

# Radiation Therapy Prophylaxis for Heterotopic Ossification in Non-Hip Sites

Ajaykumar B. Patel<sup>1\*</sup>, Katherine S. Tzou<sup>2</sup>, Megan Single<sup>3</sup>, Laeticia Hollant<sup>4</sup>, Bridget Smart<sup>5</sup>, Katherine Gaines<sup>6</sup>, Courtney E. Sherman<sup>7</sup>, Jennifer L. Peterson<sup>2</sup>, Stephen J. Ko<sup>2</sup>, Laura A. Vallow<sup>2</sup>, Robert C. Miller<sup>2</sup>, Steven J. Buskirk<sup>2</sup>

<sup>1</sup>Northside Radiation Oncology Consultants, Atlanta, GA, USA

<sup>2</sup>Department of Radiation Oncology, Mayo Clinic, Jacksonville, FL, USA

<sup>3</sup>College of Medicine, University of Kentucky, Lexington, KY, USA

<sup>4</sup>University of Central Florida, Orlando, FL, USA

<sup>5</sup>University of Florida, Gainesville, FL, USA

<sup>6</sup>University of North Florida, Jacksonville, FL, USA

<sup>7</sup>Department of Orthopedic Surgery, Mayo Clinic, Jacksonville, FL, USA

Email: \*jaykumarbpatel@gmail.com

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## Abstract

**Background:** Radiation therapy prophylaxis for heterotopic ossification is well-established for the hip, either pre or post-operatively. There is limited data for this treatment in non-hip sites. We report our institution's experience. **Methods:** From October 2004 to August 2015, a total of 39 non-hip sites in 38 patients were treated with prophylactic radiation therapy for heterotopic ossification at our institution. An IRB approved retrospective review was performed. There were 15 patients who received treatments to the elbow, 13 to the knee (1 bilateral for a total of 14 knees), and 10 to other sites (leg stump (2), pubic symphysis (2), femur (1), foot (1), humerus stump (1), abdominal wall (1), shoulder (1), thigh (1)). All but 1 patient were treated with a single fraction treatment with 700 or 800 cGy. One patient received 2000 cGy in 10 fractions to the abdominal wall for heterotopic ossification extending from the xiphoid process. **Results:** Fifteen patients underwent treatment to the elbow with a median follow-up of 5 months (0 - 99). Median age for this group was 50 years (37 - 69). Nine (60.0%) patients had evidence of heterotopic ossification prior to surgery. All (100%) of the elbow patients were free from recurrence at last follow-up. There were no acute or late toxicities noted. For treatment to the knee, there were 4 (28.6%) recurrences, all in cases where there were pre-operative heterotopic ossification. There were two other recurrences in the non-hip, elbow or knee sites: one patient who received radiation therapy to the abdominal wall and one patient who underwent treatment to the thigh. **Conclusions:** Prophylactic radiation therapy with 700 cGy or 800

cGy in 1 fraction either before or after surgery remains a safe and effective treatment for both hip and most non-hip sites. Fractionated treatment may be used for larger treatment fields, however experience is limited.

## Keywords

Heterotopic Ossification, Radiation Therapy, Knee, Elbow

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## 1. Introduction

Heterotopic ossification (HO) is the development of bone in soft tissue. It can develop in various sites around the body, usually in a postoperative or post-traumatic setting near a joint space. Heterotopic ossification can affect quality of life with symptoms including pain, swelling, and loss of joint motion. Rates of HO formation vary by risk factors, including history of previous HO or fracture. Radiation therapy (RT) is well-established in high-risk patients for prevention of HO development for the hip [1]. There are multiple randomized controlled trials showing that 7 Gy in 1 fraction within 72 hours of surgery decreases the risk of development of HO in these patients [2] [3] [4].

Prophylactic RT has been used in non-hip sites including the elbow and knee; however, this data is more limited [5]. HO of the elbow can occur in up to 56% of patients with a radial head fracture [6]. For patients with a dislocation with an associated fracture, rates can be 5% - 20% [7]. Recurrence after excision has not been well documented. There is no standard recommendation for the role of RT prophylaxis for HO of the elbow.

Literature for HO of the knee is even less common. There are multiple case reports and a retrospective study with 12 patients [8]-[15]. The development of HO has been noted after total knee arthroplasty in up to approximately 40% of patients [9] [10] [11] [12]. HO of the knee can also occur after dislocation, most notably after posterior cruciate ligament reconstruction [16]. The disease is typically characterized by bony formation near the quadriceps expansion and can result in pain or loss of mobility [13] [14] [15]. Prophylactic radiotherapy for the knee has not been well reported.

