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Topic Discussion

Radiation Therapy for the Treatment of Osteoarthritis

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Abstract

Osteoarthritis is a common cause of pain and disability in the United States. Many patients experience pain that is refractory or unable to be treated by traditional treatments such as exercise, physical therapy, nonsteroidal anti-inflammatory drugs, and/or cyclooxygenase-2 inhibitors. For patients with medically refractory disease, intra-articular corticosteroid therapy, hyaluronic acid, or surgery can be considered. However, for many older patients with significant impairment in quality of life related to osteoarthritis, radiation therapy is a noninvasive treatment option that has a long history of global use. In this topic discussion, we review the clinical evidence supporting treatment of osteoarthritis, as well as considerations for how to select which patient and joint to treat. We discuss technical considerations for treatment including dose and immobilization, assessment of treatment response, and the role of retreatment.

Osteoarthritis is a common cause of pain and disability in the United States, with a prevalence of over 32 million.[1] Nationwide, it is estimated that the direct cost (ie, medical expenditures) of osteoarthritis is approximately $85 billion.[2] Both the incidence and disability from osteoarthritis are increasing, in part as a result of aging populations as well as rising obesity rates.[3]

Osteoarthritis has been functionally defined as pain with activity or morning stiffness lasting less than 30 minutes, typically in patients older than 45 years. Osteoarthritis is a clinical diagnosis, although plain radiography can be helpful to visualize typical joint space narrowing and osteophyte formation.

Osteoarthritis management relies on various treatments, with preference for more conservative options such as exercise[4] and/or physical therapy with nonsteroidal anti-inflammatory drugs (NSAIDs) and/or cyclooxygenase-2 inhibitors. For patients with refractory disease, more invasive options such as intra-articular corticosteroid therapy, hyaluronic acid, or surgery can be considered. However, the use of NSAIDs may be limited in certain populations, and older patients or those with comorbidities may not be eligible for, or may be resistant to, joint replacement.[4] Additionally, many patients wish to avoid invasive procedures if possible given associated risks. For patients with significant impairment in quality of life related to osteoarthritis, radiation therapy is an option that is used frequently outside the United States.[1,5]

Clinical Evidence

Examples of modern studies investigating low-dose radiation therapy (LDRT) for osteoarthritis are

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summarized in Table 1.[6-10] Of note, although there is substantial retrospective and single-arm data supportive of treatment, there have also been small randomized double-blinded sham-controlled trials that have shown no benefit to low-dose radiation.[6,7] The sham-controlled studies have been criticized for small patient numbers, inadequate treatment delivery, and unrealistic endpoints for patients with severe, chronic pain.[1]

The IMMO-LDRT01 clinical trial completed in Germany is evaluating the immunophenotype of peripheral blood from 250 patients undergoing LDRT using a standard protocol.[8] Patients undergo radiation therapy with 0.5 Gy × 6 fractions delivered at least 48 hours apart. Radiation therapy was delivered using 180 kV x-rays and treatment could be repeated at 3 months after delivery if patients were not subjectively satisfied with their pain relief. An interim analysis of 125 patient has been published.[8] The analysis demonstrated on average significant pain relief from 6.5 to 3.8 on visual analog pain scale after 2 rounds of irradiation. Patients reported significantly reduced morning stiffness. Additionally, peripheral blood analysis demonstrated an overall anti-inflammatory picture: a significant decrease in the number of peripheral lymphocytes, B cells, and plasmacytoid dendritic cells.[8]

Considerations for Patient Selection

Generally, conservative treatment with exercise and/or physical therapy with or without NSAIDs are recommended before considering other treatments. Although radiation associated malignancy is thought to occur as a stochastic effect with no zero risk threshold, there has never been a reported case after LDRT for osteoarthritis in the literature or for the dose equivalent to 2 courses of LDRT. Risk of a radiation-induced malignancy likely varies by age, dose delivered, volume irradiated, comorbid conditions, and time to incidence, and therefore common practice is to limit the use of LDRT to adult patients of more advanced age, especially in cases where visceral organs may receive therapeutic dose. While the German Society of Radiation Oncology guidelines recommend LDRT for anyone aged 40 years or older, the median age of patients in the study by Rühle et al. retrospective study was 76 years.[9]

