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The forefoot in early rheumatoid arthritis: Anatomy, imaging and clinical aspects

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Introduction

Introduction

Synovium in joints, tendons and bursae

A joint consists of two bones that together form an articulation. In general the goal is movement and flexibility of the body. Generally joints are synovial lined, such as the large multidirectional joints of the shoulders and hips, and the unidirectional joints of the fingers. In addition there are fibrous and cartilaginous joints that are more stable, such as the sutures connecting the skull bones, and the symphysis. The synovial joints are the main focus of this thesis. There are several characteristic features to a synovial joint. First, it contains a layer of cartilage that covers the articulating surfaces. Secondly, a joint capsule is present consisting of an inner synovial membrane and an outer fibrous membrane. The synovial membrane attaches to the margins of the joint surfaces and encloses the articular cavity. It produces synovial fluid to lubricate the articulating surfaces. A synovial membrane can also be found outside the joint capsule, where closed sacs of synovial membrane form tendon sheaths and bursae (Figure 1).⁽¹⁾ The synovial tendon sheath, also referred to as tenosynovium, surrounds the tendon and serves to reduce friction by providing a smooth gliding surface, this helps to prevent tendon injury at locations where there is excessive movement or bone.^(2,3) Not all tendons have a synovial sheath, for example it is absent at the Achilles tendon.⁽⁴⁾ Other structures that can be found near joints are the bursae, that occur primary or secondary to friction. Primary bursae are native synovium-lined structures closely related to bone and tendon sheaths. They lie between tendons and overlying structures, like bone, where they serve to reduce the friction of one structure moving over the other.⁽²⁾ Secondary non-native bursa, also referred to as adventitious bursae, form at sites of friction, for example neobursa after upper leg amputation and friction with the prosthesis. Unlike the primary bursae, adventitious bursa do not have a synovial lining.⁽⁵⁾ Normally, only a small amount of fluid is present in a native bursa, but this increases in case of synovitis and can become symptomatic.

The small joints of the hands and feet are examples of synovial joints that are surrounded by tendons that may or may not have a synovial tendon sheath, depending on the location.⁽⁶⁻¹⁰⁾ At the small hand joints, the metacarpophalangeal (MCP)-joints, a sheath is present around the flexor tendons, but believed to be absent around the extensor tendons.⁽¹¹⁾ Regarding the small foot joints, the metatarsophalangeal (MTP)-joints, there is no consensus in anatomic literature

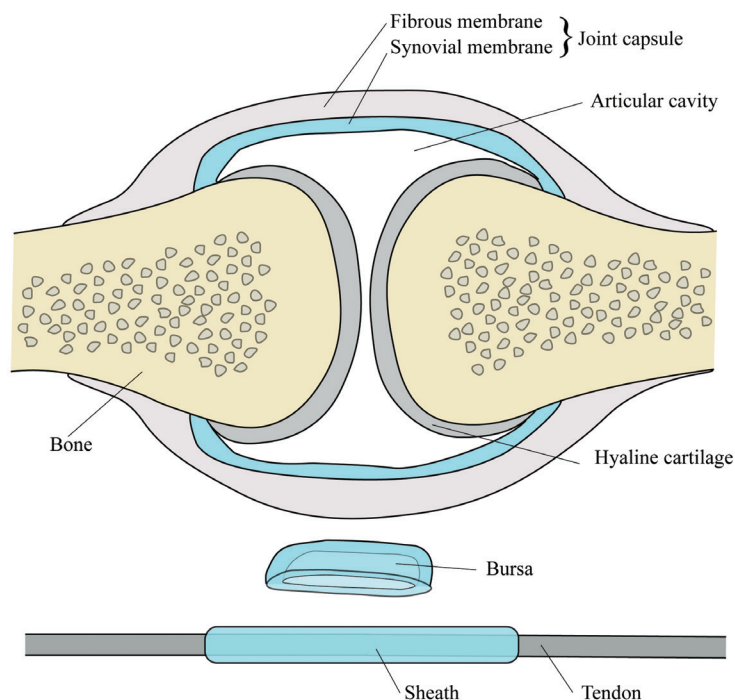


Figure 1. Example of a synovial joint with adjacent synovium-lined bursa and tendon. Synovial membranes are shown in blue. Adjusted from Gray's anatomy for students.(1)

on the presence or absence of tendon sheaths. On the extensor side of the MTP-joints, some sources portrayed extensor tendons without sheaths,(8-10) while other sources neglect to provide information on this region.(6) Regarding the flexor tendons at MTP-joints, there is controversy between sources: in some sources a sheath is described that is solely fibrous,(7) in another example it is described as both fibrous and synovial,(10) while other sources did not provide information on the matter.(8,9) The anatomical presence of tendon sheaths at the MTP-joints thus remains unclear. (Figure 2)

