

## Extra Corporeal Irradiation to Treat Osteosarcoma at a Tertiary care Institute in Central India: A Case Report

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### Abstract

Extra corporeal irradiation (ECI) is a rarely employed technique of irradiation in malignant bone tumour. In this procedure post en-bloc resection of bone it is irradiated with a dose of 50Gy in a single fraction and then it is reimplanted. This procedure ensures high rate of local control, better anatomical fit and functional outcome. In this case report we present the first case of extracorporeal irradiation in central India.

**Keywords:** Extra corporeal irradiation; Malignant bone tumour; Osteosarcoma.

### Introduction

Malignant primary bone tumours are relatively a rare entity. These are most commonly seen in children and adolescent.<sup>1</sup> The incidence of osteosarcoma cases are 4-5 per 1000000.<sup>2-5</sup>

The treatment of osteosarcoma requires multimodality approach for optimal management, requiring expertise of surgical oncologist, radiation oncologist, medical oncologist. The management of malignant bone tumours (MBT) have undergone immense advancement in last two decades. During the initial days of oncology, the preferred treatment of MBT was surgical resection (amputation). A shift in treatment strategy was developed with the aim of limb salvage. This treatment modality for limb preservation aims at better local control of the tumour and reconstruction of the limb which would result in restoration of organ function leading to better quality of life and an improved survival.

The principle we follow here, firstly we do en-bloc resection of the involved segment of the bone. After

which removal of all the grossly and macroscopically present tumour over the bone segment followed by extracorporeal irradiation (ECI) of the bone segment to achieve maximum tumoricidal effect along with sterilization and then re-implantation of the bone into the body. ECI achieves maximum tumour kill and also sterilizes the bone. Some of the techniques employed for sterilisation of bone before re-implanting it are autoclaving, microwave, pasteurizing, liquid nitrogen, and radiotherapy (extracorporeal radiotherapy).<sup>6-10</sup> With ECI we deliver a very high dose of radiation (50-300 Gy) in single fraction which results in maximum tumoricidal effect. With this case report we tried to analyse the potential benefits and limitations faced during implementation of ECI at our institute.

### Case Report

A 38-year-old, female, presented to us with initial complaint of swelling over lower end right thigh since 3 years. It was gradually progressive in



nature with no complaint of pain over the swelling initially. She had no difficulty in limb movement in the beginning. Eventually she started to experience pain while sitting in cross legged position since 2 years. On local examination there was a swelling over the lower third of right thigh involving the antero-lateral region of the thigh. Swelling was around 12 × 15 cms, well-defined margins, hard, fixed, non-tender. No popliteal lymph nodes or inguinal lymph nodes were found on palpation. Initial x-ray showed a large mass over her right distal end of femur. (figure 1). MRI distal knee joint suggestive of large mass lesion with soft tissue and calcific component seen in distal thigh arising from cortex of metaphyseal region of distal femur posteriorly and posterior-laterally. No surrounding marrow oedema or extension of lesion into medullary cavity. No significant infiltration of lesion into adjacent muscles which are displaced peripherally by lesion. Increased fluid seen in suprapatellar bursa. Findings suggestive of malignancy? Paraosteal osteosarcoma. Biopsy from the right thigh swelling suggestive of conventional osteosarcoma. Her CT scan chest was suggestive of few sub centimetric nodules in bilateral lung bases. The patient also underwent whole body scintigraphy scan which was suggestive of increased uptake of distal end of right femur. And no other evidence of distal skeletal metastasis. Her biopsy block review reported parosteal osteosarcoma (figure 2).

The patient did not seek any medical care and reported five months later to us. After a full routine and metastatic work up which revealed no evidence for lung metastasis or distant metastasis? She was started with neoadjuvant chemotherapy plan according to OGS-12 protocol. Received four cycles of neoadjuvant chemotherapy, first two cycles with cisplatin and doxorubicin for three days and then she was switched to ifosfamide and doxorubicin for three days for next two cycles. Post completion of her neoadjuvant chemotherapy her CT scan Right lower limb (figure 3) was suggestive of space occupying lesion of size 10.4 × 8 × 12 cms in the distal portion of right thigh arising from the right posterolateral parosteal aspect of femur showing areas of dense bony calcification mingled with soft tissue component. No obvious intramedullary component. The lesion is 1.5 cms proximal from the knee joint. The goal behind multi-disciplinary treatment approach at our institute is the best treatment for the patient utilising all the speciality. The patient post chemo was referred for oncology surgery and radiation oncology opinion where she was planned for wide local excision along with extra corporeal irradiation.

