

# The effect of tobacco exposure on bone healing and the osseointegration of dental implants. Clinical and molecular studies.

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i sal: Arvid Carlsson, Medicinaregatan 3, torsdagen den 8 juni 2017, klockan 9.00

av

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## Avhandlingen baseras på följande delarbeten

- I. Sayardoust S, Gröndahl K, Johansson E, Thomsen P, Slotte C. Implant survival and marginal bone loss at turned and oxidized implants in periodontitis-susceptible smokers and never-smokers: a retrospective, clinical, radiographic case-control study. *J Periodontol* 2013; 84:1775-1782.
- II. Sayardoust S, Omar O, Thomsen P. Gene expression in peri-implant crevicular fluid of smokers and non-smokers. 1. The early phase of osseointegration. *Clin Implant Dent Relat Res* 2017. doi: 10.1111/cid.12486
- III. Sayardoust S, Omar O, Norderyd O, Thomsen P. Clinical, radiological and gene expression analyses in smoker and non-smokers. 2. The late healing phase of osseointegration. *Submitted for publication*.
- IV. Sayardoust S\*, Omar O\*, Norderyd O, Thomsen P. Implant-associated gene expression in the jawbone of smokers and non-smokers. A human study using quantitative qPCR. In manuscript.

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## Abstract

**Background:** The mechanisms behind the impact of smoking on osseointegration are not fully understood. **Aim:** To correlate the clinical and molecular aspects of osseointegration in smokers compared with non-smokers. **Methodology: Study I:** In a retrospective cohort study of smokers and non-smokers, the 5-years implant survival and marginal bone loss (MBL) of machined and oxidized implants, were assessed. **Studies II and III:** In a prospective controlled study, smokers (n=16) and non-smokers (n=16) received machined, oxidized and laser-modified implants. Pain scores, implant stability quotient (ISQ) and gene expression of peri-implant crevicular fluid (PICF) and baseline bone biopsies were analyzed during 0-90d. Clinical assessments and radiology were performed at 90d. **Study IV:** Smokers (n=24) and non-smokers (n=24), each received two mini-implants with machined and oxidized surfaces. The gene expression of selected factors was analyzed in implant-adherent cells and surrounding bone after 1d, 7d and 28d. **Results: Study I:** Overall implant survival rate was lower in smokers. In smokers, machined implants failed more frequently than oxidized implants. Mean MBL at 5 years was higher at machined implants in smokers vs. non-smokers. **Studies II and III:** A higher ISQ was found in smokers compared to non-smokers. Greater MBL was found in smokers than non-smokers, particularly at the machined implant. At 90d in smokers, the PICF around machined implants revealed a higher expression of pro-inflammatory cytokine, IL-6, and a lower expression of osteocalcin compared with the surface-modified implants. Multivariate regression revealed that smoking, BoP, IL-6 expression in PICF at 90d and HIF-1 $\alpha$  baseline expression are predictors for MBL at 90d. **Study IV:** Cells adherent to machined implants revealed higher expression of pro-inflammatory cytokine, TNF- $\alpha$ . After 7d and 28d, the expression of bone formation gene, ALP, was higher at oxidized implants. Smoking was associated with initial inhibition of bone remodeling (CTR) and coupling (OPG and RANKL) genes in cells on machined implants. **Conclusions:** Smoking is associated with greater MBL during the early healing phase (0-90d), and an increased failure rate and MBL in the long-term (5 years). Whereas the machined implants were associated with a dysregulated inflammation, osteogenesis and remodeling, an increased MBL and failure rate in smokers, the oxidized implants appear to favor osseointegration by mitigating the negative effects of smoking. It is concluded that the local effects of smoking on osseointegration are modulated by host factors and implant surface properties.

**Keywords:** crevicular fluid, dental implants, gene expression, human, implant surfaces, implant survival, marginal bone loss, osseointegration, pain, periodontitis, resonance frequency analysis, smoking, titanium