

## **Intramedullary Brachytherapy for the Treatment of Long Bone Metastatic Disease: A Case Report**

**David O'Neill\***

*Department of Medicine, UT Southwestern Medical center, USA*

**\*Corresponding author:** David O'Neill, Department of Medicine, UT Southwestern Medical center, USA. Email: david.oneill@phhs.org

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### **Abstract**

**Case:** 56-year-old female with metastatic melanoma and femoral lesions with impending pathologic fracture. She was indicated for Intramedullary Brachytherapy (IMBT) and Intramedullary Nail (IMN).

**Conclusion:** IMBT + IMN is a new technique for the treatment of long bone metastases. IMBT maximizes radiation to the tumor and minimizes radiation to surrounding tissues. It allows the patient to resume systemic treatment expediently. Our cadaver model and patient were both treated for femoral metastases; however, this technique allows for the treatment of any long bones. This is a safe technique that minimizes treatment time compared to other standard radiation regimens.

### **Introduction**

Bone ranks in the top three most common sites of metastasis for solid tumors including breast, prostate, lung, thyroid and kidney carcinomas [1-3]. As life expectancy increases with improved systemic therapies, the percentage of the population affected by metastatic bone disease will continue to increase [4,5]. This necessitates an increased focus on development of effective treatments for long bone neoplasms in an effort to maintain mobility and function in this patient population.

Current surgical treatments rely on resection and reconstruction, curettage with plate fixation, or IMN followed by postoperative radiation [6-13]. Because the patients with long bone metastases by definition have advanced disease, the treatment should be locally definitive, stable enough for immediate weightbearing, and minimize the need for repeat procedures [14]. The use of adjuvant therapies such as radiation and embolization vary widely based on individual surgeon preference [15].

Postoperative radiation is typically indicated after surgical fixation of pathologic fractures or impending pathologic fractures from tumor. The benefits of postoperative radiation include local tumor cytoreduction, remineralization, alleviation of pain, return of functional status, and a reduction in the risk for subsequent fracture [16]. The chief modalities for radiation therapy include Whole Bone Radiation Therapy (WBRT), generally 8 Gy in 1 fraction, 20 Gy in 5 fractions, or 30 Gy in 10 fractions, or stereotactic body radiation therapy/stereotactic ablative radiation therapy (SBRT/SAbR) [17]. There is little consensus on the optimal dosing strategy for SBRT/SAbR; limited available guidelines recommend that biologically ef-

fective doses  $\leq 100$  Gy<sub>10</sub> should be utilized, with 20-50 Gy delivered in 1-5 fractions [18].

Brachytherapy is a form of radiation therapy in which radioactive materials sealed within needles, seeds, wires, or catheters can be placed directly into or near a tumor. Although this is one of the earliest forms of radiation therapy [19,20] its use has not gained the same popularity in the treatment of long bone disease as external beam approaches.

The purpose of this paper is to describe a novel treatment approach utilizing IMBT, in addition to IMN, in a single event approach for the treatment of long bone metastatic disease at risk of fracture.

### **Statement of Informed Consent**

This treatment falls within expected radiation treatment options through the radiation oncology department at our institution. A thorough surgical consent was obtained.

### **Case Report**

All methods were first assessed in a human cadaver model before implementation in the clinical setting. In concert with our radiation oncologist and radiation physicist, we mapped the relationship of the target tumor to the medial tip of the greater trochanter using a pre-operative CT scan. Simultaneously, the radiation oncologist and the radiation physicist created a radiation map to treat the known tumor burden.

Surgery was performed in specialized intraoperative radiation therapy operating theatre. A Smith and Nephew antegrade femoral nailing system was utilized (Smith and Nephew, Memphis,

TN), as were two 3.5mm cannulated drill bits with kirschner-wires, and brachytherapy catheters with fiducials.

The patient was positioned in a lateral position on a bean bag, in a slight decubitus position to allow for ease of lateral radiographs. Preoperative radiographs were taken using a C-arm to localize the lesions and to check for adequate visualization of the whole bone. Skin markings were drawn to superficially localize the tumor.

Skin incision was performed proximal to the tip of the greater trochanter. The 1.9mm k-wire was introduced into the appropriate start point on the greater trochanter and advanced to the level of the lesser trochanter. The cannulated drill bit was introduced taking care to avoid the peritumor region with the drill bit. The second cannulated drill bit was introduced into the wound and placed next to the first at the tip of the greater trochanter. Appropriate positioning was confirmed using fluoroscopy. The difference was measured on the field providing the surgeon with the exact measurement of the length of drill bit inside of the bone.

