Evaluation of Scrotal and Testicular Radiation Doses for Heterotopic Ossification Prophylaxis

Hejal Patel, MD, Craig L. Silverman, MD, Luis Carrascosa, MD, Arthur Malkani, MD, and Catheryn M. Yashar, MD

Abstract

The majority of patients with heterotopic ossification are males with traumatic injuries in the hip/femur region. The testes, given their proximity, are exposed to scatter radiation, which has the potential to alter sperm count and morphology.

In a prospective study, patients were treated with an 800-cGy dose of radiation without direct exposure of the testes/scrotum but with a testicular shield.

Thermoluminescent dosimeters were placed inside and outside the shield. Mean dose inside and outside the shield was 10.2 and 20.2 cGy, respectively (sperm abnormalities have been reported with 15 cGy). Given our study results, young males should be counseled and should be treated with a testicular shield.

Heterotopic ossification (HO) is the formation of mature, lamellar bone in nonskeletal tissue, usually in the soft tissue surrounding joints.[1] The first mention of HO in the literature dates to World War I with patients who sustained spinal cord injuries.[2] HO has many causes but most commonly occurs in people with traumatic injuries or after surgical interventions such as open reduction and internal fixation (ORIF) and total hip arthroplasty (THA).

The incidence of HO ranges from 11% to 75%. HO develops as early as 2 weeks and as late as 18 months after a precipitating factor.[1-3] Clinically, HO can be debilitating: 33% of patients present with loss of motion and 10% with complete ankylosis.[1] The most common prophylactic radiation referrals at the University of Louisville are young males involved in traumatic accidents. In addition, the most common etiology for any grade of HO, including Brooker grade III or IV, is after ORIF for acetabular fracture.[4,5] If HO becomes symptomatic, pain and limited mobility can significantly decrease quality of life and limit sustainable employment. The substantial risk for HO and its sequelae stimulated extensive research into prophylaxis and treatment. Research has been conducted on nonsteroidal anti-inflammatory drugs (NSAIDs), such as indomethacin, and on external beam radiotherapy.[3,6-13]

The hip is the most common site of HO prophylactic treatment. For male patients presenting for radiation HO prophylaxis, the radiation field is in close anatomical proximity to the testes. To date, the testicular dose from scatter radiation has not been investigated, and recommendations have not been made regarding counseling or testicular shielding. In the literature, very low doses of radiation have been shown to alter sperm production and morphology.[14] At our institution, patients who are to receive HO prophylaxis and want to remain fertile are routinely offered testicular shielding, even though it is not a standard recommendation in radiation textbooks.[15,16]

We conducted a prospective study to evaluate radiation doses to the scrotum/testicles during single-fraction treatment for HO to evaluate the necessity of counseling and testicular shielding.

Materials and Methods

Between 1999 and 2005, 27 male patients (age range, 16-56 years) referred for HO prophylaxis after posttraumatic ORIF or THA were evaluated as the study population. Twenty-six (96%) of these patients were referred after a motor vehicle accident. The risks and benefits of radiation HO prophylaxis were explained to each patient, and each signed an informed consent form.

These patients were treated within 24 to 48 hours after surgery. A standard dose of 800 cGy of external beam radiation was given using parallel opposed fields with dose prescribed to the central axis at midplane (Figure 1).[17] Field sizes and photon energies varied (higher energies and field sizes were used for larger, thicker patients). Energy and field size were determined by the treating radiation oncologist. Radiation was delivered with a conventional linear accelerator (Philips Electra) with a source-

Dr. Patel is Resident in Radiation Oncology, Dr. Silverman is Clinical Associate Professor of Radiation Oncology, Dr. Carrascosa is Instructor in Radiation Oncology, and Dr. Malkani is Assistant Professor of Orthopaedics, University of Louisville, Louisville, Kentucky.
Dr. Yashar is Assistant Professor of Radiation Oncology, University of California San Diego, La Jolla, California.

