and the wrist. In the study by Wang et al, the outcome of 10 patients treated with unipolar prostheses after resection of Grade III giant cell tumours in the distal radius was investigated.⁵² In their cohort, six out of 10 patients developed a complication, including two wrist subluxations and one aseptic loosening.⁵² In two patients pain associated with the implant was still present at last follow-up.

The outcome of intracalarey implants in the femur ($n = 21$), humerus ($n = 18$) and tibia ($n = 5$) was reported by Benevenia et al.⁵³ In total, 13 complications were observed

in 44 patients, most commonly due to structural failure ($n = 6$).⁵³ Of note, the majority of complications were observed in implants of the femur.⁵³ A mean MSTS score of 77.0% was observed for all locations, with cemented implants being associated with a better score.⁵³

In summary, long-term outcomes following endoprosthetic reconstruction in tumour surgery are relatively good in terms of functionality. However, complications occur frequently and do not only pose a threat to the treating team but also significantly affect a single patient's perspective on postoperative outcome.

Discussion

In the studies compiled in the present review, the authors focused on functional outcomes, complications and long-term follow-up of tumour endoprostheses used in orthopaedic oncology. Regarding functional outcomes – usually evaluated with the MSTS score – these did not significantly differ between studies dealing with identical body regions. However, there was a tendency towards poorer functional outcomes the more aggressive the resections had been and the larger the used implants

were. Moreover, the larger the implants, the more frequently complications were observed. Specifically, infections posed a major problem in endoprosthetic reconstruction with megaprotheses. Of note, only a few studies were identified dealing with preventive procedures to lower the risk of infection in tumour surgery, e.g. the use of silver-coated implants. In this field, further in-depth research should be performed in order to lower the risk of infection, which often leads to revision and implant explantation with major consequences for the patient. Another important issue in endoprosthetic reconstruction with large tumour endoprotheses is the fact that patients are getting older despite staying more active, wherefore the risk for periprosthetic fractures is raised. Of note, only one study was identified in the present review dealing exclusively with periprosthetic fractures around tumour endoprotheses.³⁴

There are some limitations in the present review. As we excluded studies journals with an impact factor ranking > 25.9% in the respective category, results on smaller patient cohorts or from small-volume centres may not have been discussed. Moreover, as we excluded all case reports, very novel advances in endoprosthetic reconstruction of tumour endoprotheses may not have been considered.

Conclusion

The long-term results of tumour endoprotheses used in orthopaedic oncology depend on several factors, including the postoperative functionality, patient satisfaction and the rate of complications.

Over the last three years, 53 studies have been published dealing with tumour endoprotheses. However, significant novelties were lacking amongst these studies. On the other hand, many studies focused on long-term results on already established reconstructive procedures, which is equally important with regard to clinical applicability of specific reconstructive techniques.

In the next few years, studies should also focus on prevention of frequently observed complications – especially deep infections of tumour endoprotheses and periprosthetic fractures, as these issues pose a major threat to orthopaedic surgeons and treated patients.

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FUNDING STATEMENT

Although none of the authors has received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article, benefits have been or will be received but will be directed solely to a research fund, foundation, educational institution, or other non-profit organization with which one or more of the authors are associated.

ICMJE CONFLICT OF INTEREST STATEMENT

DA reports honorarium and travel expenses for a lecture, unrelated to this study from Lilly and travel expenses for a meeting unrelated to this study from Implantcast GmbH.

AL reports grants/grants pending paid to his institution outside the submitted work from Metronic, Johnson & Johnson, Alphamed.

All other authors declare no conflict of interest.

LICENCE

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