Literature Review - March 5th, 2019

Bioactive-glass in periodontal surgery and implant dentistry.

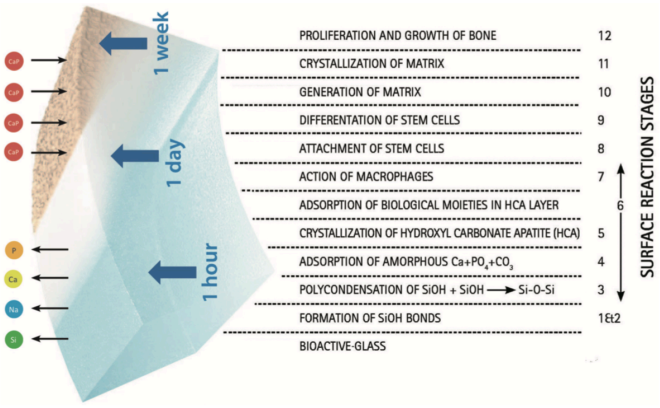
Introduction

- Several kinds of biomaterials have been employed in treatment of deep intraosseous defects over the last decade
- Among these, group of surface reactive glass ceramics (calcium sodium phosphosilicates) have attracted more and more attention
- Bioactive glass (B-G) has numerous features, most of which are a proven history of biocompatibility and capacity to act rapidly as biomimetic mineralizer
- Chemical composition is significant
- Constituents are minerals that occur naturally in the body: silica, sodium oxide, calcium oxide, and phosphorus pentoxide
- Two key composition features of B-G:
  - High CaO/P2O5 ratio, making it distinctively reactive - shows formation of outer layer of hydroxycarbonate apatite.
    - Critical concentrations of biologically active ions become available exactly at rate and location needed for cell proliferation and differentiation
    - On dissolving, activates genes that modulate osteogenesis, without occurrence of fibrous tissue encapsulation, neither causing inflammation nor toxicity
    - Antimicrobial properties exhibited due to creation of alkaline environment and resistance of material to bacterial adhesion and biofilm formation
  - Content of around 60 mol% silica
    - Plays important role in making glass easy to melt, but also contributes to form HCA, which leads to direct chemical attachment to both soft and hard tissues
- Increased literature available to support application of B-G in variety of clinical applications, including alveolar ridge preservation, maxillary sinus augmentation, treatment of various intrabony and furcation defects

Overview of the Fundamental Science

<u>Materials properties of B-G, MOA, and Biological Response</u>

- Keys to regenerative repair of bone is to:
  - Control population of cells that are capable of entering into active phases of cell cycle
  - Complete mitosis of cells with accurate replication of genes
  - Achieve cellular differentiation into a phenotype capable of synthesizing a full complement of extracellular proteins that constitute a mature osteocyte
- 3D architecture of mineralized bone is created by osteoblasts that are exposed to critical concentrations of soluble ionic constituents released from B-G
- Approx. 17-20 ppm soluble Si and 88-100 ppm soluble Ca ions required
- MOA discussed extensively in literature
- Sequence of interfacial reactions involved in forming bond between B-G and bone:



- Process involves 5 initial stages:
  - Initial ion exchange of alkali ions with hydrogen ions from liquid medium, which increases the pH at the B-G bone interface to values >7.4
  - Glass network dissolution
  - Silica-gel polymerisation
  - Formation of an over-saturated solution that exceeds the solubility product constants for a number of mineral forms, including crystal growth of HCA
- Structurally and chemically similar to mineral phase of human bone, allowing accelerated interface strength acquisition
- First three stages occur in parallel and complete in release of silicic acid, condenses to form a negatively charged gel at surface of particles
- Serves to hold glass particles in a cohesive mass and resembles HCA matrix so much to induce osteoblast differentiation
- Controlled rates of glass dissolution provide the critical concentration of biologically active ions to cells via interfacial solution
- The longer the dissolution, the better the deposition of bone tissue and growth
- Important to observe the end result of cell cycle activated by ionic products of B-G dissolution is up regulation of numerous genes that express growth factors and cytokines and extracellular matrix components
- B-G can be moulded into any desired shape and available in multiple forms

Clinical Applications
<u>Alveolar ridge preservation and/or pre-prosthetic reconstruction procedures</u>

- An ideal bone replacement material should have the following properties:
  - Available at any time and in any amount
  - Easy to handle
  - No donor site morbidity
  - Not cause foreign-body reaction or be toxic
  - Any transmission of infectious diseases must be excluded
  - No effect at follow-up examination
  - Economical, namely, it should entail no additional cost or prolong operation time
- Golden standard - autogenous bone grafts
  - But still has some disadvantages: limited availability, additional surgery, donor site morbidity
  - Resorption may be unpredictable
- B-Gs are effective in eliciting specific cellular responses
- Ability to remain where placed even with adjacent suctioning, and hemostasis during incorporation into host bone
- Possibility of employing these biomaterials to fill and repair dentoalveolar defects in a rapid and controllable way has been thoroughly investigated by OMFS
- Since introduction, original B-G released as PerioGlas for Perio regeneration, and NovaBone or Biogran used in OMFS
- One of the first commercial applications of B-Gs in dentistry was to prevent resorption of alveolar bone after tooth removal and to maintain or enhance bony ridge form for subsequent restorative treatments with implant-supported prosthesis
- There has been a number of clinical studies that have demonstrated consistent results in a variety of alternative treatments including surgical modification/reduction of maxillary sinus, regeneration of inter proximal bone defects, periodical application, management of cystic defects, treatment of peri-implantitis
- In all of applications, proven efficacy and effectiveness to bond with hard tissue and enhance its growth due to osteoconductive and osteostimulatory properties of the glass

