Background: The majority of aortic dissection cases occur below current intervention thresholds and improved methods for identifying those at highest risk are urgently required. Thoracic aortopathy has been associated with medial microcalcification, which can be visualised non-invasively, however, any relationship to disease severity has yet to be established.

Methods: One hundred and one thoracic aortic specimens were collected from 57 patients with thoracic aortopathy and 18 controls. Quantitative assessment of histological microcalcification (percentage area von kossa staining) and autoradiography (18F-sodium fluoride) was performed. Histopathological degeneration severity was assessed and correlated with microcalcification content. Nanoindentation (tissue elastic modulus) was performed. The feasibility of18F-sodium fluoride imaging as a clinical tool was assessed in vivo.

Results: Microcalcification content was higher in aortopathy samples with mild (n=28; 6.17 [2.71 to 10.39], p≤0.001) or moderate histopathological degeneration (n=30; 3.74 [0.87, to 11.80], p<0.014) compared with controlaortic samples (n=18, 0.79 [0.36 to 1.90]). Interestingly, samples with severe histopathological degeneration (n=24; 0.40 [0.15 to 0.87]) had substantially less microcalcification compared with mild or moderate degeneration (both p<0.001), a process closely linked with elastin loss (n=82; r=-0.36, p=0.001) and lower

tissue elastic modulus (n=28; r=0.43, p=0.026). Microcalcification quantified using 18F sodium fluoride was closely correlated with histological assessment (n=66; r=0.76, p<0.001), and identified areas of focal weakness in vivo.

Conclusions

In thoracic aortopathy, progression to severe medial degeneration is associated with reduced microcalcification and biomechanical weakness, mediated through elastin fibre loss. 18F-Sodium fluoride quantifies medial microcalcification and is a feasible modality for tracking disease with major translational promise.