intended site but would not permit leaching of this growth factor to an unintended site.

Summary Of Invention

[0005] In order to solve the problems of osteoinductive bone graft in the prior art, inventors of the present invention made intensive studies and found that β-TCP particles exposed on the surfaces of the biodegradable fibers of ReBOSSIS® are not covered by a thin polymer layer. Based on that finding, inventors of the present invention concluded that the exposed portion of the β-TCP particles can be used to bind BMP-2 to the particles. By binding BMP-2 to the β-TCP particles, one can use ReBOSSIS® as a scaffold for an osteoinductive bone regeneration material that allows gradual release of BMP-2 in the bone defect site but would not permit leaching of this growth factor to an unintended site.

[0005a] In one aspect, there is provided a method of producing an osteoinductive bone regeneration material comprising a targetable bone morphogenetic protein-2 (tBMP-2) comprising: preparing a fibrous scaffold material formed of a plurality of electrospun biodegradable fibers, wherein the plurality of electrospun biodegradable fibers entangle with each other to form a cotton-wool like structure having inter-fiber spaces forming a microenvironment for cell growth therein, the electrospun biodegradable fibers comprise 43-60 vol% β-TCP particles distributed in the electrospun biodegradable fibers such that a portion of the β-TCP particles is partially exposed on a surface of the electrospun biodegradable fibers without being coated by a polymer layer, and contacting the fibrous scaffold material with tBMP-2 contained in an acetate buffer solution so that the tBMP-2 is bound to the β-TCP particles exposed on the surface of the fibers forming the microenvironment throughout the cotton-wool like structure to produce the osteoinductive bone graft, wherein an area of binding site for tBMP-2 on β-TCP particles exposed on a surface of the electrospun biodegradable fibers is adjusted by an amount of the β-TCP particles contained in the electrospun biodegradable fibers.

[0006] Embodiments of the present invention relate to osteoinductive bone regeneration materials that comprise ReBOSSIS® fibers and a bone morphogenetic protein-2 (BMP-2). The BMP for use with embodiments of the invention may be a BMP-2 or a derivative of BMP-2. The BMP-2 may be a human BMP-2 or an animal (e.g., pets or livestock) BMP-2. A derivative of BMP-2 includes a BMP-2 fused with one or more β-TCP binding peptides to form a fusion protein, which will be referred to in this description as a "targetable BMP-2" or "tBMP-2." All these different forms of BMP-2, such as human BMP-2 (including recombinant human BMP-2, rhBMP-2 and wild-type human BMP-2, wtBMP-2), animal BMP-2, and tBMP-2, may be referred to generically as "BMP-2." That is, the term "BMP-2" encompasses rhBMP-2, wtBMP-2, animal BMP-2, and tBMP-2.

[0007] ReBOSSIS® has a cotton-wool like structure formed of a plurality of electrospun biodegradable fibers having a diameter of 40-320 μ m, length of 5-20mm and containing calcium compound particles (e.g., β-TCP particles) and biodegradable polymer such as poly(lactic acid) (PLLA) or poly(lactic-co-glycolic acid) (PLGA). The biodegradable fibers may contain other calcium compound particles, such as silicon releasing calcium carbonate vaterite (i.e., silicon-doped vaterite, SiV). Thus, ReBOSSIS® fibers may comprise biodegradable polymer (e.g., PLLA and/or PLGA) and calcium compound particles (e.g., β-TCP particles and/or SiV particles). As used herein, the term "calcium compound particles" may be β-TCP particles, SiV particles, or a combination of β-TCP particles and SiV particles.

[0008] An electrospun biodegradable fiber of ReBOSSIS® contains a large amount of calcium compound particles distributed on or in the fibers. A portion of the β-TCP particles are exposed on the surface of the fibers forming uneven surface topography of the fiber, and the remaining portion of the β-TCP particles are buried in the fibers. The β-TCP particles exposed on the surface of the fiber is not coated by a thin polymer layer. By