Address correspondence to: Catheryn M. Yashar, MD, Department of Radiation Oncology, University of California San Diego, Moores Cancer Center, 3855 Health Sciences Drive, La Jolla, CA 92037 (tel, 858-822-6046; fax, 858-822-5568; e-mail, cyashar@ucsd.edu).

Am J Orthop. 2008;37(9):E163-E166.

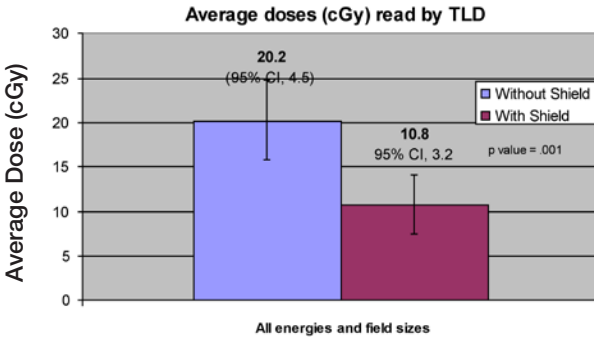

Figure 3. Thermoluminescent dosimeter readings for all field sizes and photon energies.

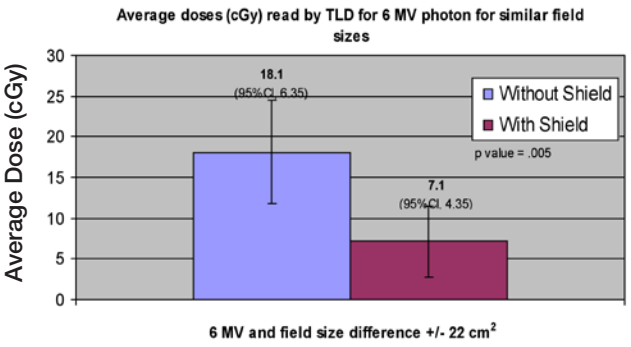

Figure 4. Thermoluminescent dosimeter readings for 6-MV energy only and field sizes within 22 cm^2.

to-axis distance of 100 cm and a dose rate of 400 cGy/min. All treatment fields excluded the testes and scrotum.

Given the differences in field size and patient anatomy, the proximity of treatment field to testes varied. For all patients, a testicular shield was applied during treatment (Figure 2) and placed midline as far from the radiation field as possible. The shield is made of half-inch lead (atomic number, 82; atomic mass, 207.2 amu), has a polyurethane coating, and comes in one standard size. Several testicular shields are described in the literature, but they all have 1- to 1.5-mm lead or lead blocks as the primary shielding.[18-20] The shield used at our institution is manufactured by Radiation Protection Design and is based on the original design described by Fraass and colleagues[21] in 1985.

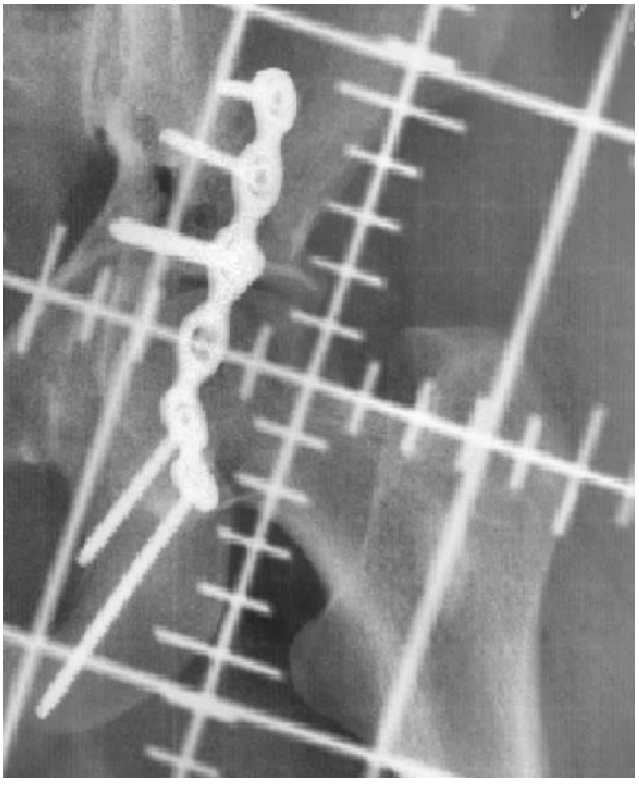

Figure 1. Typical simulation film for heterotopic ossification prophylaxis.

