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MUSCULOSKELETAL

# Dual energy CT iodine map for delineating inflammation of inflammatory arthritis

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**Abstract**

Iodine mapping is an image-processing technique used with dual-energy computed tomography (DECT) to improve iodine contrast resolution. CT, because of its high spatial resolution and thin slice reconstruction, is well suited to the evaluation of the peripheral joints. Recent developments in the treatment of inflammatory arthritis that require early diagnosis and precise therapeutic assessment encourage radiological evaluation. To facilitate such assessment, we describe DECT iodine mapping as a novel modality for evaluating rheumatoid arthritis and psoriatic arthritis of the hands and feet.

*Key Points*

- *Dual-energy CT iodine mapping can delineate inflammation of peripheral inflammatory arthritis.*
- *DECT iodine mapping has high spatial resolution compared with MRI.*
- *DECT iodine mapping has a high iodine contrast resolution.*
- *DECT iodine mapping may reflect therapeutic effects.*

**Keywords** Computed tomography · Dual energy · Inflammation · Arthritis · Enthesitis

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## Introduction

Dual-energy computed tomography (DECT) allows acquisition of two different sets of imaging data by obtaining two different energy levels of X-rays. There are currently three DECT methods including dual X-ray sources, fast kVp switching and double layer detector. DECT facilitates material characterisation because every material has a specific level of X-ray absorption from different energy X-rays [1]. In musculoskeletal research, applications to gout, bone marrow oedema, tendon and metal artefact reduction have been reported [2–5]. Iodine mapping with DECT has been clinically used for pulmonary embolism [6, 7] and other disorders such as metastatic renal cell carcinoma and squamous carcinoma of the head and neck [8–10], but otherwise very little has been reported on its application to musculoskeletal issues [11]. On iodine mapping, the iodine contrast material distribution can be displayed with colour-coding, e.g. as distinct areas of yellow-orange. This makes it a suitable imaging method for diseases in which abnormal iodine contrast material accumulation needs to be visualised.

Inflammatory arthritis is one of the most common diseases in clinical rheumatology, with rheumatoid arthritis (RA) and psoriatic arthritis (PsA) being the two most common types of peripheral arthritis. Inflammatory lesions such as synovitis and tenosynovitis are key findings for early diagnosis of inflammatory arthritis. The importance of such early diagnosis has been increasingly recognised: the European League Against Rheumatism (EULAR) recently recommended that patients with arthritis should be referred to a rheumatologist within 6 weeks after the onset of symptoms to improve outcomes [12]. The development of biologics has improved the prognosis, and correct diagnosis should result in starting biologics in the early phase, before irreversible structural changes occur. Recognition of the significance of subclinical

inflammation, which can be detected only by images, has recently increased. This asymptomatic, weak inflammation may indicate future disease development and predict progressive bone erosion [13, 14].

Magnetic resonance imaging (MRI) and ultrasound (US) have been widely used to detect inflammatory lesions, but they have several disadvantages. MRI tends to produce artefacts in the distal part of the peripheral joints and has limited spatial resolution. US cannot evaluate interosseous aspect of metacarpophalangeal (MCP) or metatarsophalangeal (MTP) joints and this modality is examiner dependent. Therefore, the emergence of new modalities is expected [15]. CT, which has seldom been used for inflammatory arthritis because of its poor iodine-contrast resolution, has several advantages for detection of peripheral inflammatory arthritis. High spatial resolution enables evaluation of small structures such as the distal interphalangeal (DIP) joints. Thin-slice image reconstruction is available in any direction without deterioration of image quality, and is suitable for evaluation of complicated structures, such as the hand and foot. Evaluation of structural changes is important to make a correct diagnosis and prediction of prognosis in inflammatory arthritis. CT has the obvious advantage of being able to evaluate structural changes because of the direct depiction of cortical bone, and has been used as the gold standard instead of histopathological reference. It has been reported that sensitivity of bone erosion of MRI and US is 0.61–0.68 and 0.42–0.44, respectively, when using CT as the reference [16]. Compared with contrast-enhanced CT with digital bone-masking technique [17], a DECT iodine map allows dose reduction and avoids misregistration between pre- and post-contrast images.

A combination of high resolution CT and iodine mapping can be a suitable modality for evaluation of early stage inflammatory arthritis. We have reported the usefulness of iodine mapping in evaluating PsA using contrast-enhanced MRI as a reference standard [11].