Overall, there is limited data for radiation prophylaxis outside of the hip. In this study, we report our institution's experience with use of RT for prophylaxis of HO in non-hip sites.

## 2. Methods

After obtaining IRB approval, a query was performed for patients with a diagnosis of heterotopic ossification treated with radiation therapy in our department. A review of electronic medical records including treatment records was performed. Our search found 255 patients who had either preoperative or postoperative prophylactic RT for HO at our institution from October 2004 to August 2015. Of those 255 patients, 218 received treatment to the hip, 15 to the elbow, 13 to the

knee (1 bilateral for a total of 14 knees), and 10 to other sites (2 leg stump, 2 pubic symphysis, 1 femur, 1 foot, 1 humerus stump, 1 abdominal wall, 1 shoulder, 1 thigh). Patient data including demographics, radiation and surgery details, acute and chronic toxicities, and follow-up were collected on all patients. We report local failure and toxicity.

All patients were treated with linear accelerators using photons with anterior-posterior-posterior-anterior (AP-PA) beams.

Data analysis was conducted using JMP statistical software (SAS Institute Inc., Cary, North Carolina).

### 3. Results

A total of 39 non-hip sites in 38 patients were treated with prophylactic RT for HO at our institution. A breakdown of sites is shown in **Table 1**. All but 1 patient were treated with a single fraction to 700 or 800 cGy. The exception was treated with 2000 cGy in 10 fractions to HO extending from the xiphoid process to the abdominal wall.

#### 3.1. Elbow

Fifteen patients underwent treatment to the elbow with a median follow-up of 5 months (0 - 99). Median age for this group was 50 years (37 - 69). Nine (60.0%) patients had evidence of HO prior to surgery. Types of surgeries are listed in **Table 2**. Thirteen (86.7%) patients had RT postoperatively. Two patients (13.3%) had treatment preoperatively. All (100%) patients were free from recurrence at follow-up. There were no acute or late toxicities noted.

#### 3.2. Knee

Thirteen patients received treatment to a total of 14 knees (1 patient had bilateral knee treatment). The median follow-up was 21.5 months (1 - 110). Median age for this group was 66.5 years (21 - 81). Eight (61.5%) patients had evidence of preoperative HO. All knees were treated with postoperative RT receiving 700

**Table 1.** A breakdown by anatomic site shows most common non-hip sites treated.

Anatomical Site	Number Treated
Elbow	15
Knee	14
Femur/femur stump	4
Non-hip joint pelvic bone	2
Humerus stump	1
Shoulder	1
Abdomen	1
Foot	1

**Table 2.** A breakdown of surgeries shows the most common elbow surgery was elbow arthroplasty.

Surgery/Procedure	Number of Patients
Elbow arthroplasty	8
Heterotopic debridement	2
Open reduction and/or fixation	2
Radial ulnar synostosis takedown	2
Contracture release	1

cGy in 1 fraction. There were 4 (28.6%) recurrences, all in cases where preoperative HO was noted. Two of the recurrences occurred in the same patient who had bilateral RT after bilateral knee manipulation. This patient had bilateral total knee arthroplasty 48 days prior to this knee manipulation and subsequent RT. She then underwent HO excision the following year. The recurrences are outlined in **Table 3**. There were no acute or late toxicities noted.

### 3.3. Other Sites

There were 10 patients who received RT to non-hip, elbow, or knee sites. These sites are outlined in **Table 4**. There were 2 recurrences in this group: 1 patient received RT to the abdominal wall, and 1 underwent treatment to the thigh. The patient who received RT to the abdominal wall had myositis ossificans extending from the xiphoid process to the pubic symphysis. His disease developed after significant abdominal wall trauma. **Figure 1** shows this patient's extent of disease. He received 2000 cGy in 10 fractions.

## 4. Discussion

Radiation therapy (RT) for prophylaxis of heterotopic ossification (HO) for the hip is well-established [1] [2] [3] [4]. The same therapy for other sites is not as widely reported. In this article, we add to the growing body of literature for knee, elbow, and other sites that are at high-risk for developing HO.

In our study, patients who received RT to the elbow had no HO recurrences and no toxicities, demonstrating that this treatment is safe and effective. Other reports for RT to the elbow found similar results [17]. A study from Cleveland Clinic reported on 36 patients who underwent surgery and postoperative single-fraction RT [18]. They found that only 3 (8%) of the patients developed new HO after therapy. A study from Rush University in 2011 evaluated 44 patients who underwent RT after surgery to the elbow and had post-therapy radiographs [19]. They found at a follow-up of 136 days that 21 (48%) of the patients had developed HO.

