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## GUIDELINES & RECOMMENDATIONS

# Radiotherapy CT-based contouring atlas for non-malignant skeletal and soft tissue disorders: a practical proposal from Spanish experience

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**Objective:** Interest in low-dose radiotherapy (LD-RT) for the symptomatic treatment of nonmalignant conditions, including inflammatory and degenerative disorders of the joints and para-articular soft tissues, has increased substantially in recent years. In the present document, we provide a CT-based contouring atlas to help identify and delineate the most common osteoarticular regions susceptible to LD-RT.

**Methods:** The clinical efficacy of LD-RT is supported by a large body of evidence. However, there is no consensus on the parameters for contouring the planning target volume (PTV). Moreover, 3D simulation and planning should be the standard of care even for nonmalignant disorders. For this reason, the present guidelines were prepared to help guide PTV contouring based on CT images, with the same quality criteria for patient immobilization, treatment simulation, planning and delivery as those routinely applied for cancer radiotherapy.

**Results:** PTV for radiotherapy requires precise identification of the target areas based on CT and other imaging techniques. Using a series of cases treated at our institution, we have defined the PTVs for each location on the simulation CT to establish the relationship between the image and the anatomical structures to be treated. We also specify the immobilization systems used to ensure treatment accuracy and reproducibility.

**Conclusions:** This comprehensive atlas based on CT images may be of value to radiation oncologists who wish to use LD-RT for the symptomatic treatment of degenerative or inflammatory osteoarticular diseases.

**Advances in knowledge:** The recommendations and contouring atlas described in this article provide an eminently practical tool for LD-RT in non-malignant conditions, based on the same quality criteria recommended for all modern radiotherapy treatments in Spain.

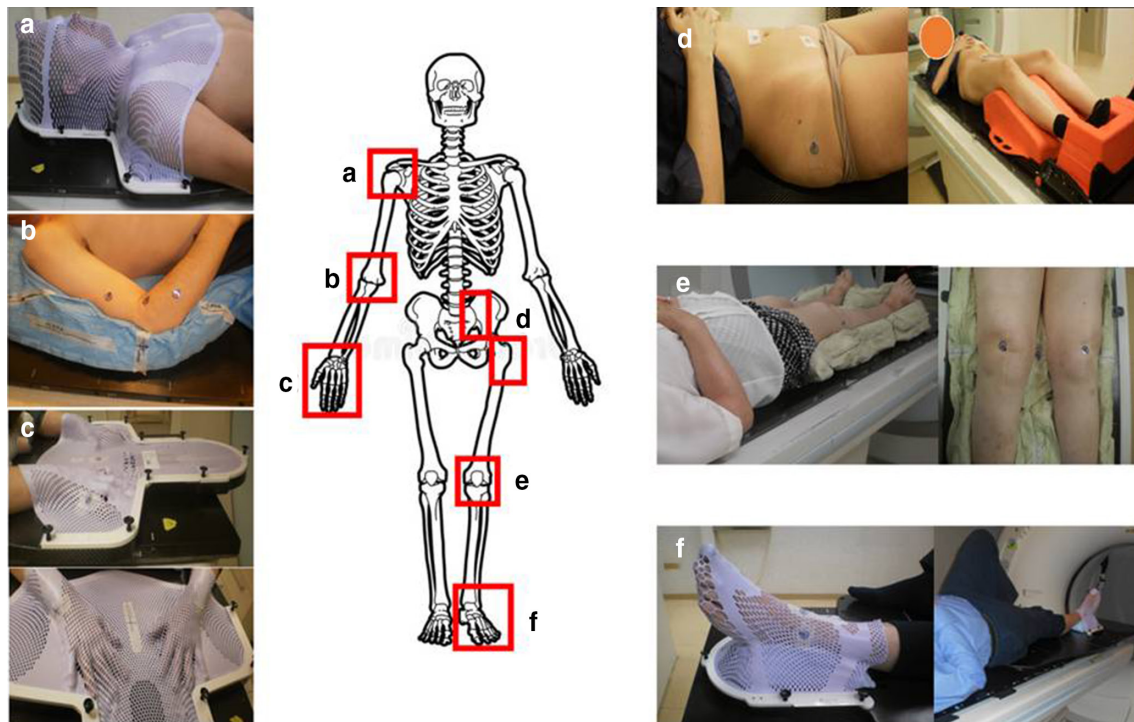
## BACKGROUND

Degenerative disorders of the joints and para-articular soft tissues are an important challenge for developed countries. It is estimated that nearly one-fourth of the general adult population in high-income countries suffers from osteoarthritis—including 10% of males and 18% of females over age 60. Osteoarthritis is a painful condition that causes stiffness and thus negatively impacts the individual's ability to perform many activities of daily living. Due to population ageing in the developed world, the prevalence of degenerative osteoarticular diseases continues to rise, leading to increasing disability, which is associated with high social

and economic costs. A recent report by the World Health Organisation (WHO) stated that osteoarthritis would be the fourth leading cause of disability by the year 2020.<sup>1</sup>

Available treatments, both pharmacological and non-pharmacological, have only a limited efficacy that commonly decreases over time. Common conservative measures include weight loss, moderate exercise and physical rehabilitation (local heat, magnetic therapy, shock waves, etc.). Analgesics and non-steroidal anti-inflammatory drugs (NSAIDs), SYSADOAs (symptomatic slow acting drugs for osteoarthritis), corticosteroids, anaesthetics and other local

Figure 1. Immobilization procedure for LD-RT of shoulder (a), elbow (b), hand (c), pelvis and hip (d), knee (e) and foot and ankle (f).



injections, have also been proposed for symptom relief. However, many patients will eventually require prosthetic replacement of the damaged joint, which requires surgery followed by a long rehabilitation process that is often not well tolerated by patients. Moreover, none of the available surgical or pharmacological treatments are without possible side-effects (e.g. gastrointestinal bleeding, kidney disorders, cardiac disorders, etc.), some of which can be severe and even compromise the patient's life.<sup>2</sup> For this reason, many groups have investigated affordable therapeutic alternatives, especially among the elderly in whom comorbidities and polypharmacy are common.<sup>3</sup>

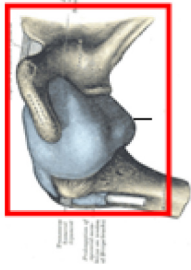
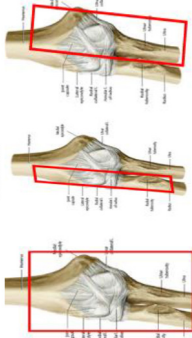
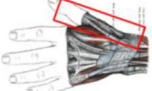

Radiotherapy is a non-invasive treatment that does not interfere with other treatments commonly offered to elderly patients. The effectiveness of radiotherapy for pain relief and improved functionality was demonstrated decades ago. Although there still exist some concerns about the risk of low-dose radiotherapy (LD-RT) to induce cancer, these fears are largely unfounded. Published data show that the risk of induced cancer is low—ranging from 0.5 to 40 cases per 1000 treatments—and up to three times lower for elderly patients.<sup>4–8</sup> In Germany, approximately 10–30% of daily activity at most radiation oncology departments involves radiotherapy for non-malignant conditions.<sup>9</sup> Moreover, in recent years, several medical associations have published clinical guidelines and recommendations for the use of radiotherapy for the treatment of non-malignant conditions, including the German Radiation Oncology Society (DEGRO) in Germany and the Royal College of Radiologists (RCR) in the United Kingdom.<sup>10–14</sup>

Ionizing radiation has long been used to treat cancer and other conditions. Due to technological advances, radiotherapy

is constantly improving and becoming safer and more effective. Naturally, treatment planning and delivery has changed as newer technologies become available. While there is a clear emphasis on offering safe and effective radiotherapy for the treatment of cancer, it is important to apply the same criteria to the treatment of non-malignant conditions. In other words, the simulation, planning procedure documentation, radiotherapy administration and subsequent monitoring processes for non-malignant diseases must be applied with the same requirements and quality control as those used in the treatment of cancer.<sup>9,10,15,16</sup> Similarly, the volume to be irradiated (planning target volume [PTV]) should be carefully contoured using the planning computed tomography (CT) scan and any other images that are necessary, such as magnetic resonance imaging (MRI) and/or ultrasound, which may help to identify soft tissue involvement.