In this article, we describe our experience and suggest the potential utility of DECT with iodine mapping for detecting and evaluating peripheral inflammatory arthritis, especially RA and PsA.

## Methods

Institutional review board approval and informed consent from all participating patients were obtained. RA and PsA patients in this report were diagnosed by experienced rheumatologists or dermatologists of our facility.

## Technical method

We used a dual-source DECT unit (Somatom Definition Flash; Siemens Healthineers, Forchheim, Germany) and scanned at 80 kV and 140 kV. The detailed parameters of DECT in our facility are shown in Table 1. Tin filter equipment on the high-energy X-ray tube reduces unnecessary radiation exposure and emphasises spectral separation between low- and high-energy X-ray beams. The average radiation dose of our protocol was as follows: the volume CT dose index (CTDIvol) was around 10 mGy and the dose length product (DLP) was around 270 mGy·cm. We scanned the unilateral hand or foot during each scan, because the entire area of interest must be equally exposed to the two different X-ray energies to obtain accurate dual-energy data. The patient was in a superman position for unilateral hand and flexed opposite knee for unilateral foot. This limitation makes it impossible to obtain sufficient dual-energy data from the shoulder or hip. We used 100 ml of iohexol (Omnipaque, 350 mg iodine/ml; Daiichi-Sankyo, Tokyo, Japan) as a contrast medium at 1.5 ml/s and started scanning 120 s after injection. The acquired data was processed with a commercial workstation (Syngo Dual Energy, Liver VNC; Siemens Healthineers) using a three-material decomposition technique that can identify iodine-containing voxels from dual-energy data and create a virtual unenhanced image. Then, the iodine map was obtained by overlaying the coloured subtracted iodine onto the virtual unenhanced image. The iodine map had 1.0-mm thick sections at 0.7-mm increments. To evaluate peripheral joints, detailed images were created in three orthogonal planes, with sagittal and axial images specific to each finger [11].

## Imaging of DECT iodine map

### Synovitis

Synovitis is a non-specific inflammation of the joint capsule synovium found in inflammatory arthritis as well as in infectious arthritis or osteoarthritis. In RA, the synovium is the primary inflammatory site, and pannus formation, its hallmark, is a major source of cartilage and bone destruction. In PsA, fibrocartilaginous entheses are regarded as the primary site, and the synovium is inflamed by spreading from the adjacent fibrocartilaginous enthesitis. This close relationship between the synovium and fibrocartilaginous enthesis is recognised as the synovio-entheseal complex [18]. The difference in the source of inflammation between RA and PsA results in image differences. Extra-articular inflammation has been reported as more apparent in PsA than RA [19]. According to Outcome Measures in Rheumatology Clinical Trial (OMERACT), synovitis on MRI is defined as an area in the synovial compartment that shows above-normal post-contrast enhancement of a thickness greater than the width of the normal synovium [20]. With MRI, synovitis is detected at high intensity inside the joint cavity on fat-suppressed T2-weighted or short tau inversion recovery (STIR) images.

**Table 1** Parameters of dual-energy CT for peripheral inflammatory arthritis in our facility

| parameters | tube voltage (kV) | effective mAs | rotation time (sec) | collimation (mm) | pitch |
|---|---|---|---|---|---|
| setting | 80/140 | 250/125 (11.60 mGy) | 0.5 | 40 ×0.6 | 0.6 |

Proliferated synovium and joint fluid is responsible for this high-signal intensity. After injection of contrast medium, proliferative synovium and leakage of contrast medium into the joint space cause abnormal joint cavity enhancement. When we observed synovitis on the DECT iodine map, both florid proliferation of synovium (pannus) and inflamed synovium were obviously enhanced (Fig. 1 a,b). However, there were cases with linear enhancement limited to the joint capsule synovium without joint cavity enhancement. Enhancement sparing of the finger joint cavity is seen rarely on MRI, and even synovitis is not seen much. Further investigation is required to explain why the joint cavity is spared in weak synovitis according to the DECT iodine map. This effect may have been caused by differences in spatial resolution or contrast medium distribution between CT and MRI. From our limited experience, synovitis in RA tends to show enhancement in the joint space, which is thought to reflect pannus (Fig. 1 a,b). However, synovitis in PsA tends to show limited enhancement along the joint capsule synovium (Fig. 1 c,d). Although synovitis findings in RA and PsA are indistinguishable by MRI, a previous histopathological study suggested that the inflamed synovial membrane in PsA differs subtly from that in RA, with less hyperplasia of the lining layer, more synovial oedema and a greater number of synovial vessels in the former [21]. These histopathological differences may contribute to the different appearance of synovitis in the two forms of arthritis in DECT iodine map.

