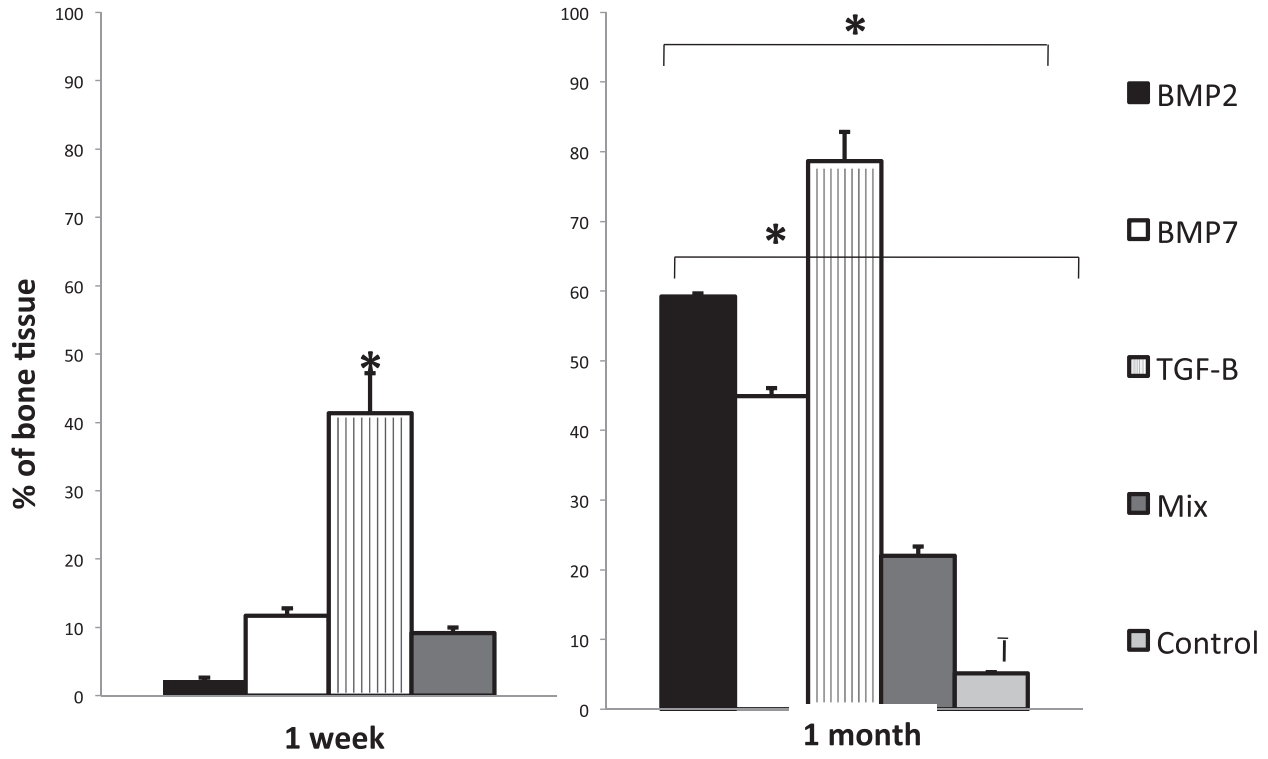

Figure 3 Determination of the percentage of bone tissue by automated morphometry after one and four weeks of implantation adding the indicated growth factors. Results are presented as means and standard deviation of three different dogs in the indicated time points. Mix means implants with the three factors in the same concentration. Asterisk represent statistical difference ($p < 0.005$) among the indicated groups. Two independent experiments were run with similar results.

factors [8]. This was clearly demonstrated by our gene expression kinetics study which showed the inflammatory tissue as the site of the highest expression of BMP and TGF-β1.

A significant focus of research on tissue engineering has been the developing of ideal carriers for bone growth factors [20]. The carrier should act as three-dimensional space scaffolding across which de novo bone formation can occur; and also should maintain an effective concentration of growth factors and containing them in order to avoid extraneous bone formation. Collagen is considered a good carrier, because it is a good source of adhesion-signaling molecules and is also a support for blood vessels and parenchymal cells. We used a type I collagen sponge as carrier, because it is also osteoinductive and favored vascular growth due to its physical characteristics. There is also a good amount of fibrous tissue in the omentum, which contributed to the confinement of the implant and growth factors, avoiding the bone production outside the implant and facilitates its surgical resection avoiding the formation of adherences.

Other essential elements in bone formation are specific growth factors, such as BMP, FGF, PDGF, IGFs [21,22]. BMP is the largest sub group of growth factors that belong to the TGF-β superfamily; they are pleiotropic regulators that mediate various sequential cellular responses such as: chemotaxis and proliferation of progenitor cells, differentiation into osteoblast, vascular invasion, bone formation, remodeling and bone marrow differentiation [6,21]. For bone induction, the most commonly utilized BMPs are BMP2 and 7. BMP2 acts upstream inducing global cellular mobilization (day 1 to 3), whereas BMP7 acts on bone differentiation (day 2 to 5) [2]. These kinetics patterns were also observed in our model, during the first week of implantation BMP2 was highly expressed, while BMP7 raised its maximal expression during the second week. We produced both factors in tobacco leaves as recombinant proteins and added into the implants. After one month, 60% and 45% of the implant was constituted by trabecular bone when added BMP-2 or BMP-7 respectively. The induction of cell proliferation by both BMPs was demonstrated by the immunohistochemistry detection of the cell proliferation marker PCNA, which showed numerous positive cells in the mesenchymal tissue around bone trabeculae. Thus both recombinant proteins are efficient inducing a more rapid bone production in this model. Indeed, both BMPs are now available in the clinical setting [2], and recent evidence has shown that heterodimeric BMPs may have a greater effect than homodimers alone [23]. However in our experimental conditions, we did not