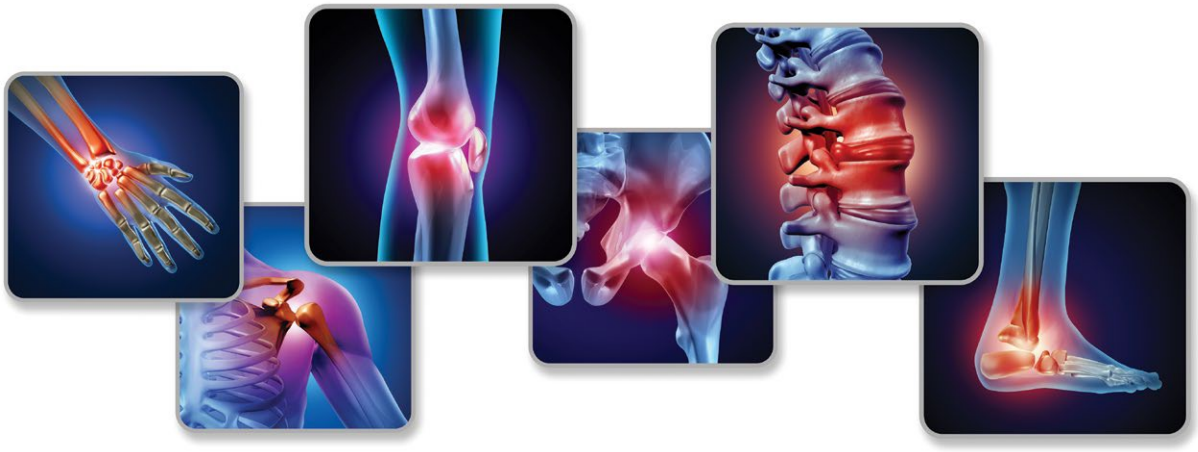


LOW DOSE RADIOTHERAPY TREATMENTS FOR OSTEOARTHRITIS

BY AUSTIN KIRSCHNER, MD, PHD, AND AUSTIN DOVE, MD

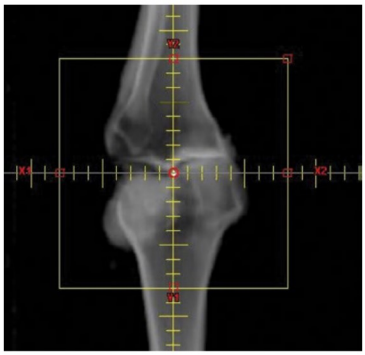
LOW DOSE RADIATION THERAPY (LDRT) has been employed for over a century to alleviate pain and improve mobility in patients with osteoarthritis (OA). Since its first documented use in 1898, LDRT for OA has been a well-accepted and utilized treatment in many countries, such as Germany where several tens of thousands of patients are treated each year.[1] In the U.S., the use of LDRT for OA has declined over the past few decades, but recently has had reemerging interest.

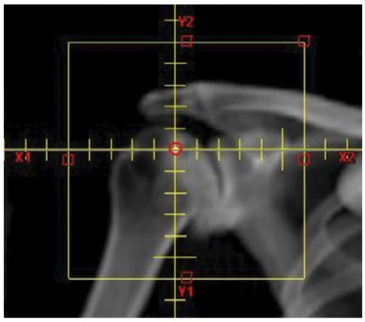
While OA is considered a "benign" disease, more than 32 million Americans suffer from it and experience considerable morbidity and associated mortality from the condition. OA is the most common type of arthritis, which results from the chronic degeneration of cartilage between bones in the joint resulting in damage to articular surfaces, bones, ligaments and surrounding structural components. OA is a clinical diagnosis for persistent usage-related joint pain, typically in patients with age greater than 45 years and morning stiffness lasting less than 30 minutes.[1] The pathophysiology of OA is complex with multiple inflammatory pathways interacting to increase pro-inflammatory cytokines and recruitment of proteases, which result in joint damage. The radiobiologic effect of LDRT has been shown by multiple preclinical studies to modulate inflammatory pathways and cellular components to reduce pain and joint stiffness. These pathways include modulation of macrophages to anti-inflammatory M2 phenotype, reduction in the production of nitric oxide and inflammatory cytokines, and decreased transmigration of pro-inflammatory cells into the extracellular space.[1]

