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Project: A new way to diagnose and measure calcium crystal arthritis with MARS imaging

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Introduction:
Calcium crystal arthritis is a form of arthritis that occurs when calcium crystals deposit in and around the joints and can cause inflammation. The main types of crystals that can potentially cause problems are calcium pyrophosphate (CPP) and hydroxyapatite (HA). Calcium crystal arthritis can look like any other inflammatory arthritis and this can be a diagnostic dilemma. Therefore, finding out if the inflammation is due to crystals and if so, which crystal type, is crucial as treatment will be very different.

The diagnosis of arthritis due to crystal formation requires a sample of fluid to be obtained from the joint and inspected by microscope. The different crystal types are distinguished by the way they appear in polarised light. Non-invasive assessment of these crystals to identify if and what crystals are causing arthritis will allow faster diagnosis. We wondered if Medipix All Resolution System (MARS CT) has a potential to improve current diagnosis of calcium crystal arthritis.

MARS CT is a spectral imaging technology that allows characterisation of materials by using X-ray spectroscopy to identify the presence of crystals and the type of crystal.

In this project, we are testing if MARS-CT can be used to diagnose and measure calcium crystal arthritis.

Aim:
The aim of our project was to test if MARS-CT is able to determine the lowest detectable concentration of calcium commonly found in crystal arthropathies and to distinguish calcium pyrophosphate crystals from hydroxyapatitie crystals.

Method:
A range of concentrations of CPP and HA were prepared in the PCR tubes. The crystals were suspended in agar to form homogenous solution and mixed well to avoid formation of air bubbles. These samples were put into phantom which was then placed inside the MARS CT to be scanned.

The resulting CT images were analysed. Attenuation values of each concentration of crystals were obtained using ImageJ. Material decomposition process was carried out to identify calcium-like material in our samples. This was done by using hydroxyapatite solution as reference.

Next, the energy profiles and attenuation curves were plotted. Graphs for CPP and HA were compared to see if there's a difference between them.

Lastly, in order to validate that our samples do indeed contain crystals, the samples were observed under light microscopy.

Results:
First and foremost, MARS CT is able to detect both CPP and HA. Higher concentrations of CPP and HA samples were shown as bright region on the CT images. The lowest detectable limit where this can happen is 6.1mg/ml for CPP and 14.7mg/ml for HA. This is a lot greater than clinical range.

At this stage, MARS CT is not capable of diagnosing calcium crystal arthritis. Increasing the sensitivity of the scanner can bring this closer to clinically relevant scale. The results indicate that there is a positive relationship between concentration and attenuation – the higher the concentration, the more attenuating the material is. Also, for the same concentration, CPP shows higher attenuation in comparison to HA. We have confirmed that samples are calcium-like by doing a material decomposition on the CT images.

MARS CT successfully identified areas in the samples that contain calcium based material. However, MARS CT cannot distinguish CPP and HA. This is because, in CT imaging, composition and atomic number play an important role. Both CPP and HA are made up of 31% and 40% calcium respectively and they have very similar atomic number (15.24 vs 15.86).

Therefore, MARS CT is not yet capable of comparing materials with very similar characteristics. The next step for the research would be to compare calcium based crystals with non-calcium based crystals. Crystal inspection under light microscopy indicates that our samples are indeed made up of crystals. However, we have found that they contain many lumps that are made up of hundreds of individual crystals joined together.

Therefore, we came to conclusion that the bright spots that are shown on the CT images are the result of aggregation of many crystals. In synovial fluid sample of calcium crystal arthritis patient, only one or two individual crystals can be found, indicating we are no way near clinical scale. Optimising the MARS CT settings used to scan crystal arthritis and customising the software for measuring calcium crystals might allow MARS CT to become a clinically useful tool to speed up diagnosis in future.

Conclusion:
This study reveals both potential and limitations of current MARS CT. It suggests the capability of scanner in detecting crystals as well as the need for improving the sensitivity of the scanner for clinical application.

However, this first step has shown promising results. It is hoped that the results of this study will help to foster an ongoing research relationship with University Hospital Lausanne to continue joint research into multispectral imaging of crystal arthropathies.