With regards to bursae, anatomic literature does not mention their presence at the MTP-joints, even though histopathologic studies have pointed out their presence in all intermetatarsal spaces.(12,13) Thus while the presence of synovial tendon sheaths and bursae is seen as a characteristic feature of synovial joints,(1) their presence at the MTP-joints seems overlooked. The MTP-joints will be the main focus of this thesis, synovial extra-articular structures at these joints, i.e. tendon sheaths and bursae will also be studied.

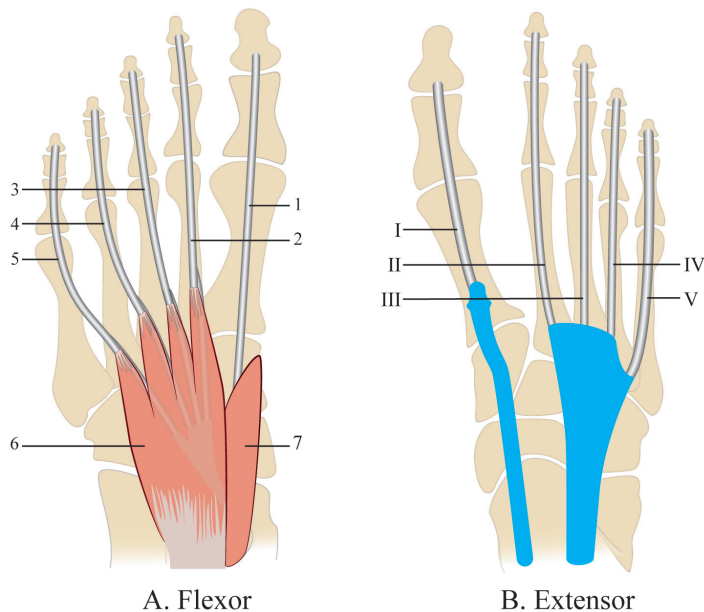


Figure 2. Anatomic absence of tendon sheaths in the forefoot according to anatomic literature. **A:** plantar view of the forefoot with flexor tendons. 1: tendon of the m. flexor hallucis longus, 2-5: tendons of the common mm. flexor digitorum longus (FDL) and common flexor digitorum brevis (FDB). Proximally the four tendons of the FDL run deep from under the FDB muscle (6) and extend distally together with the FDB tendons. The tendon of the FHL (1) proximally runs deep from under the musculus abductor hallucis (7) and the FDB. **B:** dorsal view of the forefoot with extensor tendons. The tendon sheaths are shown according to anatomic literature: the tendon sheaths of the tibialis anterior, extensor hallucis longus (I) and extensor digitorum longus tendons (II-V) end proximal of the MTP-joints. Adjusted from Netter's atlas of Human Anatomy.(8)

Relevance of anatomic knowledge in the interpretation of imaging

Anatomical knowledge is a fundamental component for the interpretation of medical practice and science. The general assumption is that every part of us that can be seen with the naked eye has already been discovered. However, ways of viewing the body change due to advances in imaging techniques, such as MRI.(14) Through advanced imaging we bring into view progressively finer detail within the human body that pose new questions on how to interpret what can be seen. This in turn may increase our anatomical knowledge, as advanced imaging may lead to the discovery of structures that have previously not been described in anatomic literature.

