



Bone Engineering

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Tissue Engineering VS Regenerative Medicine

Insitu Vs Invitro Osteogenesis

Strategy for Engineered Bone

Cells (Osteoblast or Osteoprogenitor)

Scaffold (synthetic or natural)

Growth Factor

Dentomaxillofacial Regeneration

- In situ Osteogenesis

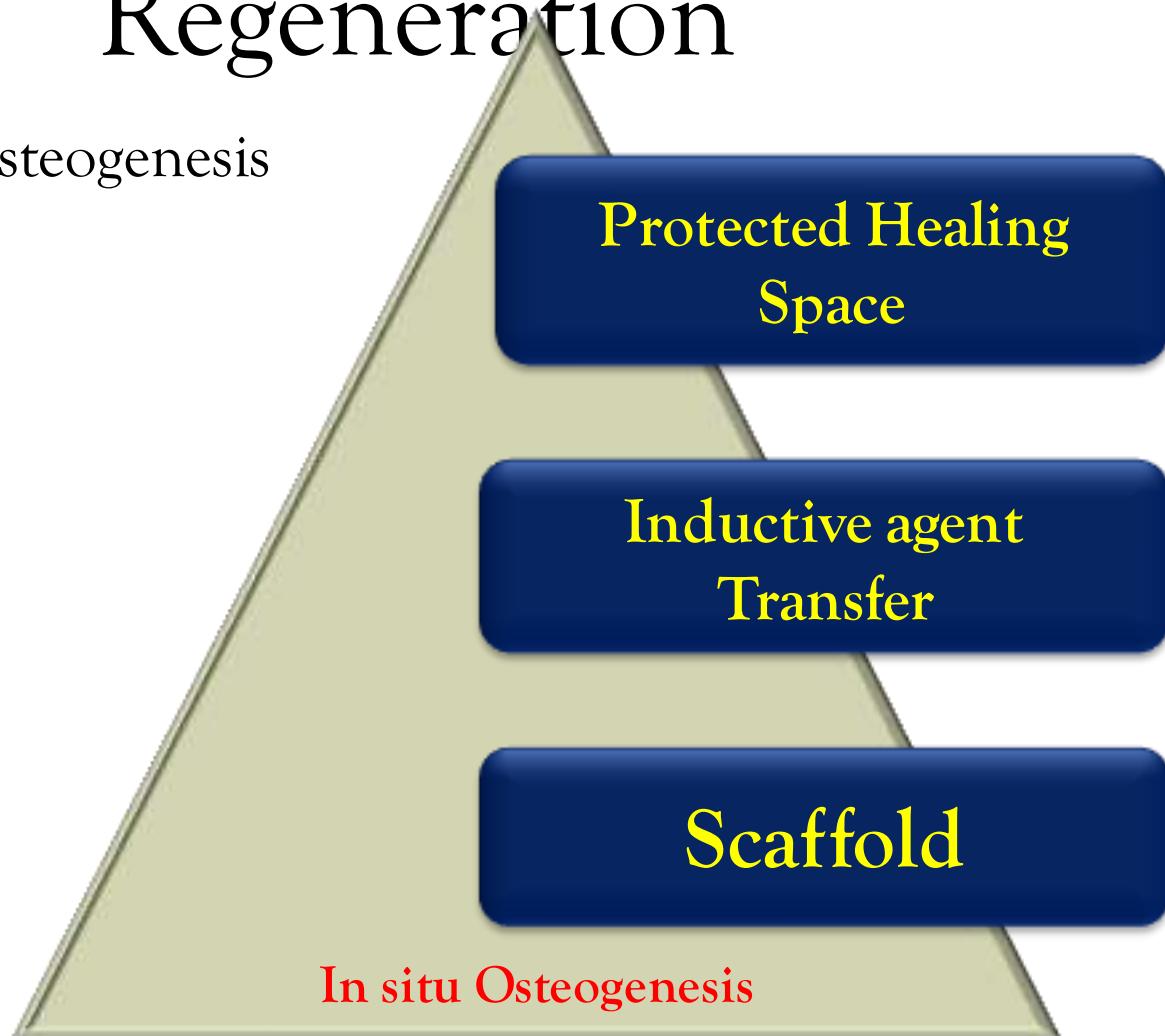


Table 1. RAT CRANIAL DEFECTS

Study	Year	Defect	MSCs	Cultured in Osteogenic Medium*	Scaffold	Growth Factor
Akita et al ²⁷	2004	4 mm × full thickness	hBMSCs	+ [†]	Gelfoam	Treated with BMP-2 (50 ng) and bFGF (2.5 ng)
Lin et al ²⁸	2008	8 mm	rADSCs	-	Alginate gel	Transfected with BMP-2
Kim et al ²⁹	2007	8 mm × 2 mm	hBMSCs from femur	-	Hydrogel	Transfected with BMP-2
Castano-Izquierdo et al ³⁰	2007	8 mm	rBMSCs from femur	+ [‡]	Titanium mesh	-
Yoon et al ³¹	2007	8 mm	hADSCs	+ [§]	PLGA	-
Khojasteh et al ³²	2008	5 mm × full thickness	rBMSCs from tibia	+	Bio-Oss or β-TCP	-
Bohnenblust et al ³³	2009	8 mm	rADSCs	+		-
Liu et al ³⁴	2009	5 mm × full thickness	hUCMSCs	-/+	3-dimensional pDBM scaffolds	-

