Look into the future of titanium implant applied in combat trauma treatment ——Endowed with sequential and multi-functional composite coating for antibiosis and osteogenesis

Weizong Weng[1,3] , Shanshan Liu[1] , Ji Tan[2] , Xuanyong Liu[2]

1. *The 73rd Army , Eastern Theater Army Command , PLA of China*

2. *State Key Laboratory of High Performance Ceramics and Superfine Microstructure, Shanghai Institute of Ceramics, Chinese Academy of Sciences, Shanghai , China,200050*
3. *Department of Orthopedics, the First Affiliated Hospital of Naval Medical University, PLA of China*

Summary : Combat trauma-related open fractures often accompany by persistent infections, which cause significant obstacles to military readiness recovery. As a traditional orthopaedics fixation implant, Titanium should be endowed with ideal antibacterial and osteogenic properties to meet the current needs of combat trauma implants.

Methods: Ca-Ti (Calcium-Titanium) and MgO (Magnesium Oxide) composite coatings were prepared for titanium surface modification by ion implantation (Ca plasma) and magnetron sputtering, respectively. The physicochemical properties were characterized by SEM, AFM, FTIR et al. The biological effects and related mechanisms were demonstrated via antibacterial analysis, cell culture and *in vivo* experiments (**Figure 1**).

Results: The composite coating presented a 'sandwich-like' multilayer structure, which can achieve antibacterial and osteogenic effects through the sequential changes of surface microenvironment. The sequential reactions covered crucial time-windows for bactericidal, bacteriostatic and osteogenic

effects, avoiding antibiotic resistance. In specific, the MgO film of the composite coating can react with water to form an alkaline microenvironment at the initial stage, which showed significant bactericidal effect. The Ca-Ti layer can react to form a relatively weak alkaline microenvironment in the later stage, which possesses ideal bacterial-inhibiting capacity. It can also promote osteogenic differentiation via activating Wnt/β-catenin signaling cascade. *In vivo* experiments in a rat model of femoral osteomyelitis showed that the composite coating can effectively inhibit infection and promote titanium's osteointegration.

Conclusion: This research may provide a possible strategy of titanium surface modification for the combat trauma fractures treatment.