On Nano Size Structures For Enhanced Early Bone Formation

Akademisk avhandling
som för avläggande av Odontologie Doktorsexamen vid Göteborgs Universitet kommer att offentligen försvaras i Föreläsningssal 3, Medicinaregatan 12, 4 tr, Göteborg, onsdag den 13:e juni 2007. kl 09.00 av

Luiz Meirelles
leg. Tandläkare, MSc

Fakultetsopponent: Lyndon F. Cooper,
Stallings Distinguished Professor of Dentistry,
University of North Carolina at Chapel Hill, USA

Paper I: *validate the model*
Meirelles L, Arvidsson A, Albrektsson T, Wennerberg A. Increased bone formation to unstable nano rough titanium implants.
Clin Oral Impl Res, In press.

Paper II: *effect of nano HA*
Meirelles L, Arvidsson A, Andersson M, Kjellin P, Albrektsson T, Wennerberg A. Nano hydroxyapatite structures influence early bone formation.
Submitted for publication.

Paper III: *nano HA in a gap model*
Meirelles L, Albrektsson T, Kjellin P, Arvidsson A, Stenport Franke V, Andersson M, Wennerberg A. Bone reaction to nano hydroxyapatite modified titanium implants placed in a gap healing model.
J Biomed Mater Res Part:A, accepted.

Paper IV: *nano- HA and titania*
Meirelles L, Melin, L, Peltola T, Kjellin P, Kangasniemi I, Fredrik C, Andersson M, Albrektsson T., Wennerberg A. Effect of hydroxyapatite and titania nano structures on early in vivo bone response.
Submitted for publication.

Paper V: *nano structures on oral implants*
Meirelles L, Currie F, Jacobsson M, Albrektsson T, Wennerberg A. The effect of chemical and nano topographical modifications on early stage of osseointegration.
Submitted for publication.

Abstract

Purpose The general aim of the present thesis was to investigate early bone response to titanium implants modified with nano size structures. Therefore, 1. a model to evaluate titanium implants modified with nano size structures was validated; 2. a suitable detection method of nano size structures was implemented.

Materials and Methods A rabbit model was selected and healing time was 4 weeks in all experiments. A smooth cylindrical implant design was selected in order to control the macro-threads and micro-structures. Thus, early bone response could be related to added nano size structures alone. A stabilization plate was utilized to ensure adequate fixation of the attached implant. Smooth implants were obtained through polishing techniques (electrical and mechanical) and were used as control surfaces and, after relevant modifications, as experimental surfaces. Six surface modifications were investigated: 1. mechanically polished, 2. electropolished, 3. nano hydroxyapatite (HA), 4. nano titania, 5. blasted (TiO_2) and 6. fluoride-modified. The implant surface topography was measured with an interferometer and an atomic force microscope. Surface roughness parameters were calculated and nano size structures dimension and distribution were characterized. Surface morphology was evaluated by scanning electron microscopy. Surface chemical composition was monitored with X-ray photoelectron spectroscopy. The bone response was measured with removal torque tests and histological and histomorphometrical analyses.

Results The model tested to evaluate smooth implants was found adequate. Atomic force measurements combined with image processor analyses software was suitable to characterize nano size structures at the implant surface. Nano HA modified implants enhanced bone formation at 4 weeks of healing compared to electropolished implants. However, placed in a gap healing model the nano HA modified implants showed similar bone formation compared to electropolished implants. If both test and control implants were modified with nano structures, so-called bioactive nano HA and bioinert nano titania, respectively; enhanced bone response of 24% was found to the "bioinert" nano titania implants, although not statistically significant. The beneficial effect of nano size structures on the experimental model was tested on screw shaped moderately rough implants. The oral implants that exhibited particular nano structures (fluoride and nano HA) showed a tendency of higher removal torque values compared to control (blasted) implants, that lacked such structures.

Conclusions Based on *in vivo* animal experiments, enhanced bone formation was demonstrated to smooth and moderately rough titanium implants modified with nano size structures with different chemical composition.

Key words: nano structures, nanotopography, surface modification, osseointegration, bone tissue, titanium implants

ISBN: 978-91-628-7202-1

Correspondence: Luiz Meirelles, Dept Biomaterials, Box 412, 405 30 Göteborg, Sweden; email: luiz.meirelles@odontologi.gu.se