Table 2. RAT FEMORAL DEFECT

Study	Year	Defect Size	MSCs	Cultured in Osteogenic Medium*	Scaffold	Growth Factor
Henrich et al ³⁵	2009	5 mm	hBMSCs	—	β -TCP	
Zhang et al ³⁶	2010	7 mm	hFMSCs	+	PCL-TCP	—

Table 4. RABBIT DEFECTS IN ORTHOPEDIC STRUCTURES

Study	Year	Defect	MSCs	Cultured in Osteogenic Media*	Scaffold	Growth Factor
Niemeyer et al ⁴¹	2009	Radial diaphysis 15 mm	hBMSCs, rBMSCs	+	CDHA ceramic cylinders	—
Wan et al ³⁹	2006	Ulna 20 mm	rPBMSCs, rBMSCs	—	PCP	—
Yoon e al ⁴⁰	2007	Femur 15 mm	rBMSCs from iliac	—	Calcitriol-loaded PLGA, plain PLGA	—

Table 5. DOG MANDIBULAR DEFECT

Study	Year	Defect	MSCs	Cultured in Osteogenic Medium*	Scaffold	Growth Factor
Yamada et al ⁴²	2004	10 mm	dBMSCs from iliac	+	—	PRP
Yuan et al ⁴³	2006	30 mm	dBMSCs from iliac	+	β -TCP	—
Ito et al ⁴⁴	2006	10 mm	dBMSCs from iliac	+	Fibrin glue	PRP
Jafarian et al ⁴⁵	2008	10 mm	dBMSCs from humerus	+	HA-TCP, Bio-Oss	—

Table 6. DOG DEFECT IN ORTHOPEDIC STRUCTURE

Study	Year	Defect	MSCs	Cultured in Osteogenic Medium*	Scaffold	Growth Factor
Li et al ⁴⁶	2007	Ulnar defect 25 mm	dADSCs	+	TCP	Engineered ADSCs, transfected with BMP-2