Although general guidelines are available for the indications and basic contouring recommendations for radiotherapy of benign diseases,<sup>17</sup> most of the series published to date did not use simulation techniques based on CT images or three-dimensional (3D) planning. We have developed a CT-based anatomical atlas to fill this gap and to allow radiation oncologists to easily identify the target volume at each location, but always keeping in mind that these recommendations should be taken exclusively as an expression of the usual practice in our department. Our clinical protocols contemplate the use of similar procedures for the simulation, planning and treatment of both oncological pathology and benign diseases. However, we are aware that CT planning could be safely omitted for reasons of radiation protection when referring to the radiation treatment of small joints of

Table 1. Proposed limits of PTV for different osteoarticular locations

	SUPERIOR	INFERIOR	MEDIAL	LATERAL	PROXIMAL	DISTAL
<p><b>SHOULDER</b></p> 	<p>POST: 1 cm above acromion ANT: coracoid process</p>	<p>1.5 cm under lesser tubercle</p>	<p>POST: 1.5 cm scapula ANT: 1.5 cm clavicle</p>	<p>Lateral side-of humeral head, neck and epiphysis and 1 cm of surrounding soft tissues</p>		
<p><b>ELBOW</b></p> 	<p>1.5 cm above trochlea and capitellum</p>	<p>1.5 cm below radial and ulnar tuberosities</p>	<p>1.5 cm around bone edges into surrounding soft tissues</p>	<p>1.5 cm around bone edges into surrounding soft tissues</p>		
<p><b>RHIZARTHROSIS</b></p> 			<p>1 cm around of the soft tissues surrounding the bones</p>	<p>1 cm around of the soft tissues surrounding the bones</p>	<p>Half of the metacarpal bone, the joint with the trapezoid bone and 1 cm through the radial bone</p>	<p>Proximal third of the distal phalanx</p>
<p><b>FINGERS 2-5</b></p> 	<p>2 mm inside the dorsal skin</p>	<p>2 mm inside the ventral skin</p>	<p>1 cm around of the soft tissues surrounding</p>	<p>1 cm around of the soft tissues surrounding</p>	<ul style="list-style-type: none"> <li>Distal third of the most proximal phalanx (arthrosis)</li> <li>Common synovia vaina (Flex-tendinosis)</li> <li>Beginning of corresponding bursa leaning on the ulna and radius (Exten-tendinosis)</li> </ul>	<ul style="list-style-type: none"> <li>Proximal third of the most distal phalanx (arthrosis)</li> <li>Distal phalanx (Flex-tendinosis)</li> <li>Distal or proximal phalanx (Exten-tendinosis)</li> </ul>

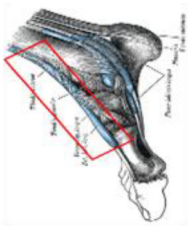
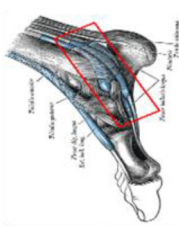
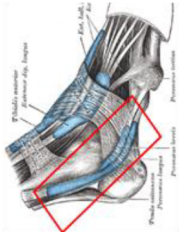
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Table 1. (Continued)

	SUPERIOR	INFERIOR	MEDIAL	LATERAL	PROXIMAL	DISTAL
<p><b>SACROILIAC</b></p> 	1 cm above sacroiliac joint	1 cm below sacroiliac joint	1 cm into sacral bone	1 cm into iliac bone		
<p><b>TROCHANTERITIS</b></p> 	Trochanter, femoral head and neck	Below lesser trochanter	1 cm around of the soft tissues surrounding	1 cm around of the soft tissues surrounding		
<p><b>KNEE</b></p> 	2 cm above femoral condyles	2 cm below tibial condyles and fibula head	1 cm around of the soft tissues surrounding	1 cm around of the soft tissues surrounding	1 cm above lateral and medial femoral epicondyle	Lateral and medial tibial condyles and fibula head
<p><b>PLANTAR FASCIA</b></p> 			1 cm around of the soft tissues surrounding	1 cm around of the soft tissues surrounding	Metacarpal-phalanx joint	Calcaneus tuberosity
<p><b>ACHILLES TENDON</b></p> 			1 cm around the tendon	1 cm around the tendon	Lateral and medial malleolus	Calcaneus tuberosity, subcutaneous calcaneus bursa, submuscular calcaneus bursa

(Continued)

Table 1. (Continued)

	SUPERIOR	INFERIOR	MEDIAL	LATERAL	PROXIMAL	DISTAL
 <p>T.A. + F.T</p>			1 cm around the tendon	1 cm around the tendon	2 cm above medial malleolus	<ul style="list-style-type: none"> <li>Plantar side of first metacarpal and first cuneiform bone (insertion of the T.A.)</li> <li>Plantar side of distal phalanges (insertion of F.T.)</li> </ul>
 <p>T.P. + E.T</p>			1 cm around the tendon	1 cm around the tendon	2 cm above lateral malleolus	<ul style="list-style-type: none"> <li>Plantar side of second, third, fourth metacarpal and second, 3<sup>rd</sup> cuneiform bones (insertion of the T.P.)</li> <li>Dorsal side of distal phalanges (insertion of E.T.)</li> </ul>
 <p>PERONEUS MUSCLES</p>			1 cm around the tendon	1 cm around the tendon	2 cm above lateral malleolus	<ul style="list-style-type: none"> <li>fifth metatarsal bone, lateral side.</li> </ul>

E.T, Extensor tendons of the toes; F.T, Flexor tendons of the toes; T.A, Tibialis anterior; T.P, Tibialis posterior.



the hands, feet, elbows, or heels, since the irradiation region can be adequately defined clinically.

## METHODS AND MATERIALS

Joints are complex structures that allow movement between different parts of the body. Diverse tissues and structures such as cartilage, synovial membrane, tendons, fascia, and bursas all play important roles in joint function. Damage to any of these structures can lead to inflammation and/or pain. Depending on the damaged structure, numerous conditions can develop, including arthritis (damage to the articular cartilage), inflammatory conditions such as bursitis (inflammation of the bursa), synovitis (inflammation of the cell layer that lines the tendons), tendonitis (inflamed tendons), and fasciitis (involvement of fascia, especially the plantar fascia).

Target volumes for these disorders should include the entire joint and articular cartilage, the specific joint capsule, the neighbouring bone and/or muscular insertion zone, and the peritendinous bursae and surrounding soft-tissue structures.<sup>15</sup>

In the present document, we have reviewed the most common osteoarticular diseases treated at our institution and defined the PTV for each condition on a cross-sectional CT scan. Following our department protocols, in all cases, the immobilization procedure for treatment was the same applied in cancer radiotherapy, using vacuum mattresses and custom thermoplastic masks or commercially available immobilizers (Figure 1). For each treatment location, we present a CT study, highlighting in the 3D reconstruction the PTV defined in each CTslice as well as its anatomical correlation on anatomical illustrations from Gray's *Anatomy of the Human Body*.<sup>18</sup>

Table 1 summarizes the proposed PTV definitions for the osteoarticular locations evaluated.

### Shoulder

The shoulder includes the acromioclavicular joint between the acromion and the clavicle, and the glenohumeral joint, which involves articulation between the glenoid cavity of the scapula and the humeral head. Shoulder osteoarthritis affects approximately 30% of the elderly population.<sup>19</sup>

After radiotherapy for benign shoulder conditions, reported improvement rates in terms of reduced pain and increased shoulder mobility range from 37 to 56% immediately after treatment, rising to 73 to 85% during follow-up (up to three years in some studies).<sup>20–24</sup> However, it is important to note that the radiation technique applied in most of these studies was either direct apposition of orthovoltage fields or simple two-dimensional (2D) planning with  $10 \times 10/12 \times 12/10 \times 15 \text{ cm}^2$  or rectangular fields that completely encompassed the shoulder joint with two beam angles (anteroposterior and posteroanterior). Very few of those studies used CT images for simulation.

Painful shoulder syndrome is a set of progressive conditions that progress from one to the next, including subacromial impingement, shoulder capsulitis, biceps longus tendinitis or rotator cuff

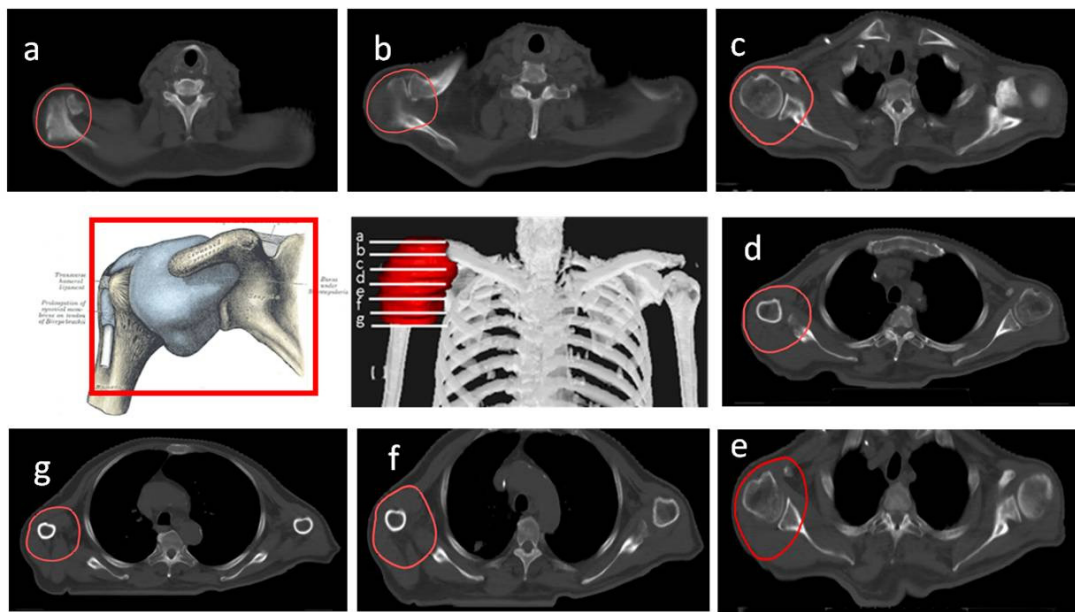
tendinitis, and true degenerative arthrosis of the acromioclavicular or glenohumeral joints. However, in most cases, there are two or more overlapping conditions present at the same time,<sup>25</sup> which is why the DEGRO recommends using the same PTV to encompass the entire shoulder joint and adjacent bony and muscular structures (acromion, glenohumeral joint, and the coracoid process; acromioclavicular ligament, coraco-acromial ligament, coraco-humeral ligament, transverse ligament and the superior-middle-inferior glenohumeral ligaments). The synovial bursae located around the shoulder should also be included. These bursae include the following: subacromial-subdeltoid (between the joint capsule and the deltoid muscle), subacromial (between the capsule and the acromion), subcoracoid (between the capsule and the coracoid process of the scapula), coracobrachial (between the subscapularis muscle and the tendon of the coracobrachialis muscle), subscapular (between the capsule and the tendon of the subscapularis muscle), and the supra acromial bursa. The tendons that should be included are those that attach to the muscles (teres minor, infraspinous, subscapular and supraspinous) and to the origin of the deltoid, the long head of the biceps brachii muscle, trapezius insertion, pectoralis minor insertion and short head of the biceps brachii muscle. (Figure 2)<sup>17</sup>

