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Review Article

Frequency and reason for reoperation following non-invasive expandable endoprostheses: A systematic review

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ABSTRACT

Background: Non-invasive expandable endoprostheses (NIEPR) utilize an external electromagnetic field to drive an innate mechanical gearbox. This lengthens the extremity following oncological resections in children with a predicted limb length discrepancy (LLD), facilitating limb-salvage. This review was conducted to assess NIEPR implant survival rates and identify modes of implant failure unique to these prostheses.

Methods: Medline, EMBASE and the Cochrane Library databases were searched for all manuscripts evaluating implant survival of NIEPRs implanted into skeletally immature patients following resection of extremity sarcomas. Minimum follow-up of 12 months or implant failure was required for inclusion. Failures were classified using the latest ISOLS classification and exact implant-specific failure modality was also identified.

Results: 19 studies met inclusion criteria. Mean age was 10.0 years (7.7 – 11.4 years). The most common locations for NIEPR implantation were the distal femur (343, 76.7%) and proximal tibia (53, 119%). Mean follow-up was 65.3 months (19.4 – 163 months). The overall implant revision rate was 46.2% (0 – 100%); implant specific revisions included maximal prosthesis lengthening with persistent LLD (10.4%), failed extension mechanism (6.1%), implant fracture (7.7%), hinge fracture (1.4%) and bushing wear (0.9%). Persistent clinically significant (>20 mm) LLD at final follow-up was present in 19.2% (0 – 50%) of patients. The mean MSTS score was 85.1% (66.7–96.3%) at final follow-up.

Conclusion: Implant-related failures are the most common reason for NIEPR revision. Implant reliability appears to be improved with current designs. A sub-classification to the current classification system based on implant-specific failures for NIEPRs is proposed.

Contents

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1. Introduction

Osteosarcoma and Ewing sarcoma are the most common primary malignant bone sarcomas in children. Management requires a multidisciplinary approach, including chemotherapy, wide surgical resection and in certain cases, radiotherapy.[1] There has been a paradigm shift towards limb-salvage surgery (LSS) in orthopaedic oncology over the last 30 years. LSS now constitutes 90–97% of extremity sarcoma resections.[2,3] LSS offers improved functional capacity and quality of life compared to those undergoing amputation, with no detriment to oncological outcomes.[4–9] Survival rates for children with localized bone sarcoma are approaching 70% at 5 years, and therefore, optimizing functional outcomes is of growing importance to survivors.[10]

Performing successful limb-salvage in the skeletally immature presents an added challenge due to the open epiphyseal growth plate, damage of which can result in a functionally significant limb-length discrepancy (LLD), risking poor gait mechanics and a reduced quality of life.[11,12] Strategies to safely resect the tumour, while sparing the physis, exist for diaphyseal-located lesions, however, tumours are most often located in the metaphysis and safe resection often includes the growing physis.[1,13] Other reconstruction options include rotationplasty, standard (non-extendable) endoprosthesis or biological reconstruction with allo- or autograft. These can be combined with later limb-lengthening or contralateral limb epiphysiodesis to address any LLD.[14] High failure, associated morbidity and difficult surgical technique associated with some of these procedures led to the advent of growing endoprostheses which are gradually lengthened, mimicking natural limb growth to prevent LLD.[15]

The first expandable prosthesis was designed in 1976 by Dr. Scales with Stanmore (Stanmore Implants Worldwide, Addison, TX) utilizing a worm-gear expansion mechanism in the Mark 1 design.[16] Subsequent generations of this prosthesis utilized ball-bearing or incremental C-collar (or sleeve) interposition, requiring open surgery and exposure of the prosthesis for extension. With second generation prostheses, extensions were done "minimally-invasively" through a small incision and manual rotation of a worm-drive mechanism with a chuck key.[17] These implants required additional operations, an anesthetic and exposure of the prosthesis.[18]

Modern, third generation expandable endoprosthesis utilize non-invasive expansion mechanisms. Within the body of these implants are telescoped segments of prosthesis which slide relative to each other. An innate magnetic disc and gearbox within the prosthesis are powered when placed at the center of a rotating electromagnetic field. This rotates, generating a steady rate of implant extension, without the need for anaesthesia or an incision (Fig. 1).[17,19–21] Compared to previous designs, this design aims to reduce the rate of infection, the most common complication following any EPR implantation.[22,23] However, due to the magnetic system, patients are unable to undergo MRI scans.

