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REVIEW ARTICLE

# DEGRO guidelines for the radiotherapy of non-malignant disorders

## Part II: Painful degenerative skeletal disorders

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**Abstract**
*Background and purpose* The purpose of this article is to summarize the updated DEGRO consensus S2e guideline recommendations for the treatment of benign painful degenerative skeletal disorders with low-dose radiotherapy.
*Materials and methods* This overview reports on the role of low-dose radiotherapy in the treatment of enthesiopathies (shoulder syndrome, trochanteric bursitis, plantar fasciitis, and elbow syndrome) and painful arthrosis (knee, hip, hand, and finger joints). The most relevant aspects of the DEGRO S2e Consensus Guideline Radiation Therapy of Benign Diseases 2014 regarding diagnostics, treatment decision, dose prescription as well as performance of radiotherapy and results are summarized.
*Results* For all indications mentioned above, retrospective and some prospective analyses have shown remarkable effects in terms of pain relief. Nevertheless, the Level of Evidence (LoE) and the Grade of Recommendation (GR) vary: LoE 1b–4 and GR A–C.
*Conclusion* Low-dose radiotherapy for painful degenerative skeletal disorders is effective in the majority of the patients and therefore it may be a reasonable therapeutic alternative when simple and non-invasive methods have been used without persistent success. For all discussed entities, single fraction doses of 0.5–1.0 Gy and total doses of 3.0–6.0 Gy/series applied with 2–3 fractions per week are recommended.

**Keywords** Enthesiopathy · Painful arthrosis · Benign degenerative disease · Low-dose radiotherapy · German S2e guideline

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## DEGRO-S2e-Leitlinie für die Strahlentherapie von gutartigen Erkrankungen

Teil II: Schmerzhafte degenerative Skeletterkrankungen

**Zusammenfassung**

*Hintergrund* Zusammenfassung der Empfehlungen der DEGRO-S2e-Leitlinie zur Niedrigdosis-Radiotherapie von gutartigen schmerzhaften degenerativen Skeletterkrankungen.

*Material und Methode* Die vorliegende Zusammenfassung berichtet über die Bedeutung der Niedrigdosis-Radiotherapie in der Behandlung von Enthesiopathien (Schultersyndrom, Ellenbogensyndrom, Bursitis trochanterica, Fasciitis plantaris) und schmerzhaften Arthrosen (Knie-, Hüft, Hand- und Fingergelenksarthrosen). Die wichtigsten Aspekte der aktuellen DEGRO-S2e-Konsensus-Leitlinie Strahlentherapie gutartiger Erkrankungen bezüglich Diagnostik, Therapieentscheidungen, Dosisempfehlungen und Durchführung einer Radiotherapie werden zusammengefasst.

*Ergebnisse* Für alle genannten Entitäten wurde in zahlreichen retrospektiven und einigen prospektiven Untersuchungen ein bemerkenswerter Effekt der Niedrigdosis-Radiotherapie im Sinne einer Schmerzlinderung beschrieben. Je nach Entität wurden Evidenzlevel (LoE) von 1b–4 festgestellt, sodass unterschiedliche Empfehlungsgrade (GR) von A–C für den Einsatz der Radiotherapie ausgesprochen wurden.

*Schlussfolgerung* Die Niedrigdosis-Radiotherapie von benignen schmerzhaften degenerativen Skeletterkrankungen ist bei der Mehrheit der Patienten effektiv im Sinne einer Schmerzlinderung und ist daher insbesondere für Patienten, bei denen andere konservative Verfahren ohne Einsatz ionisierender Strahlung zu keiner anhaltenden Verbesserung der Schmerzsymptomatik geführt haben, eine gut begründbare therapeutische Alternative. Empfohlen wird die Durchführung der Bestrahlung mit Fraktionsdosen von 0,5–1,0 Gy bis zu Gesamtdosen von 3,0–6,0 Gy/Bestrahlungsserie sowie 2–3 Fraktionen pro Woche.

**Schlüsselwörter** Enthesiopathie · Schmerzhafte Arthrose · Gutartige degenerative Erkrankung · Niedrigdosis-Strahlentherapie · S2e-Leitlinie

Low-dose radiotherapy has been proven to be an effective tool in the treatment of painful degenerative skeletal disorders. This overview reports on the role of low-dose radiotherapy in the treatment of enthesiopathies (shoulder syndrome, trochanteric bursitis, plantar fasciitis, and elbow syndrome) and painful arthrosis (knee, hip, hand, and finger joints).

