Scaffold curvature-mediated novel biomineralization process originates a continuous soft tissue-to-bone interface

Abstract

A myriad of shapes are found in biological tissues, often naturally evolved to fulfill a particular function. In the field of tissue engineering, substrate geometry influences cell behavior and tissue formation in vitro, yet little is known how this translates to an in vivo scenario. Here we investigate scaffold curvature-induced tissue growth, without additional growth factors or cells, in an ovine animal model. We show that soft tissue formation follows a curvature-driven tissue growth model. The highly organized endogenous soft matrix, potentially under mechanical strain, leads to a non-standard form of biomineralization, whereby the pre-existing organic matrix is mineralized without collagen remodeling and without an intermediate cartilage ossification phase. Micro- and nanoscale characterization of the tissue microstructure using histology, backscattered electron (BSE) and second-harmonic generation (SHG) imaging and synchrotron small angle X-ray scattering (SAXS) revealed (i) continuous collagen fibers across the soft-hard tissue interface on the tip of mineralized cones, and (ii) bone remodeling by basic multicellular units (BMUs) in regions adjacent to the native cortical bone. Thus, features of soft tissue-to-bone interface resembling the insertion sites of ligaments and tendons into bone were created, using a scaffold that did not mimic the structural or biological gradients across such a complex interface at ist mature state. This study provides fundamental knowledge for biomimetic scaffold design in the fields of bone regeneration and soft tissue-to-bone interface tissue engineering.

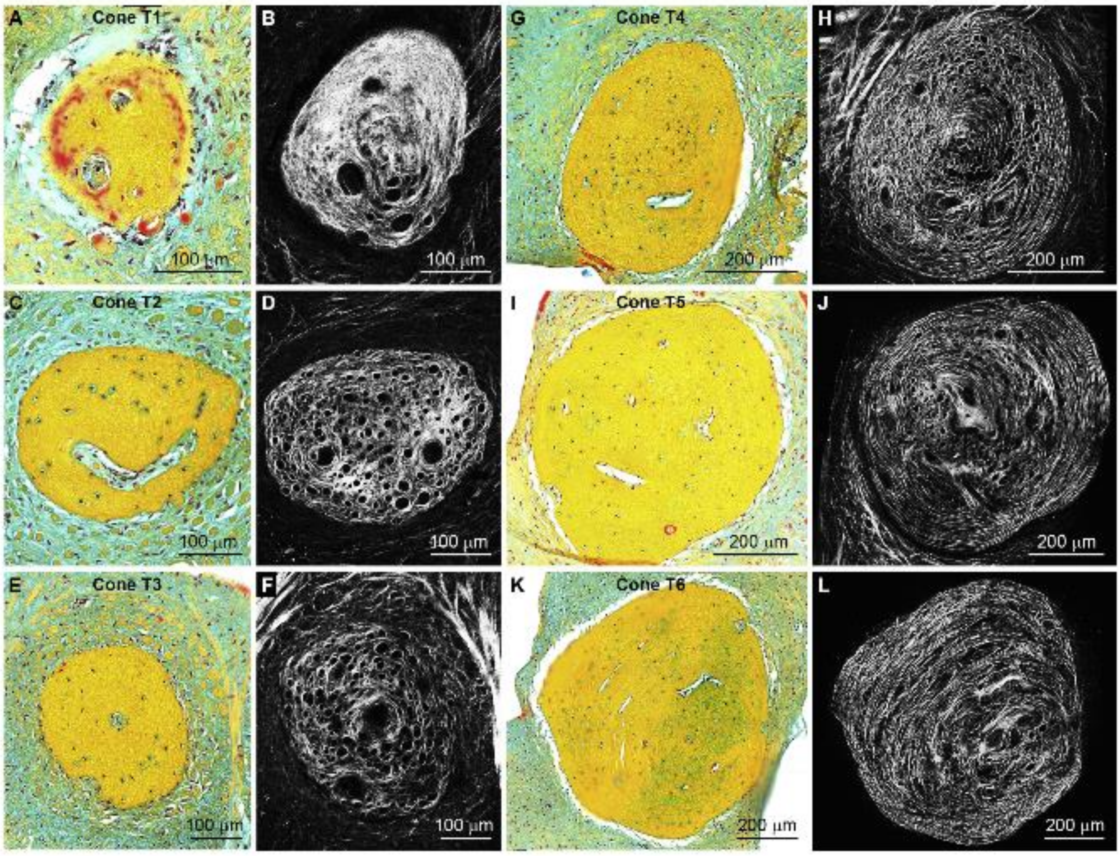

Fig. 6. Soft and mineralized tissue patterning in the transversal sections of cones T1-T6. Histology and SHG imaging of transversal sections of cones, from (A) the smallest to (K) the largest cone section diameter, which indicates proximity to the cone tip and to the cortical bone, respectively. No evidence of osteoid formation (bright red) is observed on the interface between mineralized and soft tissue. In the smallest cones (T1-T3), SHG images reveal a tubular structure in the collagen microstructure within the mineralized tissue. This morphology remains visible in the core of larger cones, on top of which lamellar bone can form (T4-T6). The largest cone, T6, exhibits a highly aligned collagen structure in the circumferential direction. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)