

An Injectable Composite of Osteogenic Protein-1 (OP-1, rhBMP-7) and Hydroxyapatite Enables Early *In Vivo* Cement Stabilization and Biointegration. A Controlled, Randomized Study in the Sheep Spine.

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INTRODUCTION: Lumbar interbody fusion by means of hydroxyapatite- or calcium phosphate-cements proved to be unsuccessful in clinical and experimental settings. Since these biomaterials cannot withstand shear and bending forces, fracture and subsequent fragmentation of the biomaterials will result along with final resorption of the debris [1].

Objective of this *in vivo* study was to investigate the ability of OP-1 to induce osseous stabilization of a hydroxyapatite-cement early enough to prevent it from fragmentation and resorption thus enabling integration of the biomaterial and spinal fusion. For this reason, an injectable composite of di-/tetra-hydroxyapatite and microencapsulated OP-1 (2.2 mg) was developed.

METHODS: Endpoints of this controlled, randomized, prospective study were total cement leftover, radiographic interbody fusion rates, and biomechanical properties at 8 weeks post op. In 14 sheep, L4/L6 were instrumented posteriorly with an internal fixator, intervertebral disc L4/L5 was removed under transpedicular endoscopic control, and end plates L4/L5 were decorticated. In 7 randomly assigned sheep, the created defect in L4/L5 was then augmented transpedicularly with the composite (HA-OP-1). The remaining 7 animals were treated with the hydroxyapatite cement without OP-1 (HA).

Following euthanasia, the ratio between total volume of cement leftover (V_{8weeks}) and total volume of cement initially applied (V_{0weeks}) was measured by means of CT-assisted volumetry. Fusion rates were evaluated radiologically (plain X-ray and CT). Range of motion and neutral zone were determined by biomechanical testing applying pure moments of ± 3.75 and ± 7.5 Nm in each principle motion plane.

RESULTS: V_{8weeks}/V_{0weeks} was significantly higher in the HA-OP-1 group ($p=0.007$): $79.9\% \pm 13.8\%$ (HA-OP-1) versus $54.0\% \pm 6.8\%$ (HA).

Radiomorphologic evaluation of the HA group revealed gross fragmentation of the formerly solid cement mass, especially within the interbody space along with loss of contact at the bone-cement interface. In contrast, cement masses in the HA-OP-1 group remained solid. Radiographic fusion rate was 5/7 in the HA-OP-1 group versus 0/7 in the HA group ($p=0.002$, Wilcoxon-test).

Biomechanical testing, however, could not show an improvement of the stability in the segments treated with OP-1:

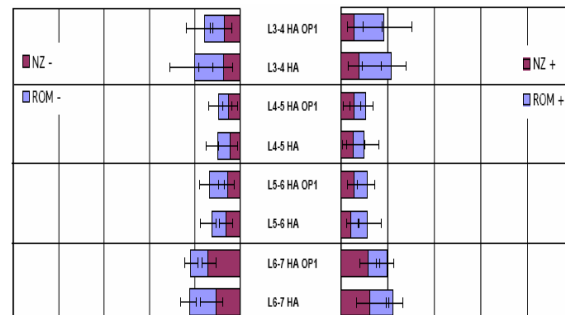


Fig. 1: Median values for range of motion (ROM) and neutral zone (NZ) during lateral bending upon ± 3.75 Nm (posterior instrumentation dismantled).

DISCUSSION & CONCLUSIONS:

Biointegration of the osteoconductive carrier without OP-1 does not occur, since shear and bending forces cause early cement fracture with subsequent fragmentation and gross resorption. In contrast, the osteoinductive effect of OP-1 enables early callus sheathing and *in vivo* stabilization of the composite resulting in biointegration and radiographic spinal fusion in 5/7 cases. The initial layers of bridging bone, however, proved to be still fragile at 8 weeks post op. to withstand biomechanical forces.

REFERENCES: ¹ T.R. Blatter, G. Delling, A. Weckbach (2003) *Eur Spine J* 12:216-23.

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