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EDITORIAL

Expandable endoprostheses in skeletally immature patients: Where we are

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Abstract

Approximately 45 percent of malignant bone tumors are seen under the age of 16 and one of the important results of growth plate sacrification in patients with immature skeletons is limb inequality. Until the early 1990s, the treatment options for these patients were rotationplasty or amputation. Multimodal approaches that combine imaging, chemotherapy, and surgical techniques have enabled the development of limb-preserving methods with satisfactory results. In order to overcome inequality problems, expandable prostheses have been developed in the 1980s. Extendable endoprosthesis replacements have been improved over the years and are now an established and safe alternative. Noninvasive prostheses appear to be advantageous compared to minimally invasive expandable prostheses that require multiple surgical procedures, but the complication rate remains high. Therefore, although expandable prostheses are not the definitive answer to the treatment of bone sarcomas in skeletally immature children, they are still a suitable interim choice until full adulthood is achieved. Due to reported high complication rates, the procedures require significant experience and are recommended for use only in specialized cancer centers.

Key Words: Bone sarcoma; Expandable endoprostheses; Limb salvage surgery; Non-invasive; Minimal-invasive; Invasive; Extendible endoprostheses

Core Tip: Extendable endoprosthesis replacements have been improved over the years and are now an established and safe alternative. Noninvasive prostheses appear to be advantageous compared to minimally invasive expandable prostheses that require multiple surgical procedures, but the complication rate remains high. Due to reported high complication rates, the procedures require significant experience and are recommended for use only in specialized cancer centers.

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INTRODUCTION

The most common malignant bone tumors are osteosarcoma and Ewing's Sarcoma, and these constitute 80% of all malignant bone tumors in children[1-3]. Approximately 45 percent of these tumors are seen under the age of 16[1]. An important consequence of growth plate resection in sarcoma surgery in patients with immature skeletons is limb inequality. Until the early 1990s, the treatment options for patients with a height difference of 4 cm or more after surgery were rotationplasty or amputation[4,5]. Although these two methods remain good options for selected patients today, technological advances, advances in prosthesis design, and multimodal approaches that combine imaging, chemotherapeutic modalities, and surgical techniques have enabled the development of limb-preserving methods with satisfactory results[1,6,]. In limb-sparing surgery, allografts, pedicled bone grafts, bone transfers and megaprostheses can be applied in approximately 85% of cases in children today[2]. Apart from this, Arthrodesis and allograft prosthesis composites are among the common options[6]. Arthrodesis is associated with poor function. Allografts are difficult to adapt to small anatomical structures, and problems such as lysis and nonunion are their limitations.

Approximately 60% of primary bone sarcomas in young patients occur in the distal femur or proximal tibia, and often require resection of the growth plate during surgery[1,2]. 35% and 30% of the growth of the lower extremity is attributed to the epiphyses of the distal femur and proximal tibia, respectively. This means that, unlike other regions, resections around the knee have a potential risk of discrepancy[1].

Extremity inequalities are accompanied by functional deficits, gait disorders, secondary obliquity in the pelvis and cosmetic problems[2,4]. In recent years, in order to overcome these problems, expandable prostheses have become an option in limb-sparing surgery for sarcoma patients with immature skeletons[1]. A growing prosthesis may potentially allow for final patient height as a result of preventing contralateral epiphysiodesis[7]. Although promising results are reported in the literature regarding these prostheses, there are also studies presenting high rates of complications and revisions[6].

The main indication for expandable prostheses is that the patient is expected to have a leg length difference of at least 3 cm in adulthood. A length difference of 3 cm or less can be compensated by making the operated side longer at the time of operation or by shoe modifications. Therefore, in these cases, it is more appropriate to use a classical adult type prosthesis[1]. After the age of 13 in boys and 11 in girls, It is accepted that an extension will not be expected to more than 3 cm. Therefore, there is no indication of expandable prosthesis in these patients[1,2].

