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Radiotherapy for non-malignant diseases in orthopaedics: efficacy and safety

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Abstract
Introduction: This review aims to assess the current evidence on the efficacy and safety of low-dose radiotherapy (LDRT) in the treatment of non-malignant musculoskeletal and orthopaedic disorders, including osteoarthritis, plantar fasciitis, calcaneal spur, enthesopathies, Dupuytren's contracture, Ledderhose disease, and heterotopic ossification. As the prevalence of such conditions rises due to aging populations and modern lifestyle factors, interest is growing in alternative therapies for patients unresponsive to standard conservative treatment.
State of the Art: LDRT has been used in Germany for decades and is now gaining wider clinical attention. Its mechanisms—primarily anti-inflammatory and immunomodulatory—include suppression of pro-inflammatory cytokines and modulation of macrophage phenotypes. Recent studies show pain reduction in 42–95% of patients, with complete remission in up to 81%, depending on the condition, dosage, and treatment schedule. Comparable efficacy is seen between lower (0.5 Gy/fraction) and higher (1.0 Gy/fraction) dosing regimens. LDRT has shown particular benefit in early-stage fibromatoses and in postoperative prevention of heterotopic ossification, where combination with NSAIDs enhances efficacy. Safety data indicate minimal adverse effects and no significant increase in malignancy risk. However, some randomized trials report outcomes similar to placebo, highlighting the need for further controlled research.

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Conclusions: LDRT is a safe and promising adjunctive therapy in selected orthopaedic conditions, especially where conventional treatments have failed or are contraindicated. While long-term safety appears acceptable, further sham-controlled trials, biomarker studies, and treatment standardization are essential. This review is primarily intended for clinicians seeking evidence-based alternatives for managing chronic musculoskeletal disorders. **Keywords:** radiotherapy, non-malignant diseases, osteoarthritis, plantar fasciitis, heterotopic ossification, Dupuytren's contracture, Ledderhose, Gorham-Stout

Table legends:

Table 1. Studies evaluating the effects of radiotherapy on osteoarthritis.
Table 2. Studies evaluating the effects of radiotherapy on musculoskeletal disorders of the foot.
Table 3. Studies evaluating the effects of radiotherapy on heterotopic ossification.
Table 4. Studies evaluating the effects of radiotherapy on other musculoskeletal disorders.

1. Introduction

In recent decades, there has been a marked increase in the number of patients presenting with orthopaedic complaints, including degenerative, inflammatory, and post-traumatic conditions. This trend is primarily attributed to population ageing and lifestyle changes, including increased mechanical load on the musculoskeletal system (e.g. due to obesity, intense physical activity, or sedentary work) [1–3]. As a result, traditional conservative treatments—such as analgesic pharmacotherapy or physiotherapy are often insufficiently effective or poorly tolerated [4].

Consequently, increasing attention is being paid to the use of low-dose radiotherapy (LDRT) as an adjunct treatment in selected orthopaedic conditions. The mechanism of action of low-dose radiation is primarily based on its anti-inflammatory and immunomodulatory effects, including inhibition of pro-inflammatory cytokine synthesis, phenotypic modulation of macrophages toward an anti-inflammatory profile, and suppression of excessive angiogenesis in diseased tissues. The resolution of inflammation leads to pain reduction and improved quality of life for patients [4,5].

In Germany, where low-dose radiotherapy has been applied in orthopaedic patients for many years, evidence supports its clinical effectiveness in alleviating symptoms associated with osteoarthritis, plantar fasciitis, calcaneal spur, painful shoulder syndrome, and enthesopathies [4,6]. Emerging data also suggest its efficacy and safety in other conditions, including heterotopic ossification prophylaxis and Dupuytren's contracture.

Retrospective analyses indicate an overall favourable safety profile of LDRT, with clinical improvement often sustained for several months or even years. However, to define its precise role in clinical practice and to optimize treatment protocols, randomized controlled trials with sham treatment arms and standardized regimens are still required [4,6].

Given the rapid rise in the number of orthopaedic patients, there is a growing need for novel therapeutic strategies. Low-dose radiotherapy may represent a valuable option, particularly in cases where conservative measures are ineffective or contraindicated due to systemic burden or surgical risks [1,2].

2. Materials and methods

To assess the efficacy and safety of radiotherapy in non-malignant orthopaedic conditions, a literature review was conducted using databases including PubMed, ResearchGate, and Google Scholar, focusing on publications from the past 10 years (2015–2025). The 10-year timeframe was chosen to ensure the inclusion of the most recent and clinically relevant studies, reflecting current radiotherapy techniques, guidelines, and evolving clinical practice patterns in non-malignant orthopaedic conditions. The search utilized keywords such as "radiotherapy," "non-

malignant diseases," "orthopaedics," and disease-specific terms including "osteoarthritis," "plantar fasciitis," "heterotopic ossification," "enthesopathy," "Dupuytren's contracture," "Ledderhose disease," and "Gorham-Stout disease."

3. Results

3.1. Osteoarthritis (OA)

Osteoarthritis affects approximately 7.6% of the global population, corresponding to an estimated 595 million individuals in 2020, with projections indicating a 60–100% increase in prevalence by 2050 [1]. In 2020, the age-standardized incidence rates were approximately 8059 cases per 100,000 women and 5780 per 100,000 men, indicating a higher disease burden among females [1–3]. Risk factors include obesity—responsible for nearly 20% of new cases—as well as age and joint injuries [2].

The mechanism of LDRT in OA is multifactorial, targeting several key processes involved in inflammation regulation. Initially, LDRT mitigates pathological changes in the vascular endothelium by reducing the overexpression of adhesion molecules, thereby limiting the migration of pro-inflammatory leukocytes into inflamed tissue. Additionally, doses around 0.5 Gy modulate the phenotype of macrophages and other antigen-presenting cells towards an anti-inflammatory profile, reducing secretion of cytokines such as IL-1β and TNF-α, and downregulating iNOS (inducible nitric oxide synthase) expression [5].

