The Multi-domain Load Hypothesis Suggests Shear Stresses are More Prevalent in the Femoral Neck than Lesser Trochanteric Region: Implications for Optimizing Interventions that Reduce Fracture Risk

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Author disclosures: none

INTRODUCTION: Preventative approaches are needed to curb the rising incidence of femoral neck (FN) fractures. Although osteogenesis is more readily enabled in young adults, pre-emptive interventions in the middle-aged need to be explored. An extensive understanding of the natural loading environment of the FN region could help develop interventions that enhance bone quality and quantity. The most important mechanical stress/strain characteristics (mode and magnitude) have differential influences on osteogenesis (e.g., compression > tension). For example, administration of low-molecular-weight parathyroid hormone (teriparatide) increases bone deposition in regions naturally subjected to compression when they are loaded in compression (vs. tension loading) **[1-3]**. Although the most commonly considered strain modes (compression and tension) are prominent in conventional (Wolffian) understanding of FN loading **[4]**, increasing evidence suggests that shear stresses may be more important **[5]**. Regional differences in the biological importance of shear stresses (most important in the FN, least important in the lesser-to-subtrochanteric region) reflects the 'multi-domain load hypothesis' (**Fig. 1**) **[6]**. Recognizing the potential biological importance of shear stresses in this context could help develop protocols where this stress/strain mode enhances osteogenesis in the FN to a greater extent than when compression and teriparatide are concurrently administered **[1-3]** (**Table 1**, various described exercise regimes). We examined finite element analyses (FEAs), other types of analytical studies, and similar robust sources of evidence relevant to exploring the hypothesis that shear stresses/strains are a critical component of the natural/habitual load environment of the FN region.

METHODS: (A) Literature review. Studies including FEAs or other computational/analytical studies of the proximal femur were examined for various terms with respect to the loading environment of the FN: shear, torsion, multiaxial loading, multidirectional loading, complex loading, shifting neutral axis. The 28 studies identified were independently examined by three investigators. These studies (and search results) can be found at https://teambone.com/themes/. **(B) Trabecular intersection angles.** These data were obtained from a prior radiographic study **[7]** of human femora (n=16, age range: 20-70). One pair of obvious arched trabecular tracts were traced in the FN and lesser trochanteric (LT) regions. Angles of intersections formed at the trabecular arch apices were measured from tracings. Oblique (i.e., non-orthogonal) intersections are known to best accommodate prevalent/predominant shear stresses **[6]**. **(C) Predominant collagen fiber orientation (CFO) analysis**, as described previously **[9]**, allows distributions of habitual strain modes (tension, compression, shear/torsion) to be inferred by regional variations in predominant CFO in thin sections, allowing habitual bending to be distinguished from torsion/shear. CFO was quantified in the contralateral bones from the same adult human femora (described above) in the cortices at: (1) mid-neck, (2) lesser/sub-trochanteric, and (3) proximal diaphysis **[10,11]**.

Results: (A) Our literature review shows that 82% (23/28) of the FEAs and other analytical studies report the presence of significant shear stresses/strains in the FN. **(B) Trabecular intersections** in the human proximal femora are typically non-orthogonal in the neck (69°$\pm$12°; range 51°-90°; **Fig. 2**), consistent with adaptation for shear loading **[8]**. In contrast, trabecular tracts were typically orthogonal in the trochanteric region (92°$\pm$6°; range: 82°-105°) (p<0.01 vs. FN), as expected in a loading environment with comparatively simpler bending (i.e., prevalent/predominant tension and compression). **(C) CFO results** are consistent with: (1) torsion/shear in the FN, and (2) medial-lateral bending in the LT region **[10,11]**.

