NovaBone Putty

Osteostimulative Composite

Putty is a new, next generation Calciumphosphosilicate bone graft material built from a bioactive glass platform with additives to improve handling and efficacy.

Composition

- Bioactive Glass – 69%
- Glycerin – 19%
- PEG – 12%

Bioactive Phase

- Consists of 2 particle sizes
  - Phase 1: 90-710 µ Bioglass particles
  - Phase 2: 32-125 µ Calcium Phosphosilicate (CPS)
- Phase 2 particles provide the initial burst of calcium phosphate and also enhance the physical characteristics to improve handling.
- Phase 2 resorbs at a much faster rate than the larger particle phase.
Additive

- Polyethylene Glycol – 12.4%
- Melts at low temperatures – 45° C
- A nontoxic material that is used in food & pharma industries
- Water soluble - gets absorbed in 24-48 hrs
- Additive fills spaces between the particles of bioactive phases
  – Enhances handling by giving a smooth surface to the putty

Binder - Glycerin

- Highly hydrophilic liquid
- Gets absorbed into the blood stream within 48 hrs – 72 hrs
- Enhances the pliability of the putty and keeps it coherent
- Used as softening agent and to keep all the phases of putty together

Putty – Properties

- 100% Synthetic – Fully resorbable
- Non toxic, non allergenic
- Osteostimulative & Osteoconductive
- No refrigeration required - 4 yr shelf life (unlike other similar products)
- May be combined with Autograft /Allograft
- Extremely easy to use
Indications

- Immediate implant surgeries
- Sinus elevation surgeries
- Socket regeneration – Ridge preservation
- Furcation defects & Periodontal pockets
- Post apicoectomy bone regeneration
- After third molar extractions
- Maxillofacial surgeries – CLP, mastoid obliteration, etc

Unique Properties

- Unique Presentation
- No Mixing, thawing required
- Excellent material retention at defect site
- Adapts well to different shapes and surfaces of defects
- Eliminates concerns of device migration
- Fool Proof – No concerns of under/over condensation

Advantages

- Overcomes the drawbacks of particulate grafts
- No mixing required – package to placement
- Excellent ease of handling
- Great adaptability
  - provides greater graft-implant surface area
- Hydrophilic - blends with blood
- Stays in place – no device migration
  - Excellent for use in Furcation defects where retention is a problem
- Smooth surface texture
  - helps prevent damage to sinus membrane during sinus elevation
Precaution

- May not be cohesive when mixed with autograft / allograft
  - Overcome by “sandwich” / layer technique
- Temperature sensitive – Has to be stored & transported < 40°C
  - Do not leave the material in a car

Putty – Mechanism of Action

- After the clot forms – PEG, Glycerin & smaller CPS particles get absorbed over 5-7 days
- A virtual porous network forms in the defect
- Smaller CPS particles provide the initial burst of calcium & phosphorous
- Spaces between particles permit rapid vascularization and bone in-growth
- Multiple foci of osseous regeneration areas appear throughout the defect thus enhancing the rate of bone formation

Mechanism of Action
**Osteostimulation**

- **Osteoconduction** - Passive mechanism by which bone formation occurs along the surfaces of an implant material
- **Osteostimulation** - “The stimulation of osteoblast proliferation and differentiation as evidenced during *in vitro* osteoblast cell culture studies by increased DNA content and elevated osteocalcin and alkaline phosphatase levels” FDA 2005
  - Stimulates osteoblast recruitment, proliferation and differentiation at the defect site
  - Increased rate of bone formation
    - New bone occurs throughout the defect
      - Not just at the edges – osteoconduction
    - Multiple areas of bone formation
      - Each particle reacts to generate bone
      - Bone formation seen within each individual particle
    - Higher rate of particle resorption
      - Putty displays higher rate of bone regeneration than particulate graft materials
  - Does not generate bone in non-osseous sites

**Osteostimulation – The Proof**

- 3 week Histo slide shows active areas of bone formation (B)
- Note bone growth around the particles (pink areas)
- Also note cracks developing in the particles and pink areas inside the cracks
  - Demonstrating bone ingrowth
  - 3 weeks

**Labels**
- B – Bone
- P – Particle
- C – Cracks
Osteostimulation – The Proof

- Histo slide shows abundant areas of bone (B)
- Cracks have progressed into the center of each particle
- Pink areas seen at the center of each particle
  - Demonstrating bone growth from inside
  - Active resorption from inside
- Multiple foci of bone formation

