

High-resolution peripheral quantitative computed tomography in patients with rheumatoid arthritis

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Valorisation

This valorisation chapter describes how the outcomes of this thesis contribute to society and specifically for research and industry. We think that the results described in this thesis are of relevance to future research using High-Resolution peripheral Quantitative Computed Tomography (HR-pQCT), especially on the role of vascular channels in bone damage in rheumatoid arthritis (RA) and in other bone affecting diseases.

First, we thank our participants for their voluntary participation in our studies. They volunteered to image their finger joints, but the results described in this thesis were not common knowledge to most of our participants. Because the gathered data and results, as described in this thesis, were not common knowledge to most of our participants we kept them informed on the progress and scientific outcomes we sent annual newsletters in layman language. This way, the subjects became more aware of the value of their participation and this simple form of information sharing was received with great gratitude. It is therefore recommendable to other research groups to do the same.

Background

RA is a chronic inflammatory autoimmune disease affecting approximately one percent of the population worldwide¹. Patients with RA often suffer from inflammation of the joints. The subsequent bone damage caused by inflammation might lead to progressive deformity and disability of, for example, the finger joints. When damage in the finger joints is present early in the RA disease course, this forms a risk factor for poor long-term disease outcome^{2,3}. In clinical practice of a rheumatologist, conventional radiography is still used as gold standard to assess damage and progression of damage in finger joints of patients with RA.

In the management of patients with RA, other and more sensitive imaging techniques are suggested for monitoring disease activity and progression of damage⁴. For example, compared to conventional radiography, HR-pQCT is proven to be a more sensitive imaging technique for detection of cortical interruptions⁵. In this thesis, we studied especially the presence of cortical interruptions in finger joints in patients with RA and healthy subjects using HR-pQCT. It was previously suggested that cortical interruptions on HR-pQCT can represent either physiological vascular channels or pathological erosions, which are considered specific for RA⁶. Pathological interruptions represent damage that has already occurred; physiological vascular channels on the other hand, may play a role in the development of a large interruption. Vascular channels allow direct communication between the bone marrow and the surrounding joint structures⁷. In one of the chapters of this thesis, we studied the nature of cortical interruptions seen on HR-pQCT, using histology as the gold standard. We studied whether cortical interruptions detected in metacarpophalangeal joints and classified as vascular channels on HR-pQCT were indeed vascular channels on histology. Also, we evaluated the image characteristics of histologically identified vascular channels on

matched HR-pQCT images. Our results showed that vascular channels can be detected using HR-pQCT, however due to the small size and heterogeneous presentation of these vascular channels, the detected number was limited and it appeared that the current definition was insufficient.

Contributions of this thesis to society

The findings in this thesis are of significant importance and of additional value for current understanding and further research in RA. If vascular channels play a role in the development of large cortical interruptions, the ability of HR-pQCT imaging to identify vascular channels in finger joints enables, in part, the detection and monitoring of these vascular channels. When large cortical interruptions indeed develop at the 'entry points' through vascular channels, HR-pQCT imaging will enable to show and follow these bone changes over time. This monitoring may be of additional value, also after treatment initiation in clinical studies in order to assess the effect of treatment on this process. Due to the high sensitivity of HR-pQCT, it is expected that fewer participants are needed in clinical trials with HR-pQCT compared to trials using conventional radiography, to observe an effect of for example drug treatment.

Some of the results in this thesis were obtained after collaboration with a team from Aarhus University, Aarhus, Denmark. Initially we met during international meetings organized by the SPECTRA (Study Group for XTrEme CT in RA) collaboration. Collaborations allow broader studies into for example, the mechanisms involved in pathological bone erosion development by combining different fields of expertise such as histology, cell research and HR-pQCT imaging. Therefore the value of the continuation of our collaboration shall be stressed out during annual meetings of SPECTRA. Furthermore, SPECTRA is a Special Interest Group (SIG) at the Outcome Measures in Rheumatology (OMERACT) initiative. This initiative aims to identify and improve relevant health outcome domains. An instrument such as HR-pQCT needs to meet the requirements of the OMERACT filters defined by "truth", "discrimination" and "feasibility". The members of the SPECTRA collaboration strive to implement the OMERACT approach in their studies. As such, the results of this thesis shall be presented during future OMERACT meetings.

Future perspectives

Currently, HR-pQCT has only been used in research settings. Further validation is needed to study the possibility of use in clinical settings. However, at the moment we also see opportunities to use HR-pQCT images for patient educational purposes. Research showed that three-dimensional reconstruction of joint prototypes helped patients to better understand the impact of a disease like RA on their bone⁸. Treatment adherence after showing the impact of the disease on bone could possibly be improved. To test this, an intervention study using three-dimensional prototypes of joints affected by RA, but also by other rheumatic disease such as psoriatic arthritis and gout,

could be initiated. When newly diagnosed patients attend the outpatient clinic, research nurses can use the prototypes to explain what happens to the bone of the joints affected by the disease over time. In addition, three-dimensional reconstructions of some of their own joints can be made, which also makes HR-pQCT imaging more comprehensive to patients.

The results described in this thesis are based on cross-sectional data, but a follow-up was planned as part of these studies. Therefore, the longitudinal data that will become available may further contribute to knowledge about the importance of vascular channels and the development and progression of cortical interruptions in RA.

The HR-pQCT device used in this thesis is the first generation of HR-pQCT scanners. With the recent introduction of the second generation HR-pQCT scanner, the higher isotropic voxel size of this new scanner (61 μm versus 82 μm) can for example provide more details on the role of vascular channels in development of large cortical interruptions. Furthermore, the information on the role of vascular channels can be translated to other types of bone disease research, for example in psoriatic arthritis or osteoarthritis.

Last, in this thesis we showed that visual scoring of HR-pQCT images was time consuming, but that the automated algorithm showed promising results to sensitively and objectively detect cortical interruptions. Future research should focus on further validation of this automated algorithm.

This thesis provides a solid basis/foundation with interesting outcomes of HR-pQCT imaging of finger joints in healthy subjects and patients with RA, which can further be explored in future research.

Current publicity

Results in this thesis have been submitted and published in scientific journals. As part of the SPECTRA collaboration we published a supplement issue in the Journal of Rheumatology on HR-pQCT imaging. Results have also been presented at national and international conferences. Oral presentations have been given at the national conference of the Dutch Rheumatology association (Nederlandse Vereniging voor Reumatologie, 2014, 2015 and 2016). Posters have been presented at the European League Against Rheumatism (EULAR 2014, 2015 and 2016) and American College of Rheumatology (ACR 2014 and 2016).

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