Fibroblasts and fibroblast-like synoviocytes (FLS) play a pivotal role in sustaining chronic inflammation in OA, producing numerous mediators that promote joint tissue degradation. LDRT suppresses activation of these cells, reducing cartilage and subchondral bone damage and supporting immune balance within bone tissue—by decreasing osteoclast activity (which drives bone erosion) while enhancing osteoblast function [8]. Furthermore, LDRT alters the cytokine and chemokine secretion profile, promoting the release of anti-inflammatory factors (e.g., TGF-β), contributing to more effective resolution of inflammation [9]. Table 1 presents a detailed summary of clinical outcomes associated with radiotherapy in OA, based on scientific evidence published over the past decade.

In 2015, Otto et al. conducted a summary analysis of 19 retrospective clinical studies involving a total of 895 patients treated with LDRT for painful osteoarthritis of the hip. In these studies, 24–89% of irradiated patients experienced significant or complete pain relief [6]. Similarly, Seegenschmiedt et al. reviewed 17 retrospective studies published before 2004, comprising 809 patients treated with LDRT for osteoarthritis of the hand and fingers, with 63–75% reporting substantial or complete reduction in pain [4].

Osteoarthritis is one of the most common musculoskeletal disorders, causing pain, reduced joint function, and decreased quality of life. In cases where conventional pharmacological treatments and rehabilitation fail to yield satisfactory results, low-dose radiotherapy may serve as an alternative therapeutic option. However, evidence on its efficacy remains mixed. For example, Kaltenborn et al. reported that approximately 70% of patients with carpometacarpal (CMC) joint OA of the thumb experienced symptom improvement lasting up to one year [10]. Likewise, Micke et al. found significant pain relief in patients with gonarthrosis following radiotherapy, with effects persisting during long-term follow-up [11]. Conversely, Mahler et al. found no significant difference between LDRT and placebo, suggesting that the observed benefits may be short-lived or attributable to placebo effects [16]. Retrospective studies point to the potential efficacy of LDRT in treating various forms of OA. Research by Juniku et al. and Hautmann et al. indicated that LDRT may provide long-term pain relief, especially for ankle and tarsal joints [15,19]. In contrast, Minten et al. observed no significant improvement in patients with hand OA,

and the ArthroRad study reported no differences between high-/low-dose and low-/very low-dose radiation groups [13,27]. Meta-analyses of retrospective data on knee and hip OA suggest LDRT effectiveness ranging from 24–91%, though robust evidence of long-term benefit is lacking [14,18].

From a safety standpoint, LDRT is generally well tolerated, with no major adverse effects such as tissue damage or increased cancer risk reported in the reviewed studies. Only van den Ende et al. reported minor nail changes in patients with hand OA following radiotherapy [17]. Ongoing clinical trials, such as RAGOCO and LoRD-KNeA (ClinicalTrials.gov IDs: NCT04424628 and NCT05562271), may provide new data regarding the long-term efficacy and safety of this treatment [28].

According to the German Society for Radiation Oncology (DEGRO) guidelines, LDRT may be considered a therapeutic option in patients with moderate to advanced knee OA (Kellgren grades 2–3) and hip OA (Kellgren grades 2–4) when surgery is contraindicated or declined by the patient. The recommended dose ranges from 3.0 to 6.0 Gy, delivered in fractions of 0.5–1.0 Gy, administered 2–3 times per week. DEGRO emphasizes the need for further research to determine the optimal dose and verify long-term efficacy, especially in comparison to placebo. The organization also notes that LDRT may be more effective in specific patient subgroups, with baseline pain intensity being a key prognostic factor [7].

In summary, low-dose radiotherapy may represent a viable treatment alternative for patients with osteoarthritis, particularly when other therapeutic modalities have failed. However, current evidence remains inconclusive, and the efficacy of LDRT appears to depend on disease location and severity. While the therapy is safe, further research is needed to define the conditions under which it offers the greatest clinical benefit.

3.2. Plantar Fasciitis and Calcaneal Spur

Radiotherapy is increasingly being employed in the treatment of plantar fasciitis and calcaneal spur, particularly in Europe. In Germany, 10,510 patients with calcaneal spur were treated with radiotherapy in 2014, representing a significant proportion of all patients receiving radiotherapy for non-malignant conditions [29]. In Turkey, between 2015 and 2020, radiotherapy was administered to 6,346 patients with non-malignant disorders, of whom 19% were treated for plantar fasciitis [30]. Table 2 provides a detailed overview of the clinical effects of radiotherapy in plantar fasciitis, calcaneal spur, heel pain (calcaneodynia), and Achilles tendon pain (achillodynia), based on scientific evidence published in the last 10 years.

In clinical studies, 73% to 95% of patients with plantar fasciitis and calcaneal spur experienced a significant reduction in pain, with many cases showing long-lasting therapeutic effects. Complete pain remission ranged from 12% to 81%, depending on the treatment regimen and length of follow-up. A key finding was the comparable efficacy of low-dose protocols, such as 0.5 Gy per fraction (total dose of 3 Gy), compared to higher-dose schedules (1.0 Gy per fraction, total of 6 Gy), which is in accordance with recommendations from the German Society for Radiation Oncology (DEGRO). This suggests that optimal therapeutic effects can be achieved with minimal radiation exposure, thereby increasing the safety of the intervention.

Safety analyses indicate that low-dose radiotherapy in plantar fasciitis treatment is well tolerated and not associated with any significant adverse effects. Most studies reported no serious side effects, and temporary pain exacerbation—observed in some patients—typically resolved within a few weeks. Long-term follow-up has not shown an increased risk of malignancies, reinforcing the safety profile of LDRT in the management of chronic pain. Retrospective data show that in

96% of patients, the efficacy of LDRT was sufficient to avoid retreatment, further highlighting its clinical value.

DEGRO also emphasizes that the lack of serious side effects and low oncogenic risk make LDRT an appealing therapeutic alternative for patients unresponsive to conservative treatments, such as rehabilitation, pharmacotherapy, or platelet-rich plasma (PRP) injections [7].

