Anatomical analysis of inflammation in hand psoriatic arthritis by Dual-Energy CT Iodine Map

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HIGHLIGHTS

• Dual-Energy CT (DECT) Iodine Map has high iodine contrast resolution with maintaining high spatial resolution.
• Variable enthesitis of peripheral joints may be key findings for diagnosis of psoritatic arthritis (PsA).
• DECT Iodine Map allowed to determine precise anatomical structures of inflammation in hand PsA.

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ABSTRACT

Objective: This study aimed to identify the detailed location of inflammatory lesions and its frequency of hand PsA on DECT Iodine Map with referring the cadaveric specimen.

Materials and methods: Thirty-eight anatomical landmarks were selected as a potential inflammatory sites in the thumb and middle finger. We included 22 symptomatic PsA patients who underwent contrast enhanced DECT of the hand. MR images and macroscopic specimens of thumb and middle finger were prepared from a cadaver. Two musculoskeletal radiologists evaluated DECT with referring the cadaveric images to determine the precise location of inflammatory sites and its frequency.

Results: The frequently observed inflammation sites of active PsA patients were either classical or functional entheses, and coincide with the well-known hypothesis that primary inflammatory sites of PsA are enthesis. We have noticed that there was remarkable enhancement around DIP joints (13.6 %–45.5 %).

Conclusion: DECT could assess the detailed anatomical sites of the inflammatory lesion in hand psoriatic arthritis, which coincided with enthesis.

1. Introduction

Psoriatic arthritis (PsA), along with rheumatoid arthritis (RA), is a common inflammatory arthritis of the small joints of the hands and feet [1]. Since early diagnosis allows early intervention of biologics and good therapeutic efficacy, there is a need for imaging studies that can evaluate early signs of enthesitis and synovitis with an ability to analyze treatment response [2,3].

We reported that Dual-Energy CT (DECT) Iodine Map enables delineation of inflammatory changes with good iodine contrast and high spatial resolution in short examination times [4]. The main locus of inflammation is thought to be different in RA and PsA. In PsA, entheses, which has been regarded as the main locus of inflammation, are present all over the finger. The location of inflammation is important in the pathogenesis of PsA and differentiating from RA. This difference is thought to create different image findings, as shown in the Table1. In this regard, DECT may evaluate precise inflammatory sites with high spacial resolution that CT has.

If the detailed anatomical inflammatory sites could be analyzed, a deeper understanding of the pathogenesis of PsA may be possible. However, detailed anatomical analysis of inflammatory sites with DECT Iodine Map has not been conducted.

Moreover, our previous study showed that the enhancement around distal interphalangeal joint (DIP) was more frequently observed on DECT Iodine Map compared to contrast-enhanced MR (CE-MR) imaging in PsA patients [5]. It is still undetermined whether this phenomenon was a false positive or true inflammatory lesion.

The purpose of this study was to identify the detailed location of...
inflammatory lesion and its frequency of hand PsA on DECT Iodine Map through comparison with gross anatomy, high resolution MR imaging, and Iodine Map of cadaveric fingers.

2. Materials and methods

2.1. Subjects

2.1.1. Patients

We included consecutive symptomatic PsA patients who presented at the dermatology outpatient clinic of our institution from June 2014 to July 2017. Subjects who underwent DECT at our institution before therapeutic intervention were included. PsA cases without the involvement of hands were excluded. Finally, we included 22 cases for this study.

2.1.2. Cadaver

Formalin-alcohol fixed cadaveric hand of an 80-year-old male without a history of joint disease was prepared. The thumb and middle finger were scanned with MR imaging, and cadaveric gross specimens of the middle finger were prepared.

2.2. DECT protocol for PsA patients

All patients underwent scanning with the SOMATOM Definition Flash (Siemens Healthineers, Forchheim, Germany) in dual energy mode with following parameters: tube energy of 80 kV and 140 kV with 0.4 mm tin filter, 250 and 125 effective mAs, 0.5-second rotation time, 40 × 0.6-mm collimation, and pitch of 0.6.

