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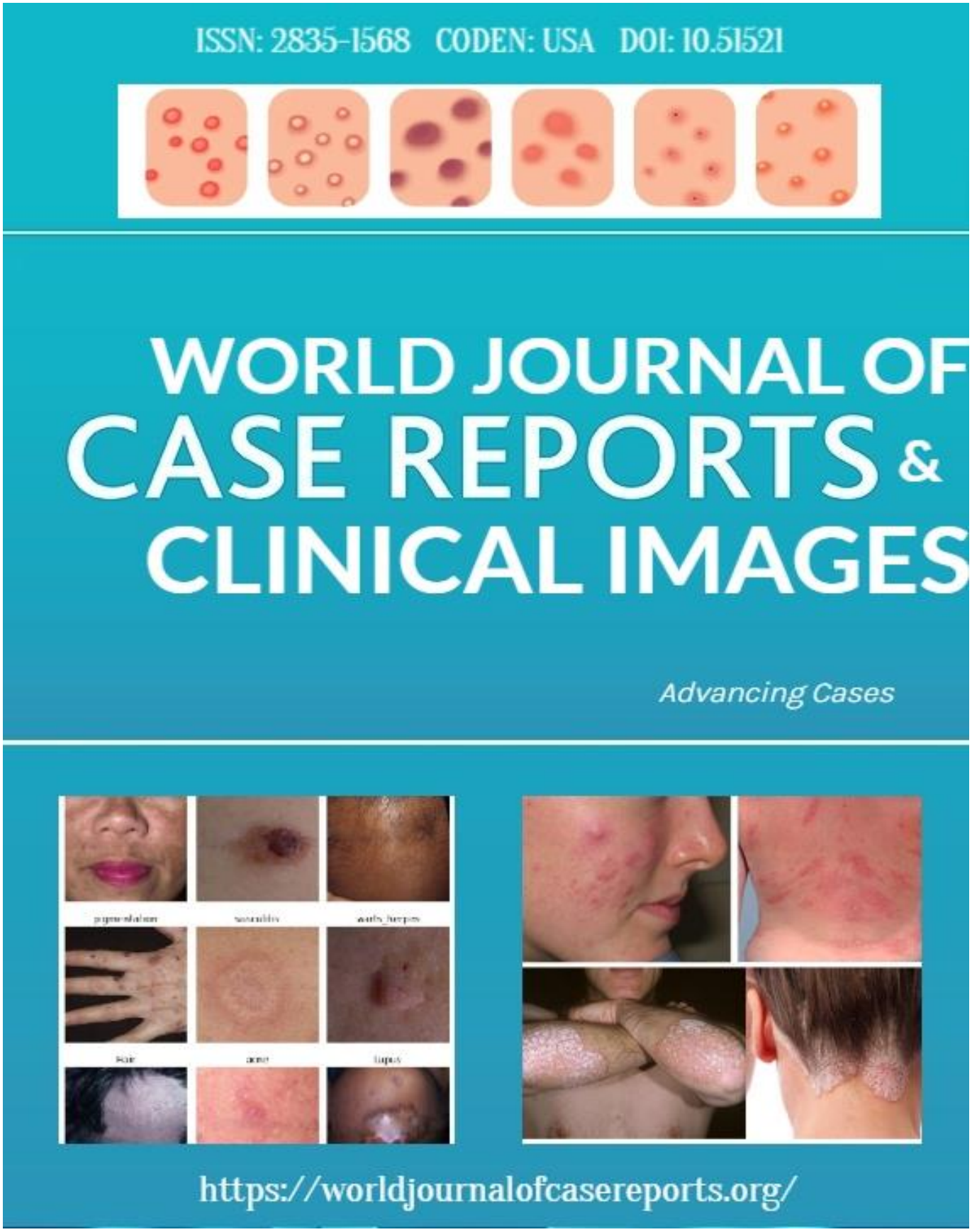

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ORIGINAL ARTICLE

Radiation Therapy in Heterotopic Ossification: Case Series

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Abstract

***Aims**: Heterotopic ossification (HO) is a diverse pathologic process, defined as the formation of extra skeletal bone in muscle and soft tissues. The study is sought to determine whether radiation therapy (RT) can prevent recurrence in patients who have had HO removed.*

***Methods and Material**: Five patients were treated after resection of manifest HO. RT was performed with 6 MV photons after simulation on the basis of CT scans.4 patients received 10 Gy in 1#, and 1 patient received 8 Gy in 1#.*

***Results**: Patients are on follow up since 2 years. Patients showed no progression of HO. No relevant adverse effects were observed.*