3.3. Heterotopic Ossification

Heterotopic ossification (HO) is the pathological formation of bone within soft tissues, most commonly around large joints such as the hip, elbow, or knee [40]. It often occurs as a complication following trauma, orthopaedic surgery, or burns, with incidence rates depending on the patient population and prophylactic strategies used [41]. Following total hip arthroplasty (THA), HO develops in 15% to 90% of patients, while in individuals with traumatic brain or spinal cord injuries, the incidence can reach up to 65% [40,41]. Key risk factors include male sex, older age, obesity, smoking, a history of HO, and the use of cemented hip prostheses [40]. The pathogenesis of HO involves the activation of mesenchymal stem cells, which, under the influence of inflammatory cytokines, differentiate into osteoblasts, initiating ectopic bone formation. Crucial molecular mediators include bone morphogenetic proteins (BMPs), interleukin-6 (IL-6), and prostaglandin E2 (PGE2). In cases involving central nervous system injury, this process may be further intensified by metabolic and hormonal alterations [41]. Radiotherapy is an effective preventive measure for HO, particularly in patients undergoing orthopaedic procedures. It may be administered either preoperatively or postoperatively, with efficacy comparable to nonsteroidal anti-inflammatory drugs (NSAIDs) [40]. Typically, a single fraction of RT is delivered within 24–72 hours after surgery. Radiotherapy is also used in treating advanced HO, especially after surgical excision, as it helps reduce the risk of recurrence. Modern radiation techniques such as three-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT) allow for minimized adverse effects, including reduced risks of infertility and secondary malignancies [42]. Table 3 provides a detailed summary of the clinical effects of radiotherapy in the context of heterotopic ossification, based on from the past 10 years.

Radiotherapy is an established method for both prophylaxis and treatment of heterotopic ossification, particularly in high-risk patients, such as those undergoing total hip arthroplasty, suffering from periarticular trauma, or undergoing amputations. Clinical studies have demonstrated that the most effective regimen involves a single dose of 7–8 Gy, which significantly reduces the risk of recurrence, with reported efficacy ranging from 76% to 97% across different patient populations [43,7]. In individuals at high risk of HO progression, higher doses (7 Gy) have proven more effective than lower doses (4–5 Gy), indicating a dose-dependent therapeutic effect [46].

Prophylactic radiotherapy can reduce the risk of HO formation by up to 71%, especially in patients undergoing extensive orthopaedic procedures and experiencing prolonged hospitalization [45]. When combined with NSAIDs, its effectiveness increases further. Studies have shown that recurrence rates dropped from 27.6% to 8% with the use of combined therapy [52]. This approach is well tolerated, with side effects such as dermatologic or gastrointestinal symptoms occurring infrequently and typically being mild in severity [47,48]. The German Society for Radiation Oncology (DEGRO) recommends that a single dose of 7–8 Gy should be the standard for HO prophylaxis. In high-risk patients, a fractionated regimen of 5 × 3.5 Gy may be considered [7]. The optimal therapeutic window spans up to 4 hours before surgery or within 72 hours postoperatively, ensuring maximal prophylactic benefit. Despite high efficacy, further

studies are needed to determine the optimal dosing for recurrent HO and to identify predictive biomarkers that could facilitate a more personalized treatment approach [59].
In conclusion, radiotherapy is a safe and effective prophylactic intervention for heterotopic ossification, particularly in high-risk patients, where it can significantly reduce recurrence rates. The combination of radiotherapy with NSAIDs appears to enhance its efficacy, and ongoing research may support even better treatment individualization [7].

3.4. Other Musculoskeletal Disorders

This section discusses additional musculoskeletal disorders, including hyperproliferative conditions, for which radiotherapy has demonstrated clinical benefit. These include common tendon and bursal inflammations, painful shoulder syndrome, Dupuytren's contracture, Ledderhose disease, and the rare Gorham-Stout disease [7]. Table 4 presents a detailed overview of the clinical outcomes of radiotherapy in these conditions, based on evidence published over the past 10 years.

Radiotherapy in enthesopathies, painful shoulder syndrome, and greater trochanteric bursitis

Clinical studies investigating the use of RT in enthesopathies, painful shoulder syndrome, and greater trochanteric bursitis have reported that 42% to 75% of patients experienced significant pain reduction, with many cases showing sustained long-term relief. Complete remission ranged from 16% to 64.6%, depending on the treatment protocol, follow-up duration, and the specific condition treated.

In patients with bursitis trochanterica, the use of two RT series improved therapeutic outcomes from 59% to 72.5%, highlighting the potential benefit of repeat radiotherapy. Studies also demonstrated that fractionation regimens using 0.5 Gy per session (total 3–4 Gy) or 1.0 Gy per session (total 6 Gy) yielded comparable effectiveness, aligning with recommendations from the German Society for Radiation Oncology (DEGRO). These findings suggest that optimal clinical outcomes can be achieved with minimal radiation exposure, improving safety and reducing the risk of long-term side effects.

Safety analyses confirm that low-dose radiotherapy is well tolerated, with no significant adverse effects. Retrospective data showed no increase in cancer risk, and the estimated risk of skin cancer or sarcoma at irradiated sites was negligible (<0.1%). In long-term follow-up, 50–70% of patients did not require retreatment, reinforcing the clinical efficacy of LDRT in managing chronic musculoskeletal pain. DEGRO emphasizes that the absence of serious side effects and minimal long-term complication risk make radiotherapy an attractive option for patients unresponsive to conservative therapies such as rehabilitation or pharmacotherapy [7].

Radiotherapy in Dupuytren's Disease

Radiotherapy is also considered an effective treatment for early-stage Dupuytren's disease, particularly when finger contractures do not exceed 10° and joint mobility remains preserved. Studies show that in such cases, up to 80% of patients experience disease stabilization, and 45–67% show symptom regression [66,67]. In the long term, radiotherapy significantly reduces the need for surgical intervention—with up to 84% of patients avoiding surgery after treatment [66]. DEGRO recommends radiotherapy in patients with active, progressive disease, as long as pathological nodules are still in the proliferative phase. Its guidelines suggest a regimen of 30Gy, delivered in 10 fractions of 3 Gy over two treatment cycles, separated by a 8-12 week interval [7].

In the context of non-malignant disorders treated with radiotherapy—particularly calcaneal spur—data from the Czech Republic show that approximately 26,000 patients undergo

radiotherapy annually, 75% of whom are treated with X-ray units, with calcaneal spur being the most common indication. In 2013, the collective effective dose from radiotherapy for calcaneal spur was 77 manSv, representing 25.6% of the total effective dose for all non-malignant conditions treated with RT in the country [79].