Thermoluminescent dosimeters (TLD) were used to measure the radiation dose received by the testes. TLD response and calculated dose are affected by previous radiation and thermal history. Typical dose–response curves are linear for doses smaller than 100 cGy and are most reliable on the linear portion. All measurements in this study were well below 100 cGy. For consistency, only one TLD reader was used. TLD readings are accurate within 3%.[22] TLDs were placed both inside the shield and outside the shield edge closest to the radiation-field edge in a predetermined and reproducible position for all patients. Measurements were taken both inside and outside to determine the reduction in dose to the testes with the shield in place. TLD measurements were analyzed and recorded for each patient.

Results

All patients received radiation treatment without complication. Mean TLD dose inside the testicular shield was 10.2 cGy (range, 3-30 cGy, Figure 3), and mean dose outside the shield was 20.2 cGy (range, 13-50 cGy). Median TLD dose inside the shield was 7.8 cGy, and median dose outside the shield was 19.6 cGy. Testicular dose was reduced by 51% with shield use and usually decreased radiation exposure by at least 10.0 cGy ($P>.001$). Dose variation may be attributable to differences in field size, photon energy, distance from radiation field to shield, and variable inherent TLD sensitivity.

To examine a more homogeneous population of patients and to verify results, we tabulated results for patients treated with 6-MV photons and field sizes within ±22 cm^2 (Figure 4). In this population, there was a 40% reduction in radiation dose, which corresponds to a drop of 11.0 cGy ($P>.001$). Mean TLD dose was 7.1 and 18.1 cGy inside

Figure 2. Testicular shield.

Table. Randomized Studies Comparing Use of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and Radiation Prophylaxis

Authors	No. Patients	Radiation Dose, cGy	Incidence of Heterotopic Ossification (%)	
			NSAIDs	Radiation Prophylaxis
Kienapfel et al[7]	154	600	36.0	25.0
Sell et al[8]	155	990	23.3	2.3
Kolbl et al[9]	113	700	16.0	11.1
Burd et al[10]	166	800	11.0	4.0
Moore et al[11]	75	800	17.9	9.0
Knelles et al[12]	723	1200 (700 Gy)	12.2	5.0
Kolbl et al[13]	100	700	47.8	11.1

and outside the shield, respectively. Median dose was 7.6 and 19.6 cGy inside and outside the shield, respectively. There was not a demonstrable effect on the dose reduction when examined by field size.

Discussion

HO is a well-described hip-surgery complication with defined risk factors. Often, as a result of trauma, referred patients are young males. NSAID use and photon radiation therapy have emerged as HO prevention methods.

Bone is an active organ, and remodeling is a dynamic balance of bone-forming osteoblasts and bone-destroying osteoclasts. HO is postulated to occur when local trauma skews this balance by invoking inflammatory factors that stimulate bone formation. NSAIDs are thought to inhibit the induction of these inflammatory factors. The highly mitotic osteoprogenitor cells themselves are thought to be particularly sensitive to radiation and are the postulated radiation target.[23]

There are concerns about both methods of prophylaxis, NSAID use and radiation therapy. NSAIDs such as indomethacin can have serious gastrointestinal side effects, including gastritis, ulceration, and bleeding. Given that anticoagulation is standard procedure after THA, hemorrhage is another concern. In addition, Burd and colleagues[24] reported a series that demonstrated an increase in long-bone nonunion in patients who received indomethacin versus radiation therapy.

