

## Deproteinized bovine bone graft remodeling pattern in alveolar socket: an immunohistological evaluation

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The biologic pattern of bone remodeling is well defined in several *in vivo* and *in vitro* studies, but the influence of bone substitutes on individual healing pattern in human is not completely defined and described. Several grafts are available on the market, homologous, heterologous and synthetic bone substitutes. Deproteinized bovine bone (Bio-Oss®, Geistlich Pharma AG, Switzerland) (DBB) is a heterologous substitute derived from bovine bone deprived of all the organic components and reduced in porous grains of different dimensions (0.25 - 2 mm). Preclinical and clinical studies widely described the biocompatibility of deproteinized bovine bone and the integration of this biomaterial in the regenerated bone, but several papers underlined the low rate resorption of the material, that still remains *in situ* until 11 years after regeneration procedures. This characteristic was also investigated *in vitro* in osteoblasts, unraveling the ability of DBB particles in down-regulating BMP-2, BMP-7, TNF-alpha and IL6 genic expression in the early phase of healing but, to the best of our knowledge, no studies checked the same parameters *in vivo*. The aim of the present study is to describe the remodeling pattern of DBB in human socket alveolar preservation in the late phase of healing. Ten patients that needed tooth extraction and implant placement were recruited. At the time of the extraction a bone biopsy (T0) was collected and the alveolar socket was filled with DBB and covered with a membrane (Bio-Guide®, Geistlich Pharma AG, Switzerland). After 6 months, before implant placement, another bone biopsy was collected (T1). All specimens were processed for immunohistochemistry to mark BMP-2, BMP-7, ALP, IL6 and TNF-alpha. Every section was mapped at 200X total magnification and the presence of these factors was quantified using a standardized method with Adobe Photoshop PS5. For every marking the normalized delta between T1 and T0 was calculated and the results were respectively: BMP2  $0.67 \pm 0.43$ , BMP7  $0.36 \pm 0.23$ , ALP  $-0.28 \pm 0.18$ , IL6  $0.81 \pm 0.60$ , TNF-alpha  $1.09 \pm 0.85$ . The Wilcoxon paired test revealed highly significant differences between T0 and T1 for all markers ( $p < 0.05$  for IL6 and  $p < 0.01$  for the others). Differently from what expressed in “*in vitro*” studies, these data underline that DBB in late phases of healing does influence bone turnover by stimulating the production of morphogenetic proteins and inducing the expression of other catabolic and anabolic markers involved in bone remodeling, thus confirming its role as a valid bone substitute.

### Key words

Bone turnover, post-extraction site, immunohistochemistry, bone substitute.