Limb-salvage with endoprostheses is associated with complications, which Henderson *et al* originally categorized into three mechanical and two non-mechanical modes of failure, with a subsequent modification to include expandable prostheses and paediatric failures.[23,24] This system has allowed for standardization and simplification of limb-salvage outcome reporting. Previous literature regarding expandable endoprostheses have reported a 43–59% revision rate; however, these combine outcomes of minimally-invasive *and* non-invasive prostheses and solely use the Henderson classification to stratify implant-related failures, which are grouped as "Structural failure; Implant breakage or wear; expandable implant lengthening malfunction."[24,25]

The primary aims of the present study are to identify and quantify the incidence of mechanical and implant-specific revision rates for non-invasive expandable endoprostheses (NIEPRs). Secondary aims were to classify implant failure by the mode of mechanical failure specific to these novel endoprostheses.

2. Methods

2.1. Search strategy

This study was carried out according to the Preferred Reporting for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[26] A literature search was performed from inception to January 10, 2021 of the MEDLINE, Embase and Cochrane Library databases. The search terms applied were: (non-invasive OR noninvasive OR expandable OR extendable OR extendible OR growing OR minimally invasive OR minimally-invasive) AND (endoprosthes* OR prosthesis OR megaprosthes* OR mega-prosthes* OR replacement OR prosthetic OR limb*salvage OR limb*preserving OR limb saving) AND (cancer OR sarcoma* OR tumour* OR tumor* OR osteosarcoma OR Ewing*) AND (paediatric* OR pediatric* OR child* OR adolescent* OR skeletally immature). Duplicate manuscripts were removed. A manual search of the reference lists of included studies was also performed, although this did not yield any additional manuscripts meeting inclusion criteria.

2.2. Inclusion and exclusion criteria

Study inclusion and exclusion criteria were defined *a priori*. Two independent reviewers (JRL and JDS) performed screening of each title and abstract with discrepancies settled by consensus discussion. Studies must have reported revision rates of NIEPRs implanted following primary extremity sarcoma resection in skeletally immature patients for inclusion. Studies of prospective or retrospective design were included. Minimum follow-up time was 12 months from index surgery or until implant failure. Case reports and reviews were excluded. In addition, to minimize false over- or underrepresentation of complication rates, studies with recruitment of less than five patients were excluded. When authors from the same institution presented case series of the same patients at