### Elbow

The distal humerus and proximal ulna and radius form the elbow joint connecting the upper arm to the forearm to allow for flexion/extension of the forearm. Chronic pain at the lateral epicondyle of the elbow is known as lateral epicondylitis or “tennis elbow”, while pain at the medial epicondyle is known as epicondylitis or “golfer’s elbow”, both of which are relatively common conditions estimated to affect from 1 to 3% of the population.<sup>26</sup> These painful conditions are associated with chronic pathologic changes in tendon origins, although the underlying causes remain unclear. Reported pain relief rates achieved with LD-RT for tennis or golfer’s elbow range from 51 to 98%.<sup>27–30</sup> Recently, Hautmann et al<sup>30</sup> comprehensively reviewed the available evidence to assess the efficacy of radiation to relieve epicondylitis humeri (EPH)-related pain, finding a mean response rate of 80%. However, as those authors observed, these findings must be interpreted cautiously given the important methodological differences in the studies included in the review, such as differences in radiotherapy techniques and the time period when they were carried out. As in other joint locations, definition of the target volumes for EPH treatment, administered with either orthovoltage or a linear accelerator, was based on the physician’s experience and clinical examination. Generally, a single portal arrangement or two opposing rectangular fields ( $6 \times 8 \text{ cm}$ ) were used.

In cases with elbow joint arthrosis, the PTV may include the whole joint and its capsule (2 cm proximally and 3 cm distally). The PTV for radial epicondylitis (tennis elbow syndrome) should include 1–2 cm above the lateral humeral epicondyle, including its trochlea and condyle, the radius head, neck and tuberosity plus 1 cm distally; and for ulnar epicondylitis (golfer elbow syndrome), the PTV should include 1–2 cm above the medial epicondyle, the ulna olecranon process, ulna coronoid process and its tuberosity, plus 1 cm distally. In terms of soft tissue, the

Figure 2. CT-based PTV contouring for painful shoulder syndrome (a-h).



following should be included: synovial bursae around the olecranon (superficial, subtendinous and intratendinous bursae) or the cubital fossa (bicipitoradial and interosseous bursae), ligaments (articular capsule, and the lateral, collateral, radial collateral, annular, accessory collateral and ulnar collateral ligaments) and tendon insertions in the area. (Figure 3a–c).

### Wrist, Hand and Fingers

The hand has numerous joints, including the distal radioulnar joint, radiocarpal joint, midcarpal joint, carpometacarpal joints and thumb and finger joints, which allow mobility of the hand and fingers. Osteoarthritis of the hand and fingers is one of the leading causes of disability worldwide. This condition affects both hand strength and function, thus leading to disability in activities of daily living. The overall prevalence of hand osteoarthritis is estimated to be 43.3%.<sup>31,32</sup> LD-RT has been reported to provide pain relief in 56–90% of patients while also achieving a significant improvement in functionality and mobility. LD-RT appears to provide better pain relief in cases with thumb involvement (osteoarthritis at the base of the thumb) compared to cases involving the second to fifth fingers.<sup>33–36</sup> In addition to osteoarthritis of the thumb and fingers, other inflammatory disorders

likely to benefit from LD-RT are tendonitis and tenosynovitis of the hand and wrist, which can develop secondary to overuse, injury, or degenerative arthritis leading to swelling, pain and functional restriction. Trigger digits (stenosing tenosynovitis of the thumb and fingers), flexor and extensor tenosynovitis, and de Quervain disease are the most common clinical presentations.<sup>37</sup>

Although none of the studies published to date have precisely defined the treatment volume beyond the use of  $6 \times 4$  cm or  $6 \times 6$  cm fields, Kaltenborn et al<sup>33</sup> analyzed the differences in symptomatic response to LD-RT, noting a significant improvement when the target volume was expanded (beyond the thumb saddle joint alone) to include the neighbouring thumb joints or the surrounding joints of the carpal bones.

Figures 4–6 illustrate the proposed PTV contouring guidelines according to the specific hand or wrist joint or tendon. For osteoarthritis of the finger joints, the PTV should include the proximal and distal phalanges in the involved joint within 1 cm around the soft tissues in the second to fifth fingers. However, in case of osteoarthritis at the base of the thumb, the proximal limit of the PTV should include half of the metacarpal bone, the joint with

Figure 3. CT-based PTV contouring for painful elbow syndrome (a-j).

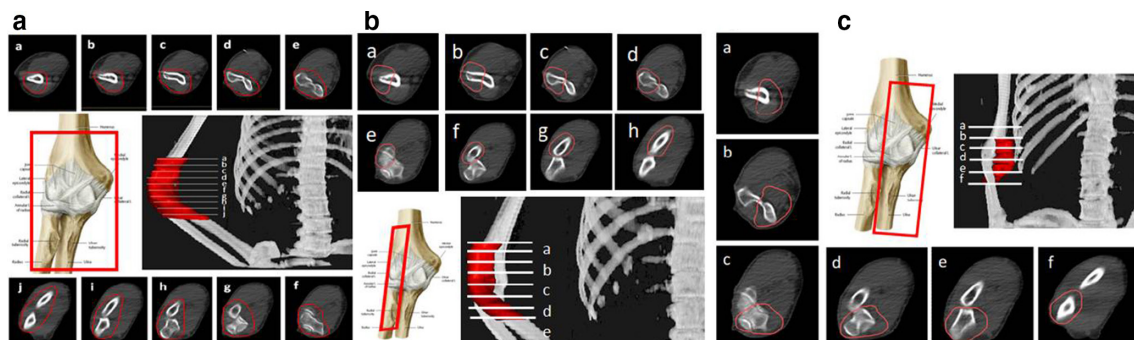


Figure 4. CT-based PTV contouring for second to fifth fingers osteoarthritis (a-i).

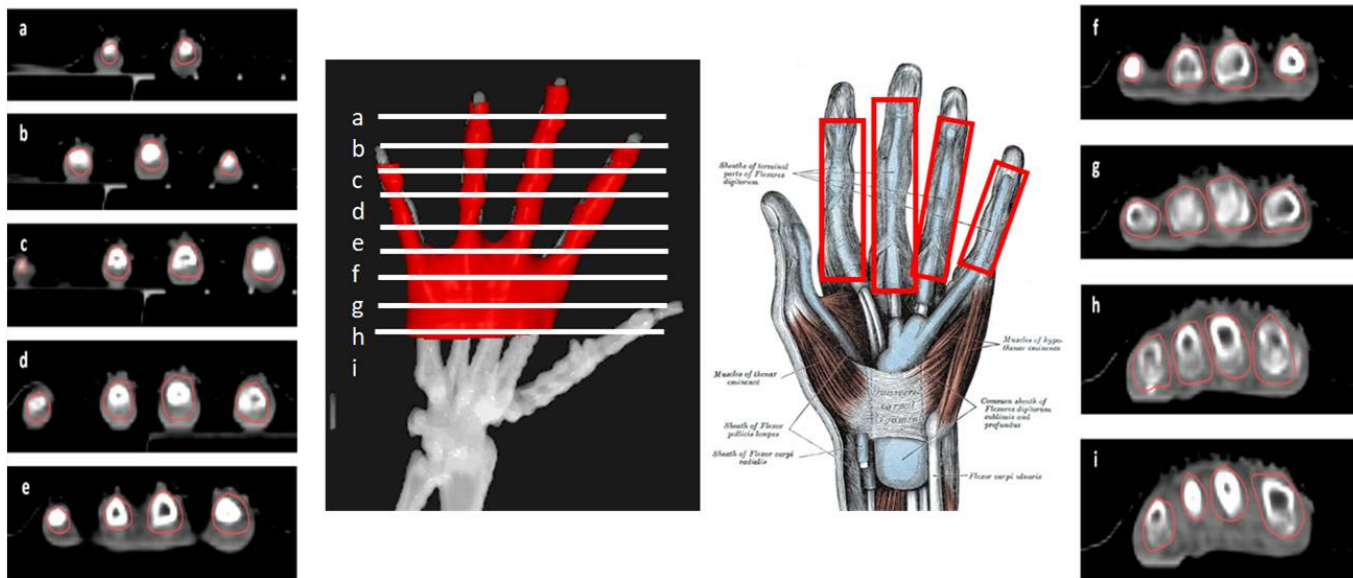


Figure 5. CT-based PTV contouring for thumb osteoarthritis (a-j).