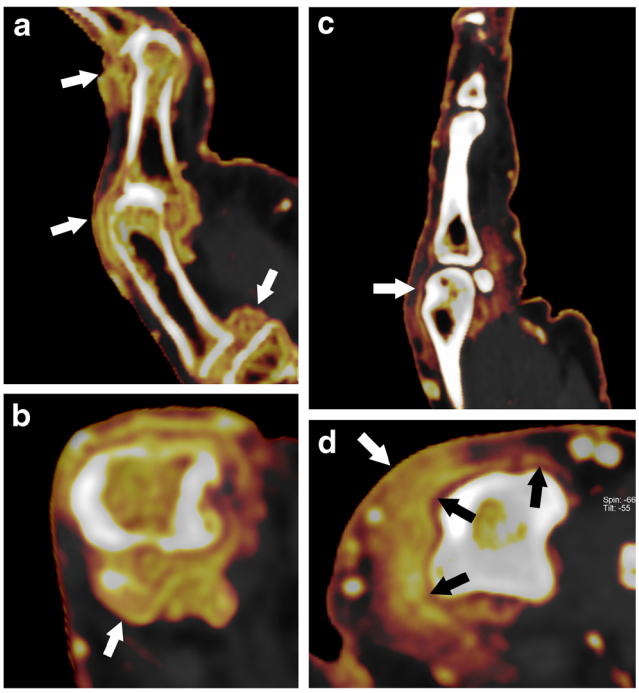


**Fig. 1** Synovitis in a 69-year-old patient with rheumatoid arthritis (RA) (**a**, **b**) and a 43-year-old patient with psoriatic arthritis (PsA) (**c**, **d**). (**a**) Sagittal dual-energy computed tomography (DECT) iodine map of the first finger shows enhancement of florid proliferative synovium, suggesting pannus formation in multiple joints (arrow). (**b**) Both inflamed synovium and pannus are apparent in the transverse metacarpophalangeal (MCP) joint image (arrow). (**c**) Sagittal image showing linear enhancement along the joint capsule (arrow). (**d**) Extra-articular inflammation is more prominent in the transverse image (arrow). Linear joint capsule enhancement suggests inflamed synovium (black arrow). Subcutaneous dot and tubular structures of enhancement are reflecting subcutaneous vessels. Normal skin also appears as a thin bright layer

## Tenosynovitis

Tenosynovitis is defined as inflammation of the synovial lining of the tendon sheath and is common in inflammatory arthritis [22]. Imaging has a higher sensitivity for evaluation of tenosynovitis than clinical assessment [23]. As with joint synovitis, tenosynovitis is a common type of inflammatory lesion in RA, and it may occur wherever tendon sheaths exist. In PsA, diffuse flexor tenosynovitis is one of the main factors for dactylitis, which is a hallmark of PsA [24]. However, in the early phase of PsA, flexor tenosynovitis tends to occur at pulley sites. Fibrocartilaginous enthesis, a target tissue of PsA, is a functional tissue that resists shear and compressive mechanical stress. In the flexor tendons of the fingers, fibrocartilaginous entheses exist between tendon sheaths and fibrous pulleys, where they are called functional entheses, which can become inflamed and cause functional enthesitis [25]. The DECT iodine map shows tenosynovitis as an abnormal enhancement along the tendon that appears similar to tenosynovitis in contrast-enhanced MRI (Fig. 2 a). Finger-specific image reconstruction with DECT enables display of the area of inflammation along the entire length of the tendon. DECT iodine mapping suggested that the pulley sites are critical for flexor tenosynovitis in PsA (Fig. 2 b,c).

## Extensor peritendinitis

Extensor peritendinitis is defined as inflammation around a tendon that is not surrounded by synovial tendon sheath. Friction sites between the extensor tendon and dorsal aspect of the phalangeal bone constitute functional enthesis, and functional enthesitis can occur in PsA. Friction sites of the extensor tendon move proximally in the extended position, and they are well recognised by the true sagittal plane of the fingers on DECT iodine map (Fig. 3). Extensor peritendinitis at the metacarpophalangeal joint has been reported as highly