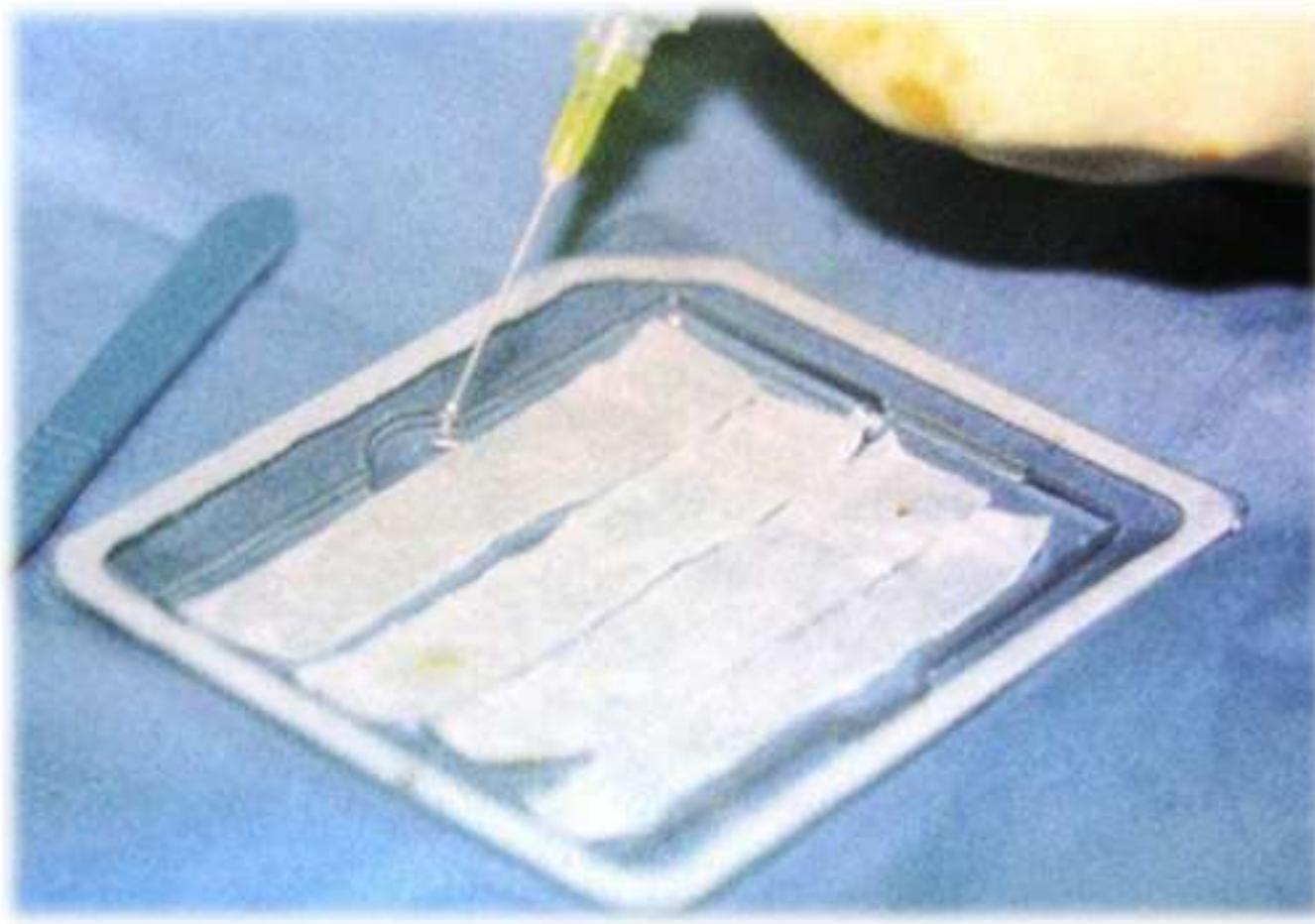
Table 7. HUMAN STUDIES

Study	Year	Number of Cases	Defect	MSCs	Cultured in Osteogenic Medium*	Scaffold	Growth Factor
Ueda et al ⁴⁷	2005	6	Sinus augmentation/ridge onlay plasty with simultaneous implant placement	hBMSCs from iliac crest	+	β -TCP	PRP
Filho Cerruti et al ⁴⁸	2007	32	Anterior-posterior maxilla deficiency	hBMSCs from iliac or sternum	-	Thrombin-calcium/coadministered with particulate allografts	PRP
Ueda et al ⁴⁹	2008	14	Sinus augmentation/ridge onlay plasty with simultaneous implant placement	hBMSCs from iliac crest	+	-	With PRP
Shayesteh et al ⁵⁰	2008	7	Sinus augmentation	hBMSCs from iliac crest	-	HA-TCP	-
Behnia et al ⁵¹	2009	2	Secondary repair of alveolar cleft	hBMSCs from iliac crest	-	DBM combined with calcium sulfate	-

Growth factor Therapy

Cell therapy

Maxillary Sinus Augmentation



Boyne PJ, Marx RE, Nevins M et al; Int J Periodontics Restorative Dent. 1997;17:11-25



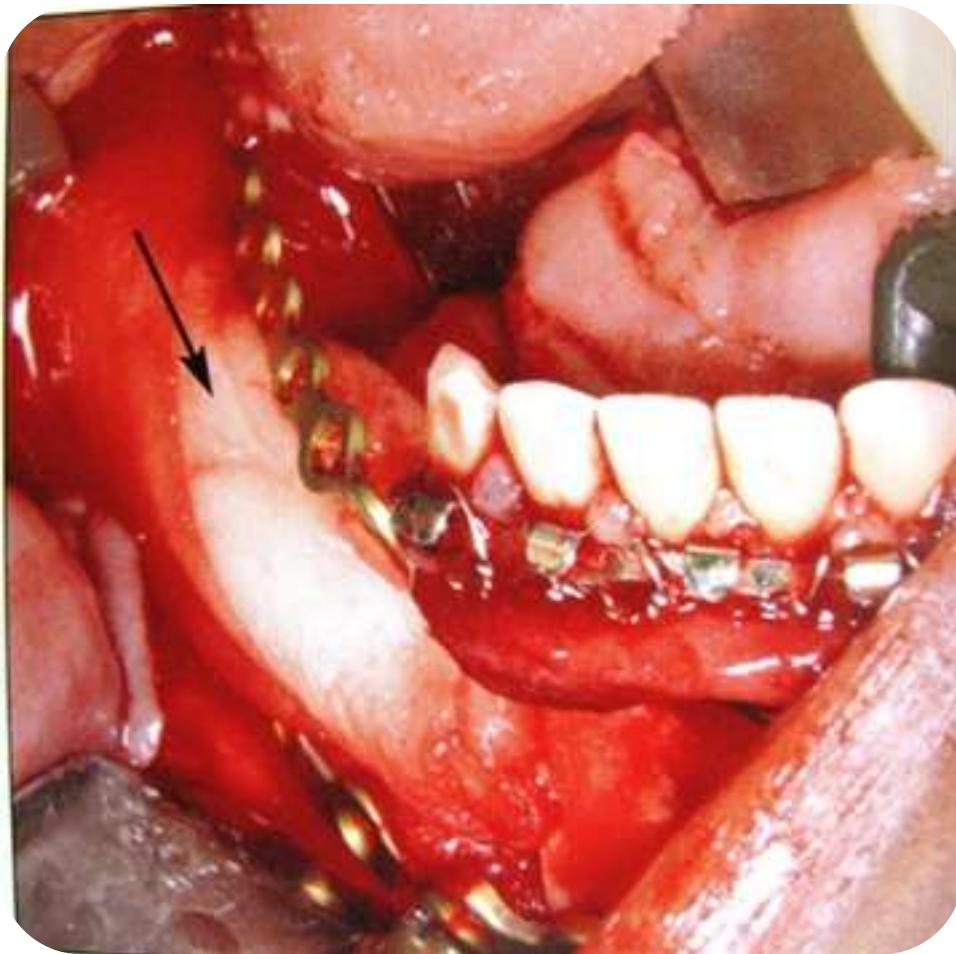
Boyne PJ, Marx RE, Nevins M et al; Int J Periodontics Restorative Dent. 1997;17:11-25



