Jaw bone regeneration – current status

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DMD, PhD, Professor, Lithuanian University of Health Sciences
Kaunas, Lithuania, on September 9-10, 2016.
The Baltic Ossoeintegration Academy (BOA) together with the Lithuanian University of Health Sciences (LUHS) and number of Universities from Europe and USA is organizing an International Dental Implant Congress and Consensus Conference devoted to the topic of Peri-implantitis.
BOA & LSMU
International Dental Implant Congress
Concensus Conference
9-10 September 2016 - Kaunas, Lithuania

PARTICIPANTS - EUROPE AND USA UNIVERSITIES
The bone sets the tone

- Bone defects often result from tumor resection, congenital malformation, trauma, fractures, surgery, or periodontitis in dentistry, as well as from diseases, such as osteoporosis or arthritis.

- After the loss of teeth atrophy of the alveolar processes occurs in a vertical as well as a horizontal plane. The term atrophy is defined in the dictionary as “a wasting away; a diminution in the size of a cell, tissue, organ, or part”

The bone sets the tone

• This process is starting and continuous throughout life because of the lack of stimuli (disuse atrophy) seen on alveolar process of the jaws

Figure 3 – Shows gradual alveolar bone resorption after tooth loss. (http://doctorspiller.com/Bone_Grafting/bone_grafting.htm)

• The glossary of prosthodontic terms. J Prosthet Dent. 2005 Jul;94(1):10-92. [Medline] [CrossRef]
The bone sets the tone

- After tooth extraction an average alveolar bone loss of 1.5–2 mm (vertical) and 40%–50% (horizontal) occurs within 6 months.


The bone sets the tone

• Most of alveolar dimensional changes occur during the first 3 months.
• If no treatment to restore the dentition is provided, then continued bone loss occurs and up to 40%–60% of ridge volume is lost in first 3 years.


The bone sets the tone

- Disuse atrophy

The bone sets the tone
Other possible etiological factors

- Drawings describes a process, which combines all of the above elements, whereby bone formation and resorption are maintained in balance.
Other possible etiological factors

• Once this balance is disrupted, excessive osteoclastic activity may lead to problems such as osteoporosis or bone resorption

• Overloading, trauma, inflammation can evoke disbalnce and bone resorbtion
Interesting facts

• Normally, about 0.7% of the human skeleton is resorbed and replaced by new healthy bone each day.
• Therefore, normal turnover of the skeleton occurs approximately every 142 days.
Interesting facts

• By age 80 both men and women typically have lost about half of their maximum bone mass value

• Women lose an estimated 35% of their cortical bone and 50% of cancellous bone as they age, while men lose only two-thirds of these amounts
The bone sets the tone

• In dental implant treatment, it is important to measure the alveolar process precisely so that the proper system may be chosen

• There are number of classifications suggested for assessment of the degree of atrophy of partially or fully edentulous jaws
The bone sets the tone

• One of the most popular classification systems for jaw anatomy (jaw shape and quality) for dental implant treatment was proposed by Lekholm and Zarb in 1985.

The bone sets the tone

• However, this classification, like many others, described changes only of jaw shapes in general and failed to indicate precise measurements

The bone sets the tone

- Juodzbalys et al. in 2004 proposed clinical and radiological classification of the jawbone anatomy for implantation based on edentulous jaw segment (EJS) anatomy assessment

The bone sets the tone
The bone sets the tone
The bone sets the tone

Dental implant operation planning should be done on three-dimensional edentulous jaw segment (EJS) pattern

The bone sets the tone
3D planning is essential

C = Type II height > 8 to ≤ 10 mm. Simultaneous implantation with augmentation are recommended.

D = Type II height > 4 to ≤ 10 mm
Simultaneous implantation with vertical alveolar process augmentation are recommended.

E = Type III height (≤ 8 mm) in mandible. Vertical alveolar process augmentation and late implantation are recommended.

F = Type III height ≤ 4 mm in maxilla. Sinus floor augmentation and late implantation are recommended.
The bone sets the tone

- Nevertheless, this classification fails to assess mandibular canal anatomy variations and risk degree of inferior alveolar nerve injury which is a serious complication with incidence ranged from 0 to 40%!