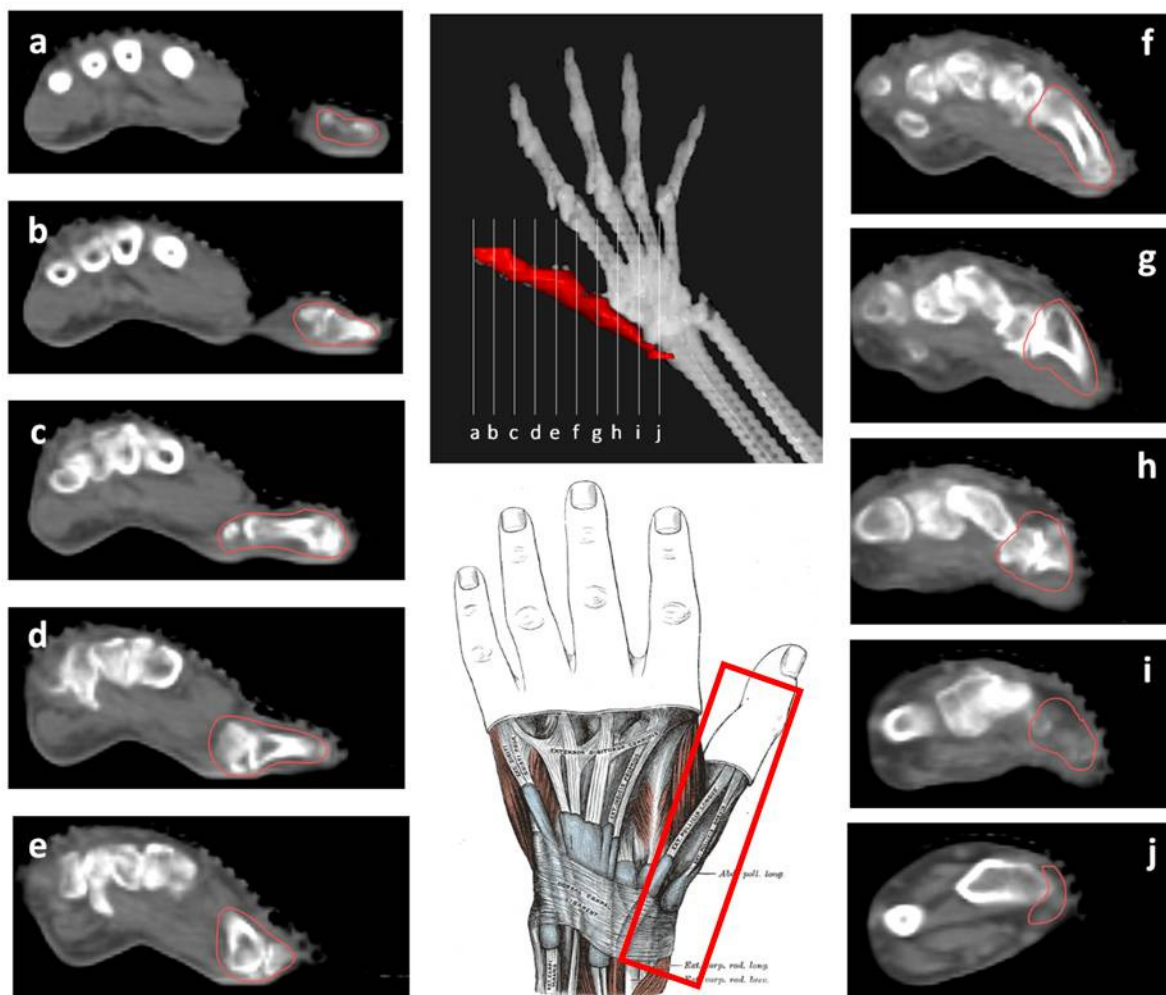
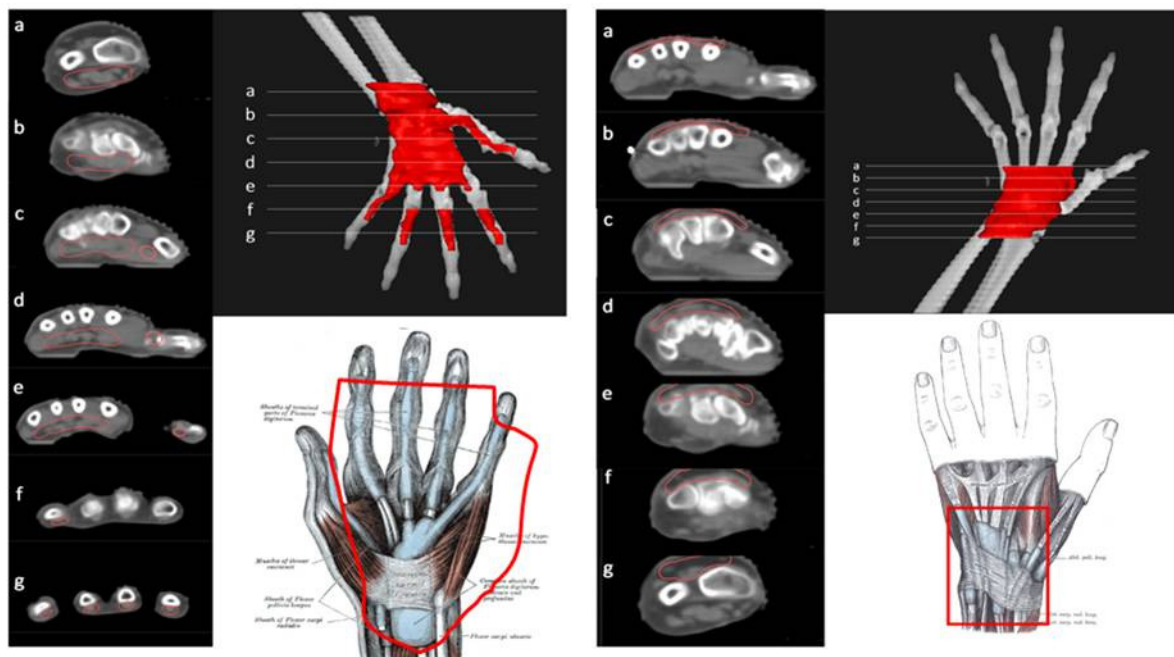




Figure 6. CT-based PTV contouring for flexor tendinitis (left, (a-g) and extensor tendinitis (right, a-g) of the hand.



the trapezoid bone and continue around 1 cm through the radial bone. To avoid damaging the fingernails, the distal segment of the fingers should be excluded.

For the treatment of tendonitis and tenosynovitis, the involved tendon should be included from its distal bone insertion point until the beginning of the corresponding muscle fibres. The PTV should be expanded medially and laterally by 0.5–1 cm around the corresponding bones. The synovial sheaths of the involved tendons should be included as follows: (1) the common synovial sheath (ulnar bursa) for tendons of the flexor digitorum for fingers 2 to 5, and radial bursa for the flexor tendon of thumb from the insertion point in the distal phalanx to the ulna and radius heads, including the whole common synovial sheath or (2) the extensor retinaculum that holds tendons of the extensor digitorum in six different but attached compartments.

If the dosimetric distribution is inhomogeneous, a 5–10 mm bolus material can be placed on top of the hand/fingers.

### Pelvis and Hip

The proximal area of the legs contains three structures that are especially vulnerable to inflammation and pain: the hip joint, the sacroiliac joint (sacroiliitis) and the trochanter (trochanteric bursitis). Sacroiliitis is a painful condition in which one or both sacroiliac joints become inflamed. This condition is often associated with other conditions, such as ankylosing spondylitis, psoriatic spondylo-arthritis, pregnancy, reactive arthritis or ligament involvement. In the general population, the prevalence of sacroiliac disorders of any aetiology is estimated at 1.9%.<sup>38</sup> Clinically, this disorder manifests as inflammatory low back pain that is exacerbated at night and improves with exercise.