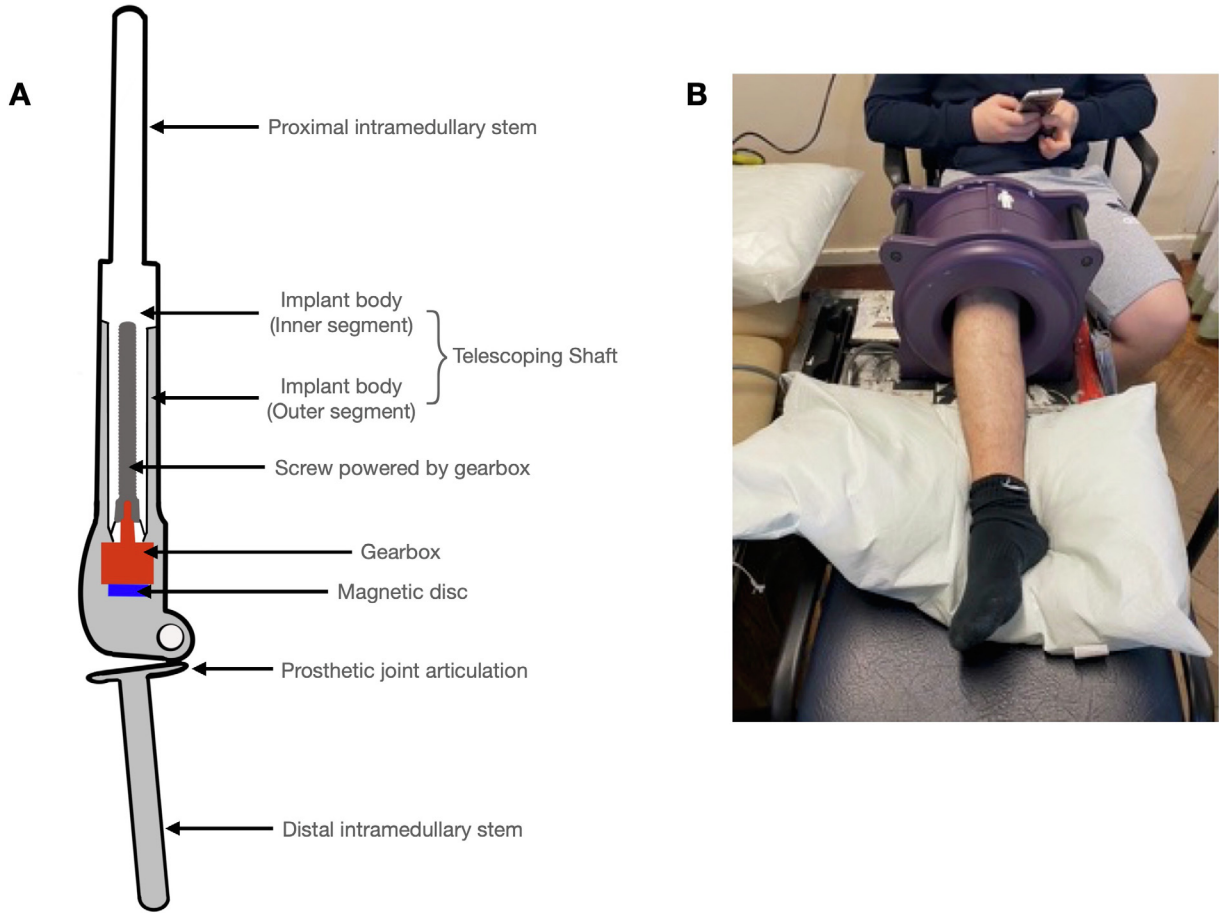

Fig. 1. Depiction of the internal mechanisms of a typical, third generation, non-invasive expandable prosthesis (A). Example of a patient undergoing prosthesis lengthening in clinic with an external lengthening drive unit (B). (Clinical photograph taken and reproduced with consent).

different follow-up periods, the study with the longest follow-up period was selected and the prior studies excluded. Studies published before 2000 or not published, or available, in the English language were excluded.

2.3. Study quality

The Methodological Index for Non-Randomized Studies (MINORS) criteria was used to determine the quality of included studies.[27] For each included study, a total score from zero to a maximum 16, for non-comparative, and 24, for comparative studies, is comprised from 12 domains, each with a score between of zero to two. This was performed by two independent reviewers (JRL and AA) with discrepancies resolved by consensus.

2.4. Data extraction

Data extraction was performed independently by two reviewers (JRL and AA) according to a standardized predesigned form. Any discrepancies were resolved by consensus after discussion with a third author (JDS). Study data recorded included; author, publication year, study design and patient number. Following this patient demographic data, tumour type, mean follow-up duration and patients lost to follow-up were collected. Surgery information including prosthesis type, mean amount lengthened, mean number of prosthesis lengthening procedures, final limb-length discrepancy in millimetres (mm) and percent of patients with LLD > 20 mm. A LLD of >20 mm was chosen as this has been considered clinically significant in several previous studies.[12,28,29] Finally, outcome data including mean Musculoskeletal Tumor Society (MSTS) score, mean number of additional operations required, and implant failures were recorded.

Implant failures were recorded and categorised according to the most recent Henderson (ISOLS) classification.[24] Endoprosthesis failures were defined as failure of the prosthesis that necessitated exchange of hardware. Implant failure (ISOLS type 3A) necessitating revision were then sub-categorised into the exact specific reason for failure, when details were available. For example, irrigation and debridement procedures were not classified as a failure according to Henderson, whereas a staged exchange of a prosthesis was. Number of additional operations included all subsequent returns to the operating room.

2.5. Statistical analysis

Average data between studies was presented as weighted means and ranges. Weighted means were calculated according to the total included patient size. Overall rates were calculated as the number of events of the outcome in question across all studies divided by the total number of patients across all studies. No statistical comparison of outcome data was performed due to the innate heterogeneity between studies and lack of available data. Data was analyzed using Stata 16.1 (StataCorp, College Station, TX). P-values of < 0.05 were considered statistically significant.

