# Revisiting Radiotherapy: Low-Dose Radiation Therapy for Refractory Osteoarthritis

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**Abstract:**

Osteoarthritis (OA) is a highly prevalent musculoskeletal disorder causing chronic pain and disability. As many patients fail conservative therapy or are unsuitable for surgery, effective non-invasive options are needed. Low-dose radiation therapy (LDRT) has re-emerged as a treatment targeting OA-related inflammation and providing symptom relief. This narrative review summarises the epidemiology and pathophysiology of OA, the radiobiological rationale for LDRT, patient selection criteria, clinical outcomes, and safety considerations. Evidence from randomised controlled trials, observational studies, and international guidelines — particularly German Society for Radiation Oncology (DEGRO) — was also reviewed. At low doses (0.5–1.0 Gy per fraction; total 3 Gy), LDRT exerts anti-inflammatory effects that translate into significant pain relief and functional improvement in OA of affected joints. Evidence from randomised and observational studies showed good tolerance, mild to no toxicity, and an extremely low theoretical risk of secondary malignancy. DEGRO guidelines endorse LDRT as an adjunctive treatment for selected patients with painful OA who have failed conservative therapy or are unsuitable for surgery. LDRT is a safe, evidence-based, non-invasive option that provides effective pain relief and functional improvement in selected patients with osteoarthritis. By addressing chronic joint inflammation, it offers a practical therapeutic “middle ground” between conservative management and surgery. Further research is warranted to optimise patient selection, timing, and predictive biomarkers of response.

**Key words:** Osteoarthritis, Low-Dose Radiation Therapy, Pain Relief.

## Introduction

Osteoarthritis (OA) affects nearly 595 million people globally and is a leading cause of pain and disability. By 2050, OA prevalence is projected to increase by 74.9% for the knee, 48.6% for the hand, 78.6% for the hips, and 95.1% for other joints.[1] In India, symptomatic OA cases rose 2.66-fold, from 23.46 million in 1990 to 62.3 million in 2019.[2]

OA is no longer viewed as a simple “wear-and-tear” disorder but as a disease of joint failure, involving cartilage degeneration and chronic low-grade inflammation.[3] OA risk increases with age and is influenced by female sex, obesity, prior injury, and genetic factors. While management ranges from lifestyle measures and pharmacotherapy to surgery, a subset of patients remains refractory to conservative treatment, yet unsuitable or unwilling for surgical intervention. For such patients, low-dose radiation therapy (LDRT) offers a non-invasive, effective therapeutic option, addressing the inflammatory component of OA.[3]

## Historical Perspective

The use of radiation for non-malignant diseases dates back nearly a century. Following the discovery of X-rays by Wilhelm Conrad Röntgen in 1895 and radioactivity by Henri Becquerel and Marie Curie, radiotherapy was rapidly adopted for a wide range of benign conditions, often without robust evidence or long-term safety data.[4] As early as 1898, X-rays were reported to provide effective pain relief in patients with arthritis.[5] However, growing recognition of the risk of radiation-induced secondary malignancies led to fear and uncertainty, resulting in a gradual global decline in the use of radiotherapy for benign diseases.

## Radiobiological Rationale for LDRT

LDRT exerts anti-inflammatory and immunomodulatory effects that result in pain relief (Figure 1). At doses used for OA (0.3–1.0 Gy),[6] LDRT downregulates pro-inflammatory cytokines (tumour necrosis factor-α [TNF-α], interleukin-1β [IL-1β], interleukin-6 [IL-6]), upregulates anti-inflammatory mediators (transforming growth factor-β [TGF-β]), reduces endothelial activation and leukocyte recruitment, and promotes macrophage polarisation towards an anti-inflammatory (M2) phenotype.[7] These combined effects suppress chronic synovial inflammation and nociceptive signalling, leading to improved pain and joint function without significant structural damage.[8]

