COST Action – MP1301 NEWGEN

March 17th-18th
Aveiro, Portugal

Jaw bone regeneration – current status

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SALUS PRO PATRIA

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


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Osseointegration
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LIETUVOS SVEIKATOS
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International Dental Implant Congress
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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 glossary of prosthodontic terms. J Prosthet Dent. 2005 Jul;94(1):10-92. [Medline] [CrossRef]

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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.

- Liu, J.; Kerns, D.G. Mechanisms of guided bone regeneration: A review. Open Dent. J. 2014, 8, 56–65.
- Van der Weijden, F.; Dell'Acqua, F.; Slot, D.E. Alveolar bone dimensional changes of post-extraction sockets in humans: A systematic review. J. Clin. Periodontol. 2009, 36, 1048–1058.

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.

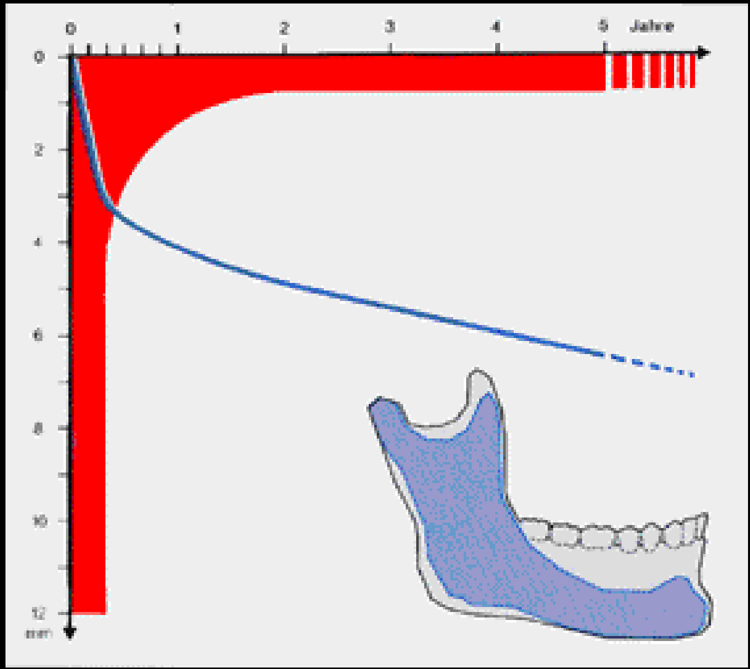
- Schropp, L.; Wenzel, A.; Kostopoulos, L.; Karring, T. Bone healing and soft tissue contour changes following single-tooth extraction: A clinical and radiographic 12-month prospective study. Int. J. Periodontics Restor. Dent. 2003, 23, 313–323.
- Tallgren, A. The continuing reduction of the residual alveolar ridges in complete denture wearers: A mixed-longitudinal study covering 25 years. 1972. J. Prosthet. Dent. 2003, 89, 427–435.
- Carlsson, G.E.; Thilander, H.; Hedegard, B. Histologic changes in the upper alveolar process after extractions with or without insertion of an immediate full denture. Acta Odontol. Scand. 1967, 25, 21–43.

The bone sets the tone

- Disuse atrophy

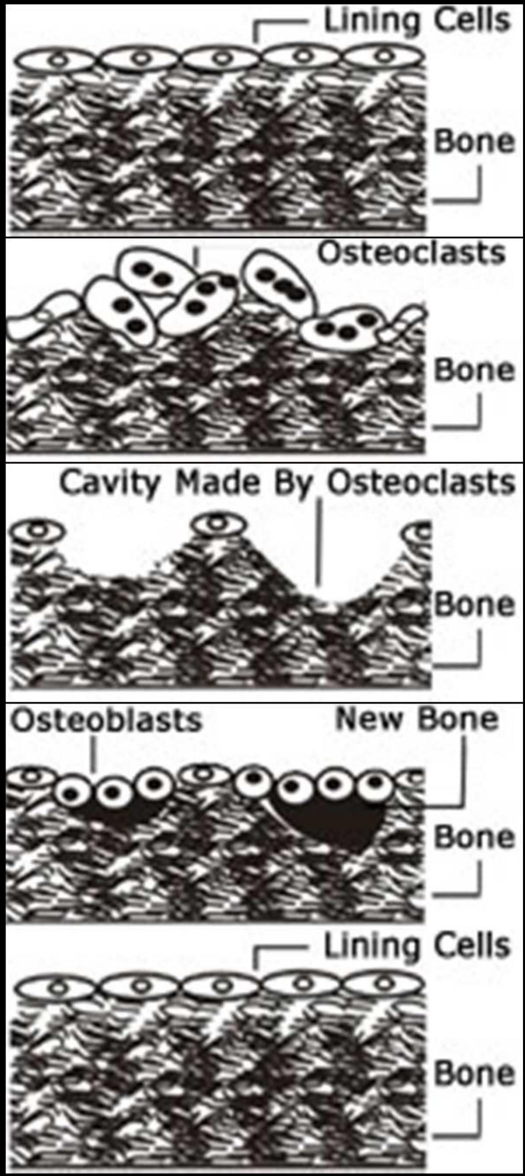
- The glossary of prosthodontic terms. J Prosthet Dent. 2005 Jul;94(1):10-92. [Medline] [CrossRef]

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



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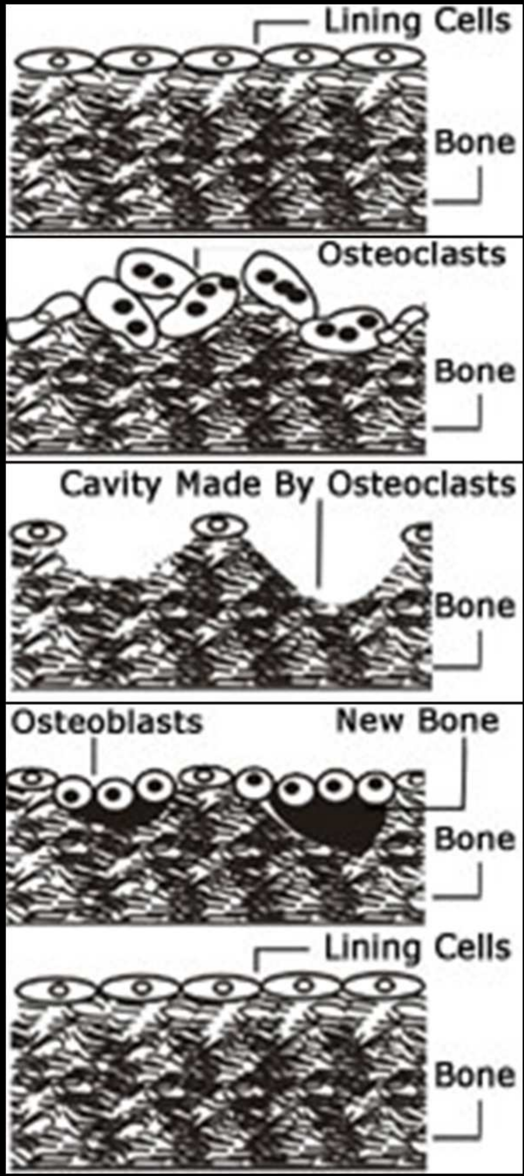
Other possible etiological factors

- 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



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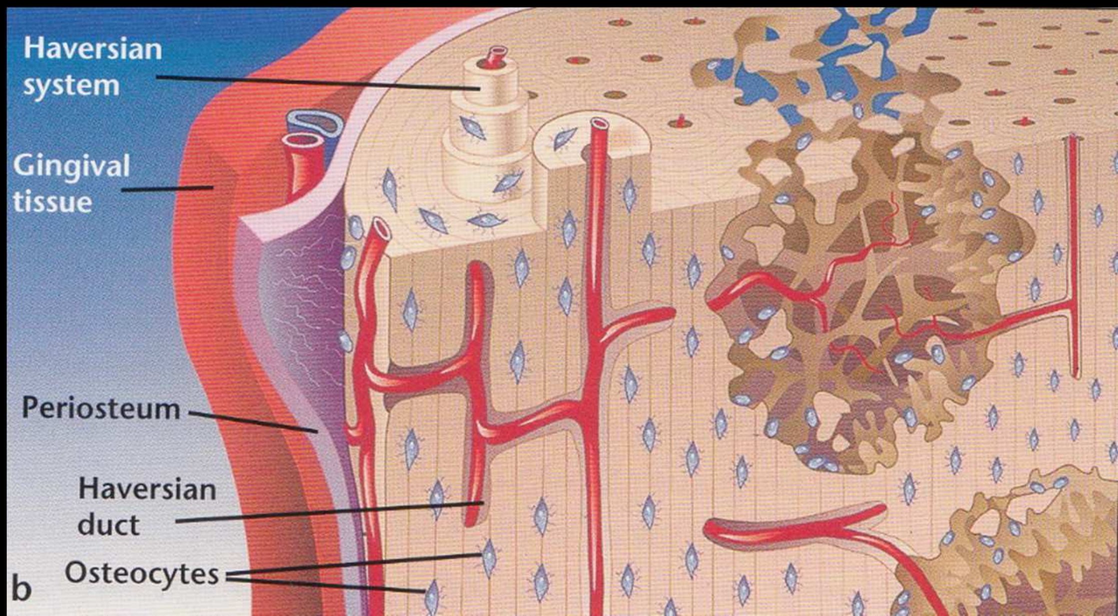
Interesting facts

- 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 man lose only two-thirds of these amounts

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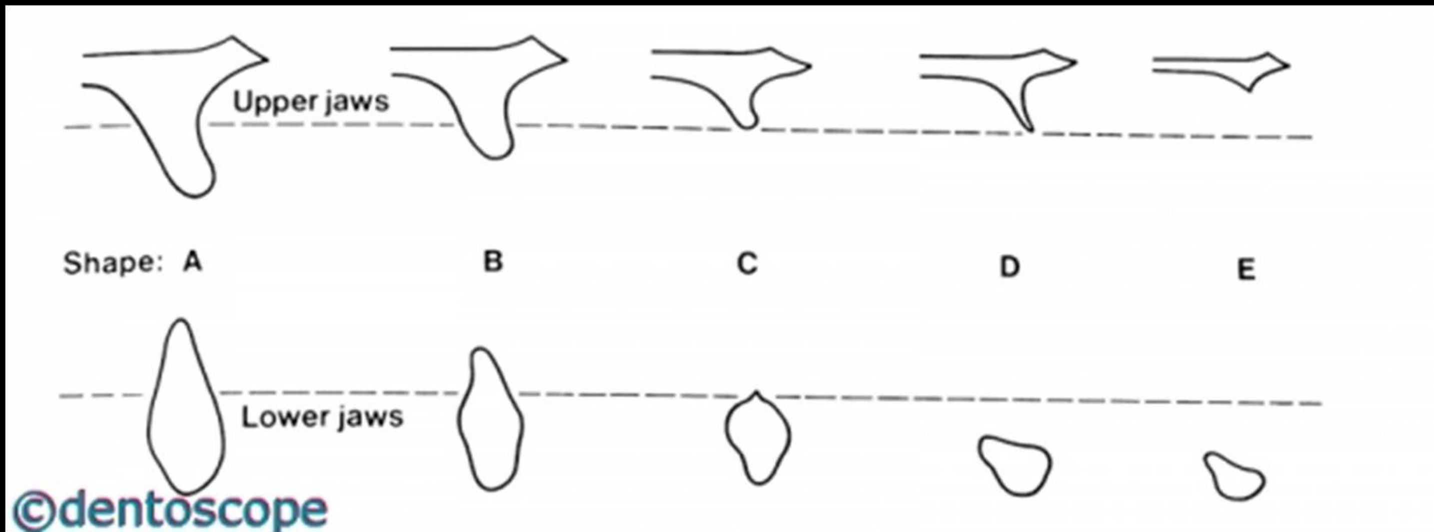
The bone sets the tone

- 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



- Lekholm U, Zarb GA. In: Patient selection and preparation. Tissue integrated prostheses: osseointegration in clinical dentistry. Branemark PI, Zarb GA, Albrektsson T, editor. Chicago: Quintessence Publishing Company; 1985. p. 199–209.

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

- Lekholm U, Zarb GA. In: Patient selection and preparation. Tissue integrated prostheses: osseointegration in clinical dentistry. Branemark PI, Zarb GA, Albrektsson T, editor. Chicago: Quintessence Publishing Company; 1985. p. 199–209.

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

Juodzbalys G, Raustia AM. Accuracy of clinical and radiological classification of the jawbone anatomy for implantation--a survey of 374 patients. J Oral Implantol. 2004;30(1):30-9. [Medline] [CrossRef]

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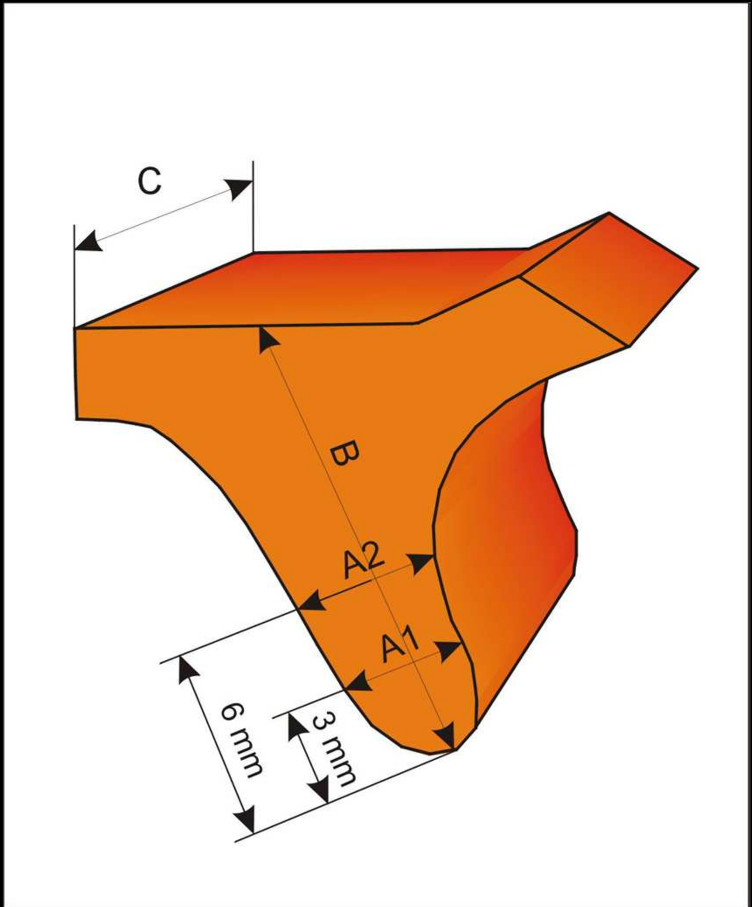
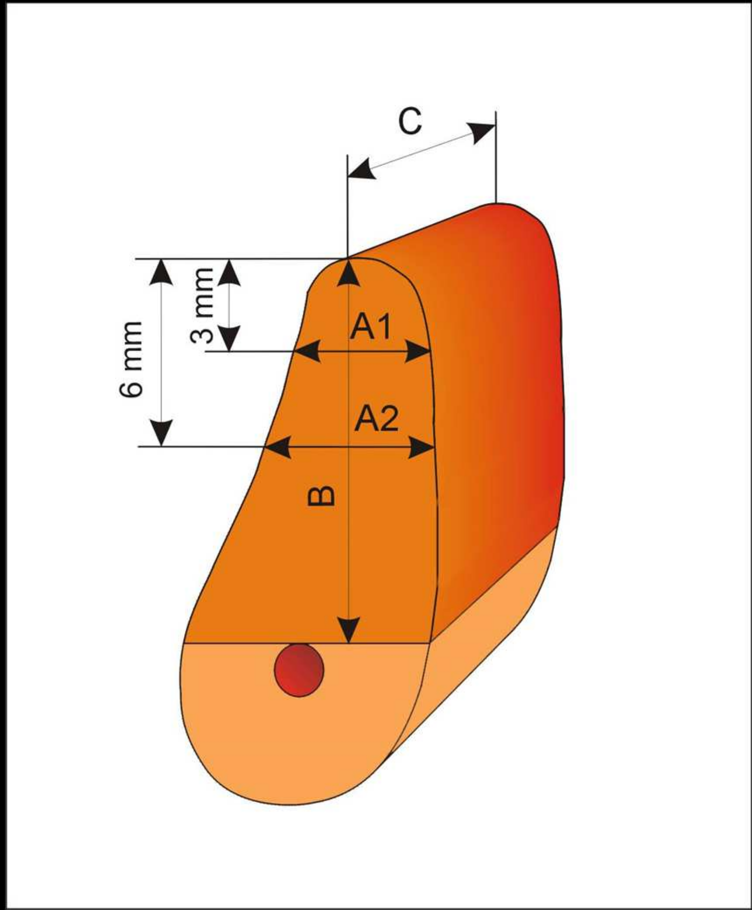
The bone sets the tone





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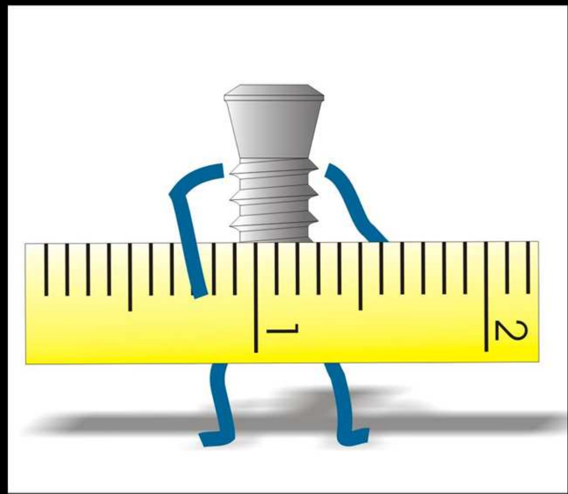
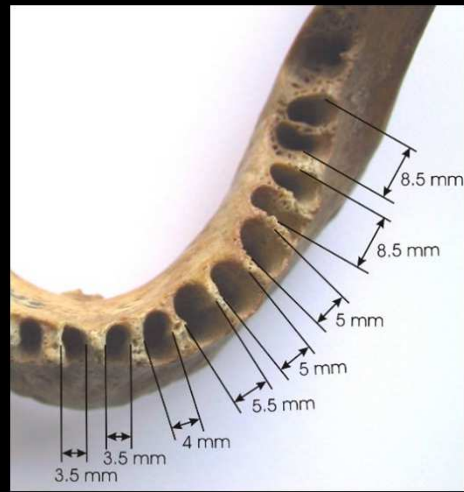
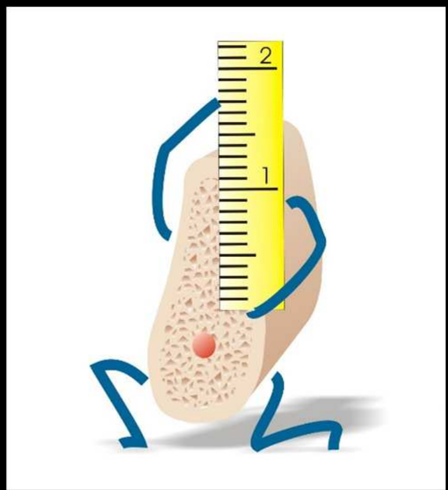
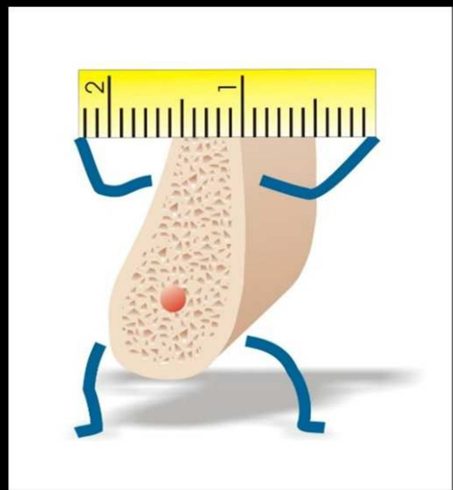
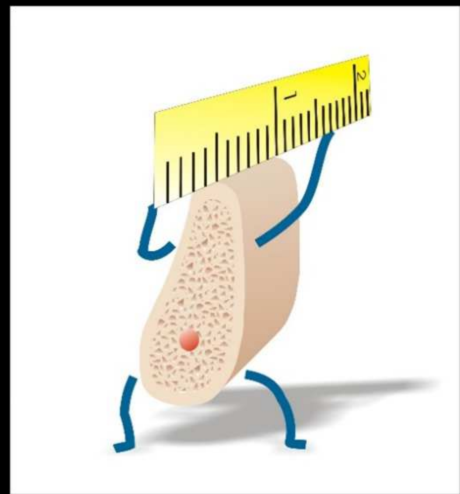
The bone sets the tone











The bone sets the tone

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

Juodzbalys G, Kubilius M. Clinical and Radiological Classification of the Jawbone Anatomy in Endosseous Dental Implant Treatment. J Oral Maxillofac Res 2013;4(2):e2

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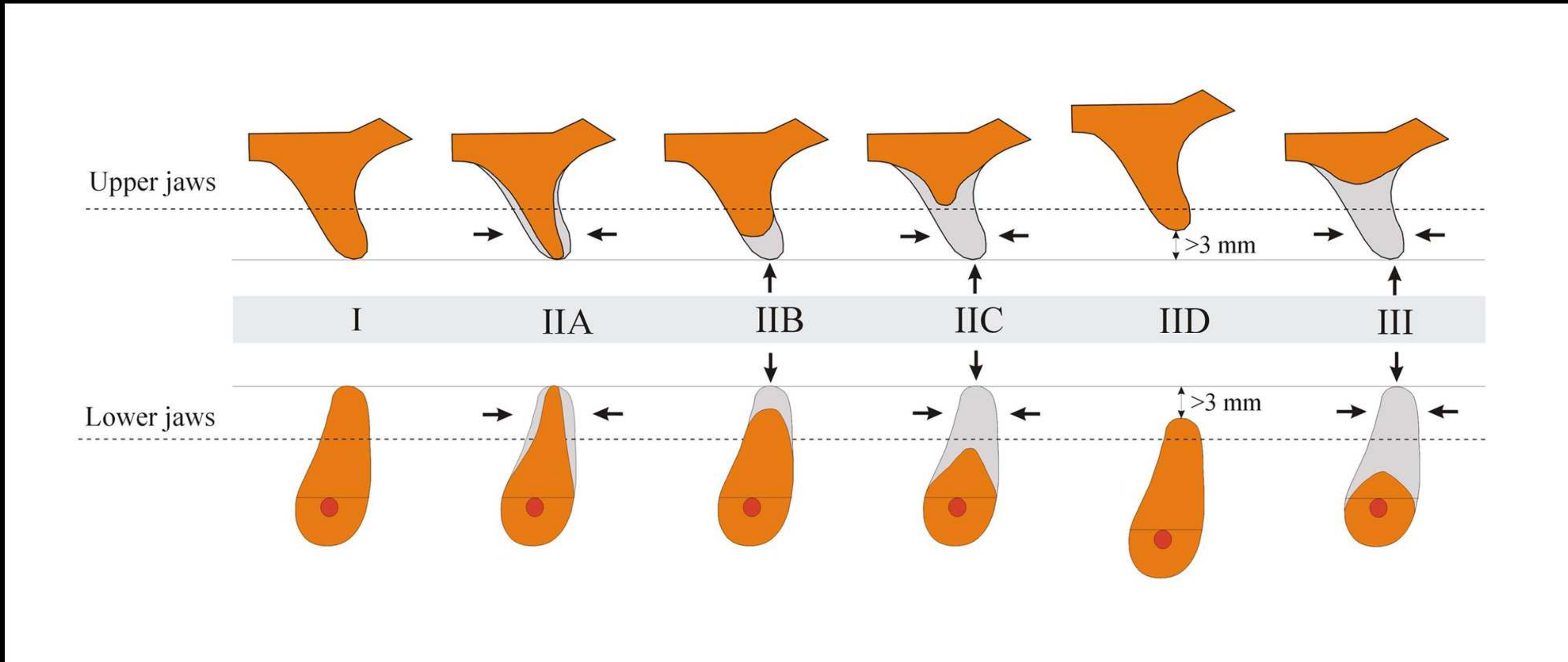
The bone sets the tone



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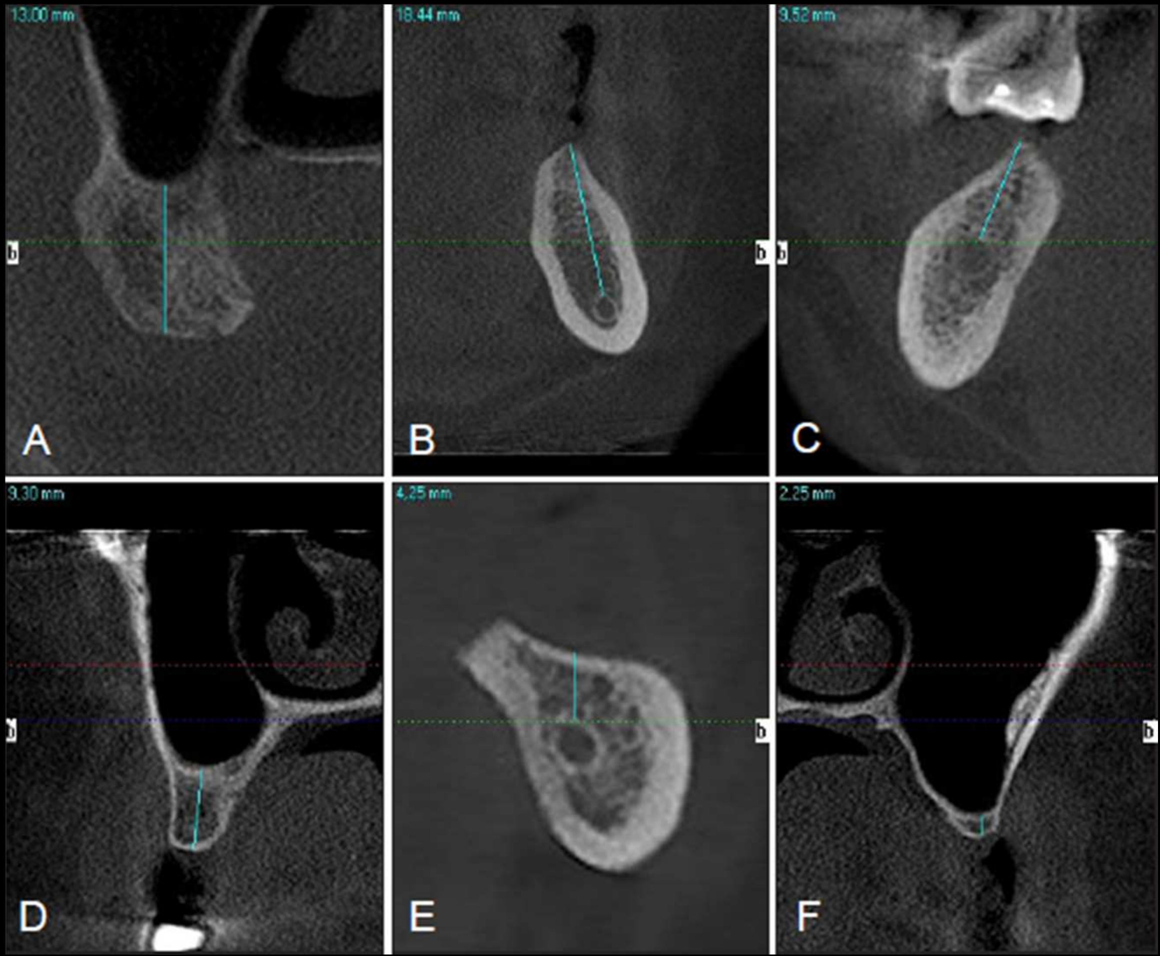
3D planning is essential



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) im 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.