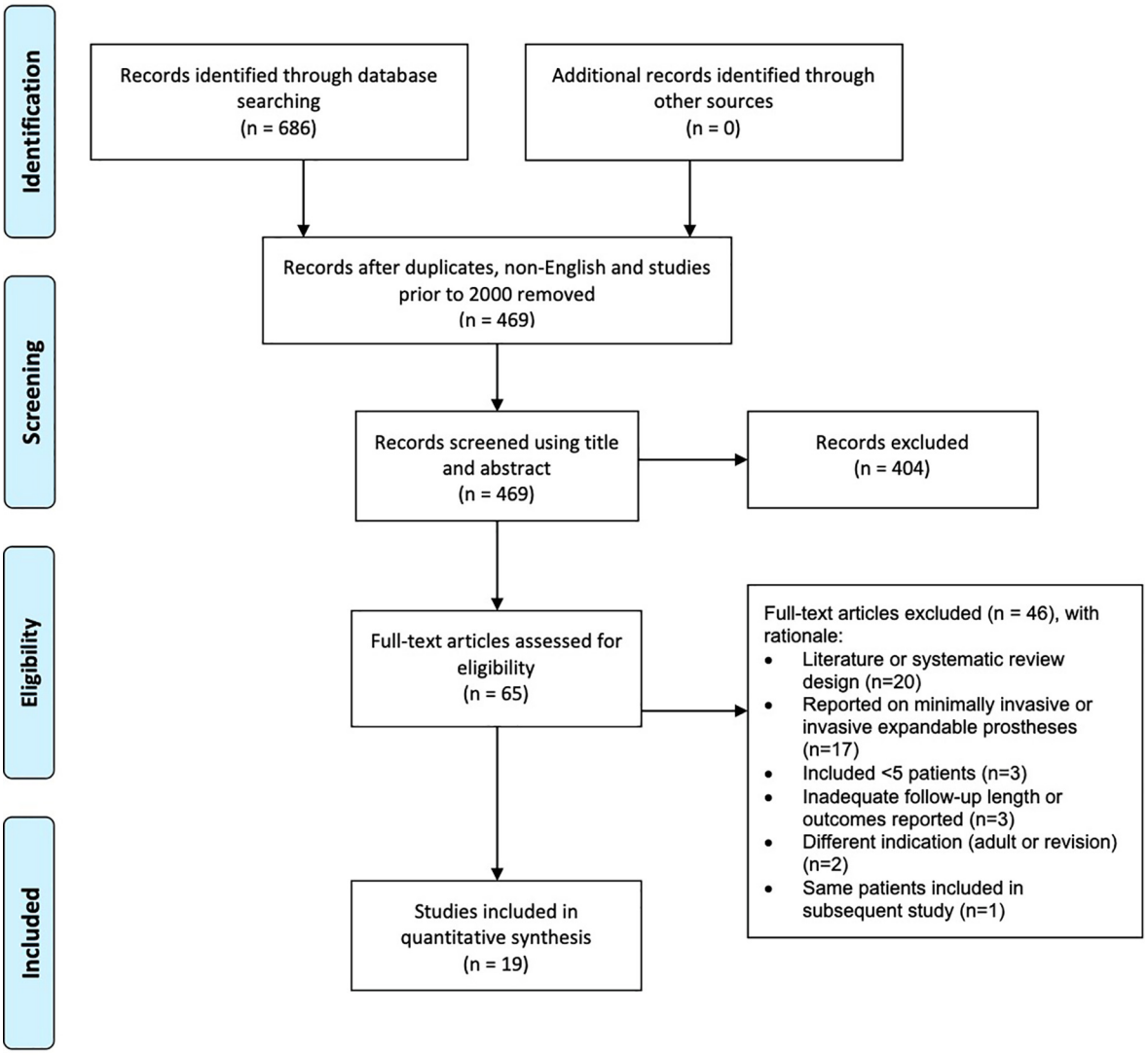

Fig. 2. Search results and study selection flowchart.

3. Results

3.1. Search results

Overall, there were 469 references identified following the initial search and removal of duplicates. Following screening and full-text review, 19 studies met the inclusion criteria (Fig. 2).[30–47] Included studies were published between 2003 and 2020. Altogether, these included a total of 495 patients, with a range of 6 to 101 patients included per study. Limiting to patients with > 12 months follow-up, there were 441 patients. There were eight studies, encompassing 132 patients (26.7%), that analyzed outcomes of the Repiphysis® prosthesis (Microport Orthopedics, Arlington, Tennessee, USA) (originally the Phenix prosthesis).[30,31,40–44] Twelve studies, including 356 patients (71.9%), evaluated the Juvenile Tumour System (JTS) (Stanmore Implants, Elstree, UK)[32–39,41,46,47] and one study with seven patients (1.4%) evaluated the MUTARS® Xpand prosthesis (ImplantCast, Buxtehude, Germany).[45] The lengthening mechanisms of these implants vary, details of each are described in Table 1.

3.2. Study quality

The mean MINORS score for included studies, was 10.2 points, with a range of 7 to 16 points. All studies had a retrospective design, there were no prospective or randomized studies. 17 of these studies were conducted at a single-centre, and two were multi-centred (Table S1).

3.3. Patient demographics

The mean age of patients at time of non-invasive EPR implantation was 10.0 years (mean range: 7.7 to 11.4 years) and included 244 (53.5%) male patients (range: 28.6% to 87.5% male patients). Resected tumours included osteosarcoma in 400 (87.7%), Ewing sarcoma in 52 (11.4%) and others in four (0.9%) patients. The most common anatomical location for NIEPR implantation was the distal femur (n = 343, 76.7%), followed by the proximal tibia (n = 53, 11.9%), total femur (n = 30, 6.7%), proximal femur (n = 14, 3.1%), proximal humerus (n = 3, 0.7%), femur intercalary (n = 3, 0.7%)

Table 1
Description of the lengthening mechanisms for each non-invasive expandable prosthesis included in this study.