For advanced stages of Dupuytren's disease, combined approaches have been explored. A study evaluating high-dose-rate (HDR) brachytherapy with ^{192}Ir following surgical aponeurectomy showed a significant improvement in finger mobility, with mean contracture decreasing from 55.4° to 15.4° ($p<0.01$), suggesting its potential in more aggressive disease forms [68].

In terms of safety, radiotherapy for Dupuytren's disease is well tolerated. Most adverse effects are mild and transient, with the most commonly reported being erythema (20.4%), dry skin (39.8%), and desquamation (3.8%) [66]. Long-term effects such as skin atrophy (3%), sensory disturbances (2%), and telangiectasia (3%) were rare, with no cases of ulceration or malignancy reported [66,67].

In the DEPART trial, which assessed adjuvant radiotherapy after surgery, collagenase injection, or needle fasciotomy, 60 patients were randomized to a control group or radiotherapy group (30 Gy in 10 fractions). Over 4 years, 114 adverse events were recorded, most (89%) of which were mild, and fewer than half were attributed to RT. Among 12 more serious events, only 3 were linked to radiotherapy, all of which resolved within 6 months, with only reduced sweating persisting long-term [80].

In summary, radiotherapy is recommended for early-stage Dupuytren's disease, especially in patients with active progression, as it may significantly reduce surgical risk and slow disease progression [66,67]. In more advanced stages, combined approaches with surgery may be considered, although further studies are needed to evaluate long-term outcomes [68].

Radiotherapy in Ledderhose Disease

Radiotherapy has also shown efficacy in early-stage Ledderhose disease, particularly in patients with progressive symptoms and pain. Studies report that 70–80% of patients experience pain reduction, with complete symptom remission in some cases [69,70]. Clinical trials also indicate that RT leads to stabilization or regression of nodules, thereby reducing the need for surgery [69].

According to DEGRO, radiotherapy should be performed during the active stage of disease, when symptoms are progressing, to prevent further pathological changes and avoid surgical intervention [7]. Randomized controlled trials have confirmed that radiotherapy not only reduces pain but also improves gait function and quality of life. In one study, patients receiving radiotherapy demonstrated significant improvements in mobility and biomechanical parameters, distinguishing them from placebo-treated individuals [71]. DEGRO notes that radiotherapy is most effective when applied as a primary treatment, whereas in recurrent disease, outcomes may be less favorable [7]. From a safety perspective, radiotherapy is well tolerated, with most side effects being mild and transient, including erythema, dryness, and burning sensations, which usually resolve within a few months [69,70]. DEGRO does not currently recommend RT as a postoperative standard, citing insufficient evidence for its impact on recurrence prevention. The recommended dosing schedule consists of 30 Gy, delivered in two courses of 5 fractions of 3 Gy, with a 6–12 week interval between cycles. This is consistent with both clinical trial data and DEGRO guidelines [7]. However, further research is needed to determine optimal dosing, particularly regarding potential dose reduction without compromising therapeutic efficacy.

4. Conclusions

Low-dose radiotherapy in orthopaedic conditions is increasingly recognized as a valuable adjunct to traditional conservative therapies such as analgesic pharmacotherapy, rehabilitation,

and intra-articular injections. Its effects are primarily based on the anti-inflammatory and immunomodulatory properties of low-dose ionizing radiation, which may lead to pain relief and improved joint mobility. Numerous observations—particularly from German centers, where LDRT has been practiced for many years—support its clinical effectiveness in conditions such as osteoarthritis, plantar fasciitis, calcaneal spur, Dupuytren's contracture, and in the prophylaxis of heterotopic ossification. This therapy is considered safe and well-tolerated, with serious adverse effects being rare and the oncogenic risk minimal when standard protocols are followed. However, some controlled studies have failed to show a definitive advantage of LDRT over placebo, emphasizing the need for well-designed, sham-controlled trials. Standardization of treatment protocols and better patient selection criteria are also essential to identify those who may derive the greatest benefit. Despite these limitations, LDRT remains a promising adjunctive treatment, particularly in cases where standard approaches fail or are associated with unacceptable side effects.

Disclosure

Author Contribution Statement

Conceptualization: AW; methodology: AW; software: n/a; check: MW, AK; formal analysis: AK; investigation: AW; resources: AW, MW; data curation: AW; writing - rough preparation: AW, MW; writing - review and editing: MW, AK; visualization: AW; supervision: AK; project administration: AW; receiving funding: n/a. All authors have read and agreed with the published version of the manuscript.

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Table 1. Studies evaluating the effects of radiotherapy on osteoarthritis.

Study	Irradiated joint	Sample size	Irradiation protocol	Outcomes	Adverse effects
Kaltenborn et. al. (2016) [10]	I carpometacarpal (CMC)	84 patients (101 joints)	6 x 1 Gy, 2x / week, (total 6 Gy) (~3 weeks)	End of radiotherapy: approximately 70% of patients experienced partial or complete symptom remission. At 3 months: approximately 60% maintained improvement. At 12 months: approximately 70% maintained improvement. Better outcomes were observed with the use of larger irradiation fields (>6 × 4 cm)	~20% of patients experienced transient pain flare at therapy onset
Micke et. al. (2017) [11]	Knee	80 patients	Max. 6 Gy, 6 x 0.5–1 Gy per session	Mean VAS pain score decreased from 6.32 to 4.74; effect sustained long-term	No adverse events reported
Micke et. al. (2018) [12]	Knee	139 patients	12 × 0.5 Gy or 6 ×1.0 Gy (total 6 Gy)	VAS before RT: 6.0 → 4.5 post-RT ($p<0.001$); immediate effect: 30.9%, at follow-up (median 19.5 months): 29.2%	No adverse events reported
Minten et. al. (2018) [13]	Hand	56 patients 28 RT vs 28 „sham”	6 × 1 Gy, 2 over weeks (every other day), (total 6 Gy)	No significant difference in improvement vs. sham; responders: 29% (RT) vs 36% (sham); inflammation markers similar	Nail changes: 29% (RT) vs 11% (sham)
Koc et. al. (2019) [14]	Hip and knee	12 patients (16 joints: 4 hip joints, 12 knee joints	6 x 1 Gy over two weeks (total 6 Gy)	Pain improvement in NRS 50% at 6 weeks, only 25% at 52 weeks	No adverse events reported
Juniku et. al. (2019) [15]	Hip and knee	60 patients (30 knee joints, 30 hip joints)	3.0–5.0 Gy, 6–10 x 0.5 Gy over 2 weeks	VAS reduction: knee 7→6, hip 8→6; improvement in 20% (knee), 26.7% (hip) after 38 months	No adverse events reported
Mahler et. al. (2019) [16]	Knee	55 patients (27 RT vs 28 „sham”)	6 × 1 Gy, over two weeks (total 6 Gy)	No significant difference in responders at 3 months: 44% (RT) vs 43% (sham); no change in pain/function or inflammation	Mild adverse events; similar profiles in RT and sham groups
van den Ende et. al. (2019) [17]	Knee and hand	Knee joint: 55 patients (27 RT vs 28 sham) Hand joints:: 56 patients (28 RT vs 28 sham)	6 × 1 Gy, over 2 weeks (total 6 Gy)	No difference in responders at 6/12 months; VAS/pain/function scores similar at 12 months	Nail changes more frequent in RT group (hand arthritis); other adverse eventss (e.g. fatigue, skin reactions) similar in both groups