The first expandable prostheses were reported in the 1980s[2]. In 1976, Scales *et al*[8] reported data on the first expandable prosthesis developed in Stanmore, England. In modular flexible prosthesis types, the middle part had to be changed for lengthening (a short module was replaced with a larger one)[9] and this required a large surgical exposure. In different models, extension was possible with a more minimal incision[2,9]. In 1992, minimally invasive expandable prostheses began to be reported[7]. Later, noninvasive prostheses were developed.

The two types of expandable prostheses currently widely used are minimally invasive and noninvasive types. An important advantage of minimally invasive type expandable prostheses seems to be that they are relatively cheap, but they require additional surgeries for lengthening with a screwdriver[1]. These open operations increase the risk of infection, and mechanical failure and aseptic loosening are among the other reported complications[10]. Noninvasive expandable prostheses do not require a surgical procedure for lengthening[11]. It is an advantage that there are no risks associated with anesthesia, and the risk of infection is considered to be less[10]. In minimally invasive prostheses, each lengthening procedure is an operation and is accompanied by pain, and intensive physiotherapy is required for a good functional result[13]. Stiffness and neurovascular injury are other problems and complications can sometimes result in amputation [14]. It is accepted that non-invasive magnetic system lengthening eliminates the risk of pain, stiffness and infection[13]. However, noninvasive expandable prostheses are relatively expensive and there is not enough literature with long-term results[1].

In 2001, there were published 7 cases of osteosarcoma in which they applied the Phenix (Phenix Medical, Paris, France) noninvasive expandable prosthesis. In 6 of the cases, they were used for revision of the previous operation[11]. They carried out a total of 21 extension transactions. Each lengthening took approximately 20 to 30 s and provided an average lengthening of 8 mm, accompanied by a slight feeling of discomfort during the procedure. Extension of the prosthesis was achieved by exposure to an external electromagnetic field. They stated that noninvasive expandable prostheses are a good alternative in difficult cases of limb-sparing surgery in children.

Gitelis *et al*[15] reported 18 cases of the Repiphysis system (originally known as the Phenix Prosthesis) in 2003. They performed a total of 58 lengthening procedures on 14 of the patients whom they followed for an average of 2 years. They performed lengthenings between 1 and 7 cm. Each lengthening session was approximately 8 mm. They performed maximum lengthening in 3 patients and then switched to conventional prosthesis. As complications, they reported expandable component fractures in 2 patients, femoral component fracture in 1 patient, 2 stem fractures, 1 stem loosening and 1 deep infection. The Repiphysis prosthesis is known to use energy stored in a spring held compressed by a locking mechanism. Controlled release of the locking mechanism *via* an external electromagnetic field allows the device to be extended. The authors suggested that complications in these prostheses could be predicted and prevented. In the same year, Neel *et al*[16] reported the results of 18 Phenix noninvasive prostheses in malignant tumors around the knee. They performed extensions on 6 of the total patients. Lengthening between 1 and 30 mm was done in one session. Extensions were done in the outpatient clinic. At an average follow-up of 21 months, MSTS was 90% and revision of the prosthesis was required in 7 cases due to fracture or loosening. While there were cases where lengthening was not required, there were also cases where lengthening was done up to 6 cm. In addition, Belthur *et al*[17] applied proximal femur expandable prosthesis to 9 children. Three different generations of the Stenmore prosthesis (Mark III, IV, and V Stanmore Implants Worldwide, Stanmore, England) were used. Four patients died, and 5 patients were followed for an average of 7.6 years. A total of 63 operations were performed on five patients. Patients were lengthened by an average of 7 cm. The authors concluded that a lot of surgery was required for lengthening and revisions.