Examples of this can be found in the rheumatologic field. Historically, rheumatoid arthritis (RA) is a disease that is characterized by inflammation of the synovial lining of the joints. In addition, it is known that inflammation of the tenosynovium,

referred to as tenosynovitis, can also occur. Tenosynovitis can clinically be found in patients with active, longstanding RA, and predisposes the risk of tendon rupture. (15) Recent detailed imaging studies of the hand have revealed that subclinical tenosynovitis can also be found in the early phases of RA.(15,16) However, MRI-detected inflammation is seen around tendons with, but also around tendons that are believed to lack a tenosynovial sheath, according to anatomic literature, referred to as peritendinitis.(11) This peritendinous enhancement may be seen with or without local synovitis, and thus represents more than just a secondary peritendinitis due to synovitis.(11) Anatomic literature does not always provide references on how its images are realized. In addition, there are inconsistencies between and within anatomical reference texts.(14,17) It may thus seem justifiable to revisit previous assumptions. Regarding the MTP-joints, MRI-detected inflammation around tendons has been described at the MTP-joints in patients with RA.(18) As stated, current anatomic literature does not provide clear information on the presence or absence of tendon sheaths that is necessary for the interpretation of these MRI-findings. Therefore, anatomical studies are warranted: if these reveal the presence of a tenosynovium, these MRI-findings can be interpreted as tenosynovitis. This way, as advanced imaging gives us an increased interest in anatomy, in turn, new anatomic findings may then increase our understanding of advanced imaging, and ultimately of disease. As imaging findings may challenge anatomic research, this in turn may lead to revision of the classic textbook images.

Rheumatoid arthritis

RA is a systemic autoimmune disease that is characterized by chronic, persistent inflammation of synovial joints. In Caucasians, its prevalence is 0.5-1%. It affects women more often than men, and its incidence increases with age. Uncontrolled, it can result in erosive joint damage, disability and an increased mortality.(19)

The classic presentation of RA is a symmetrical polyarthritis that involves the small synovial joints of hand and feet, with joint pain, stiffness and swelling. A variety of symptoms can be present, and no single symptom is specific for RA. Importantly, no diagnostic criteria for RA exist. Therefore the diagnosis is made by the rheumatologist based on a combination of clinical findings and additional investigations, such as laboratory tests and imaging.(20)

For research purposes, classification criteria are used to create relatively homogeneous groups of patients. Throughout the years different classification criteria have been held for RA. Previous classification criteria such as the 1987

ACR criteria were developed for established RA, and included radiographic erosions and rheumatoid nodules. In the last decades, substantial advances in the management of RA have been made, as it has become apparent that early treatment with disease modifying anti-rheumatoid drugs (DMARDs) improves the outcome of disease. Therefore more recently, the 2010 ACR/EULAR classification criteria have been established to allow the selection of patients in an earlier disease stage.(21) In these 2010 criteria, findings of established disease such as rheumatoid nodules and radiographic erosions are no longer included, and acute phase reactants and auto-antibodies that are associated with RA are included and are weighed heavily. It is important to note that these classification criteria can only be applied to patients with a clinical diagnosis of RA.(Table 1)

In clinical practice and trials disease activity in RA is assessed by composite indices, like the Disease Activity State (DAS). The original DAS includes a 44 swollen joint count.(22) For reasons of convenience, a reduced DAS, the DAS28, has been introduced that assesses 28 joints by excluding evaluation of ankle and foot joints. And thus, even though the feet are a preferential location of involvement in early arthritis, they are excluded from this important outcome measure. Previously it was shown that the practicality of the reduced 28 joint count comes at the cost of accuracy, as the DAS28 underestimates disease activity, particularly in patients where the ankle and foot joints are affected.(23) Indeed, tenderness and swelling of foot joints was found in a substantial number of RA-patients who were considered to be in the state of remission.(24) It has been suggested that, given the high burden of foot complaints and the imminence of walking disability, a more attentive attitude to forefoot inflammation in outcome studies in RA seems justifiable.(25)

The role of imaging in RA

Imaging is used for several purposes in the management of RA, including diagnosis, prognostication, disease monitoring and also as an outcome measure in trials. (26) On conventional radiographs joint of hands and feet damage is measured by erosions and joint space narrowing. Radiographic studies have revealed that in the early phases of disease erosive change is more common in the feet than in the hands.(27,28) Traditionally, erosive change is considered an important outcome measure. However in case of prompt treatment patients have limited bone and joint damage that can be detected by radiographs. Therefore MRI and ultrasound are gaining more recognition in the management of RA, as they are more sensitive in detecting damage and in addition allow visualization of inflammation of soft tissues.(26)

