Title: The Significance of Zeta Potential in Osteogenesis

Introduction: A direct link between an electric effect and a physiological effect was first established by Luigi Galvani in 1791 in the famous 'frogs legs' experiment. The first reported successful treatment of bone non-unions by electric fields/currents was by Hartshorne[1] and Lente[2]. Eriksson[3] reported on the relationship of surface energies and charge effects on the bone induction principle. Krukowski in a series of papers[4,5,6] demonstrated a significant *invivo* response of both hard and soft-tissue to charged resin beads and Eriksson in 1976[7], using the demineralised bone samples prepared by Urist[8], demonstrated that the materials with the highest osteoinductive potential had the greatest negative surface electric charge. In an aqueous environment all cells normally exhibit a negative surface charge. Proteins are colloidal particles having charged surfaces, and any implanted material can also show a surface charge. It is an objective of the study to assess the role of zeta potential of calcium phosphate bone graft materials in the osteogenic response.

Methods: Tricalcium phosphate and hydroxyapatite powders were prepared having a range of zeta potential values, both positive and negative. Osteoblastic cells were seeded onto the various materials in standard culture wells and the response was assessed, after various time periods in culture at 37^{o}C, microscopically for adhesion and proliferation and by RT-PCR for gene expression of osteogenic markers including alkaline phosphatase, osteocalcin, osteopontin, CBFA1 and collagen type 1.

Results and Discussion: Significant differences in the behaviour of osteoblasts to positive and negatively charged surfaces were observed. Materials with negative zeta potential were more amenable to osteoblast attachment and proliferation than positively charged samples. Negatively charged surfaces gave enhanced up-regulation of the osteogenic markers compared to positively charged surfaces. Since the cells are negatively charged and like-charges repel, then appropriate serum protein adsorption must be an enabling factor. The relative iso-electric points of the biomaterial, the cell and the (morphogenetic) proteins could be an indicator of morphogenetic activity and a significant factor in the healing cascade.

Conclusions: The zeta potential of calcium phosphate bone void fillers has been shown to have biological significance. The use of alloplastic materials with charged surfaces in the repair and augmentation of bone, and soft tissue, warrants further investigation.

References: 1. Hartshorne E, Am J Med. 1841;1:121-156.
2. Lente RW, NY State J Med. 1850;5:317-319.
3. Eriksson C, J Biomed Mats Res. 1985;19:833-849.
4. Krukowski M, J Oral Max Surg. 1990;48:468-475.
5. Krukowski M, Clin Orthop Rel Res. 1994;298:266-271.
6. Krukowski M, Plast Reconstr Surg. 1992;89:891-897.
7. Eriksson C, Clin Orthop Rel Res. 1976;121:295-302.
8. Urist M, Science. 1965;150(698):893-899