Growth Factor-induced Osteogenesis In A Novel Radiolucent Bone Chamber

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Disclosures:

Introduction: The study of osteopromotive qualities of implant components used in tissue engineering is greatly helped by bone chambers [1]. Traditionally, most bone chambers consist of titanium, which makes them unsuitable for micro computed tomography (μCT) analysis. To allow longitudinal investigation of bone growth with μCT, we developed a new radiolucent bone chamber made of polyether ether ketone (PEEK). PEEK has been used in medical devices and has good mechanical characteristics and biocompatibility [2]. To improve osteogenicity, growth factors, such as bone morphogenetic protein 2 (BMP-2), vascular endothelial growth factor (VEGF) and the chemokine stromal cell derived factor 1α (SDF-1α) can be used to induce osteogenesis, angiogenesis and attract endogenous multipotent stromal cells (MSCs), respectively. These growth factors, that have a short half life time, can be laden on gelatin microspheres (GMP) for controlled release to ensure a prolonged presence [3].

In this study the feasibility of the PEEK-bone chamber and μCT assessment of growth factor-induced bone formation within the chamber were subject of investigation.

Methods: PEEK-bone chambers were placed on rat tibiae (figure 1), and filled with vehicle (control group), with fast-released BMP-2 (gold standard) or a combined growth factor group consisting of BMP-2, VEGF and SDF-1α, all laden on GMPs for sustained release. Onset of bone formation was monitored using fluorochrome incorporation, bone volume analysis using μCT after 4, 8 and 12 weeks of implantation and histomorphometry after explantation. Furthermore, the effects of single and combined growth factor addition were investigated in ectopic ceramic-based implants.

Results: All bone chambers were correctly placed and performed well. Growth factor presence in the chambers led to a significant increase in bone formation after 8 weeks, which subsided after 12 weeks, underlining the importance of longitudinal analysis (figure 2). All ectopic constructs that contained growth factors showed a significant increase in bone formation compared to control. Furthermore, the addition of SDF-1α to BMP-2 laden scaffolds was more effective in stimulating bone formation than VEGF addition to BMP-2.

Discussion: This study showed that the PEEK bone chamber is a suitable model to assess growth factor-induced orthotopic bone formation. All chambers were easily implanted bicortically, remained in the correct position and animal discomfort was mild. In the ectopic implants the SDF-1α signal was strong enough to enhance bone formation of a group containing BMP-2/VEGF. Histomorphometry is considered the gold standard in bone volume determination in the context of BCP, as bone and BCP are very similar in radio-opacity. Although BCP presence complicated μCT analysis, resulting in an overestimation, the correlation to histomorphometrical data is statistically significant (p<0.01).

Significance: The PEEK-bone chamber is a suitable model to assess growth factor-induced orthotopic bone formation in a longitudinal manner.

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**Figure 1. The PEEK bone chamber.**
A. Design of the bone chamber. B. PEEK bone chambers, cap, screw and assembled chamber. C. Placement of the bone chamber (cutaway model). D. Bone chamber in situ after implantation in the rat tibia. Scale bar represents 3 mm.

**Figure 2. μCT analysis of bone formation in the chambers.**
A. Bone volume measured in the bone chambers after 8 and 12 weeks of implantation by μCT. B, C. Original μCT scan and segmentations of bone chambers, blue marking the region of interest for segmentation. D. 3D reconstruction of control group μCT scan. E. 3D reconstruction of combined growth factor group μCT scan.

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