Low-dose radiotherapy for osteoarthritis:
A practical adjunct for general practice

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Background
Osteoarthritis (OA) is a leading cause of pain and disability, and many patients have persistent symptoms despite first-line therapies. Low-dose radiotherapy (LDRT) has re-emerged as a potential anti-inflammatory treatment for OA, with widespread use in parts of Europe but limited awareness in Australia.

Objective
The aim of this article is to review current evidence on LDRT for OA and provide general practitioners (GPs) with practical guidance on patient selection, referral pathways and integration of LDRT into OA management.

Discussion
Recent studies suggest LDRT can yield moderate- to long-term pain relief and functional improvement in OA, especially in knee OA. Overall, approximately 60–70% of patients may experience symptomatic improvement, as supported by two reported randomised controlled trials. Ideal LDRT candidates are those with chronic refractory OA who are unsuitable for, or wish to postpone, surgery. While GPs should continue standard OA management, LDRT may offer select patients an additional non-surgical management option with minimal side effects.

OSTEOARTHRITIS (OA) is the most common degenerative joint disease and a major cause of chronic pain and disability in older adults. Current guidelines from The Royal Australian College of General Practitioners (RACGP) for knee and hip OA emphasise first-line management with patient education, exercise, weight loss and analgesics.[1] Options such as intra-articular injections or joint replacement surgery can be considered for patients when first-line management is unsuccessful. However, for patients who are not suitable surgical candidates, either through comorbidity or preference, there is renewed interest in low-dose radiotherapy (LDRT) as a potential alternative therapy for OA pain.

LDRT for OA typically consists of multiple low-dose radiation fractions (0.5–1.0 Gy per fraction to a total dose of 3–6 Gy) delivered to the affected joint, with the proposed mechanism being modulation of inflammatory pathways. More than 80% of radiotherapy centres in Germany and Eastern Europe[2] use LDRT for OA, a practice shaped by decades of clinical experience and observational studies, though historically limited by a lack of high-level evidence until recently. This contrasts with countries such as Australia and the US, where LDRT for OA remains relatively underutilised.[3]

This article aims to: (1) summarise the current clinical evidence on LDRT for OA including efficacy, safety and patient outcomes; and (2) provide general practitioners (GPs) with pragmatic advice on identifying suitable candidates and referring patients for LDRT as part of a multidisciplinary approach to OA management. While the interested reader can refer to one of several more comprehensive reviews,[4,5] the goal of this paper is to provide an update on recent randomised trials, a brief summary of previous data and a practical guide for GPs to consider and counsel suitable patients on the role of LDRT as a potential adjunct, written from a radiation oncology and GP background.

Clinical evidence for LDRT in OA

Numerous recent studies have evaluated LDRT for OA, generally reporting moderate pain reduction and improved joint function in a majority of patients.[4] A 2016 systematic review of seven studies noted that while many patients experienced symptomatic benefit, the data quality was low, and a placebo effect could not be excluded.[6] Recognising this evidence gap, randomised controlled trials (RCTs) have been conducted to explore LDRT, of which three key trials are outlined below (refer to Table 1).

An Iranian RCT involved 60 patients with knee OA and persistent pain despite standard care. The LDRT group received

Table 1. Key randomised trials of LDRT in OA

Trial (year)	Fazilat-Panah et al (2025)	Makarova et al (2023)	Van den Ende et al (2020)
Location	Iran	Russia	Netherlands (multicentre) – parallel RCTs
Treatment site	Knee	Knee	Hand (DIP/PIP joints) Knee
Sample size	60 patients	292 patients	55 patients (knee) 56 patients (hand)
Radiation protocol	**3 Gy** total (0.5 Gy × 6 fractions)	**4.5 Gy** total (0.45 Gy × 10 fractions)	**6 Gy** total (1 Gy × 6 fractions)
Selection and OA severity	Age ≥65 years Kellgren–Lawrence grade 1–3	Kellgren–Lawrence grade 0–2	Age ≥50 years >50% Kellgren–Lawrence grade ≥2
Control group	Sham radiation + routine care	NSAIDs + SYSADOA (standard care)	Sham radiation
Follow-up duration	6 months	9 years	3 months (primary) 12 months (extended)
Main outcomes	↓ Pain (VAS) and analgesia intake and ↑ function vs sham; no adverse effects	↓ Long-term pain; 50%↓ risk of disability; fewer knee replacements	No significant difference in pain or function (OMERACT-OARSI)
Conclusion	**Positive:** LDRT significantly improved knee OA symptoms with no adverse effects	**Positive:** LDRT + standard care yielded sustained pain relief and halved long-term disability/ surgery risk	**Negative:** No substantial positive effect of LDRT on symptoms and inflammation in patients with hand OA

DIP/PIP, distal/proximal interphalangeal joints; LDRT, low-dose radiotherapy; NSAID; nonsteroidal anti-inflammatory drug; OA, osteoarthritis; OMERACT-OARSI, Outcome Measures in Rheumatology Osteoarthritis Research Society International; RCT, randomised controlled trial; SYSADOA, symptomatic slow-acting drugs for osteoarthritis (eg glucosamine); VAS, Visual Analog Scale.

