Southampton

IDENTIFICATION OF REGIONAL DIVERSITY IN BLOOD VESSEL STRUCTURE WITHIN MURINE CORTICAL BONE

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INTRODUCTION AND OBJECTIVES

Bone is a dynamic tissue which is actively remodelled throughout life. It relies upon a constant blood



DISTINCT VASCULAR STRUCTURES IN ANTERIOR AND POSTERIOR REGIONS OF THE YOUNG ANIMALS

supply for the provision of oxygen and nutrients. The cortex or outer shell of most of our bones is perforated by an interconnected network of vascular canals¹ and bone cell survival depends on the proximity to this vascular network. Recent evidence has emerged that low bone mass, deterioration of bone tissue and disruption of bone microarchitecture in osteoporosis may be driven by reduced angiogenic signals and vascular supply²⁻⁴. A thorough investigation of this hypothesis is currently limited by challenges related to imaging of the bone vascular network, which is deeply enclosed in mineralised bone tissue.

The goal of this study was to assess local distribution of vascular intracortical canals in the murine tibia-fibula junction and quantify changes with age.



□ 15-week- and 10-month-old C57BL/6 females

Synchrotron radiation-based CT imaging

Image processing and analysis



Figure 1. Diagram of the tibia with scanned area centred at the fibula-tibia junction.



(D). 3D rendering of Intracortical vascular canals for anterior (E) and posterior (F) regions. Percentage of canal volume for anterior and posterior compartments (G).



Figure 4. Distance analysis with exclusion of intracortical vascular canals. 2D slice with canals (A). Removal of canals to investigate effect on tissue perfusion (B). 3D distance transform on mask without canals (C) and region in red where distances to nearest bone surface have been altered (D). Tissue distances to nearest bone surface in the presence and absence of canals (E). Effect of the exclusion of canals in the maximum tissue distance (F).

Figure 3. Intracortical vascular structures in anterior and

posterior regions of the tibia-fibula junction. Separation of

the analysed region (A) in anterior (B) and posterior (C)

compartments. Intracortical vascular canals in 2D slice

% Canal Volume - Young

1.5

Volume/Bone

(Canal









□ SITE SPECIFIC CHANGES OF THE INTRACORTICAL VASCULATURE WITH AGE







Figure 5. Reduction in intracortical vascular canal volume in the posterior region with age. 3D rendering of vascular intracortical canals in the posterior regions of young (A) and old (B) animals. Local changes in the percentage of vascular canals with age (C). Thinning of the cortex with age (D).



3D DISTANCE TRANSFORM

distance image



Figure 2. Image Processing and Analysis Workflow. µCT datasets are binarised by global thresholding to capture the mineralised tissue. Porosity is extracted and classified into canals and osteocyte lacunae. 3D distance transform computes distances to the nearest canals and bone surfaces. Distances are used as tissue perfusion indicators.



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CONCLUSIONS

• Our studies reveal age-related and site-specific changes of the intracortical vascular canals that are associated with a bone loss due to thinning of the cortex.

Our future studies will investigate the functional significance of the vasculature using transgenic animals that represent human bone diseases phenotypes.

[1] D. M. L. Cooper, a L. Turinsky, C. W. Sensen, and B. Hallgrímsson, "Quantitative 3D analysis of the canal network in cortical bone by micro-computed tomography.," Anat. Rec. B. New Anat., vol. 274, no. 1, pp. 169–79, Sep. 2003.

[2] P. Carmeliet, V. Ferreira, G. Breier, S. Pollefeyt, L. Kieckens, M. Gertsenstein, M. Fahrig, A. Vandenhoeck, K. Harpal, C. Eberhardt, C. Declercq, J. Pawling, L. Moons, D. Collen, W. Risau, and A. Nagy, "Abnormal blood vessel development and lethality in embryos lacking a single VEGF allele.," Nature, vol. 380, no. 6573, pp. 435–439, Apr. 1996.
[3] Y. Liu, A. D. Berendsen, S. Jia, S. Lotinun, R. Baron, N. Ferrara, and B. R. Olsen, "Intracellular VEGF regulates the balance between osteoblast and adipocyte differentiation.," J. Clin. Invest., vol. 122, no. 9, pp. 3101–3113, Sep. 2012.

(4) F. A. Dinenno, P. P. Jones, D. R. Seals, and H. Tanaka, "Limb blood flow and vascular conductance are reduced with age in healthy humans: relation to elevations in sympathetic nerve activity and declines in oxygen demand.," Circulation, vol. 100, no. 2, pp. 164–170, Jul. 1999.

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