

# Limb Salvage in Malignant Bone Tumours - A Prospective Follow-Up Study Conducted at Government Medical College, Thrissur from 2017 to 20

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## ABSTRACT

### BACKGROUND

Limb salvage surgeries - Are they useful compared to amputation in bone tumours (malignant/recurrent). Starting from 1980s, bone tumour treatment has seen a revolution with the advent of limb salvage surgeries. From an era where amputation was the only option to the current day function preserving resections and complex reconstructions has been a major advance. The surgeon must ensure adequate resection of the involved bone and soft tissue so as to minimize chance of local recurrence. At no stage must adequate disease clearance be compromised in an attempt to achieve limb salvage. We analyzed its relevance among our rural population at a tertiary level care centre. Limb salvage surgery basically involves resection and reconstruction. Reconstruction can be either biological or endoprosthesis. Biological can be autograft or allograft. Endoprosthesis can be fixed (custom-made) or modular. Expendable bones like fibula or ulna may not require reconstruction after resection. Prosthesis provide an immediate return to function and unlike bone they are not affected by ongoing adjuvant chemotherapy and radiotherapy.

### METHODS

We conducted an 18-month prospective follow-up study on 10 patients (6 males and 4 females) who had undergone limb salvage surgeries during 2017 - 20 at Government Medical College, Thrissur. Wide excision, wide excision & biological autograft reconstruction, wide excision & modular endoprosthesis reconstruction are the different surgical modalities used. Patients were followed up clinically and radiologically in the orthopaedic out-patient department (OPD) at 6 weeks, 12 weeks and up to 1 ½ years at every 3 months. Functional scoring has been done using musculoskeletal tumour society (MSTS) - 87 scoring system. Study duration: 2017 October to 2020 October (3 years).

### RESULTS

The average score is 64.6 % using the MSTS - 87 system. Maximum score was 83 % and the minimum was 62 %. Most of our patients are doing well and pursuing near-normal life with limb salvage surgeries with very minimal complications. One of our patients succumbed to the disease during the follow-up period.

### CONCLUSIONS

Limb salvage is a better alternative to amputation in malignant and recurrent bone tumours in carefully selected and thoroughly evaluated patients.

### KEYWORDS

Limb Salvage, Malignant & Recurrent Bone Tumours, MSTS - 87 Score, Wide Excision, Biological Autograft, Modular Endoprosthesis Reconstruction

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**BACKGROUND**

Limb salvage (limb sparing) surgeries were initiated in the orthopaedic arena during the early 1980s.<sup>1</sup> Amputation was the single answer to malignant tumours of the extremity till then.<sup>2</sup> Today, limb salvage is the safe routine practice in almost 90 % of the malignant skeletal neoplasms.

Limb salvage is a beautiful combination of the knowledge of anatomy, orthopaedic expertise, oncologic outlook of surgical margins, safe surgical resection and a careful rehabilitation. It also involves the current modalities of adjuvant chemotherapy and radiotherapy.<sup>3</sup>

Limb salvage surgeries are a boon to patients with malignant & recurrent skeletal neoplasms. Proper selection of patients, careful pre-operative evaluation and meticulous surgical planning and a selfless team-work are the backbone of success for these surgeries.

**Objectives**

1. To evaluate prospectively the functional results of limb salvage surgeries in 10 patients with malignant skeletal neoplasms done at Government Medical College, Thrissur from October 2017 to October 2020.
2. To evaluate the anatomical and functional aspects of modular endoprosthesis in limb salvage surgeries.

**METHODS**

This is a prospective observational study conducted at the Department of Orthopaedics, Government Medical College Thrissur, Kerala, India for a period of three years from October 2017 to October 2020. 10 patients with malignant bone tumours – (6 males and 4 females). There were 4 cases (2 males, 2 females) of chondrosarcoma of the distal femur and 2 cases of proximal tibia (2 males). Two cases (both females) were osteosarcoma of the proximal tibia. Giant cell tumour (GCT) recurrence occurred in 2 male patients in the distal femur.

| Type of Tumour | Age of the Patient | Sex |
|----------------|--------------------|-----|
| Chondrosarcoma | 60 years           | M   |
|                | 36 years           | F   |
| Distal femur   | 57 years           | M   |
|                | 42 years           | F   |
| Proximal tibia | 65 years           | M   |
|                | 59 years           | M   |
| Osteosarcoma   | 15 years           | F   |
| Proximal tibia | 12 years           | F   |
| Recurrent GCT  | 58 years           | M   |
| Distal femur   | 50 years           | M   |

**Table 1. Case Distribution According to Age & Sex**

We had embarked on different surgical modalities depending on the site, type, pathological grade of the lesion and patient characteristics like suitability, post treatment mode of job etc.

