



# Calcium carbonates are novel positive birefringent crystals in synovial fluid

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## Presentation

A 78-year-old female patient with history of monoarthritic episodes of the wrist and ankle presented to our outpatient clinic with a swollen and painful right wrist. The X-ray showed presence of radiocarpal narrowing, chondrocalcinosis, erosion of lateral triquetrum and processus styloideus ulnae, and degeneration of the first carpo-metacarpal joint (Fig. 1A). The rheumatoid factor and anti-citrullinated protein were negative. Furthermore, radiographs of both knees showed presence of chondrocalcinosis; the left wrist however did not. The wrist was punctured, and the synovial fluid was examined with compensated polarized light microscopy (CPLM). Analysis revealed the presence of positive-birefringent microcrystals in a matrix (Fig. 1B). Positive birefringence with rhomboid or tubular forms is indicative for calcium pyrophosphate (CPP) crystals, compatible with the radiographic chondrocalcinosis.

Additional analysis with hyperspectral Raman imaging (H-iRPolM, Hybriscan technologies B.V., Nijkerk, the Netherlands), however, identified these particles as calcium carbonate crystals (Fig. 1C). Calcium carbonate crystals, i.e. calcite, have a moderately strong positive

birefringence (birefringence index + 0.175 [1]) and are therefore easily mistaken with CPLM for CPP (birefringence + 0.0155 [2]). With Raman spectroscopy, calcium carbonate can be identified with a sharp characteristic peak at  $1085\text{ cm}^{-1}$ , whereas CPP has a typical peak at  $1050\text{ cm}^{-1}$ . In this specimen, CPP but also hydroxyapatite or calcium oxalate crystals could not be identified by Raman.

## Discussion

Although the presence of calcium carbonates in the human body is widely recognized, the exact role of this compound in synovial fluid is unknown. Intra-articular presence of calcium carbonate crystals can be found and is probably not rare with sensitive techniques such as Raman spectroscopy (2022, [3]). CPLM is widely used for the detection of negative birefringent monosodium urate crystals, and these can easily be differentiated from CPP. But when positive birefringence is encountered, calcium carbonate might be considered, and a possible other clinical presentation deserves our attention.

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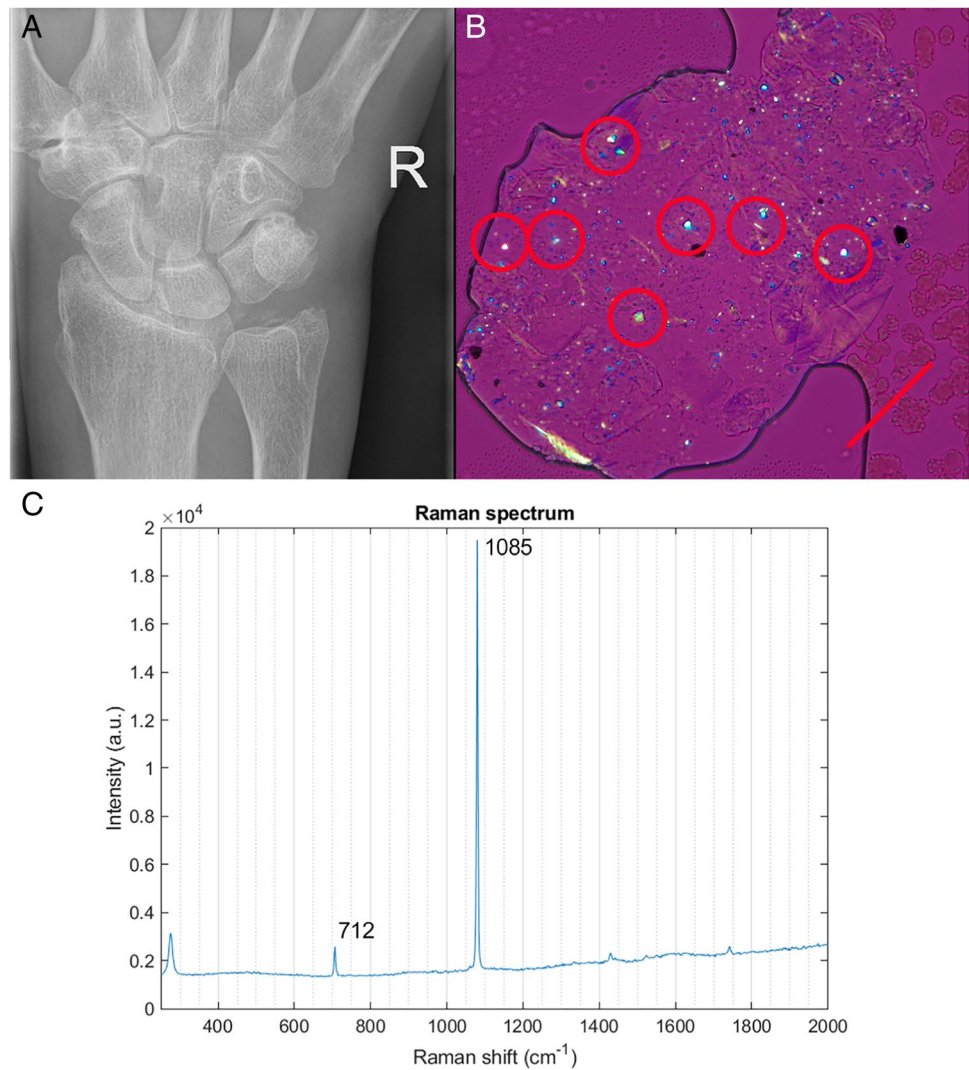
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**Fig. 1** **A** X-ray of swollen joint demonstrating both chondrocalcinosis and degenerative joint disease. **B** Compensated polarized light microscopy image of found object containing calcium carbonate crystals, which show positive birefringence. Red circles mark some of the measured crystals, the red line shows the direction of the compensator. **C** Raman spectra of crystals shown in **B**



**Author contribution** Tom Niessink drafted the manuscript and analyzed the sample. Cees Otto analyzed the spectrum and reviewed and altered manuscript. Matthijs Janssen analyzed the data and reviewed and altered manuscript. Tim L Jansen contributed to the patient care and sample retrieval and drafted manuscript.

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## Declarations

**Conflicts of interest** Cees Otto: CEO of Hybriscan Technologies B.V., a company which produces and sells Raman spectrometer devices, including H-iRPoLM which was used for this study.

Matthijs Janssen, Tim Jansen: Owners of Human Crystal Research B.V., a company interested in development of tools used for clinical identification of synovial crystals.

Tom Niessink has no potential conflicts of interest to disclose.

## References

1. Sklute E, Stephen S, Peltier C, Padova E (2015), Calcite - petrographic data file. Smith's college, 2015. (Accessed 6–9–2022, 2022, at <https://www.science.smith.edu/geosciences/petrology/petrography/calcite/calcite.html>.)
2. Takanabe A, Tanaka M, Taniguchi A, Yamanaka H, Asahi T (2014) Quantitative analysis with advanced compensated polarized light microscopy on wavelength dependence of linear birefringence of single crystals causing arthritis. *J Phys D Appl Phys* 47:285402. <https://doi.org/10.1088/0022-3727/47/28/285402>
3. Niessink T, Kuipers C, de Jong BZ, Lenferink ATM, Jansen M, Jansen TLJ, Otto C (2022), Raman hyperspectral imaging detects novel and combinations of crystals in synovial fluids of patients with a swollen joint. - 2022;n/a. <https://doi.org/10.1002/jrs.6452>

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