BonGold™ Synthetic Cancellous Bone Void Filler

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White Paper
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Introduction

Synthetic bone substitutes are increasingly being used in orthopedic surgeries and medicine. In fact, 2nd generation synthetic bone void fillers are the fastest growing bone graft material segment growing at a 11.5% growth rate. This is approximately double the DBM growth rate, the 2nd fastest growth category. Synthetic bone void fillers promote bone formation and degrade over time. However, there is still no ideal synthetic bone substitute in the market today. Why is this the case? The simple fact is that no BVFs have been designed from both a composition and hierarchical structure approach, where it resembles the native bone matrix. More than 50% of human bone is made of hydroxyapatite (HA) and at present synthetic bio-ceramics used for filling bony defects are primarily made of HA or related calcium phosphates (CaP), i.e. beta tri-calcium phosphate. Beta tri-calcium phosphate constructs are used as synthetic bone graft in treatment of long bone defects (1). However, human bone matrix has an important component of collagen where very few BVFs have this component. BonGold is a BVF that has HA and collagen assembled in such a way that resembles the native matrix.

Mineralized Collagen Matrix Resembling Natural Bone Matrix

BonGold™ synthetic cancellous bone void filler is a 2nd generation synthetic bone void filler. BonGold™ represents an improved form of nano-sized hydroxyapatite (HA) that is deposited onto a collagen matrix in the same manner as natural bone via a proprietary in-vitro mineralization process. The use of nano-sized particles increases the structure’s micro-porosity so that the resulting scaffold is 90% interconnected with pores sizes ranging from 50-550 µm. This exposed surface area creates more exposure to biologic milieu, that directly contributes to a faster absorption rate and is consistent with the rate of bone tissue in-growth.

Composition and Microstructures

BonGold’s chemical composition is composed of collagen and HA. This is similar to natural bone. Bone mineral is a carbonate containing approximately 35% calcium, 15% phosphorous and 4.5% carbonate by weight in a Ca/P molar ratio of 1:71. BonGold contains approximately 18% calcium and 8% phosphorous in a ratio of 1.67:1. This ratio is achieved through a patent manufacturing process. During this process, HA is deposited onto the collagen fibrille in the same manner as natural bone matrix as shown in the below figure. HA provides the structural rigidity while the collagen component serves two critical functions:

1. Adds flexibility to the matrix significantly improving handling characteristics, and
2. Serves to absorb local osteogenic factors that are critical to bone regeneration.
Allgens Matrix

C-axis of the HA in BonGold™ is parallel to the longitudinal direction of the mineralized collagen fibril, in the same way as HA is deposited on the collagen in the natural bone matrix.

Biological Properties

Histologically, osteoblasts are seen only on the bone surface where normal bone is engaged in turnover and repair. In the case of BonGold™, the body regards it as normal bone tissue and osteoid formation is seen throughout the scaffold. Replacement of BonGold™ by natural bone seems to occur due to resorption of this mineralized collagen matrix with osteogenesis occurring simultaneously.

Biodegradability

The nano-sized hydroxyapatite particles are absorbed by the body by being engulfed by phagocytes. In an acidic environment, several cell types, i.e. monocytes, fibroblasts, osteoclasts, multi-nucleated cells and macrophages have been observed to biodegrade the hydroxyapatite implant. During this process, there was no chronic inflammatory response identified to this material. Thereby rendering it non-immunogenic. BonGold degrades in 3-6 months, matching the in-growth rate of new bone formation. Bone cement products degrade well beyond 2-4 years. Other TCP bone void fillers, depending on porosity, will generally degrade in 1-2 years, all much longer than normal new bone in-growth.

The Regenerative Bone Matrix Facilitator

BonGold can be readily mixed with allograft, autograft, stem cells, PRPs, BMA, or antibiotic solutions to better address specific clinical needs. The porous structure allows the fluid portion of this mix to penetrate into BonGold 3D structure, thereby facilitating osteogenic factors and cells to start depositing and forming new bony structure. Additionally, the collagen component serves to be an adsorber of locally free osteogenic proteins and cells that greatly contributes to new bone regeneration.
The following are examples that demonstrate the benefits of combination use of BonGold with other biologics products.

**PRP**: The regenerative bone area of PRP on the BonGold Matrix (Group C) is significantly higher than BonGold alone (Group B), or negative control (Group A) as seen in the below table.

**Table 1. The regenerative bone area of Groups A, B, C at different time point.**

<table>
<thead>
<tr>
<th>Week</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>2w</td>
<td>0.89+0.45</td>
<td>11.50+3.19</td>
<td>19.68+4.04</td>
</tr>
<tr>
<td>4w</td>
<td>5.73+3.64</td>
<td>23.35+0.58</td>
<td>41.50+10.88</td>
</tr>
<tr>
<td>8w</td>
<td>17.48+3.52</td>
<td>39.40+3.32</td>
<td>42.10+1.57</td>
</tr>
<tr>
<td>12w</td>
<td>17.57+1.57</td>
<td>43.64+13.00</td>
<td>49.70+6.81</td>
</tr>
</tbody>
</table>

**Radiolucency**

BonGold™ is radiolucent, unlike most other BVFs which are usually radiopaque. This is a desirable feature for a BVF because it equips a surgeon with greater confidence when reviewing X-rays during the healing process.

**Placement Technique**

BonGold™ is available as blocks, strips or granules. Blocks can be sculpted to fit the shape of the defect. Granules can be gently taped into irregularly shaped defect areas. BonGold has excellent wettability characteristics and handles best when soaked in blood or marrow. Additionally, BonGold doesn’t require heat or setting time as other BVFs do. It can also be combined with any BVFs, PRPs, autografts, allografts and DBMs.

In conclusion, the combination of HA and collagen along with BonGold® patented and proprietary manufacturing process clearly differentiates BonGold™ from other existing bone graft substitutes. Furthermore, BonGold™ equips surgeons with a multi-faceted material that provides the necessary porosity that leads to faster absorption rates than calcium phosphate bone cement based products. The collagen component attracts the necessary osteogenic factors that leads to bone regeneration along the matrix. BonGold synthetic cancellous bone void filler appears to be a “Regenerative Bone Matrix Facilitator” for cancellous bone.

**References**