The contrast medium, Iohexol 100 mL (Omnipaque, 350 mg of iodine per milliliter; Daiichi-Sankyo, Tokyo, Japan) was injected from the antecubital vein at a rate of 1.5 mL/sec. Scan was started 120 s after injection.

All images were reconstructed from DE data with 1.0-mm-thick sections in 0.7-mm increments. A commercial workstation (Syngo Dual Energy, Liver VNC; Siemens Healthineers) was used for three-material decomposition analysis and to make the Iodine Map. The image was reconstructed in three orthogonal planes for each finger. Window center and window width of images were fixed as 55 and 70 Hounsefield unit (HU), respectively, for image standardization.

2.3. Imaging for cadaveric finger

Cadaveric fingers were scanned with MR imaging and DECT. MR Images were obtained by using 1.5-T unit, either the MAGNETOM Avanto (Siemens Healthineers, Erlangen, Germany) or the MAGNETOM Symphony with Tim System (Siemens Healthineers). Proton density weighted image (PDWI) in three orthogonal planes where obtained (Repeating Time:4500 msec, Echo Time:24 msec). Slice thickness were set at 1 mm.

Cadaveric gross specimens of the middle finger were prepared in axial section of the metacarpophalangeal (MCP) joint and mid-sagittal section from the proximal interphalangeal (PIP) to the tip of the finger. After diluted Iohexol (Omnipaque, 350 mg of iodine per milliliter; Daiichi-Sankyo, Tokyo, Japan) with saline at 1/200 was applied on the inner lining of the articular capsule of the MCP-DIP joint where the capsular synovitis can be occurred, DECT Iodine Map was obtained by using the same protocol as for the PsA patinet.

| Table 1 | Typical findings of RA and PsA in MRI, US and DECT. |
|---------|-----------------------------------------------------|
| MR imaging | Joint capsule synovitis | Enthesitis |
|          | Tenosynovitis | Joint capsule synovitis |
|          | Bone marrow edema | Tenosynovitis and periostinitis |
|          | Bone erosion | Periarticular inflammation |
|          | Joint space narrowing | Bone marrow edema |
| US | Same as MRI but unable to detect bone marrow edema | Same as MRI but unable to detect bone marrow edema |
| DECT | Same as MRI but unable to detect bone marrow edema of small bones | Same as MRI but unable to detect bone marrow edema of small bones |

| Table 2 | The anatomical structure evaluated. |
|---------|-----------------------------------|
| Middle finger | Thumb |
| Metacarpo-phalangeal joint | Articular capsule |
| Lumbrical muscle/interosseous muscle | Articular capsule |
| Sagital band | Interphalangeal joint |
| A1 pulley | Metacarpo-
| Proximal phalanx | Articular capsule |
| A2 pulley | Articular capsule |
| Transverse retinacular band | Interphalangeal joint |
| C1 pulley | Metacarpo-
| Proximal interphalangeal joint | Articular capsule |
| Medial collateral ligament | Medial collateral ligament |
| Lateral collateral ligament | Lateral collateral ligament |
| Volar plate | Volar plate |
| Insertion of central slip | Insertion of flexor digitorum profundus |
| Insertion of flexor digitorum superficialis | Insertion of flexor digitorum |
| A4 pulley | Insertion of flexor digitorum |
| Insertion of conjoined tendon | Insertion of flexor digitorum |
| Middle phalanx | Articular capsule |
| Insertion of flexor digitorum superficiais | Articular capsule |
| Medial collateral ligament | Medial collateral ligament |
| Lateral collateral ligament | Lateral collateral ligament |
| Volar plate | Volar plate |
| Distal interphalangeal joint | Articular capsule |
| Medial collateral ligament | Medial collateral ligament |
| Lateral collateral ligament | Lateral collateral ligament |
| Volar plate | Volar plate |
2.4. Image analysis

DECT Iodine Map of the thumbs and middle fingers of 22 PsA patients were evaluated for the presence of iodine accumulation in 38 peri-articular anatomical structures by 2 musculoskeletal (MSK) radiologists (S.O. and K.F., with 8 and 27 years of experience in interpreting musculoskeletal CT and MR images, respectively). The evaluated 38 anatomical structures are shown on the Table 2. To determine which anatomy corresponds to the sites of iodine accumulation on DECT Iodine Map, gross specimens and high-resolution MR images of cadaveric fingers, and also DECT Iodine Map of iodine applied cadaveric fingers were used as references. Through the discussion by the 2 MSK radiologists, the frequency of iodine accumulation in each anatomical structure was calculated.