For extra corporeal irradiation the involved segment of bone was excised, all the grossly involved tumour over the bone was removed (figure 4), in order prevent contamination it was then transferred to a different sterile tray over a different trolley where at first it cleaned with normal saline, all the bone marrow present in the excised section was removed using suction and then wrapped with a layer sterile wet drape soaked with 2 gm of vancomycin (figure 5) and then another two-layer surgical plastic packing. The thickness of wrapping around the bone segment was of 3cm. The wrapping ensured no air gaps were left and would help in achieving homogenous dose distribution. The 3 cm of layered wrapping helped us achieve the 'build-up' effect to the bone. The sealed segment of bone was transferred to Computed tomography (CT) console for imaging and then the images were transferred to treatment planning system (TPS). Eclipse version 13.7 (Varian medical Systems Pvt. Ltd., Palo Alto, CA, USA), where CTV and PTV were contoured. Plan was generated. Bone was shifted to Medical Linear Accelerator Clinac DMX (Varian Medical Systems Pvt.Ltd., Palo Alto, CA, USA) treatment couch ensuring proper immobilization. 2 D treatment was planned. Plan was approved in two parts of 25 Gy each since a single fraction plan of 50Gy was difficult to approve. Matching was seen with beam light and source to surface distance (SSD) was checked just like cobalt. The appropriate field size for radiation treatment was selected making sure it covered the entire segment of bone. A single fraction dose of 50 Gy using 6 MV photons was delivered in two parts to the mid plane of bone segment using a parallel-opposed antero-posterior and postero-anterior fields. Treatment time for each part was 10 minutes. Treatment was done on service mode and not on routine mode. After completion treatment delivery the bone segment was returned to operation theatre maintaining proper chain of aseptic precaution without any delay. The total time required was almost 40 minutes in which radiation delivery time was 20 minutes and the rest of the 20 minutes in shifting of bone segment, imaging and planning. Post ECI biopsy samples were taken from various sites of the bone which turned out negative for presence of malignancy (figure 6). Post ECI the bone segment was pale and lost all its tumour which present after resection (figure 7). The bone was autoclaved and then re-implanted into the body. And post procedure x-ray done. (figure 8) The patient started to weight bearing over her lower limb with support on post procedure day 7 and there after ambulation with support began post procedure day 15. Patient is on regular follow up

walking comfortably with support. Follow up to continue every 3 monthly for two years.

