

## **Activation and biomechanical assessment of an injectable hybrid osteoconductive – osteogenic bone substitute**

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**INTRODUCTION:** Current research is focusing on injectable osteoconductive materials. Injectable CaP cements offer a minimal-invasive use, but lack osteogenic properties. In order to create a combined osteoconductive / osteogenic bone substitute we used in this study a synthetic, injectable and resorbable Brushite /  $\beta$ -tricalcium-phosphate ( $\beta$ -TCP) scaffold (chronOS Inject) and impregnated it with a transglutaminase (plasmatransglutaminase – F XIII). We evaluated the activity of the osteogenic protein and the biomechanics of the mixture.

**METHODS:** Activation study: In order to evaluate the reaction of the osteogenic protein F XIII to the fluid phase of chronOS Inject (sodium hyaluronate), different pH solutions (pH 4 – 7), sodium hyaluronate and chronOS Inject were mixed with F XIII and the protein activity and F XIII release was detected with ELISA.

Biomechanical study: The injectability of the chronOS Inject / F XIII mixture was assessed measuring the force required to inject the mixture through a 1 ml standard syringe without a cannula. 3 repeats were performed with and without F XIII.

**RESULTS:** Activation study: F XIII is not influenced by low pH and the sodium hyaluronate. The release of F XIII from chronOS Inject could not be measured due to clouding of the liquid.

Biomechanical study: We saw an increase of the injection force in the presence of F XIII which increased with time after mixture.

**DISCUSSION & CONCLUSIONS:** F XIII is not affected by the liquid phase of chronOS Inject, which therefore may be a good carrier for the osteogenic protein. In a further test we could remove the clouding by filtration, however to what extent the amount of protein was also reduced needs to be further investigated. Furthermore the osteogenic protein affects the injectability of the cement which may be due to the fact, that the sodium hyaluronate and the protein increase cement viscosity or a change of the liquid / powder

ratio. The injectability needs to be optimized testing various liquid / powder ratios in the future in order to produce a hybrid injectable bone substitute.

**REFERENCES:** <sup>1</sup>Benfer J, Struck H. Factor XIII and fracture healing. An experimental study. *Eur Surg Res.* 1977;9(3):217-23 <sup>2</sup>Claes L, Burri C, Gerngross H, Mutschler W. Bone healing stimulated by plasma factor XIII. Osteotomy experiments in sheep. *Acta Orthop Scand* 1985;56(1):57-62 <sup>3</sup>Schlenzka R, v. Garrel T, Pistro C. Does fibrogammin significantly accelerate bone healing? *JBJS [Br]* 1993;75B:Suppl II:100 <sup>4</sup>Kienapfel H, Swain R, Hettel A, Wilke A, Koller M, Griss P. Recombinant and nonrecombinant factor XIII and its effect on bone ingrowth and strength of fixation. *Arch Orthop Trauma Surg.* 1997;116(4):239-43 <sup>5</sup>Ponomarev I, Becker S, Stoll T, Wrabetz E, Alini M, Wilke I. Preliminary results of enhanced osteogenesis by Fibrogammin and mesenchymal stem cells. *Eur Cell Mater* 2003;5,2:80