DISCUSSION: Conventional understanding of the loading environment of the human FN is largely based on Wolff's trajectorial theory; namely, the superior cortex and trabecular tract experience net tension, while the inferior cortex and trabecular tract experience net compression **[4,5]**. However, subsequent studies have challenged this view, as experimental and computational data suggest that the strain distribution within the FN is relatively complex/shear-dominated. This is in stark contrast to the habitual bending in the LT and proximal diaphyseal regions. These proximal-to-distal differences in load history reflect the 'multi-domain load hypothesis' of the human proximal femur **[6]**. As shown in our prior investigation exploring the suspected etiologies and antecedent load environments of FN stress fractures **[4]**, very few mention the role of shear (~4%). In contrast, shear is considered to be important in the FN region in the relatively more robust studies examined in the present investigation. Regional variations in strain mode have important mechanobiological implications because net tension, compression and shear differentially induce osteogenesis **[12,13]**. Future studies are needed to evaluate the hypothesis that when shear is appropriately imposed on the FN through exercise and coupled with a biochemical agent (e.g., teriparatide), osteogenesis occurs to a greater extent than compression **(**i.e., potentially: shear > compression > tension). Recognizing that the FN is relatively complexly loaded (hence shear-dominant) provides a framework for developing novel biophysical/biochemical strategies aimed at enhancing bone quantity and quality of this fracture-prone region.

Significance: Osteogenesis in the femoral neck can be enhanced when an anabolic agent is co-administered with a specific imposed loading environment. Such interventions should be explored with the aim of developing protocols that can help curb the rising incidence of femoral neck fractures.

REFERENCES: **[1]** Rooney et al. (2020) Bone 136:115373; **[2]** Rooney et al. (2022) Bone 157:116342; **[3]** Rooney et al. (2023) J Bone Min Res 38:59-; **[4]** Walker et al. (2023) ORS abstract 0503; **[5]** Richards et al. (2024) ORS abstract 1475; **[6]** Skedros (2025) Chapter 5, *In:* Bone Histology, A Biological Anthropological Perspective. CRC Press; **[7]** Skedros and Baucom (2007) J Theoretical Biology 244:15- ; **[8]** Pidaparti and Turner (1997) J. Biomech 30:997-; **[9]** Skedros et al. (2009) Bone 44:392-; **[10]** Skedros et al. (2013) ORS abstract 1419; **[11]** Skedros et al. (2016) ORS abstract, 734; **[12]** Zhong et al. (2013) Eur J Orthod 35:59-; **[13]** Li et al. (2015) J Orthop Res 33:1008-

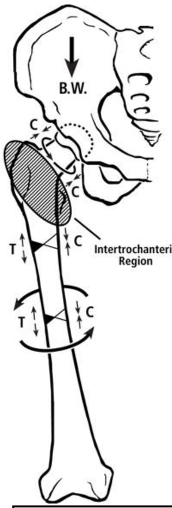

Fig. 1: Multi-domain load hypothesis of the human femur. **B.W.** = body weight; **T** = tension; **C** = compression; the circular lines in the FN and mid-shaft suggest torsional/shear loading.

Fig. 2

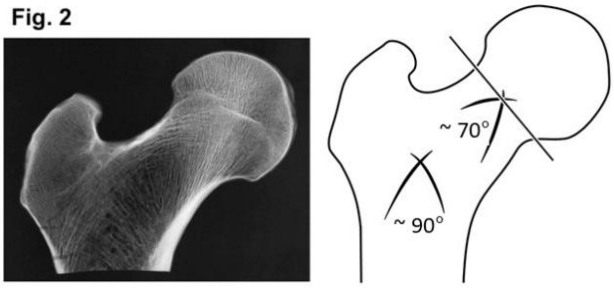

Table 1: Potential Prophylactic Osteogenic Interventions

Old Age	Young Age
Progressive Resistance Training *	Odd impact exercise such as soccer or squash§
Weight bearing impact exercises*	High impact such as long jump and triple jump§
Challenging balance, stepping, and mobility exercises*	Hopping, Running and Fast Walking*
Standing on a slightly vibrating table§	Jump roping§
Whole Body Low-magnitude high frequency vibrations‡	Regularly Standing up from a squatted position†
Fast walking and stair climbing*	High intensity jumping and hopping exercises*

Interventions were identified as *T/C, †C/C, ‡Shear, or §not specified