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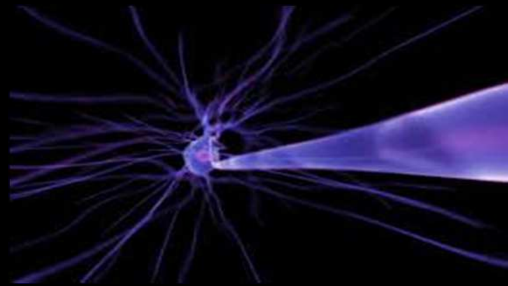
The bone sets the tone

- 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



1. **Juodzbalys G, Wang HL, Sabalys G. Anatomy of Mandibular Vital Structures. Part I: Mandibular Canal and Inferior Alveolar Neurovascular Bundle in relation with Dental Implantology.**

   J Oral Maxillofac Res 2010;1(1):e2

   URL: http://www.ejomr.org/JOMR/archives/2010/1/e2/e2ht.htm

   doi:10.5037/jomr.2010.1102

2. **Juodzbalys G, Wang HL, Sabalys G. Anatomy of Mandibular Vital Structures. Part II: Mandibular Incisive Canal, Mental Foramen and Associated Neurovascular Bundles in Relation with Dental Implantology.**

   J Oral Maxillofac Res 2010;1(1):e3

   URL: http://www.ejomr.org/JOMR/archives/2010/1/e3/e3ht.htm

   doi:10.5037/jomr.2010.1103

3. **Juodzbalys G, Wang HL. Guidelines for the Identification of the Mandibular Vital Structures: Practical Clinical Applications of Anatomy and Radiological Examination Methods.**

   J Oral Maxillofac Res 2010;1(2):e1

   URL: http://www.ejomr.org/JOMR/archives/2010/2/e1/e1ht.htm

   doi:10.5037/jomr.2010.1201

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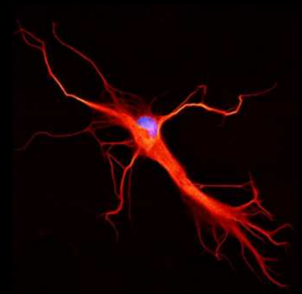
Published articles



4. **Juodzbalys G, Wang HL, Sabalys G, Sidlauskas A, Galindo-Moreno P. Inferior alveolar nerve injury associated with implant surgery.**

   Clinical Oral Implants Research 00, 2011, 1–8

   doi: 10.1111/j.1600-0501.2011.02314.x

5. Juodzbalys G, Wang HL, Sabalys G. Injury of the Inferior Alveolar Nerve during Implant Placement: a Literature Review.

   J Oral Maxillofac Res 2011;2(1):e1

   URL: http://www.ejomr.org/JOMR/archives/2011/1/e1/v2n1e1ht.htm

   doi:10.5037/jomr.2011.2101

6. **Juodzbalys G, Daugela P. Mandibular Third Molar Impaction: Review of Literature and a Proposal of a Classification. J Oral Maxillofac Res 2013;4(2): e1**

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

   doi: 10.5037/jomr.2013.4201

7. **Juodzbalys G, Kubilius M. Clinical and Radiological Classification of the Jawbone Anatomy in Endosseous Dental Implant Treatment. J Oral Maxillofac Res 2013;4(2):e2**

   URL: http://www.ejomr.org/JOMR/archives/2013/2/e2/v4n2e2ht.htm

   doi: 10.5037/jomr.2013.4202

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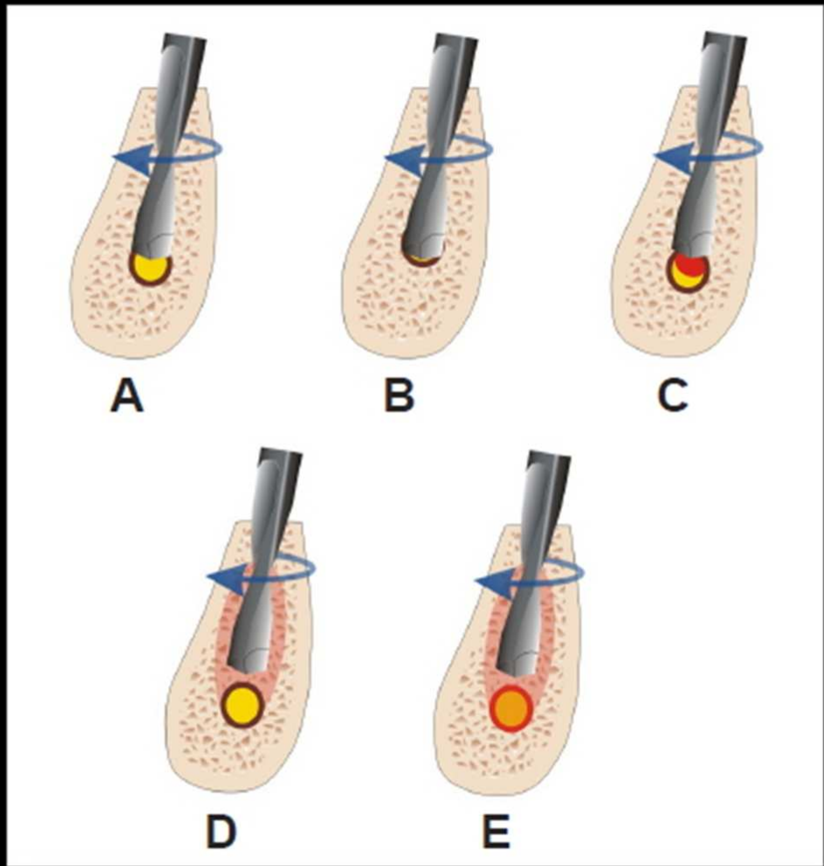
The bone sets the tone

- The most severe types of injuries are caused by implant drills and implants themselves



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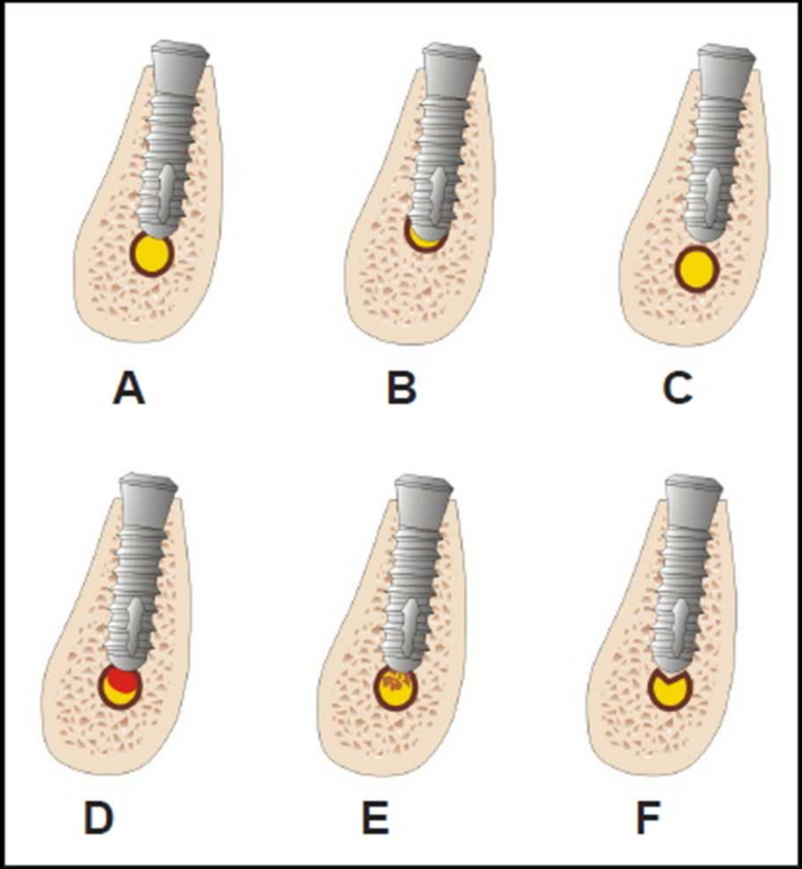

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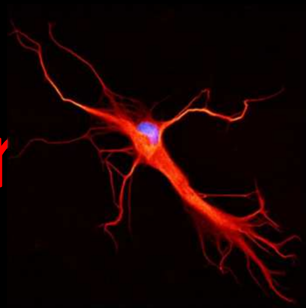
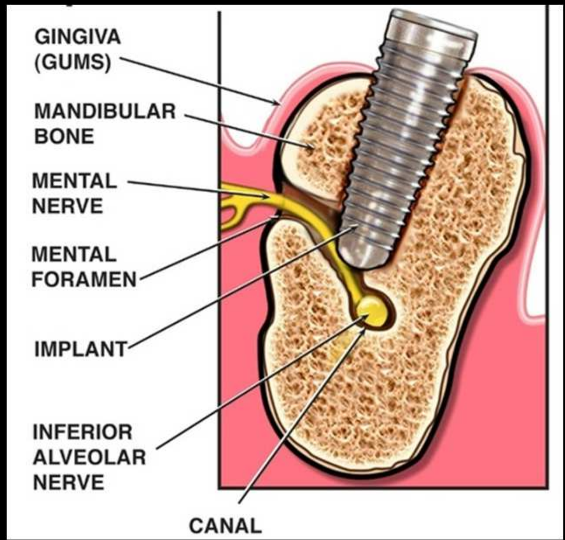
Injury of the Inferior Alveolar Ner



- 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).



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Insufficient aesthetic result

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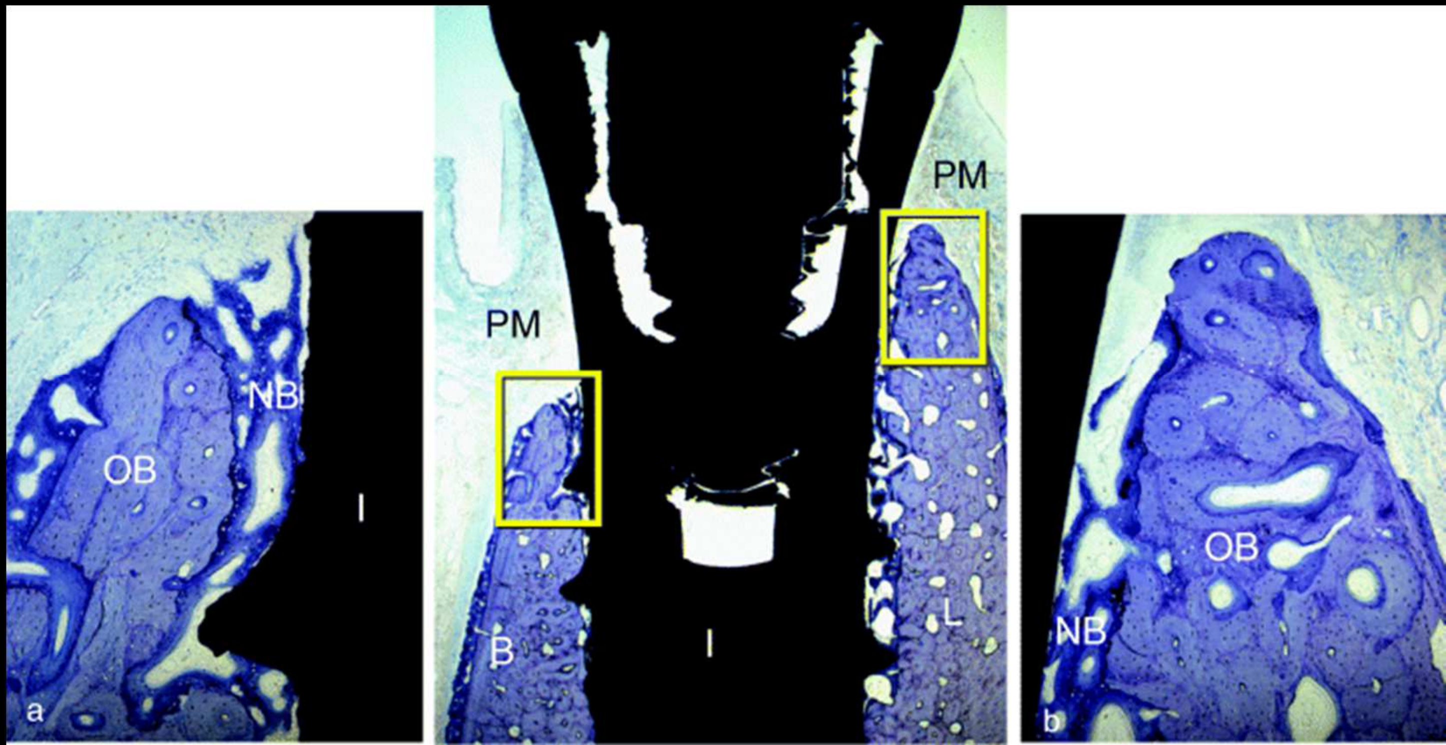
Extraction socket walls remodeling, especially of labial cortical plate

- **Mauricio G. Araújo & Jan Lindhe, 2005**



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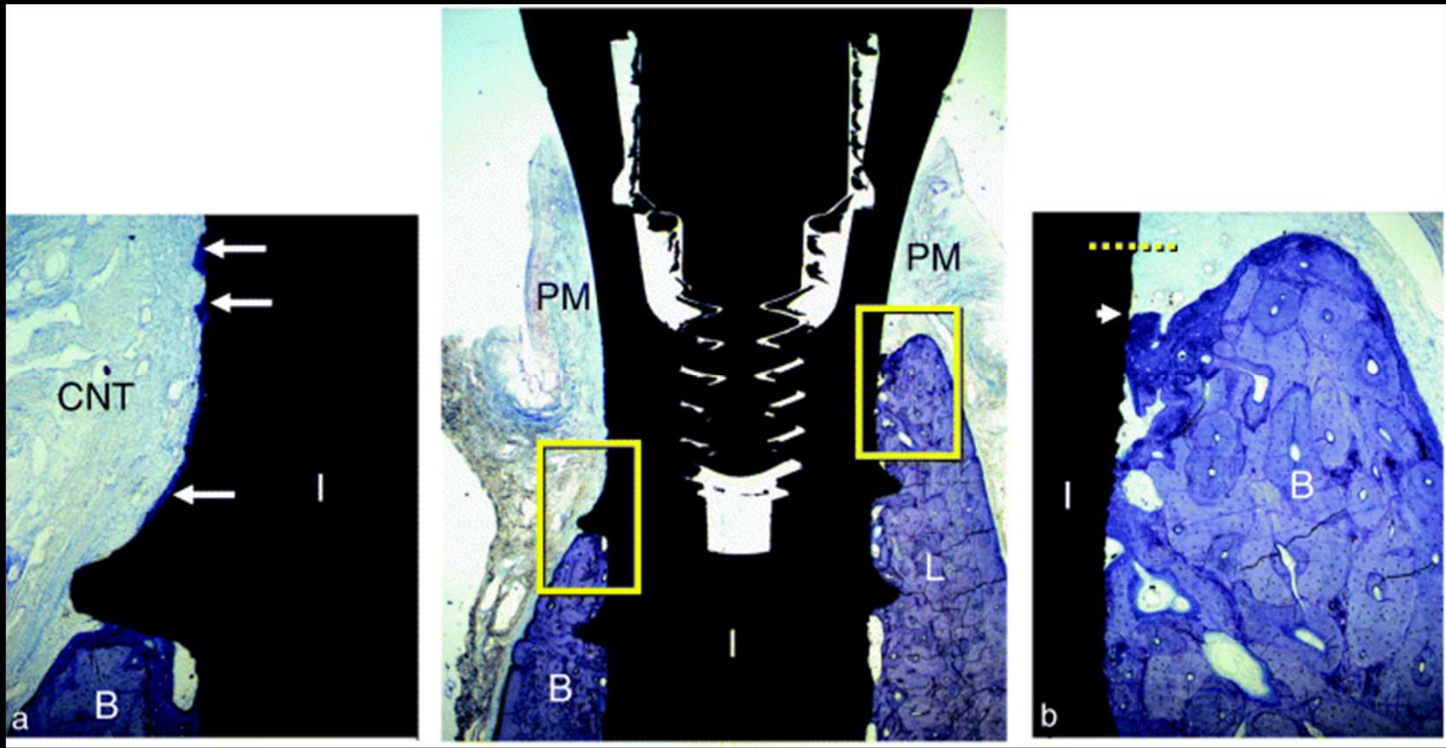

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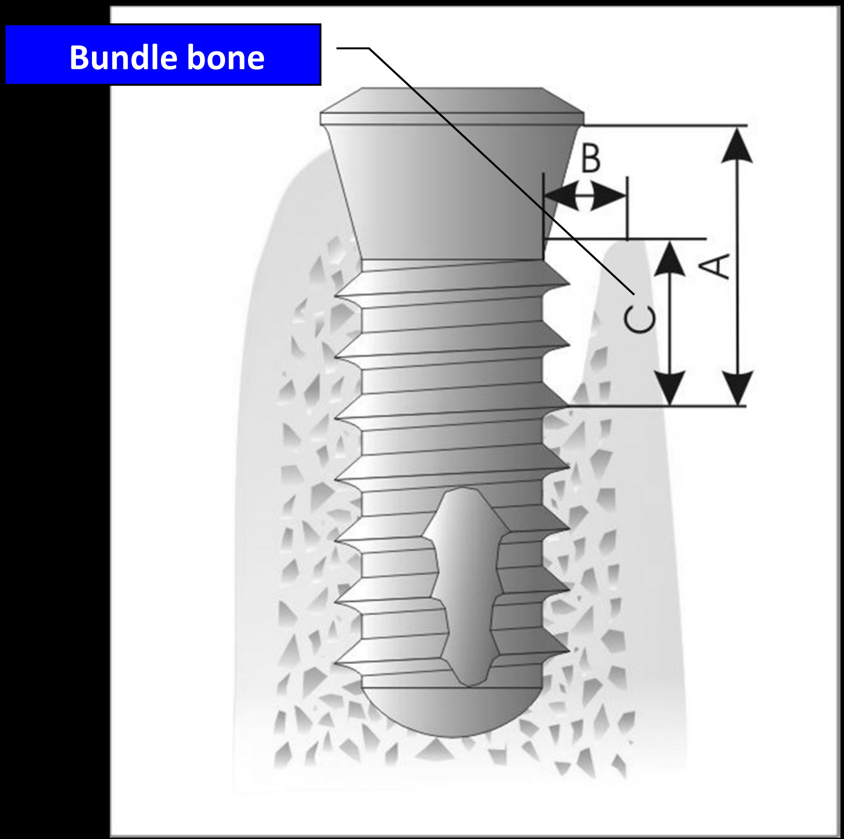
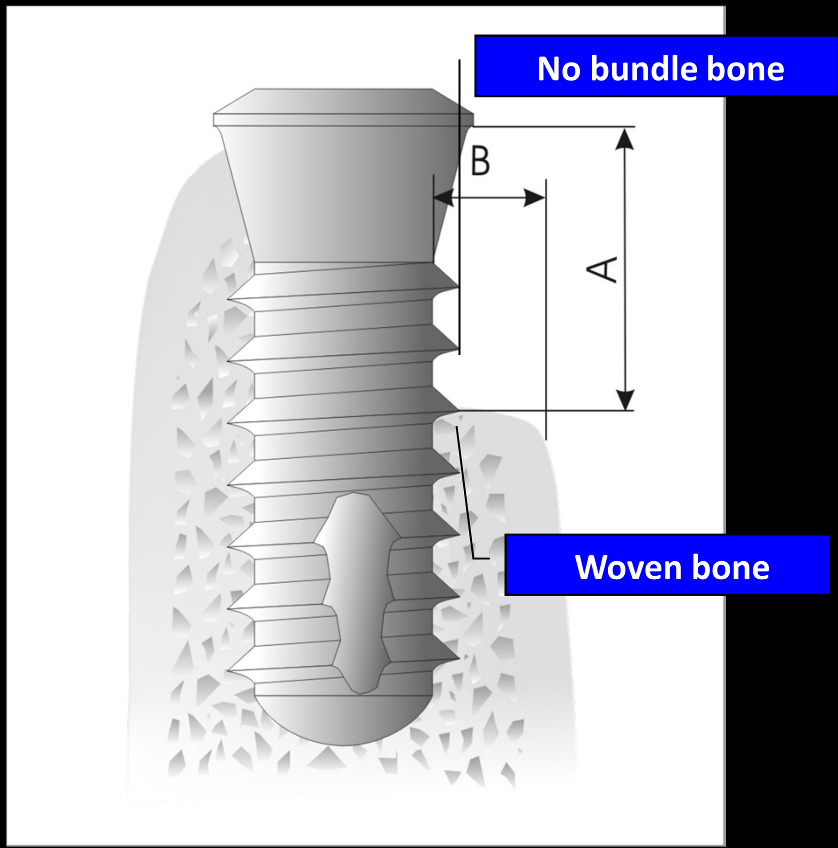
We can’t to stop extraction socket walls remodeling!