Osteostimulative effect - Bone penetration into the particles through the cracks clearly visible

6 weeks
Effect of NovaBone on bone marrow stromal cell differentiation

“.. The purpose of this study was to investigate the ability of three bioactive glasses (45S, 58S and 77S) to induce osteogenic differentiation and cell mineralization. A significant effect of the 45S and 77S bioactive materials was seen on early differentiation of the marrow stromal cells into osteoblast-like cells. 45S evidenced also the highest effect on cell mineralization …”

M Bosetti, M Cannas, Biomaterials, 26(18):3873-3879, 2005


“The results obtained demonstrated that the three new bioglasses enhanced the proliferation response of osteoblasts compared with osteoblasts alone….and did not induce stimulation of proinflammatory markers iNOS and IL-1B…”


Bioglass 45S5 stimulates osteoblast turnover and enhances bone formation In vitro: implications and applications for bone tissue engineering.

“In conclusion, this study shows Bioglass 45S5 has the ability to stimulate the growth and osteogenic differentiation of human primary osteoblasts. These findings have the potential for tissue engineering where this bioactive glass substrate could be used as a template for the formation of bioengineered bone tissue.”

Osteostimulation – References

A genetic basis for design of biomaterials for In Situ tissue regeneration

“Gene array analysis confirmed genetic activation controlled the osteoblast’s cell cycle to favor proliferation and differentiation of only the cells that proceed towards the creation of mineralized extra-cellular matrices, osteocytes, and new bone”


Ease of Use

- No special preparation required
- No refrigeration required
- Easily placed into defect site
- Does not set like a cement
- Can be formed into various shapes and sizes

Enhanced Handling
Animal Study - 1

- Rabbit study – distal femur
- 5 mm diameter x 10 mm depth
- Approx 0.3 cc of putty was used
- Histological sections were obtained at 6 & 12 weeks

Histology

- Bone penetration into the particles at 6 weeks
- Osteostimulative effect – Bone in-growth into the particles visible
- Good bone growth both at 6 & 12 weeks
- Minimal inflammatory reaction

Results

<table>
<thead>
<tr>
<th>% New Bone</th>
<th>6 weeks</th>
<th>12 weeks</th>
</tr>
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<tbody>
<tr>
<td>48</td>
<td>30</td>
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- As a comparison, the mean compressive modulus & mean toughness were equivalent to particulates
- Putty forms a great osteoconductive & osteostimulative scaffold for rapid bone regeneration & turn over
Animal Study - 2

- Sheep study – Intravertebral Defects
- 10 mm diameter x 15 mm depth
- Particulate vs. Putty vs. Empty
- Histological sections were obtained at 6 & 12 weeks

Histology - Putty

- Healthy osseous tissue seen at both 6 & 12 weeks (red area)
- Significant reduction in the number & size of particles seen at 12 weeks
- Blue areas are remnants of the stain used
- Minimal inflammatory reaction

Results

<table>
<thead>
<tr>
<th>% New Bone</th>
<th>Particulate</th>
<th>Putty</th>
<th>Empty</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 wk</td>
<td>26.98</td>
<td>47.32</td>
<td>42.00</td>
</tr>
<tr>
<td>12 wk</td>
<td>42.00</td>
<td>51.38</td>
<td>1.20</td>
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- At six weeks % new bone growth is significantly higher for Putty
- At six weeks there is no statistical difference on the volume of residual graft material
- At twelve weeks new bone growth seen with putty is statistically significant
- At twelve weeks, there is no statistical difference on the volume of residual graft material
**Completely Absorbable**

*DM Gaisser, DL Wheeler, DC Greenspan* - Presented at Society for Biomaterials annual meeting, Tampa, Florida, April 2002

- **In Vivo Evaluation**  
  - Critical sized defects in distal femur of goats  
  - Evaluate absorption rates at periods up to 12 months

- **Procedures**  
  - 10mm dia. defect in distal femur

- **Results**  
  - 6 weeks - Bone formation in grafted areas between particles, with particles linked by new bone  
  - 52 weeks – Extensive new bone formation and remodeling, with few particles remaining

