Fabrication and biological evaluation of the coating co-doped strontium and zinc nanoparticles on porous pure titanium surface by hydrothermal method

Yanqi Chen, Fuming He*
Department of Prosthodontics, The Affiliated Stomatology Hospital, School of Medicine, Zhejiang University, Hangzhou 310006, China

Key words: Hydrothermal synthesis；Antimicrobial effect；Osteogenesis；Strontium；Zinc

Background

For dental implants, early infection and peri-implantitis after implant restoration are major reasons for implant failure[1]. Plaque biofilm formation is the initiator for implant-related infection[2]. Therefore, it's urgent to develop a new antibacterial implant materials or treatment methods. It is found that nanostructured titanium surface can resist bacterial adherence and promote bactericidal capability[3]. Zinc (Zn) not only exhibits excellent antibacterial behavior with broad spectrum and limits drug-resistance bacteria induction, but also is active in osteogenesis[4]. Strontium (Sr) has various effects of improving immunologic reaction, promoting osteogenesis and inhibiting osteoclastic differentiation[4].

Aim

In this study, Sr- and Zn- incorporated micro/nano-structured titanium surface with nanorods (MNT-Sr/Zn) was fabricated by a two-step hydrothermal process, aiming to improve osseointegration and reduce implant failure caused by implant-related infection and broaden new ideas for the future research on the antibacterial properties of biological materials.

Materials & Methods

The Mod Ti surfaces were used as a control. The characterization of different surfaces was detected by a field emission scanning electron microscope (FE-SEM) equipped with energy dispersive spectra (EDS) detector. Meanwhile, *Staphylococcus aureus (S. aureus)* was selected to evaluate antibacterial properties through Live/Dead Staining and watching the adhesive bacterial morphology under FE-SEM. What's more, rat bone marrow-derived mesenchymal stem cells (rBMSCs) were cultured on the surfaces to detect their early osteogenic properties, like the alkaline phosphatase(ALP) activity and the expressions of osteogenesis related genes.

Results

The results confirmed that nanorod-like particles with a diameter of about 30-50 nm of MNT-Sr/Zn. In the EDS spectra, the elements of Zn and Sr were evenly distributed, and approximately 1.49 ± 0.16 wt% and 21.69 ± 2.74 wt% respectively. More importantly, Zn-containing nanorod-like particles and the morphology could work together, slightly decreasing adhesion of *S. aureus* but increasing the proportion of dead cells, thus inhibiting subsequent biofilm formation, compared with the controlled group. In addition to this, MNT-Sr/Zn could enhance the osteogenic differentiation via the upregulation of the transcription of osteogenic related genes *in vitro.*

Conclusions

This research provides a new surface modification method on titanium substrate for multi-functional implant material development. Due to the co-doping of Sr and Zn in the coating, biomechanical stability, antibacterial capability and early osteogenic inductive effect are enhanced, which has the potential to be applied in dental implantation in the future.

References

[1] Hickok, N. J. , Shapiro, I. M. , Chen, A. F. (2018). The impact of incorporating antimicrobials into implant surfaces. Journal of Dental Research, 002203451773176.
[2] Chouirfa, H., Bouloussa, H., Migonney, V., Falentin-Daudre, C (2019). Review of titanium surface modification techniques and coatings for antibacterial applications. Acta biomaterialia 83:37-54
[3] Jaggessar, A., Shahali, H., Mathew, A., Yarlagadda, P. K. D. V. (2017). Bio-mimicking nano- and micro-structured surface fabrication for antibacterial properties in medical implants. Journal of Nanobiotechnology, 15(1), 64.
[4] Edward O'Neill, Awale, G., Daneshmandi, L., Umerah, O., & Lo, W. H. (2018). The roles of ions on bone regeneration. Drug Discovery Today.

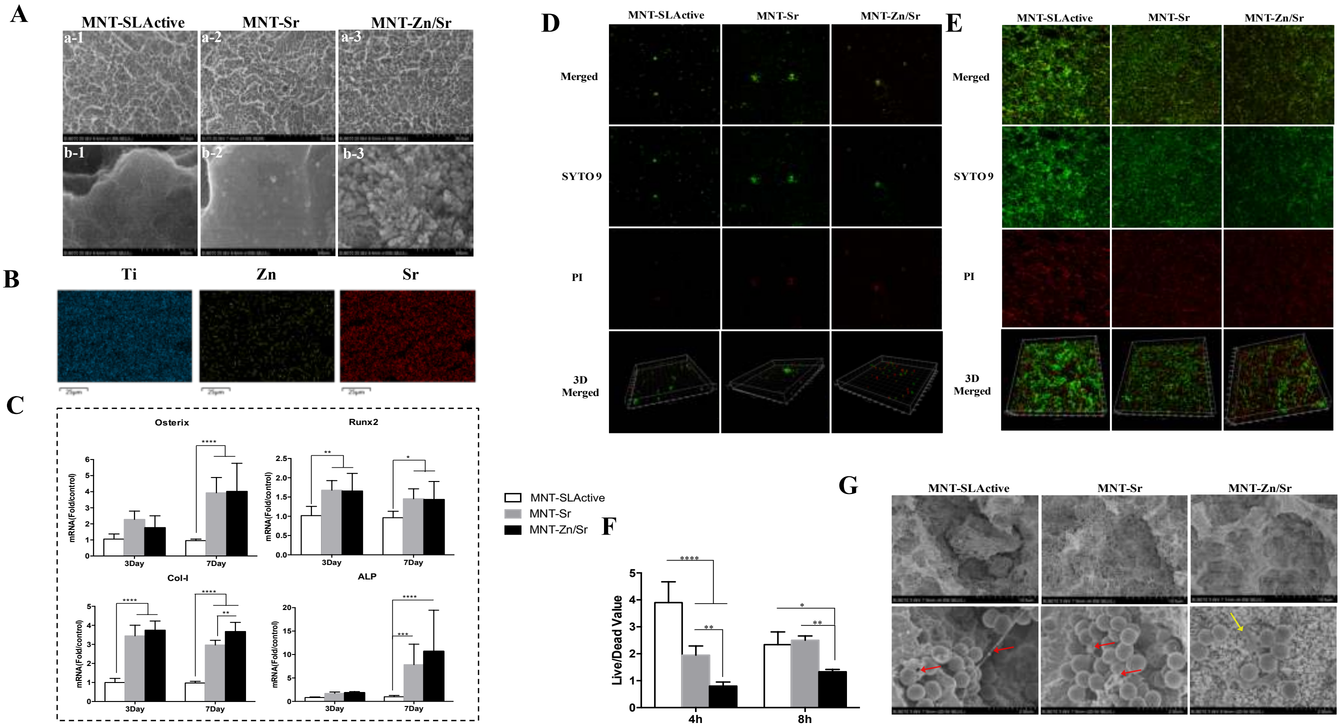

Figure 1 (A) Representative FE-SEM images showed that morphology of micro/nano rough surfaces of MNT-SLActive, MNT-Sr, MNT-Zn/Sr. (B) EDS mappings of MNT-Zn/Sr. (C) The osteogenic markers of rBMSCs on different surfaces. (D-E) Fluorescent images of *S. aureus* after adhesion on various surfaces for 4 h and 8 h, respectively. (F) The values of live/dead bacteria on different surfaces. (G) FE-SEM images of *S. aureus* after adhesion on various surfaces for 24 h. Red arrow: polysaccharide-like substances; yellow arrow: bacterial debris. Error bars represented the SD of three independent experiments. Significant differences were found for (*) $p < 0.05$, (**) $p < 0.01$.