Multiple retrospective and prospective observational studies have shown significant improvement in both pain and mobility in OA patients treated with LDRT. A recently published review paper highlights numerous studies published on the benefit of LDRT.[1] Notable studies for OA treated with LDRT include a retrospective analysis of almost 1,000 patients with 65% having improvement in pain symptoms and a prospective study of 100 hand OA patients with 94% having pain improvement. However, efficacy of LDRT in OA has been questioned by two small randomized clinical trials that have been criticized for low patient numbers with possible underpowering and no option for reirradiation for poor responders. Nevertheless, there remains no randomized evidence for LDRT over sham RT. A large multi-institutional randomized trial of sham versus LDRT is ongoing in South Korea with anticipated completion date in 2025.[2]

Continued on following page

In clinical practice, it is crucial to correctly identify patients with OA who are most likely to benefit from LDRT treatment. Patients should have a formal diagnosis of OA before considering LDRT evaluation. Other potential causes with similar presentations should be ruled out before establishing a diagnosis of OA, such as rheumatoid arthritis, psoriatic arthritis, crystalline arthritis or avascular necrosis. Educating potential referring providers about LDRT for OA through outreach programs helps establish appropriate referrals from primary care providers, rheumatology, sports medicine, orthopedic surgery, interventional anesthesiologists and others. Additionally, many patients seen in radiation oncology clinics for other reasons may have OA and could be considered for LDRT.





During initial patient evaluations, understanding the duration and severity of symptoms as well as other attempted interventions can help determine the likely benefit from LDRT. Patients with a symptom history greater than five years or with extensive prior treatment history are less likely to benefit from LDRT. An X-ray evaluation of the affected joint can determine severity of OA on the Kellgren and Lawrence classification (grade 0-4).[3] Severe OA (grade 4) is less likely to benefit from LDRT. Consideration of secondary malignancy (SM) risk should be evaluated on an individual basis, with the general recommendation of limiting offering LDRT to patients whose age is 50 years and older. However, there has not been a reported case of secondary malignancy attributed to LDRT for OA, and the risk of SM for extremity LDRT is estimated to be equivalent to the risk associated with a CT of the abdomen/pelvis.[4] LDRT has minimal risk of skin erythema given low dose used. No evidence suggests LDRT could negatively affect future ability to undergo joint replacement, if needed in the future.[1]

Regarding simulation, our institutional practice depends on the joint to be treated. A CT simulation with appropriate immobilization devices is reasonable for reproducibility, although with wider-open field design for LDRT the extreme rigor of setup can be relaxed. The recommended dose for LDRT is 3 Gy in 6 fractions (0.5 Gy per fraction), each treatment given

Continued on next page

A PATIENT'S PERSPECTIVE

AFTER SUFFERING FROM OSTEOARTHRITIS for years, Philip Vicari, 85 years of age, had tried everything short of joint replacement to improve his condition. Despite daily use of Tylenol and Tramadol, his Visual Analogue Pain Score (VAS) remained an average of eight out of 10. After undergoing radiotherapy for an unrelated condition, Mr. Vicari became aware of low dose radiotherapy for OA. Within a few weeks after the treatment, he noticed significant improvement in both his pain and mobility.

"I began to see little things in everyday life improve — things you wouldn't think about until you can do them. After treatment, I had significantly more mobility than before. For example, I have long hair that I have to put in a bun to keep out of my face. Prior to treatment, I couldn't lift my arms up so I would have my wife help. Now, I can do it myself again."