In expendable bones, resection was done. In distal femur and proximal tibia lesions, the vascularity of the lesion, the involvement of major vessels and the distal vascularity of the limb were assessed by doing MR angiogram. In lesions with cortical break and soft tissue extension, wide excision and modular endo prosthetic reconstruction was done. In two lesions of the proximal tibia (chondrosarcoma) without much soft tissue component, wide resection of tibia and reconstruction with autograft (fibula and iliac crest) were attempted.

The soft tissue cover was obtained from the non-resected muscles and other soft tissue structures in almost all of our cases. We did not have to depend upon any plastic surgical procedure for any of our cases.

Role of tumour markers: Recurrent GCT was evaluated by serial measurements of acid phosphatase. For osteosarcoma and chondrosarcoma, no other specific tumour markers were analyzed except alkaline phosphatase.

**Inclusion Criteria**

Malignant bone tumours of the appendicular skeleton where there is adequate distal vascularity and no evidence of metastasis.

**Exclusion Criteria**

All benign bone tumours, bone tumours of the axial skeleton, bone tumours on limbs where distal vascular status is not satisfactorily salvageable, bone tumours with distal metastasis.

**Statistical Analysis**

Since small number of cases (10) it was not necessary. Observational analysis using musculoskeletal tumour rating scale was done.

**RESULTS**

We had operated on 10 patients during this period. In all of them, we did wide excision of the tumour with adequate margins and reconstructed the structural anatomy with either modular endoprosthesis or biological reconstruction with bone graft (autograft).The follow up patients were functionally analysed based on the MSTS - 87<sup>3</sup> scoring system which included the following criteria master chart.

1. Pain
2. Range of motion
3. Strength
4. Stability
5. General functional ability
6. Emotional acceptance
7. Deformity

| Complications                          | Tumour                        | Nature of Surgery        | No. of Patients |
|--|-------------------------------|--------------------------|-----------------|
| Proximal fragment splintering of femur | Chondrosarcoma distal femur   | Endoprosthesis           | 1               |
| Tumour spillage into the knee joint    | Chondrosarcoma distal femur   | Endoprosthesis           | 1               |
| Surgical wound skin necrosis           | Chondrosarcoma distal femur   | Endoprosthesis           | 1               |
|  | Chondrosarcoma proximal tibia | Autograft reconstruction | 1               |
|  | Osteosarcoma proximal tibia   | Endoprosthesis           | 1               |
| Surgical wound infection               | Chondrosarcoma distal femur   | Endoprosthesis           | 1               |
|  | Chondrosarcoma proximal tibia | Autograft reconstruction | 1               |
| Pulmonary metastasis & death           | Chondrosarcoma distal femur   | Endoprosthesis           | 1               |

**Table 2. Surgical Complications**

|   |   |  |   |
|---|---|--|---|
|    | <p><b>Figure 1a.</b><br/><i>OS Proximal Tibia-Preop X-Ray</i></p>                   |    | <p><b>Figure 1b.</b><br/><i>Intraop Picture</i></p>                                       |
|   | <p><b>Figure 1c.</b><br/><i>Chondrosarcoma Distal Femur-Excised Specimen</i></p>    |   | <p><b>Figure 1d.</b><br/><i>X-Ray</i></p>   |
|  | <p><b>Figure 1e.</b><br/><i>Clinical Picture at 18 Months</i></p>                   |  | <p><b>Figure 1f.</b><br/><i>Recurrent GCT Distal Femur-Clinical Picture at 1 year</i></p> |
|  | <p><b>Figure 1g.</b><br/><i>Chondrosarcoma Proximal Tibia-X-Ray at 9 Months</i></p> | <p><b>Figure 1.</b><br/><i>Chondro and Osteosarcomas Undergone Limb Salvage</i></p>  |   |

### MSTS-87 Scoring

The score was maximum (83 %) for the male patient with recurrent GCT of the (R) distal femur for whom endo prosthetic reconstruction was done. Except for the female patient with chondrosarcoma of (L) distal femur who died 4 months post op due to pulmonary metastasis, the score was minimum (62 %) for the female patient with chondrosarcoma (R) distal femur for whom modular endoprosthesis reconstruction was done. The average MSTS - 87 score was 64.6 %.