3 Gy total over six sessions to the knee, while the control group received sham (no radiation) in addition to continued routine care.[7] The LDRT arm showed improved pain scores present by the first month after treatment and persisting through 6 months, as well as improved function. The authors concluded that LDRT appears to be effective for symptom relief in knee OA. Strengths of this trial include minimisation of bias by using double blinding and a sham control arm, appropriate patient selection with early-stage knee OA (majority Kellgren–Lawrence grade 2) and the use of a more modern regimen of 3 Gy. While the selection of patients aged 65 years or greater may be seen to limit generalisability, it highlights the importance of minimising the time-dependent risk of secondary malignancy. The major limitation in this trial was the small sample size, but overall, this trial sets a promising foundation for a well-designed sham-controlled RCT with greater numbers.

A Russian RCT studied 292 patients with knee OA (Kellgren–Lawrence grade 0–2) over a long follow-up of 10 years. Patients were randomised to standard medical therapy with or without adjunct radiotherapy (total 4.5 Gy over 10 sessions).[8] The actuarial disability-free rates at 10 years were 90.2% in the LDRT arm and 79.6% in the control arm. The authors calculated that a quarter of disability cases could be prevented if all patients received LDRT in addition to standard of care. Two factors limiting generalisability were the lack of clear definition of the endpoint 'disability' and the recruitment of a younger population of patients (mean age 37.3 years in the treatment arm). Additionally, this trial was not a sham-controlled trial. However, the analysis of a relatively large sample size over a long duration is a notable strength of this paper and supports LDRT's efficacy and durable benefit in knee OA.

The drive for randomised data arose from the foundation established by decades of non-randomised data supporting the use of LDRT for OA, largely from Germany. Several review papers have previously summarised the data,[4,5] including 12 retrospective studies and two observational studies with level III evidence supporting the benefit of LDRT using different metrics such as the Visual Analog Scale (VAS) or the von Pannewitz score. Acknowledging the heterogeneity of assessment, recorded response rates ranged from 25% to nearly 100%.[5] For example, a large retrospective analysis of 1185 joint sites in 970 patients aged ≥65 years treated with LDRT demonstrated a significant reduction in pain intensity using the numerical rating scale in almost two-thirds of the cohort.[9] Six prospective OA studies with level II evidence reported significant improvements in the numerical rating scale, VAS and von Pannewitz score following LDRT, including one that analysed 100 patients with hand OA. It was found that 94% of patients had a significant improvement in pain using the VAS score at 6 months.[10]

Although no consensus guidelines currently exist in Australia, the German Society of Radiation Oncology (DEGRO) has published evidence-based recommendations for the radiotherapeutic management of benign diseases, including OA.[11] Drawing on the significant body of retrospective and prospective data, as well as newer randomised data, they have made recommendations regarding the use of LDRT in OA. While recommending treatment primarily for patients over the age of 40 years, they assign a recommendation level of C for LDRT to the knee, hip and hands, equating to 'can be performed, if indicated'. The indications include painful OA where surgical interventions are not yet indicated or desired and where conservative therapies are ineffective, not tolerated or contraindicated.

In contrast to the above studies, a pair of Dutch RCTs ran in parallel yielding negative results using LDRT in hand and knee OA.[2,12] As part of these trials, 55 patients with knee OA and 56 patients with hand OA were randomised to LDRT (6 Gy total in six sessions) or sham radiation. The primary outcome for these studies used the Outcome Measures in Rheumatology Osteoarthritis Research Society International (OMERACT-OARSI) responder criteria, which includes pain, function and global assessments. There was no significant difference between the groups at 3 months in primary (composite pain/function improvement) or secondary (pain scores, quality of life [QOL] and ultrasound measures of inflammation) endpoints. While these trials had methodological strengths of reasonable blinding (single) and the use of sham control arms, a notable limitation is the small sample size. These trials were powered for large clinical effects (40% difference in proportion of responders), with resultant wide confidence intervals that may not necessarily exclude the presence of a modest, clinically meaningful analgesic effect. Furthermore, while not a methodological fault, the strong placebo response associated with the use of sham controls in OA has been proposed as a potential confounder that can minimise perceived clinical effect.[13,14] Additional criticisms have focused on inconsistent adherence to the contemporary European standard regimen of 3 Gy delivered in six fractions, with the option of a second course of radiotherapy offered in cases of inadequate pain relief.[15] Furthermore, with almost 50% of the participants having longstanding pain >5 years before radiotherapy, there is a possibility that there was a significant cohort of treatment-refractory patients whose disease had progressed beyond analgesic response to non-operative measures. Finally, there is evidence that the analgesic effect from LDRT can improve over time.[15,16] While the Dutch RCTs report a 12-month analysis, they acknowledge that the trial was not powered for this, and that unmasking at 3 months may have introduced additional bias.

