A Biofunctional Coating Of Sulfated Hyaluronan Enhances Osseointegration Of Dental Implants

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Aim

High success rates for dental implants are achieved in healthy bone. Considering the demographic development in industrialized countries an increasing number of patients potentially receiving dental implants is suffering from general diseases. Systemic diseases e.g. osteoporosis are affecting the bone metabolism and might negatively influence the osseointegration of dental implants. An increase of peri-implant bone formation is desirable to enable a sufficient osseointegration in compromised bone. One possible approach is the coating of dental implant surfaces using components of the extracellular matrix. Recent studies showed a positive effect of surfaces modified with collagen I on peri-implant osteogenesis. The aim of the present animal study was to evaluate the influence of two regioselectively low-sulfated hyaluronan derivates on early bone formation in maxillary bone.

Material and Methods

In vitro and *in vivo* examinations were performed to evaluate the hypothesis. The implants used in the animal experiments were screw type titanium implants with a length of 15 mm and a diameter of 5 mm. Three different surface modifications were evaluated after healing times of four and eight weeks.

In vitro

The coating was performed using a dip coating procedure. The following surface modifications were examined:

grit-blasted and acid-etched titanium	(titanium)
titanium + collagen I + at C6 position sulfated hyaluronan	(sHA1)
titanium + collagen I + not at C6 position sulfated hyaluronan	(sHA1Δ6s)

To evaluate the stability of the implant coating removal torque testing was performed. The implants were inserted in artificial bone (Sawbones Europe AB. Malmö. Sweden) applying a torque of 35 Ncm. Subsequently, the implants were dissected and the content of collagen I being adherent to the surface was quantified using Sirius Red staining as described [1].

In vivo

After extraction of the premolar teeth, each six implants were inserted into the maxilla of six adult female miniature pigs and allowed to heal submerged. Following healing times of four and eight weeks the jaws were dissected and fixed in formaldehyde. Histologic samples were prepared according to Donath’s sawing and grinding technique [2]. The longitudinal sections of the implants were analyzed using light microscopy (Olympus BX 61, Olympus Deutschland GmbH, Hamburg, Germany). Histomorphological and histomorphometrical evaluation regarding bone implant contact (BIC), osteoid implant contact (OIC), bone volume density (BVD) and osteoid volume density (OVD) followed. The statistical analysis was performed using the SPSS software (IBM Corporation, Armonk, NY, USA).

Results

In vitro results

Applying the Sirius Red staining comparable amounts of collagen I were detected before and after insertion into artificial bone indicating the implant coating remains stable on the surface.

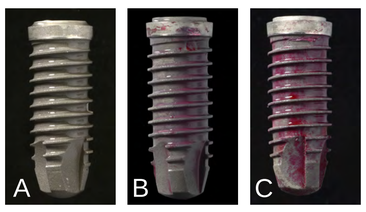


Figure 1 – Sirius Red staining of the implant coatings prior insertion in artificial bone. A) titanium; B) collagen I + sHA1Δ6s; C) collagen I + sHA1

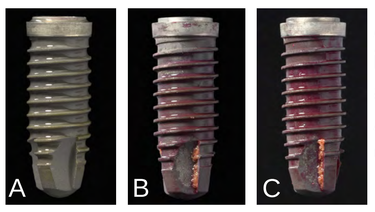
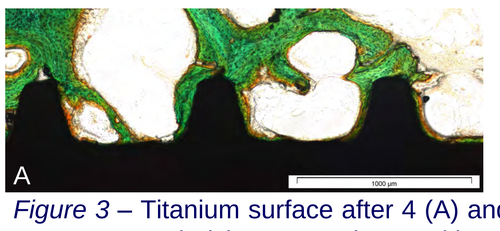


Figure 2 – Sirius Red staining of the implant coatings after insertion in artificial bone and explantation. A) titanium; B) collagen I + sHA1Δ6s; C) collagen I + sHA1

In vivo results

All animal completed the study. Two implants (1 x titanium, 1 x sHA1) were lost during the eight week healing period.