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**Results**

- Graft content decreased significantly with time.
- Residual graft material occupied an average of 1.5% of the defect area at six months
- Less than 0.5% graft material at 1 year
Human Clinical Cases
NovaBone Putty
Illustrations
Radiographs

- Note the excellent adaptation of putty against the surface of implant
- Immediate post op radiograph shows presence of putty around implant – radiodense with no trabecular pattern

Radiographs

- 6 week post op radiograph demonstrates presence of trabecular pattern around implant – indicative of bone regeneration
- 9 month post op radiograph demonstrating a fully loaded implant in completely regenerated natural bone
Human Clinical Cases
Predicate Particulate

Periodontal Osseous regeneration

This patient presented with a 7 mm anterior periodontal defect also displaying extensive horizontal bone loss.

The defect was thoroughly debrided and particulate was used for bone regeneration.

Radiographic Evaluation

- Radiographs
  - Preoperative – probe showing the extent of bone loss
  - Postoperative (8 months) – probe displaying bone regeneration
  - Also notice good horizontal bone regeneration
Radiographic Analysis

Pre-operative radiograph showing severe osseous intrabony defect.

Post-operative radiograph at 24 months following graft procedure. Evidence of significant bony fill at the defect site.

Pre-operative radiograph showing a huge periodontal intrabony osseous defect.

Post-operative radiograph at 3 months following showing bone formation and presence of particulate graft

Post-operative radiograph at 6 months showing regenerated mature periodontal bone
Post Extraction Ridge Maintenance

Trauma causing the tooth fracture; ridge regeneration required to proceed with implantation

After extraction of the root fragments, the site was prepared and PerioGlas was placed into the defect

4-month postoperative photograph shows well-conformed soft tissue over the regenerated ridge
**Ridge Augmentation**

Highly resorbed mandibular ridge

Holes are drilled at the graft site and graft particulate is placed

Membrane overlying the graft to help retain and support the material

Augmented ridge at 6 months displaying good soft tissue contour over the regenerated bone

**Implant Placement After Ridge Augmentation**

Surgical preparation of the site facilitating the placement of 3 implants – 6 month post surgery

Implants at the grafted site showing good healthy bone around – 6 month post implantation
Case Report - Clinical History

- 27 year old female
- **Diagnosis:** Odontogenic keratocyst, left mandibular third molar, extending into the ramus
- **Treatment:** Mandibular molars extracted; cyst enucleated; residual defect grafted with NovaBone particulate and covered with a collagen membrane.
- **Results:** At six months, the graft site is filled with radiodense tissue.
  - No recurrence at three years post-operatively
Sinus Elevation

Radiograph showing the proximity of the bone to the floor of the sinus membrane

Sinus floor elevated and an immediate implant placed in the anterior area

Augmented sinus showing mature bone in the posterior areas, ready for implant placement (6 month post-op)
Immediate Implants

Pre-operative radiograph showing the fractured root necessitating extraction

Photograph showing the implant in position immediately after the tooth was extracted

Particulate graft was placed in the space around the implant and the socket wall

6 month post-operative radiograph showing healthy osseous tissue around the implant
Clinical / Animal Studies

- Rabbit femur study – Complete
- Sheep spine study 1 – Complete
- Sheep spine study 2 – Complete
- 10 patient – Private Practice – Sinus Elevation study done by Dr. Ron Nevins (Harvard)
  - Histo analysis expected March 09
- Sheep study comparing PerioGlas Putty vs. Bio-Oss vs. Grafton DBM – begins June /July 08
  - Data expected March 09
- Human Clinical Studies
  - Grafton DBM vs PerioGlas Putty – Dr. Saroff - Data expected Dec 09
  - Putty in Immediate vs Delayed implants – Dr. Anderegg – Data expected – Dec 09
  - Putty in sinus elevations – Luton College London – Data expected - Dec 09

Case studies from Craniofacial and Orthopedic Surgeries

Hemi-Mandibulectomy

57 year old male with recurrent ossifying fibroma of the mandible

Resection of the affected part of the mandible was the only treatment

SS, U Oklahoma
Hemi-Mandibulectomy

Reconstruction with bone plate, rib allograft, and allogenic cortico-cancellous bone mixed with 12cc of NovaBone

16 month postoperative panoramic x-ray of reconstruction and graft site
Adult Cranial Remodeling

