ARE THE CRACKS STARTING TO APPEAR IN BISPHOSPHONATE THERAPY?
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Introduction: Osteoporosis is a global health issue with 200 million people suffering worldwide and it is a common condition in the elderly. Bisphosphonates including alendronate and risendronate are considered as the first line treatment for osteoporosis. However, there is increasing evidence that bisphosphonate (BP) therapy is associated with atypical fractures. Animal studies have reported a dose-dependent association between the duration of BP therapy and the accumulation of micro-damage. We tested the hypothesis that hip fracture patients treated with BP exhibit greater micro-damage density than untreated fracture and ‘healthy’ aging non-fracture controls.

Method: Trabecular bone cores from patients treated with BP were compared with patients who had not received any treatment for bone metabolic disease (ethics reference: R13004). Non-fractured cadaveric femora from individuals with no history of bone metabolic disease were used as controls. Cores were imaged in high spatial resolution (~1.3µm) using Synchrotron X-ray tomography (Diamond Light Source Ltd.) A novel classification system was devised to characterise features of micro-damage in the Synchrotron images: micro-cracks, diffuse damage and perforations. Synchrotron micro-CT stacks were visualised and analysed using ImageJ, Avizo and VGStudio MAX.

Results: Our findings show that the BP group had the highest micro-damage density across all groups. The BP group (7.7/mm³) also exhibited greater micro-crack density than the fracture (4.3/mm³) and non-fracture (4.1/mm³) controls. Furthermore, the BP group (1.9/mm³) demonstrated increased diffuse damage when compared to the fracture (0.3/mm³) and non-fracture (0.8/mm³) controls. In contrast, the BP group (1.9/mm³) had fewer perforations than fracture (3.0/mm³) and non-fracture controls (3.9/mm³).

Conclusion: BP inhibits bone remodelling, thereby reducing the number of perforated trabeculae, but over-suppression leads to micro-damage accumulation. Accumulated damage could weaken the trabecular bone in the femoral head and neck, increasing the risk of a fracture during a trip or fall.