In 2006, Gupta *et al*[14] reported 7 cases in which they lengthened all patients by 4 or 5 cm using a Stanmore noninvasive prosthesis due to sarcoma located in the distal femur. The mean extension was 25 mm and mean knee flexion was 110 degrees. They calculated the average MSTS score as 68%. One patient died of disseminated disease. And they observed knee flexion deformity in one patient. By reversing the mechanism, they applied a 2 mm shortening and then full extension was achieved.

In 2010, Beebe *et al*[18] reported 12 cases in which they used repiphysis noninvasive expandable prosthesis in the upper and lower extremities and lengthened between 1 and 10 cm. They performed a total of 38 lengthening procedures on nine patients. In 3 patients, the tumor was in the proximal humerus. They reported that this noninvasive prosthesis provided acceptable functional results for both upper and lower extremity implantation. In the same year, Saghieh *et al*[19] reported the results of 17 custom-made Repiphysis prostheses, which they followed for an average of 61 months. 5-10 mm lengthening was applied at each session with an oral analgesic and the patient was discharged 30 min after the procedure. However, general anesthesia was required in 3 patients. One was due to pain during the procedure, one was due to anxiety, and one was due to extension mechanism malfunction. A total of 38 lengthening procedures between 2 and 15 mm were performed on 13 of the patients. The complications they reported were extension mechanism failure, femoral stem fracture, tibial fracture distal to the tibial stem, and infection. In this year, Dotan *et al*[20] reported the long-term results of 38 cases in which they applied 4 different expandable prostheses over the years. Model, which was elongated with sleeves in two cases, Lewis expandable adjustable prosthesis in five cases, and Kotz (minimally invasive) endoprosthesis in 29 cases and noninvasive prosthesis in 2 cases. They observed complications in 58% of the patients. The most common complication was infection, and they were diagnosed the infection 56 times. They detected early nerve damage in 8 patients and nerve damage after lengthening in 1 patient. All fully recovered with splints on follow up. They reported that approximately 3 cm of limb inequality was acceptable for good function. In these cases, planning a new operation to achieve equality brings the risk of complications. And, when skeletal growth is completed, replacement with a non-expanding prosthesis may be beneficial.

In 2010, Henderson *et al*[21] examined emotional acceptance by interviewing 15 patients who received expandable prostheses and their families. They reported that patients could have levels of happiness similar to people without the disease and that patients had good or excellent functional outcomes. In 2014, Ness *et al*[12] compared the functions of 13 patients, with an average age of 15 years, who received expandable prostheses, and 29 patients, with an average age of 19 years, who received modular prostheses. They found that there was no functional difference between the two groups. Also scores and revision rates were the same.

In 2013, Ruggieri *et al*[22] published 32 cases with noninvasive and minimal invasive prostheses in which they lengthened approximately half a cm to 16 cm and had an average MSTS of 79. They found that there was no functional difference in their study in which they used both types of expandable prostheses.

In 2015, Arteau *et al*[23] reported the results of 23 distal femoral expandable noninvasive prostheses. They used Repiphysis prosthesis in 14 patients, custom-made Biomet prosthesis in 8 patients, and Stanmore Juvenile Tumour System (JTS) in 1 patient. The tibial physis was preserved in all cases, except for the tibial stem entry point. In 15 of the cases, the growth of the tibia was less than the opposite side. Overgrowth was observed in the proximal tibia in 1 patient. In a total of 5 patients, an inequality of more than 2 cm was observed in the last follow-up, and epiphysiodesis was performed on the opposite side in 3 of these cases[24]. In 2015, Benevenia *et al*[25] published the results of 20 Repiphysis prostheses. They reported 15 complications at an average of 57 months. There was one dislocation, one contracture, 4 aseptic loosening, 5 structural failures, 3 deep infections and 1 relapse.