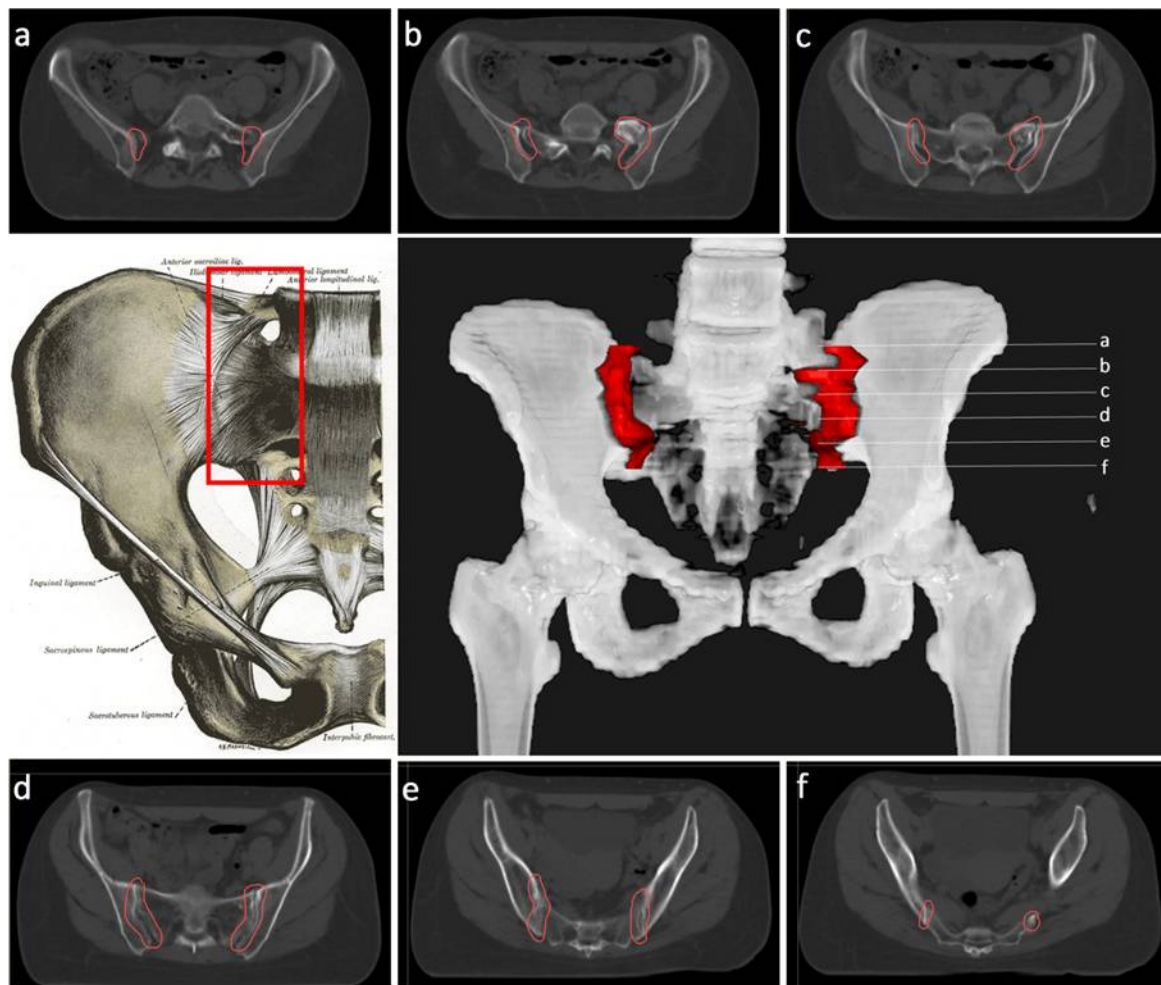
Trochanteric bursitis is defined as the inflammation of any of the bursa around the trochanters, usually the greater trochanter. The pain caused by this condition is also known as meralgia paresthetica, typically occurring when walking up stairs or lying in the lateral position at night. This pain syndrome secondary to trochanteric bursitis affects 15% of females and 6.6% of males.<sup>39</sup> The use of LD-RT to treat trochanteric bursitis has been shown to provide overall pain response rates (partial or total relief) ranging from 46–72%.<sup>40–42</sup>

Coxarthrosis is the consequence of series of events. First, there is a loss of cartilage, then bone spurs form around the joint, and finally, muscle weakness of the extremity appears.

Contrary to the lack of contouring evidence for other joints, several authors describe target volume based on planning CT that includes the trochanteric region and the peritendinous bursae of the great trochanter and femoral neck.

For the treatment of sacroiliitis, the PTV should include the whole joint between the sacral and iliac bones with a margin  $\geq 1$  cm on each side, including the sacroiliac ligaments (Figure 7). To treat greater trochanteric pain syndrome, the PTV should include the existing synovial bursae around the greater trochanter of the femur, as follows: the trochanteric bursa (superficial and posterior to the greater trochanter of the femur and subjacent to the iliotibial band), the gluteus medius bursa (between the gluteus medius muscle and the greater trochanter) and the gluteus minimus bursa (located beneath the gluteus minimus tendon at the anterosuperior edge of the greater trochanter) (Figures 7 and 8). In cases with major inflammation, the gluteus femoral bursa should be included caudally, with a final extension up to

Figure 7. CT-based PTV contouring for sacroiliitis (a-f).



7 cm in the craniocaudal direction. In addition, the musculature surrounding the trochanter must be included.

For the treatment of coxarthrosis, the PTV might include the whole joint between the iliac bone (acetabulum) and the femoral head, and 1 cm distally through the femoral head (Figure 9).

### Knee

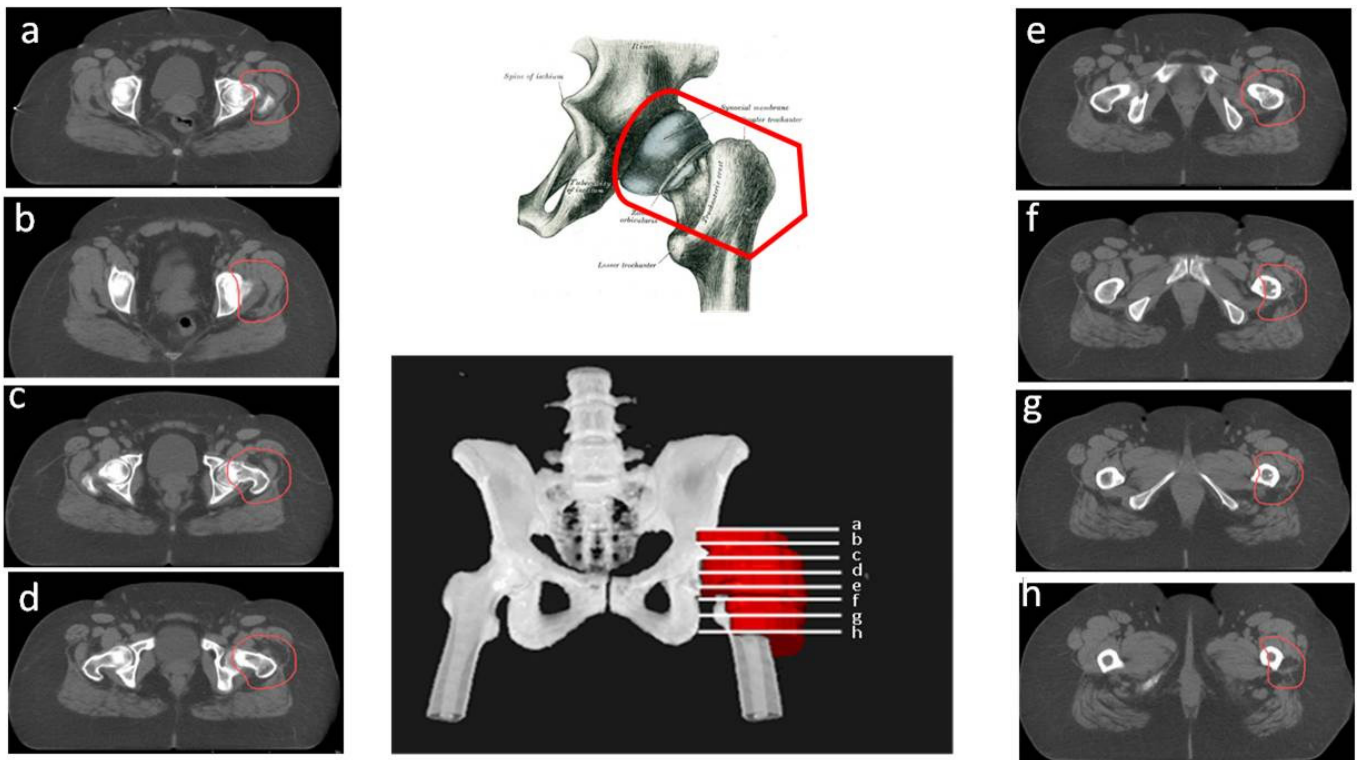
Knee osteoarthritis is estimated to affect 10% of the population over age 55 and up to 40% of people aged 70–74 years.<sup>43,44</sup> Painful gonarthrosis is probably one of the degenerative conditions most refractory to conservative treatment; nevertheless, LD-RT has been shown to achieve pain relief rates ranging from 29 to 49%.<sup>45–48</sup> Most published studies have used either direct ventral and dorsal fields, or lateral and medial fields to plan radiotherapy treatments. Mucke et al<sup>46</sup> evaluated the role of radiotherapy for the treatment of painful gonarthrosis in a national patterns of care study (2006 to 2008) that included 248 German radiotherapy centres.<sup>45</sup> Data were collected on patient accrual, patient numbers, pre-treatment, pain record, treatment indications, RT technique, and target volume concepts. Notably, of the 238 responding centres (96%), only one reported using CT-based 3D planning technique