Álvarez et. al. (2019) [18]	Finger, I CMC, knee joint	84 patients (26 finger joints, 25 I CMC joints, 33 knee joints)	6 x 1Gy (3x/ week over 2 weeks)	Statistically significant VAS improvement across all joint groups: finger joints: 6.62→3.69),I CMC: 7.59→3.48, knee: 7.59→3.21	Nie odnotowano istotnych działań niepożądanych
Hautmann et. al. . (2020) [19]	Ankle and tarsal	44 patients: 66 ankle / tarsal joints	6× 0,5 Gy (total 3 Gy) lub 6 × 1 Gy (total 6 Gy) over two weeks	Median NRS pain drop from 7→4 (up to 12 months); After 12 months 19,6% joints NRS 0/1 ROM improved in 56.7%; effect lasted ≥24 months	No adverse events reported.
Donaubauer et. al. (2020) [20]	Finger joints	483 patients	6 × 0,5 Gy (total 3 Gy) lub 6 × 1,0 Gy (total 6 Gy)	70% showed ≥20% pain reduction; 0.5 Gy was more effective than 1 Gy; Thumb-only cases had poorest outcomesl; Pain relief: 73.7% (0.5 Gy) vs 83.3% (1.0 Gy)	No serious adverse events; only 2% reported worsening pain
Rogers et. al. (2020) [21]	Finger joints	59 patients	8 × 0,5 Gy, 2×/week, total 4 Gy over 4 weeks (repeated after ~8 weeks, in case of pain)	Resting pain (VAS) median 2, slight decrease (p=0.056 at 12 months), exercise pain (VAS) median 5, dropped ~3 points (p<0.001), grip strength increased by ~2–3 kg (p=0.004)	No significant adverse events noted
Hermann et. al. . (2021) [22]	I CMC joint	25 patients	6 × 0,5 Gy (total 3 Gy); 2×/week.; (insufficient improvement after 3 months – an additional course up to 6 Gy)	80% of patients had partial pain relief; VAS global pain: median dropped from 7 to 3 (3 mo) and 2 (12 mo) PRWE global: 0.50 → 0.36 (3 mo) → 0.27 (12 mo), indicating improved function and QoL Thumb flexion improved from 64° to 73°	No significant adverse events noted
Aramburu et. al. (2021) [23]	Peripheral joints and lumbar spine	67 patients - peripheral joints 8 patients - lumbar spine	6 x 1 Gy over 2 weeks.	Overall, 70.1% of patients with osteoarthritis achieved ≥50% pain reduction	No significant adverse events noted
Rühle et. al. (2021) [24]	Knee, hip, shoulder, finger and foot joints	970 patients, 1185 joints	6×1 Gy, total 6 Gy or 6×0,5 Gy total 3 Gy (2–3 sessions weekly)	Immediately post-RT: ~60% pain reduction; ~66% at ~8 weeks; VAS decreased from 66 → 53 (end of RT) → 44 (first follow-up); After re-RT (in 32%): ~61% improvement	No significant adverse events noted
Álvarez et al. (2022) [25]	Hand and wrist joints	100 patients	1 Gy every second day total 6 Gy, 17, 0,5 Gy every second day (total 3 Gy)	94% reported pain relief; VAS dropped from 8 → 5 post-RT, and to 4 at 3 months	No adverse events reported
Weissmann et al. (2022) [26]	Foot and tarsal joints	196 patients	0.5 Gy or 1.0 Gy; 6x over 3 weeks, 2 days pause	75% showed >20% improvement; 37% achieved 80–100% relief (median ~55–60%)	2 patients reported worsening symptoms
Niewald et. al. (2024) [27]	Knee and hand joints	133 patients (3Gy: 77 hands, 33 knees, 0,3 Gy: 81 hands, 30 knee	0.05 Gy or 0.5 Gy 2x/week over 3 weeks (total 0.3 Gy or 3 Gy)	At 12 months: pain improved in both groups. ΔVAS: 3 Gy: -19.5, 0.3 Gy: -16.2; KOOS-PS: 0.3 vs 7.2; SF-SACRAH: -7.5 vs -6.6.	No adverse events reported.

Legend: VAS - Visual analogue scale, RT - radiotherapy, NRS - Numeric rating scale, PWRE - Patient-rated wrist evaluation, KOOS-PS - Knee injury and osteoarthritis outcome score physical function short-form, SF-SACRAH - Short form score for the assessment and quantification of chronic rheumatic affections of the hands

Table 2. Studies evaluating the effects of radiotherapy on musculoskeletal disorders of the foot.