All the 9 patients are doing well after a mean follow-up period of 18 months (varying from 6 months to 30 months). A female patient of 36 years with chondrosarcoma of the (L) distal femur succumbed to lung metastasis after 4 months of the surgery.

## DISCUSSION

### Osteosarcoma

Malignant bone tumour in which cells synthesize bone. Osteosarcoma (OS) is a primary malignant bone tumour, described as a spindle cell neoplasm. It is an osteogenic tumour, most commonly occurring in the metaphyseal region. "It has a worldwide incidence of 3.4 per million people per year". It is the second commonest 1<sup>0</sup> malignant tumour of bone next to multiple myeloma and the commonest primary sarcoma of bone.<sup>4</sup>

Primary osteosarcoma: the bone of origin is otherwise normal. Secondary osteosarcoma: bone of origin is altered<sup>2</sup> (e.g.: Paget's disease, radiation Rx, infarction etc.) The common age group is 10 – 14 years, more in males (primary os); where as for the secondary tumour it is 60 - 65 years. Osteoid (new bone) is a must for the pathological diagnosis of osteosarcoma.<sup>1</sup> Radiologically, osteosarcoma is an aggressive lesion. Morphologic sub-types of conventional osteosarcoma are osteoblastic, chondroblastic and fibroblastic. Prior to 1980s, high-grade OS was treated by amputation. Chemotherapy and limb salvage is now considered as the first treatment of choice. The current survival rate has increased to > 70 %. Prognosis and choice of therapy is determined by metastasis, tumour grade and response to neoadjuvant chemotherapy.<sup>5</sup>

### The World Health Organization's Divided Osteosarcoma Histologically into-

- Central OS – conventional (high grade), telangiectatic, small cell, giant cell rich
- Intramedullary OS - well differentiated low grade OS
- Surface OS - parosteal, periosteal, high grade surface

### Conventional Osteosarcoma

Conventional OS represents 90 % of all osteosarcoma cases and is the most common variant. It is commonly seen in ages of 10 – 30 years. It is further subdivided into osteoblastic, chondroblastic, and fibroblastic groups. On

radiographs, OS is mostly seen in metaphyseal region extending into epiphysis/diaphysis and it can be osteolytic or osteoblastic, or both. Most common site is around the knee - distal femur and proximal tibia. Histologically, high grade spindle cell stroma is seen with anaplastic malignant osteoblast producing malignant osteoid, which is key for diagnosis.

### Telangiectatic Osteosarcoma

Telangiectatic osteosarcoma (TOS) is a rare variant and accounts for 3 to 4 % of OS. It is a high-grade variant of OS. Histologically, high-grade anaplastic sarcoma cells are seen on the septae and peripheral rim of dilated blood-filled cavities characterize TOS. Radiographically, a purely lytic lesion and a wide zone of transition is seen in the metaphysis. Moth-eaten appearance or permeative pattern of destruction is usually seen.

### Small-Cell Osteosarcoma

Small-cell osteosarcoma (SOS) constitutes 1 % of all cases of OS. The histological features of SOS show small cells with hypochromatic round nuclei and nuclear polymorphism, maybe confused with Ewing's sarcoma (production of osteoid is key to diagnosis for OS).

### Low-Grade Osteosarcoma

Low-grade osteosarcoma (LOS) accounts for around 1 % of all cases of OS, most commonly affecting in age group of 20 – 40 years. When treated with curettage, there is high risk of transformation to conventional OS but the prognosis is better.

### Surface OS

#### *Parosteal Osteosarcoma*

Parosteal osteosarcoma (PAOS) originates from the periosteum and is a low grade tumour representing 5 – 6 % of cases of OS. It is the most common surface OS. Radiographs demonstrate a densely ossified arising from the cortex, while the medullary cavity is spared. Histologically, regular arrangement of trabeculae with a high degree of parallel orientation, similar to what may be seen in a periosteal new bone reaction, with atypical spindle cells between them.