- Case Study
  - Subject: 40 yr old female
  - Diagnosis:
    - Crouzon’s syndrome
  - Treatment:
    - Frontal osteotomy with supraorbital bandeau advancement
    - Absorbable plates / mesh
    - Grafting with NovaBone (Bioglass) bone-blood mixture

  - AG - Milwaukee, WI

Preoperative view

Osteotomy for frontal advancement
Adult Cranial Remodeling

Repositioning bone flaps

Placement of NovaBone C/M into the osteotomy site

Three days post-op

Six months post-op
NovaBone Putty

- Taking 20 yrs of technology one step ahead
- The next generation graft material
- Enhanced bone formation
- Unsurpassed ease of handling

Instructions for Use

- PerioGlas Putty has been engineered to simplify surgical procedures and is one of the easiest products to use clinically for osseous regeneration
- No mixing is required
- Putty can be placed into the defect immediately after opening the package
- Putty is engineered such that the material cannot be over-packed into the defect site

- The material becomes adhesive and cohesive enabling easy handling with instruments
- The material does not stick to instruments or gloves and hence can be manipulated easily into the defect site
Mixing with Autograft / Allograft

- Putty does not require any mixing, however if mixing is desired with Autograft or Allograft a “layer technique” is advocated
- Place Putty & Autograft (or allograft) in layers instead of premixing them outside
- This will help maintain the handling properties of Putty

Use of Membrane

- Putty demonstrates a natural ability to prevent epithelial down-growth in periodontal cases
- If primary closure is achievable, no membrane is required in periodontal surgeries
- Membrane not required
  - Periodontal surgeries / Furcation surgeries
  - Small extraction sockets
  - Cystic regeneration with mucosal coverage
- Membrane required
  - Large extraction sockets – Ridge Augmentation – to obtain ridge shape

Unique Usage

- Putty can be used in unique ways and indications
- Putty is the easiest to use around implants during immediate implant surgeries as it gives good adaptation against the implant
- Putty is ideal for furcation defects where most particulate materials have retention issues
- Also in ridge augmentation surgeries in the mandible, where putty can be molded to the desired shape
Putty Benefits

- Unlike other putties, no mixing or handling is required
- No refrigeration required
- Easiest to mold, shape & conform to defect
- Osteostimulative – Enhanced bone regeneration
- Material does not flow – No device migration
- Excellent material retention – use suction around defects
- Helps clot stabilization & healing
- No over / under condensation issues

Ease of Use

- No special preparation required
- No refrigeration required
- Easily placed into defect site
- Does not set like a cement
- Can be formed into various shapes and sizes
Competition

- **Putty / Gel**
  - Grafton DBM – Demineralized Bone Matrix
  - Pepgen-P15 – synthetic peptide
  - Gem21s – B-TCP + Platelet Growth Factor
    - Currently not approved for Implant surgeries!! (Jan 09)

- **Morsels**
  - Bio-Oss – Bovine bone
  - Puros & Other DFDBA’s – Human cadaver bone
  - Pro-Osteon – Sea coral

- **Particulate**
  - Bioplast HTR – denture material
  - B-TCP – Tri calcium phosphate
  - Calcium Sulfate

**Putty vs. Bio-Oss**

- No clinical comparison yet
- Putty is technologically far superior to Bio-Oss
- Animal study in progress – sheep study
- Bio-Oss – non resorbable & bovine derived
- Putty has high resorption and enhanced bone regeneration
- Bio-Oss is only Osteoconductive while Putty is Osteostimulative

**Putty vs. Any Particulate**

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NovaBone® C/M
Bioglass® Synthetic Bone Graft Particulate

CRANIOFACIAL BONE GRAFT PARTICULATE

- Bioactive Synthetic Compound
- Enhances Bone Regeneration and Healing
- Bone Graft Replacement and Extender
- More than 650,000 Procedures Performed

CRANIOPLASTY
ORBITAL RIM AND OSSEOUS DEFECT RECONSTRUCTION
MANDIBLE RECONSTRUCTION
ALVEOLAR CLEFT GRAFTING

PUREX
SURGICAL PRODUCTS GROUP

A Revolutionary Bone Graft Extender!
Primary Repair of an Osseous Defect in the Superolateral Orbital Roof Utilizing a NovaBone-C/M® Bone Fragment Slurry