- New bone formation has been demonstrated histologically in human oral bone defects treated with B-G
- Also evidence the replacement and infiltration of osseous tissue starts at 4 months, and all B-G particles completely disappear at 16 months following procedure

Maxillary sinus lift surgery

- Maxilla grafting with composite grafts of B-G granules and autogenous bone chips was shown to be as good as treatment with autogenous bone alone, yielding same quality and volume of mineralized tissue when a reasonable healing period allowed
- Bone formation in defects filled with B-G originates from margins of defect and proceeds up to certain distance, but not necessarily throughout the defect space
- Thus, harvesting of autogenous bone may still be necessary, but the amount of bone needed is considerably decreased
- Use of autogenous bone dictated by its osteogenic potential related to number of surviving osteoblasts and osteoinductive effect brought about by release of bone morphogenic proteins and other growth factors, which have the capacity to accelerate deposition of new bone along graft material
- When using biomaterials for bony deficiencies, advisable to know their resorption behaviour, and this should closely match the bone formation rate at regeneration or implant sites
- B-G granules start to resorb postoperatively while new bone is formed within and around them, unlikely for glass remnants to interfere with bone dynamics at implant-bone interface after fixtures have been installed
- Been shown B-G able to produce more new bone than SHA

Treatment of periodontal defects

- Limited human histologic evidence to show renewal of integrated bone, cementum and connective tissue attachment coronal to base of previous osseous defect
- Large amount of clinical and radiological data supporting the application of B-Gs in treatment of teeth that have advanced periodontal destruction
- Several clinical studies have shown better results employing B-G in comparison with conventional treatment methods
- Study by Mengel et. al showed B-G treated sites showed a greater trend to improvement compared to conventionally treated sites is consistent with the findings of a recent systematic review of literature by Sohrabi et. Al
- Evidence presented suggests that B-G induced a “repair” response rather than a true regenerative response
- Consequently, gain in clinical attachment level could be due to chemical bonding between newly formed HCA layer and host tissue as well as the soft tissue bonding property of B-G
- All evaluated B-G materials in included studies appeared to be biocompatible, and no reports of adverse effects, such as allergies, abscess formation, or rejection of grafting materials
- Main limitation inherent in B-G products that are currently available is their granular nature, and as such, cannot serve reliably as space-making materials in sites where there is no support for a membrane and soft tissue coverage may cause its collapse during healing

Metal surface biofunctionalization: coating material for dental implants

- B-G is regarded as a viable alternative to cover metallic implants in order to combine best properties of both materials
- B-G coating may improve rate of commitment of bone precursor cells to osteoblastic lineage differentiation and the resultant implants display a more rapid interfacial bone formation, with consequent stabilization at an early stage

- Several studies identified importance of thermal expansion coefficient of B-G, making the coatings prone to crack if stresses arise due to glass shrinking at a different rate from metal substrate during processing
- Difficult to match high TEC of glass coating with its predisposition to crystallize throughout heat treatment to that of titanium
- However, in case of conventional coating methods, matching the TEC of glass coating to that of titanium is an essential step
- Glass should have a slightly lower TEC than the metal
- May induce only small compressive stresses passing from processing temperature to room temperature
- TEC of glass can be reduced by increasing the silica content, but this reduces bioactivity as well
- Also can be reduced by a partial substitution of CaO with MgO and of Na2O with K2O
- Another approach to combine thermal expansion of coating to that of metallic substrates is represented by preparation of multi-layer coatings
- Coated implants were integrated into host bone without a connective tissue capsule and were surrounded by significantly more bone than the non-coated implants
- Effectiveness of interfacial adhesion depends on proper elemental interdiffusion, chemical bonding, and physical interlocking between dissimilar phases

- Number of methods utilized to manufacture bioactive coatings on metal prostheses
- In recent short-term clinical study, newly developed B-G/coated dental titanium implants were fabricated using a conventional enamelling technique and evaluated following implantation in partially edentulous patients
    - Application of small amounts of borosilicate containing titania to experimental implants, and glass composition optimized to show a lower tendency to crystallization during thermal coating treatment
    - Resultant thickness in range of 70-100 micrometers
    - After 12 months, no apparent retardation of normal bone healing process around fixture occurred

- Peri-implantitis has been discussed extensively
- B-G has shown to be active against supra- and sub-gingival bacteria, further underlining its potential benefits as part of an implanted device

Conclusions

- B-Gs are an important consideration when choosing the optimal biomaterial to be used as a bone substitute in periodontal and implant therapy
- B-G is a versatile replacement material, since it is available in multiple forms and can be moulded into desired shapes
- Its unique bioactive properties allow for an osteoproductive environment in which the bone-biomaterial interface is uniquely stronger than it would be with other forms of alloplasts
- B-G represents an important and exciting field of study