PTV delineation may include the whole knee joint (lateral and medial supracondylar ridges, capitulum, medial and lateral epicondyles, popliteal fossa, femoral trochlea, lateral and medial tibial condyles, tibial tuberosity, fibula head and the patella bone), the entire synovial capsule and surrounding soft tissues and musculature, including the main knee bursae (prepatellar, infrapatellar [deep and superficial], suprapatellar, Pes Anserine, semimembranosus (popliteal), and the iliotibial and medial collateral ligament bursae). The collateral (lateral and medial) and cruciate tendons (anterior and posterior) in this area can also be considered for inclusion in the PTV. The tendons included are those located at the insertion at the fibula of the biceps femoris, origin of the peroneus longus, proximal third of the extensor digitorum longus, proximal third of the tibialis anterior, sartorius, semitendinosus, and gracilis insertions, medial head of the gastrocnemius, semimembranosus, popliteus, proximal third of the tibialis posterior and origin of the soleus on the fibula head (Figure 10) (Figure 9).

### Foot and ankle

The efficacy of LD-RT to treat calcaneodynia secondary to degenerative irritation of the plantar fascia originating at the medial calcaneal tuberosity of the heel and the surrounding perifascial

Figure 8. CT-based PTV contouring trochanteric bursitis (a-h).



structures is supported by a large body of evidence (Table 2). This syndrome affects approximately 10% of the general population, with prevalence rates among runners as high as 22%.

Plantar fasciitis accounts for 11 to 15% of all foot symptoms in adults.<sup>49,50</sup> Several studies have shown that pain relief rates range from 61–98%.<sup>51–64</sup> In most of these studies, the target volume was determined by physical examination and conventional 2D-simulation. This volume generally covers the calcaneus with plantar aponeurosis, with an additional margin to include the neighbouring areas. However, heterogenous radiation fields have been reported.<sup>53</sup> In our routine clinical practice, we define the field based on CT images encompassing the entire calcaneus, including the insertion points of the plantar fascia and the Achilles tendon. Nonetheless, other groups have suggested a more restrictive approach limited to the painful region with 2 cm margins extending into the neighbouring areas (Figure 10).

In addition to plantar fascia, LD-RT can provide symptomatic relief of other inflammatory lesions affecting the foot and ankle. The Achilles tendon crosses the ankle at its posterior aspect. Achilles tendinopathy is the most common ankle and heel injury, especially in athletes, with an incidence of 2.35 cases per 1000 persons per year in adults aged 20 to 60 years of age.<sup>65</sup> LD-RT provides achillodynia relief in 90–95% of cases.<sup>24,66</sup> Tarsal tunnel syndrome involving the foot arch can occur due to trauma, inflammatory diseases, or to the position of the valgus. In this case, the tendons under the retinacula of the flexors (posterior tibial tendon, flexors tendons) should be included in the PTV (Figure 11.1).

In addition to the Achilles tendon, other tendons located in the medial, lateral and anterior aspects of the ankle and foot may also be affected. These tendons include the tibialis posterior tendons and flexor tendons of the toes (flexor hallucis longus and digitorum brevis), and the peroneus longus and brevis or tibialis anterior and toe extensor tendons (extensor hallucis longus and digitorum brevis). All of these tendons can suffer from overload and inflammation leading to tendonitis, which may benefit from treatment with LD-RT. Although smaller volumes limited to the insertion of the plantar fascia and the calcaneal spur have been proposed by some authors,<sup>51–64</sup> we recommend a PTV that encompasses the entire calcaneus and the region of the plantar aponeurosis, including insertion of the plantar fascia and the Achilles tendon (Figure 10). If the dosimetric distribution is not homogenous, a 5–10 mm bolus can be placed at the top of the Achilles tendon. For the treatment of tendonitis or tenosynovitis of the foot and ankle, the PTV should include the tendons and synovial sheaths appropriate to each anatomic location (Figure 11).

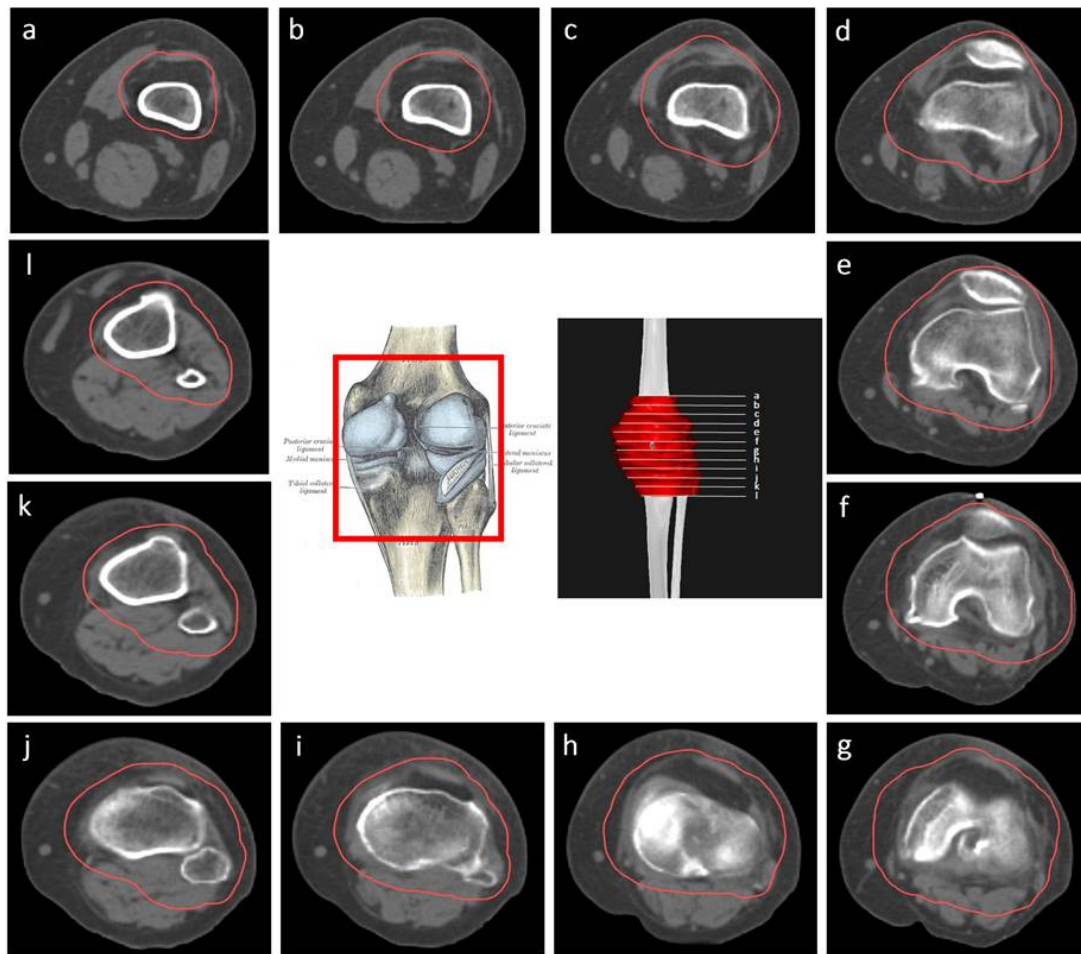
## DISCUSSION

The main objective of this review is to provide the radiation oncologist, when considered necessary, a set of simple tools to define radiotherapy treatment volumes for degenerative disorders of the joints and para-articular soft tissues based on current 3D planning criteria on CT images.

The efficacy of LD-RT for symptomatic relief of non-neoplastic degenerative or inflammatory disorders of joints and para-articular soft tissues has been demonstrated through numerous studies conducted over the past 100 years. However, those



Figure 9. CT-based PTV contouring for knee osteoarthritis (a–l).



studies are highly heterogeneous in terms of the number of patients treated, anatomic locations, total doses, fractionation schedules, treatment volumes, irradiation technique, and methods used to assess response. As a result, it is difficult to draw firm conclusions supported by strong evidence. In fact, many of those studies had only a short follow-up, even although the analgesic effects of LD-RT typically increase over time, thus significantly improving long-term efficacy of LD-RT compared to the immediate post-RT results. In addition, a second course of local irradiation is typically necessary from 10 to 12 weeks after the first treatment for degenerative conditions with inflammation of joints and periarticular soft tissues. A patterns of care study carried out in Germany ( $n = 238$  institutions) to assess the role of LD-RT for symptomatic osteoarthritis showed symptomatic pain relief in 79.5% of patients, although nearly 30% of the 4544 patients required a second course of radiotherapy 6–12 weeks after completion of the first treatment.<sup>16</sup> Table 1 summarizes the results of studies published in the last 20 years (since the year 2000). In this table, we included only studies with at least 50 patients and adequate data about treatment volumes, total dose and fractionation.<sup>20–24,27,30,33–36,40,45–48,51,52,54–64,66</sup> In most of these studies, a key limitation is the lack of a control group, which is important as the placebo effect cannot be ruled out.

