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IDENTIFICATION OF HIGH DENSITY MINERALISED PROTRUSIONS IN HUMAN KNEES BY CLINICAL SCANNING TECHNIQUES

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High density mineralised protrusions (HDMPs) from the mineralising front into hyaline articular cartilage (HAC), initially found in horses have recently been confirmed in *ex-vivo* human hip joints. Postulated to be the extension of a naturally occurring microcrack self-healing mechanism, these phenomena are extremely densely mineralised and have the potential to fragment under normal loading conditions. It is likely that their presence would have consequences for the biomechanical performance of surrounding tissues and they have been associated with osteoarthritis (OA).

Investigation of HDMPs in human knees was performed by means of parallel *in-* and *ex-vivo* imaging studies. A retrospective analysis was conducted using the clinical MRI scans of 36 patients (age 19-67) with Alkaptonuria, a genetic condition invariably comorbid with early-onset OA. Patient MRI data were acquired sagitally at 1.5mm intervals with an in-plane resolution of 0.58mm. Potential protrusions were assigned a confidence value (1-5; 5=most confident) based on observable characteristics, representing likelihood of misinterpretation. Nine cadaveric knees (age 74-97) were also studied by MRI. Dual echo steady state (DESS) MR data were produced isotropically at 0.26mm resolution. Each knee was assessed for OA using the Kellgren-Lawrence (KL) scale.

Potential protrusions were identified in all knees across both studies, with 210 reported in total (*in-vivo*=180, *ex-vivo*=30). Ninety-two percent of those noted *in-vivo* had a confidence score of ≥3, indicating a low likelihood of misinterpretation. Each study reported protrusions in all areas of the knee joint. There was considerable variability in morphology and distribution. They were observed both in isolation and in clusters. The ratio of femoral to tibial protrusions for *in-vivo* scans was 4.6:1, compared with 1.7:1, *ex-vivo*. The percentage of protrusions found in regions central to articulation *in-* and *ex-vivo* was 50 and 74, respectively. Signs of OA (KL score ≥1) were recognised in all cadaveric knees.

High incidence, twinned with distribution of protrusions in OA knees suggests a role within the progression of arthropathy. Presence in all knees across both studies further demonstrates the phenomenon is not limited to individuals with ochronotic OA. Clustering may account for several protrusions, or may be attributable to a single fragmented HDMP. Observed morphological variation may be normal for the HDMP phenotype, or possibly representative of different stages within the HDMP pathogenesis. Regions central to articulation typically experience the greatest strain within the knee. Therefore, it is likely that the high proportion of HDMPs observed in these areas would be subjected to fragmentation, at the detriment of surrounding HAC.

The detectability of HDMPs in clinical practice is demonstrable by both the *in-* and *ex-vivo* studies as they were conducted using clinical MRI scanners with clinically-achievable parameters. Clinical detection of HDMPs should be considered as a potential imaging biomarker for predicting joint destruction. The application of a confidence scale was useful in compensating for the reduced image quality of patient, compared with cadaveric scans. However, the validation of a standardised detection protocol is needed in order to distinguish which are genuine HDMPs and which are not.

Ideally, this would involve microCT and histological analysis of all potential protrusions identified in a joint by clinical scanning techniques, such as those we describe here.