Radiation toxicities

Secondary malignancies

Secondary malignancies are a recognised late complication of radiotherapy, with the associated risk typically justified by the therapeutic imperative of achieving tumour control in the primary malignancy. As such, careful consideration must be applied in the use of radiotherapy for patients without a diagnosis of cancer. Accurately estimating the risk of secondary malignancies is challenging, as available evidence is largely derived from older datasets necessitated by the long latency of onset. These data may overestimate contemporary risk, given the substantial advances in modern radiotherapy techniques. There are multiple factors specific to the use of LDRT in OA that likely mitigate the risk of secondary malignancies. The incidence of radiation-induced secondary malignancies increases with higher dose regimens,[17-19] and inherent to the use of radiotherapy in OA is the radiobiological principle of using a low dose. The relative risk of secondary malignancies is inversely related to age at exposure,[17,20,21] reflected in the DEGRO recommendations to limit LDRT for OA to patients above the age of 40 years.[11] Finally, there are variable tissue-dependent risks of radiation-induced malignancies, and for peripheral joints such as the hand and knee, the risk is felt to be exceedingly low.[11] A retrospective trial compared the rates of breast cancer following LDRT for non-malignant shoulder conditions in a specific geographic cohort, and it found no increased rate when compared with the expected spontaneous incidence for this cohort.[22]

Other toxicities

Acute radiation toxicities from LDRT would be expected to be mild and minimal, as indicated by a review of multiple studies including over 1000 patients, of which only one patient reported mild skin erythema.[4] Non-carcinogenic late radiation toxicities generally follow a predictable dose-threshold model and are labelled 'deterministic' effects. As such, LDRT doses fall well below the expected threshold expected to cause clinically significant toxicities in tissues other than nail changes in the relatively radiosensitive nail beds in hand OA.[12] The RCTs previously discussed, as well as another that randomised between two low-dose regimens and followed up over 12 months, did not identify any other adverse effects attributable to LDRT.[7,12,23] Another consideration is the potential impact of prior LDRT on subsequent surgical procedures; however, current evidence does not demonstrate any adverse association.

Defining ideal candidates for LDRT

A critical role for the GP is to identify which patients with OA might be suitable for referral for LDRT. Drawing from the evidence and expert consensus, ideal candidates for the consideration of LDRT have the following profile:

- Diagnosed OA with significant symptoms: the patient should have radiologically and clinically confirmed OA with moderate-to-severe pain and/or functional impairment. Typically, these patients have chronic OA (symptoms for >3 months) with a substantial impact on their QOL or daily activities (eg shortened walking distance because of pain).
- Inadequate response to standard therapies: LDRT should only be considered after conventional non-surgical treatments have been optimised and found insufficient. Patients should have already engaged in exercise/physiotherapy programs, managed their weight, optimised analgesia and possibly tried steroid injections, as reflected in RAGCP and international guidelines.[1]
- Not an immediate surgical candidate: although surgery remains the standard of care for appropriately selected patients, many face prolonged wait times,

are deemed medically unsuitable or decline operative intervention. For these individuals, therapeutic options beyond conventional analgesia are limited. In such circumstances, LDRT may serve either as a temporising 'bridging' therapy prior to surgery or as an adjunct to established pharmacological and non-pharmacological pain management strategies.

- Mild-to-moderate radiographic severity: in the Russian trial showing excellent outcomes, patients were limited to Kellgren–Lawrence grade ≤2,[8] whereas the negative Dutch trial included many patients with erosive changes,[2] suggesting that LDRT might work best in earlier stages of OA rather than in bone-on-bone end-stage OA.
- No contraindications to radiotherapy: key contraindications are pregnancy (because of risk to the foetus) and active joint or surrounding infection (because of risk of impaired healing). While the risk of secondary malignancy is thought to be very low, as reflected in the DEGRO guidelines,[11] LDRT is more appropriate for the older population to further minimise risk. Overall, for most older adults with OA, there is no prohibitive contraindication to LDRT.

Practical considerations

Familiarity with the process for referral, treatment and follow-up is essential for facilitating LDRT as a management option for appropriate patients (refer to Figure 1).