John W. Shore, M.D., F.A.C.S
Malena M. Amato, M.D. (f)
Sean M. Blaydon, M.D. (f)
Texas Oculoplastic Consultants Austin, Texas

Pre-op: A 42-year-old female presented with a presumed aneurysmal bone flap cyst of the right orbit. The pre-operative CT shows the osseous defect in the right superolateral orbital roof. (Fig. 1)

A lateral orbitotomy was performed and the 22mm x 20mm lesion was excised. (Fig. 2) A NovaBone-C/M and bone fragment slurry was prepared and placed to fill the defect site and to cover and smooth the bone flap. (Fig. 3)

Post-op: At eight months post-op the patient was symptom free. The CT shows bone in position with a radiographic interpretation of the area as "new bone" formation. (Fig. 4)

Surgeons should utilize proper surgical techniques and their clinical experience to determine appropriate surgical procedures.

Successful implantations are technique sensitive. Sound surgical judgement should be used in the selection, shaping, handling, and implantation of NovaBone-C/M.

NovaBone-C/M Bone Graft Particulate is provided STERILE and packaged individually in a sterile mixing cup.

References


NovaBone-C/M is a synthetic bioactive particulate bone graft extender or replacement that facilitates a healing response in the graft site when combined with body fluids. In situ, it forms a macroporous structure that allows bone ingrowth and progressively resorbs as it is replaced by living bone. Because it bonds with both bone and soft tissue, it remains in the defect, allowing reconstruction of normal tissue.

**An "Osteostimulatative" Graft Material**

NovaBone-C/M is a synthetic bioactive particulate bone graft extender or replacement that facilitates a healing response in the graft site when combined with body fluids. In situ, it forms a macroporous structure that allows bone ingrowth and progressively resorbs as it is replaced by living bone. Because it bonds with both bone and soft tissue, it remains in the defect, allowing reconstruction of normal tissue.

**More Predictable Autograft Success**

NovaBone-C/M can reduce variability in autograft success that comes from factors like graft particle size or source location. Combining NovaBone-C/M with autografts may provide better results than with particulate autograft alone (faster regeneration of new bone).4

**A Record of Success**

The material in NovaBone-C/M has been used in more than 650,000 implanted graft cases in oral, dental, and craniofacial surgery.

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**Adult Cranial Remodeling Utilizing NovaBone-C/M® and Bone Particles**

**Pre-op:**
A 50-year-old male presented complaining of severe headaches, which appeared to be caused by previously untreated Crohn’s syndrome. (Fig. 1)

A fronto-orbital advancement using a supraorbital bandeau was performed to relieve pressure on the brain and reduce the relative orbital proptosis.

Bone particles were collected at the time the bone was intact (Fig. 2). A manual drill was used to keep the bone cells intact. This bone material was mixed with NovaBone-C/M and used to fill the craniotomy gaps and bone holes.

**Post-op:**
At six months, the patient noted a reduction in headaches and improved cosmesis. CT scans of the cranium at three days post-op (Fig. 3) and at six months post-op (Fig. 4) detail significant bone in-fill and consolidation of the defect areas.

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**Mandible reconstruction utilizing donor graft, and 12cc of Bioglass® [NovaBone-C/M®]**

Steven M. Sullins, DDS
Professor and Chairman
Department of Oral and Maxillofacial Surgery
University of Alabama Health Sciences Center

**Pre-op:**
A 57-year-old male presented with a recurrent ossifying fibroma of the hemi-mandible. He had been previously treated approximately 25 years ago and noticed that there was gradual enlargement of his jaw and inability to wear a partial denture. The radiographic evaluation revealed extensive involvement of the left mandible necessitating resection and immediate reconstruction. (Fig. 1)

A hemimandibulectomy (Fig. 2) was accomplished followed by immediate reconstruction utilizing a reconstruction plate, donor graft, and a mixture of cortico cancellous bone from the posterior ilium and approximately 10-12cc of particulate Bioglass. Immediate post-op radiograph of reconstruction and graft site shows NovaBone-C/M mixture in place. (Fig. 3)

**Post-op:**
Following six months of graft consolidation dental implants were placed, and following integration, a hybrid fixed prosthesis fabricated. Follow-up radiograph at 16 months indicates significant consolidation in graft areas. (Fig. 4)