#### *Periosteal Osteosarcoma*

Periosteal osteosarcoma (PIOS) is an intermediate grade tumour and is less common. It has a matrix component that is mainly cartilaginous. PIOS tends to arise between the cortex and the cambium layer of the periosteum, and therefore a periosteal reaction is usually visible on radiographs.<sup>6</sup>

#### *High-grade Surface Osteosarcoma*

High-grade surface osteosarcoma (HGSOS) constitutes less than 1 % of all OS. It manifests as a high-grade surface lesion with an appearance similar to conventional type.

Localized invasion of endosteum and cortex is seen as it has the same malignant potential as that of a conventional OS.

### Management

Conventional treatment of osteosarcoma includes neoadjuvant chemotherapy + surgical excision + adjuvant chemotherapy.<sup>6</sup> Limb salvage – wide resection + reconstruction with endoprosthesis & biological replacement. Amputation in non-salvageable cases. Van Ness rotational arthroplasty.<sup>6</sup> Chemotherapy: 4 agents - methotrexate with leucovorin rescue, doxorubicin, cisplatin & ifosfamide. In metastatic disease – Etoposide<sup>4</sup>

### Chondrosarcoma

Chondrosarcoma is a malignant chondrogenic tumour of bone which does not produce osteoid.<sup>7</sup> It is the 3<sup>rd</sup> most common bone malignancy next to multiple myeloma and osteosarcoma. Chondrosarcoma (CS) represents a group of heterogeneous, usually slow-growing, primary malignant tumours of bone characterized by the formation of neoplastic hyaline cartilaginous tissue. It is most often seen beyond 40 years of age. It is the second most common primary solid tumour of bone after osteosarcoma. They constitute about 20 % of all primary malignant tumours of the bone. 75 % of the cases occur in males.<sup>8</sup> About a small % of patients are below 20 years which are usually high grade. Recurrence of this malignancy usually occurs through satellite nodules, distant metastasis to the lungs and very rarely through lymph nodes.<sup>9</sup> Usually recurrent tumour has higher histological grade.

Primary or conventional chondrosarcoma – tumour arises in a normal bone. Secondary chondrosarcoma - occur in a pre-existing enchondroma or osteochondroma. Conventional chondrosarcoma is the more common variant and accounts for 80 % – 90 % of chondrosarcomas is subdivided into the central, periosteal, and peripheral subgroups. Non-conventional variants of primary chondrosarcoma include mesenchymal chondrosarcoma, clear cell chondrosarcoma, and dedifferentiated chondrosarcoma. Radiological features: large size, rapid growth, fluffy calcification, poor margins, erosions or thickening of cortex, no periosteal new bone formation. Histological behaviour can be predicted by grading of chondrosarcoma and is essential prior to intervention. Histopathologically, chondrosarcomas can be divided into three grades depending on the cellularity and nuclear changes in chondrocytes.

- Grade I: low-grade and locally aggressive, also called atypical cartilaginous tumour. Lesions will often closely resemble normal cartilage or the benign enchondroma. It is moderately cellular and contain increased chondroid matrix.
- Grade II tumours contain a greater degree of nuclear atypia and hyperchromasia, and nuclear size and are more cellular. Mitoses can be found.
- Grade III tumours are highly cellular with more pleomorphic and atypical cells than grade II and absence

of matrix. Mitoses are easily detected. Peripheral cells are less differentiated and spindle.

- Grade IV tumours is also called as dedifferentiated chondrosarcoma and makes up 10 % of all chondrosarcomas. It is defined histologically by the presence of a high-grade, often spindle or pleomorphic tumour without significant cartilaginous matrix.

### Management

Surgical excision is the primary treatment of choice. Chemotherapy<sup>10</sup> has no role. Low grade tumours can be managed by intralesional excision<sup>11</sup> and phenol/hydrogen peroxide cauterization as we do in a GCT. High grade tumours with intraarticular or soft tissue extension need wide surgical excision and endo prosthetic replacement. Radiotherapy may have a role in dedifferentiated tumours or deep seated in-operable tumours.

