### Accepted Manuscript

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PII: S8756-3282(18)30178-9

DOI: doi:10.1016/j.bone.2018.04.024

Reference: BON 11635

To appear in: Bone

Received date: 15 November 2017

Revised date: 27 April 2018 Accepted date: 28 April 2018

Please cite this article as: Rémy Gauthier, Hélène Follet, Max Langer, Evelyne Gineyts, Frédéric Rongiéras, Françoise Peyrin, David Mitton, Relationships between human cortical bone toughness and collagen cross-links on paired anatomical locations. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Bon(2017), doi:10.1016/j.bone.2018.04.024

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### **ACCEPTED MANUSCRIPT**

# Relationships between human cortical bone toughness and collagen crosslinks on paired anatomical locations

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Abstract: Human cortical bone fracture processes depend on the internal porosity network down to the lacunar length scale. Recent results show that at the collagen scale, the maturation of collagen cross-links may have a negative influence on bone mechanical behavior. While the effect of pentosidine on human cortical bone toughness has been studied, the influence of mature and immature enzymatic cross-links has only been studied in relation to strength and work of fracture. Moreover, these relationships have not been studied on different paired anatomical locations. Thus, the aim of the current study was to assess the relationships between both enzymatic and non-enzymatic collagen cross-links and human cortical bone toughness, on four human paired anatomical locations. Single Edge Notched Bending toughness tests were performed for two loading conditions: a quasi-static standard condition, and a condition representative of a fall. These tests were done with 32 paired femoral diaphyses, femoral necks and radial diaphyses (18 women, age  $81 \pm 12$  y.o.; 14 men, age  $79 \pm 12$  y.o.; 15 men, age  $79 \pm 12$  y.o.; 16 men, age  $79 \pm 12$  y.o.; 17 men, age  $79 \pm 12$  y.o.; 18 men, age  $79 \pm 12$  y.o.; 19 men, age  $79 \pm 12$  y.o.; 19 men, age  $79 \pm 12$  y.o.; 10 men, age  $79 \pm 12$  y.o.; 10 men, age  $79 \pm 12$  y.o.; 11 men, age  $79 \pm 12$  y.o.; 12 men, age  $79 \pm 12$  y.o.; 12 men, age  $79 \pm 12$  y.o.; 14 men, age  $79 \pm 12$  y.o.; 15 men, age  $79 \pm 12$  y.o.; 16 men, age  $79 \pm 12$  y.o.; 17 men, age  $79 \pm 12$  y.o.; 18 men, age  $79 \pm 12$  y.o.; 19 men, age  $79 \pm 12$  y.o.; 19 men, age  $79 \pm 12$  y.o.; 10 men, age  $79 \pm 12$  y.o.; 11 men, age  $79 \pm 12$  y.o.; 12 men, age  $79 \pm 12$  y.o.; 13 men, age  $79 \pm 12$  y.o.; 14 men, age  $79 \pm 12$  y.o.; 15 men, age  $70 \pm 12$  y.o.; 15 men, age  $70 \pm 12$  y.o.; 15 men, age  $70 \pm 12$  y.o.; 16 men, age  $70 \pm 12$  y.o.; 17 men, age  $70 \pm 12$  y.o.; 18 men, age  $70 \pm 12$  y.o.; 18 men, age  $70 \pm 12$  y.o.; 18 men, age  $70 \pm 12$  y.o.; 19 men, age  $70 \pm 12$  y.o.; 19 men, age  $70 \pm 12$  y.o.; 10 men, age  $70 \pm 12$  y.o.; 8 y.o.). Collagen enzymatic and non-enzymatic crosslinks were measured on the same bones. Maturation of collagen was defined as the ratio between immature and mature cross-links (CX). The results show that there was a significant correlation between collagen cross-link maturation and bone toughness when gathering femoral and radial diaphyses, but not when considering each anatomical location individually. These results show that the influence of collagen enzymatic and non-enzymatic cross-links is minor when considering human cortical bone crack propagation mechanisms.

**Keyword:** Human cortical bone, fracture toughness, strain rate, inter-sites, collagen cross-links

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