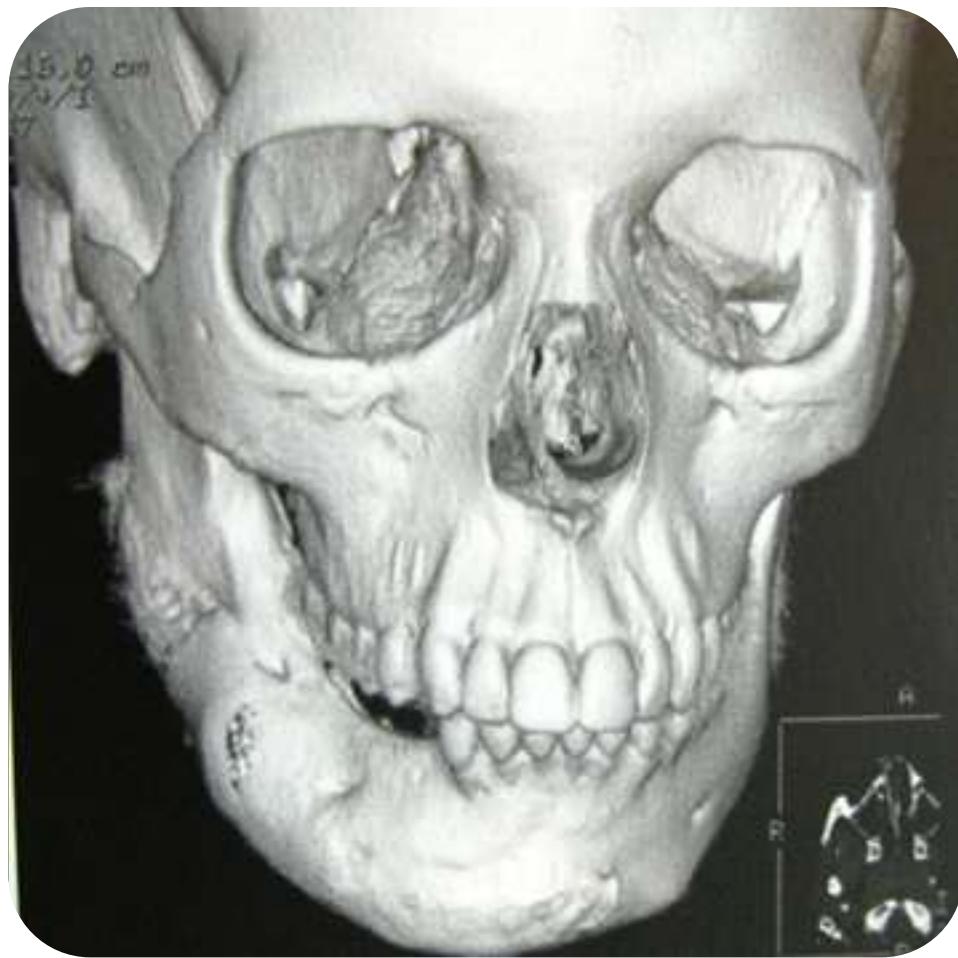
Boyne PJ, Marx RE, Nevins M et al; Int J Periodontics Restorative Dent. 1997;17:11-25