As outlined in the literature, LDRT should be regarded as an adjunctive option for carefully selected patients rather than a standard therapy. Its integration can be conceptualised within a stepped care framework (Figure 2), comprising four tiers of escalating intervention, with LDRT positioned as a potential option prior to the consideration of surgical management. The national accessibility of LDRT for OA in Australia is expected to grow following the experience in Europe and more recently the US, where certain centres have experienced a significant expansion in their rates of benign treatment.

In Australia, GPs may refer suitable patients directly to a radiation oncology service. As with other benign indications for radiotherapy, such as keloid scarring and thyroid eye disease, treatment is covered under Medicare. Following referral, patients are triaged within the oncology service, with their non-malignant status taken into account during prioritisation. The patient journey involves a consultation and consent by the radiation oncologist, including a

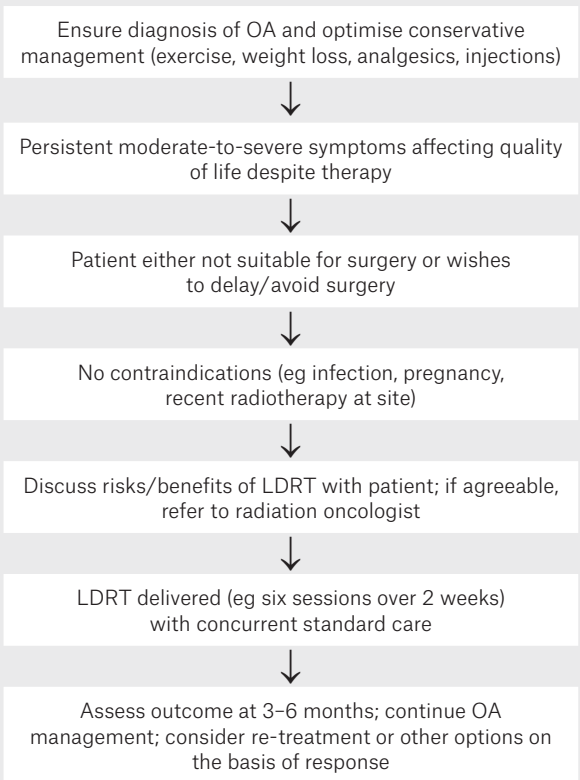

Figure 1. Example clinical decision flowchart for considering referral of a patient with osteoarthritis (OA) for low-dose radiotherapy (LDRT).

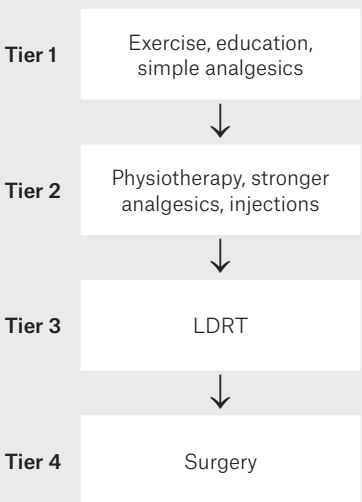

Figure 2. Osteoarthritis (OA) stepped care model.

All patients with OA receive Tier 1 interventions. If inadequate, move to Tier 2. If this is still inadequate and surgery is not imminent or desired, low-dose radiotherapy (LDRT) could be a Tier 3 option. Beyond that, Tier 4 would be surgery for those who fail or are inappropriate for LDRT or other measures.

discussion of the expected minimal adverse effects and theoretical low risk of a secondary malignancy. Patients will then undergo a planning computed tomography scan of the joint, following which they will undergo treatment, lying on a treatment couch with X-rays directed towards the affected joint for a few minutes per session, usually 2–3 times per week over 2–3 weeks.

Following treatment, there will be a typical 6–12-week post-treatment assessment by the radiation oncologist, following which the GP can continue to gauge the response.

Conclusion

LDRT offers a practical and underutilised option for patients with persistent OA pain despite first-line therapy. While LDRT is yet to be integrated into current Australian guidelines, there is growing evidence supporting its use to reduce pain, improve function and potentially slow progression to disability or joint replacement. Acknowledging two negative sham-controlled RCTs, when considering notable flaws such as small numbers, they should not override the significant body of supporting randomised, prospective and retrospective data. They should, however, highlight that LDRT is not universally effective and that appropriate patient selection is crucial. The GP can consider referral for LDRT for patients with chronic OA (typically knee or hip) without further conservative options and for whom surgery is undesirable. The relative ease of delivery, minimal toxicities and improvement in QOL highlight LDRT as an attractive option that should complement, not replace, standard care.

Key points

- LDRT may reduce OA pain via anti-inflammatory effects.
- LDRT for OA has shown significant benefits for pain relief in European centres.
- Two RCTs show significant pain reduction and functional benefit in knee OA.
- LDRT is ideal for OA pain refractory to first-line therapies or where surgery is not an option.
- LDRT has minimal acute side effects and an extremely low theoretical cancer risk.

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