***Conclusions**: The use of postoperative radiation therapy is an effective and safe treatment in the prevention of heterotopic bone formation in a high-risk group of patients*

Keywords: *Heterotopic Ossification, Radiation Therapy*

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Introduction

The process of aberrant bone growth in non-osseous tissue is known as heterotopic ossification (HO). The hip is the most frequently involved site followed by elbows, knees, shoulders or other soft tissues around joints. Joint stiffness and limited range of motion are potential symptoms of HO, other symptoms are fever, local rise of temperature, redness, tenderness and swelling. Although no specific etiological factors have been found in HO patients, prior research indicates that ankylosing spondylitis, osteoarthritis, spinal cord injury, hereditary diseases, and previous history of ipsilateral or contralateral HO may be risk factors for this condition [2]. The most widely used method in the world, the HO assessment classification was created by Brooker *et al* [5]. (Table 1).

Table 1: Brooker classification system of HO

[adapted from Brooker *et al*]

Stage	Description
I	Bone islands within the soft tissue
II	Bone spurs from the pelvis or proximal end of the femur, with at least 1 cm between opposing bone surfaces
III	Bone spurs from the pelvis and/or proximal end of the femur, with less than 1 cm between opposing bone surfaces
IV	Apparent bone ankylosis of the hip

Following hip arthroscopy, radiographic imaging can reveal an incidence of HO ranging from 4.7% to 44%. Twelve weeks following surgery, 37 (57.8%) of 64 patients with displaced fractures of the acetabulum disclosed by a Kocher-Langenbeck technique had HO, according to Karunakar et al [9]. It has been reported that in individuals with a prior history of HO formation on the opposite side, the incidence of HO following hip arthroplasty might reach up to 92%. Clinically, after total hip replacement, the incidence of substantial HO (Brooker classification; grade III or grade IV with symptoms) ranges from 3% to 7%. Non-steroidal anti-inflammatory drugs (NSAIDs) are often used to prevent heterotopic ossification (HO) [1]. NSAIDs are contraindicated in patients with peptic ulcer, renal failure, or other comorbidities, even if they can be used as preventive treatments against HO. One alternative therapeutic option that tries to lower the postoperative risk of developing HO is radiotherapy (RT) [3]. It was discovered that osteogenic progenitors were susceptible to radiation therapy during bone repair research conducted in 1950s. These early investigations tapped into the mechanism of HO, which is the conversion of primitive mesenchymal cells in the surrounding soft tissues into osteoblastic tissue. From a defective bone formation/remodelling process, this tissue subsequently generates mature lamellar bone. The reason why osteogenic progenitor cells are assumed to be radiosensitive, according to Craven et al, is because of their high rate of mitosis during their differentiation into osteoblasts and chondrocytes. The study aims to assess the safety and effectiveness of PORT in advanced-stage HO patients.

Subjects & Methods:

We provide a case series of HO patients who had adjuvant radiotherapy following surgical resection.

Case Series:

Case 1: A-20-year old gentleman presented with complaint of hard swelling over bilateral hips and restriction of B/L hip movements since 6-7 months. He gives history of RTA 2 years back and has undergone B/L acetabular plating. On CT Scan diffuse hyperdense area of bone attenuation noted extending from the bilateral iliac bones extending inferiorly upto lesser trochanter with bridging. Patient underwent B/L hip heterotopic ossification excision.

Case 2: A 33-year-old gentleman presented with complaints of right leg pain associated with stiffness since 2 to 3 months. He gives history of RTA following which he underwent right leg exploration with right tibia intramedullary nailing with right acetabular plating 3 years back. A CT showed plating in acetabulum with callus formation, intramedullary nail noted in right femur. Patient underwent right hip heterotopic ossification excision

