

In Vitro And In Vivo Evaluation Of A Third Generation Guided Bone Regeneration Membrane Which Combines Biodegradability With Bioactivity

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INTRODUCTION: The first generation of biomedical materials developed in the 60s and 70s aimed to achieve a suitable combination of physical properties to match those of the replaced tissue with a minimal toxic response in the host (1). The second generation of biomedical materials were designed to be either resorbable (biodegradable suture or fracture fixation plates and screw) or bioactive (bioglass). The combination of both properties will lead to a third generation of biomedical materials which are biodegradable and bioactive and help the body to heal itself (2).

In the last decade guided bone regeneration (GBR) was considered to be a predictable and effective method for enhancing bone healing especially in the dental field (3). In GBR the membrane serves as a barrier for the connective tissue and maintains the open space for the time bone needs to fill it up. The only matter of controversy remains the choice of the membrane. The expanded poly-tetrafluoroethylene membranes are the most widely used, but require a secondary surgical procedure to remove them after they have fulfilled their task. Using biodegradable membranes a second surgery is not needed but if they are of biological origin like in the case of collagen a certain risk of the transmission of diseases remains. To avoid this problem resorbable, fully synthetic polymer membranes are an attractive alternative. The aim of this study was to evaluate a new biodegradable PLGA membrane developed for GBR, which proved to be a biomedical material of the 3rd generation because it combines biodegradability with bioactivity.

METHODS: The protocol for these studies was approved and controlled by the local authorities. Rabbits were sedated and four 6 mm craniotomy defects were created (2 in the parietal and 2 in the frontal bone) with a 6 mm trephine in a dental hand piece. The surgical area was flushed with saline to remove bone debris and membranes of 7 mm in diameter were placed above and below the defect. The InionGTR membranes were used according to the recommendations of the manufacturer. After 4 weeks the calvarial bones were removed and Goldner stained histosections

prepared. For each condition the percentage of defect area filled with new bone of 8 middle sections was determined. In vitro tests were performed MC3T3-E1 cells, which resemble preosteoblastic cells.

RESULTS: The evaluation of bone regeneration in standardized defects generated in the calvarial bone of rabbits showed that compared to untreated control defects (31±4%, N=17), the Osseoquest (Gore, USA) (61±5%; N=8, P<0.001) and InionGTR membrane (Inion, Finland) (79 ± 5%, N=8, P<0.001) improved the bone healing significantly. Due to the fact that the InionGTR membrane performed significantly better than the Osseoquest membrane (N=8, P<0.048) we determined the effect of the InionGTR membrane on different cell lines. If InionGTR membrane was applied to MC3T3-E1 cells a dose dependent increase in alkaline phosphatase activity was achieved. At 2 mg InionGTR membrane the alkaline phosphatase activity was 2,5±0.3 times (N=6, P<0.001) the control level. With 2 mg of InionGTR membrane mineralization of MC3T3-E1 cells determined after 4 weeks with alizarin-staining had increased 1,5±0.05 times

DISCUSSION: InionGTR membrane is a biomedical material of the third generation because it combines biodegradability with bioactivity. The increase in alkaline phosphatase activity and mineralization of MC3T3-E1 cells indicates that the InionGTR membrane accelerates the maturation of preosteoblasts to osteoblasts leading to an acceleration of bone healing in vivo. This extra enhancement of bone healing due to a third generation GBR membranes could make GBR a principle which can also be applied on the orthopedic field.

REFERENCES: ¹ LL Hench; *Science* **208**, 826 (1980) ² LL Hench and JM Polak; *Science* **295** 1014 (2002) ³ C Dahlin, U. Lekholm and A. Linde *Int J Periodontics Restorative Dent* **11**, 273-281 (1991)