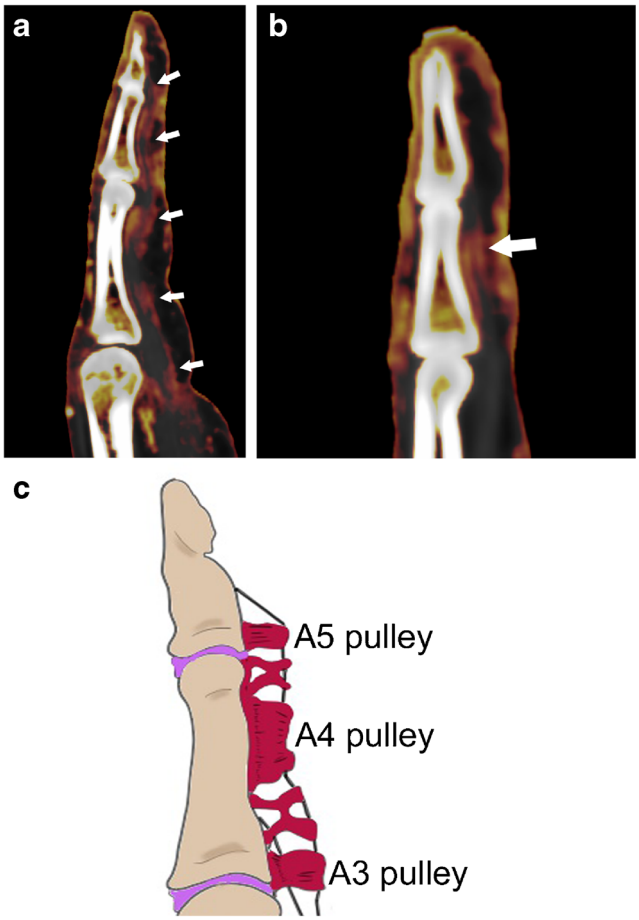


**Fig. 2** Flexor tenosynovitis. (**a**) Dual-energy computed tomography (DECT) iodine map of an 81-year-old patient with psoriatic arthritis (PsA) shows contrast enhancement at multiple pulley levels (arrow). (**b**) A 41-year-old patient with early stage PsA and only 3 weeks' history of arthralgia. Localised enhancement is present in the tendon sheath at A4 pulley (arrow), suggesting that flexor tenosynovitis occurs at pulley sites in the early phase of PsA. (**c**) Anatomical illustration showing the fibrous pulley that works as a functional enthesis

characteristic of PsA in differential diagnosis from RA with US [26]. However, inflammatory lesions of the extensor tendon were not included in the recent MRI scoring system for PsA by Outcome Measures in Rheumatology Clinical Trials (OMERACT) because of poor inter-rater reliability [27]. That result is understandable, because an image in the true sagittal plane with high spatial resolution, while ideal for evaluation of the extensor side of the finger, is not always available by MRI. DECT can generate the preferred image, and we may evaluate extensor peritendinitis with confidence.

## Extensor tendon enthesitis

Extensor tendons attach to the dorsal base of the distal phalanges, and the superficial lamina of the extensor tendon encloses the proximal part of the nail root. This anatomical feature explains the association between extensor tendon

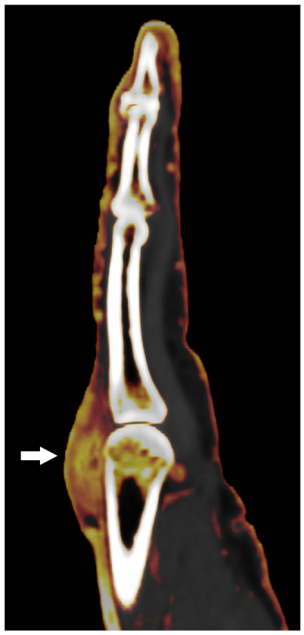

**Fig. 3** Extensor peritendinitis. Dual-energy computed tomography (DECT) iodine map of a 66-year-old patient with psoriatic arthritis (PsA) showing swelling and marked proximal enhancement in the dorsal part of the second metacarpophalangeal (MCP) joint (arrow)

enthesitis and abnormal nail bed enhancement in PsA [28]. Those inflammatory complexes are considered contributors to nail abnormalities, which are a unique feature of PsA. In the DIP joint, extensor peritendinitis occurs very close to extensor tendon enthesitis, and these types of inflammation are usually continuous. DECT iodine mapping can show abnormal enhancement in the responsible area clearly, even though it is a very peripheral part of the finger (Fig. 4).