Herford and PJ Boyne

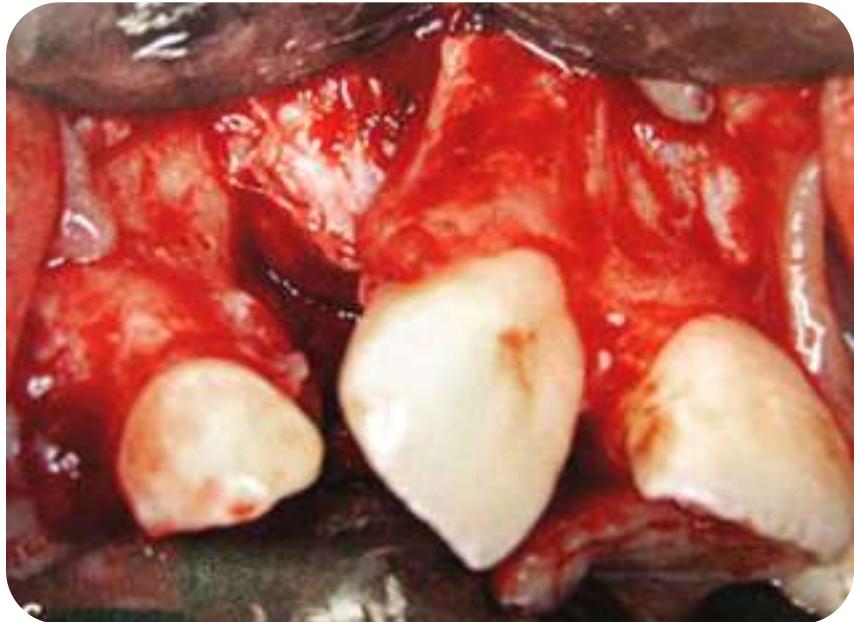






*Alan S. Herford . Philip J. Boyne. Rick Rawson. Roland P.
Williams*



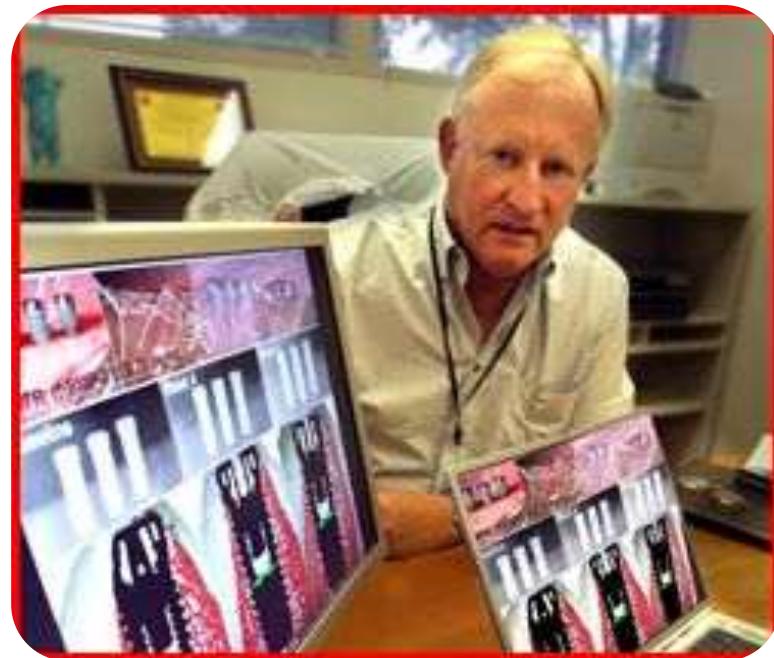






RhBMP-2

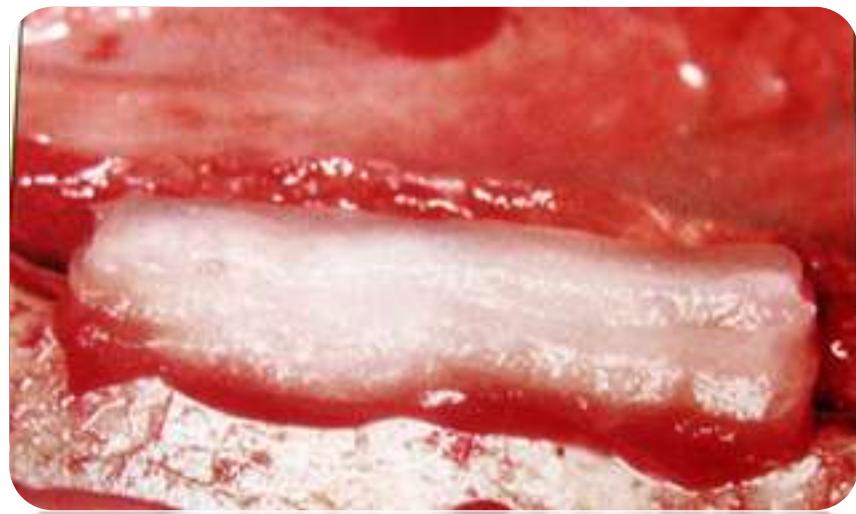
- Animal Critical Size defect Study (Wikesjo)
- Human studies