### Recurrent GCT

Giant cell tumour of bone is usually benign but locally aggressive neoplasm comprising of mononuclear round to spindle cells with numerous evenly dispersed osteoclast like giant cells. They constitute about 5 % of primary bone tumours. The usual age group is 20 – 45 years. The common location is the epiphysis and the adjacent metaphysis. Most common sites are distal femur, proximal tibia, distal radius and the proximal humerus. Other bones like proximal sacrum, vertebrae, skull bones are also involved. > 95 % of the tumours are unifocal. 5 - 10 % cases present with pathologic fractures. Malignancy is rare in GCT (less than 2 % of cases) and is more common among older patients (30 – 50 years). It is rarely associated with Paget's disease of bone and also focal dermal hypoplasia (Goltz' syndrome). It involves epiphysis and adjacent metaphysis of the long bones. The osteoclast like multinucleated giant cells are evenly distributed throughout the lesion and is also known as osteoclastoma. Primary malignant GCT of bone is a high-grade sarcoma arising in a GCT of bone at initial diagnosis. Secondary malignant GCT of bone is a high-grade sarcoma arising at the site of an initially treated GCT after surgery or after low-dose radiation therapy. Secondary malignant GCT is more common than the primary one. Histologically, benign neoplastic lesion consisting of three cell types: mononuclear histiocytic cells, multinucleated giant cells that resemble osteoclasts, and neoplastic stromal cells. The giant cells per se are not neoplastic. The neoplastic cells are primitive mononuclear mesenchymal stromal cells which appear as preosteoblasts. They express the tumour markers like RANKL & preosteoblast markers like ALKP, RUNX<sub>2</sub>, SP7, osteoclastin. X ray – lobulated, eccentric, expansile, osteolytic lesion. (Soap-bubble appearance)

### Radiographic Grading

#### *Campanacci Grading*

- Grade 1 - quiescent,
- Grade 2 - active,
- Grade 3 - aggressive

Prognostic factors: approximately 2 % of cases produce pulmonary metastasis. "They are usually slow-growing and some regress spontaneously. Local recurrence, high Campanacci grade and curettage may be risk factors for metastasis.<sup>3</sup> Secondary malignancy has got poorer prognosis than the primary one.

#### *Differential Diagnosis*

1. Brown tumour
2. Central giant cell granuloma
3. Chondroblastoma
4. Non-ossifying fibroma
5. Aneurysmal bone cyst (ABC)
6. Tenosynovial GCT

### **Treatment**

#### *Medical Management*<sup>12</sup>

1. Bisphosphonates
2. Denosumab – anti RANKL monoclonal antibody"

Surgery – Curettage (intralesional excision) with proper adjuncts is the treatment of choice. Intralesional curettage is associated with recurrences, 15 - 50 % of which recur within 2 years,<sup>13</sup> hence wide resection is preferred as it decreases the risk of multiple recurrences but often requires complex skeletal reconstructions associated with higher rates of surgical complications and decreased function. Although better functioning is seen with intralesional curettage, there is an unacceptably high re-recurrence rates and increased frequencies of pulmonary metastases.

#### *Causes of Recurrence*

1. Incomplete curettage
2. Curettage without proper adjuncts like PMMA/burring
3. Secondary malignant change

Recurrent GCT is considered as a severe disease due to the risk of pulmonary metastasis. Diagnosis of recurrence<sup>14</sup>: clinical features show signs of recurrence. Radiologically, there will be peripheral osteolysis in the existing lesion. Magnetic resonance imaging (MRI) is more conclusive. Biochemically, there will be elevation of markers, serum tartrate resistant acid phosphatase<sup>15</sup> is such a useful marker."

#### *Management of Recurrence*<sup>16</sup>

1. Repeat curettage/intralesional excision with proper adjuncts.
2. Wide excision
3. Endoprosthesis"

### **Limb Salvage**

Surgical ablation of the diseased bone with oncologically safe margins is the best means of local control in malignant bone tumours. From an era, amputation was the only option to the current day function preserving resections and complex reconstructions has been a major advance. At no stage must adequate disease clearance be compromised in an attempt to achieve limb salvage. The salvaged limb will provide function superior to that offered by a prosthetic limb after an amputation. Limb salvage surgical techniques

provide a safe methodology of treatment for 85 – 90 % of patients.<sup>17</sup> There are three essential steps of limb salvage - resection, skeletal reconstruction and soft tissue and muscle transfers.