- Even after the accurate measurement of available bone, the nerve injury can occur as the result of over penetration of the drill owing to low resistance of the spongy bone; this can lead to slippage of the drill even by experienced surgeons.
Published articles

   URL: http://www.ejomr.org/JOMR/archives/2010/1/e2/e2ht.htm
doi:10.5037/jomr.2010.1102

   URL: http://www.ejomr.org/JOMR/archives/2010/1/e3/e3ht.htm
doi:10.5037/jomr.2010.1103

   J Oral Maxillofac Res 2010;1(2):e1
   URL: http://www.ejomr.org/JOMR/archives/2010/2/e1/e1ht.htm
Published articles

   Clinical Oral Implants Research 00, 2011, 1–8

   J Oral Maxillofac Res 2011;2(1):e1
   URL: http://www.ejomr.org/JOMR/archives/2011/1/e1/v2n1e1ht.htm

   URL: http://www.ejomr.org/JOMR/archives/2013/2/e1/v4n2e1ht.pdf

   URL: http://www.ejomr.org/JOMR/archives/2013/2/e2/v4n2e2ht.htm
The bone sets the tone

• The most severe types of injuries are caused by implant drills and implants themselves
The bone sets the tone

• The most severe types of injuries are caused by implant drills and implants themselves
Injury of the Inferior Alveolar Nerve

• It was discerning remark, however, it remains a serious complication and many had reported the incidence, varies from 0 to 40%, of implant related inferior alveolar nerve (IAN) injuries (Tay & Zuniga 2007; Misch 2008; Alhassani & AlGhamdi 2010; Misch & Resnik 2010).
Insufficient aesthetic result
Extraction socket walls remodeling, especially of labial cortical plate

- Mauricio G. Araújo & Jan Lindhe, 2005
Extraction socket walls remodeling, especially of labial cortical plate

- Mauricio G. Araújo & Jan Lindhe, 2005
We can’t to stop extraction socket walls remodeling!

- Bundle bone
- No bundle bone
- Woven bone
Soft tissue contour variations

Keratinized gingival width
Keratinized gingival thickness
Mesial papillae
Distal papillae

SOFT TISSUE ASSESSMENT

Soft tissue contour variations

Keratinized gingival width
Keratinized gingival thickness
Mesial papillae
Distal papillae

Soft tissue vertical deficiency

Height of alveolar process
Bone beyond the apex of extraction socket
Labial plate vertical position
Facial bone thickness
Intra-dental bone peak height
Distance between adjacent teeth

Presence of bone lesions

Extraction socket morphology – parameters evaluation

Type I - Adequate

Type II - Compromised

Type III - Deficient
Insufficient bone volume
In order to achieve successful implantation, the perfect model would be if implants were surrounded by at least 1 mm of bone

What decisions can be made in case of inadequacy between jaw bone volume and dental implant size?

• To reduce dental implant measurements to a minimum and to identify minimal alveolar bone volume
What decisions can be made in case of inadequacy between jaw bone volume and dental implant size?

• To augment alveolar ridge by utilizing guided bone regeneration technique either in conjunction with implant placement (simultaneous approach), or, as ridge augmentation procedure before implant placement (staged approach)
Autologous bone

Figure 17. Intraoral autogenous graft harvest sites (the tuberosity, ramus, and symphysis).
Autologous bone
Autologous bone
Gabriele bone regeneration

GBR primarily relies on 4 principles

1. Excluding unwanted tissues and cells from migrating into the area
2. Space creation and maintenance
3. Protection of the underlying blood clot
4. Wound stabilization
1. Excluding unwanted tissues and cells from migrating into the area

I and III type collagen bilayer membrane
2. Space creation and maintenance
3. Protection of the underlying blood clot