Histomorphologic results



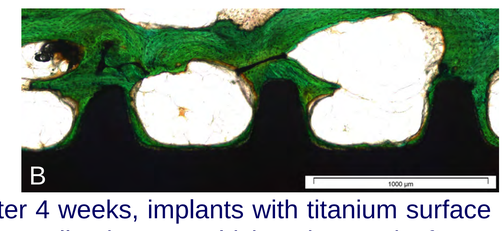
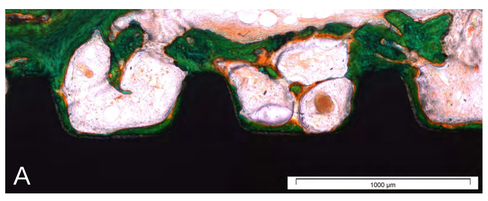


Figure 3 – Titanium surface after 4 (A) and 8 (B) weeks: After 4 weeks, implants with titanium surface were surrounded by woven bone with an osteoid layer. Lamellar bone could be observed after a healing period of 8 weeks (Masson Goldner trichrome, magnification: 100x).



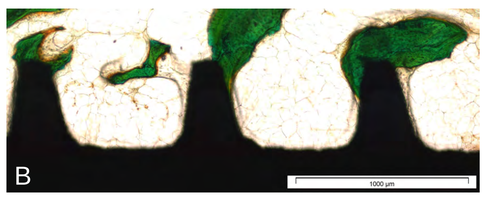
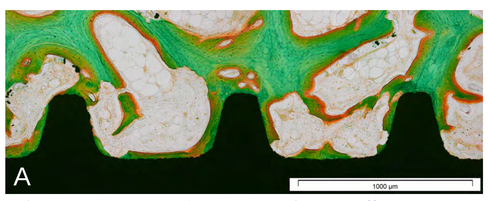


Figure 4 – Surface coating collagen I + sHA1Δ6s after 4 (A) and 8 (B) weeks: This surface modification showed pronounced formation of lamellar bone after 4 weeks. After 8 weeks, signs of remodeling could be found (Masson Goldner trichrome, magnification 100x).



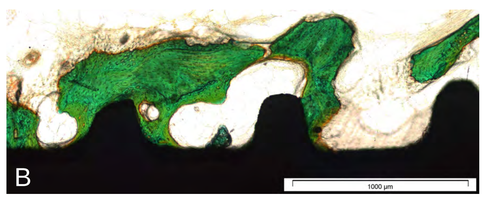


Figure 5 – Surface coating collagen I + sHA1 after 4 (A) and 8 (B) weeks: A pronounced layer of osteoid was found on the implant surface after 4 weeks. After a healing period of 8 weeks, the implants were mainly covered by lamellar bone (Masson Goldner trichrome, magnification 100x).

Histomorphometric results

	surface	4 weeks mean ± SD in %	8 weeks mean ± SD in %
BIC	titanium	33.3 ± 11.8	31.4 ± 17.6
	sHA1Δ6s	37.0 ± 17.0	37.0 ± 14.8
	sHA1	33.1 ± 14.0	48.0 ± 13.5
OIC	titanium	2.6 ± 1.3	0.7 ± 0.3
	sHA1Δ6s	2.6 ± 2.4	1.0 ± 0.9
	sHA1	3.0 ± 1.8	1.3 ± 0.6
BVD	titanium	22.4 ± 14.9	9.6 ± 8.0
	sHA1Δ6s	23.2 ± 11.0	13.3 ± 6.8
	sHA1	24.4 ± 7.9	21.0 ± 15.3
OVD	titanium	8.0 ± 8.0	3.7 ± 3.3
	sHA1Δ6s	6.4 ± 7.2	3.9 ± 3.5
	sHA1	8.4 ± 5.9	5.1 ± 4.5

Table 1 – Means (MW) and their standard deviation (SD) for bone implant contact (BIC), osteoid implant contact (OIC), bone volume density (BVD) and osteoid volumen density (OVD). Only the decrease in osteoid implant contact from 4 to 8 weeks for titanium showed a statistical significance ($p < 0.05$).

Conclusion

In the present study, the applied coating consisting of collagen I and regioselectively low-sulfated hyaluronan derivates showed a sufficient stability on grit-blasted and acid-etched titanium surfaces. After the eight week healing period, a higher, however not statistically significant, peri-implant bone formation was observed for both sulfated hyaluronan modifications compared to titanium [3]. Further studies are necessary to evaluate the influence of the degree of sulfation and the influence of the position of the sulfated groups on peri-implant osteogenesis.

Literature

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TRR67 MATRIX ENGINEERING

The study was supported by the Transregio 67 grant of the German Research Foundation (DFG)

Deutsche Forschungsgemeinschaft DFG