Distal radius cortical microstructure and calculated strength predict incident fractures independently of FRAX in postmenopausal women

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Objective
Operational diagnosis of osteoporosis is based on areal bone mineral density (aBMD). However, a large proportion of fractures occur in subjects without osteoporosis. This suggests that aBMD, despite being a good predictor of fracture, does not capture all components of bone fragility. We investigated the contribution of bone microstructure to fracture risk in postmenopausal women, independently of aBMD and clinical risk factors integrated in FRAX.

Methods
Seven hundred thirty nine women (age 65.0 ± 1.4 years), enrolled in the Geneva Retirees Cohort (GERICO) study, were prospectively followed for fracture occurrence over 3.5 ± 1.0 years. At baseline, cortical (Ct) and trabecular (Tb) volumetric bone density (vBMD) and microstructure at distal radius and tibia were assessed by HR-pQCT (Xtreme CT, Scanco Medical, Bassersdorf, Switzerland), and aBMD by DXA. A principal component analysis was applied for the radius and the tibia separately.

Results
Seventy six women (10.3%) sustained an incident clinical fracture (excluding fingers, toes and skull) or a morphometric vertebral fracture. Three principal components were identified at the radius and the tibia (Tb microstructure, Ct microstructure, and bone scanned projected area), representing in both sites 89% of the variability of the HR-pQCT parameters. All components were associated with incident fractures. Hazard ratios [HR] for one standard deviation decrease of each component varied from 1.27 to 1.79 (p<0.05 to <0.001). After adjustment for femoral neck aBMD, all components except tibia Tb microstructure remained significantly associated with fracture risk [HR for one standard deviation decrease of each component varied from 1.28 to 1.69 (p<0.05 to <0.001)]. After adjustment for FRAX (with aBMD), only Ct microstructure components [HR (95%CI) 1.56 (1.22-2.04), p<0.001 and 1.45 (1.14-1.85), p=0.003 at the radius and the tibia respectively] and radius Tb component [HR (95%CI) 1.30 (1.01-1.67), p=0.043] remained significantly associated with fracture risk. After adjustment for FRAX with aBMD and TBS, only Ct microstructure components remained significantly associated with fracture risk [HR (95%CI) 1.43 (1.11-1.85), p=0.006 and 1.32 (1.02-1.69), p=0.033 at the radius and the tibia respectively].

Conclusion
Cortical bone alterations predict incident fractures independently of aBMD and FRAX. This highlights the additive contribution of Ct bone microstructure assessment to aBMD and FRAX in identifying women at increased risk of incident fracture.