Study	Irradiated area	Sample size	Irradiation protocol	Outcomes	Adverse effects
Ott et. al. (2015) [31]	Achilles tendon (Achillodynia)	112 patients	6 × 0.5 or 1 Gy, 2×/week (total 3–6 Gy) (~3 weeks)	Early response in 84%, delayed in 88%, long-term in 95%; complete pain remission: 1% immediate, 12% at 6 weeks, 45% long-term	No adverse events reported
Seegenschmiedt et. al. (2015) [4]	Plantar fascia	11,909 patients (various study groups)	6 × 0.5–1.0 Gy, 2–3×/week (total 3–6 Gy)	Complete pain relief in 12–81%, partial improvement in 7–74%; optimal dose: 3 Gy	No adverse events reported
Gogna et. al. (2016) [32]	Plantar fascia	40 patients (20 PRP vs 20 RT)	6 × 0.5 Gy, 2×/week (total 3 Gy) (~3 weeks)	VAS: pain reduced from 6.5 to 2.35 at 6 months; AOFAS improved from 52.5 to 89.65; plantar fascia thickness decreased	No adverse events reported
Kędzieraws ki et. al. (2017) [33]	Plantar fascia	47 patients (no control group)	6 × 1 Gy, 2×/week (total 6 Gy) (~3 weeks)	Complete pain remission in 96%; 4% required retreatment	No adverse events reported
Prokein et. al.(2017) [34]	Plantar fascia	127 patients	6 × 0.5 or 1 Gy, 2–3×/week (total 6 Gy) (60 vs 67 patients)	VAS reduction: 59.4 (1 Gy group) vs 61.6 (0.5 Gy group); no significant difference between doses	No adverse events reported
Micke et. al. (2018) [12]	Plantar fascia or Achilles tendon	286 patients (calcaneodynia), 46 patients (achillodynia)	6 × 0.5–1.0 Gy, 2–3×/week (total 6 Gy)	Calcaneodynia: 46% good response post-RT, 80.7% after follow-up. Achillodynia: 39.1% post-RT, 88.9% after follow-up	No adverse events reported
Rogers et. al. (2020) [21]	Plantar fascia	54 patients	8 × 0.5 Gy, 2×/week (total 4 Gy) (~4 weeks)	93% pain-free at 12 months (VAS = 0); 4-point VAS reduction; 5 s improvement in walking test	No adverse events reported
Zahnreich et. al. (2020) [35]	Plantar fascia	22 patients (RT)	6 × 0.5 Gy, 2×/week (total 3 Gy) (~3 weeks)	Improvement in 89%; 50% achieved complete pain relief	No adverse events reported
Rudat et. al. (2021) [36]	Plantar fascia	666 patients, 864 heels	6 × 0.5 Gy, 3×/week (total 3 or 6 Gy)	45.9% had insufficient pain relief after 10 years; 40% improved after re-irradiation	No adverse events reported
Djiepmo et. al. (2022) [37]	Plantar fascia	102 patients, 117 heels	6 × 0.5–1.0 Gy, 2–3×/week (total 3 or 6 Gy)	73% pain-free after long-term follow-up; pain duration before RT significantly affected outcome	No adverse events reported

Pluta et. al. (2022) [38]	Plantar fascia and Calcaneal spur	46 patients	6 × 1 Gy, daily on weekdays (total 6 Gy) (~6 days)	Median NRS before RT: 8.0 → 5.5 (1 month) → 1.0 (6 months); 7-point drop; lasting improvement 85%	No adverse events reported
Karimi et. al. (2024) [39]	Plantar fascia and Calcaneal spur	100 patients	6 × 0.5 Gy (total 3 Gy)	Over 70% reported significant improvement	No adverse events reported

Legend: PRP - platelet-rich plasma, RT - radiotherapy, VAS - Visual Analogue Scale, AOFAS- American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Score, Numeric Rating Scale - Skala numeryczna

Table 3. Studies evaluating the effects of radiotherapy on heterotopic ossification.

Study	**Irradiated joint**	**Sample size**	**Irradiation protocol**	**Outcomes**	**Adverse effects**
Boffeli et. al. (2015) [43]	Foot (after partial metatarsal amputation)	11 patients	7 Gy single dose within 72 h after postoperatively	82% of patients had no HO recurrence; 18% had mild HO	No significant adverse effects
Weng et. al. (2015) [44]	Hip (after total arthroplasty in patients with ankylosing spondylitis)	91 patients 129 hip joints (53 without RT vs 76 irradiated with 5 Gy)	5 Gy single dose within 2 days postoperatively	HO incidence: 26% (no RT) vs 36% (5 Gy); no significant difference Harris Hip Score (HHS) improvement similar in both groups (93.4 vs 93.1)	No significant adverse effects
d'Heurle et. al. (2016) [45]	Hip joint (after acetabular fractures)	141 patients	7 Gy single dose	HO risk reduced by 71% (OR = 0.29); higher risk with prolonged hospitalization (OR = 7.6)	No significant adverse effects
Liu et. al. (2017) [46]	Hip joint (after total arthroplasty)	147 patients (71 received 4 Gy vs 76 received 7 Gy)	4 Gy vs 7 Gy single dose administered 1–2 days postoperatively	HO incidence: 42.3% (4 Gy) vs 25.0% (7 Gy); 7 Gy significantly more effective ($p = 0.035$)	No significant adverse effects
Müseler et. al. (2017) [47]	Hip joint (after spinal cord injury)	244 patients (444 hip joints)	7 Gy single dose	HO recurrence: 5.9% of cases; mean time to recurrence 47.7 days; all retreated with 7 Gy	No significant adverse effects
Ruo Redda et. al. (2018) [48]	Hip joint (after arthroplasty and trauma)	30 patients (31 joints)	7 Gy (87.1%), 8 Gy (6.5%), 12 Gy in 3 fractions (3.2%), 15 Gy in 5 fractions (3.2%)	76% achieved complete remission, 22.6% partial response; 6.5% had recurrence after 12–19 months	No significant adverse effects
Honore et. al. (2020) [49]	Hip joint (after spinal cord and brain injuries)	19 patients (RT) vs 76 (no RT)	7.5 Gy single dose one day preoperatively	No statistically significant difference in HO recurrence between groups	Increased risk of sepsis requiring surgical revision ($p < 0.05$)