When asked about the procedure, he states, "The actual procedure is very simple. You get on the treatment table and lay there. You don't feel anything, no discomfort." Following treatment, he continues to stay active. "I can walk further without pain. I take less Tramadol now. I'm currently redoing my kitchen. I'm able to do much more than I could before." When asked if he would recommend the treatment, his response was simple: "I would certainly encourage others. You have nothing to lose. [You] definitely come away with more positives than before."

on non-consecutive days two to three times per week. Prior to LDRT for OA, we recommend documentation of a visual analogue pain score (VAS) to determine severity of pain. Following treatment, we recommend obtaining additional VAS as well as a Von Pannewitz Score at six weeks to determine adequate response. If less than desired response is achieved, reirradiation could be considered with the same dose/fractionation schedule, which provides response in about 50% of patients who do not initially respond to treatment.[5] In summary, LDRT is a standard-of-care treatment for OA that provides good efficacy and minimal risks and should be offered in the setting of multidisciplinary care.

Austin Kirschner, MD, PhD, is an associate professor in the Department of Radiation Oncology at Vanderbilt University Medical Center. He is a specialist in radiotherapy for GU malignancies, lymphomas and benign disorders.
@AKRadDoc

Austin Dove, MD, is one of the radiation oncology chief residents at Vanderbilt University Medical Center and will be joining Tennessee Oncology in Chattanooga, Tennessee, following completion of training.
@A_Dove5

REFERENCES

1. Dove APH, Cmelak A, Darrow K, et al. The use of low-dose radiation therapy in osteoarthritis: A review. *Int J Radiat Oncol Biol Phys*. 2022; 114(2):203-220.
2. Kim BH, Shin K, Kim MJ, et al. Low-dose radiation therapy for patients with knee osteoarthritis (LoRD-KNeA): A protocol for a sham-controlled randomized trial. *BMJ Open*. 2023;13(2).
3. Kohn MD, Sassoon AA, Fernando ND. Classifications in brief: Kellgren-Lawrence Classification of Osteoarthritis. *Clin Orthop Relat Res*. 2016;474(8):1886-93.
4. Jansen JT, Broerse JJ, Zoetelief J, et al. Estimation of the carcinogenic risk of radiotherapy of benign diseases from shoulder to heel. *Radiother Oncol*. 2005;76(3):270-7.
5. Ott OJ, Hertel S, Gaipl US, et al. Benign painful elbow syndrome. *Strahlentherapie und Onkologie*. 2012;188(10):873-877.

A 'Beacon of Hope' FOR OSTEOARTHRITIS

The Leonard Ferguson Cancer Center Experience

BY BOBBY KONERU, MD, AND RICHARD SHAFFER, MBBS

LOW DOSE RADIOTHERAPY (LDRT) is given for osteoarthritis, tendinopathy and bursitis due to its anti-inflammatory and pain relieving properties. It typically consists of single fraction sizes of 0.5-1.0 Gy and total doses of 3-12 Gy.

It is mainly used in Central Europe, particularly in Germany. Guidelines have been developed by the German Benign Radiotherapy Group,[1] outlining optimal dosage and treatment protocols for osteoarthritis with LDRT. However, in North America, LDRT remains underutilized. A recent review article in the Red Journal by Dove et al.[2] (co-author of previous article on page 23) about radiotherapy for osteoarthritis has prompted significant interest in developing this service throughout the United States.

The Leonard Ferguson Cancer Center experience

Motivated by these findings, discussions with FHN Memorial Hospital administration resulted in the establishment of a program within the Leonard Ferguson Cancer Center for LDRT, yielding remarkable symptomatic responses in the initial patients. For instance, a 68-year-old artist with hand osteoarthritis regained the ability to paint, and another patient who was painfully limping for years, was now walking pain-free after six LDRT sessions.

Encouraged by the success of our early cases, we initiated marketing efforts through print and radio advertisements, leading to a substantial increase in patient volumes. We discussed our program with local orthopedic surgeons, rheumatologists, and primary care physicians, although most of our patients were self-referred. Since 2023, our LDRT program has treated over 75 new osteoarthritis patients, addressing more than 125 joints, evolving from a curiosity-driven initiative into one of the larger LDRT programs in the country.