Considerations for Joint Selection

In patients presenting with osteoarthritis affecting multiple joints, we prioritize treatment based on the joint that has the greatest impact on quality of life. There is variability in our collective practices as to whether the vertebral column is treated. As well, most practices do not typically treat more than 3 sites at a time. After LDRT to the highest priority joint, patients undergo follow-up evaluations at 3-month intervals to assess treatment response. Subsequent treatment for the next highest priority joint is determined based on this reassessment. This approach addresses practical constraints related to patient time on the treatment table, as treating multiple joints in a single session can be physically taxing and result in poor patient experience. Additionally, this strategy ensures that treatment availability for cancer patients is not compromised by the scheduling of LDRT for benign conditions.

Table 1 Selected clinical evidence

Study	No. of patients	Anatomic site	Radiation dose	Outcome
Rühle et al,[9] 2021	970; retrospective	Multiple sites	0.5 Gy × 6 or 1 Gy × 6	Pain reduction in about 2/3 of treated sites
Alvarez et al,[11] 2022	100; prospective	Hand	0.5-1 Gy every other day × 6; total 3-6 Gy	Reduction in pain at 3, 6, and 12 mo; 63/100 underwent retreatment
Mahler et al,[6] 2019	55 (27 LDRT, 28 sham)	Knee	1 Gy × 6 over 2 weeks; total 6 Gy	No substantial effect
Minten et al,[7] 2018	56 (28 LDRT, 28 sham)	Hand	1 Gy × 6 over 2 weeks; total 6 Gy	No substantial effect
Niewald et al,[12] 2022	133 patients/244 joints (LDRT vs very low-dose RT)	64 knees and 172 hands	0.5 Gy × 6, twice weekly (vs 0.05 Gy × 6, twice weekly)	LDRT

Abbreviations: LDRT = low-dose radiation therapy; RT = radiation therapy.

Table 2 Treatment recommendations

Treatment site	Technical consideration	Positioning of patient
Hands	May or may not consider blocking the nail beds; treat entire hand; use bolus	Prone with hands over head or supine with hand on side with arm akimbo; Aquaplast for hand immobilization
Feet	May or may not block nail beds; treat entire foot; can consider using bolus over dorsal surface	Supine, knee flexed, may consider Aquaplast for foot and ankle immobilization if patient needs assistance holding still; alternately, may use a Vaclock setup in frog leg position to allow for more beam angles
Shoulders	Block lung	Supine
Hip	Treat entire joint space	Supine
Knees	Include entire joint, at least 2.5 cm medial and lateral margins	Supine
Spine	Include level above and below (at minimum)	Supine, arms at sides

Treatment Recommendations

Table 2 reports general treatment recommendations for the treatment of osteoarthritis. Our practice is to treat with 0.5 Gy per fraction, 2 to 3 treatments per week, for a total of 3 Gy. Treatment planning is relatively straightforward, using opposed beams (typically anterior to posterior/posterior to anterior (AP/PA)) and 2-dimensional complex isodose technique.

Example fields

Figures 1-6 show examples of treatment fields for treatment of osteoarthritis of the hand (Fig. 1a, b), knee (Fig. 2; opposing field not shown), hip (Fig. 3; opposing field not shown), shoulder (Fig. 4; opposing field not shown), wrist (Fig. 5; opposing field not shown), and ankle and foot (Fig. 6; opposing field not shown). These radiation field sizes may seem large for radiation oncologists who are