Georgakopoulos et. al. (2020) [50]	Hip joint (after total hip arthroplasty)	14 patients	7–10 Gy single dose postoperatively	0% HO recurrence after a median follow-up of 126 months	No significant adverse effects
Lee et. al. (2020) [51]	Hip joint, femur, knee joint (in advanced heterotopic ossification)	9 patients	6–9 Gy	5/9 patients had ≥50% HO volume reduction	No significant adverse effects
Pakos et. al. (2020) [52]	Hip joint (after total hip arthroplasty)	97 patients 50 (RT + NSAID) vs 47 (NSAID only)	7 Gy single dose within 3 days postoperatively	HO incidence: 8% (RT + NSAID) vs 27.6% (NSAID only)	No significant adverse effects
Dass et. al. 2021 [53]	Index finger	1 patient	7 Gy single dose within 24 h postoperatively	No HO recurrence after 8 months; full range of motion; no pathological scarring	No significant adverse effects
Geller et. al. (2022) [54]	Elbow joint	54 patients	7 Gy single dose within 72 h postoperatively	HO occurred in 16.7% (primary prophylaxis) and 11.1% (secondary); 5.6% required surgery	One case of delayed bone union (11 months)
Zorn et. al. (2024) [55]	Thigh (post-amputation)	1 patient	8 Gy single dose	Significant pain relief and limb function improvement	No significant adverse effects
Osório et. al. 2023) [56]	Hip joint (after hip arthroplasty)	1 patient	20 Gy in 2 Gy/day fractions over 2 weeks	No HO recurrence after 2 years; improved hip ROM; HHS improved from 44 to 87	No significant adverse effects
Mohamed et. al. (2022) [57]	Hip and elbow joints (after traffic-related trauma)	39 patients (35 hip, 4 elbow)	7–8 Gy single dose within 3 days postoperatively	97% regained partial ROM; 5-year HO recurrence prevention efficacy: 97.2%	13% of patients experienced transient gastrointestinal and skin symptoms
Zampogna et. al. (2023) [58]	Hip joint (after arthroplasty)	26 patients	7 Gy single dose 24 h preoperatively	Forgotten Joint Score (FJS) increased from 21.3 to 76.5; VAS pain decreased from 7.2 to 1.8	Four cases of local complications: nerve injury (3.8%), prosthesis dislocation (3.8%), hematomas (7.5%)
Xin et. al. 2024 [59]	Elbow joint (after post-traumatic injuries and surgeries)	76 patients	7–8 Gy single dose 24 h preoperatively	HO recurrence in 6.6% of patients. Elbow function improved (Mayo Elbow Score: 56.05 → 93.88) Elevated $IFN\gamma^{+}CD8^{+}T$ and $IL17^{+}CD4^{+}T$ cells suggest immune role in HO pathogenesis	No significant adverse effects

Legend: RT- radiotherapy, HO - heterotopic ossification, OR - odds ratio, NSAID - nonsteroidal anti-inflammatory drug, ROM - Range of motion, IFNγ - Interferon gamma, IL - Interleukin

Table 4. Studies evaluating the effects of radiotherapy on other musculoskeletal disorders.

Study	Irradiated joint	Sample size	Irradiation protocol	Outcomes	Adverse effects
Miszczyk et. al. (2015) [60]	Elbow joint (humeral epicondylopathy)	48 patients (50 elbow joints)	6 × 1 Gy, 7–12 days (total 6 Gy)	Mean pain reduction: 22.8% post-RT, 70.2% at 8–12 months, 57.5% at 26–30 months (Brief Pain Inventory)	No significant adverse effects
Hautmann et. al. (2018) [61]	Elbow joint (humeral epicondylopathy)	124 patients (138 elbow joints)	6 × 1 Gy over 2 weeks (total 6 Gy)	Median NRS: 7 pre-RT → 4 at 6 weeks → 0 at 12 & 24 months; 64.6% had NRS 0–1 at 12 months	No significant adverse effects
Hautmann et. al. (2020) [62]	Elbow joint (humeral epicondylopathy)	86 patients (99 elbow joints – re-irradiation)	6 × 0.5–1 Gy over 2–3 weeks (total 3–6 Gy)	Re-RT: median NRS 6 → 3 at 6 weeks → 2 at 12 months → 1 at 24 months; 50.9% had NRS ≤1 at 24 months	No significant adverse effects
Rogers et. al. (2020) [21]	Elbow joint (humeral epicondylopathy)	44 patients (35 lateral epicondylitis, 9 medial epicondylitis)	8 × 0.5 Gy, 2x / week, 4 weeks (total 4 Gy); optional repeat after 8 weeks	Lateral epicondylitis: VAS improvement, handgrip ↑ 5.2 kg (flexion), ↑16 kg (extension) at 12 months	No significant adverse effects
Pluta et. al. (2022) [38]	Elbow joint (humeral epicondylopathy)	27 elbow joints	6 × 1 Gy, 1 session / day, 6 days (total 6 Gy)	Median NRS: 8.0 → 5.0 (1 month) → 4.0 (6 months); median difference: -4.25	No significant adverse effects
	Knee joint (PT, HT)	10 knee joints		Median NRS: 8.0 → 5.0 (1 month) → 2.5 (6 months); median difference: -4.5	
	Shoulder joint (PPS)	6 shoulder joints		Median NRS: 5.5 → 3.0 (1 month) → 2.0 (6 months); median difference: -3.5	
Micke et. al. (2018) [12]	Shoulder joint (PPS)	162 patients	6 or 12 × 0.5–1 Gy (total 6 Gy)	Median VAS: 7.0 → 5.0 post-RT; responders: 32.7% (immediate), 60% (long-term)	No significant adverse effects
	Greater trochanter of the femur (GTPS)	70 patients		Median VAS: 7.0 → 5.0 post-RT; responders: 27.1% (immediate), 46.3% (long-term)	
Leist et. al. (2024) [63]	Shoulder joint (PPS)	236 patients	Various fractionation schemes: max. 6 × 1 Gy or 12 × 0.5 Gy (total 6 Gy)	Therapeutic effect: 30.9% immediate, 55.2% at long-term follow-up	No significant adverse effects