3. Results

3.1. Patient characteristics

A total of 22 patients who had symptomatic PsA of digital joints and completed DECT were included. The group included 15 men and 7 women, with a mean age of 54.8 (±17.6) years. The mean duration of psoriasis was 11.8 (±11.3) years, and the mean joint symptom duration was 19.5 (±35.6) months. All subjects fulfilled Classification Criteria for Psoriatic Arthritis (CASPAR) criteria. The demographic and clinical characteristics of enrolled patients are shown in Table 3.

Table 4

The detection rate of iodine accumulation assessed by MSK radiologist.

| Middle finger | Detection frequency | Thumb | Detection frequency |
|---------------|---------------------|-------|---------------------|
| Metacarpophalangeal joint | | | |
| Lumbrical muscle/interosseous muscle | 13.6 % | Abductor pollicis brevis | 4.5 % |
| Sagital band | 13.6 % | Flexor pollicis brevis | 4.5 % |
| A1 pulley | 18.2 % | Adductor pollicis muscle | 9.1 % |
| Articular capsule | 9.1 % | Extensor pollicis brevis | 9.1 % |
| Medial collateral ligament | 13.6 % | Sagital band | 22.7 % |
| Lateral collateral ligament | 9.1 % | Medial collateral ligament | 9.1 % |
| Metacarpophalangeal joint | | | |
| Volar plate | 9.1 % | Lateral collateral ligament | 4.5 % |
| Proximal phalanx | | | |
| A2 pulley | 22.7 % | Volar plate | 9.1 % |
| Transverse retinacular band | 13.6 % | Articular capsule | 0% |
| C1 pulley | 22.7 % | Extensor pollicis longus | 22.7 % |
| Articular capsule | 4.5 % | Flexor pollicis longus | 13.6 % |
| Proximal interphalangeal joint | | | |
| Medial collateral ligament | 22.7 % | Medial collateral ligament | 18.2 % |
| Lateral collateral ligament | 18.2 % | Lateral collateral ligament | 13.6 % |
| Volar plate | 13.6 % | Articular capsule | 0% |
| Distal interphalangeal joint | | | |
| Insertion of central slip | 9.1 % | Volar plate | 4.5 % |
| Middle phalanx | | | |
| Insertion of flexor digitorum superficialis | 18.2 % | | |
| A4 pulley | 27.2 % | | |
| Insertion of conjoined tendon | 22.7 % | | |
| Insertion of flexor digitorum profundus | 13.6 % | | |
| Articular capsule | 36.4 % | | |
| Medial collateral ligament | 45.5 % | | |
| Lateral collateral ligament | 36.4 % | | |
| Volar plate | 13.6 % | | |

Fig. 1. A 28-year-old man with PsA.
a) Axial DECT Iodine Map shows iodine accumulation consistent with the A1 pulley on the palmar side of MCP joint (arrow).
b) Axial section of the gross cadaveric specimen and c) axial section of PDWI image of the cadaver delineates the corresponding A1 pulley (arrow).
3.2. Assessment of iodine accumulation of each anatomical structure

The frequency of iodine accumulation in each anatomical structure is shown in Table 4.

3.2.1. Pulley system

Many pulleys are known to exist on the palmar side of the fingers, that support the function of the flexor tendon. DECT Iodine Map showed abnormal enhancement along the pulleys, which could be regarded as functional enthesitis (Fig. 1). The frequency of inflammation was relatively high at all pulleys we assessed (18.2 %–27.2 %) and inflammation tended to be more prevalent in the distal part.