The guidewire was removed and replaced with the appropriately sized brachy-catheter with radiopaque markers which was advanced to the target position. The radiation oncologist confirmed placement of brachytherapy catheter and confirmed no blood, contaminant, or kinks were found therein. The catheter was then secured to operative field and attached to intraoperative radiation therapy afterloader device. Radiation physicists confirmed safety and ready position of device. At this point in the procedure, the surgeons and all operating room personnel left the operative suite and the patient received planned intraosseous radiation dose. After radiation was completed, we proceeded with IMN placement. We utilized the reamer irrigator aspirator (RIA) (DePuy Synthes, Warsaw, IN) for a one pass reaming and removal of intramedullary tumor burden. The IMN was placed in standard fashion with a single cephalomedullary screw and a single distal interlocking screw.

IMBT was then performed on a 56-year-old female with metastatic melanoma and impending fracture to the left femur with three lesions visible on radiographs and MRI. We cannulated her femoral canal, placed the brachytherapy catheter in the appropriate location and sequentially irradiated the tumors with a goal peripheral dose of 20 Gy. After her radiation treatment, the brachytherapy catheter was removed and IMN was placed. We encountered no complications. She was ambulating post-operative day one and discharged post-operative day three. She recovered without any wound complications, no evidence of associated fibrosis, or any nerve damage four months post-operatively. She continued to ambulate with a walker. Unfortunately, she developed further disease and died of progressive metastatic melanoma 4 months 28 days post-operatively.

## Discussion

Post-operative radiation after surgical fixation of an impending pathologic fracture is considered standard of care and is recommended by several professional groups, including the American Society for Radiation Oncology (ASTRO), and the American College of Radiology (ACR) [21]. Such radiation typically takes the form of External Beam Radiotherapy (EBRT) in single- or multi-fraction regimens, at the discretion

of the treating radiation oncologist, with 30 Gy in 10 fractions being a commonly accepted post-operative dosing regimen [18]. Such doses are commonly delivered using Anterior-Posterior (AP) and Posterior-Anterior (PA) beams to an area encompassing the entire length of implanted hardware. As a result of this technique, a large area of bone and soft tissue receives the full prescription dose, thereby increasing the risk of treatment-related toxicity. The dose ranges commonly used in EBRT may also be inadequate for certain tumor histologies, such as renal cell carcinoma or melanoma, which are more sensitive to higher per-fraction doses of radiation [22]. Moreover, these treatments can delay systemic therapy, as they require a simulation session, planning period, and up to 2 weeks to deliver treatment.

High Dose Rate brachytherapy (HDR) is form of brachytherapy that involves the temporary placement of radioactive sources in, or adjacent to areas of tumor. The treatment typically involves the use of an afterloader, which guides a radioactive source (most often Iridium-192) under robotic control through catheters or needles into areas that harbor or are at risk of harboring cancer. Unlike EBRT, where the radiation beam must traverse healthy tissue in order to reach the tumor, HDR delivers radiation from within the tumor. Furthermore, HDR enables rapid dose fall off, with dose at a given location expected to be inversely proportional to the distance from the radioactive source squared. As a result, the dose to the tumor can be significantly higher and the dose to surrounding healthy tissues is greatly reduced.

Toxicity from brachytherapy is related to the dose of radiation delivered to nearby organs at risk (OARs). To our knowledge, HDR has not previously been used for the treatment of long bone metastases; thus, potential toxicities to long bones and other OARs must be extrapolated from other radiation techniques and other indications for treatment with HDR.

Although the use of HDR in long bones has not been previously documented, it has been studied in the re-irradiation setting for patients with progressive spinal lesions. In a study of five patients from Memorial Sloan Kettering Cancer center treated to a median dose of 14 Gy (range 12-18 Gy), there were no reported toxicities [23].

## Conclusion

Given the ability of brachytherapy to deliver high doses of radiation with excellent conformality to sites of tumor burden while sparing nearby tissues, the utilization of IMBT for long bone metastatic disease has great potential for tumor ablation with less toxicity. This is a proof-of-concept study with successful result. We were able to identify metastatic bone lesions via MRI and CT scan to develop an intraosseous brachytherapy radiation plan with subsequent IMN stabilization. This treatment enabled significantly smaller treatment volumes with higher radiation dose to tumor burden and reduced dose to soft tissue relative to external beam radiation therapy approaches. A higher single fraction dose allows for the potential for improved control of certain radioresistant cancer cell lines. With a single radiotherapeutic treatment dose that is complete at the time of surgery, the patient is able to consolidate their treatment plan for metastatic bone disease and resume systemic treatment expeditiously.

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