## Collateral ligament enthesitis

The collateral ligament enthesis is also inflamed in patients with PsA. The collateral ligament consists of the side wall of the joint capsule, and inflammation of the collateral ligament easily extends into the adjacent joint synovium. DECT iodine mapping can show the exact inflammatory site because of their high spatial resolution and thin slice thickness.

## Extra-articular enthesitis

Achilles tendon enthesitis is a well-known extra-articular inflammatory lesion in PsA and other types of spondyloarthropathy. Inflammation is not limited to the insertional site but extends to the proximal part along the tendon. There is a functional enthesis between the Achilles tendon and the calcaneus, which is a part of the retrocalcaneal bursa [18]. Functional enthesitis of this component contributes to abnormal enhancement along the tendon. This inflammation spreads to the adjacent synovium of the retrocalcaneal bursa. DECT iodine mapping can delineate linear

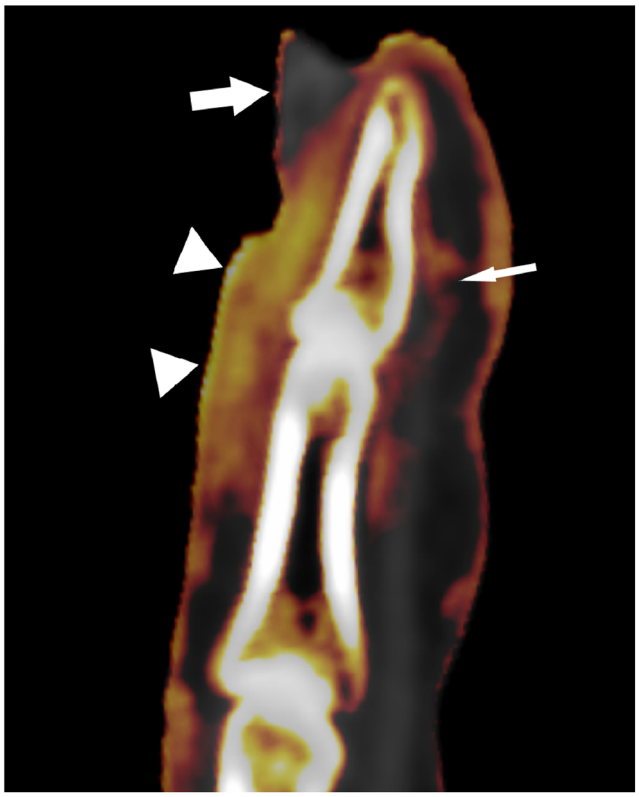

**Fig. 4** Diffuse inflammatory lesion in the DIP joint. A 42-year-old patient with psoriatic arthritis (PsA) and marked nail deformity (arrow). Dual-energy computed tomography (DECT) iodine map shows swelling and enhancement along the extensor tendon at the distal interphalangeal (DIP) joint, suggesting extensor peritendinitis and enthesitis in the tendon attachment site at the distal phalangeal base (arrowhead). Abnormal enhancement spreads into the nail bed. Flexor tendon enthesitis and tenosynovitis are also present (thin arrow)

abnormal enhancement along the Achilles tendon and the retrocalcaneal bursa (Fig. 5).

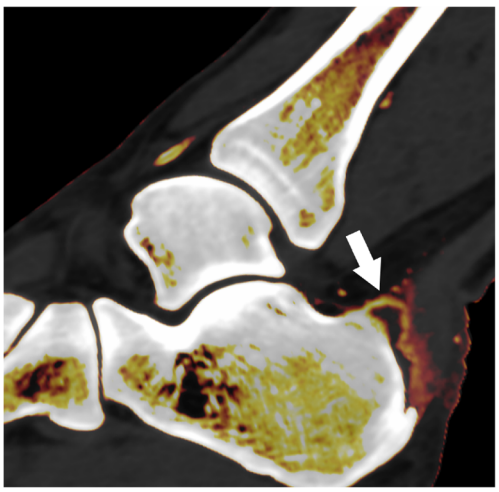

**Fig. 5** Achilles tendon enthesitis. Dual-energy computed tomography (DECT) iodine map of a 38-year-old patient with psoriatic arthritis (PsA) shows abnormal enhancement along the Achilles tendon and adjacent synovium of the retrocalcaneal bursa (arrow). There is bone proliferation at the Achilles tendon entheseal site of the calcaneus

## Evaluation of therapeutic effect

Rapid development of therapeutic options has made it necessary to establish efficient methods to monitor the response to the treatment. Biologics are effective, but they cost more than other drugs [29], and some of them increase the risk of infections including tuberculosis [30]. Thus, it is particularly important to monitor the response to them. Semi-quantitative evaluation with MRI for RA and PsA has been presented by OMERACT [27, 31], and standardization of imaging evaluation has progressed. These scoring systems have been validated in several recent reports [32–35]. MRI, however, is usually not as accessible as CT, and its limited spatial resolution and MRI artefacts can affect evaluation. On the other hand, patients prefer CT to MRI because of fast acquisition and less noise [17]. Therefore, DECT might be a suitable modality for arthritis patients who need repeated monitoring of therapeutic effects. DECT iodine mapping can reveal obvious improvement in inflammatory lesions in accordance with symptom relief after therapy with biologics (Fig. 6).