Table 1. Classification criteria for Rheumatoid Arthritis

Revised ACR 1987 criteria	2010 ACR/EULAR criteria
Morning stiffness \geq 1 hour	Joint involvement
Arthritis \geq 3 joint areas	- 1 large joint (0)
Arthritis of hand joints	- 2-10 large joints (1)
Symmetric arthritis	- 1-3 small joints (2)
Rheumatoid nodules	- 4-10 small joints (3)
Presence of RF	- $>$ 10 joints, including at least 1 small joint (5)
Radiographic changes (erosions)	Serology
	- ACPA and RF negative (0)
	- Low-positive ACPA or RF (2)
	- High-positive ACPA or RF (3)
	- Acute-phase reactants
	- Normal CRP and ESR (0)
	- Abnormal CRP or ESR (0.5)
	Duration of symptoms
	- $<$ 6 weeks (0)
	- \geq 6 weeks (1)
4/7 criteria must be present to fulfil criteria	6/10 points must be present to fulfil criteria

ACR: American college of rheumatology; EULAR: European league against rheumatism; RF: rheumatoid factor; ACPA: anti-citrullinated protein antibodies; CRP: c-reactive protein; ESR: erythrocyte sedimentation rate.

MRI and ultrasound both show synovitis and tenosynovitis. A unique feature of MRI is its capability to detect change in the bone marrow described as osteitis or bone marrow edema (BME). All three features are considered to be inflammatory in nature. Both ultrasound and MRI have advantages and disadvantages. Ultrasound is easily accessible but is operator dependent, and while MRI is more expensive it is generally considered to yield more reproducible results. Finally MRI is more sensitive than ultrasound in detecting tenosynovitis and synovitis.(29,30)

Because of the advantages of MRI, it is increasingly used for research purposes. As the complexity and the amount of information provided by MRI pose a challenge, the OMERACT MRI RA Working Group has developed a scoring system: The RA MRI scoring system (RAMRIS) that scores erosions, synovitis and BME. It was developed to standardize MRI-scoring of the small joints of the hands for research purposes and is recognized as a valid outcome measure in trials.(31) Regarding the development, application and validation of this MRI-score, only the small joints of the hands were addressed. The MTP-joints, however, have been neglected.(32) In addition to the RAMRIS a score was developed by Haavardsholm that scores tenosynovitis.(33)

Regarding imaging of the feet, radiographic studies have revealed the important added value of imaging the feet to the hands.(34) Regarding MRI this has not been evaluated, although MRI findings may be as prevalent at MTP-joints as the hands. (18,35) It would therefore be of interest to study the added benefit of MRI of the foot to that of the hand.

Aims and outline of this thesis

RA is an evolving disease, where patients nowadays are treated early in the disease course. Because of the shift to treat early disease phases, MRI has gained increased recognition and is increasingly utilized. And while RA is a disease where the small joints of both the hands and feet are involved, the focus in research has primarily been on involvement of the hands, as the DAS28 excludes the feet and the RAMRIS is not even validated for the MTP-joints. Perhaps most surprisingly, even anatomic literature seems to be incomplete when it comes to the description of the normal anatomy of the feet.

Therefore, this thesis has three general aims:

- To validate the use of the RAMRIS for MRI of MTP-joints
- To increase understanding of the anatomy of soft tissues in the forefoot and to study its involvement in RA by MRI
- To study the association of MRI-detected inflammation at the MTP-joints to clinical outcomes

All studies in this thesis were performed using the Leiden Early Arthritis Clinic (EAC). This is a longitudinal inception cohort that contains consecutive included patients that present to the rheumatology outpatient clinic of the Leiden University Medical Center with clinically confirmed arthritis and a symptom duration of <2 years.(36) At baseline, swollen joint counts were performed, serum samples were obtained, and an MRI of a unilateral hand and foot was performed. All patients were naïve to DMARDs at the moment of inclusion in the cohort, and patients received regular rheumatologic care. It is important to note that the results of the MRI were blind for the treating physician.

To provide an overview of studies available on the application of the RAMRIS on MRI of the MTP-joints, a systematic literature review was performed in **chapter 2**. The aim of this review was to summarize studies evaluating the validity of the RAMRIS applied to MRI of the MTP-joints according to the OMERACT Filter criteria:

Truth, Discrimination and Feasibility. Truth is further subdivided into Face, Content and Construct validity. Discrimination is divided into test-retest reliability, ability to discriminate in trials, longitudinal construct validity and thresholds of meaning. Finally a research agenda was set. In subsequent chapters of this thesis, we aimed to resolve some of the items from this research agenda.