Prosthesis	Manufacturer	Mechanism
Repiphysis	Microport Orthopedics, Arlington, Tennessee, USA	The implant locking mechanism is heated using an electromagnetic field. This heat also softens the polymer tube within the prosthesis. Potential energy from a compressed spring in the inner tube of the prosthesis is released. Elongation occurs in 20 s.
Juvenile Tumour System	Stanmore Implants, Elstree, UK (Now part of Stryker Corporation, Kalamazoo, Michigan, USA)	An external rotating electromagnetic field powers a magnetic disc. The disc is connected to the input shaft of a gearbox. The output shaft of the gearbox is connected to the inner segment of the telescopic shaft. Rotation of the gearbox therefore causes the segments of the telescopic shaft to separate, and lengthen. Elongation occurs at 023 mm/minute (1 mm/4 min) and can be performed in clinic.
MUTARS Xpand	ImplantCast, Buxtehude, Germany	Mechanical growing module with electric motor. Energy is transmitted through an electromagnetic inductive field through the skin to a small receiver in the subcutaneous tissue that is connected to a mechatronic actuator in the prosthesis. Elongation occurs at 1 mm/day in 5 min and can be performed at home.

and total humerus (n = 1, 0.2%). The mean follow-up was 65.3 months (range: 19.4 to 163 months) (Table 2).

3.4. Implant survivorship and complications

The overall implant revision rate was 46.2% (range: 0 to 100%). This appeared to be higher in studies evaluating the Repiphysis implant, 66.0% (range: 42.9 to 100%), compared to the JTS prosthesis, 36.9% (range: 0 to 78.6%). There were no revisions in the study evaluating the MUTARS implant. The mean number of additional surgeries required following the implantation of a NIEPR is 0.81 (range: 0.08 to 2.10). In the Repiphysis studies the mean was 1.21 additional surgeries (range: 0.6 to 2.10) and 0.62 (range: 0.30 to 1.50) in the JTS study groups. Implant failures according to the ISOLS classification are listed in Table 3. The most common indication for implant revision was structural, implant failure (Type 3A), with a 16.1% incidence, followed by aseptic loosening (Type 2A and 2B) at 8.8%, and infection (Type 4A and 4B) at 8.8%. Soft-tissue failure (Type 1A) also necessitated subsequent surgery in 8.6% of patients.

The more specific modes of implant failure identified were: (1) maximal prosthesis lengthening achieved with a persistent LLD; (2) premature extension mechanism failure; (3) prosthesis body or stem fracture; (4) implant hinge articulation fracture; (5) implant bushing or articulation wear (Table 4). The most common indication for revision surgery was achieving the maximum extendable length, which occurred in 46 patients, 10.4%. The extension mechanism failed in 27 patients, 6.1%. Extension mechanism failure (7.8% and 5.2%) and prosthesis fracture (21.9% and 2.0%) appeared to be more frequent with the Repiphysis prosthesis than with JTS, respectively. However, the JTS implant was revised more commonly for achieving the maximum extendable length (4.7% and 13.1%, for Repiphysis and JTS, respectively). The lengthening mechanism of one (14.3%) MUTARS implant failed.

3.5. Limb lengthening and functional scores

For all patients, the mean lengthening achieved was 38.1 mm (range: 6 to 88 mm), including patients that underwent no prosthesis lengthening sessions because they were unwell and/or

Table 2
Baseline study and patient characteristics by study and prosthesis subgroup.

Study Characteristics				Patient Characteristics		
Lead Author, Year	Patient Number (n)	Mean Follow-up (months)	Prosthesis	Mean Age (years)	Male Sex (n, %)	Anatomic Location
Dukan R (JTS), 2021	12	73.2	JTS	8.2	5 (41.7)	DF 11; PT 1
Tsuda Y, 2020	12	163.0	JTS	11.1	7 (87.5)	DF 10; PT 1; PF 1
Gundavda MK, 2019	16	49.6	JTS	10.3	11 (68.8)	DF 13; IC 3
Coathup MJ, 2019	42	22.0	JTS	10.1	23 (54.8)	–
Sambri A, 2019	101	64.0	JTS	9.5	50 (49.5)	DF 99; PT 1; TF 1
Medellin MR, 2018	13	158.4	JTS	11.0	–	TF 13
Tsagozis P, 2018	6	72.0	JTS	10.0	–	PT 6
Gilg MM, 2016	50	64.0	JTS	10.4	24 (48.0)	DF 40; PT 6; TF 4; PF 1
Ruggieri P (JTS), 2013	7	19.4	JTS	8.6	4 (57.1)	DF 7
Hwang N, 2012	34	44.0	JTS	11.0	18 (52.9)	DF 25; PT 3; TF 5; PF 1
Picardo NE, 2012	55	41.2	JTS	11.4	33 (60.0	DF 33; PT 12; TF 2; PF 8
Henderson ER, 2012	8	48.0	JTS	10.4	–	DF 6; PF 2
Dukan R (Repiphysis), 2021	28	117.6	Repiphysis	7.7	15 (53.6)	DF 22; PT 6
Cipriano CA, 2015	10	72.0	Repiphysis	10.1	6 (60.0)	DF 10
Staals EL, 2015	15	75.4	Repiphysis	8.0	9 (60.0)	DF 14
Benevenia J, 2015	20	57.0	Repiphysis	9.8	9 (45.0	DF 9; PT 3; TF 4; PH 3; TH 1
Ruggieri P (Repiphysis), 2013	15	50.3	Repiphysis	9.1	9 (60.0)	DF 14
Saghieh S, 2010	17	61.7	Repiphysis	10.5	10 (58.8)	DF 10; PT 7
Haidar R, 2008	12	31.0	Repiphysis	11.0	–	DF 4; PT 3
Neel MD, 2003	15	22.0	Repiphysis	11.0	9 (60.0)	DF 10; PT 4; TF 1
Torner F, 2016	7	65.3	MUTARS Xpand	9.8	2 (28.6)	DF 6; PF 1
Mean, (range)	23.6 (6–101)	65.3 (19.4–163.0)		10.0 (7.7–11.4)	53.5% (28.6–87.5)	

