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## HYALURONIC ACID | HYHA

of the materials to supporting the soft tissues

### HYALURONIC ACID

Partial surface treatment on the body implant with hyaluronic acid. Cold plasma decontamination









Sa 0,50 µm overall mean value on a measuring area of 30x30 µm decontamination



Sa 1,90 µm overall mean value on a measuring area of 30x30 µm sand-blasting, double etching, cold plasma

Biochemical methods of surface modification endeavor to utilize current understanding of the biology and biochemistry of cellular function and differentiation. "Biochemical surface modification utilizes critical organic components of bone to affect tissue response". The goal of biochemical modifications is to immobilize proteins, enzymes or peptides on devices surfaces for the purpose of inducing specific cell and tissue responses. Puleo da, nanci a (1999): understanding and controlling the bone-implant interface, biomaterials, 20:2311-2321.

# HA & OSTEOGENESIS

In 1904 Pfaundler hypothesized that calcium binding was an important step during the calcification of the bone and that some unknown component of the bone was responsible; It was later discovered that GAGs play an important role and that HA enhances proliferation and growth of hydroxyapatite crystals; Iwata and Urist found that large amounts of HA were secreted when implants of decalcified bone remineralized as bone (Clin. Orthop. Rel. Res., 90, 236, 1973); In vitro studies using fetal calvarial cells and bone marrow osteogenic stem cells show that osteogenesis in vitro is significantly enhanced by HA 30-160 kDa, while high Mw HA (550-1300 kDa) shows weak inhibitory effect as compared to the control (G. W. Bernard et al. Redefining Hyaluronan, Abatangelo and Weigel Eds., Elsevier, 2000, pp. 215-231); 800 kDa HA added to bone marrow stromal cells cultured in vitro accelerates cell proliferation, increases ALP activity and osteocalcin gene expression. HA interacts with BMP-2 to generate direct and specific cellular effects (X. Zou et al. Biomaterials 25, 5375, 2004); 900 kDa HA has a positive effect in bone ingrowth in Titanium fiber mesh implant in rats (S. Itoh et al. J. Mat. Sci. Mat. Med., 12, 575, 2001); HA shows a positive effect in early bone consolidation in distraction osteogenesis (B. C. Cho et al., J. Craniofacial Surg., 13, 783, 2002)

# HA TO TI IMPLANTS

Hyaluronan from bacterial fermentation was supplied by Lifecore Inc.



## RESULTS

100

87.5

75

62.5

50



BIC: the length of bone directly opposed to the implant without the presence of a fibrous membrane/the total length of the bone-implant interface x 100

Bone ingrowth: bone area between the screw and the line connecting the thread crests divided by the total screw thread area x 100

Microhardness measurements were performed in the tangential direction to the interface with a Vickers indenter (four-sided pyramid with square base and an apex angle between opposite sides of 136°±15') applied at a load of 0.05 kgf and dwell time of 5 sec.

## RESULTS

Histomorphometric results for uncoated and coated screws IN TRABECULAR BONE at 4 weeks (n=5)

Parameter		Uncoated (screw)	Coated (screw)
BIC (%)	Median	22.5	69.0**
	SEM	5.8	5.8
	(Min - Max)	(16.1 - 47.4)	(45.4 - 80.7)
Bone Ingrowth (%)	Median	30.3	56.3**
	SEM	2.0	3.4
	(Min - Max)	(23.9 - 33.9)	(41.9 - 59.4)
Wilcoxon signed rank test: *, p<0.05; **, p<0.01			

# **DISCUSSION & CONCLUSIONS**

HA covalently linked to nanoporous Ti implant surfaces significantly increases bone growth at 4 weeks (histomorphometry). There's not only more bone (histomorphometry) but interfacial bone is significantly more mature in the case of HA coated implants (microhardness). Functional studies (push-out force) confirm the significant improvement of osteointegration at early stages. HA coating effects are magnified in the more biochemically rich (and clinically more difficult) trabecular bone. Hypotheses&mechanisms that could account for the observed results: Increased hydrophilicity of the HA coated surface, Charge effects (Ca2+ binding, Ca2+ mediated mechanisms), Role of HA in wound healing, HA is found whenever there is need for rapid cell proliferation, repair and regeneration. During an early stage of osteogenesis, when only undifferentiated mesenchymal cells are found, HA reaches peak levels.

### Cortical bone





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The push-out test was carried out by placing the femoral segments on a support jig (ø 3.5 mm) using a MTS apparatus (Sintech-1/M, MTS Adamel Lhomargy, Ivry sur Seine, France). A force was applied to the implant from the medullar side at a constant crosshead speed of 2 mm/min, pushing it out from its bony bed.

### Trabecular bone