3.2.2. Joint capsules

Synovitis in PsA tended to show linear enhancement along the joint capsule synovium. They were similar to DECT Iodine Map of cadaveric finger joint after application of diluted contrast medium on the inner articular capsule surface (Figs. 2 and 3). Our results showed varying detection frequency of joint capsules. In the thumbs, the frequency was 0 %. On the other hand, the linear enhancement along the joint capsule was detected in the middle fingers and the highest frequency showed in the DIP joint (MCP 9.1 %, PIP 4.5 %, DIP 36.4 %).

3.2.3. Collateral ligament

The inflamed collateral ligament enthesis was also delineated on DECT Iodine Map with its high spatial resolution and thin slice.
thickness. The collateral ligament consists of the radial and ulnar side wall of the joint capsule.

3.2.4. Enthesis of the flexor and extensor tendon

In the thumb, the extensor pollicis brevis tendon inserts onto the dorsal base of the proximal phalanx and the extensor pollicis longus tendon continues distally and inserts onto the dorsal base of the distal phalanx. The flexor pollicis brevis tendon inserts onto the radial sesamoid bone and radial base of the proximal phalanx with abductor pollicis brevis. The flexor polices longus tendon inserts onto the base of the distal phalanx. Cadaveric high resolution MR image showed these enthesis. Despite the considerable anatomical complexity, DECT managed to distinguish each inflamed anatomical structure. (Fig. 4).

In the other digit, extensor tendons which originate from both extrinsic and intrinsic extensor muscles create central slip and terminal tendon through complex connectivity. Inflammation of extensor tendon enthesis at the base of distal phalanx was relatively frequent (22.7 %) and could spread to nail bed continuously (Fig. 5).

The flexor tendon consists of two tendons: the flexor digitorum superficialis, which inserts on the midportion of the middle phalanx, and the flexor digitorum profundus, which inserts on the volar base of the distal phalanx. Not only attachment sites of the tendon, but also enhancement along tendon sheath was detected as tenosynovitis (Fig. 6).

4. Discussion

The current study revealed that the frequently observed inflammation sites of active PsA patients could be classified as either classical or functional entheses. In the thumb, sagittal band around the MCP joints, medial collateral ligament of the IP joints, and around the extensor pollicis longus tendon were the three most prevalent sites. In the middle finger, variable pulleys, collateral ligaments, and articular capsule of the PIP joints, and various entheseal structures in the DIP joints were dominant inflammatory sites. Functional enthesis, coined by Benjamin and McGonagle, is referred to the sites where bones and tendons/ligaments are closely in contact but not attached [6]. Pulleys and sagittal band are representative tissue of functional enthesis of the fingers whereas the attachment sites of tendon and ligament are named as classical enthesis. Enhancement along tendon sheath was seen occasionally on DECT Iodine Map. Because tendon sheath has synovium,
tenosynovitis is known to have a close relationship with RA. However, since tendon sheath runs near bones, pulleys, volar plates and other fibrous structures, the enhancement along the tendon sheath may indicate secondary tenosynovitis from classical/functional enthesitis. Hence, our results may coincide with the hypothesis that primary inflammatory sites of PsA are enthesis, which is different from RA [7].

In this study, we have noticed that there was remarkable enhancement around DIP joints. This may be explained by the fact that variable enthesis are crowded in a small DIP joint. For example, as classical enthesis, all attachment of flexor tendon, extensor tendon, radial collateral ligament, and ulnar collateral ligament are existing in the DIP joint. This finding was also consistent with the previous reports that the DIP joints are predominantly involved in PsA and are also associated with characteristic nail psoriasis [8,9]. Capsular synovitis has been regarded as the secondary inflammation due to adjacent enthesitis and the iodine accumulation of articular capsule was also often observed in DIP joint rather than the MCP and the PIP joint. Among the 22 active PsA patients, one case showed an enhancement of articular capsule of the DIP joint without any inflammation of surrounding enthesis. It can be suspected that conjoint osteoarthritis may cause iodine accumulation in the articular capsule of the DIP joint.