Effectiveness of LDRT for OA

When evaluating the effectiveness of LDRT for osteoarthritis, we have found an average pain reduction from 7/10 to 3/10 (on a numerical rating scale of 0 to 10). Additionally, patients have benefited from improvements in range of motion, stiffness,

Continued on following page

Figure 1: Proportion of patients with a good pain response to radiotherapy for osteoarthritis

Site	Response Rate (weighted average)	Studies	Patients
Hands	68%	7	994
Foot and Ankle	75%	2	262
Knee	79%	33	5116
Hip	64%	23	914
Total	75%	65	7286

functional abilities, and quality of life. Various baseline factors such as symptom duration, radiological stage, age, gender, inflammatory status, radiotherapy dose parameters, total dose, timing, and number of phases are known to influence the treatment response.

Figure 1 (R Shaffer, unpublished) shows data from multiple trials, illustrating pain responses at different body sites. While the average response rate ranges from 64% to 79%, it is crucial to acknowledge the high uncertainty associated with these figures. The variability in responses may be attributed to prognostic characteristics within different patient populations studied at each anatomical site, and caution is warranted as variations may be artefactual.

The place of radiotherapy in the osteoarthritis treatment pathway

Radiotherapy is a valuable intervention in the landscape of osteoarthritis treatment, particularly in addressing the substantial gap that exists between conservative measures and surgical options (Figure 2). Recent research highlights the limited impact of medications, underscoring the need for alternative solutions. With an overall success rate of 75% in reducing pain, radiotherapy becomes a pivotal player in filling this treatment void for patients grappling with pain and functional impairment.

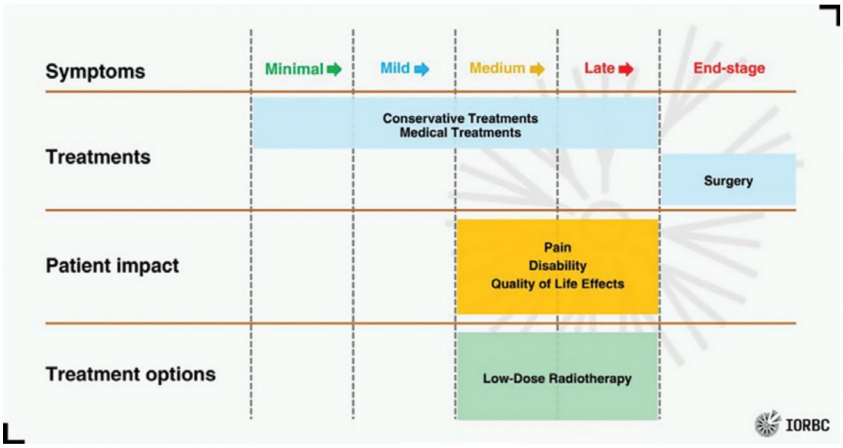
The identified gap between conservative measures and surgical interventions leaves a considerable population dealing with the impact of osteoarthritis on their daily lives. Importantly, at our clinic, we offer education in self-care, for instance, exercises and weight loss, as a crucial aspect of their overall management which is vital for all patients with this disabling condition. For individuals for whom surgery is not an option or who face prolonged waiting times due to extensive surgical queues or disease eligibility criteria, radiotherapy emerges as a viable and impactful alternative.

Radiotherapy serves as a beacon of hope for these patients, offering the prospect of pain relief, enhanced functionality, and the potential to either postpone or altogether avoid surgical procedures. We have seen this have a transformative effect on many of our patients' overall quality of life.

Bobby Koneru, MD, is a radiation oncologist at the Leonard Ferguson Cancer Center in Freeport, Illinois, and adjunct Assistant Professor at Loyola University Stritch School of Medicine. He is a board member of the International Organization for Radiotherapy for Benign Conditions (IORBC).

Richard Shaffer, MBBS, is a specialist in radiotherapy for benign conditions and president and founder of the IORBC.

Figure 2 – Radiotherapy's place in the landscape of osteoarthritis treatment



REFERENCES

1. Ott OJ, Niewald M, Weitmann HD, et al. DEGRO guidelines for the radiotherapy of non-malignant disorders. Part II: Painful degenerative skeletal disorders. *Strahlenther Onkol.* 2015;191(1):1-6.
2. Dove APH, Cmelak A, Darrow K, et al. The Use of Low-Dose Radiation Therapy in Osteoarthritis: A Review. *Int J Radiat Oncol Biol Phys.* 2022;114(2):203-220.