

Osteocytes as indicators of bone quality

Multiscale structure-composition characterisation of the bone-implant interface

Akademisk avhandling

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av

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Avhandlingen baseras på följande delarbeten

- I. Shah FA, Zanghellini E, Matic A, Thomsen P, Palmquist A. The Orientation of Nanoscale Apatite Platelets in Relation to Osteoblastic–Osteocyte Lacunae on Trabecular Bone Surface. *Calcif Tissue Int.* 2016;98:193-205.
- II. Shah FA, Lee BEJ, Tedesco J, Wexell CL, Persson C, Thomsen P, Grandfield K, Palmquist A. Micrometre-sized magnesium whitlockite crystals in micropetrosis of bisphosphonate-exposed human alveolar bone. *Submitted for publication.*
- III. Shah FA, Palmquist A. Evidence that Osteocytes in Autogenous Bone Fragments can Repair Disrupted Canalicular Networks and Connect with Osteocytes in *de novo* Formed Bone on the Fragment Surface. *Calcif Tissue Int.* 2017;101:321-327.
- IV. Shah FA[#], Johansson ML[#], Omar O, Simonsson H, Palmquist A, Thomsen P. Laser-Modified Surface Enhances Osseointegration and Biomechanical Anchorage of Commercially Pure Titanium Implants for Bone-Anchored Hearing Systems. *PLoS One.* 2016;11:e0157504. [#]Contributed equally.
- V. Shah FA, Nilson B, Brånemark R, Thomsen P, Palmquist A. The bone-implant interface – nanoscale analysis of clinically retrieved dental implants. *Nanomedicine.* 2014;10:1729-37.
- VI. Shah FA, Wang X, Thomsen P, Grandfield K, Palmquist A. High-Resolution Visualization of the Osteocyte Lacuno-Canalicular Network Juxtaposed to the Surface of Nanotextured Titanium Implants in Human. *ACS Biomater Sci Eng.* 2015;1:305-313.
- VII. Shah FA, Snis A, Matic A, Thomsen P, Palmquist A. 3D printed Ti6Al4V implant surface promotes bone maturation and retains a higher density of less aged osteocytes at the bone-implant interface. *Acta Biomater.* 2016;30:357-367.
- VIII. Shah FA, Omar O, Suska F, Snis A, Matic A, Emanuelsson L, Norlindh B, Lausmaa J, Thomsen P, Palmquist A. Long-term osseointegration of 3D printed CoCr constructs with an interconnected open-pore architecture prepared by electron beam melting. *Acta Biomater.* 2016;36:296-309.

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Abstract

By virtue of certain design features, bone anchored metal implants can be made to elicit a strong initial osteogenic response, i.e., the amount of bone formed. While quantitative differences are often lost at longer follow up times, do differences in the initial osteogenic response lead to long-term alterations in bone quality? This thesis investigates osseointegration in terms of bone quality, with an emphasis on the osteocyte lacuno-canalicular network (Ot.LCN) in relation to compositional and ultrastructural patterns observed at intermediate or late healing. A series of investigations was undertaken to study osteocyte lacunae on the forming bone surface (Paper I), hypermineralised lacunae of apoptotic osteocytes (Paper II), autogenous bone fragments found within healing sites (Paper III), bone formed adjacent to surface modified implants (Papers IV–VI), and bone formed within macroporous implants (Papers VII and VIII) using a range of analytical microscopy and complementary spectroscopic techniques. A directional relationship exists between the shape of the osteocyte lacuna and the underlying bone surface. The physico-chemical environment of the lacunar space is, however, different from the surrounding bone matrix, resulting in formation of a calcium phosphate phase more stable than apatite at lower pH, i.e., magnesium whitlockite. Connectivity between osteocytes within unintentionally generated autogenous bone fragments and *de novo* formed bone on their surface indicates a regenerative capacity of osteocytes. Laser-ablation creates a hierarchical micro- and nanotopography on titanium implants and enhances their biomechanical anchorage. Osteocytes attach directly to such surfaces, while mineralised collagen fibril organisation at bone-implant and bone-osteocyte interfaces is similar. More osteocytes are retained in the vicinity of Ti6Al4V surface as manufactured by electron beam melting than machined Ti6Al4V. In addition to cp-Ti and Ti6Al4V (ASTM F136), osteocytes also attach to CoCr (ASTM F75) thus indicating a favourable osteogenic response of a material generally considered inferior to Ti6Al4V. Therefore, osteocytes reveal vital information about bone quality and are important structural markers of osseointegration. Evaluation of the Ot.LCN can be extremely beneficial in characterising the bone response to materials intended for bone anchored, load bearing applications.

Keywords: 3D printing; apatite; biomaterials; biomineralisation; bone; bone quality; canaliculi; CoCr; collagen; electron beam melting; electron microscopy; implant; interface; in vivo; lacuna; micropetrosis; osseointegration; osteocyte; Raman spectroscopy; surface modification; Ti6Al4V; titanium; ultrastructure; whitlockite