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**Osseointegration of Titanium Implants with Biologically Active  
Coatings in a Gap Model:  
Bone Morphogenetic Protein-2 vs. Titanium Plasma Spray in the Göttingen  
Minipig**

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This study compares measures of osseointegration for two differently coated titanium implant types in a gap model in 18 Göttingen minipigs. The two coatings were: 1) biologically active, immobilized bone morphogenetic protein-2 and 2) a standard titanium plasma spray. Within the two equal sized groups of nine animals, each animal received 4 implants (for the group  $n=36$ ) and was sacrificed at 4, 8, or 12 postoperative weeks. Implants were placed in the intertrochanteric and intercondylar site of both femora. Histomorphometrical analyses examining bone and osteoid volume (measures of osteoinduction) as well as bone and osteoid ongrowth (measures of osteoconduction) were performed. Additionally, three different polyfluorochrome labels were applied in each of the postoperative times, enabling dynamic tracking of bone turnover. Finally, scintillation examinations were employed to rule out heterotopic bone formation as well as to test the suitability of this method for quantifying differences in bone activity in implantology.

Histomorphometrical results showed significantly greater means for the bone morphogenetic protein-2 than titanium plasma spray for all four parameters: bone volume (11.407% with 95% CI: 9.614% – 13.201%; 6.775% with 95% CI: 5.071% – 8.479%;  $p=0.0004$ ), osteoid volume (4.070% with 95% CI: 3.420% – 4.721%; 1.789% with 95% CI: 1.171% – 2.408%;  $p<0.0001$ ), bone ongrowth (4.047% with 95% CI: 2.650% – 5.443%; 0.266% with 95% CI: 0.000% – 1.593%;  $p=0.0002$ ) and osteoid ongrowth (5.905% with 95% CI: 4.474% – 7.335%; 0.341% with 95% CI: 0.000% – 1.700%;  $p<0.0001$ ). Examining the temporal dimension at 4, 8, and 12 weeks revealed that bone volume was significantly greater in the bone morphogenetic protein-2 group than in the titanium plasma spray group at 12 weeks ( $p=0.0027$ ) and at 8 and 12 weeks for osteoid volume ( $p=0.0341$  and  $p=0.0266$ , respectively). For the osteoconductive parameters, the bone morphogenetic protein-2 group showed greater values in bone ongrowth at 12 weeks ( $p=0.0052$ ) and greater values in osteoid ongrowth at 4 and 8 weeks ( $p=0.0002$  and  $p=0.0313$ , respectively) than the titanium plasma spray group. The polyfluorochrome analysis showed bone turnover in both groups from at least the 8<sup>th</sup> to the 80<sup>th</sup> postoperative day, while semiquantitative values were largely inconclusive. No heterotopic bone could be found by means of scintillation examination.

The results of this study – one of the largest of its kind – largely mirror the results in other experiments in that biologically active, immobilized bone morphogenetic protein-2 showed significantly

greater osseointegration. Furthermore, the temporal analyses showed continued greater values at 12 weeks, indicating that the full benefit of immobilized bone morphogenetic protein-2 may extend beyond this time period in the Göttingen minipig.