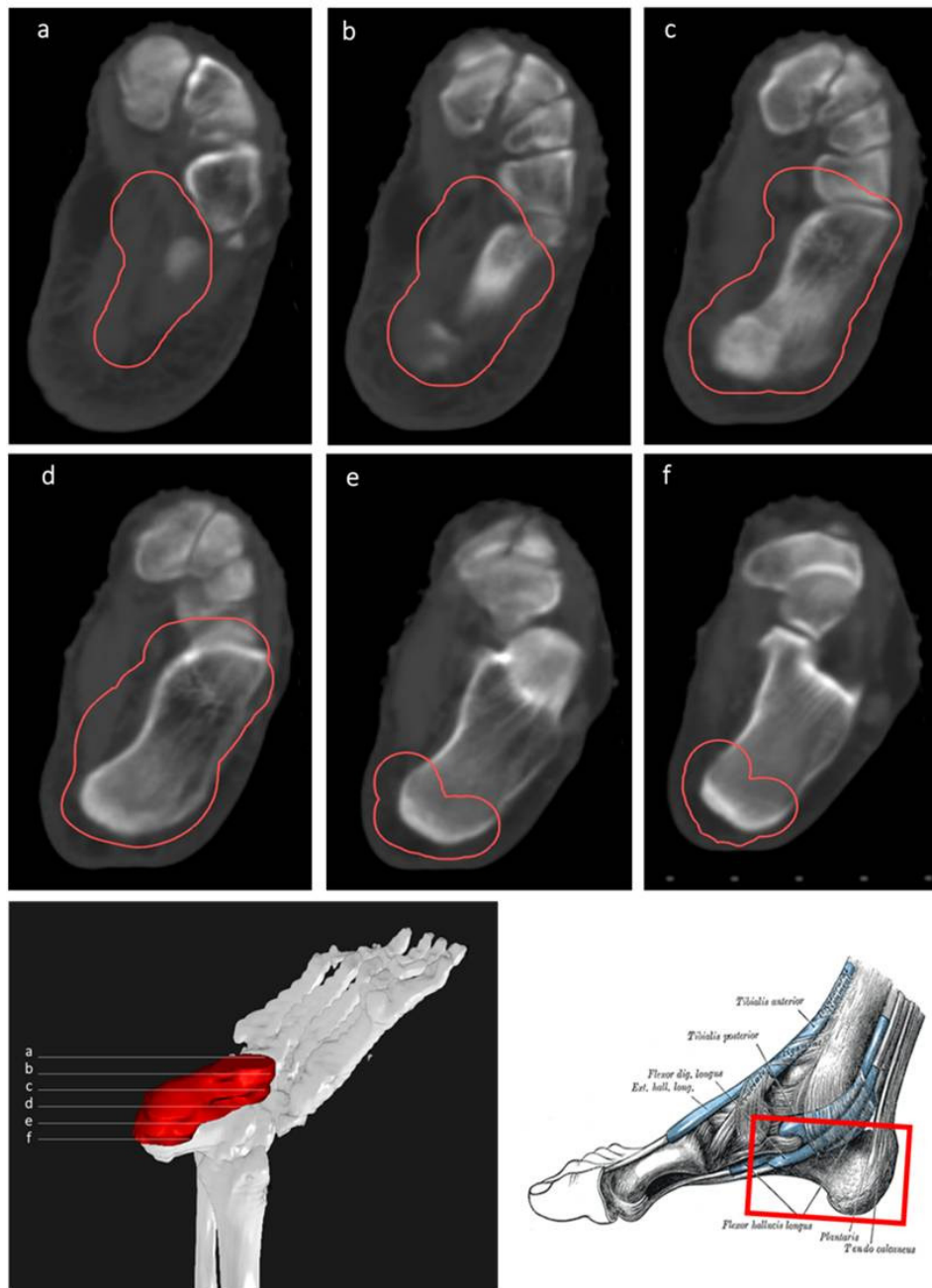
In this regard, well-designed, randomised controlled trials are needed.

Of the studies that have used modern radiotherapy planning and delivery techniques, the only study to randomise patients was the trial performed by Canylmaz et al<sup>62</sup>, who randomized 124 patients with plantar fasciitis to receive radiotherapy (6 Gy in six fractions of 1 Gy) or local injections of corticosteroids and anaesthetics. At a median follow-up of 12.5 months, pain relief was significantly higher in the radiotherapy group (68% vs 28%,  $p < 0.001$ ).

Recently, the results of two well-designed trials were published. Minten et al<sup>26</sup> evaluated the efficacy of LD-RT in 56 patients with hand osteoarthritis (finger joint or base of the thumb). Mahler and colleagues<sup>48</sup> evaluated 55 patients with knee osteoarthritis. Both studies used a smart randomized, double-blind study design comparing active treatment—LD-RT (6 Gy in fractions of one Gy, three fractions/week) to sham radiotherapy. Reirradiation was not permitted in patients who showed partial response, and the final follow-up was three months after treatment completion. Importantly, neither study found between-group differences (radiotherapy vs sham RT) on any of the parameters



Figure 10. CT-based PTV contouring for plantar fasciitis (a-f).



evaluated. Despite these negative findings, it is important to underscore the relevant limitations of both studies: (1) the three month follow-up period is insufficient to conclude that LD-RT is not effective; (2) a second RT treatment was not performed when total relief was not achieved; and (3) the patient population had a pain history >5 years before irradiation and the available evidence suggests that it is more difficult to improve pain in patients with long-term pain.<sup>16,46,67,68</sup>

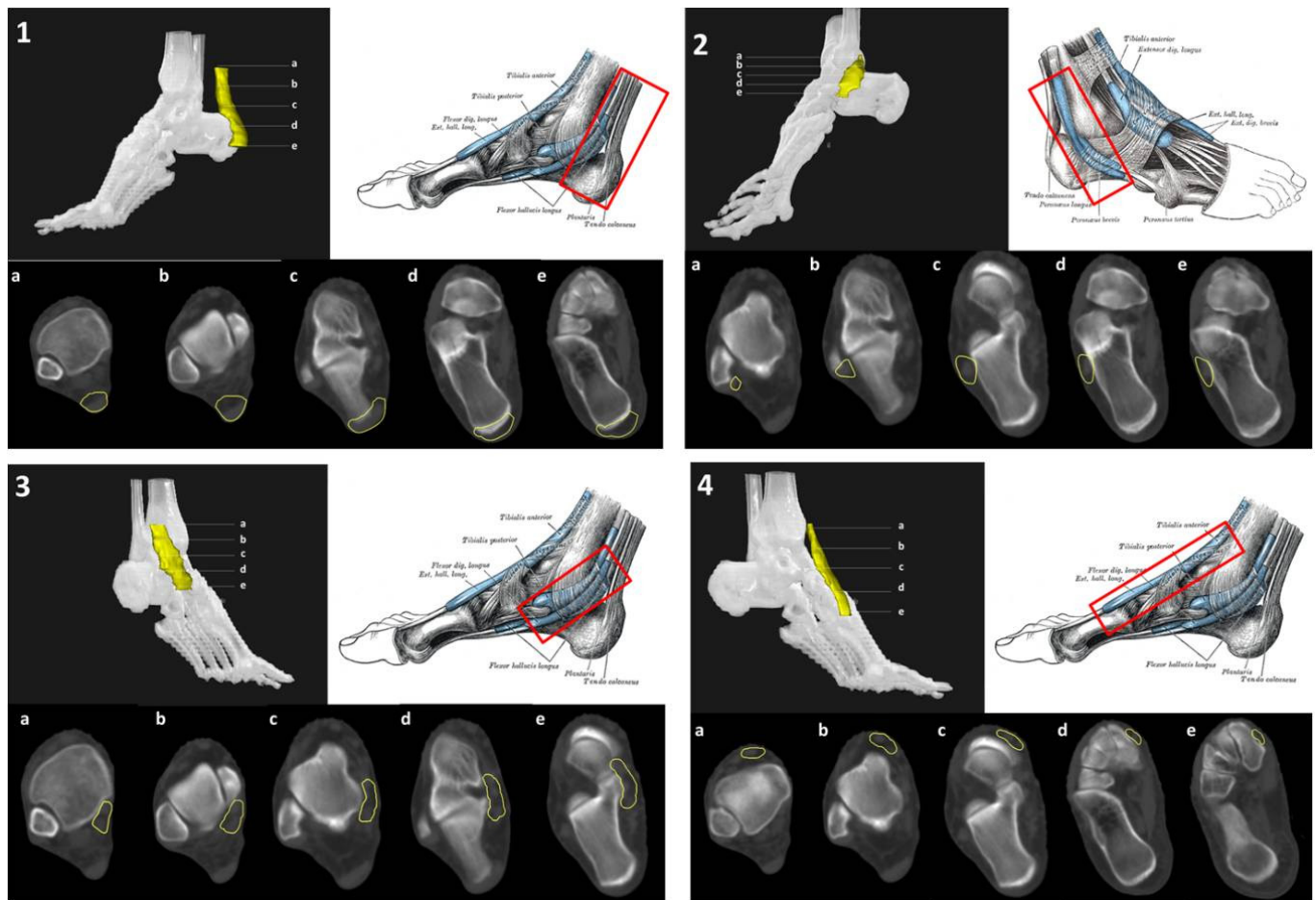
Even though the available data support LD-RT for symptomatic relief of degenerative and inflammatory diseases of the joints and periarticular soft tissue, many radiation oncologists remain reluctant to consider this approach as a standard therapeutic