Resection must be wide and appropriate and is crucial for the elimination of disease and must include excision of previous biopsy tracts and sites with at least 2 cm margin. 6 – 7 cm of bone to be osteotomized distal to the lesion to ensure clear margins.<sup>18</sup> Preoperative evaluation including imaging and intra operative computer assisted tumour surgery or using Kawaguchi's concept of barrier effect should be kept in mind for safe margins. At the met diaphyseal end, a marrow margin of 3 cm as evaluated on T1 - weighted MRI is adequate. Most bone sarcomas occur in metaphyseal portion of bone. The articular cartilage serves as a barrier to extension of tumour and joint itself is rarely involved but in order to achieve adequate margins resection usually involves the articulating or joint surface.

Diaphyseal tumours option of intercalary resection and reconstruction with either metallic diaphyseal prosthesis or bone in the form of a strut allograft or fibular autograft (with additional internal fixation). In skeletally immature patients there comes the problem of physeal destruction and the possibility of growth disturbances. Location of the tumour through the growth plate was a contraindication for limb salvage and an indication to amputate. But now, current treatments include resection with expandable growth endoprosthesis, allograft endo prosthetic composites, or rotationplasty.<sup>19</sup> Reconstruction is the next essential step in limb salvage. In weight-bearing bones, it can be divided into 2 types – endo prosthetic replacement and biological reconstruction.

Endo prosthetic replacement is a form of reconstruction in limb salvage surgery, and is reported to have good functional outcomes and better cosmetic and psychological benefits in comparison to other forms of treatment.<sup>20</sup> The design of these implants includes modular, custom-made, and growing implants for the skeletally immature. The growth plates of the affected bone are removed, and the prosthesis is lengthened by 1 – 2 cm per surgery, in order to correlate with the contralateral, healthy extremity. Metallic prosthesis (Mega prosthesis) which span the resection gap and allow for movement of joint form the main stay providing both mobility and stability.

Biologic replacement is another form of limb reconstruction, which includes autograft, allograft, recycled autografts, and allograft prosthetic composite reconstructions. Allograft prosthetic composites (APC) is a method of combining allograft with implants for reconstruction.<sup>21</sup> Autografts is used in a number of ways. Ideal bone for autograft is the fibula, as it is long, tubular, relatively superficial, and minimally load sharing. It can be vascularized or not, however non-vascularized graft is dependent on the blood supply and bone quality it is placed into.<sup>22</sup>

### **Advantages of Endoprosthesis**

- Limb salvage with metallic prosthesis provide an immediate return to function and unlike bone they are

not affected by ongoing adjuvant chemotherapy or radiotherapy.

- Intra operative flexibility of implant according to size and fitting
- Low risk of deep infection
- No issue regarding no union compared to other allografts
- No risk of disease transmission
- Complications of modular (Endoprosthesis)

#### *Early Complications*

- Wound necrosis
- Infection
- Neuropraxia due to handling of soft tissues
- Deep vein thrombosis (DVT)

#### *Late Complications*

- Aseptic loosening, it is the most common cause for revision surgery in reconstruction failures.
- Persistent infection - most serious and dreadful complication. Also, infection is the most common cause of failure of reconstruction leading to amputation. Commonly seen in Tibial endoprosthesis reconstruction.
- Extensor lag as seen in proximal tibial reconstructions due to issues with reattachment of patellar tendon. Most surgeons do a gastrocnemius flap so that it acts as a soft tissue cover and also biological attachment for patellar tendon.
- Fatigue fracture of prosthesis due to continuous loading and micro fractures. But modern-day prosthesis are manufactured to withstand fatigue in long term run as seen in 10 year studies.

#### **Advantages of Biological Replacement**

- Osteoarticular / Bulk allograft is ideal in younger patients since it provides biological healing, also there is direct attachment of remaining muscle and soft tissues
- Disadvantages of biological reconstruction
- Non-union
- Wound infection
- Disease transmission (in case of allografts)
- Fracture of allograft Berry Classification' Type 1 - immediate post operatively due to graft lysis by immune reaction, Type 2 - fracture through shaft of allograft, Type 3 - fracture through articular surface.

#### **CONCLUSIONS**

Limb salvage surgeries in bone tumours are useful and beneficial to the patients if carefully selected with proper evaluation, meticulous planning and cautious follow-up. The functional results for the modular endoprosthesis are good in musculoskeletal tumours.

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