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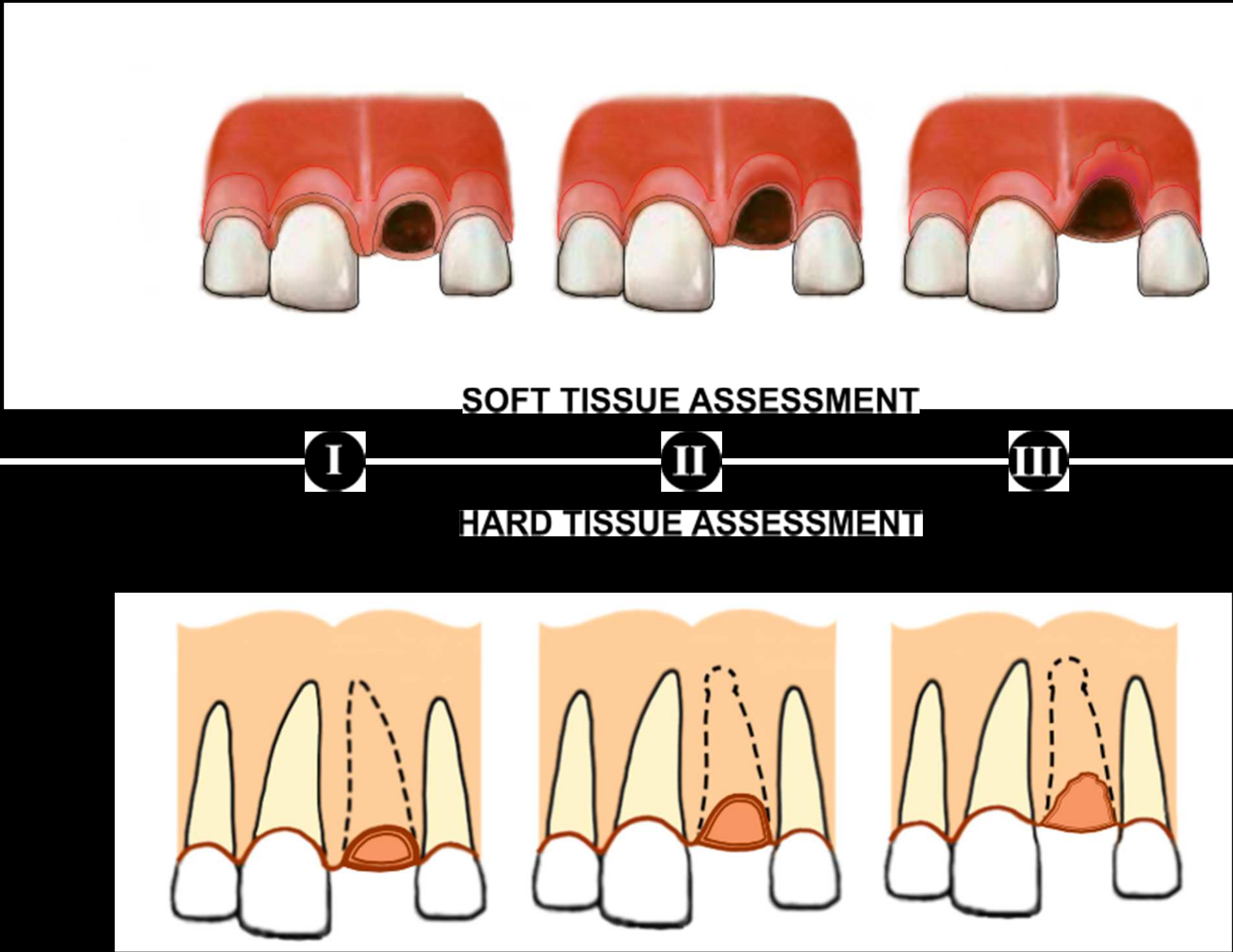
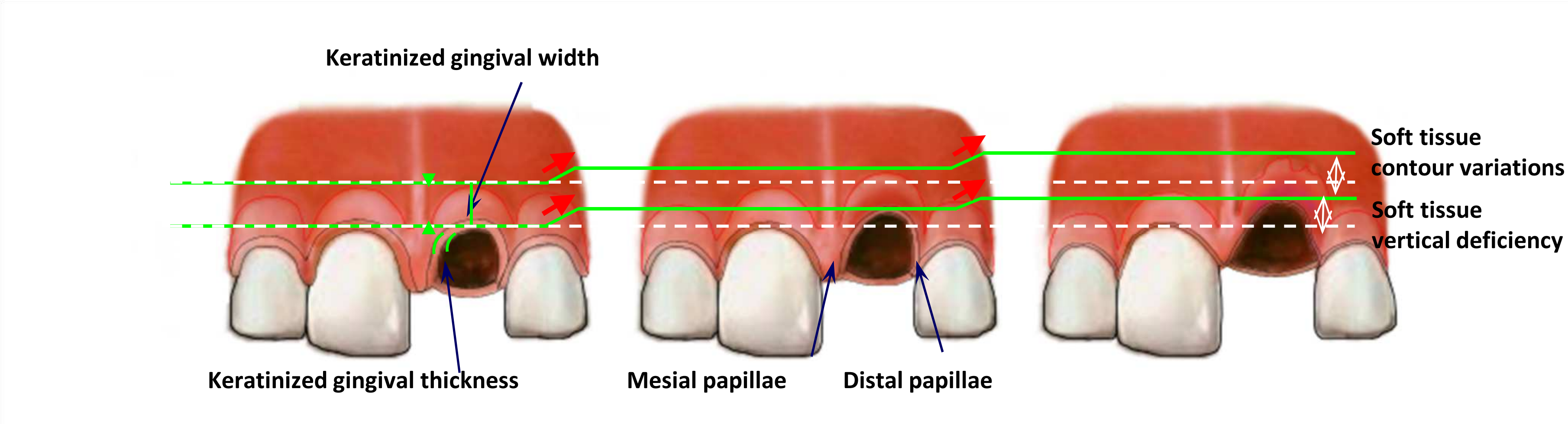


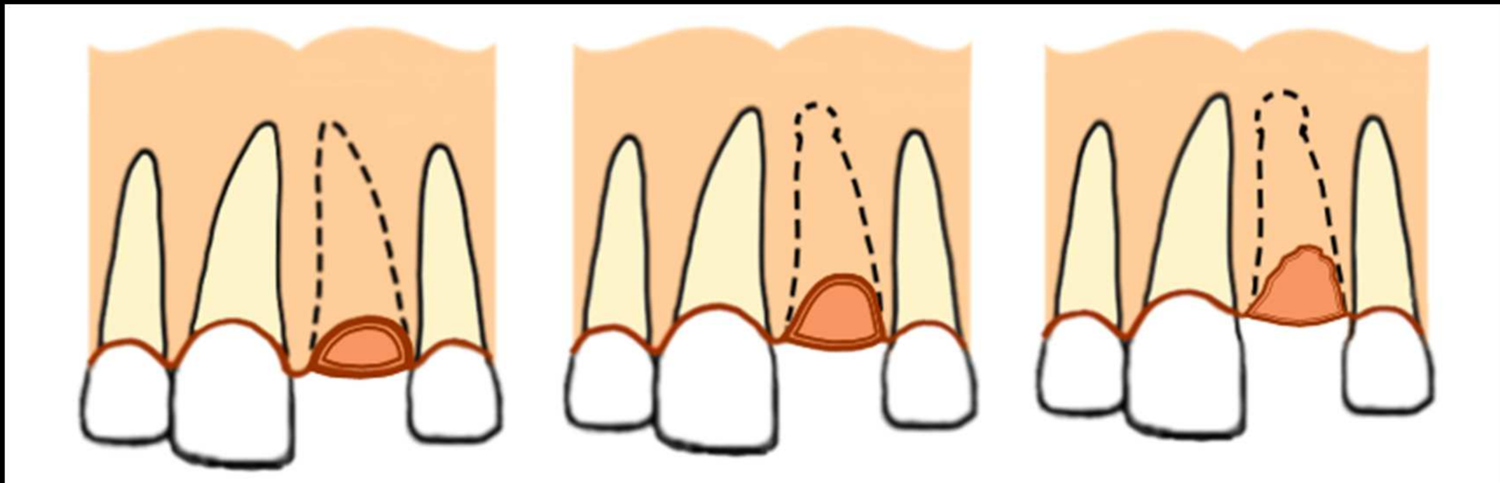
Gintaras Juodzbalys, Dalius Sakavicius, Hom-Lay Wang. Classification of Extraction Socket based upon soft and hard tissue components // Journal of Periodontology. 2008 March;79(3):413-424.



SOFT TISSUE ASSESSMENT

I | II | III

HARD TISSUE ASSESSMENT



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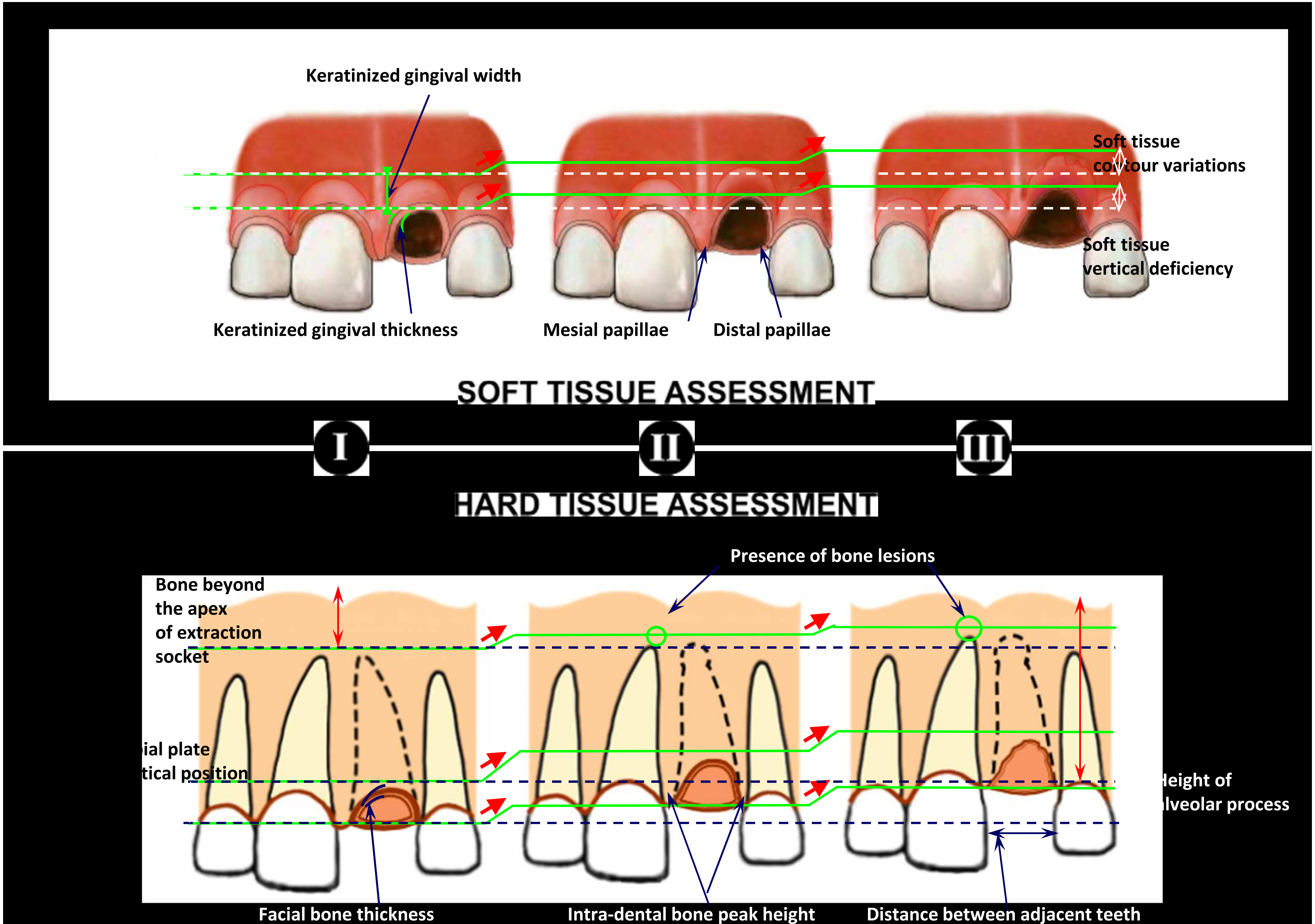

Gintaras Juodzbalys, Dalius Sakavicius, Hom-Lay Wang. Classification of Extraction Socket based upon soft and hard tissue components // Journal of Periodontology. 2008 March;79(3):413-424.

Extraction socket morphology – parameters evaluation

Type I - Adequate

Type II - Compromised

Type III - Deficient

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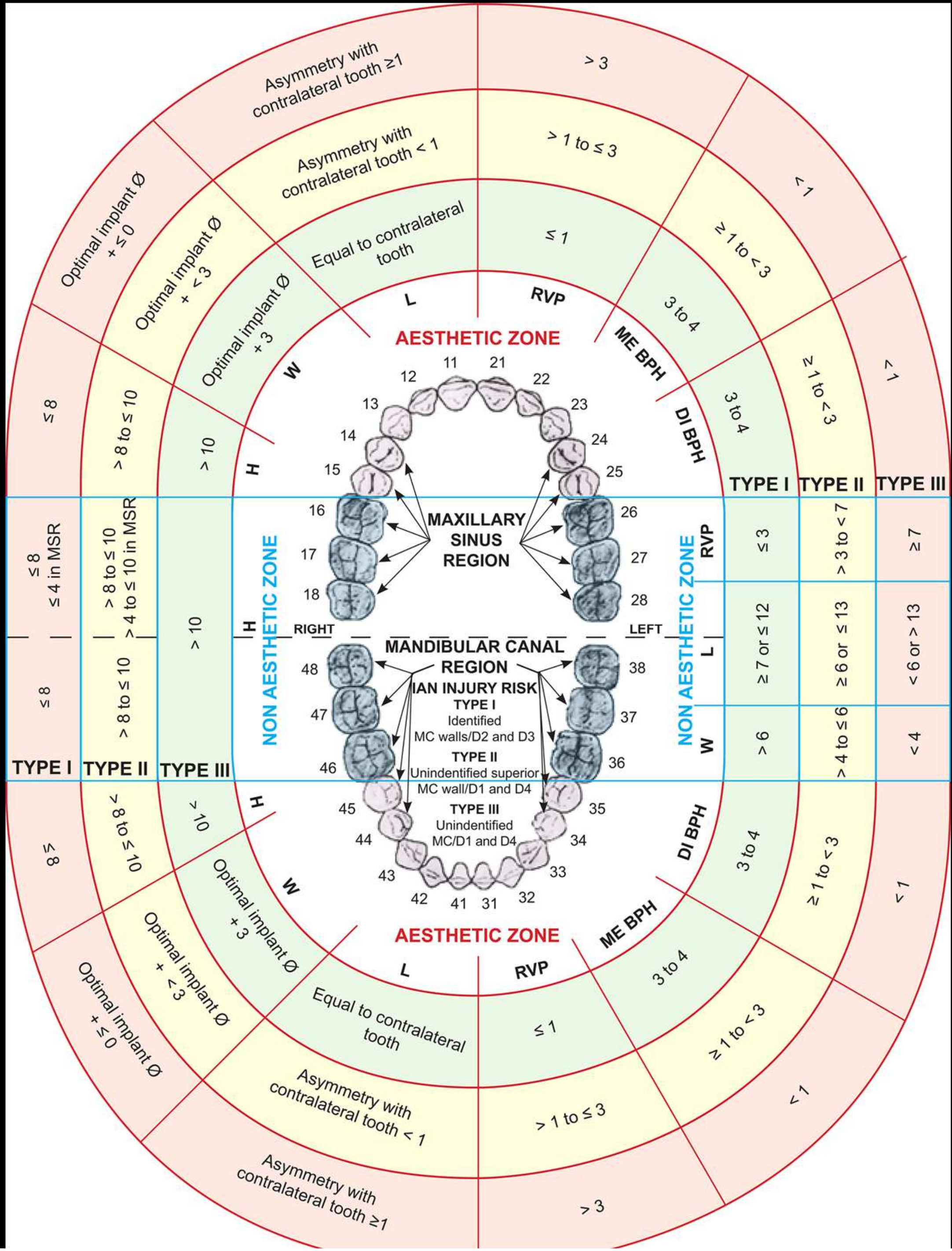

AESTHETIC ZONE
NON AESTHETIC ZONE
MAXILLARY SINUS REGION
MANDIBULAR CANAL REGION
IAN INJURY RISK
TYPE I
Identified MC walls/D2 and D3
TYPE II
Unindentified superior MC wall/D1 and D4
TYPE III
Unindentified MC/D1 and D4
RIGHT
LEFT
TYPE I
TYPE II
TYPE III
RVP
L
W
H
ME BPH
DI BPH
Equal to contralateral tooth
Asymmetry with contralateral tooth < 1
Asymmetry with contralateral tooth ≥1
Optimal implant Ø + 3
Optimal implant Ø + < 3
Optimal implant Ø + ≤ 0
≤ 1
> 1 to ≤ 3
> 3
3 to 4
≥ 1 to < 3
< 1
≤ 3
> 3 to < 7
≥ 7
≥ 7 or ≤ 12
≥ 6 or ≤ 13
< 6 or > 13
> 6
> 4 to ≤ 6
< 4
> 10
> 8 to ≤ 10
> 4 to ≤ 10 in MSR
≤ 8
≤ 4 in MSR

Insufficient bone volume

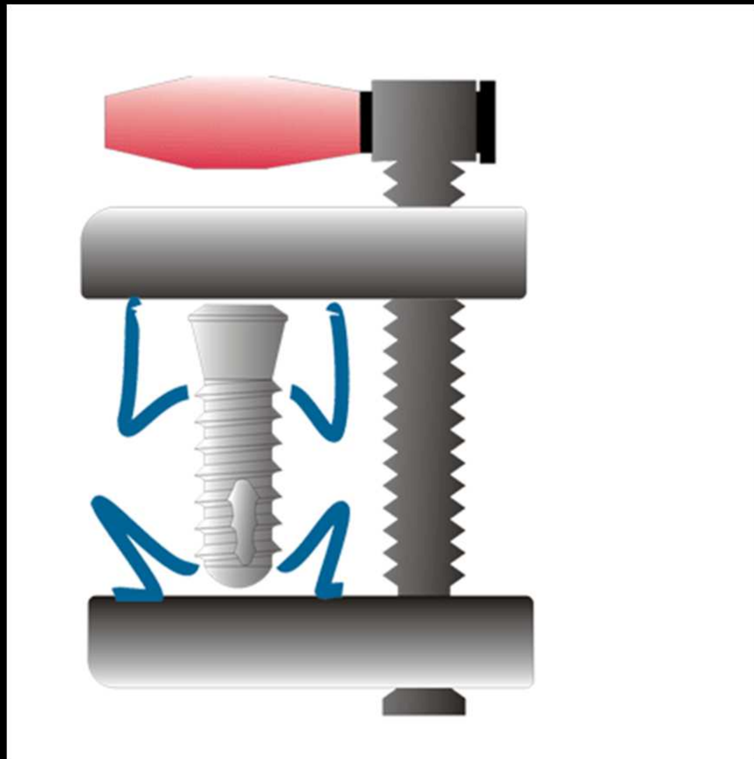
Insufficient bone volume

In order to achieve successful implantation, the perfect model would be if implants were surrounded by at least 1 mm of bone

Allen F, Smith DG. An assessment of the accuracy of ridge mapping in planning implant therapy for the anterior maxilla. Clin Oral Implants Res 2000;11:34-38.

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



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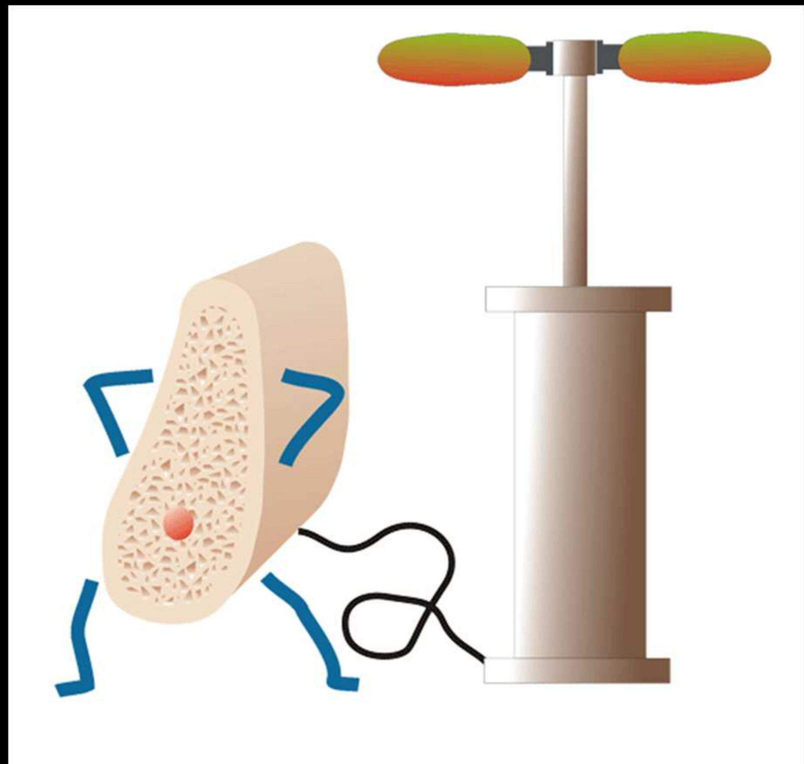
What decisions can be made in case of inadequacy between jaw bone volume and dental implant size?

