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# Collagen Fiber Orientation (CFO) and CFO Heterogeneity (CFO-Het) in the Human Femoral Neck Cortex: Do these Characteristics Demonstrate Age-Related Changes in Load-History?

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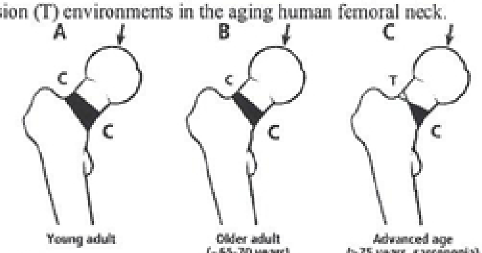
## INTRODUCTION

Because loss of bone mass does not fully explain the age-related propensity for fractures [1], investigating bone quality is of particular importance in preventing fragility fractures. Age-related changes in collagen/organic matrix characteristics play an important role in the degradation of tissue mechanical properties seen with aging [2,3]. Additionally, predominant collagen fiber orientation (CFO) strongly correlates with load history where habitual "tension" regions show longitudinal CFO and habitual "compression" regions show oblique-to-transverse CFO [4]. Consequently, the presence of habitual bending can be distinguished from habitual torsion (where CFO variations are less obvious or seem paradoxical) [5]. Because of the additional importance of collagen in conveying bone toughness [6], we are interested in relationships of predominant CFO and CFO heterogeneity (CFO-Het = variation in CFO) with age and load history. In this context we used these two characteristics to consider an important hypothesis stated by Mayhew and co-workers [7] regarding changes in the distributions of strains across the femoral neck region with aging. They predicted that with aging the superior aspect of the hip becomes relatively underloaded (compared to the inferior aspect) as a result of reduced gluteus medius strength (sarcopenia) and increased percentage of walking (overall ambulation is also reduced). We further predict that net tension also occurs in the superior cortex with age (see figure). This is important because the accumulation of tension-specific microdamage, coupled with the thinning superior cortex, could be the "1st stage" of the two-stage process that increases the probability of low-energy/fragility fractures of the femoral neck (the "second stage" is compression from a fall that overloads the previously tension-loaded and shell-like superior and postero-superior cortex). We hypothesize that there are regional CFO and CFO-Het changes that reflect shifting compression (C) and tension (T) environments in the aging human femoral neck.




## METHODS

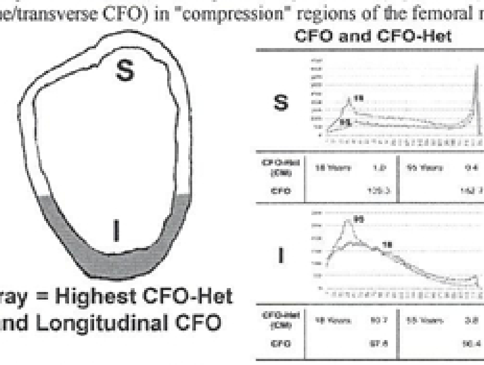
29 human femoral necks (4 male, 25 female; 18-95 years) were embedded in polymethyl methacrylate. A 1mm thick mid-neck transverse section was obtained from each bone, mounted on a glass slide and ultramilled to achieve an overall thickness of 100$\pm$5 µm [8]. 50X images were obtained in octants of each sectioned bone. Images were taken in circularly polarized light and CFO was expressed as the weighted mean gray-level (WMGL) in each image [8]. CFO-Het was measured using full width at 1/2 maximum (FWHM) of the GL profile obtained from each image. Spearman correlations and Kruskal-Wallis Z tests were used for statistical analysis.

## RESULTS

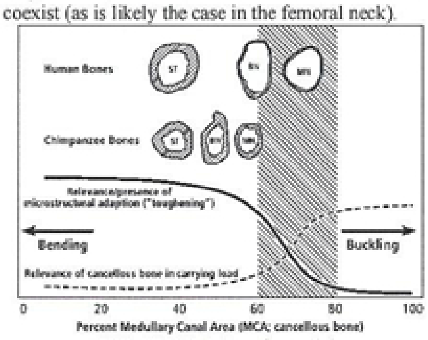
The inferior cortex of the human femoral neck showed significantly higher CFO-Het than the superior cortex ($p < 0.0001$) (see figure below). By contrast, and unexpectedly, the inferior "compression" cortex had more longitudinal CFO (i.e., darker WMGLs, which are typically found in "tension" regions ($p = 0.005$)). CFO-Het did not correlate with CFO ($r = -0.1$). Superior/inferior (S/I) CFO and S/I CFO-Het did not correlate with age ($r = -0.004$, $r = 0.2$ respectively), which was also not expected. The figure below shows GL/CFO profiles from S and I cortices from our youngest (18-year-old) and oldest (95-year-old) bones.

## DISCUSSION

Our results show no evidence of the predicted age-related emergence of CFO patterns that reflect net tension in the superior cortex. Also, through the broad age range (18-95 years) there is significantly higher CFO-Het and, unexpectedly, more longitudinal ("tension" CFO) in the inferior cortex (typically considered the "compression" cortex). Based on our previous studies, we expected higher CFO (significantly more oblique/transverse CFO) in "compression" regions of the femoral neck




[9]. It is difficult to conclude that our paradoxical CFO data actually reflect the presence of greater compression in the <u>superior</u> cortex, and less compression (or tension) in the inferior neck. Caution must also be exercised in interpreting the CFO-Het data in terms of adaptation/load-history. This is because CFO and CFO-het are 'composite' measures that summarize all possible explanations for gray-level variations in a polarized image, including osteon morphotypes and the percentage of interstitial bone. In fact, these latter two variables could be more sensitive for detecting load-history variations than CFO-Het. Nevertheless, among a myriad of isolated histomorphological characteristics of bone that have been studied as potential predictors of regional "tension" and "compression" cortices produced by habitual bending, CFO is the most sensitive and specific [4]. But what could invalidate CFO's utility is if the cortical area of the bone cross-section is sufficiently low, placing it beyond a "cortical robusticity threshold" where conventional histomorphological adaptations are no longer valid [10]. For example, the shaded region shown below represents a threshold where the cortical thickness of a region is so thin that it no longer exhibits conventional histomorphological evidence of bending. This hypothesis could help explain our paradoxical findings. The use of histomorphological characteristics in drawing simple interpretations of load history is also confounded in situations when habitual bending and torsion coexist (as is likely the case in the femoral neck).




## SIGNIFICANCE

The organization of bone collagen is important in ensuring toughness in addition to being correlated with strain history. Establishing regional patterns in the collagen component of bone can help in determining how bone microstructure might be adapted for variations in load history. This knowledge helps to advance understanding of the specific characteristics of normal bone matrix organization that degrade with age and disease (e.g. osteoporosis) in the fracture-prone femoral neck.

## REFERENCES

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