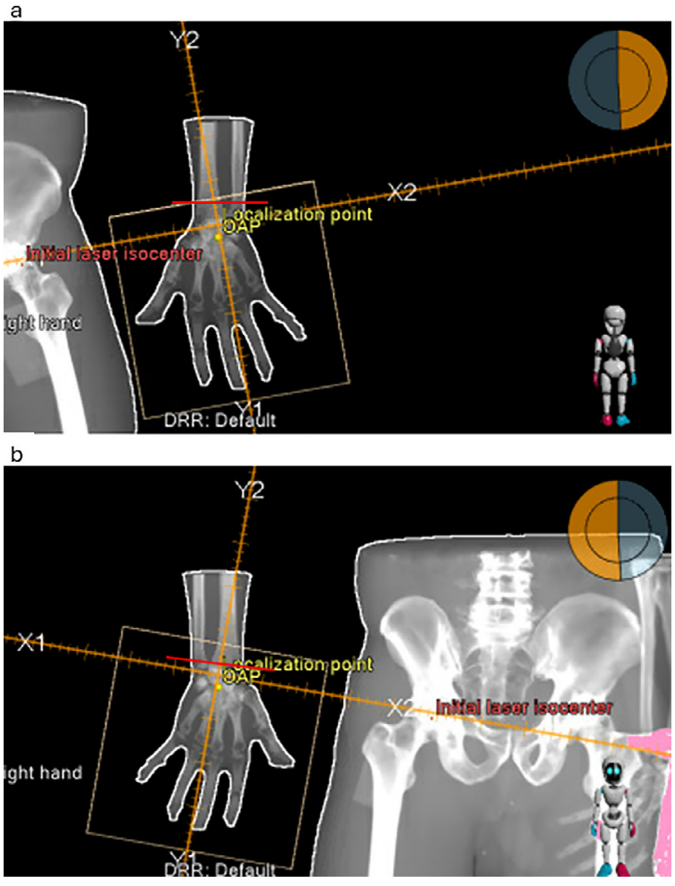

Figure 1 (a, b) Hand (no nail blocking).

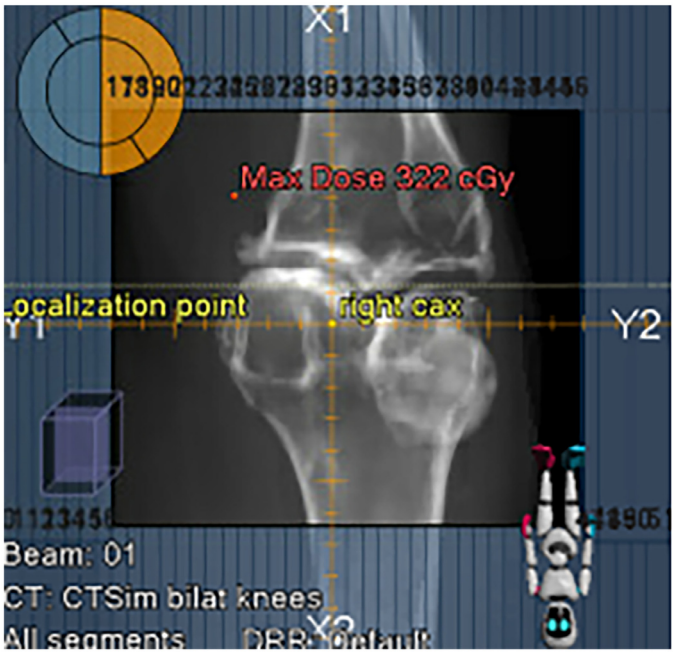

Figure 2 Knee.