An important aspect of Discrimination is the reliability of scoring.(37) Therefore, in **chapter 3** we studied whether applying the RAMRIS to the MTP-joints is reliable. As the focus in rheumatology is shifting from established erosive RA to early arthritis and even to patients with arthralgia that are suspect to progress to arthritis,(38) this study was performed in patients with early arthritis and also in patients with clinically suspect arthralgia without apparent arthritis upon physical examination.

As part of Face and Content validity it is important that MRI is able to capture the intended pathophysiological feature.(39) In the case of tenosynovitis, the pathophysiological feature is the synovial sheath surrounding the tendons. Besides that anatomic literature leaves it undetermined if tendons at the MTP-joints have a synovial sheath,(6-10) it is also unknown whether tenosynovitis at the MTP-joints is associated with RA. In **chapter 4** we therefore studied the anatomical presence of a tenosynovium of the tendons at the MTP-joints in an anatomical study. The main goal of this was clarify whether MRI-detected contrast-enhancement around the tendons can be interpreted as tenosynovitis. Subsequently the association of these MRI-lesions with RA was studied in a large cross-sectional study in patients with early RA.

Besides classic MRI-inflammation defined by synovitis, tenosynovitis and BME, other MRI findings have gained little attention. Intermetatarsal and submetatarsal areas may be involved in RA and reveal abnormalities on MRI such as intermetatarsal bursitis, Morton's neuroma and submetatarsal bursitis.(40) In **chapter 5** we therefore studied the occurrence of these lesions in early RA.

Next, Construct validity was assessed by studying MRI with physical examination and disability as clinical outcomes. Physical joint examination for swelling is a crucial element in the assessment of the clinical status of RA-patients. However, physical examination of the MTP-joints is generally considered difficult.(41) Therefore in **chapter 6** the association of arthritis upon physical joint examination and MRI-detected inflammation at the MTP-joints was assessed. In addition, in RA-patients walking disabilities are common,(42) therefore in **chapter 7** we studied whether walking difficulties were associated with MRI-detected inflammation.

The value of MRI-detected inflammation of the MTP-joints to recognize patients that will develop RA is still unknown. In addition, in clinical practice, radiographs of both hands and feet are obtained as previous studies have shown that this combined assessment provides better sensitivity and specificity than the hands and feet alone.⁽⁴³⁾ In analogy to conventional radiography, a combined hand and foot MRI score might state an important advancement to the present RAMRIS that only images the hand. For Feasibility, it is important to know whether imaging of the foot is of additional value to the hand, as it prolongs the scan time and thereby costs. Therefore in **chapter 8** we aimed to answer both questions: first we studied whether MRI-detected inflammation of the foot is predictive for RA-development. Secondly we studied whether combining MRI-detected inflammation of the foot to that of the hand is of additional value.

Chapter 9 consists of a summary and general conclusions of the studies performed in this thesis. In **chapter 10** the summary and general conclusions are provided in Dutch.