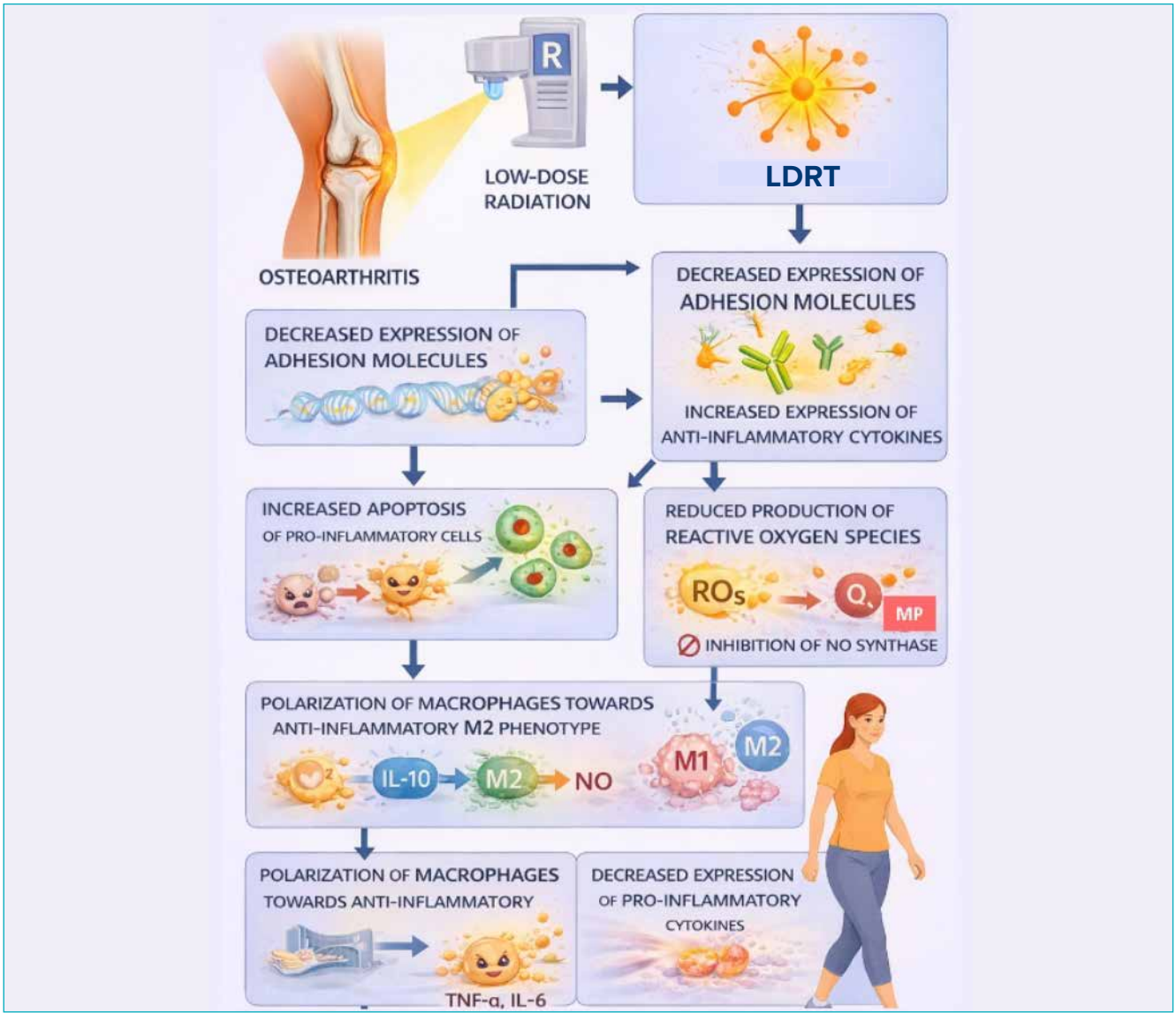


**Figure 1:** Radiobiological mechanisms of the anti-inflammatory effect of low-dose radiation therapy. **Abbreviations:** DNA: Deoxyribonucleic Acid; IL-6: Interleukin-6; IL-10: Interleukin-10; LDRT: Low-Dose Radiation Therapy; M1: Classically Activated Macrophages; M2: Alternatively Activated Macrophages; MP: Metalloproteinases; NO: Nitric Oxide; O4: Tetraoxygen; ROS: Reactive Oxygen Species; TNF-α: Tumour Necrosis Factor-α.

## Indications and Contraindications for LDRT in OA

Appropriate patient selection for LDRT in OA is essential, as it plays a key role in determining the treatment outcomes shown in Table 1.

| Indications | Contraindications |
|---|---|
| Age > 40 years | Spine osteoarthritis |
| Sites - Upper and lower limbs | Active pregnancy |
| Kellgren-Lawrence (KL) stage ≤ 3 | Kellgren-Lawrence stage 4 |
| Pain score of at least ≥ 4 on Visual Analog Scale (VAS) | Active infection of the joint (e.g. septic arthritis) |
| History of chronic pain > 3 months, refractory to conservative line of treatment | Active infection of the affected joint |
| Surgical options contraindicated or opted against by the patient | Active cancer or undergoing cancer treatment |

**Table 1:** Indications and contraindications of low-dose radiation therapy for osteoarthritis.

## Treatment Planning

LDRT planning involves patient consent, computed tomography (CT) simulation with immobilisation, and target volume delineation, with careful shielding of adjacent critical structures (Figures 2, 3A and 3B). Based on clinical studies and international guidelines, the standard dose for OA is 3 Gy in 6 fractions (0.5 Gy each) over 2 weeks.[9] Treatment response is assessed at 6–8 weeks using the Visual Analogue Scale (VAS), Numeric Rating Scale (NRS), or Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores.[10,11] In cases of partial or no response, a second LDRT course may be delivered 8–12 weeks after the initial treatment.[12,13]