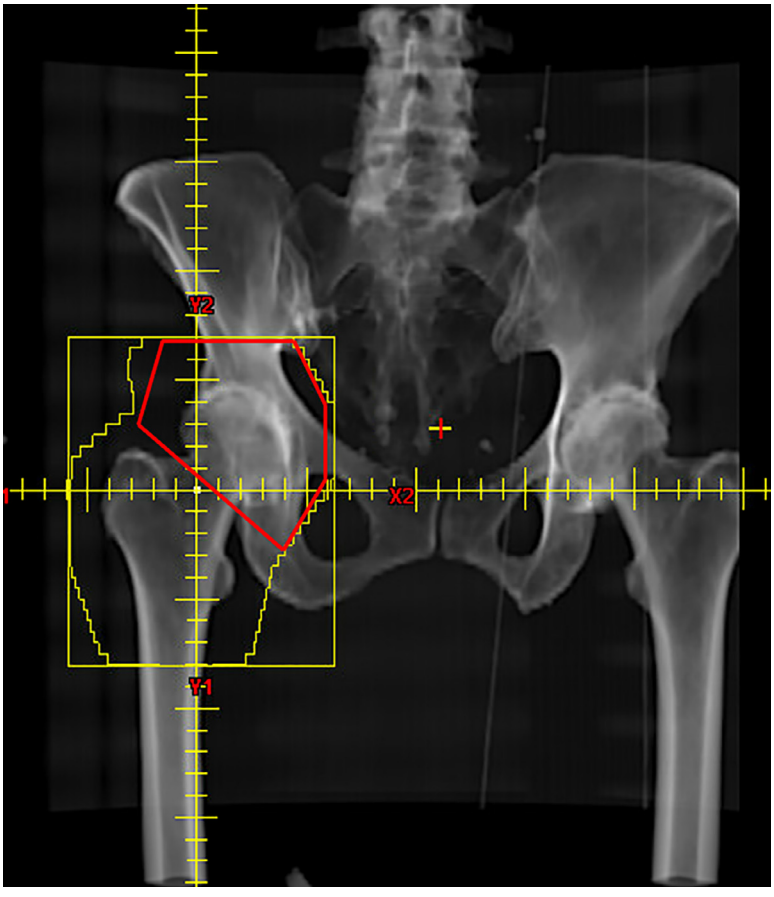

Figure 3 Hip.

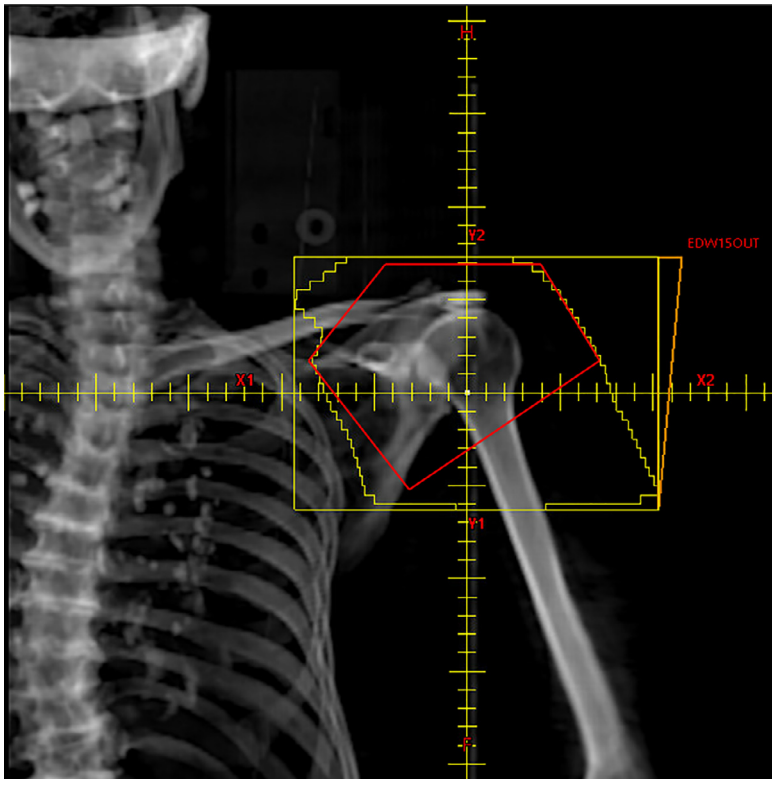

Figure 4 Shoulder.