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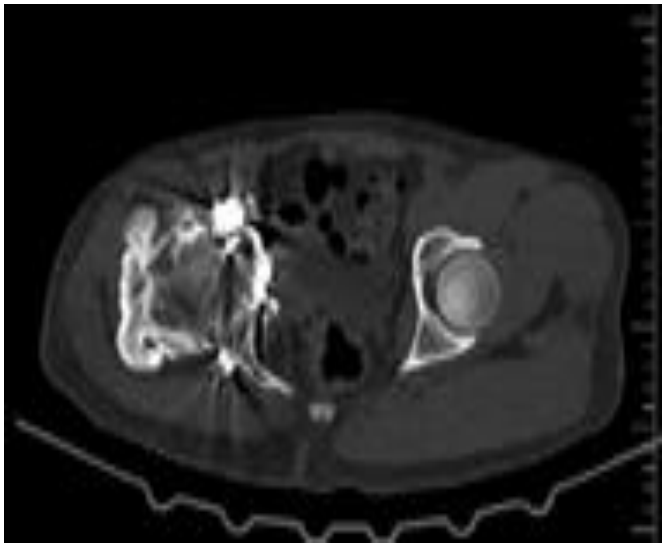
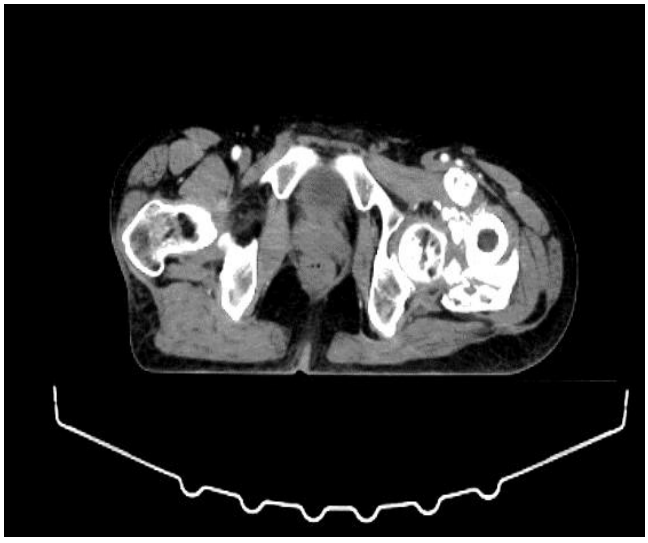


Case 3: 23year old gentleman came with complaint of stiffness in right elbow joint since 8 months. Give H/O RTA a year back and has undergone right shoulder closed reduction and right elbow closed reduction with percutaneous Steinmann pin. On CT of Right elbow – old fracture with excess callus formation seen around the proximal end of ulna and radius. He underwent heterotopic excision of right elbow

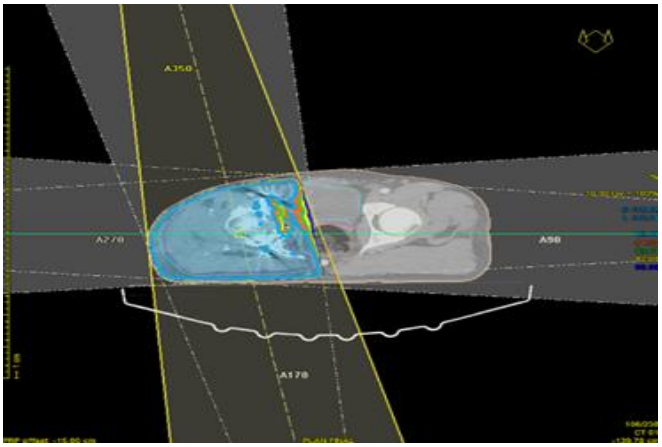
Case 4: A 40 years old gentleman presented with alleged history of fall following an episode of seizures 3 months back, he sustained injury to left hip and was managed conservatively. On evaluation with CT there was communicated fracture neck, inter trochanteric, sub trochanteric and proximal left femur with superior and anterior displacement of femoral shaft. Multiple fracture fragments are noted in anterior and posterior aspects of proximal femoral neck, he underwent left femoral dynamic hip screw stabilization.



Case 5: A 45year old gentleman presented with complaint of left knee pain since 2 months, gives H/O RTA a year back and injury to the knee. On evaluation with X ray he was diagnosed with HO of left tibia and underwent excision.

Following appropriate disease and treatment counselling, the patients had a CT simulation in comfortable immobilization device and was scheduled for radiation therapy for the site of excision. The treatment volumes were contoured on 3mm slice thickness CT, delineation of the target volumes of interest followed: Clinical Target Volume (CTV) which included periarticular tissues with the post-operative tumor bed and Planning Target Volume (PTV), which corresponded to CTV plus extra margin in order to compensate for inter- and intra-fraction uncertainties consequent to daily setup errors and to potential internal organ motion. Radiation therapy was administered using a 6 MV linear accelerator. Patients were treated with three dimensional conformal radiotherapy (3DCRT) technique with 10 Gy delivered in 1#, with the exception of case #3, which got 8 Gy in 1# within 24hrs post-surgery. Patients are stable and have a decent range of motion during follow-up.