It can be ensured using appropriate supporting bone plastic material
<table>
<thead>
<tr>
<th>Table 1. Bone replacement grafts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human bone</td>
</tr>
<tr>
<td>Autogenous grafts (autografts)</td>
</tr>
<tr>
<td>Extraoral</td>
</tr>
<tr>
<td>Intraoral</td>
</tr>
<tr>
<td>Allogeneic grafts (allografts)</td>
</tr>
<tr>
<td>Fresh frozen bone</td>
</tr>
<tr>
<td>Freeze-dried bone allografts</td>
</tr>
<tr>
<td>Demineralized freeze-dried bone allografts</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bone substitutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xenogeneic grafts (xenografts)</td>
</tr>
<tr>
<td>Bovine-derived hydroxyapatite</td>
</tr>
<tr>
<td>Coralline calcium carbonate</td>
</tr>
<tr>
<td>Alloplastic grafts (alloplasts)</td>
</tr>
<tr>
<td>Polymers</td>
</tr>
<tr>
<td>Bioceramics</td>
</tr>
<tr>
<td>Tricalcium phosphate</td>
</tr>
<tr>
<td>Hydroxyapatite</td>
</tr>
<tr>
<td>dense, nonporous, nonresorbable</td>
</tr>
<tr>
<td>porous, nonresorbable (xenograft)</td>
</tr>
<tr>
<td>resorbable hydroxyapatite derived at low temperature</td>
</tr>
<tr>
<td>Bioactive glasses</td>
</tr>
</tbody>
</table>
4. Wound stabilization

We should use proper suturing technique
Clinical case
Clinical case
Clinical case
Clinical case
Guided bone regeneration

GBR contains one or more of three critical components:

1. Osteoprogenitor cells (osteocits, osteoblats)
2. Growth and differentiation factors (PDGF, BMP, TGF ...)
3. Extracellular matrix (Bio-Oss, Cerasorb, Biogran ...)

JUOZASILYS DENTAL IMPLANT INSTITUTE
Ideal grafting material
Conventional grafting

<table>
<thead>
<tr>
<th></th>
<th>Osteoconductive</th>
<th>Osteoinductive</th>
<th>Osteogenic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alloplast</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Xenograft</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Allograft</td>
<td>+</td>
<td>+/-</td>
<td>-</td>
</tr>
<tr>
<td>Autograft</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
What do we seek by grafting the cystic cavity?

• Regenerate the bone  +/-
• Prevent soft tissue collapse  +/-
• Improve bone quality and strength  –
• Accelerate bone healing  –
• Avoid infections and healing disturbances  –

Is it possible with osteoconductive grafting materials?
Alternatives?
Evolution of bone grafts

Progress in regenerative periodontal/bone therapies.

Hiroshi Egusa, Wataru Sonoyama, Masahiro Nishimura, Ikiru Atsuta, Kentaro Akiyama

Stem cells in dentistry – Part II: Clinical applications

Leukocyte-Platelet Rich Fibrin (L-PRF)
Platelet Rich Fibrin (L-PRF)

Platelet Activation: Natural coagulation → Fibrin Clot

<table>
<thead>
<tr>
<th>Factor</th>
<th>Target cell/tissue</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-EGF</td>
<td>Blood vessel cells, outer skin cells</td>
<td>Cell growth, recruitment</td>
</tr>
<tr>
<td></td>
<td>Fibroblasts and many other cell types</td>
<td>Differentiation, skin closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cytokine secretion</td>
</tr>
<tr>
<td>PDGF, A+B</td>
<td>Fibroblasts, smooth muscle cells, chondrocytes, osteoblasts, mesenchymal stem cells</td>
<td>Potent cell growth, recruitment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Blood vessel growth, granulation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Growth factor secretion; matrix formation with BMPs (collagen and bone)</td>
</tr>
<tr>
<td>TGF-β1</td>
<td>Blood vessel tissue, outer skin cells</td>
<td>Blood vessel (+/-), collagen synthesis</td>
</tr>
<tr>
<td></td>
<td>Fibroblasts, monocytes</td>
<td>Growth inhibition, apoptosis (cell death)</td>
</tr>
<tr>
<td></td>
<td>TGF gene family (includes BMPs)</td>
<td>Differentiation, activation</td>
</tr>
<tr>
<td></td>
<td>Osteoblasts (highest levels of TGF-β1)</td>
<td></td>
</tr>
<tr>
<td>IGF-1,2</td>
<td>Bone, blood vessel, skin, other tissues</td>
<td>Cell growth, differentiation, recruitment</td>
</tr>
<tr>
<td></td>
<td>Fibroblasts</td>
<td>Collagen synthesis with PDGF</td>
</tr>
<tr>
<td>VEGF/EGF</td>
<td>Blood vessel cells</td>
<td>Cell growth, migration, new blood vessel growth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antiapoptosis (anti–cell death)</td>
</tr>
<tr>
<td>bFGF</td>
<td>Blood vessels, smooth muscle, skin</td>
<td>Cell growth</td>
</tr>
<tr>
<td></td>
<td>Fibroblasts, other cell types</td>
<td>Cell migration, blood vessel growth</td>
</tr>
</tbody>
</table>

