Introduction: Growth factor enhanced allograft incorporation could improve clinical outcome after revision surgery by accelerating new bone formation and thereby improving implant stability. In a previous study, we studied the early effects of OP-1 device on the incorporation of impacted morsellized cancellous bone and TCP/HA in an unloaded bone chamber in goats [1]. After four weeks, new bone formation was not promoted by the OP-1 device, no signs of accelerated resorption. However, a dose-dependent inhibition of vascularization and fibrous tissue ingrowth was found. Bone ingrowth into densely impacted allografts is delayed by impaction, as compared to bone ingrowth in allografts that are not impacted. An impacted graft acts as a hindrance for the ingrowing tissue or vessels. By adding OP-1 solution to the impacted bone grafts in a bone chamber, bone ingrowth increased dramatically [2]. In contrast, in our previous study, the collagen carrier initially might have additionally delayed bone and fibrous tissue ingrowth into the impacted graft material by filling up the space between the impacted graft material. Although the collagen type I carrier therefore may not be optimal for use in bone impaction grafting, in clinical cases the better late ingrowth may appear despite an early delay. The current study was designed to see if the decrease represented a final loss or was just a delay, and if so, can the OP-1 device overcome this initial delay and does this ultimately result in a better late ingrowth?

Methods: In a bone chamber study, two concentrations of OP-1 device were tested in combination with allografts and TCP/HA. The OP-1 device consists of 3.5mg rhOP-1 combined with 1g type I bovine-derived collagen. Non-OP-1 treated allografts and TCP/HA served as controls (Table 1). Cancellous allografts were obtained from the sternum of six donor goats. TCP/HA particles (BoneSave™, Stryker Orthopaedics, Limerick, Ireland) were used as synthetic bone substitute. The particles consisted of a TCP/HA percentage of 80/20, with a size of 2-4mm and 50% porosity. We used the bone conduction chamber (BCC) which is a model for membranous ossification [3]. The BCC consists of a titanium screw with a cylindrical interior space. It is made up of two threaded half cylinders held together by a hexagonal closed screw cap (Fig. 1). Impaction was performed by gradually filling the BCC followed by impaction of the material by a constant force of 40N for 2 minutes. The applied pressure was calculated to be 12.5MPa.

Results: In the TCP/HA groups no difference in fibrous tissue ingrowth between the medium-dose OP-1 to the allograft control group. In contrast, after 4 weeks, a significantly less fibrous tissue was measured comparing the medium-dose OP-1 to the allograft control [1]. No differences between TCP/HA with or without the addition of OP-1 device were found. However, in the allograft control total tissue ingrowth distance was significantly less than in the TCP/HA control (p=0.02).

Discussion: Within impacted bone chips, the migration of cells into the impacted allograft is compromised and vascularization is delayed for several weeks. It seems that the delayed or reduced new bone ingrowth seen in experiments with impaction therefore is less important and even may be beneficial, as long as the graft/fibrous tissue composite remains strong enough to withstand forces acting on it during remodeling. From the present study the lack of ingrowth appeared to be a delay rather than an inhibition. After 8 weeks however, the delay was only partly overcome. Similar to our results after 4 weeks, no difference in bone ingrowth between OP-1 device groups and their controls were observed. However, after 8 weeks significantly more fibrous tissue ingrowth was measured in allografts mixed with OP-1 device compared to the allograft control. In contrast, after 4 weeks, a significantly less fibrous tissue was measured comparing the medium-dose OP-1 to the allograft control. In the TCP/HA groups no difference in fibrous tissue ingrowth between OP-1 device groups and their controls were observed, where after 4 weeks a strongly significant dose-dependent decrease in fibrous tissue existed. Our data demonstrated the difficulty of applying a biological enhancer of bone healing, such as an osteoinductive growth factor, in a situation where the access to blood supply and stem cells are limited and also bone healing is impaired. Our data again indicates that lack of effect of OP-1 in different clinical situations could be related to the problem that various biological environments require different growth factors dosage and carriers for optimal stimulation.

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