In 2016, Cipriano *et al*[26] reported on 10 patients with Repiphysis expandable prosthesis for distal femoral osteosarcoma whom they followed for an average of 6 years. They identified 37 implant-related complications and performed 15 revision surgeries. Six of these were aseptic loosening surgeries. Deterioration of the metadiaphyseal area surrounding the prosthesis stem was observed in all patients, deterioration in femoral length and cortical thinning were also common, which they thought would complicate potential future treatment with standard stem prostheses. Because there may be a problem with sufficient bone stock. As a result, the average MSTS score were 67.

In 2016, Torner *et al*[2] reported 7 cases between the ages of 8 and 12 in which Mutars Xpand noninvasive expandable prosthesis was applied. The average follow-up period was 65 months. The average MSTS score after rehabilitation was 26.3. They detected extension device malfunction in one patient and late infection in one patient. Extension intervals varied between 1 and 6 cm. In the knee megaprostheses used in these cases, the proximal physis of the tibia remained open and was allowed to grow naturally, thus minimizing limb inequality. In 2016, Schinhan *et al*[27] reported 71 cases in which they applied invasive, minimally invasive or non-invasive prostheses and followed up for more than 2 years. The average MSTS was approximately 88%. They reported a total of 184 complications in 58 of the patients. 46% of these were soft tissue failures, 28% structural failures and 17% were infections. One of the structural failures mentioned in many series is stress shielding. It is more pronounced in children than in adults. It usually occurs in the first 2 years and no significant deterioration is observed afterward. In fact, it is not clear whether these findings lead to a risk of fracture.

Decilveo *et al*[1] published the results of 8 extremities of 7 patients in 2017. Four of the prostheses were noninvasive and 4 were minimally invasive. The mean functional outcome (MSTS scores) at the final follow-up was 93.3%. Functional outcomes for the noninvasive and minimally invasive expandable prostheses were 97% and 85%, respectively. Complications included temporary peroneal nerve palsy, infection, stiffness, and wound healing problems. Both appear to be safe and reliable means of reconstruction that permit limb salvage and provide good functional results considering the alternative is amputation. In 2018, Gilg *et al*[28] reported 21 cases in which primary arthroplasty was performed due to sarcoma and revision was performed with an expandable prosthesis due to complications. They followed all patients for at least one and a half years. They observed deep infection in 2 patients. The mean residual leg length difference was 15 mm. They stated that noninvasive growing prostheses are a successful option in eliminating leg length in revision surgery.

Gundavda *et al*[13] reported the results of 18 noninvasive prostheses in 2019. The mean MSTS score was 28.83. The number of lengthening procedures they performed on patients varied between 1 and 12. They followed patients for an average of 50 months. They stated that the high cost of noninvasive prostheses can be considered recovered because they do not require additional lengthening procedures. In addition, small lengthening at frequent intervals seems to be more physiological than the minimally invasive method. As a complication, revision was performed on 2 patients due to malfunction of the extension mechanism. Prosthesis infection was observed in one patient after release surgery due to flexion contracture. In addition, delayed infection requiring new surgical interventions and medical treatments was observed in 2 patients. In 2019, Ajit Singh *et al*[29] reported 20 cases in which they used minimally invasive expandable prostheses. They followed all cases for at least 2 years and 85% of cases for at least 5 years. During this period, they performed a total of 124 surgical interventions, 56 of which were extension surgeries.

Staals *et al*[30] reported a study containing data from 15 European reference centers in 2020. According to an average follow-up of 80 months in 299 cases, noninvasive prostheses had a lower risk of infection and there was no difference in aseptic loosening rates between cemented and cementless stems. In 2020, Portney *et al*[31] published a meta-analysis in which they examined 292 cases. There was an average follow-up period of 67 months. 89% of the cases were followed for at least 10 years. Limb inequality was present in 36% of the cases, and the rate increased as the follow-up period increased. Minimally invasive expandable prostheses had significantly lower complication rates than noninvasive prostheses, especially in terms of mechanical complications. Because there were many extension problems in noninvasive prostheses.