We had similar outcomes with patients undergoing treatment to the knee. While 4 (28.6%) patients experienced recurrent disease, all of them had evidence of HO prior to surgery. One patient who had bilateral recurrence had knee

**Table 3.** Three patients had knee recurrences with time to progression ranging from 1 to 13 months.

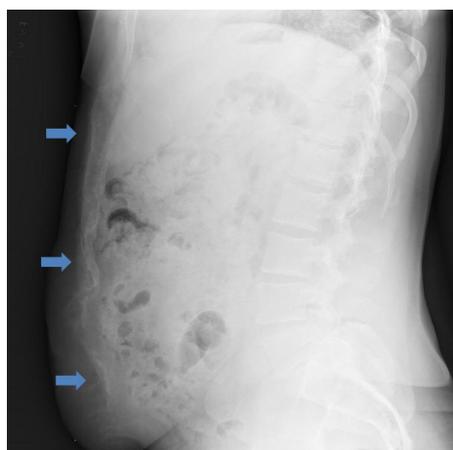
Patient	Surgery/Procedure	Time to RT	Preoperative HO	Time to Recurrence/Progression
1	Revision of total knee arthroplasty	1 day	Present	13 months
2	Total knee arthroplasty	<1 day	Present	1 month
3	Bilateral knee manipulation	2 days	Present (bilateral)	1 month

HO: Heterotopic ossification; RT: Radiation therapy.

**Table 4.** Other sites.

Site	Type of Surgery	Radiation Dose/Fraction	Recurrence?
Iliac crest and pubic symphysis	HO excision	700 cGy/1 fx	No
Superior pubic ramus and obturator foramen	HO excision	700 cGy/ 1 fx	No
Femur	HO excision	700 cGy/1 fx	No
Femur	HO excision	700 cGy/1 fx	Yes
Femur stump	Above-the-knee amputation	700 cGy/1 fx	No
Femur stump	Above-the-knee amputation	700 cGy/1 fx	No
Foot	HO excision	700 cGy/1 fx	No
Abdomen	HO excision	2000 cGy/10 fx	Yes
Humerus stump	Above-the-elbow amputation, HO excision	700 cGy/1 fx	No
Shoulder	HO excision	700 cGy/1 fx	No

HO: Heterotopic ossification.

**Figure 1.** This image is a lateral X-ray of abdominal heterotopic ossification in a 40-year-old male with myositis ossificans extending from the xiphoid process to the pubic symphysis (blue arrows).

manipulation and RT 48 days after an initial bilateral arthroplasty. There was no report of HO excision at the time of knee manipulation prior to RT. This leads to the question of whether or not the timing of RT this late after bilateral arthroplasty contributed to this patient having recurrence and progression of disease. Overall, there were no toxicities, acute or late, noted.

One report from Drexel University with 12 patients who underwent RT for knee HO prophylaxis had no HO recurrence after treatment [8]. This patient group differed from ours as 8 (61.5%) of our patients versus none of their patients had evidence of HO prior to surgery. A report by Chidel *et al.* detailed their experience with 5 patients who received knee HO prophylaxis with RT [13]. They had no progression or recurrence of HO, reporting that the treatment was well tolerated.

Although acute side effects are minimal, the risk for secondary malignancy is always an important concern in the treatment of benign disorders. There have been case reports for developing soft tissue sarcomas within the field of single-fraction RT for HO [20] [21]. However, none of the larger series of both hip and non-hip sites have shown any evidence of the development of secondary malignancy within the treatment field. A study by Berris *et al.* outlined peripheral organ doses from radiotherapy for non-hip sites [22]. They found for shoulder, elbow, and knee treatments that equivalent peripheral organ doses were 0.85 - 62 mSv, 0.28 - 1.6 mSv, and 0.04 - 1.6 mSv, respectively. This corresponded to cancer risks of 0 - 5.1, 0 - 0.6, and 0 - 1.3 cases per 10,000 persons. The highest risks were with treatment to the shoulder in developing malignancies of skin (5.1 cases per 10,000) and breast (3.8 cases per 10,000). Though the risk for secondary malignancy remains, it is evidently extremely rare, especially in elbow and knee treatments.

A noted obvious limitation of this study is its retrospective nature and heterogeneous patient cohort.

## 5. Conclusion

RT prophylaxis with 700 cGy in 1 fraction either before or after surgery remains a safe and effective treatment for both hip and most non-hip sites.

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