PRFM = platelet-rich fibrin matrix; PD-EGF = platelet-derived epidermal growth factor; PDGF = platelet-derived growth factor; TGF-β1 = transforming growth factor beta 1; IGF = insulin-like growth factor; VEGF/EGF = vascular endothelial growth factor/endothelial cell growth factor; bFGF = basic fibroblast growth factor; BMP = bone morphogenetic protein.

L-PRF vs PRP – fibrin architecture

- **PRP** – bovine thrombin and CaCl$_2$ induces sudden fibrin polymerization with tetramolecular junctions
- Incorporation of cells and growth factors is difficult

- **L-PRF** – natural slow polymerization leads to three dimensional fibrin polymerization
- Favorable to cytokine enmeshment and cellular migration

L-PRF – importance of fibrin matrix

• Fibrin is natural scaffold for angiogenesis attracted MSCs
• Fibrin network is able to enmesh leukocytes, platelets and growth factors and furthermore to promote leukocyte migration
• Fibrin matrix guides epithelial cell migration to its surface

L-PRF leukocyte content

• L-PRF – contains ~50% of blood leukocyte count

• Leucocytes trapped in the fibrin matrix continue to produce high quantities of TGFβ-1 and VEGF

• Leukocytes secret interleukins and have antimicrobial potential

L-PRF Clinical Use

- Socket healing optimization
- Socket preservation
- Periodontal defects treatment
- Bone augmentation in combination with particulate grafts
- Sinus lift surgeries
- Root coverage and gingival surgery
- Periimplant defect regeneration


Horowitz R. Optimizing Root Coverage With L-PRF-The allogeneic and xenogeneic tissues have shown excellent results in the short term. Inside Dent. 2011 Nov;7(10).

L-PRF Clinical Use

• The advantage of PRP is the release of significantly higher proteins at earlier time points whereas PRF displayed a continual and steady release of growth factors over a 10-day period.

• The new formulation of PRF (A-PRF) released significantly higher total quantities of growth factors when compared to traditional PRF.

• Clinical relevance Based on these findings, PRP can be recommended for fast delivery of growth factors whereas A-PRF is better-suited for long-term release.

Clinical case
4 months post op

10.4 mm 3D

12.9 mm 3D
L-PRF optimized healing in third molar surgeries
Grafting shift from inert to bioactive materials is prospective biomimetic treatment approach
Schematic diagram illustrating the current clinical approaches to stem-cell-based bone augmentation.

Mesenchymal stem cells

• Mesenchymal stem cells (MSC) are multipotent progenitor cells that were originally isolated from various tissues, including adult bone marrow, adipose tissue, skin, umbilical cord, and placenta.

• Bone marrow-derived MSCs have been used in clinical trials for the effective treatment of osseous defects.

Mesenchymal stem cells

• However, bone marrow aspiration is an invasive and painful procedure for the donor and is a difficult procedure for a general practitioner.
• Furthermore, MSCs constitute heterogeneous cell types, and the potential for proliferation and differentiation of the MSCs depends on a patient’s age, sex, or the presence of certain medical conditions, such as diabetes or hypertension.

Mesenchymal stem cells

• Several cell populations with stem cell properties have been isolated from different parts of the tooth, including the pulp of both exfoliated and adult teeth, the periodontal ligament, and the dental follicle.