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



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Autologous bone

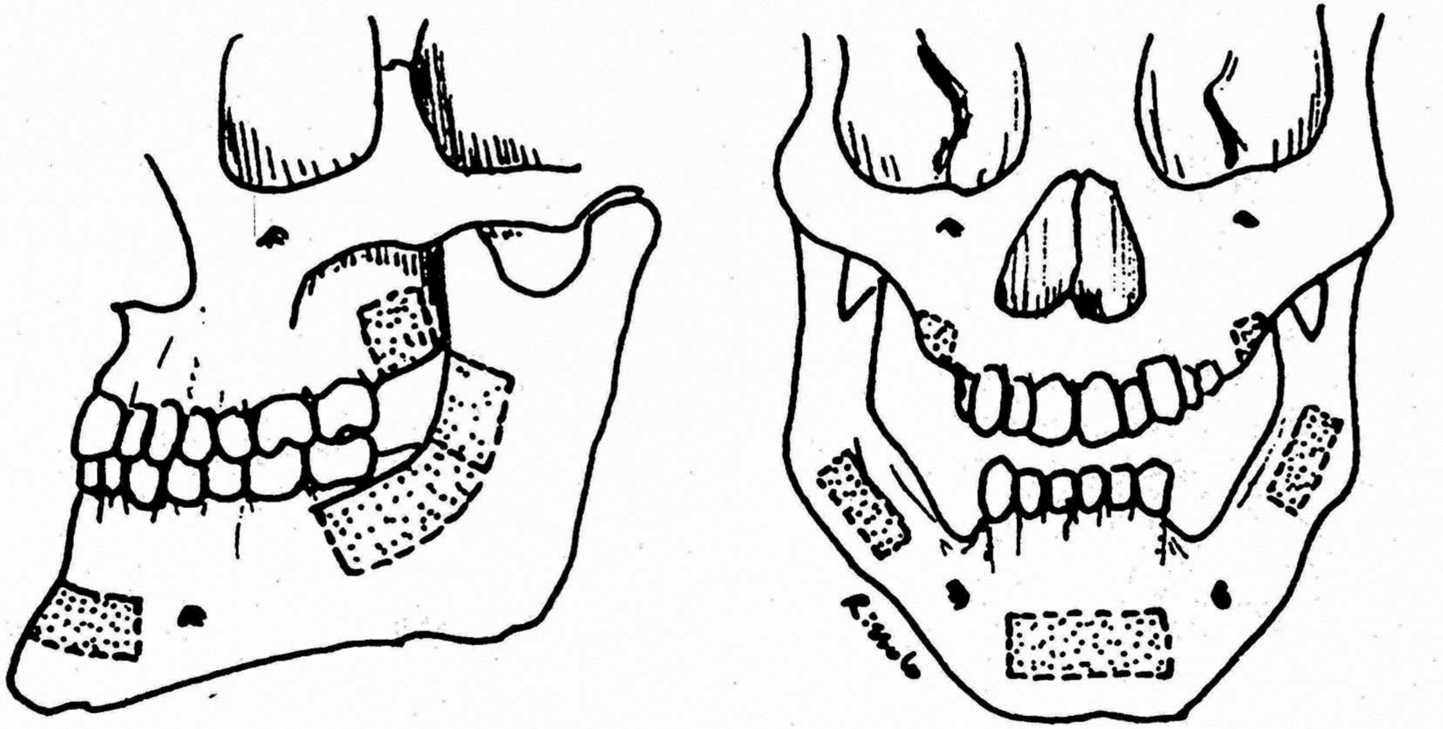
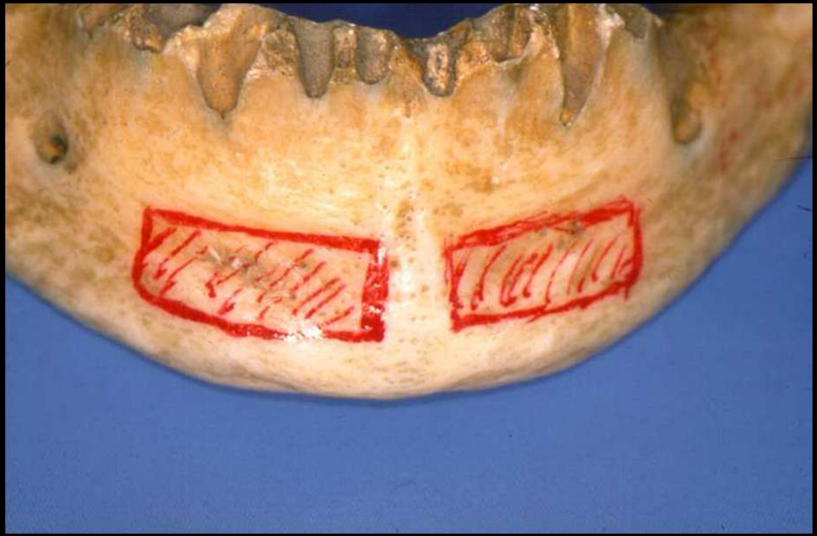
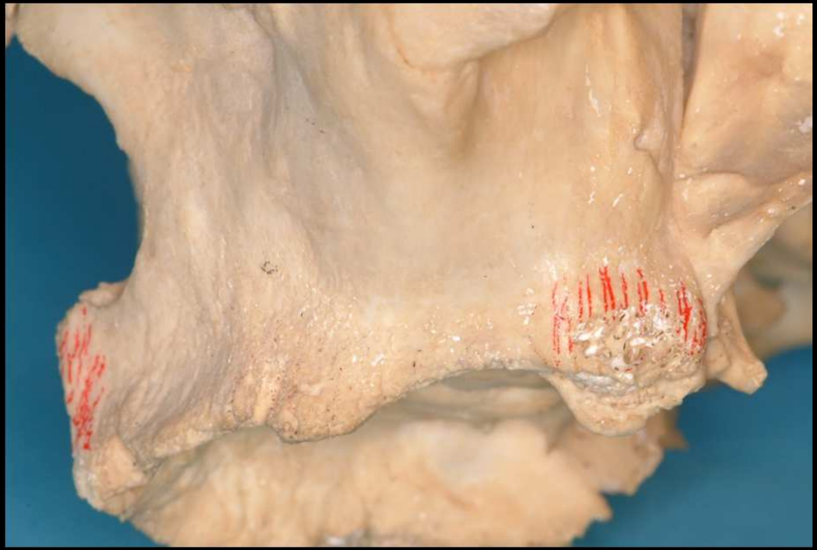
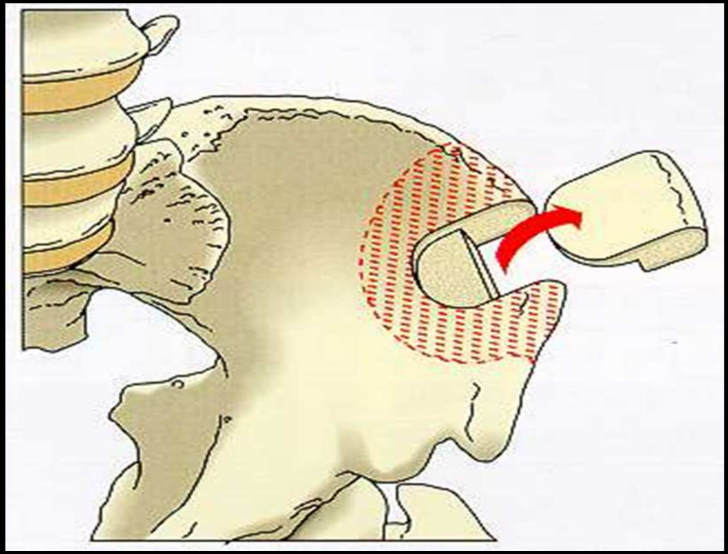


Figure 17. Intraoral autogenous graft harvest sites (the tuberosity, ramus, and symphysis).

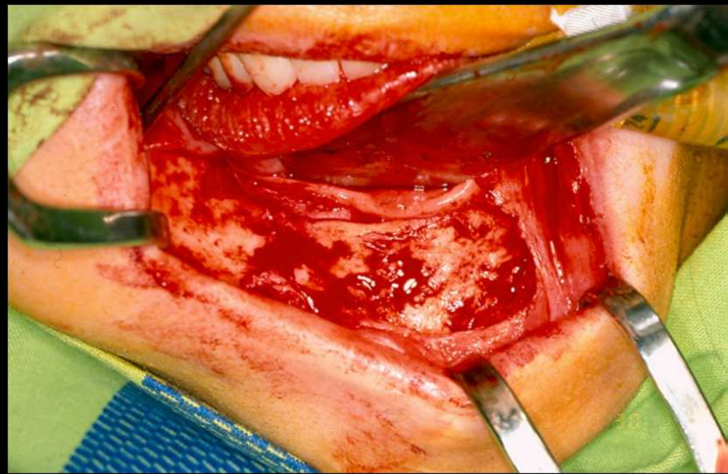
Autologous bone

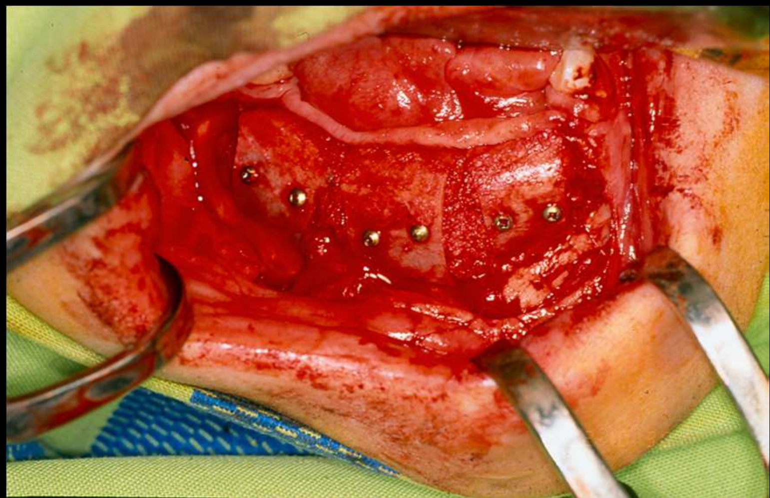




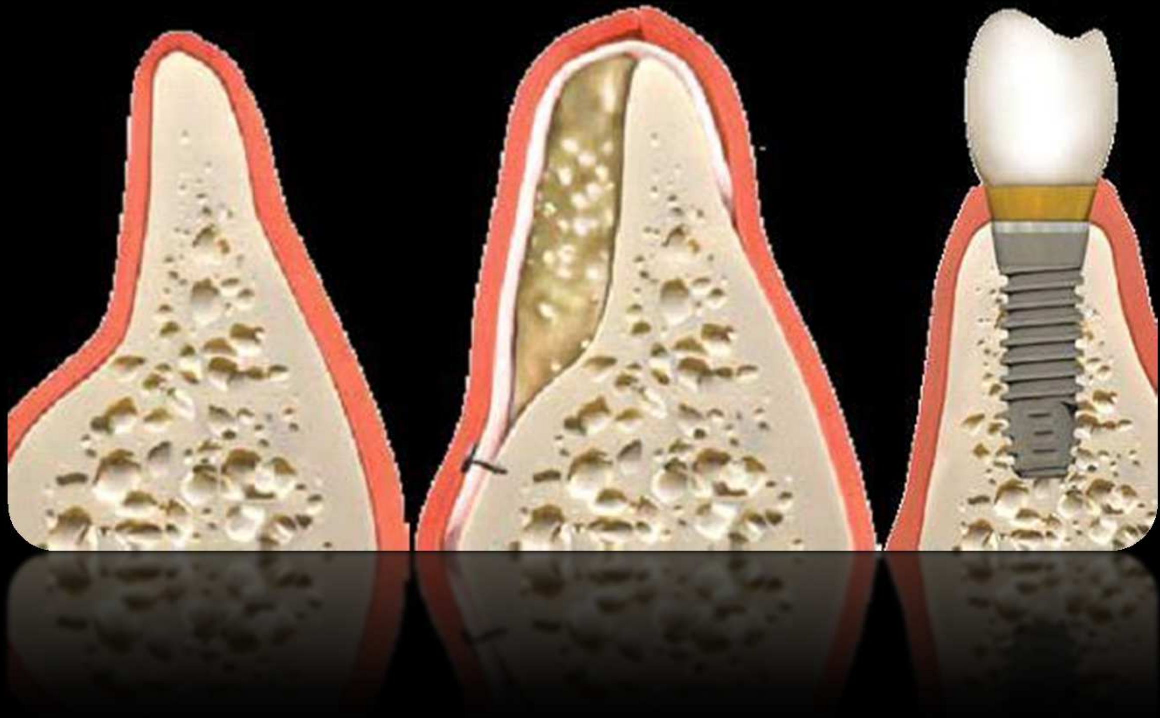


Autologous bone





Guided bone regeneration

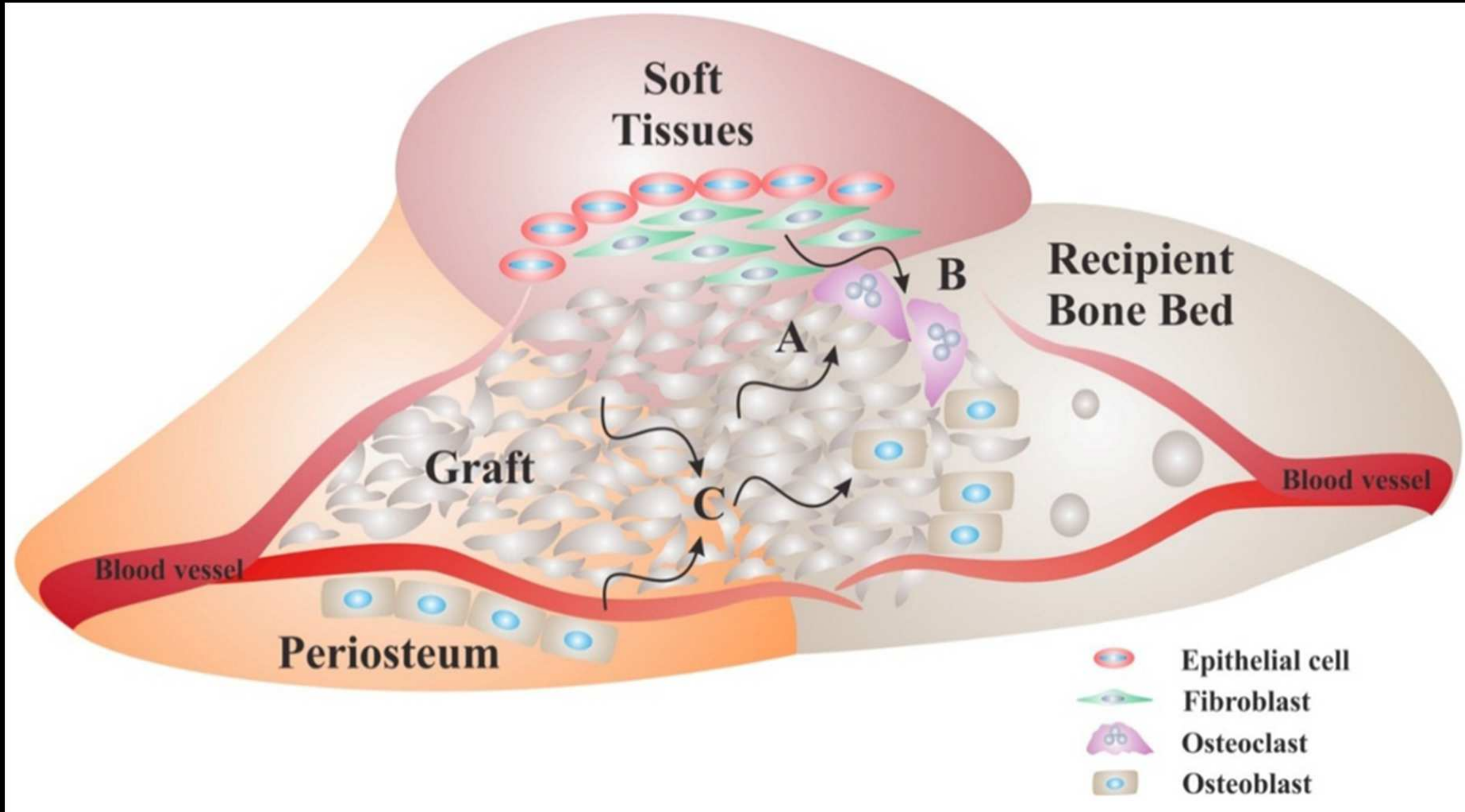


Nyman S, Gottlow J, Karring T,Lindhe J. The regenerative potential of the periodontal ligament. An experimental study in the monkey. J Clin Periodontol. 1982;9;257–265.
Gottlow J, Nyman, S, Lindhe J,et al. New attachment formation in the human periodontium by guided tissue regeneration. Case reports. J Clin Periodontol.1986;13:604–616.

Guided bone regeneration

GBR primarily relies on 4 principles

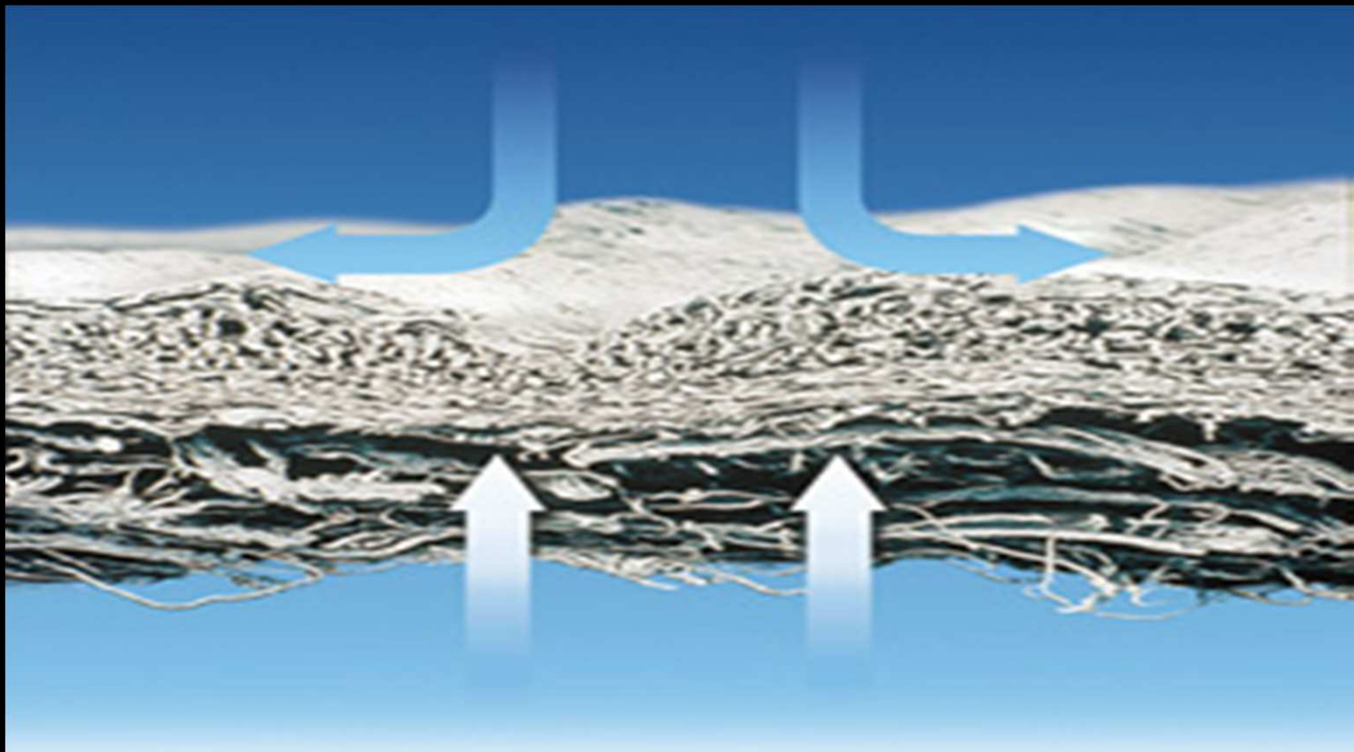
1. Excluding unwanted tissues and cells from migrating into the area
2. Space creation and maintenance
3. Protection of the underlying blood clot
4. Wound stabilization



Soft Tissues
Recipient Bone Bed
B
A
Graft
C
Blood vessel
Blood vessel
Periosteum
Epithelial cell
Fibroblast
Osteoclast
Osteoblast

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

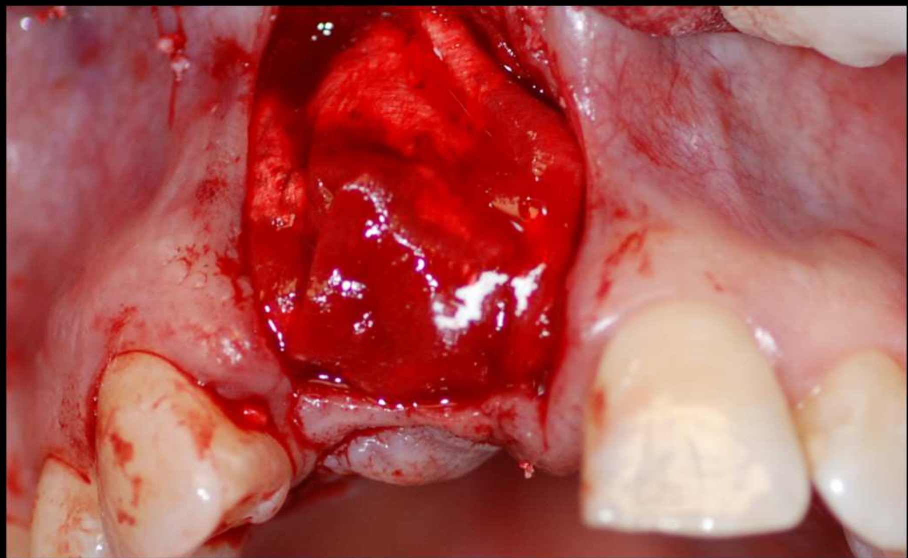
It can be ensured using appropriate supporting bone plastic material

Table 1. Bone replacement grafts

Human bone
Autogenous grafts (autografts)
Extraoral
Intraoral
Allogeneic grafts (allografts)
Fresh frozen bone
Freeze-dried bone allografts
Demineralized freeze-dried bone allografts
Bone substitutes
Xenogeneic grafts (xenografts)
Bovine-derived hydroxyapatite
Coralline calcium carbonate
Alloplastic grafts (alloplasts)
Polymers
Bioceramics
Tricalcium phosphate
Hydroxyapatite
dense, nonporous, nonresorbable
porous, nonresorbable (xenograft)
resorbable hydroxyapatite derived at low temperature
Bioactive glasses

4. Wound stabilization

We should use proper suturing technique



Clinical case

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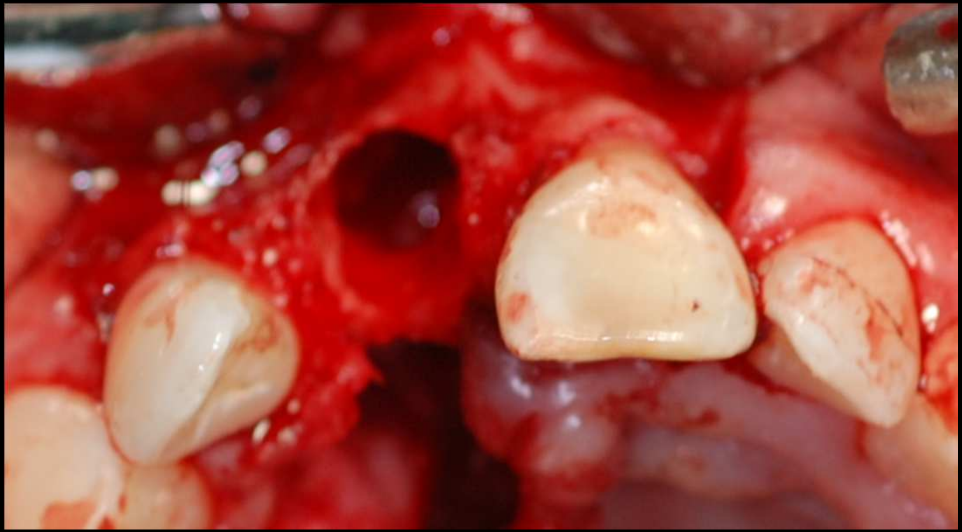
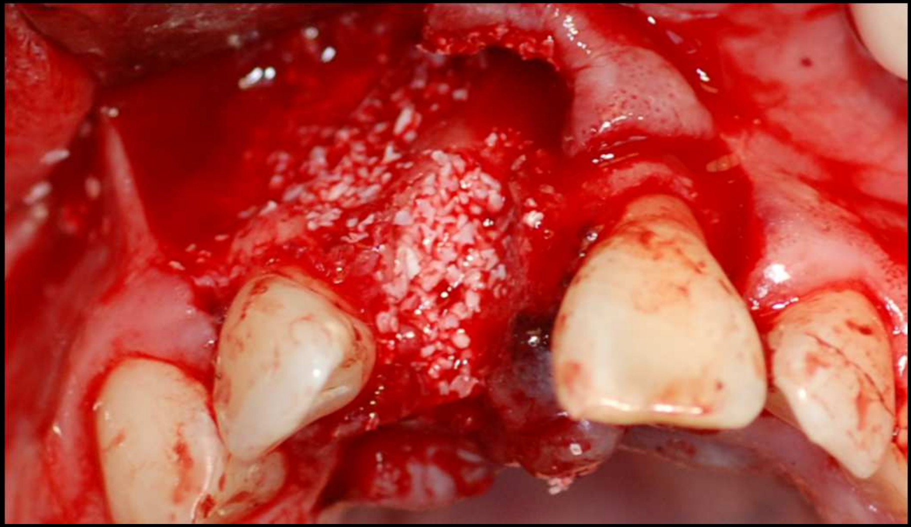
Clinical case