Enthesiopathies are usually described as painful degenerative disorders of the connective tissue located at specific tendon insertion areas of bones with some involvement of nearby soft tissues, e.g., tendons and bursae. Prevalence rates range from 1–10 % of the population. Enthesiopathies usually occur between the 4th and 6th decade and in most entities women are more frequently affected. Pathogenetic hypotheses are generally based on the assumption that mechanical overstressing, cyclic, repetitive, and intense movements with eccentric exposure will lead to submicroscopic structural damages with accompanying inflammatory, inflammatory–degenerative, degenerative, or microtraumatic changes [8]. The characteristic symptom is a localized load-dependent pain at the involved insertion area [21], which in some cases may spread in the distal or proximal direction [1]. The clinical examination should include inspection and palpation, and further functional tests if appropriate. Visible external signs of inflammation, motoric or sensible deficits, or perfusion disturbances are usually not associated with enthesiopathies.

Arthrosis is defined as a chronic, degenerative disorder of unknown cause characterized by a gradual loss of articular cartilage. Also involved in the disorder are joint structures, such as the bones, joint capsule, and near-joint musculature. Arthrosis is the most prevalent disease in Western societies but occurs worldwide. Approximately 10–15 % of adults over 60 years of age have some degree of arthrosis, and with an aging population it is becoming an increasingly important disease. Potential causes of arthrosis are mechanical overstressing and imbalance, acquired injuries, chronic arthropathies, congenital malformations, rheumatoid and bacterial arthritis, and others. The clinical lead symptom is pain during physical strain. Persistent pain at rest or during the night might be a sign of a more advanced stage of disease. The clinical examination should include inspection and palpation, joint mobility assessment, and further functional tests if necessary.

For all painful degenerative disorders, conventional X-ray diagnostic is routinely recommended to detect accidental neoplastic processes [2] and in unclear clinical situations additional ultrasound or magnetic resonance imaging (MRI) may be helpful.

More detailed information on all parts of this report including a comprehensive collection of the published data may be found in the complete version of the guideline, which is available at the DEGRO homepage (www.degro.org).

## Non-radiotherapeutic treatment options

A large variety of treatment non-radiotherapeutic options is under ongoing discussion with no clear advantage of a single method: avoidance of mechanical stress, ultrasound or extracorporeal shock wave therapy, iontophoresis, laser therapy, various physiotherapeutic approaches, acupunc-

ture, steroid or hyaluronate injections and oral NSAIDs, Botox injections, surgical interventions up to joint replacement, etc.

## Pain control after low-dose radiotherapy

Although an adequately powered placebo-controlled trial is lacking to formally prove the efficacy of radiotherapy in selected benign degenerative painful diseases and may never be performed due to ethical reasons, a huge body of evidence demonstrates low-dose radiotherapy as a very effective tool in the symptomatic treatment of benign degenerative diseases including enthesiopathies and painful arthrosis, especially in patients who did not persistently benefit from other non-radiation conservative therapies.

### Shoulder syndrome

Response rates (complete and partial response: CR and PR) usually reached 58–100 % 2–3 months after radiotherapy [14, 17]. In 7928 retrospectively evaluated patients, Heyd et al. [6] reported response rates of 55 % with CR, and 33 % with PR; 12 % of the patients did not benefit. Early treatment less than 6 months after onset of pain seemed to be more effective than with chronic pain. Data about a higher success rate for patients with calcifications were inconsistent.

### Elbow syndrome

Between 1923 and 2011, the outcome after low-dose radiotherapy for elbow syndrome had been reported in more than 2000 patients within 22 retrospective and prospective analyses. Approximately 82 % of the patients experienced significant pain reduction. The CR and PR rates were 45 % (range 5–94 %) and 35 % (range 7–73 %) [13].

### Trochanteric bursitis

Glatzel et al. [3] reported on 34 patients who were treated with total doses of 6 Gy in single fractions of 1.0 Gy. After 3 months, 38 % had a CR, and 18 % had a PR. Olschewski and Klein [12] reported on another 26 patients. They found an overall response rate of 73 %, with 23 % CR and 50 % PR rates.

### Plantar fasciitis

Retrospective analyses reported on CR rates in 12–81 %, and PR rates in 7–74 % [9, 15, 18]. In a randomized trial, Heyd et al. [7] randomly compared two dose regimens: 3.0 Gy/0.5 Gy vs. 6.0 Gy/1.0 Gy in 130 patients. Radiotherapy led to a highly significant reduction of pain symptoms in both groups, and the lower dose regimen was equally effective. In another randomized trial Niewald et al. [11] evaluated the efficacy of two other dose concepts in 62 evaluable patients: 6.0 Gy/1.0 Gy vs. 0.6 Gy/0.1 Gy. After one year, compared to the very low-dose arm the higher-dose arm led to a significant advantage in terms of pain control.