Animal Critical Size defect Study

RhBMP-2 and ACS

Clinical Oral Impl Res 1997;8
367-384

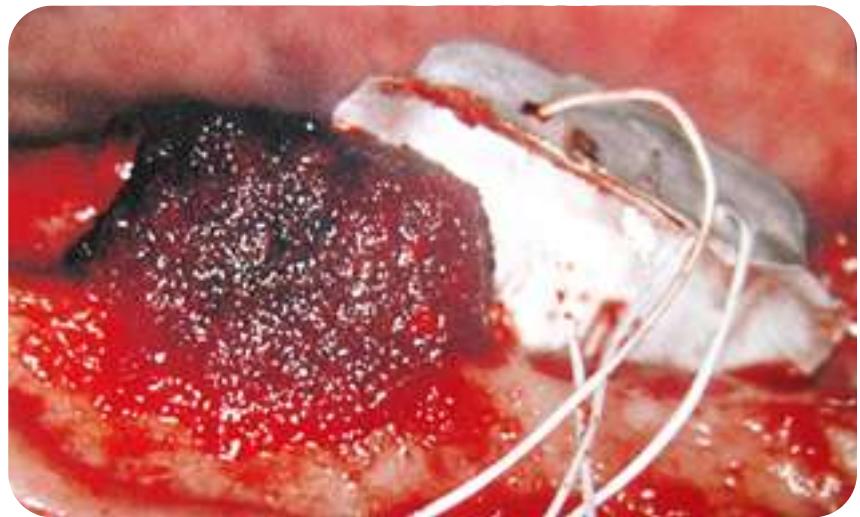


**Clinical Oral Impl Res 1997;8
367-384**



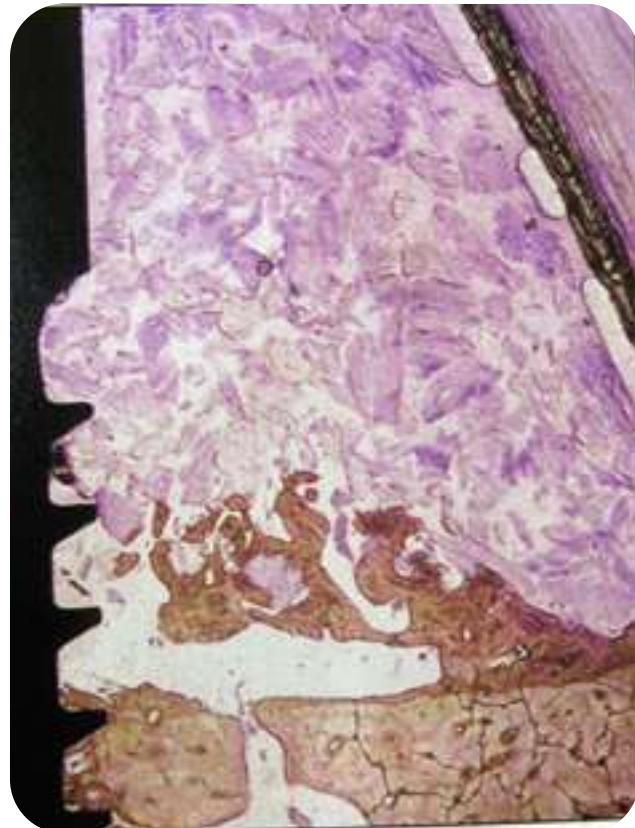
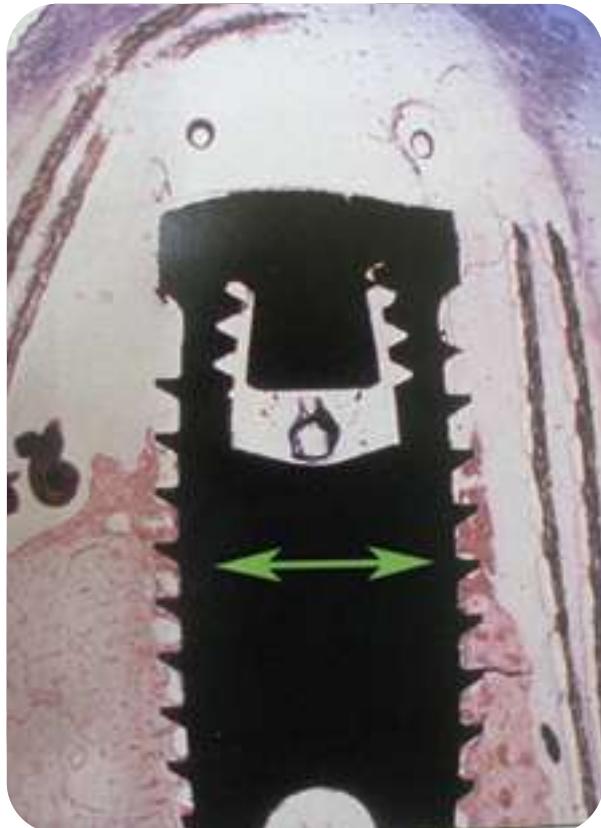
Protected Bone Healing with DFDBA

JOMI 1997; 12: 634-642



Protected Bone Healing with DFDBA

JOMI 1997; 12: 634-642



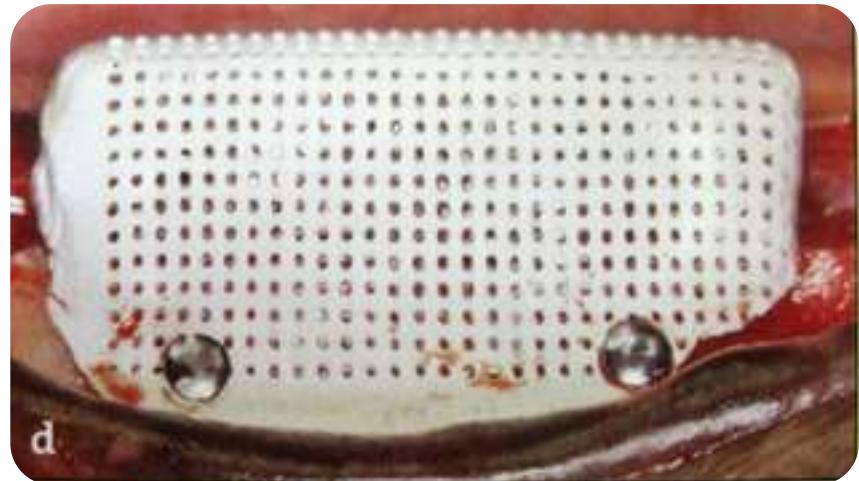
Protected Healing Space Vs Inductive transfer

Clinic Oral Impl Res 2004;;
15: 194-204



Protected Healing Space Vs Inductive transfer

Clinic Oral Impl Res 2004; ; 15: 194-
204



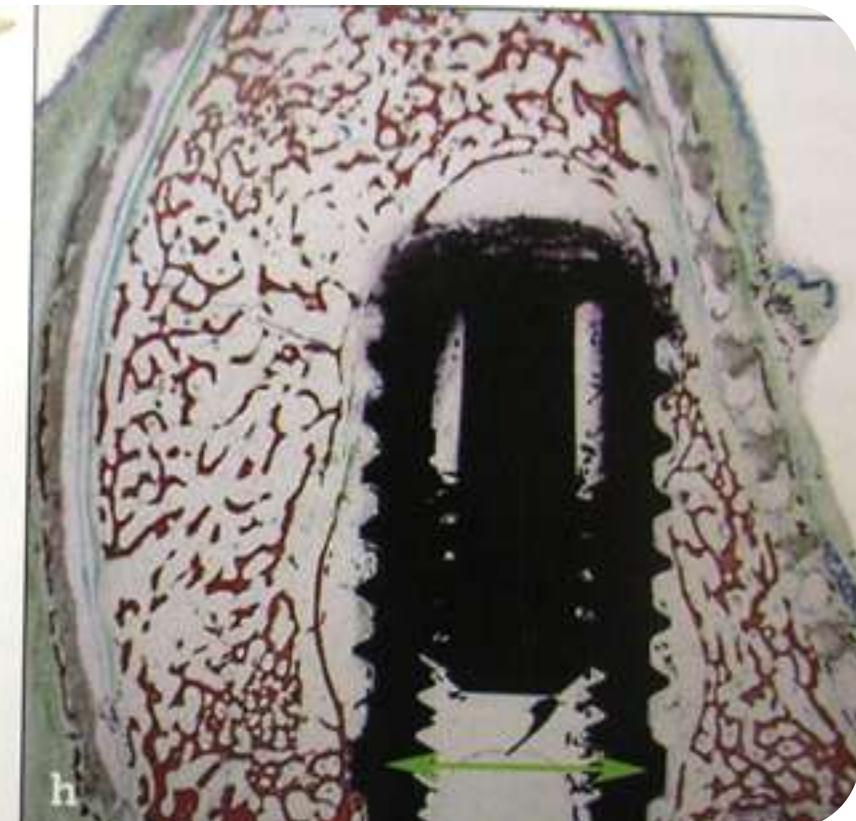
Protected Healing Space Vs Inductive transfer