alternative, even after other therapeutic measures have failed,<sup>69</sup> mainly due to the risk of radiation-induced malignancy. However, it is important to consider the following: (1) most evidence on the carcinogenic risks associated with ionising radiation comes from studies on survivors of the atomic bombs, which is obviously completely different from clinical radiotherapy; (2) current radiotherapy techniques allow us to deliver the radiation with a much greater accuracy than was possible with obsolete techniques used in the past; (3) molecular studies have demonstrated that LD-RT, in particular a single dose per fraction of 0.5 Gy, has no harmful effects on healthy non-inflamed joints, and 4) age is a determining factor in carcinogenic risk, which is markedly lower in elderly patients who are the usual candidates for LD-RT.<sup>4-7,70</sup>

Table 2. Main findings of studies published since the year 2000 that have evaluated the efficacy of LD-RT for degenerative or inflammatory musculoskeletal disorders

Author & year	Type of study	N	Total dose (dose per fraction)	MFU (months)
Painful shoulder syndrome: periarthritis humeroscapularis				
Schultze 2004 <sup>13</sup>	Retrospective	94	6 Gy (0,75 Gy)	4
Niewald 2007 <sup>14</sup>	Retrospective	141	4–8 Gy (0.5–7 Gy) & Gy (1 Gy): 89%	47
Adamietz 2010 <sup>15</sup>	Retrospective	102	3 Gy (0.5 Gy) x two series	18
Ott 2014 <sup>16</sup>	Randomized	312	3 Gy (0.5 Gy) (51%) 6 Gy (1 Gy) (49%)	35
Micke 2018 <sup>17</sup>	Retrospective	162	12 × 0.5 Gy (74%) 6 × 1 Gy (26%)	42
Painful elbow syndrome: epicondylitis humeri				
Ott 2014 <sup>19</sup>	Randomized	216	3 Gy (0.5 Gy) (52%) 6 Gy (1 Gy) (48%)	35
Leszek 2015 <sup>20</sup>	Retrospective	50	6 Gy (1 Gy)	12
Hautmann 2019 <sup>21</sup>	Retrospective	138	3 Gy (0.5 Gy) (9.4%) 6 Gy (1 Gy) (89.9%) Other (0.8%)	29
Hautmann 2020 <sup>22</sup>	Retrospective	99	Reirradiation: 3 Gy (0.5 Gy) (62.6%) 6 Gy (1 Gy) (37.4%)	28
Finger joint osteoarthritis				
Kaltenborn 2016 <sup>25</sup>	Retrospective	84	6 Gy (1 Gy)	3
Minten 2018 <sup>26</sup>	Randomized	56	6 × 1 Gy vs Sham radiotherapy	3
Alvarez 2020 <sup>27</sup>	Prospective	51 (25 rizarthrosis; 26 other finger joint osteoarthritis)	6 Gy (1 Gy)	8
Rogers 2020 <sup>28</sup>	Retrospective	99	4 Gy (0.5 Gy)	NE
Trochanteric bursitis				
Valduvico 2016 <sup>32</sup>	Retrospective	60	10 Gy (1 Gy)	18.5
Kaltenborn 2017 <sup>33</sup>	Retrospective	60	3 Gy (0.5 Gy) (39%) 6 Gy (1 Gy) (61%)	18
Micke 2018 <sup>17</sup>	Retrospective	70	12 × 0.5 Gy (94%) 6 × 1 Gy (4%)	29
Gonarthrosis				
Glatzel 2002 <sup>37</sup>	Retrospective	114	3–6 Gy (median, 6 Gy) (0.5–1 Gy, median 1 Gy)	29
Mucke 2010 <sup>38</sup>	Retrospective	4544	Total dose: 3–12 Gy (median 6 Gy) Dose/fraction: 0.25–3 Gy (median 1 Gy)	NE
Keller 2013 <sup>39</sup>	Retrospective	1037	Total dose: 0.5–10 Gy (median 4 Gy) Dose/fraction: 0.5–1.5 Gy (median 1 Gy)	NE
Micke 2018 <sup>17</sup>	Retrospective	139	12 × 0.5 Gy (80.6%) 6 × 1 Gy (19.4%)	19.5
Mahler 2019 <sup>40</sup>	Randomized	55	6 × 1 Gy vs Sham radiotherapy	3
Plantar fasciitis and Achilles tendinopathy				
Glatzel 2001 <sup>43</sup>	Retrospective	141	6 Gy (1 Gy)	30
Schneider 2004 <sup>44</sup>	Retrospective	62	5 Gy (0.25 Gy-1 Gy)	40
Muecke 2007 <sup>46</sup>	Retrospective	502	5–6 Gy (0.5–1 Gy)	26
Heyd 2007 <sup>47</sup>	Randomized	130	3 Gy (0.5 Gy) (50%) 6 Gy (1 Gy) (50%)	6
Hajtmanova 2010 <sup>48</sup>	Retrospective	323	4 Gy (1 Gy)	3
Niewald 2012 <sup>49</sup>	Randomized	62	0.6 Gy (0.1 Gy) (53%) 6 Gy (1 Gy) (47%)	12
Hermann 2013 <sup>50</sup>	Retrospective	250	3 Gy (0.5 Gy) (18%) 6 Gy (1 Gy) (72%)	11
Koca 2014 <sup>51</sup>	Retrospective	62	8 Gy (4 Gy)	28
Badakhshi 2014 <sup>52</sup>	Retrospective	171	3 Gy (0.5 Gy)	54
Uysal 2014 <sup>53</sup>	Retrospective	450	8 Gy (4 Gy)	12
Canyilmaz 2015 <sup>34</sup>	Randomized	124: 60 RT 64 Injection CE + AN	6 Gy (1 Gy) vs Injection CE + AN	12.5
Niewald 2015 <sup>54</sup>	Randomized	117	6 Gy (1 Gy)x6 vs 6 Gy (0.5 Gy)x12	3
Ott 2014 <sup>55</sup>	Randomized	457	3 Gy (0.5 Gy) (46%) 6 Gy (1 Gy) (54%)	32
Micke 2018 <sup>17</sup>	Retrospective	286	6 Gy (0.5 Gy) (92.6%) 6 Gy (1 Gy) (7.4%)	34
Ott 2015 <sup>56</sup>	Randomized (Achilles tendinopathy)	112	6 Gy (0.5 Gy) 6 Gy (1 Gy)	24

Figure 11. CT-based PTV contouring for Achilles tendinopathy (11.1, a-e); peroneus longus and brevis tenosynovitis (11.2, a-e); tibi-  
alis anterior tendinopathy (11.3, a-e); tibialis posterior tendinopathy (11.4, a-e).



Nevertheless, as a precaution, we do not offer LD-RT to patients under age 40.

Treatment volume definition (PTV) in radiotherapy for non-cancerous conditions requires an appropriate compromise between selecting a volume size that is sufficient to provide benefits while offering maximum protection of surrounding healthy tissues. PTVs should be tailored to the area of interest, but it is essential to keep in mind that excessive restriction of the PTV may decrease treatment effectiveness.<sup>25</sup> On the other hand, given the low dose per fraction and low total dose administered in treatments that have an anti-inflammatory intention, no clearly defined constraints are currently available. Consequently, we strongly recommend application of the ALARA (as low as reasonably achievable <https://www.cdc.gov/nceh/radiation/alara.html>) principle for organs at risk for radiation doses outside the PTV.

To our knowledge, no CT-based imaging atlases are currently available to guide PTV contouring of benign osteoarticular diseases. For this reason, we have developed the present PTV

definition atlas for the most common osteoarticular diseases, which will allow for the systematic definition of target volumes in patients who may benefit from low-dose radiotherapy. These recommendations are based on our clinical experience and aim to ensure the application of the same quality standards we use for the treatment of malignant tumours. We strongly believe that the CT-based contouring atlas and recommendations provided here will be of value to radiation oncologists interested in LD-RT for the symptomatic treatment of degenerative or inflammatory disorders of the joints and para-articular soft tissues, although, as we have said in the introduction, in certain cases it may not be necessary if there is sufficient experience and there is a way of clinical delimitation.

#### CONFLICTS OF INTEREST

All authors have made substantive contributions to the manuscript, read and approved the manuscript, and assume full responsibility for its content. All authors declare no sources of funding or financial interests, nor other conflicts of interest, regarding any part of this manuscript.

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