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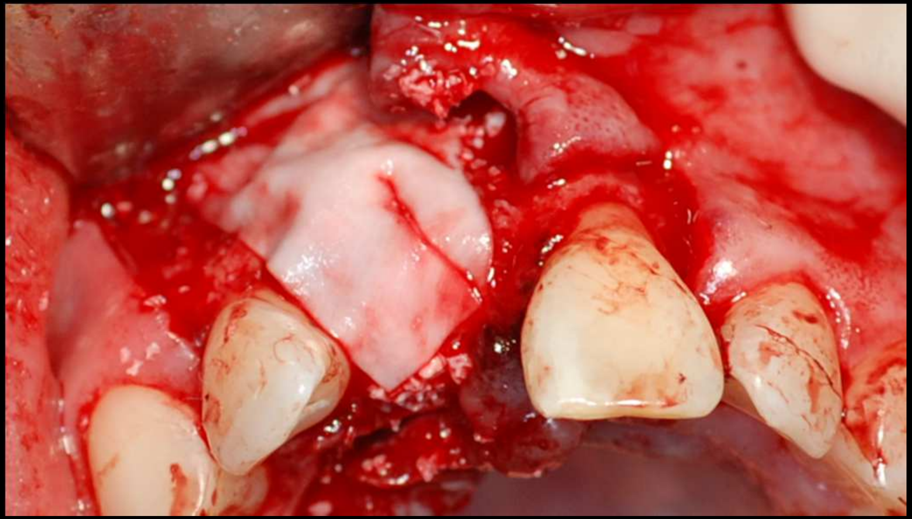
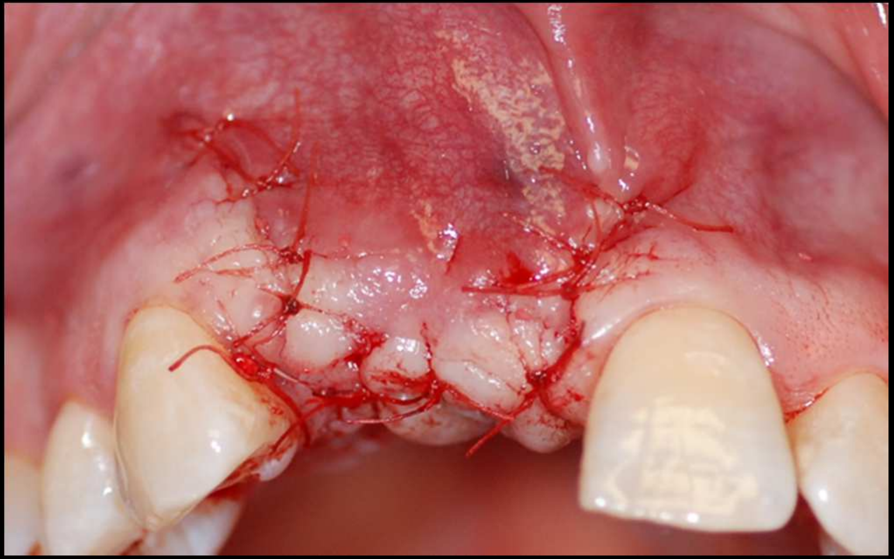
Clinical case





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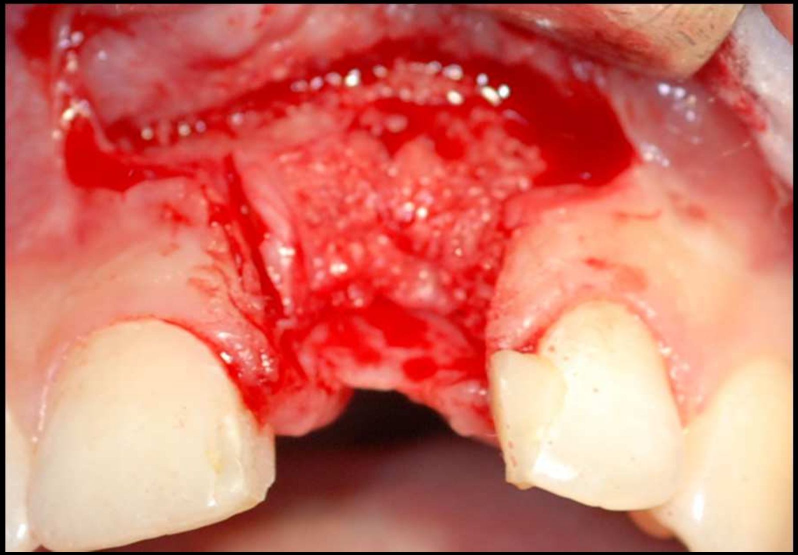
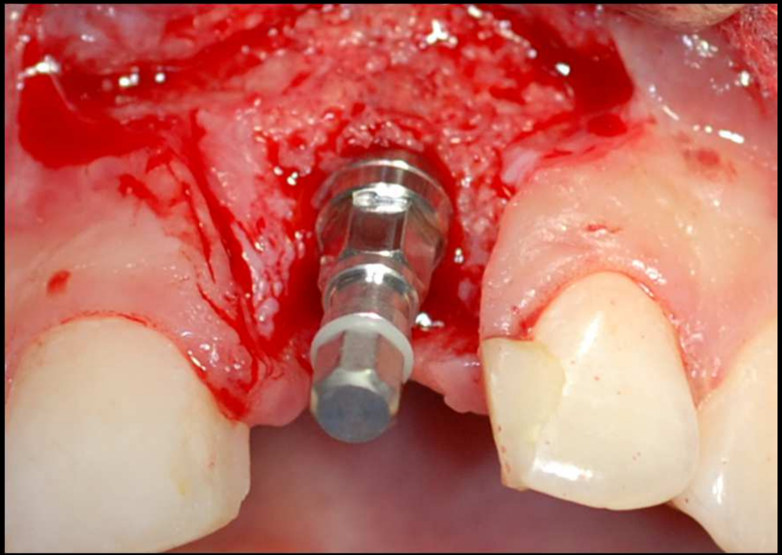
Clinical case





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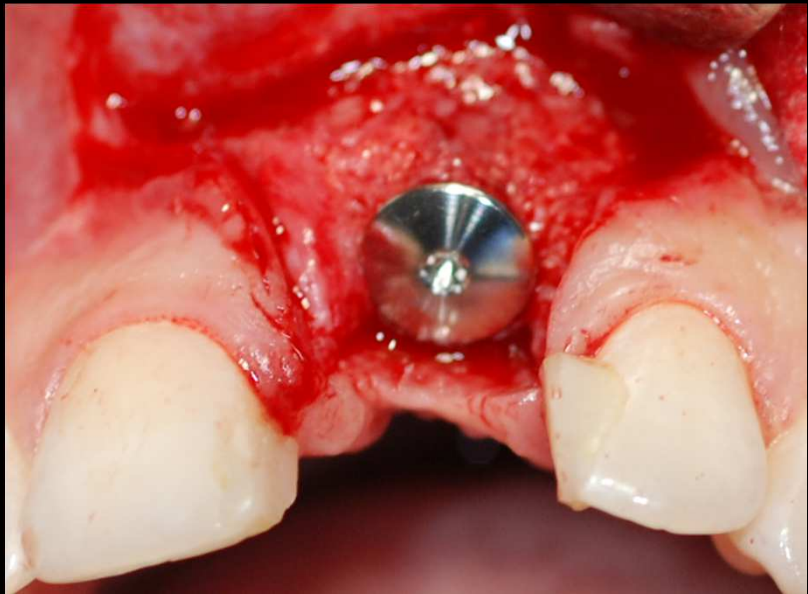
Clinical case



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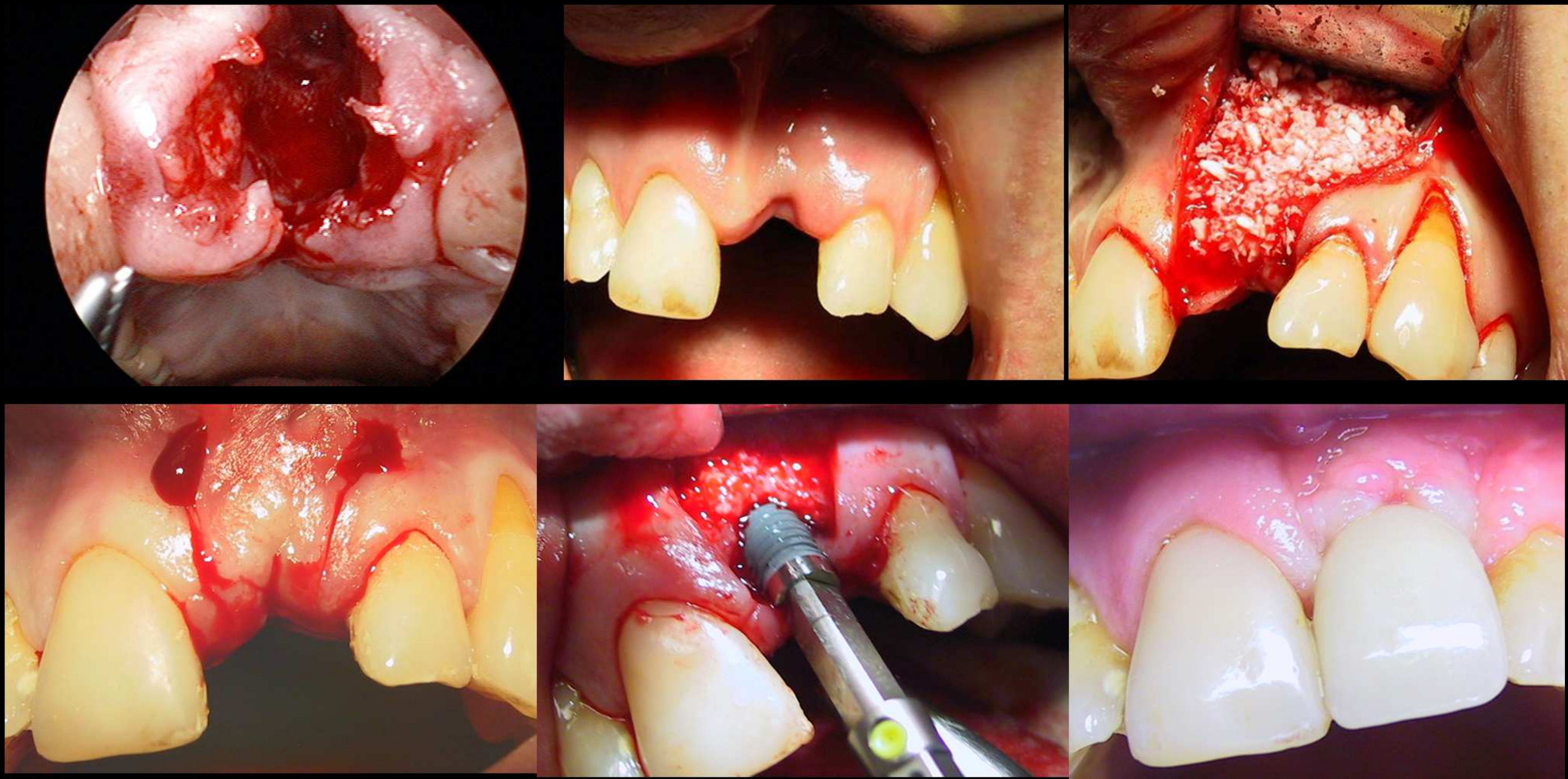
Clinical case



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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 ...)

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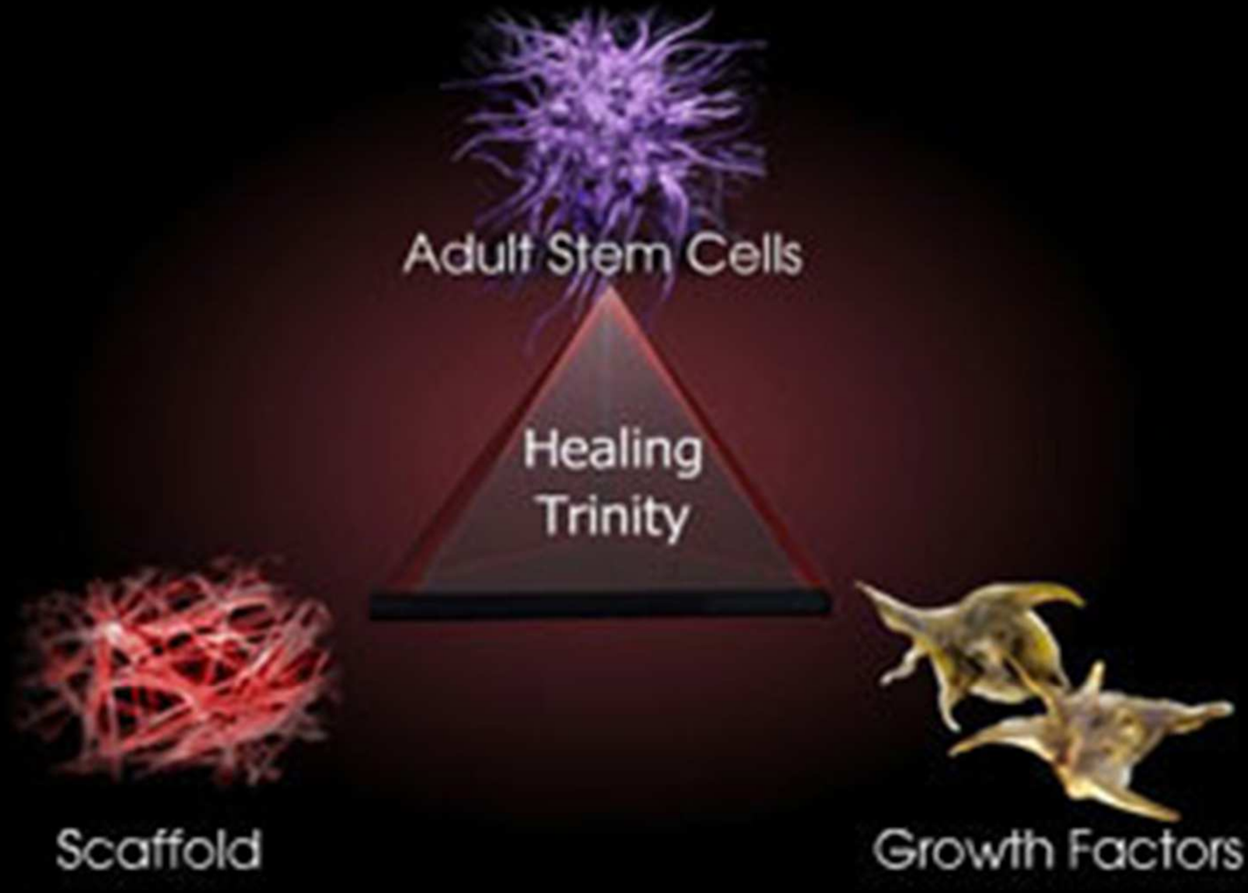
Ideal grafting material



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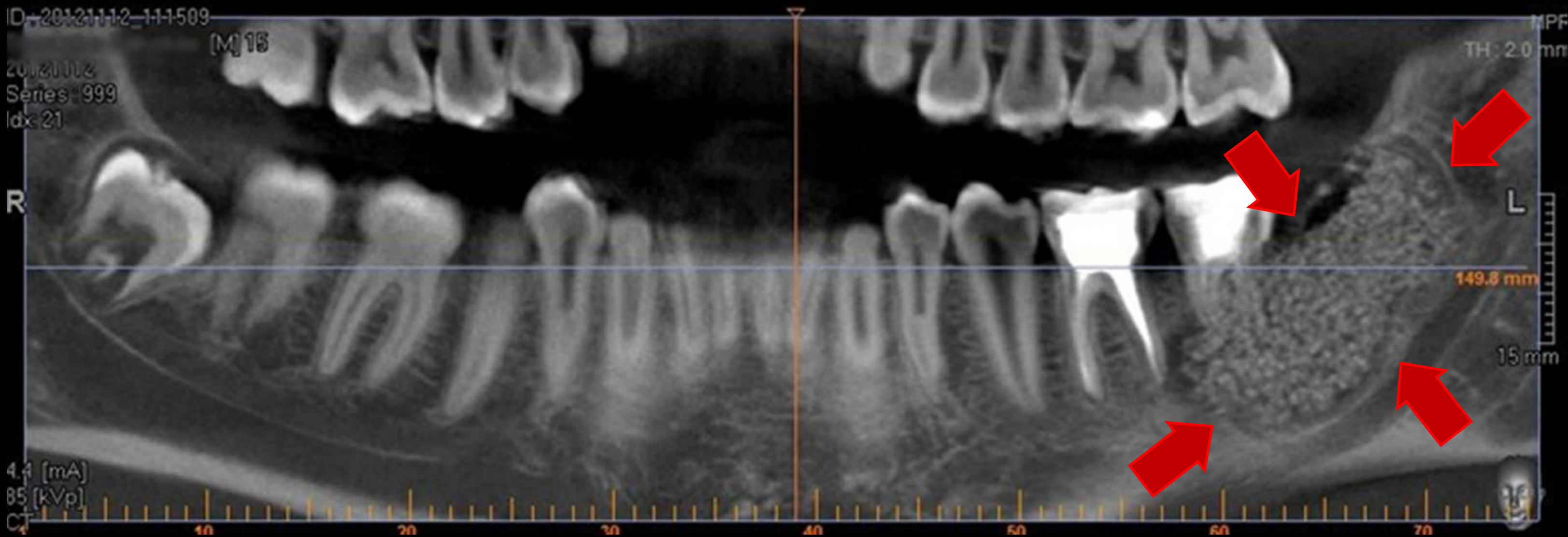
Conventional grafting

	Osteoconductive	Osteoinductive	Osteogenic
Alloplast	+	–	–
Xenograft	+	–	–
Allograft	+	+/–	–
Autograft	+	+	+



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?

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Alternatives?

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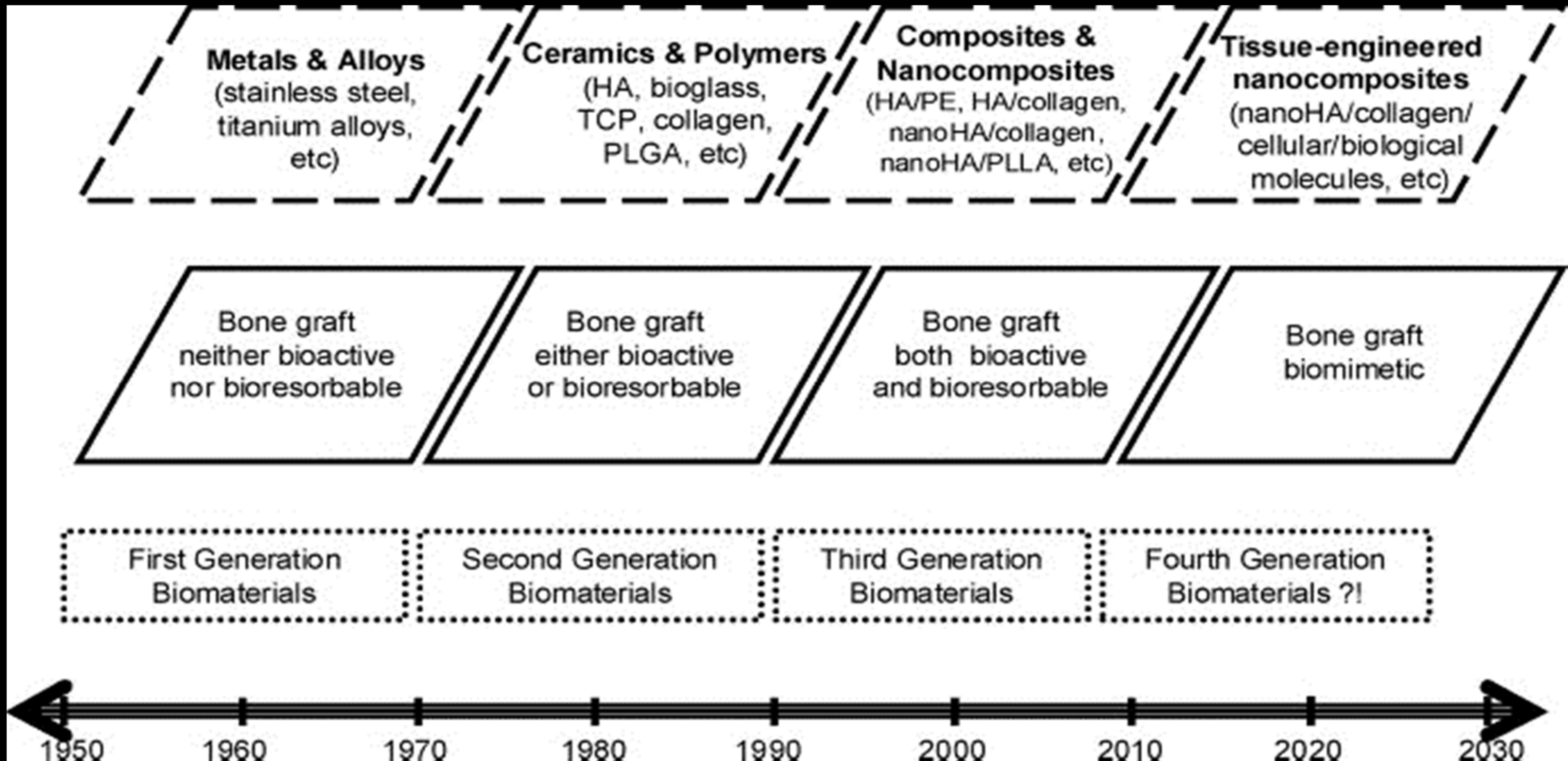

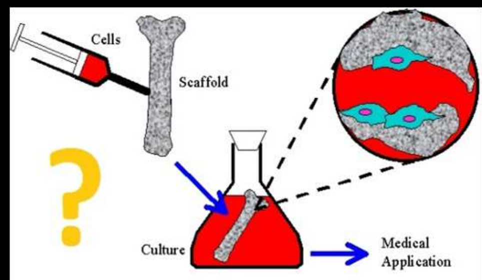

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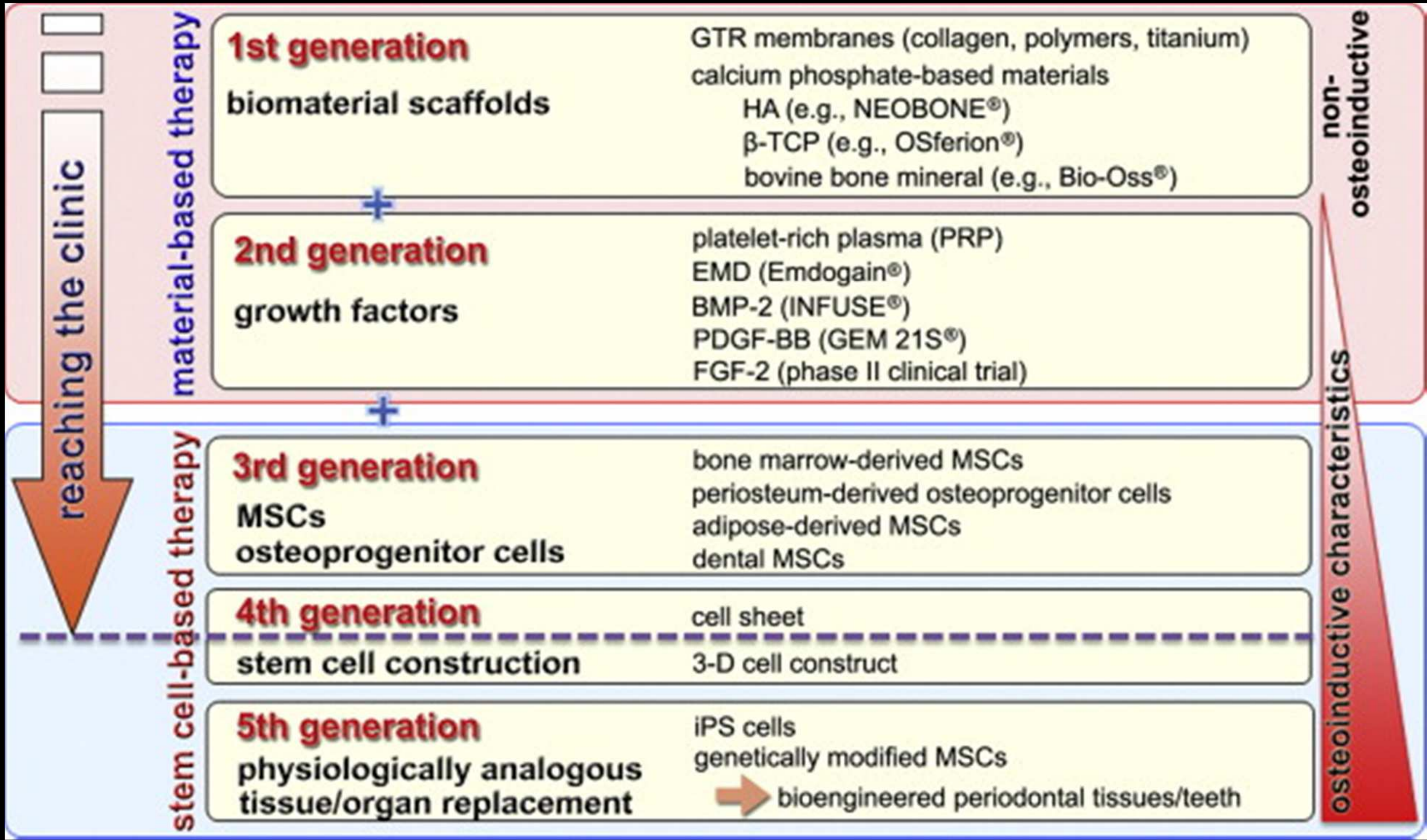

Progress in regenerative periodontal/bone therapies.