Although no single case has been reported with HO prophylaxis, the possibility of second malignancies after radiation therapy, especially in young patients, is a theoretic concern. Investigating this in their review of soft-tissue sarcomas, Kim and colleagues[25] noted no second malignancies when radiation doses were below 30 Gy. Standard prophylactic HO doses are below 10 Gy. In addition, trochanteric nonunion and prosthetic failure from bony ingrowth inhibition have been theoretic concerns with radiation therapy.[17,26] However, treatment with open fields has not clinically demonstrated decreased prosthetic failure, and shielding the prosthesis has not demonstrated increased efficacy.[27,28]

Seven randomized trials have directly compared NSAID use and radiation therapy for prophylaxis (Table). Most recently, Pakos and Ioannidis[29] reported a meta-analysis of these prophylactic methods in 7 randomized trials with 1143 patients. Radiation therapy was more effective than NSAID use in preventing Brooker III or IV HO.[9-13,29]

The radiation dose needed for optimal prophylaxis has also been explored. Brooker and colleagues[30] found no difference between single- and multiple-fraction regimens. Acceptable radiation doses for single-fraction treatment range from 400 to 800 cGy.[12,17] A typical simulation film can be seen in Figure 1. Although the testicles are near the treatment field, the amount of scatter dose they receive is unreported in the literature. Further, risk for altered sperm production and morphology from scatter radiation is uncharacterized, thereby making the need for shielding or counseling unknown.

Hall and colleagues[14] reported a temporary reduction in number of spermatozoa with radiation doses as low as 10 cGy and temporary sterility at doses of 15 cGy. Martin and colleagues[31] reported the incidence of chromosomal aberrations in 13 seminoma patients who had received a median radiation dose of 3000 cGy and testicular doses ranging from 40 to 500 cGy. Chromosomal abnormalities continued to be identified up to 24 months after completion of irradiation. Freund and colleagues[32] reported on testicular function in 8 seminoma patients treated with radiation. Absorbed gonadal radiation dose ranged from 15 to 157.5 cGy. Two patients remained azoospermic 10 to 24 months after radiation treatment. The largest study evaluating testicular dose and sperm function was reported by the Southwest Oncology Group[33] (53 patients). Median gonadal dose in this study was 79 cGy. Recovery of fertility occurred approximately 1 year after radiation, and it appeared that recovery was both dose- and time-dependent.

Fraass and colleagues[21] described using testicular shielding for dose reduction in 1985. Dose reduction has been reported to be as high as 90% with use of a testicular shield.[34] Shields are commercially available and, though considered a standard part of therapy when treating young males in the setting of Hodgkin's disease or seminoma, are not recommended for HO prophylaxis in the literature.

In our study, the minimum dose recorded outside the testicular shield was 13 cGy, and the maximum dose was 50 cGy (mean dose, 20 cGy). The published threshold dose for temporary azoospermia and sperm chromosomal abnormalities is 13 cGy. Twenty (74%) of the 27 patients in this series had a recorded dose higher than 15 cGy outside the shield, placing them at risk for sperm alteration without shielding.

All patients were treated with anterior–posterior opposed fields with varying field sizes. Mean field size was 150 cm^2. Radiation scatter dose to the testicles depends on field size and energy. All energies were in the megavoltage range and varied from 4- to 22-MV photons, depending on machine availability, patient size, and physician preference. Figure 4 tabulates results for patients with field sizes of 22 cm^2 treated with 6-MV photons; it demonstrates that, even with smaller fields, low-energy testicular dose is significantly reduced with shielding.

According to the literature, sperm abnormalities (including oligospermia, azoospermia, and chromosomal abnormalities) may occur with radiation doses as low as 15 cGy. The present study demonstrates that patients who received HO prophylaxis may routinely receive doses higher than 15 cGy. Use of a testicular shield during treatment consistently reduces radiation dose to the scrotum/testicles by 50%. These findings support routine use of a testicular shield for young male patients receiving radiation HO prophylaxis. If a testicular shield is not used, male patients should be counseled regarding possible alteration in sperm production and morphology, even though these changes are unlikely to be permanent at this dose. In addition, using the smallest field possible to achieve the aim would also be prudent to maximize the distance between the testicles and the radiation field, though we could not demonstrate a clear effect in this study. There were insufficient data to recommend low- versus high-energy photons, but realistically the energy is unlikely to make a significant difference in testicular dose.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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