In our previous study, we speculated that the linear enhancement surrounding the joint space on DECT images represents inflammation of the joint capsular synovium [4,5]. However, this finding differs from typical capsular synovitis on CE-MR imaging, which showed enhancement not only in synovium but also joint space. Yamato et al. reported that enhancement of synovium and leakage of the contrast media into the joint space in patients with RA is a time-dependent phenomenon [10]. Our DECT Iodine Map of cadaveric finger, created by applying diluted iodine on the synovium, showed a linear enhancement around the joint space. Thereby, we believe the linear enhancement surrounding the joint space on DECT Iodine Map corresponds to capsular synovitis. We suspect that this discrepancy in capsular synovitis between CE-MR images and DECT images probably due to different timing of scanning after contrast injection because CE-CT is much quicker than MR scan. Another possibility is that the difference in the permeability between Gadolinium chelates and Iodine contrast media.

MR imaging and ultrasound (US) have been widely used to detect inflammatory lesions, but they have advantages and disadvantages compared with DECT. As one of the advantages, both MR imaging and US do not need radiation exposure. However, MR imaging tends to produce artifacts in the distal part of the peripheral joints, which are common sites for PsA. Also, the spatial resolution of MR imaging is sometimes inadequate. As for the disadvantages of US, it is an examiner-dependent modality and has limited objectiveness. Although DECT needs irradiation, it has the potential to overcome these problems with a much shorter scanning time. Especially, when it comes to PsA which frequently involves peripheral joints, high spatial resolution and the ability to reconstruct images with optimal section by DECT are beneficial.

Besides inflammatory arthritis, DECT has been applied in many musculoskeletal disorders. As to rheumatologic diseases, utility of DECT for gout and sacroiliitis has been reported. Detection of monosodium urate crystal deposition by DECT showed the high diagnostic performance of gout [11]. Diagnostic performance in the evaluation of sacroiliitis with axial spondyloarthritis by DECT was also excellent with its ability to delineate bone marrow edema [12]. Other representative application of DECT for musculoskeletal disease are traumatic bone marrow edema, tendon, metal artefact reduction, bone metastasis detection in oncologic patients, and bone mineral density measurement [13].

The major disadvantage of DECT is radiation exposure. We used tube current modulation and tin filters with high energy spectrum to reduce the radiation dose. Several studies have shown that radiation dose of DECT is maintained similar to conventional single-energy multi-detector CT [14–16]. In addition, the hands are distant from radiosensitive organs, such as the lens, breasts, reproductive organs, and hematopoietic bone marrow. Hence, the effect of repeated scans is limited. The accessibility of DECT is still facility-dependent, compared with MR or US. 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 recommended on MRI for accurate evaluation of
inflammatory arthritis according to a recent publication [17].

There are several limitations in our study. First, anatomy of cadaveric finger can be affected by formalin-alcohol fixation which may have effect on strict correlation with in-vivo cases. The second limitation is that we did not analyze all fingers of PsA cases. However, our highest priority was to determine the anatomical location and identify the typical appearance of a variety of inflammatory lesions of PsA with correlating cadaveric specimen. Hence, we thought selecting thumb adding to middle finger which share the almost common anatomy with other fingers are sufficient to cover all types of enethes.

5. Conclusion

In conclusion, by using cadaveric specimen as a reference, DECT Iodine Map allowed to determine various inflamed anatomical structures of the hands in PsA. Majority of the inflammatory sites were consistent with either classical or functional enethes and DECT Iodine Map could be a valid tool in evaluation of detailed inflammatory sites of PsA.

Ethical approval

This study was approved by the institutional review board (IRB number 30-252(9273)).

The requirement for informed consent was waived because of its retrospective design.

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CRediT authorship contribution statement

Sho Ogiwara: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft. Takeshi Fukuda: Formal analysis, Writing – review & editing. Reina Kawakami: Investigation, Writing – review & editing. Hiroya Ojiri: Investigation. Kunihiko Fukuda: Conceptualization, Investigation, Writing – review & editing.

Declaration of Competing Interest

The authors report no declarations of interest.

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