References

1. Drake RC, Vogl AW, Mitchell AWM. Gray's Anatomy for Students. Elsevier 2009;2nd Edition:20-1.
2. Benjamin M, Kaiser E, Milz S. Structure-function relationships in tendons: a review. *J Anat.* 2008;212:211-28.
3. Ettema AM, Amadio PC, Zhao C, Wold LE, O'Byrne MM, Moran SL, et al. Changes in the functional structure of the tenosynovium in idiopathic carpal tunnel syndrome: a scanning electron microscope study. *Plast Reconstr Surg.* 2006;118:1413-22.
4. Stiskal M, Szolar DH, Stenzel I, Steiner E, Mesaric P, Czemberek H, et al. Magnetic resonance imaging of Achilles tendon in patients with rheumatoid arthritis. *Invest Radiol.* 1997;32:602-8.
5. Ruangchaijatuporn T, Gaetke-Udager K, Jacobson JA, Yablon CM, Morag Y. Ultrasound evaluation of bursae: anatomy and pathological appearances. *Skeletal Radiol.* 2017;46:445-62.
6. Agur AMR, Dalley AF. Grant's Atlas of Anatomy. Lippincott Williams And Wilkins 2013;13th edition, international:439.
7. Moore K.L. DAF, Agur A.M.R. Clinically Oriented Anatomy. 2017;7th edition:769.
8. Netter FH. Atlas of Human Anatomy. Elsevier. 2014;5th edition:557-8.
9. Paulsen F, Waschke J. Sobotta Atlas of Human Anatomy, Vol. 1. Elsevier. 2013;15th edition:318-9.
10. Standring S. GH. Gray's Anatomy: The Anatomical Basis of Clinical Practice. Elsevier 2015;41th edition:1419+42.
11. Nieuwenhuis WP, Krabben A, Stomp W, Huizinga TW, van der Heijde D, Bloem JL, et al. Evaluation of magnetic resonance imaging-detected tenosynovitis in the hand and wrist in early arthritis. *Arthritis Rheumatol.* 2015;67:869-76.
12. Chauveaux D, Le Huec JC, Midy D. The supra-transverse intermetatarsocapital bursa: a description and its relation to painful syndromes of the forefoot. *Surgical and Radiologic Anatomy.* 1987;9:13-8.
13. Theumann NH, Pfirrmann CW, Chung CB, Mohana-Borges AV, Haghghi P, Trudell DJ, et al. Intermetatarsal spaces: analysis with MR bursography, anatomic correlation, and histopathology in cadavers. *Radiology.* 2001;221:478-84.
14. Eizenberg N. Anatomy and its impact on medicine: Will it continue? *Australas Med J.* 2015;8:373-7.
15. Niemantsverdriet E, van der Helm-van Mil AHM. Imaging detected tenosynovitis of metacarpophalangeal and wrist joints: an increasingly recognised characteristic of rheumatoid arthritis. *Clin Exp Rheumatol.* 2018;36 Suppl 114:131-8.
16. van Steenberg HW, Mangnus L, Reijniere M, Huizinga TW, van der Helm-van Mil AH. Clinical factors, anticitrullinated peptide antibodies and MRI-detected subclinical inflammation in relation to progression from clinically suspect arthralgia to arthritis. *Ann Rheum Dis.* 2016;75:1824-30.
17. Cornwall J. Perhaps we don't know what we thought we knew: Why clinicians need to re-visit and re-engage with clinical anatomy. *Australas Med J.* 2013;6:339-40.

18. Boutry N, Larde A, Lapegue F, Solau-Gervais E, Flipo RM, Cotten A. Magnetic resonance imaging appearance of the hands and feet in patients with early rheumatoid arthritis. *J Rheumatol*. 2003;30:671-9.
19. Scott DL, Wolfe F, Huizinga TW. Rheumatoid arthritis. *Lancet*. 2010;376:1094-108.
20. van der Woude D, van der Helm-van Mil AHM. Update on the epidemiology, risk factors, and disease outcomes of rheumatoid arthritis. *Best Pract Res Clin Rheumatol*. 2018;32:174-87.
21. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, 3rd, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/ European League Against Rheumatism collaborative initiative. *Arthritis Rheum*. 2010;62:2569-81.
22. van der Heijde DM, van 't Hof M, van Riel PL, van de Putte LB. Development of a disease activity score based on judgment in clinical practice by rheumatologists. *J Rheumatol*. 1993;20:579-81.
23. Landewe R, van der Heijde D, van der Linden S, Boers M. Twenty-eight-joint counts invalidate the DAS28 remission definition owing to the omission of the lower extremity joints: a comparison with the original DAS remission. *Ann Rheum Dis*. 2006;65:637-41.
24. van der Leeden M, Steultjens MP, van Schaardenburg D, Dekker J. Forefoot disease activity in rheumatoid arthritis patients in remission: results of a cohort study. *Arthritis Res Ther*. 2010;12:R3.
25. Buchbender C, Scherer A, Miese F, Sewerin P, Haferkamp A, Brinks R, et al. Patterns of magnetic resonance imaging of the foot in rheumatoid arthritis: which joints are most frequently involved? *Rheumatol Int*. 2013;33:1731-6.
26. Colebatch AN, Edwards CJ, Ostergaard M, van der Heijde D, Balint PV, D'Agostino MA, et al. EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis. *Ann Rheum Dis*. 2013;72:804-14.
27. Brinkmann GH, Norli ES, Boyesen P, van der Heijde D, Grovle L, Haugen AJ, et al. Role of erosions typical of rheumatoid arthritis in the 2010 ACR/EULAR rheumatoid arthritis classification criteria: results from a very early arthritis cohort. *Ann Rheum Dis*. 2017;76:1911-4.
28. Landewe RB, Strand V, Conaghan PG, van der Heijde D. Damage and progression on radiographs in individual joints: data from pivotal randomized controlled trials. *J Rheumatol*. 2011;38:2018-22.
29. Ohrndorf S, Boer AC, Boeters DM, Ten Brinck RM, Burmester GR, Kortekaas MC, et al. Do musculoskeletal ultrasound and magnetic resonance imaging identify synovitis and tenosynovitis at the same joints and tendons? A comparative study in early inflammatory arthritis and clinically suspect arthralgia. *Arthritis Res Ther*. 2019;21:59.
30. Wakefield RJ, O'Connor PJ, Conaghan PG, McGonagle D, Hensor EM, Gibbon WW, et al. Finger tendon disease in untreated early rheumatoid arthritis: a comparison of ultrasound and magnetic resonance imaging. *Arthritis Rheum*. 2007;57:1158-64.
31. D'Agostino MA, Boers M, Kirwan J, van der Heijde D, Ostergaard M, Schett G, et al. Updating the OMERACT filter: implications for imaging and soluble biomarkers. *J Rheumatol*. 2014;41:1016-24.
32. Ostergaard M, Peterfy CG, Bird P, Gandjbakhch F, Glinatsi D, Eshed I, et al. The OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging (MRI) Scoring