Case 1:



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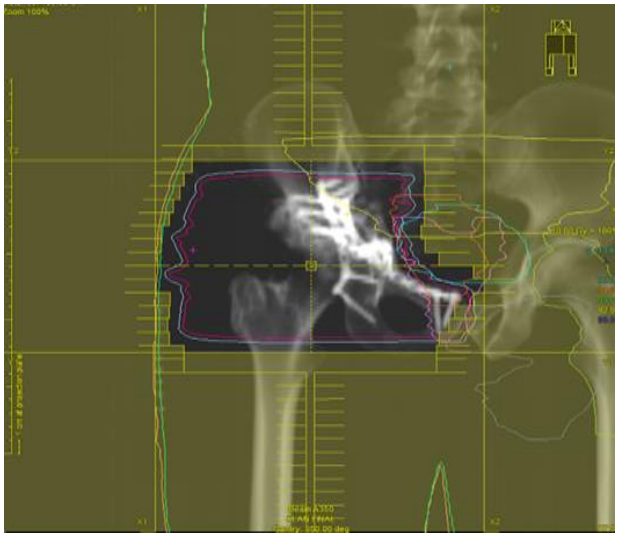
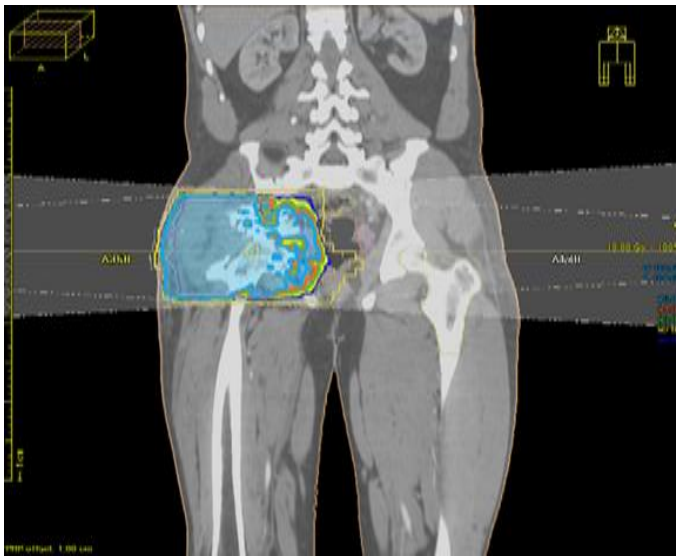
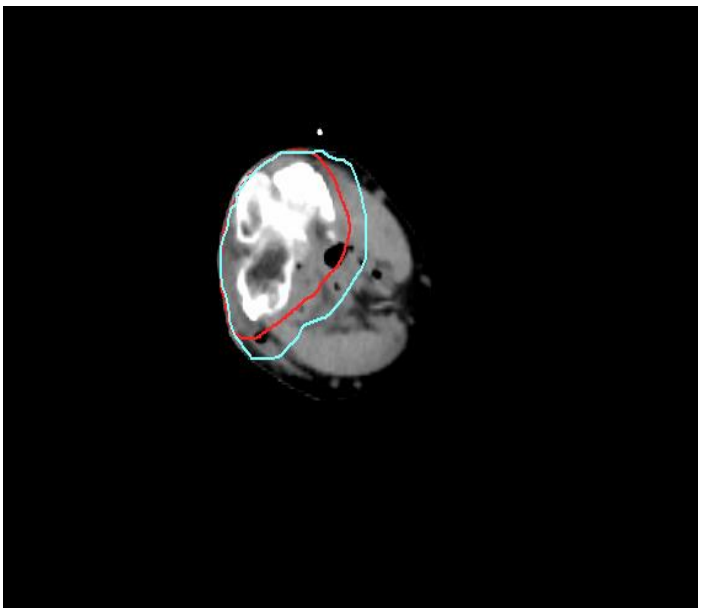


Case 2:

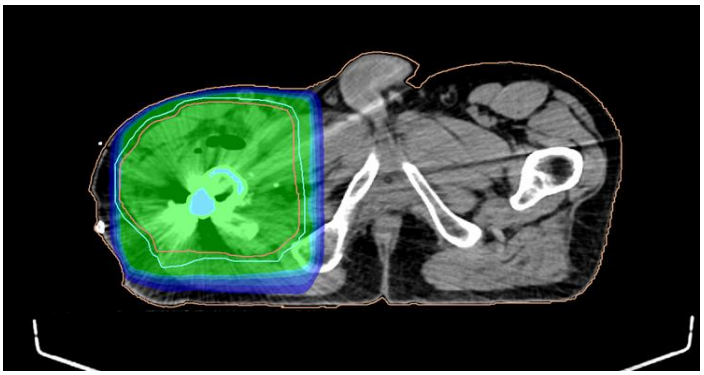
ROI	Dose [%]	Dose [Gy]	Volume [%]	Volume [ccm]
Urinary Bladder	93.02	8.3022	50.00	63.08
Anorectum	90.15	8.0151	50.00	73.09
Left Femoral Head	36.07	3.6066	50.00	104.74
Bowel Bag	29.72	2.9724	50.00	239.97
Seminal Vesicle + Prostate	39.69	3.9687	50.00	28.02
Penis + Scrotum +	3.74	0.3740	50.00	51.41
CTV PO Soc	90.07	9.0073	95.00	1665.36
PTV	87.63	8.7627	95.00	1902.47