## Risk-Benefit Profile

### Benefits of LDRT for OA:

- Reduction in pain, improvement in joint function and improved quality of life
- Non-invasive treatment option
- Minimal to no acute toxicity and good overall tolerance
- Potential benefit in patients with refractory OA who have failed conservative therapies
- Long-term effect

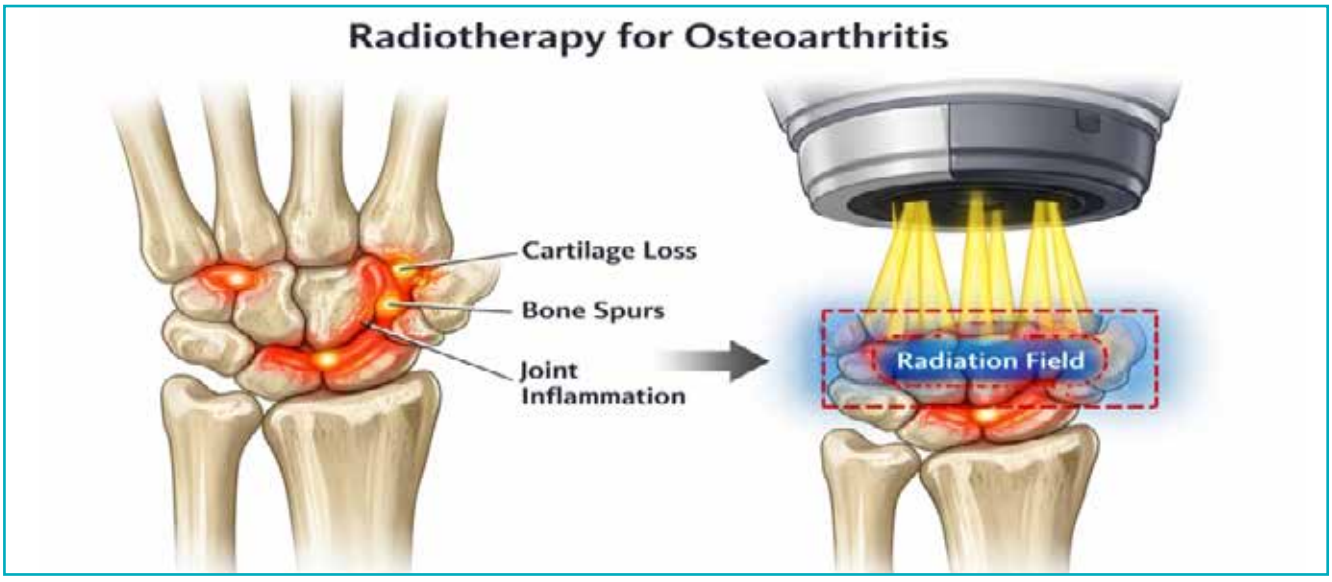


**Figure 2:** Graphic representation of a wrist joint showing changes of osteoarthritis. Only the affected area is targeted as per guidelines and treated with low-dose radiation therapy.

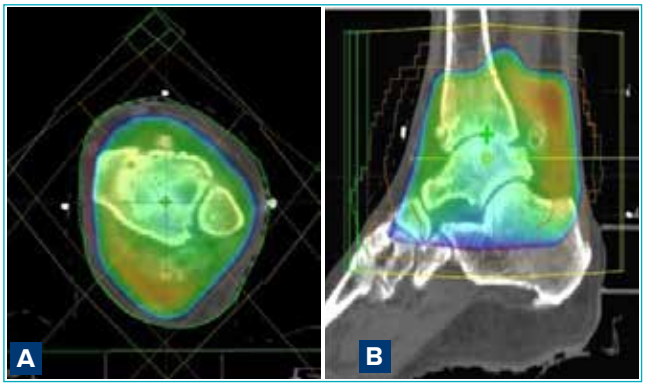


**Figure 3A and B:** Computed tomography-based target delineation and dose distribution for ankle osteoarthritis.

### Risks of LDRT for OA:

- Acute (early) toxicities (< 1%). A small but non-negligible theoretical risk of radiation-induced malignancy has been described; however, contemporary evidence suggests this risk is extremely low when low-dose regimens and appropriate patient selection are employed.[13]

## LDRT for OA in Randomised Trials and Guidelines

Some randomised trials exist in the literature, highlighting the promising role of LDRT for OA, as shown in Table 2.

