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Editorial

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Bone erosions in rheumatoid arthritis

Looking over the edge

This editorial refers to Segmentation and quantification of bone erosions in high-resolution peripheral quantitative computed tomography datasets of the metacarpophalangeal joints of patients with rheumatoid arthritis, by Dominique Töpfer et al., Rheumatology 2013;doi:10.1093/rheumatology/ket259.

In patients with RA, the presence, number and size of bone erosions and the number of joints with erosions on conventional radiographs (CRs) are hallmarks for diagnosis, staging and prediction of damage progression and are used for treatment monitoring in randomized controlled studies and in daily practice [1–3]. In this issue, Töpfer *et al*. [4] introduce a precise three-dimensional (3D) segmentation technique using high-resolution peripheral quantitative computer tomography (HRpQCT) to quantify the volume, surface area and shape of erosions in MCP joints in patients with RA.

The study of bone erosions in the joints is a challenge. First, the presence of erosions is not specific for RA; they are also found in healthy subjects and may occur in other joint diseases such as PsA, OA and crystal arthropathies such as gout [3]. Second, CR is the gold standard to evaluate bone erosions in clinical trials and daily practice, but compared with US, MRI and HRpQCT, it is one of the least sensitive methods to detect them [5]. Additionally CR does not provide a 3D evaluation of the erosions. Third, RA is a multicompartmental disease involving not only the cortical bone margin, but also bone marrow, synovium, cartilage and tendons [6]. A more exact evaluation of the presence, number and size of bone erosions in RA is therefore a promising development in understanding the changes in the bone compartment, especially when it can be performed automatically with high reproducibility [4].

What is the clinical relevance of bone erosions? An articular bone erosion is a radiological term that refers to a break in cortical bone with destruction of the natural barrier between the extraskeletal tissue and the bone marrow compartments, preferentially at the bare area of the joints, at the mineralized cartilage, or adjacent to the insertion sites of periarticular ligaments and at sites of overlying tenosynovitis [3]. Small bone channels that perforate cortical bone and carry microvessels that bridge the outer synovial membrane and the inner bone marrow space can mimic bone erosions. However, in RA, bone erosions are accompanied by the loss of adjacent trabecular and cortical bone and by the presence of bone marrow oedema on MRI in contrast to the cortical vessel channels. In addition, bone marrow oedema, as an expression of osteitis, is a strong predictor for future occurrence and progression of bone erosions. The presence of osteitis, a rich inflammatory bony tissue containing plasma, T and B cells that can be considered as secondary lymphoid tissue, indicates that the bone marrow component is essentially involved in the occurrence of inflammation and bone erosions [3].

In RA, inflammatory cells and cytokines induce an imbalance in local bone turnover resulting in increased osteoclastic bone resorption inducing cortical and trabecular bone loss (erosion and disappearance of adjacent trabecular bone), suppressed osteoblastic bone formation within the osteitis so that it rarely repairs and increased surrounding bone formation (sclerosis) [3]. The combination of these characteristics is clearly visible on the images presented by Töpfer *et al.* [4], as well as in one of our RA patients in the MosaHand project (Fig. 1).

With these new insights in RA and the possibility of high-resolution imaging with HRpQCT, the clinical significance of bone erosions shifts from a clinical tool towards a more sophisticated non-invasive means to describe and investigate joint pathology [7]. In healthy subjects, bone erosions are attributed to repair of microdamage induced by mechanical stress at the entheses of ligaments around the joints [8]. In contrast, in early RA, bone erosions allow the bone marrow component to contribute to bone destruction and inflammation [6], while later in the disease bone destruction is one of the components that contributes to joint destruction, besides destruction of cartilage, tendons and ligaments [1]. Several scenarios are hypothesized in this context [3]. First, assuming that synovitis is the driver, inflammatory cytokines and ACPA attract circulating osteoclast precursors such as dendritic cells that can differentiate into osteoclasts from the circulation towards the joint or local inflammatory cells. The combination of ACPA and active osteoclasts results in erosions formed from synovitis towards bone, the outside-in scenario. Second, when osteitis is considered the driver, ACPA produced by B cells within the bone marrow activate osteoclasts, resulting in periarticular bone loss and perforation at the extremely thin cortex in and around the bare area of the joints, the inside-out scenario. Third, in patients with erosions due to mechanical stress before the occurrence of RA or once erosions have developed during the disease, both scenarios are possible and could amplify each other.

Recently it has been suggested that preserving the structural integrity of the joint on CR rather than

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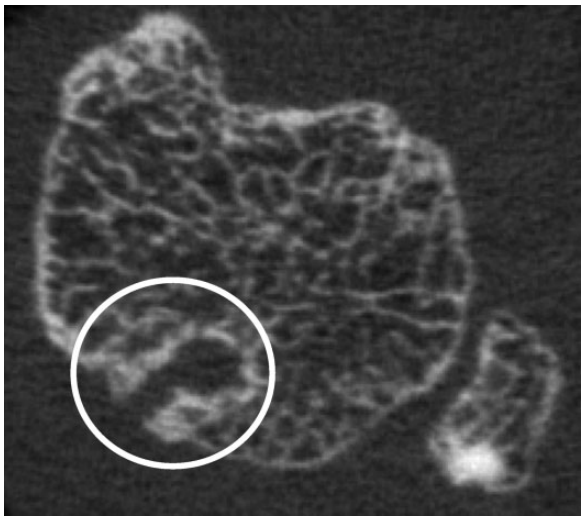
Fig. 1 Example of a bone erosion in an MCP joint of a patient with RA by HRpQCT.



Note the combination cortical break (erosion), the intramedullary disappearance of adjacent trabecular bone and the perilesional sclerosis (image of the MosaHand study, Maastricht University Medical Centre).

suppression of progression of joint lesions on CR should be the framework to study new treatments in RA [9]. Given the high level of performance of HRpQCT to identify and quantify bone erosions in more detail and probably at an earlier stage, as shown by Töpfer *et al.* [4], HRpQCT could be a welcome alternative for CR for this purpose.

However, further research is needed using HRpQCT in patients with early RA and in subjects with ACPA without clinical RA. Indeed, the osteoclasts in RA have diverse origins and functions [10]. In view of the complex changes in the joints of RA, it is important to study the presence, location, size and number of erosions as detected by HRpQCT in relation to clinical parameters, but also in the context of other aspects of joint involvement that can now be assessed with other available techniques, such as cortical and trabecular bone structure (by digital X-ray absorptiometry, high-resolution radiography, dual-energy absorptiometry), osteitis (by MRI), synovial tissue involvement (synovial thickness, vascularization and effusion by US and MRI), cartilage destruction (by CR, MRI and HRpQCT), enthesitis (by MRI and US) and tendinitis (by MRI and US).

These techniques allow evaluation of the small joints of the hands in great detail and, together with semi-automated and highly reproducible analysis using HRpQCT with a high-resolution 3D, they open a window of opportunity to better understand the extent and timing of joint damage in the different compartments, not only in RA, but also in microdamage in healthy subjects and in other diseases affecting the hand joints, such as PsA and hand OA. Looking over the edge of erosions indeed gives a dazzling view of its content.

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