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Project: Gout - diagnosis and monitoring using MARS spectral imaging

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Sponsor: Christchurch Radiology Group

Introduction:

Gout is a painful and potentially disabling form of inflammatory arthritis which is caused by deposit of needle-shaped uric acid crystals within joints when uric acid level in blood is high. These needle-like crystals could also form in soft tissues outside joints, where collections of these crystals are known as tophi. Typical invasive diagnosis requires confirmation of the presence of monosodium urate (MSU) crystals by detecting birefringent crystals in aspirated joint fluid with polarised light microscopy. However, gouty tophi can also be a valuable clue for diagnosis as the crystals that form them could be removed with a needle for microscopic examination. Research shows that gout has been affecting 1-2% of the New Zealand population and its prevalence among Maori and Pacific people is about 10-15% which is one of the highest Gout rates worldwide. Therefore, effective diagnosis and monitoring of gout is highly demanded. Non-invasive diagnosis is considered desirable as it would facilitate faster detection of articular crystals. As far as we know, conventional computed tomography (CT) could not detect MSU crystals. Dual-energy CT has shown some promise in crystal detection only at high concentrations. Therefore, we hypothesised that multi-energy CT might be more capable of crystal characterisation. Recently, MARS multi-energy CT was developed in Christchurch. This is a new imaging modality which allows characterisation and quantification of materials without loss of spatial resolution, utilising data collected from multiple narrow energy bins. Thus, it may help determine if MSU crystals are present and observable, thereby having the potential to bridge the gap between conventional CT and current molecular imaging and eventually facilitate capability of non-invasive diagnosis of gout.

Aim:

1. To detect MSU crystals using MARS imaging.
2. To determine lowest detectable concentration of MSU crystals using MARS imaging.

Method:

Samples of MSU crystals were first prepared by the sponsor, University Hospital Lausanne and brought to Christchurch. The crystals were first scanned in air which were found causing problems in the images. Several attempts were then made on suspending crystals in media such as PBS solution, ultrasound gel and agar. Agar gel was finally chosen to be the most suitable media of all. Thus, five different amounts of synthetic MSU crystals were suspended homogenously in 1.5% agar gel, which were 137 mg/ml, 74.5 mg/ml, 35.5 mg/ml, 20.5 mg/ml, and 0.5 mg/ml respectively. These MSU samples, together with a sample of agar gel were arranged in a phantom and scanned using MARS scanner. To verify MSU crystal presence in the vials, crystal inspection using polarised light microscopy was later completed. Raw images obtained were first pre-processed using software ImageJ. Then, transverse slices through the vials were used for post-analysis of spectral responses of MSU and agar.

Finally, attenuation profiles of MSU crystals and agar gel were plotted and compared, in order to characterise types of material and determine the lowest detectable concentration of MSU using current MARS scanner.

Results:

Generally, uric acid starts to crystalise in synovial fluid when its concentration reaches 0.068 mg/ml and above. As MSU crystals require certain spatial resolution to be observed, clumps of crystals might be detectable based on voxel size and given spatial resolution of the scanner. However, from the observation of the MARS images, MSU crystals could not be detected and differentiated from agar gel due to limited spatial resolution of the images. From further inspection of crystals using microscopy, a great amount of needle-shaped MSU crystal clumps were observed. This finding verified that MSU crystals could not be detected directly by MARS imaging at this stage. To further detect MSU crystals from post-processing of the images, attenuation profiles of the samples were utilised. Attenuation is known as absorption of photons when x-ray beam passes through materials. Thus, the difference in their x-ray penetration represents the contrast in the image. This means each material has its unique attenuation profile, which allows characterisation of the materials. It was observed from the graphs that profiles of MSU samples had the same slope of trend, indicating they were the same type of material. This trend could also be clearly differentiated from the profile of agar gel and the lowest detectable concentration of MSU using MARS CT scanner was determined to be 74.5 mg/ml. This result was comparable to the data obtained from a commercialised dual-energy CT which was 68.4 mg/ml. The detected high concentration of MSU indicated that these MSU components in the vials were indeed dense clumps of MSU crystals which were likely to be found in gouty tophi.

Conclusion:

The primary finding from the project is that current low-contrast sensitivity of MARS scanner is probably good enough to determine presence of MSU crystals in gouty tophi outside the joints but not high enough to observe them inside the joints. As this project is a pilot study of detecting and measuring gout crystals using MARS imaging, current methodologies require much more work before getting translated to human scanning. For future extension of the project, refinement of current approaches is required, such as improving sample preparation techniques, scanning samples under different imaging protocols, checking reproducibility of data, etc. This project also fits into a broader objective to provide new insights on developing better non-invasive spectral imaging for early detection and characterisation of articular crystals.