Table 3
Non-invasive endoprosthesis revisions categorized by the latest ISOLS prosthesis failure classification system, stratified by prosthesis type.

ISOLS EPR failure classification	Total Patients, n (%)	By Prosthesis Type	
		Repiphysis	JTS
Type 1A (Soft-tissue - Functional)	38 (8.6%)	14 (10.9%)	24 (7.8%)
Type 1B (Soft-tissue - Coverage)	16 (3.6%)	3 (2.3%)	13 (4.3%)
Type 2 (Aseptic loosening)	38 (8.8%)	18 (18.8%)	15 (4.9%)
Type 3A (Structural - Implant)	71 (16.1%)	39 (30.5%)	31 (10.1%)
Type 3B (Structural - Bone)	13 (3.0%)	4 (3.1%)	9 (2.9%)
Type 4 (Infection)	39 (8.8%)	12 (9.4%)	26 (8.5%)
Type 5 (Tumour progression)	24 (5.4%)	6 (4.7%)	18 (5.9%)
Type 6 (Paediatric)	9 (2.0%)	1 (0.8%)	8 (2.6%)

Table 4
Implant-related failures specific to non-invasive endoprostheses, stratified by prosthesis type.

Mode of Structural Implant Failure	Patients, n (%)	Prosthesis	
		Repiphysis	JTS
Maximal prosthesis length achieved with persistent LLD (Type 1)	46 (10.4%)	6 (4.7%)	40 (13.1%)
Premature failure of the extension mechanism (Type 2)	27 (6.1%)	10 (7.8%)	16 (5.2%)
Implant body or stem fracture/breakage (Type 3)	34 (7.7%)	28 (21.9%)	6 (2.0%)
Fracture of implant hinge	6 (1.4%)	0 (0.0%)	6 (2.0%)
Implant bushing or articulation wear or loosening between components	4 (0.9%)	1 (0.8%)	3 (1.0%)

undergoing therapy for their disease. The mean amount lengthened was 38.3 mm (range: 19.2 to 58 mm) in the Repiphysis studies and 38.1 mm (range: 6 to 88 mm) in the JTS studies. The mean number of lengthening sessions for patients was 5.8 (range: 0 to 40 sessions), with 4.0 (range: 2.2 to 6.0 sessions) in the Repiphysis and 7.2 (range: 1.4 to 15.5 sessions) in the JTS studies. At final follow-up, there was an average LLD of 8.8 mm (range: 0 to 25 mm), with a mean 14.6 mm LLD in the Repiphysis studies and 4.5 mm in the JTS studies.

The mean proportion of patients with a clinically significant, >20 mm, LLD at final assessment was 19.2% (range: 0 to 50%). There appeared to be a higher proportion of patients with a significant LLD (>20 mm) for those who received a Repiphysis (25.8%, range: 0 to 50%) rather than a JTS prosthesis (13.7%, range: 0 to 41.7%). The overall mean MSTS score was high, at 85.1% (range: 66.7 to 96.3%). MSTS scores were similar between prostheses, at 81.7% (range: 66.7 to 93%) and 87.6% (range: 79.3 to 96.3%) in the Repiphysis and JTS studies, respectively (Table 5).