### Gonarthrosis

Low-dose radiotherapy is an effective therapeutic option for painful Kellgren stage 2–3 arthrosis of the knee joint and can be recommended even if surgical interventions are not possible or desirable or if other conservative treatment methods are associated with excessive side effects or contraindicated. The results from 10,046 patients treated with low-dose radiotherapy for painful arthrosis of the knee joint have been published. Of these patients, 5069 were surveyed within the framework of a German patterns of care study performed in 2010 [10]. A response to radiation therapy in terms of a marked and complete reduction of pain was shown in 58–91 % of the irradiated patients.

### Coxarthrosis

Considering the results of the retrospective studies, low-dose radiotherapy may be an effective therapeutic option for painful Kellgren stage 2–4 arthrosis of the hip joint, even if surgical interventions are not possible or desirable, or if other conservative treatment methods are associated with excessive side effects or contraindicated. The results from 895 patients treated with low-dose radiotherapy for painful arthrosis of the hip joint have been published. A response to radiation therapy in terms of a marked and complete reduction of pain was shown in 24–89 % of the irradiated patients [19].

### Arthrosis of the hand and finger joints

Considering the results of the retrospective studies, low-dose radiotherapy may be an effective therapeutic option for painful arthrosis of the hand and finger joints, even if other conservative treatment methods are associated with excessive side effects or contraindicated. The results from 809 patients treated with low-dose radiotherapy for painful arthrosis of the hand and finger joints have been published. A response to radiation therapy in terms of a marked and complete reduction of pain was shown in 63–75 % of the irradiated patients [4].

## Current recommendations on radiotherapy

### General recommendations

Because of general radiation protection considerations radiotherapy should be recommended if non-radiotherapeutic approaches did not succeed [5, 20]. Furthermore, patients <40 years should be irradiated in very exceptional cases and after careful evaluation of the potential risk versus the expected benefit. Orthovoltage or megavoltage techniques may be applied. Generally, the target volumes for enthesiopathies should encompass the complete involved insertion area together with the nearby bony and muscular tissues, and for painful arthrosis the target volumes must include the articular cartilage, the nearby bony structures, the entire synovia, the surrounding muscles, and the periarticular connective tissue, as well. In case of persisting pain or insufficient pain relief 6–12 weeks after radiotherapy, a second series may be recommended [13, 16]. Radiotherapy recommendations were summarized in Table 1 including the Oxford Level of Evidence (LoE) and the Grade of Recommendation (GR).

### Shoulder syndrome

The target volume comprises the whole shoulder joint including the nearby bone and muscular structures; lung and female breast should be spared. In case of exclusive acromioclavicular pain a more limited volume may be treated. If a linear accelerator is used, an opposing field technique should be applied with 6 MV photons. Orthovoltage technique is usually performed with two opposing fields (ventrodorsal and dorsoventral) directly positioned on the painful shoulder covering the whole joint. Single doses of 0.5–1 Gy up to total doses of 3–6 Gy/series should be applied 2–3 times a week.

**Table 1** DEGRO guideline recommendations for the radiotherapy of painful degenerative skeletal disorders

| Skeletal disorder | Total doses/ series [Gy] | Single doses/ fraction [Gy] | Frequency of fractions | LoE | GR |
|---|---|---|---|---|---|
| Shoulder syndrome | 3.0–6.0 | 0.5–1.0 | 2–3/week | 4 | C |
| Elbow syndrome | 3.0–6.0 | 0.5–1.0 | 2–3/week | 2c | B |
| Trochanteric bursitis | 3.0–6.0 | 0.5–1.0 | 2–3/week | 4 | C |
| Plantar fasciitis | 3.0–6.0 | 0.5–1.0 | 2–3/week | 1b | A |
| Gonarthrosis | 3.0–6.0 | 0.5–1.0 | 2–3/week | 2c | B |
| Coxarthrosis | 3.0–6.0 | 0.5–1.0 | 2–3/week | 4 | C |
| Hand and finger joint arthrosis | 3.0–6.0 | 0.5–1.0 | 2–3/week | 4 | C |

*Gy* Gray, *LoE* Oxford Level of Evidence, *GR* Grade of Recommendation

### Elbow syndrome

The target volume should encompass the complete lateral or medial epicondyle together with the nearby bony and muscular tissues. Using Orthovolt therapy, usually a single field is clinically positioned over the medial or lateral epicondyle. At the linear accelerator, usually two orthogonal fields with low photon beam energy are used or a single field with electrons of appropriate energy. The reference point is determined on the central beam with a half joint diameter in tissue depth. Single fraction doses of 0.5–1.0 Gy are recommended, with total doses of 3.0–6.0 Gy/series with 2–3 fractions per week.