- System: Updated Recommendations by the OMERACT MRI in Arthritis Working Group. *J Rheumatol*. 2017.
33. Haavardsholm EA, Ostergaard M, Ejbjerg BJ, Kvan NP, Kvien TK. Introduction of a novel magnetic resonance imaging tenosynovitis score for rheumatoid arthritis: reliability in a multireader longitudinal study. *Ann Rheum Dis*. 2007;66:1216-20.
 34. Knevel R, Kwok KY, de Rooy DP, Posthumus MD, Huizinga TW, Brouwer E, et al. Evaluating joint destruction in rheumatoid arthritis: is it necessary to radiograph both hands and feet? *Ann Rheum Dis*. 2013;72:345-9.
 35. Calisir C, Murat Aynaci AI, Korkmaz C. The accuracy of magnetic resonance imaging of the hands and feet in the diagnosis of early rheumatoid arthritis. *Joint Bone Spine*. 2007;74:362-7.
 36. de Rooy DP, van der Linden MP, Knevel R, Huizinga TW, van der Helm-van Mil AH. Predicting arthritic outcomes--what can be learned from the Leiden Early Arthritis Clinic? *Rheumatology (Oxford)*. 2011;50:93-100.
 37. Wells G, Beaton DE, Tugwell P, Boers M, Kirwan JR, Bingham CO, 3rd, et al. Updating the OMERACT filter: discrimination and feasibility. *J Rheumatol*. 2014;41:1005-10.
 38. van Steenberg HW, Aletaha D, Beart-van de Voorde LJ, Brouwer E, Codreanu C, Combe B, et al. EULAR definition of arthralgia suspicious for progression to rheumatoid arthritis. *Ann Rheum Dis*. 2017;76:491-6.
 39. Boers M, Kirwan J, Tugwell P, Beaton D, Bingham CO, 3rd, Conaghan P, et al. The OMERACT Handbook. 2017:1-111.
 40. Cherry L, King L, Thomas M, Roemer F, Culliford D, Bowen CJ, et al. The reliability of a novel magnetic resonance imaging-based tool for the evaluation of forefoot bursae in patients with rheumatoid arthritis: the FFB score. *Rheumatology (Oxford)*. 2014;53:2014-7.
 41. Salaffi F, Filippucci E, Carotti M, Naredo E, Meenagh G, Ciapetti A, et al. Inter-observer agreement of standard joint counts in early rheumatoid arthritis: a comparison with grey scale ultrasonography--a preliminary study. *Rheumatology (Oxford)*. 2008;47:54-8.
 42. Grondal L, Tengstrand B, Nordmark B, Wretenberg P, Stark A. The foot: still the most important reason for walking incapacity in rheumatoid arthritis: distribution of symptomatic joints in 1,000 RA patients. *Acta Orthop*. 2008;79:257-61.
 43. Devauchelle Pensec V, Saraux A, Berthelot JM, Alapetite S, Jousse S, Chales G, et al. Ability of foot radiographs to predict rheumatoid arthritis in patients with early arthritis. *J Rheumatol*. 2004;31:66-70.