4. Discussion

The aim of this study was to determine the cause and incidence of implant failure following NIEPR prosthesis insertion. We believe this is the first comprehensive systematic review to focus on the complications following modern, third-generation expandable prostheses. With improving technology and more reliable outcomes, use of endoprostheses to reconstruct segmental osseous defects has been increasing.[48] The rates and figures presented in this study should aid clinicians to counsel and educate patients and their families on the risks associated with NIEPRs. Prior to this study, the available evidence to estimate risk of NIEPR revision, functional outcomes and number of lengthening sessions was based on small patient cohorts. Moreover, structural implant failures specific to these modern implants have not been defined or quantified to date. These are important factors to consider during patient follow-up and for focusing efforts for further technical improvements.[36,49]

Table 5
Lengthening and functional outcomes by study and prosthesis subgroup.

Study Characteristics Lead Author, Year	Patient Number (n)	Prosthesis	Functional Outcomes Mean amount lengthened (mm)	Final LLD (mm)	% patients with LLD > 2 cm	Mean lengthening sessions	Mean MSTS score (%)
Dukan R, (JTS), 2021	12	JTS	49.0 mm	–	16.7%	8.0	87.6%
Tsuda Y, 2020	12	JTS	–	2.0	0.0%	6.3	93.0%
Gundavda MK, 2019	16	JTS	27.7	11.8	41.7%	7.9	96.3%
Coathup MJ, 2019	42	JTS	21.0	–	–	4.0	–
Sambri A, 2019	101	JTS	–	–	21.5%	–	86.7%
Medellin MR, 2018	13	JTS	–	–	–	6.6	90.0%
Tsagozis P, 2018	6	JTS	–	–	–	–	–
Gilg MM, 2016	50	JTS	42.7	4.3	–	6.0	88.3%
Ruggieri P (JTS), 2013	7	JTS	6.0	–	–	1.4	79.3%
Hwang N, 2012	34	JTS	32.0	–	–	5.0	85.0%
Picardo NE, 2012	55	JTS	38.6	–	2.3%	11.3	82.3%
Henderson ER, 2012	8	JTS	88.0	0.0	0.0%	15.5	87.8%
Dukan R (Repiphysis), 2021	28	Repiphysis	58.0	–	21.4%	6.0	83.3%
Cipriano CA, 2015	10	Repiphysis	39.0	–	–	3.8	67.0%
Staals EL, 2015	15	Repiphysis	39.0	18.0	40.0%	4.6	81.0%
Benevenia J, 2015	20	Repiphysis	48.0	–	–	4.5	82.2%
Ruggieri P (Repiphysis), 2013	15	Repiphysis	29.1	25.0	50.0%	2.6	66.7%
Saghieh S, 2010	17	Repiphysis	19.2	0.8	17.6%	2.2	90.0%
Haidar R, 2008	12	Repiphysis	37.8	–	–	4.0	93.0%
Neel MD, 2003	15	Repiphysis	36.3	–	0.0%	4.3	90.0%
Torner F, 2016	7	MUTARS Xpand	36.4	–	–	–	87.7%
Mean, (range)	23.6 (6–101)		38.1 (6.0–88.0)	8.8 (0.0–25.0)	19.2% (0.0–50.0)	5.8 (1.4–15.5)	85.1% (66.7–96.3)

There is a 19.1% revision rate for structural failures (Type 3A + B) in NIEPRs. This was primarily due to implant-specific failures (Type 3A), 16.1%, rather than osseous failures (*peri*-prosthetic fractures) (Type 3B), 3.0%. The other causes of revision including; functional soft tissue failures (12.2%), aseptic loosening (8.8%), infection (8.8%), local tumour progression (5.4%) and paediatric failures (2.0%) occurred at similar rates to previous reports. [15,22,25,50,51] Amongst adults with endoprostheses, a large review by Thornley *et al* identified structural (implant or bone) complications to be the number one cause for revision, occurring in 16% of causes. This was followed by aseptic loosening (12%) and infection (9%).[50]

Overall revision rate for NIEPRs is around one in four patients for structural or implant-related complications (117/441 patients, 26.5%). This includes revisions for exchange of prosthesis that achieved maximum lengthening (10.4%) and may be considered to be expected, as there is limited potential for length within the physical constraints of the body of the NIEPR. The most common implant-specific failures identified were achieving maximum length and failure of the extension mechanism which are both unique complications to NIEPRs. As the largest proportion of failures are those exclusive to the prosthesis (not soft-tissue, bone, infection, local recurrence), the design and reliability should be optimized. As these modes of failure are potentially modifiable, and addressing them may prevent revision surgeries, more research and development should be invested into addressing these causes of revision.

The current system for reporting complications of EPRs following oncological resection is the ISOLS classification.[24] This classification system is easily understandable and reproducible to facilitate clear communication in clinical and research settings for any EPR complication. The two main failure modes specific to expandable endoprostheses are failure of the lengthening mechanism and reaching the maximum degree of implant length with a residual LLD. These may be considered Type 3A (structural – implant) and Type 6A (paediatric – physeal arrest) failures, respectively. However, as these complications are unique to expandable EPRs, we believe having a more specific sub-classification system will help categorize and quantify these complications and may help steer future research and implant development.