| Trial | Patients | Randomised arms | Results |
|---|---|---|---|
| Kim *et al.*[11] | 114 patients with hip or knee OA | 3.0 Gy in 0.5 Gy treatments versus 0.3 Gy in 0.05 Gy treatments versus sham | Significant pain relief at 4 months |
| Niewald *et al.*[14] | 229 patients with hand/ finger or knee OA | 3.0 Gy in 0.5 Gy given bi-weekly versus 0.3 Gy in 0.05 Gy given bi-weekly | Favourable pain relief in both arms |
| Fazilat-Panah *et al.*[15] | 60 patients with knee OA | 3.0 Gy in 0.5 Gy treatments versus sham | VAS pain score, Lysholm scale, PS, and analgesic consumption were improved from the 1st month to the end of assessment |

**Table 2:** Randomised trials highlighting the successful role of low-dose radiation therapy in osteoarthritis.
**Abbreviations:** Gy: Gray; OA: Osteoarthritis; PS: Pain Score; VAS: Visual Analogue Scale.

Few case series and observational studies are mentioned in Table 3.

| Trials | Study design | Patients | Follow-up (months) | Response |
|---|---|---|---|---|
| Koneru *et al.*[16] | Retrospective | 69 | 3 and 12 | 12 m = 80% |
| Alvarez *et al.*[17] | Prospective | 100 | 10.5 (median) | 3–12 m = 70%–94% |
| Donabauer *et al.*[18] | Retrospective | 483 | 3 and 6 | 3 m = 70%<br>6 m = 70% |

**Table 3:** Case series and observational studies highlighting the role of low-dose radiation therapy in osteoarthritis.

### DEGRO guidelines:

These comprehensive guidelines by the German Society for Radiation Oncology support the use of LDRT as a non-invasive, adjunctive option for painful OA, and are summarised below (Table 4).[9]

| Category | Recommendation |
|---|---|
| Indications | Painful knee OA (Kellgren stage 2–3): recommended when conservative treatment fails or is contraindicated |
| | Painful hip OA |
| | OA of small joints (e.g. hand, foot) |
| Patient selection | LDRT is typically considered only after conservative therapies fail (e.g., medications, physical therapy) |
| | Patients > 40 years |
| Dose and fractionation | - Single fraction dose: 0.5 Gy |
| | - Total dose per series: 3.0 Gy |
| | - Schedule: 2–3 fractions per week |
| Target volume/ technique | Entire affected joint, including adjacent bone, synovium, muscles/connective tissue |
| Response assessment | Evaluate clinical benefit with pain scores/functional scales at the end of radiation and then at 3, 6, 12 months post-therapy and so on (as per department protocol) |
| Safety/radiation considerations | Mild to no acute toxicity<br><br>The risk of secondary malignancy is very rare |
| General recommendation | LDRT can be performed for selected patients of OA if, after other conservative treatments have failed or are not suitable, and if surgery is contraindicated |

**Table 4:** Summary of the German Society for Radiation Oncology (DEGRO) guidelines for use of LDRT in OA.
**Abbreviations:** LDRT: Low-Dose Radiation Therapy; Gy: Gray; OA: Osteoarthritis.

A summary of common queries and their evidence-based responses are mentioned in Table 5.

## Future Directions

Given the rising global burden of OA, LDRT offers a valuable non-surgical option for pain relief, supported by four randomised trials and multiple case series showing significant benefits. Future research should refine timing, predictive inflammatory markers, concurrent therapies, and site-specific efficacy.

| Query | What does the evidence say? |
|---|---|
| Issue of secondary malignancies with the use of LDRT? | Based on current evidence and long-standing clinical experience, the risk of secondary malignancy from LDRT in osteoarthritis is theoretical and extremely low, and when appropriately delivered, LDRT is a safe and effective option for pain relief |
| What are the acute and late side effects of LDRT? | Available evidence indicates minimal to no acute or late toxicity with LDRT, with only rare, mild, and transient skin erythema reported, and no significant long-term risks such as secondary malignancy or joint damage |
| Will LDRT replace surgery for knee OA? | No, LDRT does not replace surgery; it is a complementary, evidence-based non-surgical therapy that provides symptomatic relief and may delay surgery in selected patients |
| Is surgery possible if LDRT has been given previously? | Yes, surgery after LDRT is feasible. The low dose (3 Gy) targets inflammation without harming healthy tissue, and post-RT fibrosis or negative surgical outcomes have not been reported |

**Table 5:** Queries and concerns about LDRT.
**Abbreviations:** LDRT: Low-Dose Radiation Therapy; Gy: Gray; OA: Osteoarthritis; RT: Radiotherapy.

### Conclusion

As evidence continues to evolve, LDRT could emerge as a practical "middle-ground" treatment for osteoarthritis, offering an effective bridge between conservative management and surgical intervention.

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