Clinic Oral Impl Res 2004;; 15:194-204



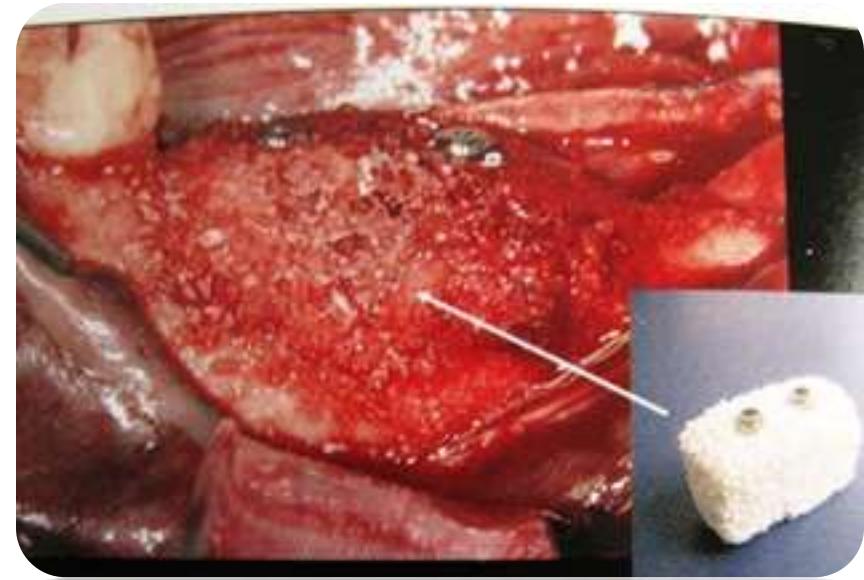
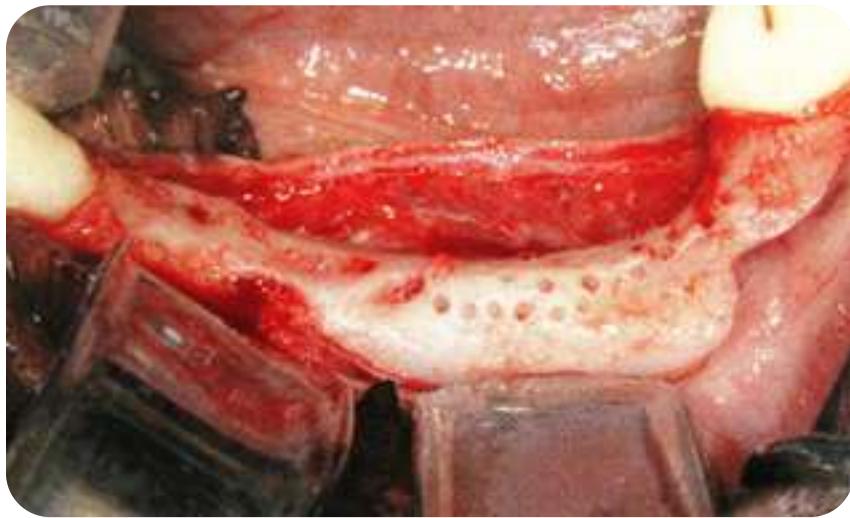
Protected Healing Space Vs Inductive agent transfer

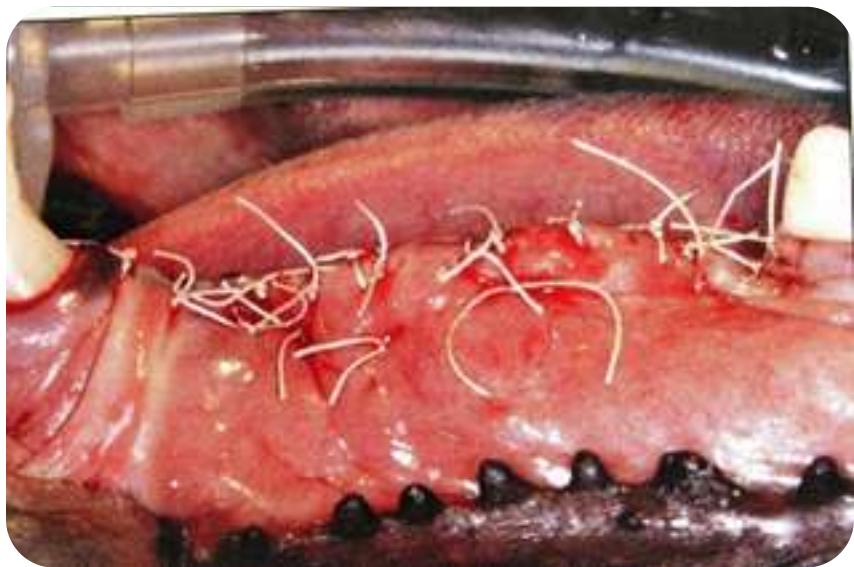
- Clinic Oral Impl Res 2004; 15: 194-204