Lex *et al*[32] published their systematic review in 2021, in which they reviewed 19 articles reporting noninvasive expandable prostheses. They found the average implant revision rate to be 46%, and while this rate was zero in some studies, it was 100% in some studies. When the reasons for revision were examined starting from the most common, 10% of the revisions were caused by maximal lengthening, 8% were due to implant-related fractures, 6% were due to extension mechanism malfunctions, and 1% were due to wear. Approximately 20% of all patients had limb disparity of more than 2 cm at the time of last follow-up. The average MSTS score was approximately 85%. They stated that noninvasive Xpandible prostheses have a high risk of revision during follow-ups, but functional results are good in 5-year follow-ups, and it is a successful method in reducing limb inequality. Masrouha *et al*[33] reported the long-term results of 11 cases with the Repiphysis prosthesis in 2022. They followed all patients for at least approximately 12 years and reported failure of all implants at an average of 36 months. While the earliest failure was seen in the 3rd month, the latest was in the 72nd month. They reported 18 mechanical failures. They also described wound dehiscence, infection, implant collapse due to physeal damage, and periprosthetic fracture. They stated that there are high complication and revision rates in Repiphysis prostheses, similar to other expandable prostheses, and that all options should be carefully evaluated when determining the indication.

In 2022, Huang *et al*[6] published the results of an average of 9 years of follow-up of 29 cases in which they applied minimally invasive expandable prosthesis. All the patients were younger than 15 years of age, and they reconstructed the prosthesis on the resection side 2 cm longer than the resection length. When they detected a height difference of more than 3 cm in the follow-up radiographs, they planned an extension. To eliminate the incompatibility, they planned to lengthen it by 2 cm every 10 months. A total of 17 patients were lengthened by an average of 4 cm. The average MSTS score was 27. They reported a total of 2 revision surgeries, one due to infection and one due to aseptic loosening.

Shehadeh *et al*[34] reported the noninvasive results of 14 JTS Prostheses and 6 Mutars in 2022. They analyzed the cases for the presence of tibial multiplanar deformities. They found tibial deformity and/or growth abnormality in 14 of the patients (10 JTS, 4 Inplantcast) whom they followed for at least 2 years. They followed 11 of 14 cases with height inequality conservatively. They performed epiphysiodesis on the opposite side for two of them and replaced them with a long prosthesis for one. They found an average rotation of 13 degrees in the tibia in 11 of the patients. They also detected coronal angulation in 3 patients and sagittal angulation in 1 patient. No surgical intervention was required in any of the rotations and angulations. In the same year, Dukan *et al*[35] reported the results of 40 cases around the knee, which they followed for an average of 8.8 years. 28 Phenix and 12 Stanmore used prostheses. They found functional results to be significantly better in the Stanmore group. In addition, while implant survival was 100% in the Stanmore group, the prosthesis was explanted in all surviving patients in the Phenix group. The main reason for the revision operations was mechanical failure. At last follow-up, limb length equality was noted in 79% of Phenix-Repiphysis patients and 84% of Stanmore patients. The authors concluded that both prostheses were good and feasible. In addition, although long-term follow-up results of the prostheses are needed, it appears that Stanmore prostheses can be kept after skeletal maturity.

CONCLUSION

Extendable endoprosthesis replacements have been improved over the years and are now an established and safe alternative. Noninvasive prostheses appear to be advantageous compared to minimally invasive expandable prostheses that require multiple surgical procedures, but the complication rate remains high. There is an increased risk associated with the elongation and mechanical reliability of extendable implants compared to adult endoprostheses. Therefore, although expandable prostheses are not the definitive answer to the treatment of bone sarcomas in skeletally immature children, they are still a suitable interim choice until full adulthood is achieved. Due to reported high complication rates, the procedures require significant experience and are recommended for use only in specialized cancer centers.

FOOTNOTES

Author contributions: Öztürk R, designed the study; performed the research; analyzed the data and wrote the manuscript.

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