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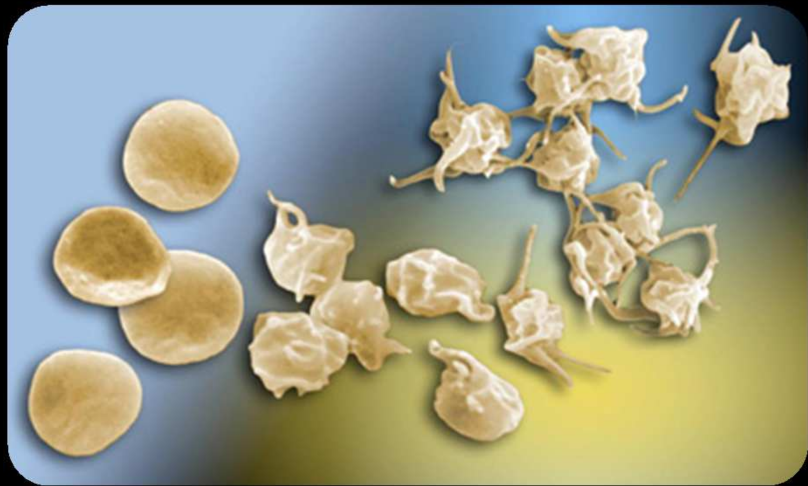
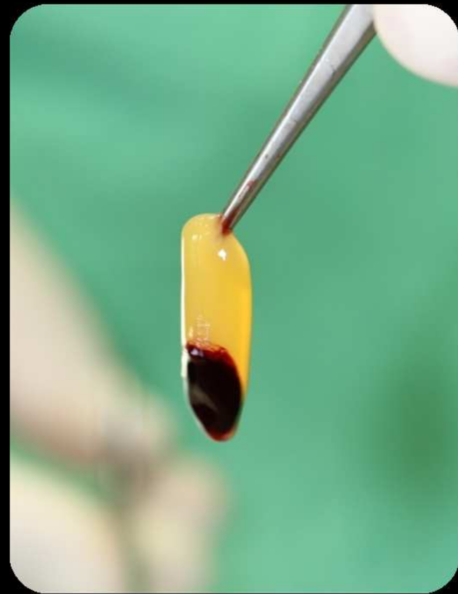
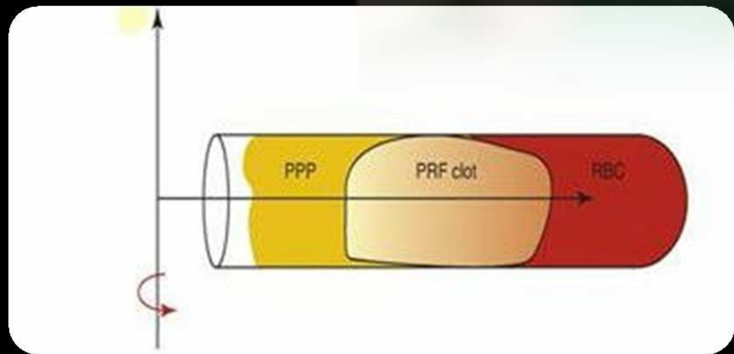
Hiroshi Egusa, Wataru Sonoyama, Masahiro Nishimura, Ikiru Atsuta, Kentaro Akiyama Stem cells in dentistry – Part II: Clinical applications Journal of Prosthodontic Research, Volume 56, Issue 4, 2012, 229–248

Leukocyte- Platelet Rich Fibrin (L-PRF)







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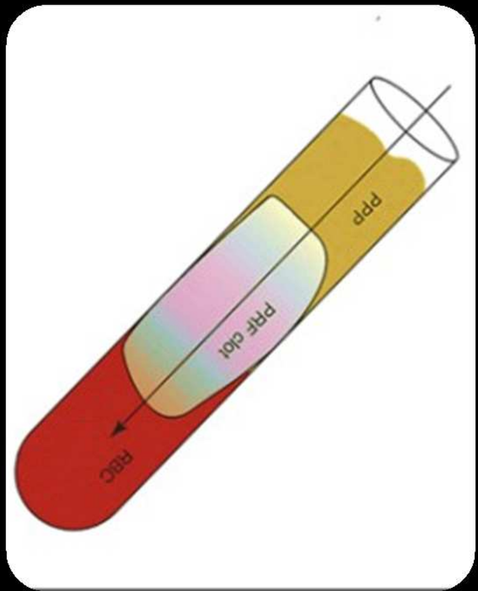
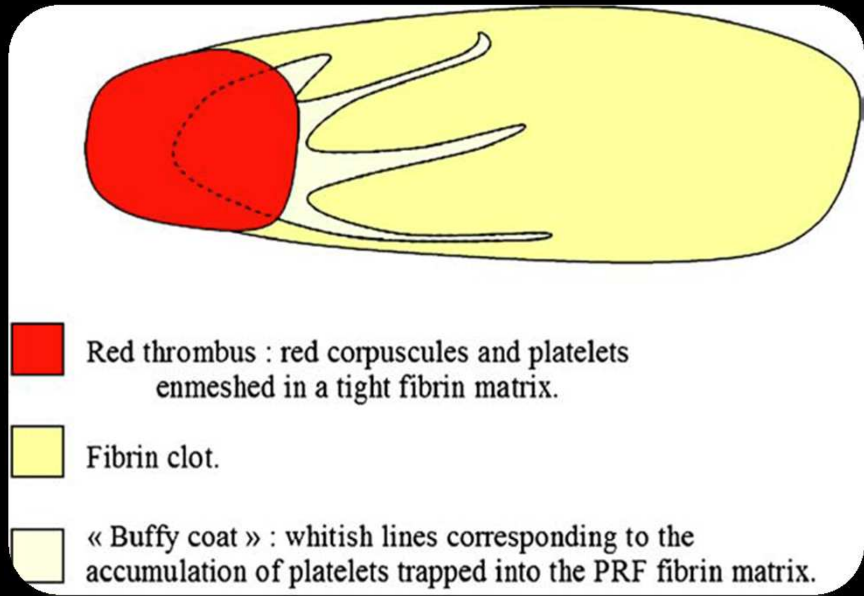
Platelet Rich Fibrin (L-PRF)

Platelet Activation: Natural coagulation → Fibrin Clot





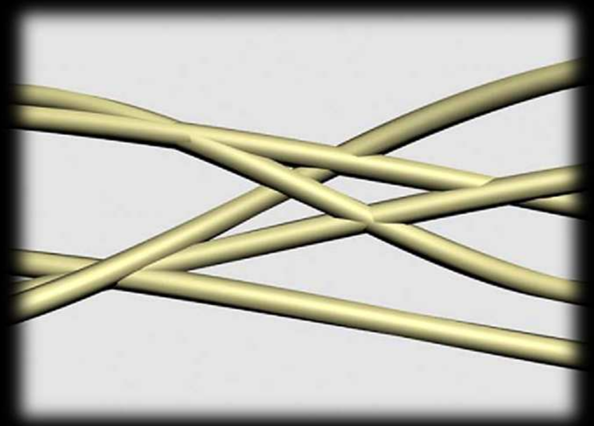
Choukroun J, Adda F, Schoeffler C, Vervelle A. Une opportunite en paro-implantologie: le PRF. Implantodontie 2001;42:55-62.
Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, Gogly B. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006 Mar;101(3):e37-44. Epub 2006 Jan 19.

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

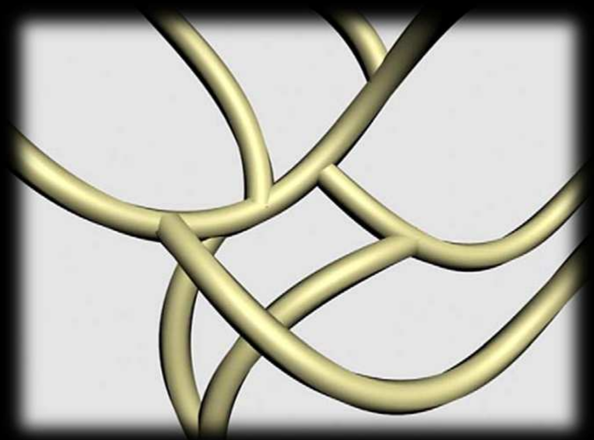
PRFM = platelet-rich fibrin matrix; PD-EGF = platelet-derived epidermal growth factor; PDGF = platelet-derived growth factor; TGF-β1 = transforming growth factor beta1; IGF = insulinelike growth factor; VEGF/ECGF = vascular endothelial growth factor/endothelial cell growth factor; bFGF = basic fibroblast growth factor; BMP = bone morphogenic protein.

Simon BI, Gupta P, Tajbakhsh S. Quantitative evaluation of extraction socket healing following the use of autologous platelet-rich fibrin matrix in humans. Int J Periodontics Restorative Dent. 2011 Jun;31(3):285-95.

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

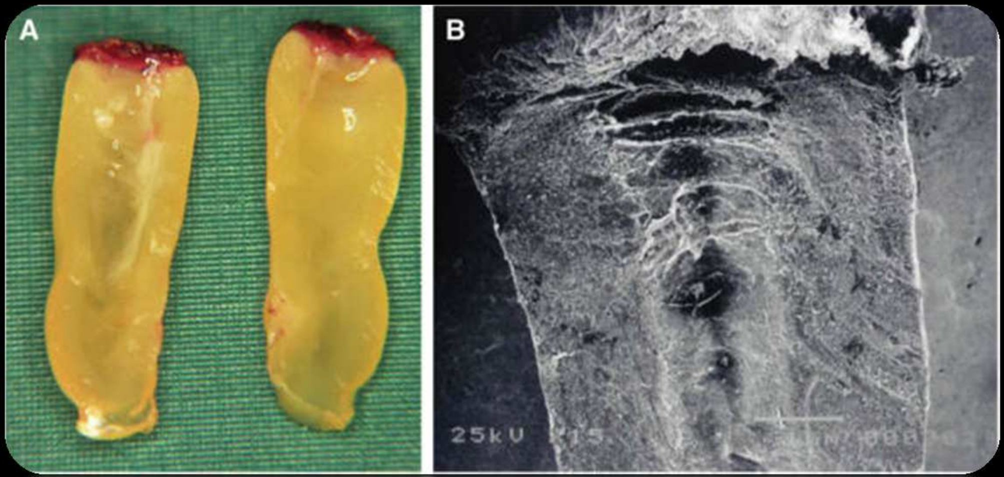


- **L-PRF** – natural slow polymerization leads to three dimensional fibrin polymerization
- Favorable to cytokine enmeshment and cellular migration

Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, Gogly B. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part II: platelet-related biologic features.Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006 Mar;101(3):e45-50.

L-PRF – importance of fibrin matrix

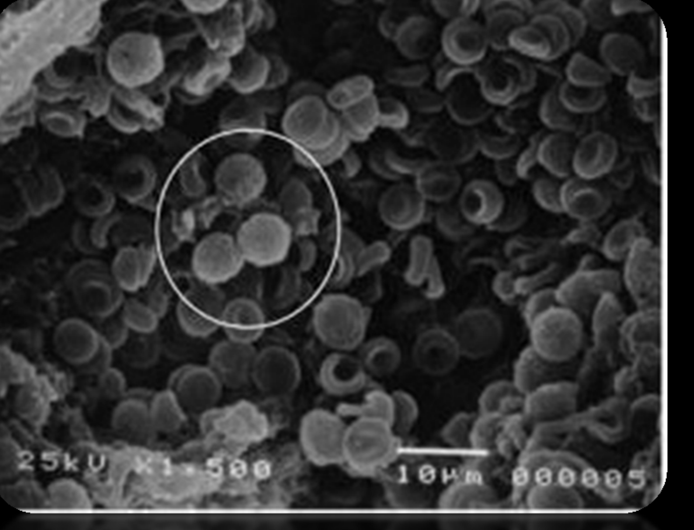
- Fibrin is natural scaffold for angiogenesis attracted MSCs
- Fibrin network is able to enmesh leukocytes, platelets and growth factors and furthermore to promote leukocyte migration
- Fibrin matrix guides epithelial cell migration to its surface



Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, Dohan AJ, Mouhyi J, Dohan DM. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part IV: clinical effects on tissue healing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006 Mar;101(3):e56-60.

L-PRF leukocyte content

- **L-PRF – contains ~50% of blood leukocyte count**
- Leucocytes trapped in the fibrin matrix continue to produce high quantities of TGFß-1 and VEGF
- Leukocytes secret interleukins and have antimicrobial potential



Dohan Ehrenfest DM, Del Corso M, Diss A, Mouhyi J, Charrier JB. Three-dimensional architecture and cell composition of a Choukroun's platelet-rich fibrin clot and membrane. J Periodontol. 2010 Apr;81(4):546-55.
Dohan Ehrenfest DM, de Peppo GM, Doglioli P, Sammartino G. Slow release of growth factors and thrombospondin-1 in Choukroun's platelet-rich fibrin (PRF): a gold standard to achieve for all surgical platelet concentrates technologies. Growth Factors. 2009 Feb;27(1):63-9.
Moojen DJ, Everts PA, Schure RM, Overdevest EP, van Zundert A, Knape JT, Castelein RM, Creemers LB, Dhert WJ. Antimicrobial activity of platelet-leukocyte gel against Staphylococcus aureus. J Orthop Res. 2008 Mar;26(3):404-10.

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

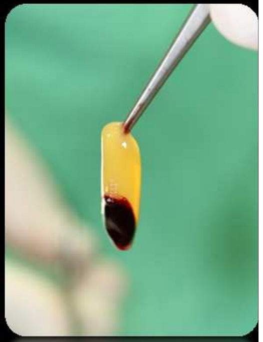
Del Corso M, Toffler M, Dohan Ehrenfest DM. Use of an Autologous Leukocyte- and Platelet-Rich Fibrin (L-PRF) Membrane in Post-Avulsion (Extraction) Sites: An Overview of Choukroun's PRF JIACD, 2009; 9: 27-35.

Chang YC, Zhao JH. Effects of platelet-rich fibrin on human periodontal ligament fibroblasts and application for periodontal infrabony defects. Aust Dent J. 2011 Dec;56(4):365-71.

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).

Mazor Z, Horowitz RA, Del Corso M, Prasad HS, Rohrer MD, Dohan Ehrenfest DM. Sinus floor augmentation with simultaneous implant placement using platelet-rich fibrin as the sole grafting material: a radiologic and histologic study at 6 months. J Periodontol. 2009 Dec;80(12):2056-64.

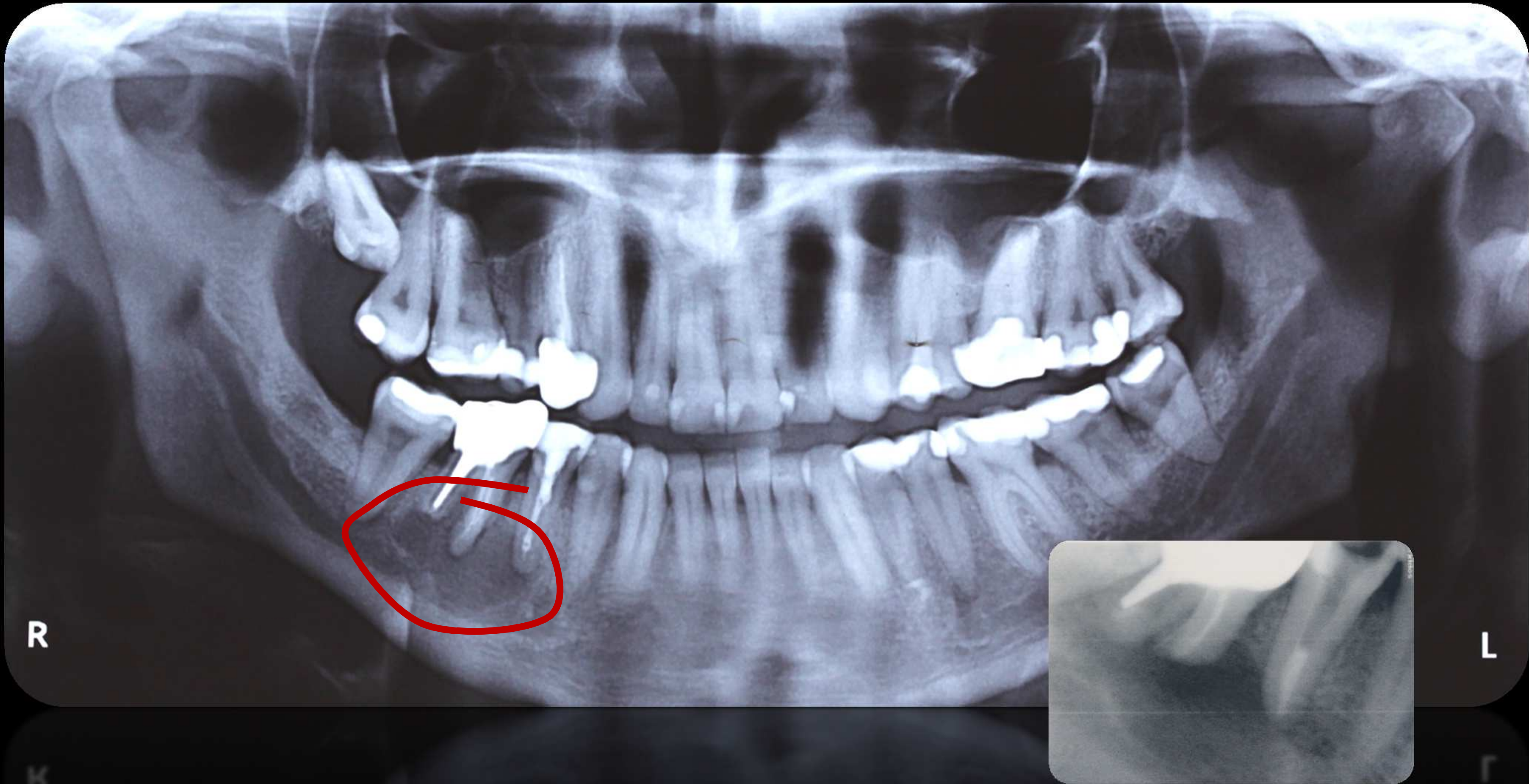
L-PRF Clinical Use



- 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.

Kobayashi E, Flückiger L, Fujioka-Kobayashi M, Sawada K, Sculean A, Schaller B, Miron RJ. Comparative release of growth factors from PRP, PRF, and advanced-PRF. Clin Oral Investig. 2016 Jan 25.

Clinical case



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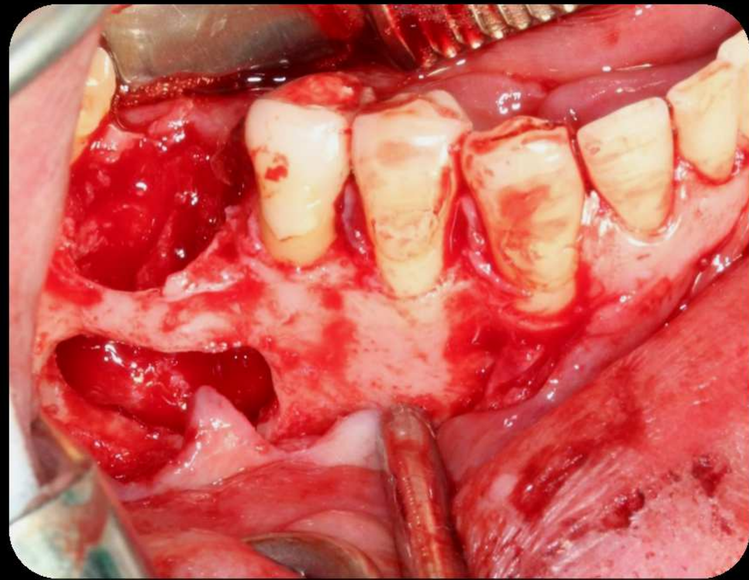


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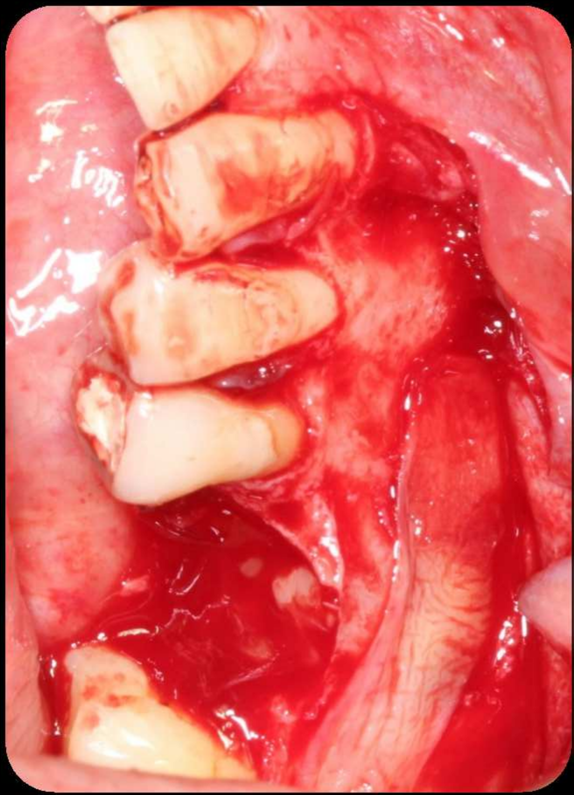

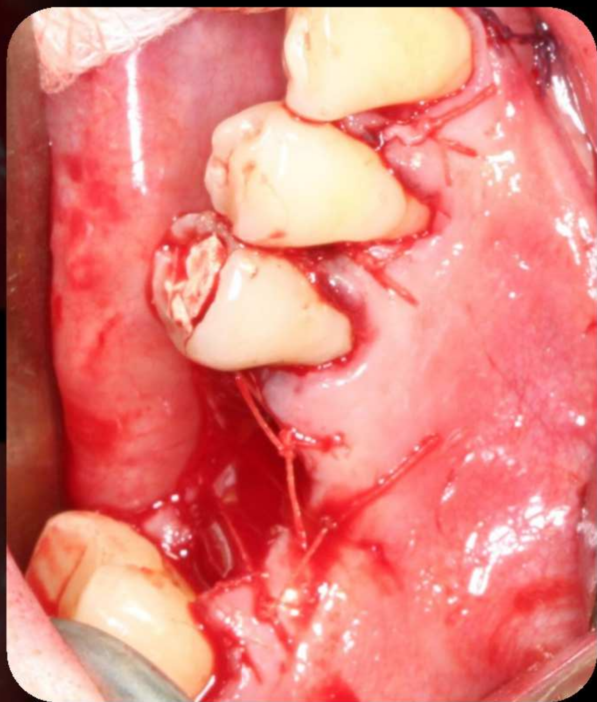

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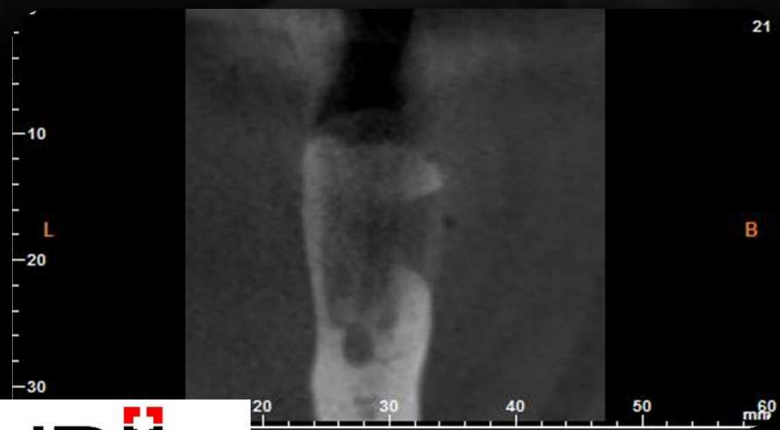
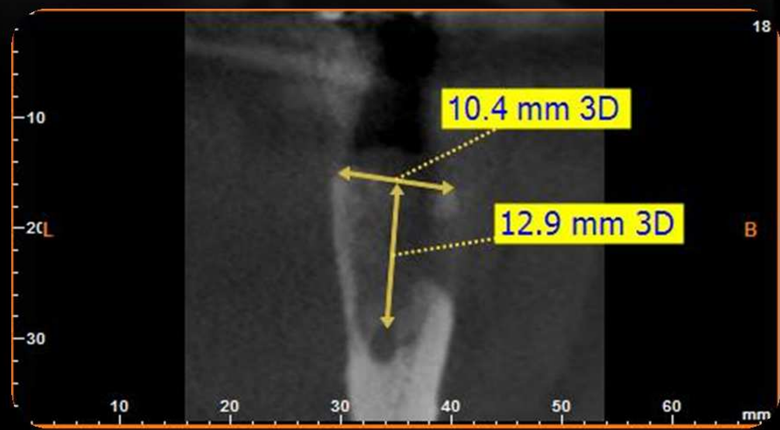
4 months post op