Yamada Y, Fujimoto A, Ito A, Yoshimi R, Ueda M. Cluster analysis and gene expression profiles: a cDNA microarray system-based comparison between human dental pulp stem cells (hDPSCs) and human mesenchymal stem cells (hMSCs) for tissue engineering cell therapy. Biomaterials. 2006;27(20):3766–3781.
Mesenchymal stem cells

- Dental pulp stem cells (DPSCs) and stem cells from human exfoliated deciduous teeth (SHED) have generic mesenchymal stem cell-like properties, such as self-renewal and multilineage differentiation.


Yamada Y, Fujimoto A, Ito A, Yoshimi R, Ueda M. Cluster analysis and gene expression profiles: a cDNA microarray system-based comparison between human dental pulp stem cells (hDPSCs) and human mesenchymal stem cells (hMSCs) for tissue engineering cell therapy. Biomaterials. 2006;27(20):3766–3781.
Regulation of osteoblast differentiation

• Several hormones and cytokines, such as bone morphogenetic proteins (BMP), TGF-β, Wnt, hedgehog, bFGF, and estrogen, are involved in the regulation of mesenchymal cell differentiation by stimulating intracellular signaling pathways.

• Among them, BMP is one of the most powerful cytokines to induce ectopic bone formation, and it strongly promotes the differentiation of mesenchymal cells into osteoblasts.

Conclusion

• Although regenerative medicine has been tried in various fields, there is much demand for regenerative medicine in dentistry, particularly in bone regeneration.
• Depending on the state of periodontitis or jaw resection, it might take more than 6 to 12 months for occlusal reconstitution.
• Thus, the development of an efficient and high-quality bone derivation method is necessary.
**Table 1—Characteristics of an Ideal Synthetic Bone Substitute**

- Be biocompatible.
- Serve as a scaffold (framework) for new bone formation.
- Be resorbable in the long-term and have potential for replacement by host bone.
- Be osteogenic, or at least facilitate new bone formation.
- Be radiopaque.
- Be easy to manipulate.
- Not support growth of oral pathogens.
- Be hydrophilic (to attract and hold the clot in a particular area).
- Be available in particulate and molded forms.
- Be microporous (for added strength to the regenerating host bone matrix and allow biological fixation).
- Be readily available.
- Be nonallergenic.
- Have a surface that is amenable to grafting.
- Act as a matrix or vehicle for other materials (e.g., bone protein inducers, antibiotics).
- Have high compressive strength.
- Be effective in GTR procedures.
Study of the preparation of the three-dimensional matrix of regenerated cellulose for bone tissue engineering using freeze-drying method was performed. Regenerated cellulose-based gel was prepared by saponification of cellulose acetate. SEM photographs of the lyophilized cellulose matrix from: (a) water; (b) 15% ethanol; (c) 20% ethanol; (d) 25% ethanol; (e) 40% ethanol; (f) 60% ethanol.
SEM photographs of the lyophilized cellulose matrix used in study
2D and 3D micro-CT images of cellulose matrix.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total volume</td>
<td>625</td>
<td>mm$^3$</td>
</tr>
<tr>
<td>Scaffold volume</td>
<td>156</td>
<td>mm$^3$</td>
</tr>
<tr>
<td>Pore volume</td>
<td>470</td>
<td>mm$^3$</td>
</tr>
<tr>
<td>Porosity</td>
<td>75</td>
<td>%</td>
</tr>
<tr>
<td>Mean scaffold thickness</td>
<td>0.212</td>
<td>mm</td>
</tr>
<tr>
<td>Mean pore diameter</td>
<td>0.749</td>
<td>mm</td>
</tr>
</tbody>
</table>
Aditional suggestions

• Clinician needs different bone plastic material consistencies:
  1. Granules
  2. Block
  3. Gel or pasta
Aditional suggestions

• We need material shaping during operation
• Material should incorporate stem cells and growth factors
Aditional suggestions

• We need material shaping during operation
Aditional suggestions

• We need material shaping during operation
Additional suggestions

• We need material shaping during operation
Additional suggestions
Additional suggestions

• Or maybe material which will stiffen and will hold implants stable?
Thank you