Based on the identified modes of failure specific to expandable EPRs, we propose using the three following failure types when describing and reporting outcomes of expandable EPRs:

Type 1: Maximum prosthesis length achieved, with a residual limb-length discrepancy

Type 2: Failure of the extension mechanism

Type 3: Implant body or stem fracture/breakage

Type 1 failures are specific to when the implant reaches a maximum expandable capacity, but the patient has open physes and continues to grow, resulting in a significant LLD at skeletal maturity.

Although no statistical comparison could be made from the available literature, the newer prosthesis, JTS (Stanmore Implants, Elstree, UK), appeared to have a lower overall revision, re-operation, extension mechanism failure, prosthesis fracture, aseptic loosening and final LLD (>20 mm) rate. However, the JTS prosthesis had a greater number of mean lengthening sessions and patients who achieved maximum prosthesis length requiring revision, which indicates a more robust implant completing the job it was designed to do. This may reflect the technical differences in the expansion mechanisms between implants (Table 1). However, it may also be due to the fact the Repiphysis prosthesis has a larger expansion capacity, with options from 35 mm to 110 mm, compared to 50 mm to 90 mm with the JTS. Lengthening options for both systems are dependent on the resected bone length. There was no clinically significant difference in functional MSTS scores between prosthesis types. Re-operation rates and functional and lengthening outcomes at similar follow-up were comparable between the MUTARS Xpand and other implants.[45] However, the single study evaluated the outcome of seven patients, of which five died of disease. There were no revisions for implant-related reasons, although the lengthening mechanism of one implant broke due to the patient undergoing an MRI.

Limb-length discrepancies of >20 mm have a significant impact on gait patterns and induce early quadriceps fatigue in the longer limb.[29] However, this study shows that on average, the growing nature of the prostheses are effective, with an average LLD of 8.8 mm, and a LLD within 20 mm in over 80% of cases at final follow-up. This difference of 8.8 mm is a clinically insignificant degree of variance for a skeletally mature patient. Moreover, there were high average MSTS scores among studies. This is comparable, and slightly higher than previously reported in reviews.[25]

NIEPRs are one proposed solution to managing limb length discrepancies in children following resection of extremity sarcomas, however other previously mentioned methods exist. Rotationplasty can be performed for tumours of the distal femur or proximal tibia.[52] This procedure is associated with a similar rate of complications as NIEPRs, although these are often more severe, such as vascular compromise and wound necrosis.[53,54] Rotationplasty has also been described as a salvage procedure following failed endoprostheses.[55,56] A combination of epiphysiodesis and distraction osteogenesis techniques are performed more frequently. These methods require use of novel growing intramedullary nails or a prolonged period (average 300 days) in an external fixator.[57,58] However, these methods are also associated with risks such as infection, contractures, non-union, secondary deformities and nerve injuries.[57,59] Despite these risks, this technique preserves native bone and may provide the best chance at a normal functioning extremity long-term.[57] In contrast, NIEPRs allow early rehabilitation, limb preservation and have easy limb lengthening mechanisms. In the setting of revision, the stem may be retained, only requiring modular exchange of the shaft and joint components to larger prostheses. Further studies directly comparing different surgical techniques are required.

There are several limitations to this study. Inherent to most research in orthopaedic oncology due to the condition rarity, all included manuscripts were of retrospective design and small patient cohorts. This reason, in addition to the heterogeneity of outcome reporting, limited the ability to perform a formal statistical comparison between studies. Despite trying to have a minimum follow-up time of 12 months, there were some studies which did not report follow-up time by individual patient, and therefore may have included patients who suffered from early mortality or without 12 months of clinical follow-up. This may result in an artificially lower reported complication rate in this review. It is also important to note the potential for reporter bias, as the accuracy of complication frequency in the literature was recorded via retrospective chart review in all studies. Publication bias may be present as this review only collected data from peer-reviewed, published manuscripts in the English language. Unfortunately, there was only one study of seven patients evaluating the MUTARS Xpand prosthesis, precluding any comparison. Finally, this study was unable to determine risk factors for NIEPR failure.

5. Conclusion

Non-invasive expandable endoprostheses carry a high risk of re-operation during the implant's lifespan. Despite this, functional outcomes and residual LLD after five-years follow-up are good. The latest NIEPR systems appear to have improved outcomes relative to their predecessors. Implant-related failures are the most common

reason for patients requiring a revision of a NIEPR and we present a novel sub-classification system to classify these in future. We hope these findings aid in prioritizing and incentivizing the development of more reliable endoprosthetic options for children with extremity sarcomas.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

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