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The periosteal microcirculation in health and disease: An update on clinical significance

Andrea Szabó [a,*], Ágnes Janovszky [b], Levente Pócs [c], Mihály Boros [a]

[a] Institute of Surgical Research, University of Szeged, Szeged, Hungary
[b] Department of Oral and Maxillofacial Surgery, University of Szeged, Szeged, Hungary
[c] Department of Traumatology and Hand Surgery, Bács-Kiskun County Teaching Hospital, Kecskemét, Hungary

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ABSTRACT

Apart from its nutritive functions, the periosteum critically affects bone regeneration via its stem/osteoprogenitor cell content. Normal healing after bone fractures, trauma–orthopedic interventions and invasive dental procedures is critically linked to the reestablishment of the periosteal microcirculation, but the reconstruction, replacement or repair of lost tissues may also be performed with autologous periosteum. Besides the initiation of cell differentiation during bone repair and remodeling processes, the periosteum together with the endosteum plays significant roles in the pathogenesis of both hormone-related and trauma-induced osteoporotic alterations in the bone metabolism. Nevertheless, the axial bones, and in particular the jawbones, and the appendicular bones display differences not only in their blood supply and fracture healing characteristics, but also in respect of the development of osteoporosis and their reactions to treatment modalities (i.e. bisphosphonates). These reactions may also be linked to the differences in periosteal microcirculatory reactions. The present overview summarizes the relevant data of microcirculatory studies focusing on the periosteal reactions in different anatomical locations together with the optimal background methodologies, study models and the most significant observations.

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1. Introduction

The periosteal membranes separate the bones from the surrounding tissues and also bind to them the elements of the skeletal system, the tendons, septa and ligaments. Although it is well recognized that the periosteum is more than simply an envelope of the bone, it is a relatively infrequent site for microcirculatory studies. Despite several decades of research, the regenerative potential of the periosteum and the distinct role of the microcirculation in a range of important physiological and pathological events are only incompletely characterized, mainly due to methodological limitations. Functional changes within the periosteal microvasculature in different experimental settings can dynamically be assessed using intravital microscopy (IVM). In the present overview, the periosteal microcirculatory reactions are summarized based on IVM findings in clinically-relevant animal models of reconstructive surgery, orthopedic-trauma interventions and systemic diseases. Differences in

* Corresponding author at: Institute of Surgical Research, University of Szeged, Szőkefalvi-Nagy B. u. 6, Szeged H-6720, Hungary.
E-mail address: szabo.andrea.exp@med.u-szeged.hu (A. Szabó).

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the physiology and microcirculatory reactions between the axial (i.e. the skull, facial bones, vertebrae, ribs, sternum and the shoulder and pelvic girdles) and appendicular bones are also discussed.

2. Brief anatomy and physiology of the periosteum

The periosteum is composed of an outer fibrous and an inner osteogenic cellular layer (for reviews, see Augustin et al. 2007; Dwek, 2010; Lin et al., 2014). From a structural aspect, the superficial portion of the outer layer is the most vascularized part, supplying the deeper periosteal layers and the superficial layer of cortical bone. The endosteum has a similar histological structure to that of the periosteum with a rich blood supply and (albeit to a lesser extent) mesenchymal stem cells (Brighton et al., 1992). Providing a highly vascular connective tissue coverage, the endosteum also plays an active role in the regulation of the metabolism and regeneration of the bone.

The application of IVM methods has led to detailed descriptions of the morphological and functional characteristics of the periosteal microvasculature in different species (representative micrographs taken in rats are shown in Figs. 1, 2, see details later). The microvascular architecture has been most extensively examined in rats, in which certain differences in the organization of the microvessels can be observed. The microvascular network within the rat mandibular periosteum comprises mainly arterioles and venules (Varga et al., 2014). In rabbits, the