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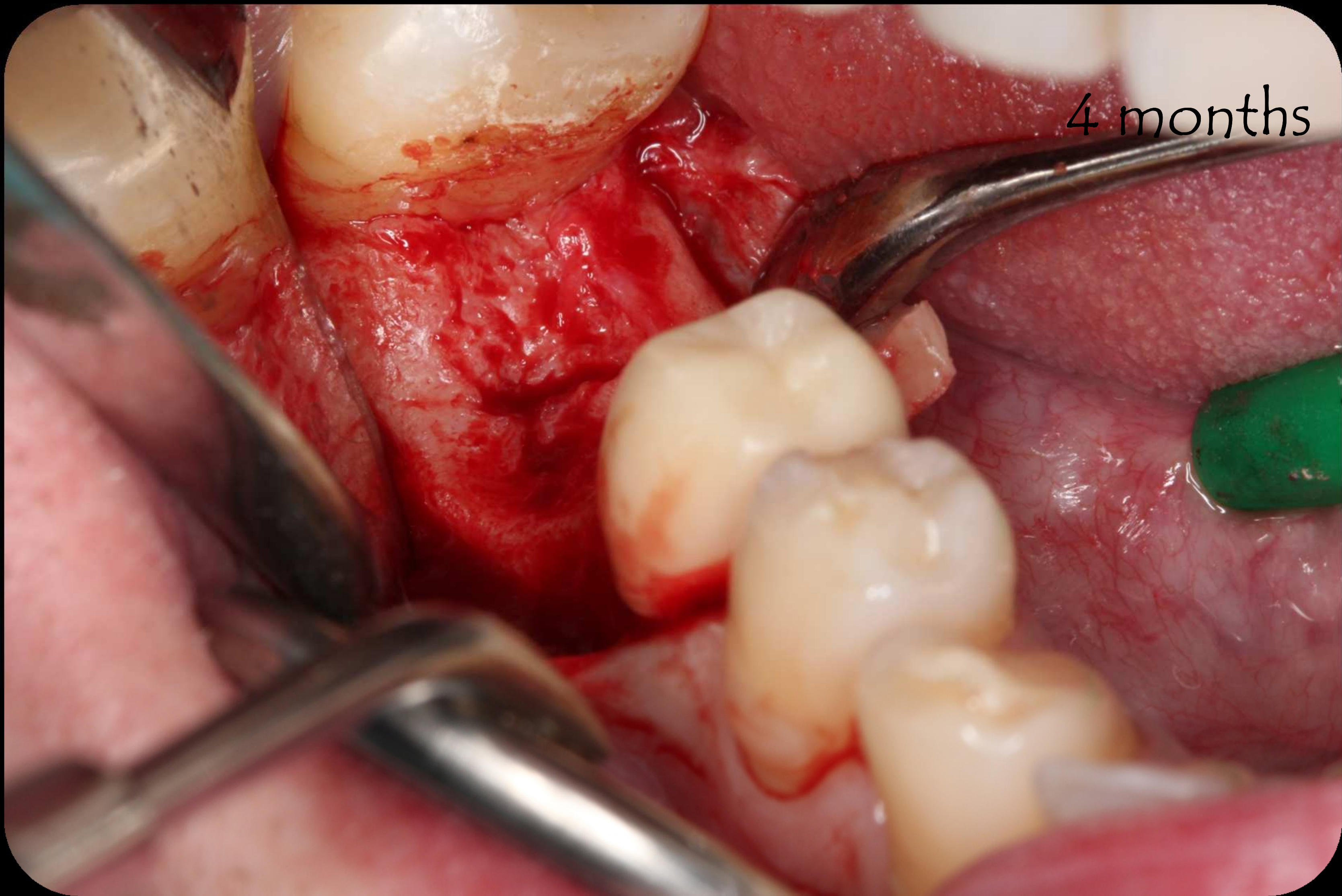

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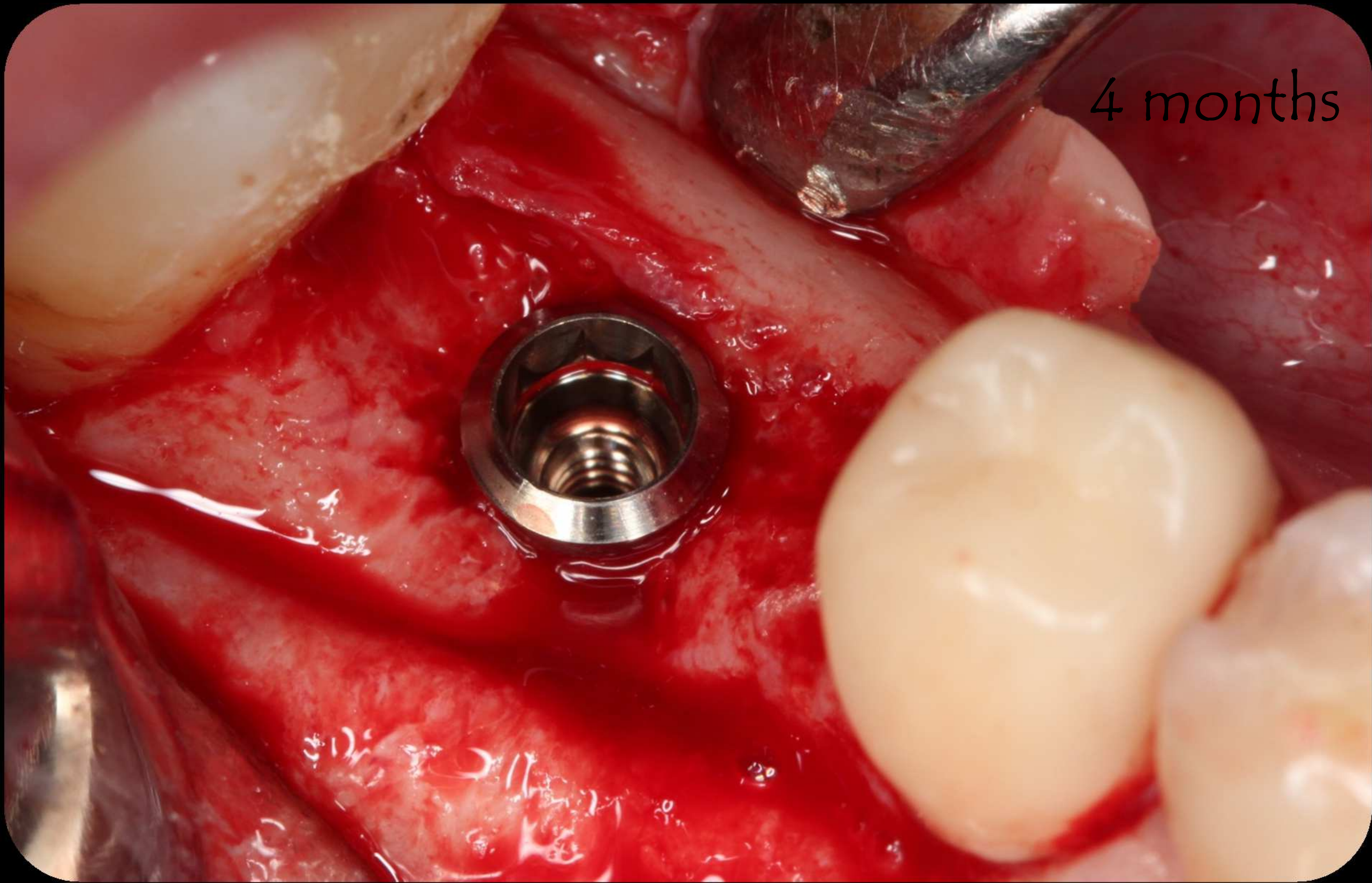

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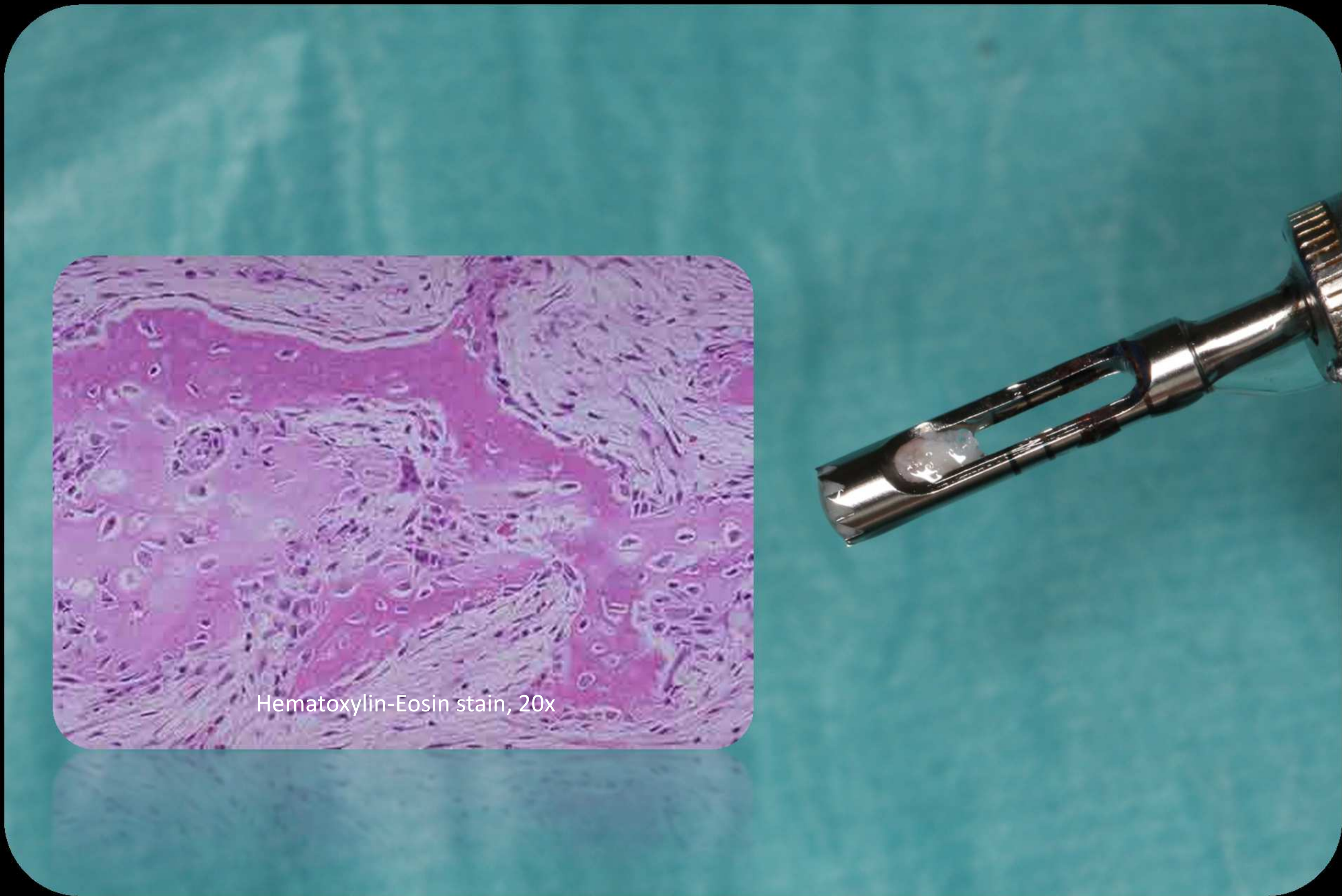
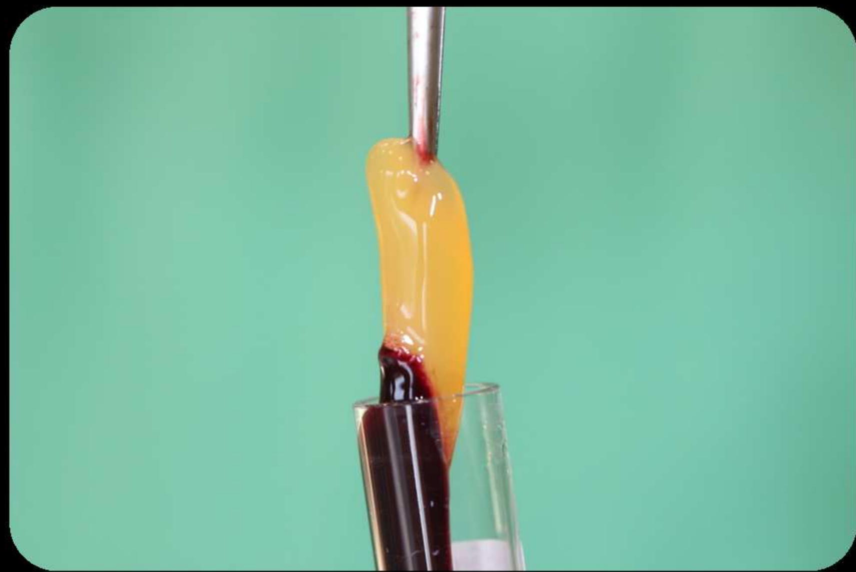
L-PRF optimized healing in third molar surgeries


Hematoxylin-Eosin stain, 20x

Grafting shift from inert to bioactive materials is prospective biomimetic treatment approach

Inert graft



L-PRF

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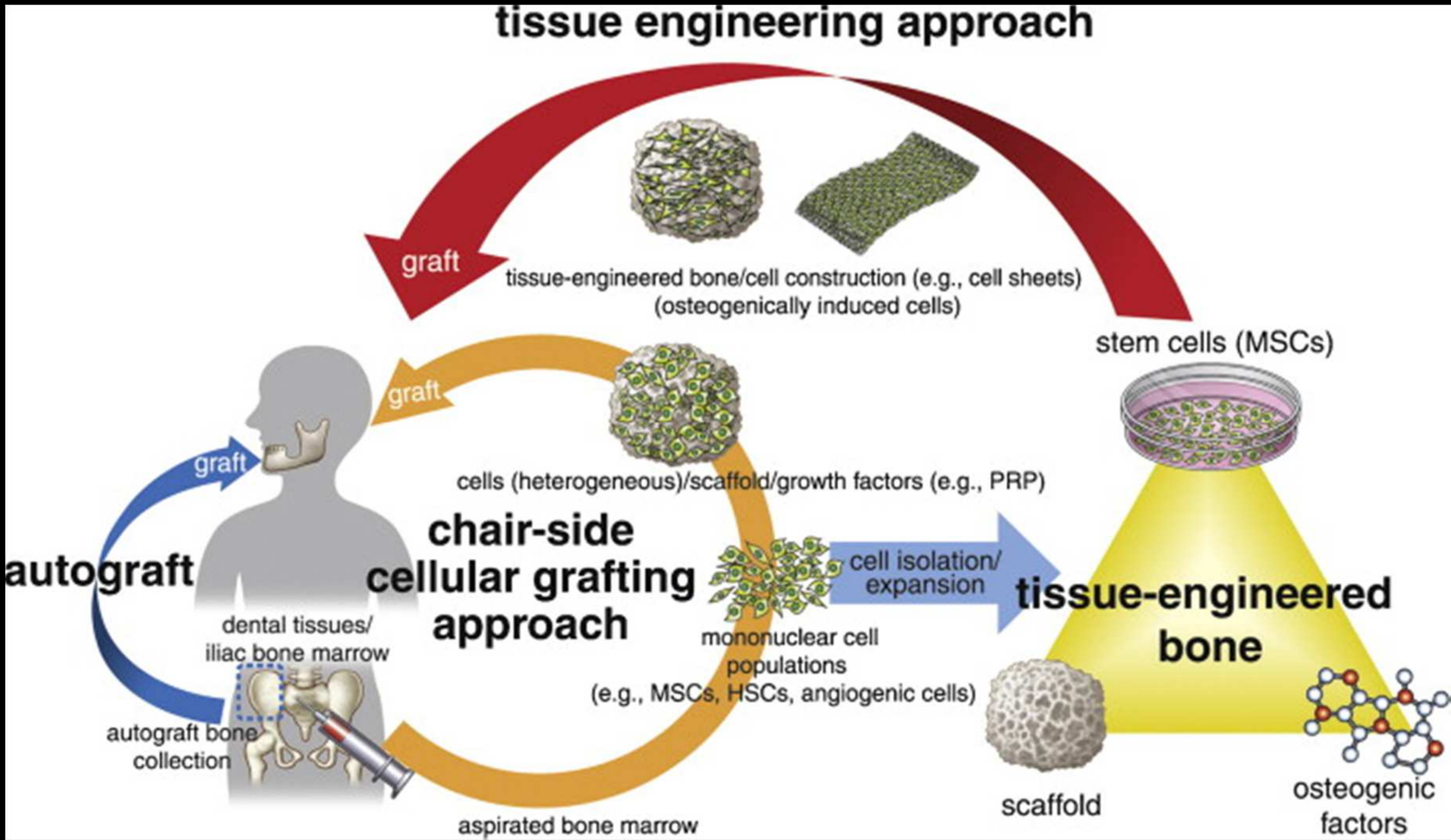

Schematic diagram illustrating the current clinical approaches to stem-cell-based bone augmentation.

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Hiroshi Egusa, Wataru Sonoyama, Masahiro Nishimura, Ikiru Atsuta, Kentaro Akiyama Stem cells in dentistry – Part II: Clinical applications Journal of Prosthodontic Research, Volume 56, Issue 4, 2012, 229–248

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.

Kern S, Eichler H, Stoeve J, Klüter H, Bieback K. Comparative analysis of mesenchymal stem cells from bone marrow, umbilical cord blood, or adipose tissue. Stem Cells. 2006;24(5):1294–1301.

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.

Kern S, Eichler H, Stoeve J, Klüter H, Bieback K. Comparative analysis of mesenchymal stem cells from bone marrow, umbilical cord blood, or adipose tissue. Stem Cells. 2006;24(5):1294–1301.

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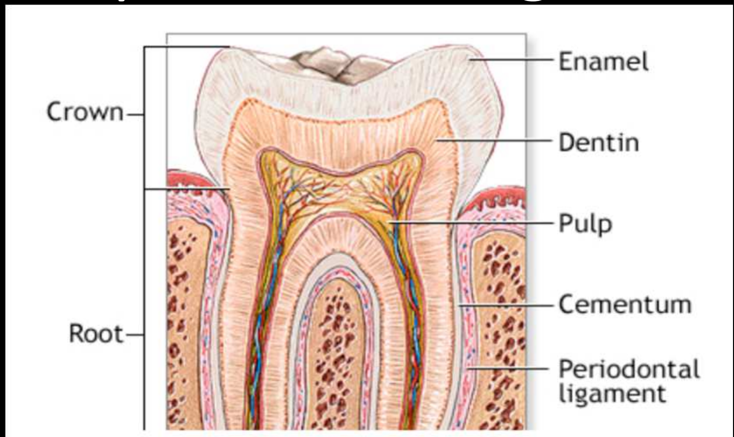
Mesenchymal stem cells

- 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.

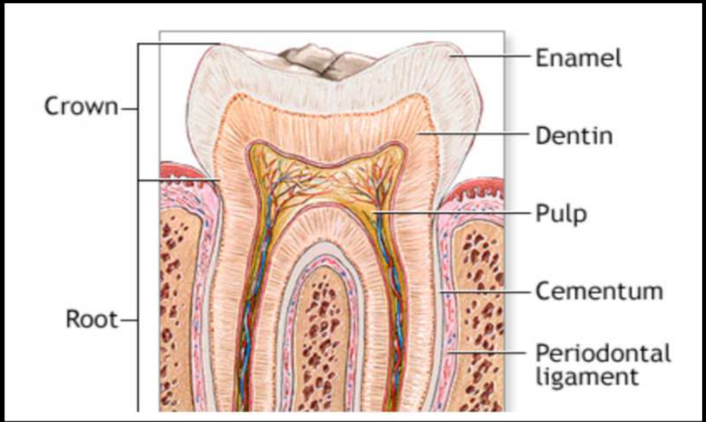


Miura M, Gronthos S, Zhao M, et al. SHED: stem cells from human exfoliated deciduous teeth. Proceedings of the National Academy of Sciences of the United States of America. 2003;100(10):5807–5812.

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.



Miura M, Gronthos S, Zhao M, et al. SHED: stem cells from human exfoliated deciduous teeth. Proceedings of the National Academy of Sciences of the United States of America. 2003;100(10):5807–5812.

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.

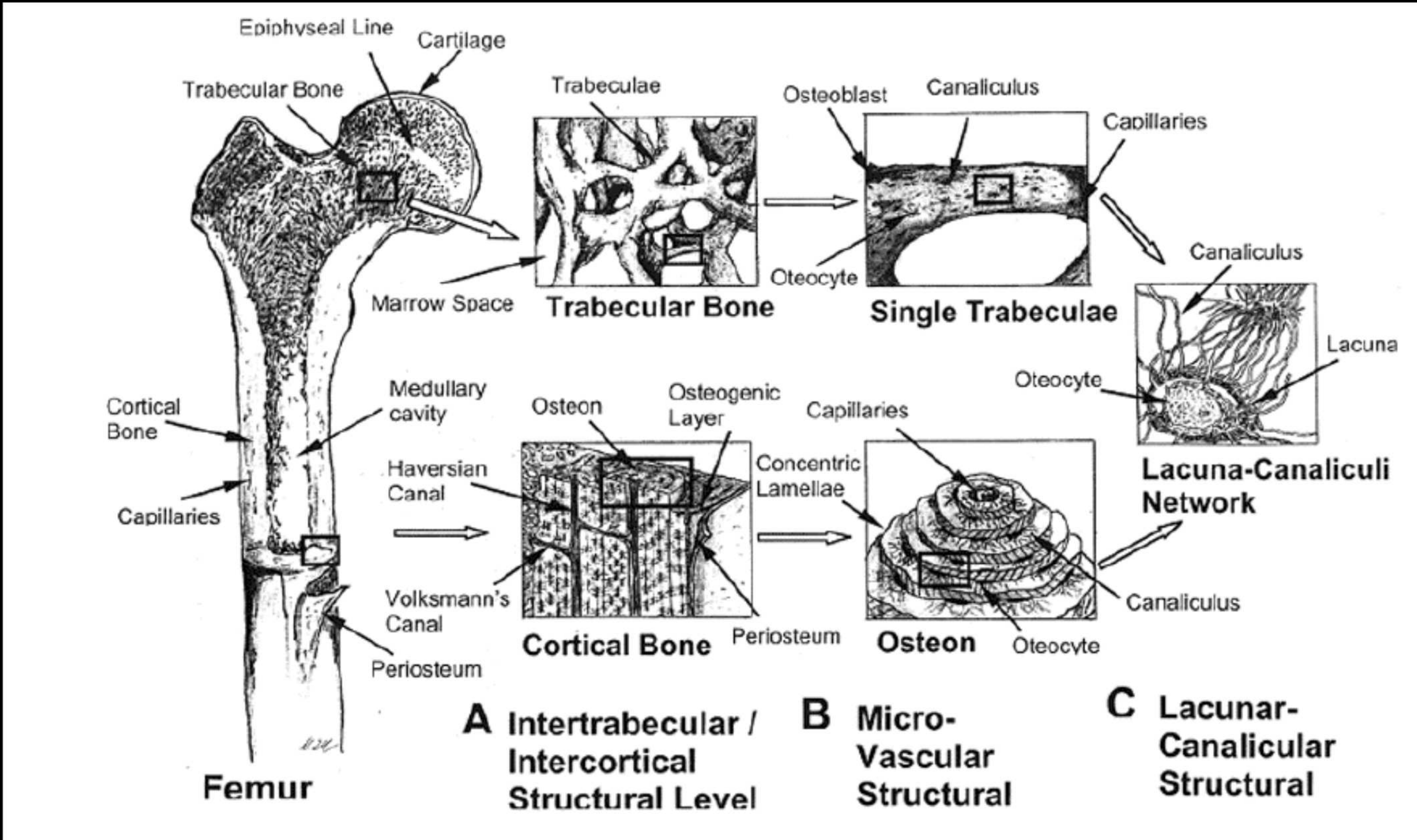
Jimi E, Hirata S, Shin M, Yamazaki M, Fukushima H. Molecular mechanisms of BMP-induced bone formation: cross-talk between BMP and NF-κB signaling pathways in osteoblastogenesis. Japanese Dental Science Review. 2010;46(1):33–42.
Katagiri T, Suda K, Miyazono . The bone morphogenetic proteins. In: Derynck R, Miyazono K, editors. Cold Spring Harbor Monograph. 2007. pp. 121–149. (The TGF-β Family).