### Trochanteric bursitis

The target volume should include the superficial and deep, primary and secondary bursae of the gluteus maximus region. If a linear accelerator is used, ventrodorsal parallel opposing portals should be applied with 6–10 MV photons. Using Orthovolt therapy, usually a single field is positioned at the most painful pressure point (clinical examination) above the trochanter major region. Like in other degenerative diseases, single doses of 0.5–1 Gy up to total doses of 3–6 Gy should be applied 2–3 times per week.

### Plantar fasciitis

Orthovoltage therapy or megavoltage therapy may be used. In the former, bolus material is recommended to be attached to the edge of the heel in order to avoid local underdosage. The reference point should be in a constant tissue depth. In the latter, 4–6 MV photons of a linear accelerator should be used, applying lateral opposing portals, and the reference point should be in the midpoint of the heel. A total dose in the range of 3–6 Gy is recommended, applied in 2–3 single fractions a week of 0.5–1.0 Gy.

### Gonarthrosis

The target volumes for painful knee joint arthrosis must include the articular cartilage, the nearby bony structures, the entire synovia, the surrounding muscles, and the periarticular connective tissue as well. Two opposed ventro-dorsal or lateral fields offer reliable distribution in the target volume. The dosage has to be determined at a uniform depth (e.g., middle of the knee joint). Appropriate radiation energy should be selected depending on the diameter of the joint. Single doses of 0.5–1.0 Gy and total doses of 3.0–6.0 Gy/series with 2–3 fractions per week are recommended.

Coxarthrosis

The target volumes for painful hip joint arthrosis must include the articular cartilage, the nearby bony structures, the entire synovia, the surrounding muscles, and the periarticular connective tissue as well. Two opposed ventro-dorsal fields offer a reliable distribution in the target volume. The dosage has to be determined at a uniform depth (e.g., middle of the hip joint). Appropriate radiation energy should be selected depending on the diameter of the joint. Single doses of 0.5–1.0 Gy, total doses of 3.0–6.0 Gy/series with 2–3 fractions per week are recommended. Radiation protection measures for the gonads are recommended.

Arthrosis of the hand and finger joints

The target volumes for painful hand and finger joints arthrosis must include the articular cartilage, the nearby bony structures, the entire synovia, the surrounding muscles, and the periarticular connective tissue of the involved joints. One dorsal or ventral field offers a reliable distribution in the target volume. The dosage has to be determined at a uniform depth (e.g., middle of the joint). Appropriate radiation energy should be selected depending on the diameter of the joint. Single doses of 0.5–1.0 Gy and total doses of 3.0–6.0 Gy/series, and 2–3 fractions per week are recommended. Radiation protection measures for the nails are recommended.

Treatment response evaluation

Success rates for pain relief and freedom of pain should be assessed 2–3 months after radiotherapy because of delayed response effects. Symptomatic outcome should be graded according to the classification published by von Pannewitz [22, 23] and/or conventional visual analogue scales.

## Summary

In all indications mentioned above, retrospective and some prospective analyses have shown a remarkable effect in terms of pain relief. Nevertheless, the Level of Evidence (LoE) and the Grade of Recommendation (GR) vary: LoE 1b–4 and GR A–C. In summary, low-dose radiotherapy for painful degenerative skeletal disorders is effective in the majority of the patients and therefore it may be a reasonable therapeutic alternative when simple and non-invasive methods have been used without persistent success. Considering general radiation protection recommendations patients should be aged >40 years, and the duration of the pain history should exceed 3 months to exclude self-limiting acute disorders. For all discussed entities single fraction doses of 0.5–1.0 Gy, and total doses of 3.0–6.0 Gy/series applied with 2–3 fractions per week are recommended.

## Compliance with ethical guidelines

**Conflict of interest** Oliver J. Ott, Marcus Niewald, Hajo-Dirk Weitmann, Ingrid Jacob, Irenaeus A. Adamietz, Ulrich Schaefer, Ludwig Keilholz, Reinhard Heyd, and Ralph Muecke state that there are no conflicts of interest. The accompanying manuscript does not include studies on humans or animals.

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