Kaltenborn et. al. (2017) [64]	Greater trochanter of the femur (GTPS)	60 patients (74 hip joints)	6 × 0.5–1 Gy, 2x / week (total 3–6 Gy)	Remission post-RT: 69% partial, 4% complete; 3 months: 33% complete; 18 months: 51% complete	No significant adverse effects
Staruch et. al. (2023) [65]	Greater trochanter of the femur (GTPS)	65 patients (71 hip joints)	6 × 0.5–1 Gy, 2x / week (total 3–4 Gy)	Remission post-RT: 42% partial, 16% complete; 2 months: 59% full/major improvement; double RT boosted efficacy to 72.5%	No serious adverse effects; transient pain flare in 20% of patients
Zirbs et. al. (2015) [66]	Palmar surface of the hand (Dupuytren's contracture)	206 patients (297 hands)	4 × 4 Gy on consecutive days, 4 cycles, 8-week intervals (total 32 Gy)	Mean follow-up: 40 months; 45% symptom reduction, 80% halted disease progression; satisfaction 7.9/10	Erythema (transient): 20.4%, skin dryness: 39.8%, desquamation: 3.8%, chronic skin atrophy: 3%, sensory disturbances: 2%, telangiectasia: 3%
Seegenschmiedt et. al. (2015) [67]	Palmar surface of the hand (Dupuytren's contracture)	1,762 patients (meta-analysis of 12 studies)	10 × 3 Gy, 5x / week, repeat after 12 weeks (total 30 Gy)	Symptom regression: 67–84%; surgery avoided in 84%; disease progression: 35% (control), 7% (21 Gy), 4% (30 Gy)	No serious complications; possible transient skin effects
Ciernik et. al. (2021) [68]	Palmar surface of the hand (Dupuytren's contracture)	6 patients (13 fingers)	10–12 Gy single brachytherapy dose, 0–2 mm depth; catheters removed 6–12 h post-treatment	Finger contracture reduced from 55.4° → 15.4° ($p<0.01$); one untreated finger progressed	No complications; no palmar skin atrophy; no additional treatment required
Schuster et. al. (2015) [69]	Palmar surface of the hand and plantar surface of the foot (PPF)	33 patients (60 feet and hands)	7 × 3 Gy (21 Gy) or 10 × 3 Gy (30 Gy) with 6–8 week break after 15 Gy	Pain relief: 81% (load-related), 70% (at rest); tension improved in 95%. Patient satisfaction: 94%	Adverse effects in 39% of patients (erythema 20%, skin dryness 25%)
de Haan et. al. (2022) [70]	Plantar surface of the foot (Ledderhose disease)	67 patients (102 feet)	2 cycles × 5 fractions per day × 3 Gy, 10-week break (total 30 Gy)	Pain relief: 74% (RT) vs 56% (placebo); improved gait speed. Pain remission: 41% complete, 37% partial; 78% reported meaningful pain relief; QoL comparable to age-matched population	15% skin dryness; 3% erythema
de Haan et. al. (2023) [71]	Plantar surface of the foot (Ledderhose disease)	84 patients (42 RT, 42 sham)		At 12 months: pain intensity significantly lower vs placebo (2.5 vs 3.6; $p = 0.03$) Pain relief: 74% (RT) vs 56% (placebo; $p = 0.002$); better gait speed & step count	Adverse effects included erythema, skin dryness, and burning sensation. 95% of adverse events were mild; 87% resolved within 18 months
Yerganyan et. al. (2015) [72]	Tibia, fibula (GSD)	1 patient	20 × 2 Gy (total 40 Gy) + bisphosphonates	MRI: lymphangiomatous infiltration ↓; bone structure stabilized, mineralization ↑ (X-ray & MRI); BAP/CTX ↓; pain & mobility improved	No adverse effects reported
Liu et. al. (2016) [73]	Pelvis, spine, ribs, skull, limbs (GSD)	12 patients	20 × 2 Gy (total 40 Gy) in 4 pts + bisphosphonates in 9 pts	Osteolysis stabilized in all treated patients. BMD ↑ in bisphosphonate group; β-CTX ↓	Chylothorax group: high mortality (43.6%); one patient showed disease progression despite therapy

Tolis et. al. (2016) [74]	Pelvis (GSD)	1 patient	45 Gy (fractionation not specified) + bisphosphonates	Osteolysis stabilized but irreversible bone destruction in some cases. Progressive hip degeneration → walking aid required	No adverse effects reported
Tateda et. al. (2017) [75]	Cervical spine (C1–C5) (GSD)	1 patient	36 Gy (unspecified fractions) + interferon α-2b + pamidronate	Osteolysis stabilized after 1.5 years of treatment. No disease progression over 5 years C2–C5 spinal fusion successful; osteolysis halted	Transient chylothorax treated with pleurodesis
Srivastava et. al. (2017) [76]	Thoracic spine (Th1–Th12), ribs (GSD)	1 patient	1 × 8 Gy + bisphosphonates	Full neurological recovery 5 weeks post-surgery No progression of spinal deformity at 1-year follow-up	No complete bone graft fusion achieved Secondary surgery required with maternal bone graft
Tena-Sanabria et. al. (2019) [77]	Pelvis, upper cervical spine (C1–C3) (GSD)	2 pediatric patients	25 × 1.8 Gy (total 45 Gy) + bisphosphonates + vitamin D	Patient 1: pelvic osteolysis stabilized; Patient 2: cervical spine bone destruction progressed	Patient #2 death due to spinal cord compression
Koto et. al. (2019) [78]	Ribs, thoracic spine (Th6–Th7) (GSD)	1 patient	5 × 4 Gy, every 5 days (total 20 Gy) + bisphosphonates + vitamin D + propranolol	No radiologic osteolysis progression; no neurological recovery (lower limb paralysis)	Hemorrhagic pleural effusion causing mediastinal shift and patient death

Legend: RT - radiotherapy, PT - patellar tendonitis, HT - hamstring tendinopathy, PPS - Painful shoulder syndrome, GTPS - Greater trochanteric pain syndrom, PPF - Palmar and plantar fibromatosis (Dupytren's contracture and Ledderhose disease, GSD - Gorham-Stout Disease, MRI - Magnetic resonance imaging, BAP - Bone alkaline phosphatase, CTX - C-terminal telopeptide,