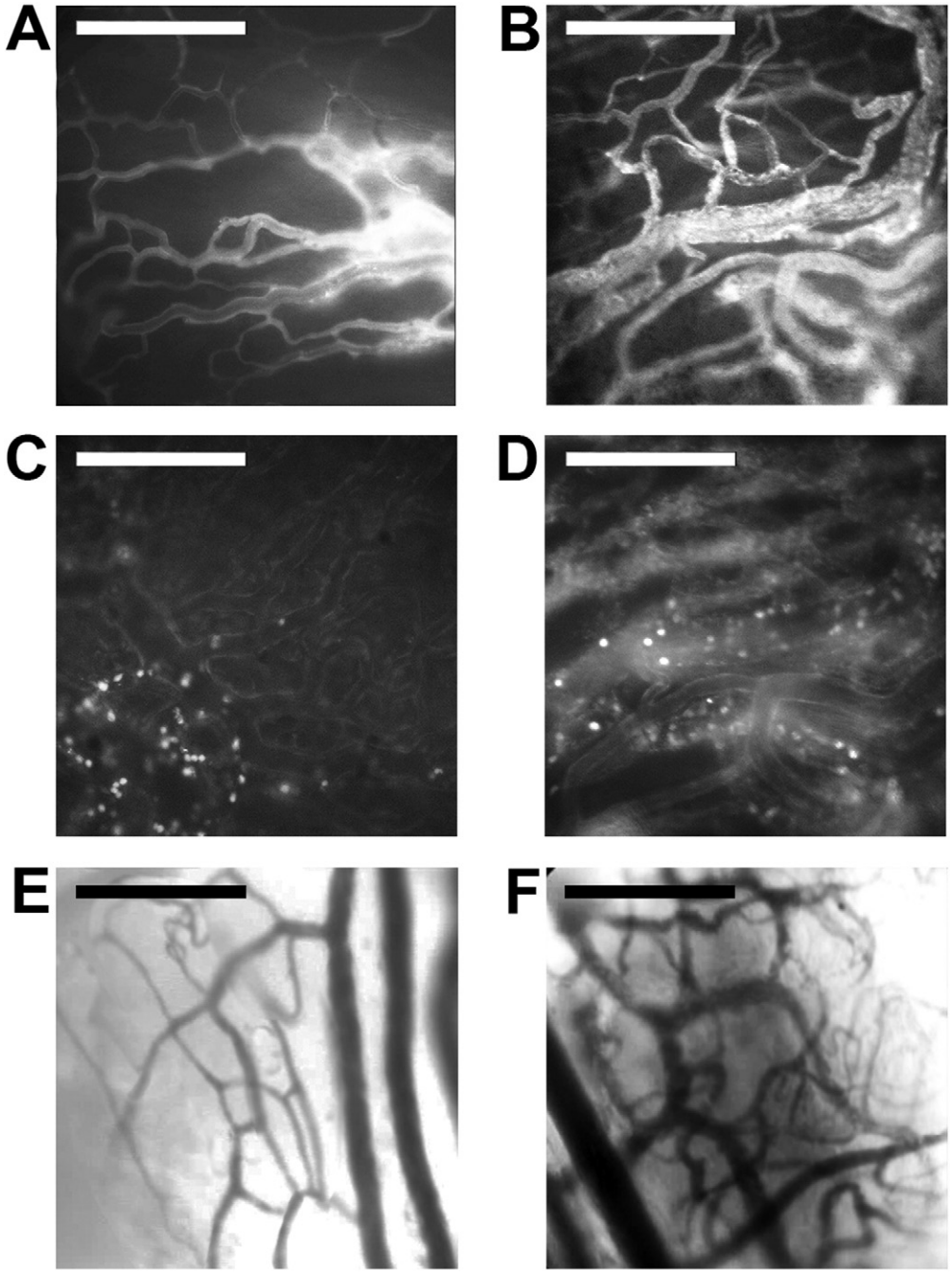

Fig. 1. Fluorescence intravital microscopic (IVM) and orthogonal polarization spectral (OPS) images of the anteromedial tibial (A, C, E) and mandibular periosteum (B, D, F) in Sprague-Dawley rats. Upper two panels: IVM images; plasma labeling with fluorescein isothiocyanate-dextran (150 KDa, Sigma, St. Louis, MO, USA) (A, B) and rhodamine 6G (Sigma, St. Louis, MO, USA)-labeled neutrophil leukocytes (C, D), respectively. The images were taken by using a Zeiss Axiotech Vario 100HD IVM microscope, 100W HBO mercury lamp, Acroplan 20× water immersion objective, Carl Zeiss GmbH, Jena, Germany) and a CCD camera (Teli CS8320Bi, Toshiba Teli Corporation, Osaka, Japan). On the lower panels, OPS images (taken by the Cytoscan A/R device; Cytometrics, Philadelphia, PA, USA) of the tibia (E) and the mandible (F) are shown. The bar denotes 200 μm (original recordings of the authors).