Conclusion

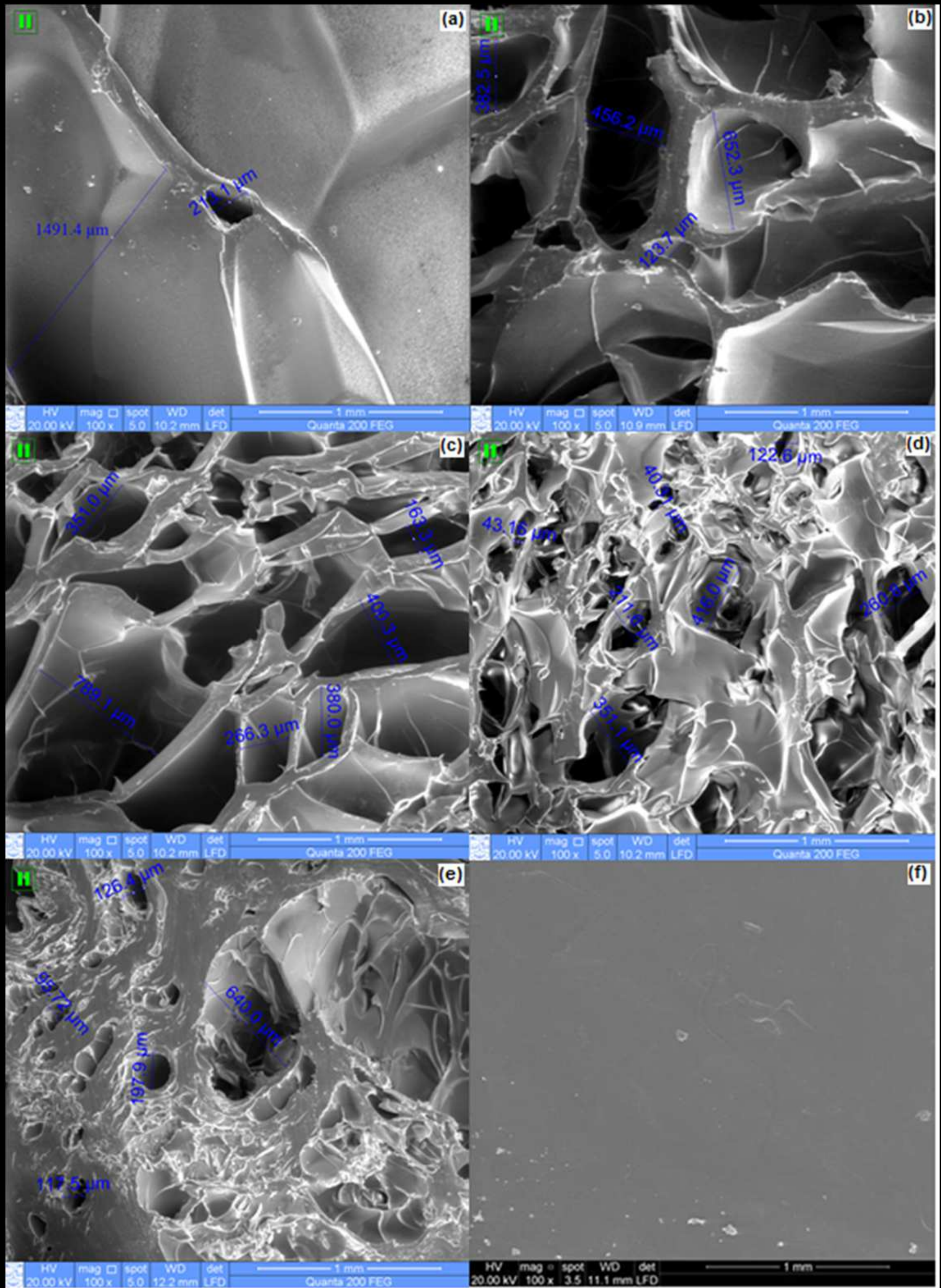
- Although regenerative medicine has been tried in various fields, there is much demand for regenerative medicine in dentistry, particularly in bone regeneration.
- Depending on the state of periodontitis or jaw resection, it might take more than 6 to 12 months for occlusal reconstitution.
- Thus, the 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 (eg, bone protein inducers, antibiotics).
- Have high compressive strength.
- Be effective in GTR procedures.



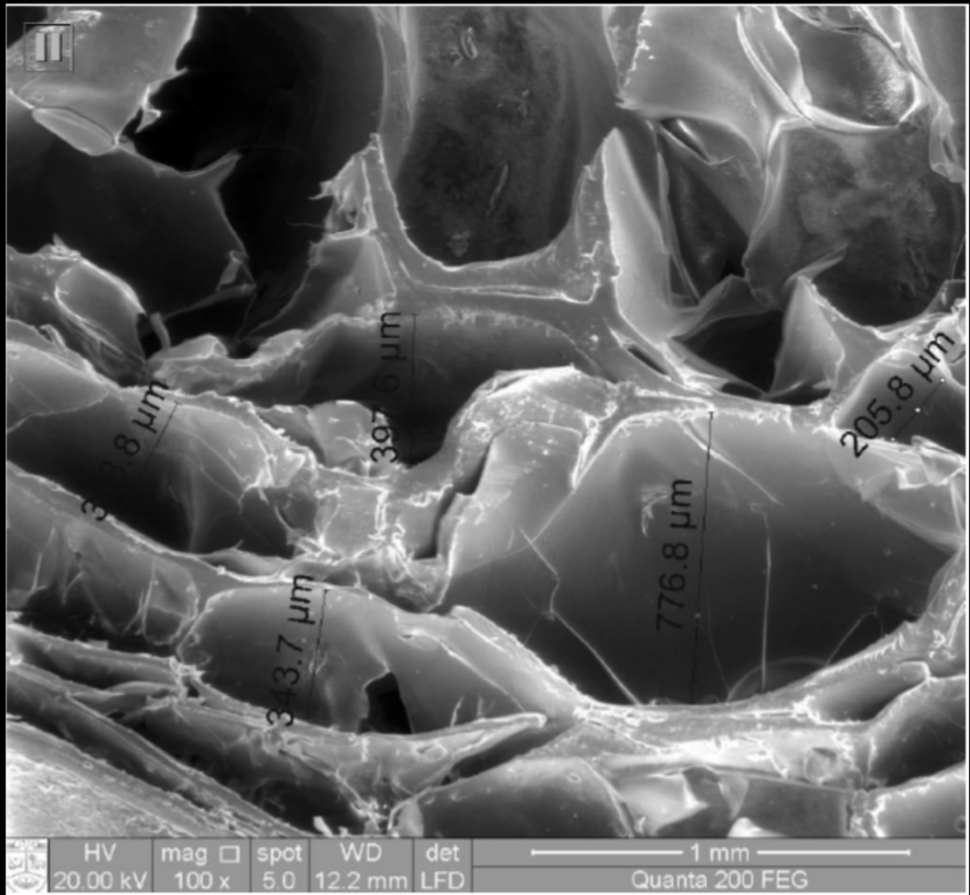
Epiphyseal Line
Cartilage
Trabecular Bone
Trabeculae
Osteoblast
Canaliculus
Capillaries
Marrow Space
Trabecular Bone
Oteocyte
Single Trabeculae
Canaliculus
Lacuna
Oteocyte
Cortical Bone
Medullary cavity
Osteon
Osteogenic Layer
Capillaries
Haversian Canal
Concentric Lamellae
Lacuna-Canaliculi Network
Capillaries
Volksmann's Canal
Canaliculus
Periosteum
Cortical Bone
Periosteum
Osteon
Oteocyte
Femur
A Intertrabecular / Intercortical Structural Level
B Micro-Vascular Structural
C Lacunar-Canalicular Structural



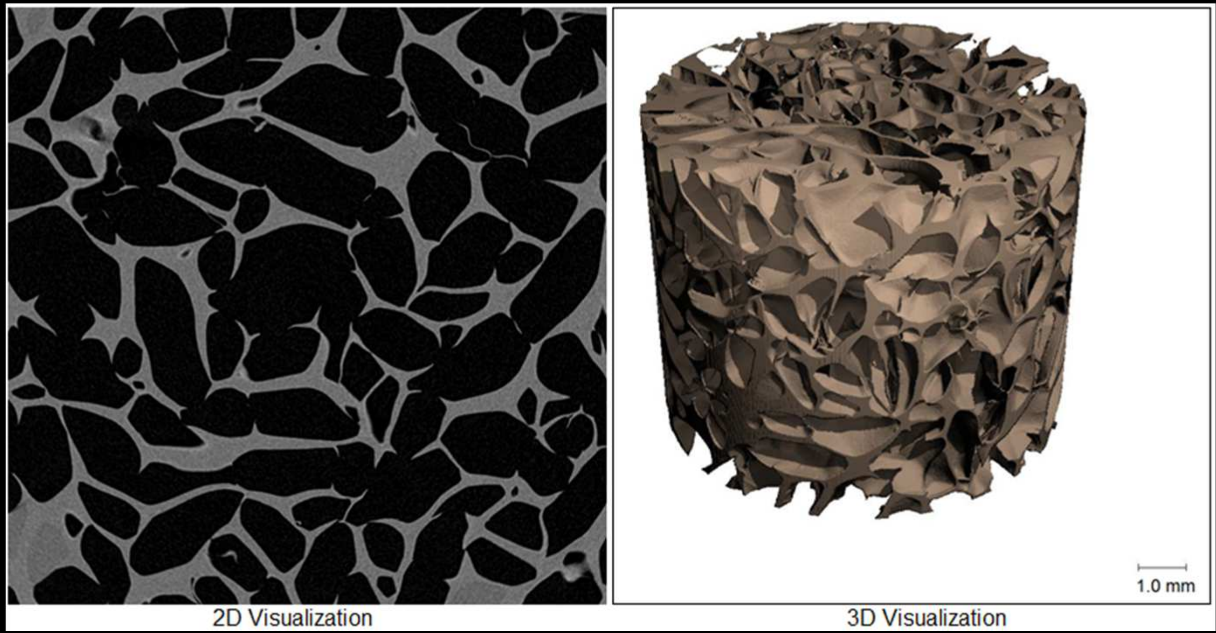
Study of the preparation of the three-dimensional matrix of regenerated cellulose for bone tissue engineering using freeze-drying method was performed.

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.

Characteristics	Value	Unit
Total volume	625	mm^3
Scaffold volume	156	mm^3
Pore volume	470	mm^3
Porosity	75	%
Mean scaffold thickness	0.212	mm
Mean pore diameter	0.749	mm

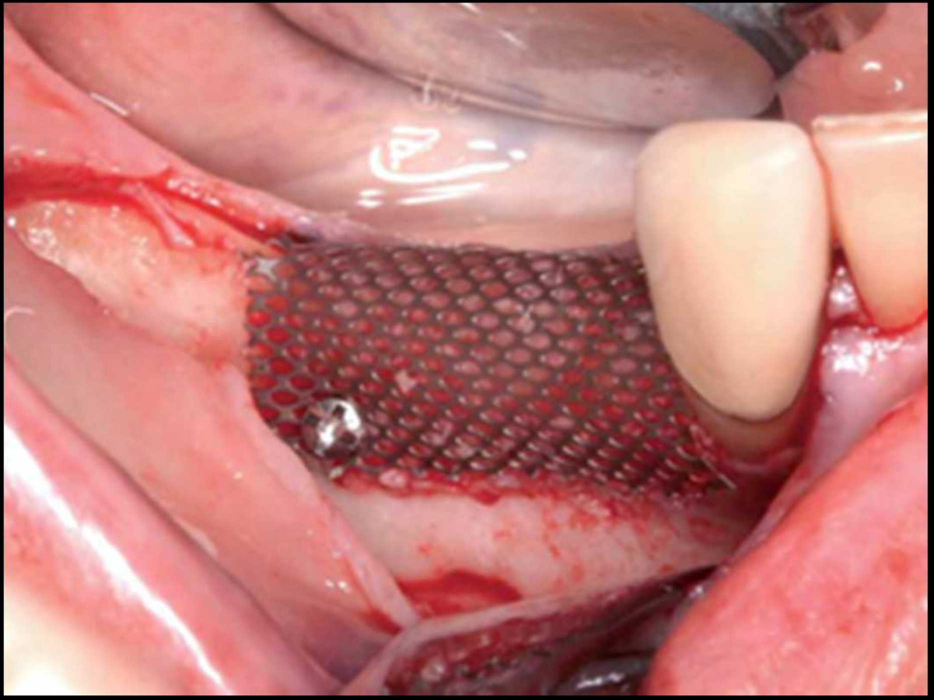
Aditional suggestions

- 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



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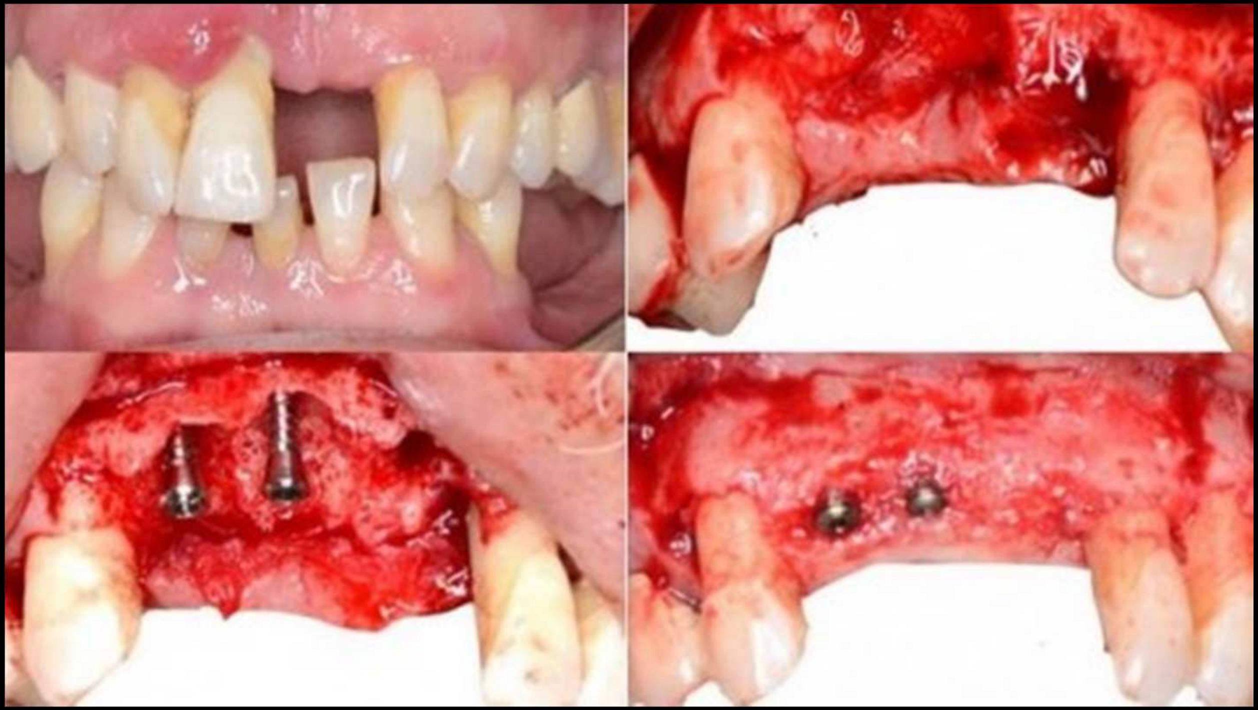
Aditional suggestions

- We need material shaping during operation



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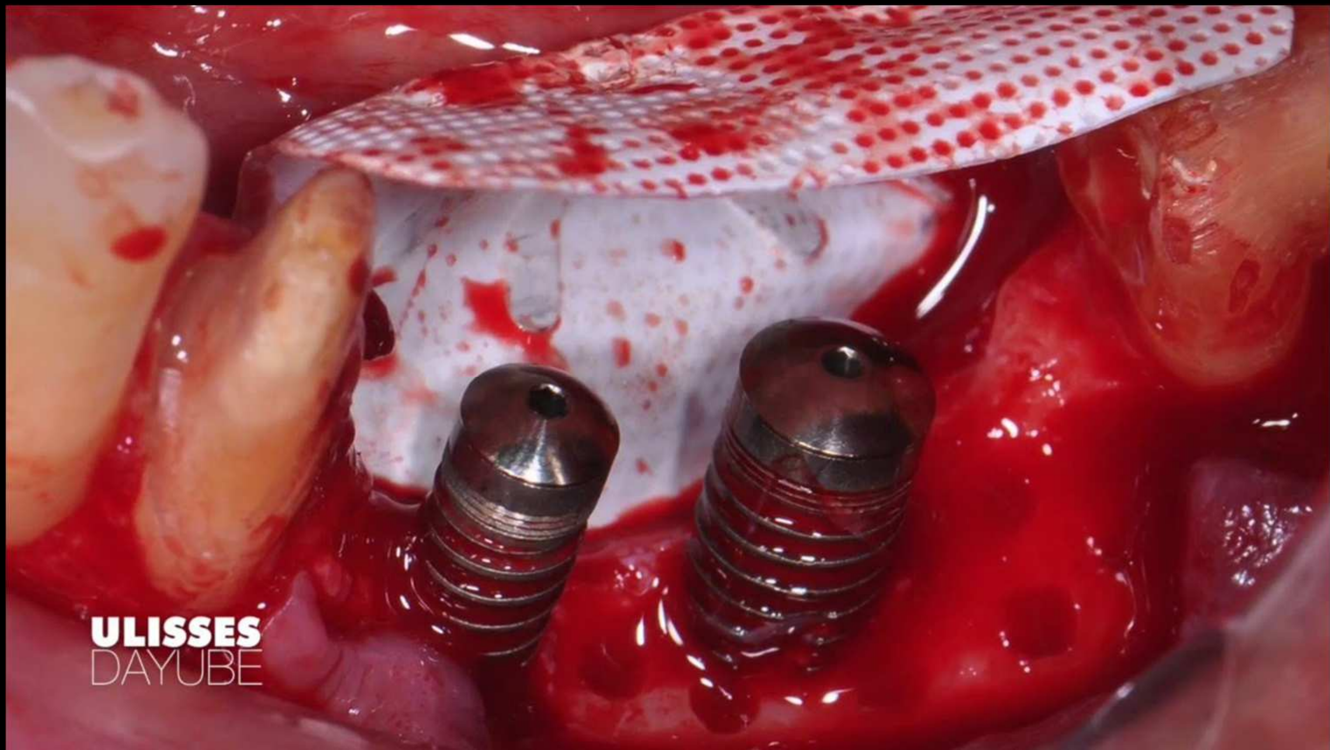

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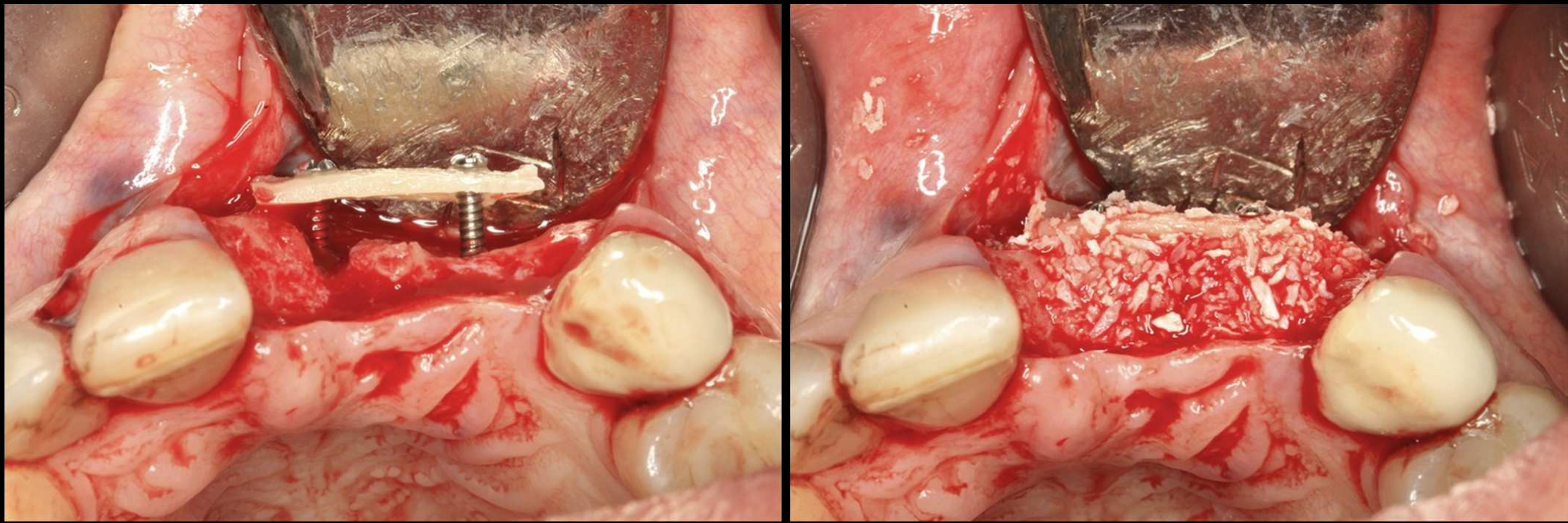
Aditional suggestions



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Aditional suggestions

- Or maybe material which will stiffen and will hold implants stable?

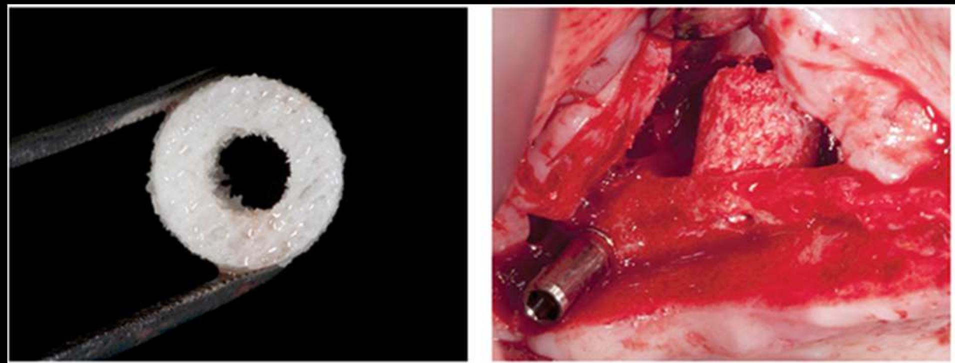

Figure 6: The bone ring measures 10 mm in height, with an exterior diameter of 7 mm and an internal diameter of 3.5 mm

Figure 7: The bone ring is placed above the osteotomy after filling the back side wall of the sinus with a xenograft

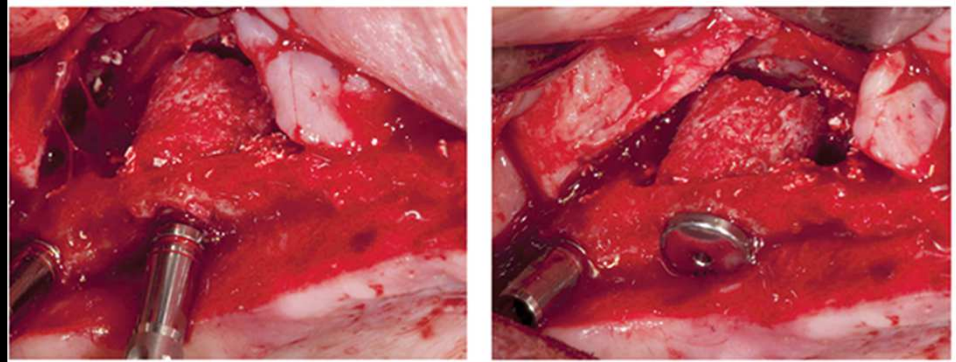

Figure 8: The implant is completely inserted into the ring, so the crestal bone and the bone ring are touching

Figure 9: A membrane screw (6 mm in diameter, with a 1 mm pin height) is used to fix the implant and bone ring to the crestal bone

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Thank you