The Potential of Reference Point Microindentation for Fracture Risk Assessment

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Introduction: Current fracture risk assessment tools, primarily bone mineral density (BMD), have limitations and do not identify a large proportion of individuals who go on to suffer a hip fracture [1]. Reference Point Indentation (RPI) is a novel tool that assesses the mechanical properties of bone [2], with the aim to supplement existing techniques for improved prediction of hip fracture. Clinically, this device has shown the potential to differentiate fractured from non-fractured patients, reporting no pain or complications [3]. To further investigate the device’s suitability as a diagnostic tool, we compared the tool to BMD and used RPI to investigate explanted osteoporotic (OP) bone in comparison to a non-disease control at the site of most clinically significant fracture, the femoral neck.

Methods: Clinically, the RPI tool is intended to be inserted through soft tissue, with the reference probe anchoring against the bone’s surface and the test probe cyclically indenting into the bone. The difference between the first and last (tenth) cycle depth, the indentation distance increase (IDI), is the main output measure (Fig - A). In this study, the Biodent HfcTM RPI device (Active Life Scientific) was used to test 42 OP femoral neck samples explanted from hip replacement patients and 10 cadaveric control samples with no history of bone disease or fracture. The femoral neck samples were indented around the entire circumference at 20° spacing at 10 N and 2 Hz with the device held freehand. Our previous studies [4, 5] highlighted heterogeneity of the bone and the optimal sample thickness, spacing and number of measurements for reduced variability and, hence, we focused a further 15 measurements within a 20° section of the inferomedial neck (the calcar) for 30 of the OP samples and all of the control. For 16 of the clinical samples, the patients returned for a DXA (Dual-Energy X-Ray Absorptiometry) BMD scan of their contralateral limb between one and two months post-operatively. The non-parametric Mann-Whitney U-Test and Spearman’s Rank Correlation were used as applicable.

The study was conducted under ethical approval (12/SC/0325 - Southampton A).

Results: Indenting the whole femoral neck (20° spacing, 18 measurements) demonstrated an elevated IDI in the osteoporotic group relative to control (47% higher - median = 20.9 µm osteoporotic vs. 14.2 µm control, p < 0.001, Fig - B.). RPI focused on the inferomedial neck also showed a similarly elevated IDI in the osteoporotic group, though with a reduced magnitude (14% higher - median = 15.5 µm...
osteoporotic vs. 13.6 µm control, p = 0.017). The ROC AUC (Receiver Operator Characteristic Area Under the Curve - where a value of 0.5 indicates a random detector and 1.0 indicates a tool that can perfectly separate the two groups) showed the RPI tool to have high sensitivity and specificity on the total neck (AUC = 0.93), which was reduced when testing the inferomedial side alone (AUC = 0.75).

As the osteoporotic group is older and contains more females than the control group (median 83 years vs. 63 years and 67% vs. 60% female, respectively) and there may be a weak relationship between age and IDI (r = 0.27, p = 0.057 - close to significance) this could be a confounding factor. However, in a smaller age and sex matched group (±2 years) the same observations remained (total neck, n = 5, p = 0.01 and inferomedial neck, n = 4, p = 0.058 - close to significance with small sample size).

In comparison to clinical BMD (OP samples), there is some correlation when considering the total femoral neck (r = -0.59, p = 0.017), but not when only considering indents at the inferomedial side (r = 0.11, p = 0.72).

Discussion: IDI was elevated in osteoporotic bone relative to the control regardless of age and sex and the ROC AUC shows that the tool can discriminate well between osteoporotic and control groups. This suggests that RPI is effective to discern osteoporotic and healthy (age matched) bone at the femoral neck, close to the site of fracture, similarly as at the tibial midshaft investigated previously [3]. Cortical thickness [4] and (considering the indent size is similar to pore diameter [7]) porosity, both influence IDI. As the cortex is thicker [5, 6] (critically, being substantially thicker than 10 times the indentation depth [4]) and less porous [7] in the inferomedial compared to the superolateral region, further measurements were focussed here. Additionally, the larger number of measurements in this region (15) and the closer proximity of measurements (20° section) intends to further reduce the variability associated with porosity and heterogeneity [5] aiming to obtain a more representative measure of the bone’s material properties. However, in doing this, the ability of RPI to differentiate between the groups is diminished and the correlation to BMD is lost. This is likely a consequence of factors such as heterogeneity, and with it, thickness and porosity, which relate to both BMD and fracture risk (e.g. elderly osteoporotic cortical bone is thinner and more porous and bone density is also heterogeneous). Additionally, with its increased thinning [6], the superolateral region is likely more affected by age and disease. Thus, when RPI is controlled for improved repeatability and a better representation of the material properties of bone by taking more measurements in the inferomedial region, it appears to be a less effective stand-alone tool. Yet, by measuring a property distinct from BMD, when measuring in this way, we hypothesize that the predictive power of RPI and BMD together (to be assessed through measuring cadaveric BMD) will create an improved combined fracture risk assessment tool.

Significance: RPI shows the ability to differentiate osteoporotic from healthy bone, with the translational potential to truly improve fracture risk assessment through supplementing existing techniques such as FRAX and BMD measurement.
Fig: B – RPI around the total neck: OP vs non-disease control.
Fig: C – Correlation between IDI and BMD, measuring around the total neck (All - 360°, shown - *p < 0.05) and 15 measurements within ±10° of the inferomedial point (Medial - 20°)