

CAN INDIVIDUALISED MODELS DISCRIMINATE BONE FRACTURE PREVALENCE FROM CONTROLS?

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Introduction

The predictivity of tools routinely used to assess the risk of bone fracture *in-vivo* (bone mineral density BMD, or derived indices e.g. FRAX) is far from ideal [Tremollieres, 2010]. Bone strength prediction based on finite element (FE) models from CT is superior to BMD *in vitro* on femora and vertebrae [Crawford, 2003], but preliminary tests on clinical data have not been able to confirm this superiority [Orwoll, 2009; Amin, 2011]. This may be due to the lack of consideration of important multiscale fracture determinants, such as the loading conditions and the bone remodelling over time.

A full multiscale model of bone fracture is currently unavailable, at least for the axial skeleton, where it is not yet possible to obtain personalised data at the tissue level. However, the fracture risk prediction through FE models could plausibly be improved by accounting for load variability using musculoskeletal model atlases, and by accounting for bone remodelling through simplified continuum level approaches.

The aim of this work was therefore to verify if such improved FE models at the lumbar spine can discriminate between individuals with prevalent osteoporotic fractures and controls.

Methods

Lumbar spine CT scans were acquired for 43 women aged over 60 (19 subjects classified as skeletally fragile having a history of osteoporotic fractures, 24 controls). Cases and controls did not differ significantly for age or height, although weight was slightly lower in the controls (mean 610 vs 680N, $p=0.02$). For each patient, DXA images and a questionnaire were available, and FRAX was calculated.

FE models were generated for each vertebra using the CT data of the L1-L3 segment, obtaining iso-topological meshes [Grassi, 2011] with mapped bone density and Young's modulus from baseline CT.

A continuum-level bone resorption rate as a function of age was estimated from literature data [Müller, 2005] and applied uniformly to the FE bone density at one-year increments.

The loading conditions were derived from a musculoskeletal model capable of estimating physiological loads [Han, 2012], together with an estimation of annual frequency of nine activities of daily living (standing, walking, flexion-extension, bending, rotation, lifting, asymmetric carrying, elevation). All loads were scaled to each patient's height and weight. The boundary conditions applied to each vertebra were obtained in terms of force and moment acting at the cranial endplate.

All models were combined to obtain the Personalised Fracture Risk (PFR). At yearly time-steps from 0 to 10: (i) the resorption module modified baseline bone density; (ii) the loading database was queried (iii) the organ scale FE model was run for each loading activity, (iv) the PFR was calculated as the risk level for each activity (maximum principal / limit strain ratio, with 0.73% limit in tension and 1.04% in compression) weighted over the frequency of the activities.

Results and Discussion

The mean values of both PFR and FRAX were higher for the group of 19 cases with respect to the 24 controls. However, differences between cases and controls were statistically significant only for PFR (PFR $p=0.005$, FRAX $p=0.31$).

These early studies indicate that a multi-scale computational framework for establishing PFR can discriminate subjects with skeletal fragility and fracture prevalence with a greater accuracy than FRAX. Clinical assessment of elderly subjects might therefore benefit from PFR to individually and prospectively discriminate cases at risk.

References

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