## Disadvantages of DECT

DECT has several disadvantages. First is radiation exposure. This is a general problem with radiology, and there is ongoing research being done to reduce the required radiation dose. Dual source-type DECT scanners carry two X-ray tubes, allowing the use of tube-current modulation and tin filters. Tin filtration of the higher-energy spectrum eliminates unnecessary low-energy X-ray exposure, enhancing the energy separation between high- and low-energy X-rays from the two tubes. The

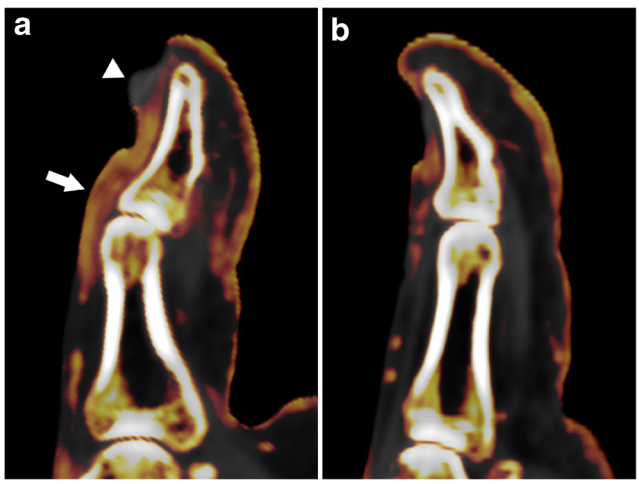


**Fig. 6** Therapeutic assessment of a 44-year-old patient with psoriatic arthritis (PsA). (**a**) Swelling and enhancement of extensor tendon enthesis spreading to the nail bed can be seen in the interphalangeal joint (arrow). Nail deformity is also present (arrowhead). (**b**) After 6 months of infliximab treatment, improvement of inflammation is apparent. The nail deformity is also improved. Enhancement of normal subcutaneous vessels and skin brightness remain

hands and feet are not close to radiosensitive organs, such as the lens or reproductive organs, and they can be scanned by CT repeatedly at appropriate intervals. The average CT dose index volume of our cases is around 10 mGy. Second, although there are reports about bone marrow visualization using DECT in several bones [36–38], its use in bone marrow oedema in peripheral bones has not been fully developed and there are only a few reports about DECT and peripheral bone. Diekhoff et al. suggested a good correlation between DECT and MRI in terms of the detectability of bone marrow oedema in peripheral arthritis from a study using seven hands and four feet [39], but prospective studies with large numbers are still needed to determine the utility of DECT for imaging bone marrow in peripheral bones. Third, not every CT has dual-energy modes, and its availability is facility-dependent compared with US or MRI. Finally, the use of iodine contrast material requires careful assessment of risks, such as renal function and history of allergy. However, contrast medium is also required on MRI for accurate evaluation of inflammatory arthritis according to a recent publication [40].

## Conclusion

DECT iodine mapping is an image-processing technique to improve iodine contrast resolution with preserving the features of CT such as high spatial resolution and multiplanar reconstruction. Adding to the high reliable evaluation of structural changes, DECT iodine mapping can delineate inflammatory lesions of inflammatory arthritis, even though detection of bone marrow oedema in peripheral bones is under development. High spatial resolution and an optimal reconstructed image may contribute early diagnosis of inflammatory arthritis. Therapeutic assessment is also available. We suggest that DECT iodine mapping is a promising area for future research as a novel approach to managing peripheral inflammatory arthritis.

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**Compliance with ethical standards**

**Guarantor** The scientific guarantor of this publication is Takeshi Fukuda.

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**Informed consent** Written informed consent was obtained from all subjects (patients) in this study.

**Ethical approval** Institutional Review Board approval was obtained.

**Methodology**
- retrospective
- observational
- performed at one institution

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