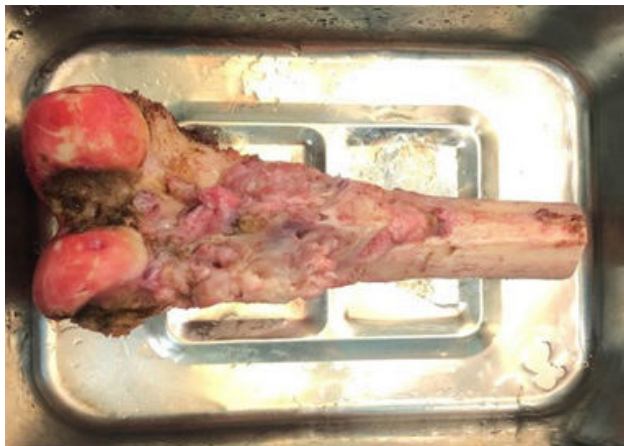


Fig. 1. Post Resection Femur with Residual Tumor



Fig. 4. Post ECI Bone Segment



Fig. 2. Post Fixation X-Ray



Fig. 3. Layered Wrapping of Bone Segment for Radiation

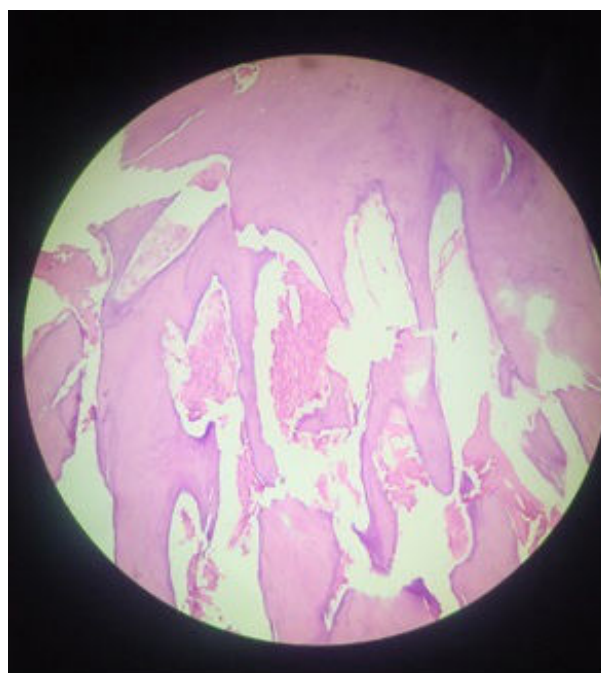


Fig. 5. Post ECI Biopsy Showing no Active Cells



Fig. 6. Pre op CT scan

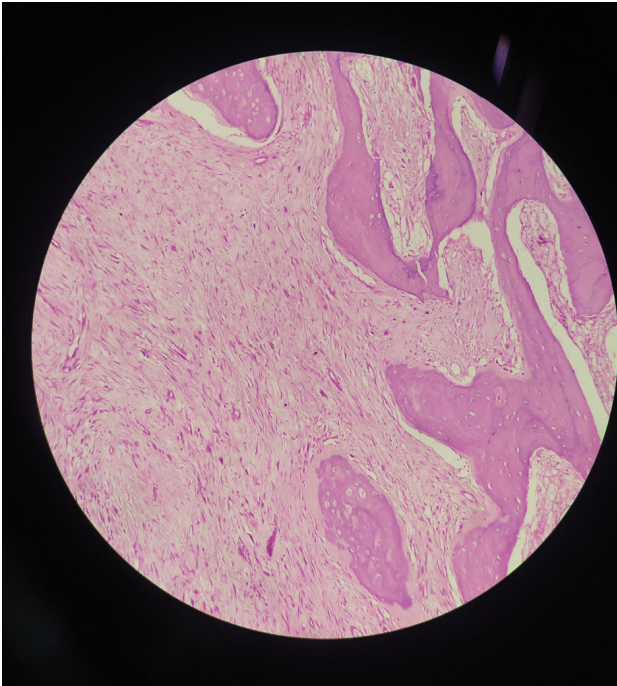


Fig. 7. Histopathology



Fig. 8. Pre Op X-ray Distal end Femur

## Discussion

The entire appeal of multi-modality approach lies in providing the best care utilising all the faculties of oncology and to achieve the best outcome for the patient. In MBT limb preservation could lead to a better quality of life. One of the key requisites of delivering ECI is the availability of all the modalities at one institute. The need of proper operating

room, CT scanmachine for imaging, and the linear accelerator to deliver radiation at one centre in close proximity is of utmost importance since time management is very crucial while executing ECI. Limb salvage would result in better quality of life and functional outcomes for the patient. Limb reconstruction can be done using artificial prosthesis, allografts and autografts. Allografts which are biologically reconstructed<sup>11</sup> require access to large bone banks and to find a matching bone donor and immunogenicity is difficult, and also expensive. This also arises concerns regarding the increased chances of transmission of infections from allografts. So, the role of ECI hold simmense importance in utilizing patients' own bone segment (autograft) as it provides a perfect anatomical fit, high dose of radiation ensures tumour kill, convenient, cost effective and also minimizes the risk of any disease transmission. Recycled irradiated autograft was first reported by Spira and Lubin in 1968.<sup>12</sup> Before re-implanting the bone segment into body bone sterilisation is a must. One of the advantages that we see with ECI is limb function preservation which translates into weight bearing and ambulation. In a study conducted by Uyttendaele et,<sup>13</sup> 15 patients with primary malignant bone tumours were treated with ECI and they were followed up for 5 years and showed excellent weight bearing. Similar studies were conducted Hong et al,<sup>14</sup> and Chen et al,<sup>15</sup> exploring the potential advantages of ECI and autograft implantation. With ECI very high radiation dose (50-300Gy) can be delivered. We delivered ECI with 50Gy in a single fraction since previous studies which states no added benefit with increase in dose and states chances of detrimental effect of with higher doses of radiation.<sup>16,17,19</sup> The advantages with delivery of such high dose is the maximum tumoricidal effect can be achieved which minimizes the chances of local recurrence which was also evident in a study conducted by Poffyn et al,<sup>18</sup> where they had 0% recurrence post treatment with ECI. And another study conducted by Davidson et al<sup>19</sup>, with 50 patients where 4 patients had recurrences. Most of the studies that we have been conducted with ECI for MBT had a heterogenous group of primary malignancy which makes it hard to conclude if the recurrence was due to tumour biology or due to failure of ECI.<sup>1,12,13, 14, 15,18</sup> The dose rate for ECI is still a matter of discussion and area that needs to be explored. Though, with ECI we can deliver doses without any radiation related toxicity to the normal tissue since the bone has been removed from the body. There is no chances of unnecessary radiation exposure to surrounding

structures. In study conducted by Ahmad fauzi et al<sup>20</sup> comparing various methods of limb salvage ECI was found to be good and convenient option. ECI can only be executed successfully in patients where biomechanical properties of the bone segment are intact.

The potential benefits of the procedure and a few limitations faced during the procedure as summarised in the table below:

Benefits	Limitations
Higher local tumour control	Single Plan approval could not be done due to high prescription dose.
Minimal chances of recurrence	Time is limiting factor since the bone is to be irradiated and transported back into the OT within a limited interval.
No dose related normal tissue toxicity	Technically feasible set up is needed to execute the treatment.
Anatomically perfect fit with autografts	To draw conclusion between local tumour control and overall survival large scale study with a higher sample size needs to be done.
No requirement of finding a matching donor bone and immunogenicity	Chances of graft failure
No need to have an access to bone banks	Perioperative complication
Cost effective	Delayed healing of wound.

## Conclusion

ECI and autograft reconstruction procedures for limb salvage are good, cost effective, and convenient treatment option with good anatomical and functional outcome. The relation between overall survival and local tumour control needs to be studied since most of the studies in literature had a small sample size. Further studies with a much larger patient cohort. The radiation delivery requires prior preparation to be carried successfully within limited time frame. This technique when employed with proper selection of patient could do wonders in regards to local control and post procedure life style of patient.

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