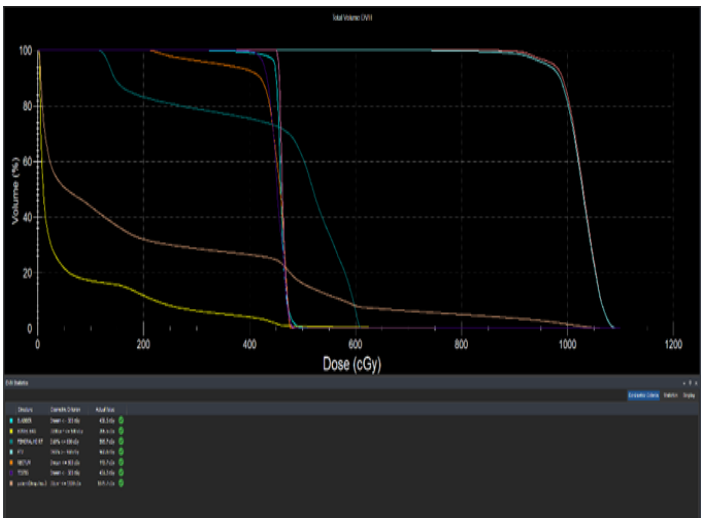


Case 3:



Case 4:





Results:

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5 patients were treated for prevention of HO after surgery. All patients were at high risk for developing HO after surgery for various reasons, but typically due to previous history of ectopic bone formation. After a median follow up of 2 years none of our patients developed HO. Impaired wound healing or other post-surgery complications. No early or late radiation induced toxicity was documented in all our patients.

Discussion:

Heterotopic ossification is defined as the formation of mature, lamellar bone in soft tissues where bone does not normally exist. HO is commonly seen following trauma or surgical intervention in periarticular tissue and is commonly associated with injury to hip. The three primary causes can be grouped into traumatic, neurogenic and genetic etiologies. Hip is the most common site followed by elbow. Classical presentation of non-genetic HO is in young adults with clear history of trauma or surgery. Approximately half of the patients are in their second and third decades of life, however broad age distribution is present from infancy to late adulthood Clinical features includes limited range of movements around involved joints, complete bony ankylosis in severe cases and deformity in the cervical spine, elbow, shoulders and temporomandibular joint. Sometimes HO can be detected as asymptomatic finding on a radiograph. Despite the risk that it can trigger another round of HO, surgery remains the only treatment option to date once bone tissue has formed. Currently most popular drugs for HO are cyclooxygenase – 2 inhibitors and nonsteroidal anti-inflammatory drugs, both target pro inflammatory prostaglandins. Traditional NSAIDs such as aspirin, ibuprofen and indomethacin inhibit the formation of both physiological and inflammatory prostaglandins. The recommended dose of indomethacin is 75 to 100 mg/ day for 7 to 14 days postoperatively.

Radiation therapy is also used in treatment of benign diseases. In order to prevent clinically significant heterotopic ossification, preoperative radiotherapy of the operative site 4 hours prior to elective hip surgery and total hip arthroplasty appears to be as beneficial to currently recommended postoperative radiotherapy regimens. A single fraction RT seems to be sufficient, cost effective and a safe treatment regimen [7]. Radiation therapy is indicated as a prophylaxis to prevent recurrence, post-surgery. It is shown that RT is more effective in early phase of HO [8]. It is recommended that surgery alone increases recurrence rates and radiotherapy should be given at pre-operative and early post-operative period to prevent recurrence. It is recommended that RT should be given within 72 hours after surgery. In the above-mentioned cases, patient's symptoms reduced after post-operative radiation therapy during the 2 year follow up. Further follow up is required to completely study the effects of radiation therapy in heterotopic ossification.

Conflict of Interest: None

Ethical Approvals: Not required

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