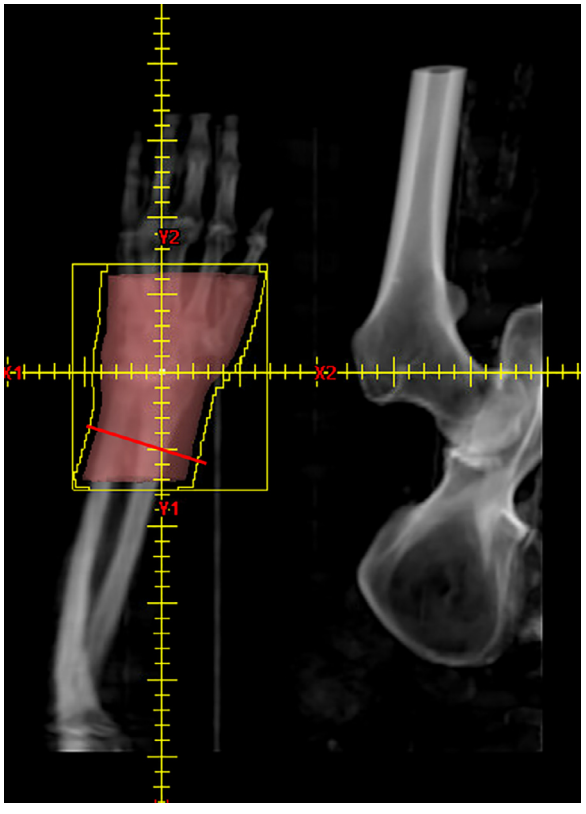

Figure 5 Wrist.

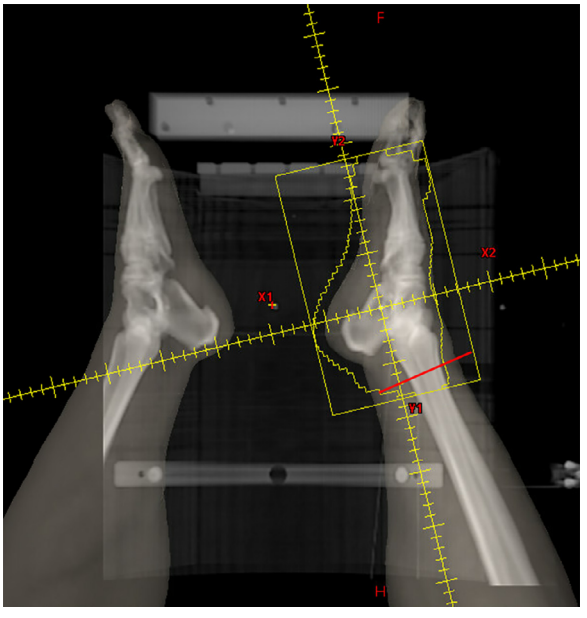

Figure 6 Ankle and feet.

used to treating only joint spaces for heterotopic ossification or limiting normal tissue volume when treating malignant disease. There may be acceptable variability in field sizes among practitioners. Smaller fields that encompass the joint space plus a margin of 2.0 to 3.0 cm are also reasonable. These smaller fields are delineated with a red line in the figures. However, the origin of pain from osteoarthritis involves not only inflammation to the joint space itself but also the joint capsule, joint ligaments, and tendons inserting or originating around the joint. We hypothesize that larger field sizes (within reason) are more likely to reduce pain and inflammation, although there are limited data in the literature.

Moreover, our fields are consistent in size with fields from a recent review of the literature.[1] One study of radiation therapy for thumb carpometacarpal osteoarthritis did show improved symptom relief with larger field sizes that extended beyond the joint space.[10] Therefore, we believe that the hypothesized greater likelihood of pain relief with larger fields outweigh the minimal to absent side effects from LDRT.

Considerations for Assessment of Treatment Response and Retreatment

Retreatment is common and technically feasible after LDRT. For this reason, we recommend not immediately discarding custom treatment immobilization devices. We recommend waiting at least 3 months to assess full treatment effect of the first course of radiation. If patients are still experiencing significant pain and discomfort, we believe a single course of retreatment is reasonable. In a retrospective series of 217 joints treated, 21% were retreated owing to no reported response to initial treatment, 42% for partial response, and 37% owing to recurrent pain.[13] Although there are some authors who mention a third or fourth course of radiation for osteoarthritis,[10,13] we generally do not treat a joint more than twice. Retreatment doses in our practice are the same as initial treatment (0.5 Gy, given twice a week, for a total of 3 Gy).

Disclosures

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