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**SUPPRESSION OF NICKEL RELEASE IN  
NICKEL-TITANIUM ALLOYS BY PLASMA  
IMMERSION ION IMPLANTATION SURFACE  
TREATMENT: TOWARDS A NEW GENERATION OF  
"SMART" ORTHOPAEDIC IMPLANTS**

K.W.K. Yeung<sup>1</sup>, Y.L. Chan<sup>1</sup>, S.C.W. Chan<sup>1</sup>, X.Y. Liu<sup>2</sup>,  
C.Y. Chung<sup>2</sup>, P.K. Chu<sup>2</sup>, W.W. Lu<sup>1</sup>, K.D.K. Luk<sup>1</sup>, D. Chan<sup>3</sup>,  
K.M.C. Cheung<sup>1</sup>

*1*Division of Spine Surgery, Department of Orthopaedics and  
Traumatology, Queen Mary Hospital,

*The University of Hong Kong, Pokfulam, Hong Kong*

*2* Department of Physics and Materials Science,

*City University of Hong Kong, Kowloon, Hong Kong*

*3*Department of Biochemistry, Faculty of Medicine,

*The University of Hong Kong, Pokfulam, Hong Kong*

Nickel-titanium shape memory alloys (NiTi) are potentially very useful in spinal deformity correction due to their super elastic properties and their ability to change shape with temperature. However, release of toxic nickel particulate debris remains a major concern. We have developed a novel method of altering the surface of the material to reduce nickel release by using plasma immersion ion implantation (PIII). This study compares the corrosion resistance and mechanical properties of PIII treated samples with untreated NiTi. NiTi discs containing 50.8% Ni were implanted with nitrogen using PIII technique. Their elemental depth profile, surface chemical composition, surface hardness and corrosion resistance were compared with untreated NiTi. The amount of Ni released into simulated body fluids after the accelerated corrosion tests were determined. The biocompatibility was assessed by culturing mouse osteoblasts expressing an enhanced green fluorescent protein on the surface of these materials. After PIII treatment, a layer of titanium nitride formed on the surface. Compared to untreated NiTi, the corrosion resistance is better by five times, and the surface hardness and elastic modulus are better by a factor of 2. The concentration of Ni in the simulated body fluid for the untreated sample was 30ppm compared to undetectable levels in the PIII treated sample. There was no difference in the ability of cells to grow on either surface. PIII results in enhanced corrosion and wear resistance, and negligible Ni release. This technique will allow NiTi alloys to be safely implanted in the human body. A new generation of "smart" orthopaedic implants will likely result.

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**ELECTRICAL PULSE INDUCED CHANGES IN CELL  
POPULATION DYNAMICS**

Allen L. Garner, Ho Yin Chan, Deepak Mangla, Arthur Holtz,  
Michael D. Uhler, Ronald M. Gilgenbach, and Y. Y. Lau  
*Bioelectromagnetism Laboratory, University of Michigan  
Ann Arbor, MI 48109 USA*

Pulsed electric fields (PEFs) are frequently used to permeabilize the cell membrane so that chemotherapeutics, DNA, and other molecules unable to enter the cell can traverse the cell membrane.<sup>1</sup> Our laboratory recently used intense, ultrawideband (UWB) electrical pulses with chemotherapeutics to kill leukemia cells in numbers greater than predicted by simple addition of the killing effects for the individual modalities.<sup>2</sup> Another group observed that applying UWB pulses to neoplastic mammary cells can actually increase cell proliferation.<sup>3</sup> In these and other cancer treatment methods, the stage of the cell cycle targeted is crucial to the treatment's overall effectiveness because a method that targets proliferating cells has a greater probability of long-term success than one that targets the quiescent (resting) cells.<sup>4</sup> We present results for a population study of Jurkat (human leukemia) cells exposed to multiple 400  $\mu$ s, 1 kV/cm electrical pulses and various levels of bleomycin, a standard chemotherapeutic. We assess the cell stage targeted by these treatments by fitting the data to a simple mathematical model, which considers the cells as being either proliferating or quiescent.<sup>4</sup> Based on the resulting parameters, we predict how the treatments alter the steady-state behavior and the transition rates between the cell states. We also discuss the possible implications of these results with respect to cancer treatment. The mathematical model used here is general and can also be applied to the population dynamics changes induced by other modalities, such as ultrashort PEFs.<sup>2,5</sup>

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