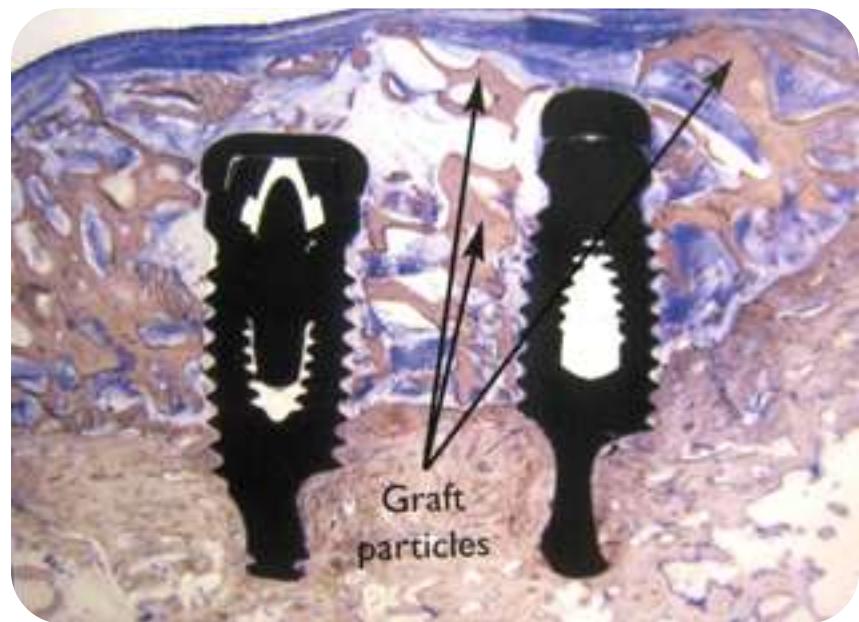


Simion et al. 2009









Group A

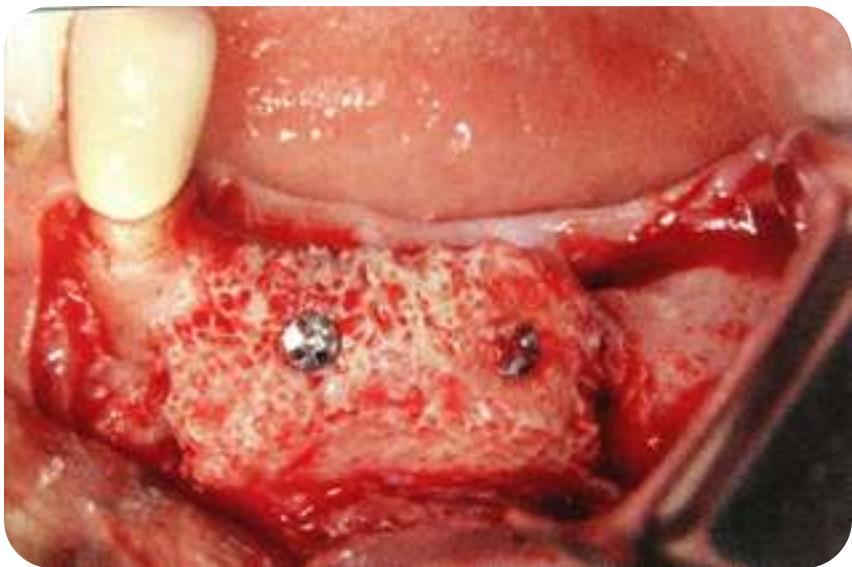


Group B



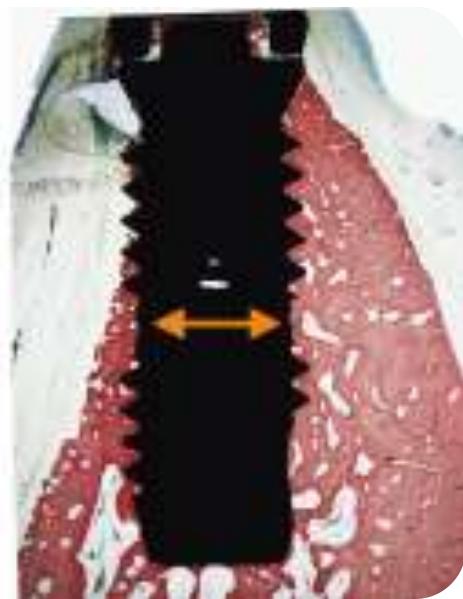
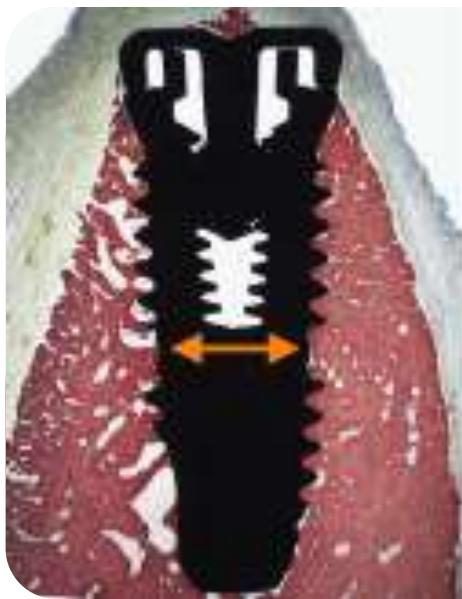
Group C





Susin et al:
J Clin Periodontol 2010; 37: 574–
581







Cell therapy

- Differentiated cell Therapy
- Mesenchymal Stem Cell Therapy
- Bone marrow aspirate therapy

Differentiated cell Therapy



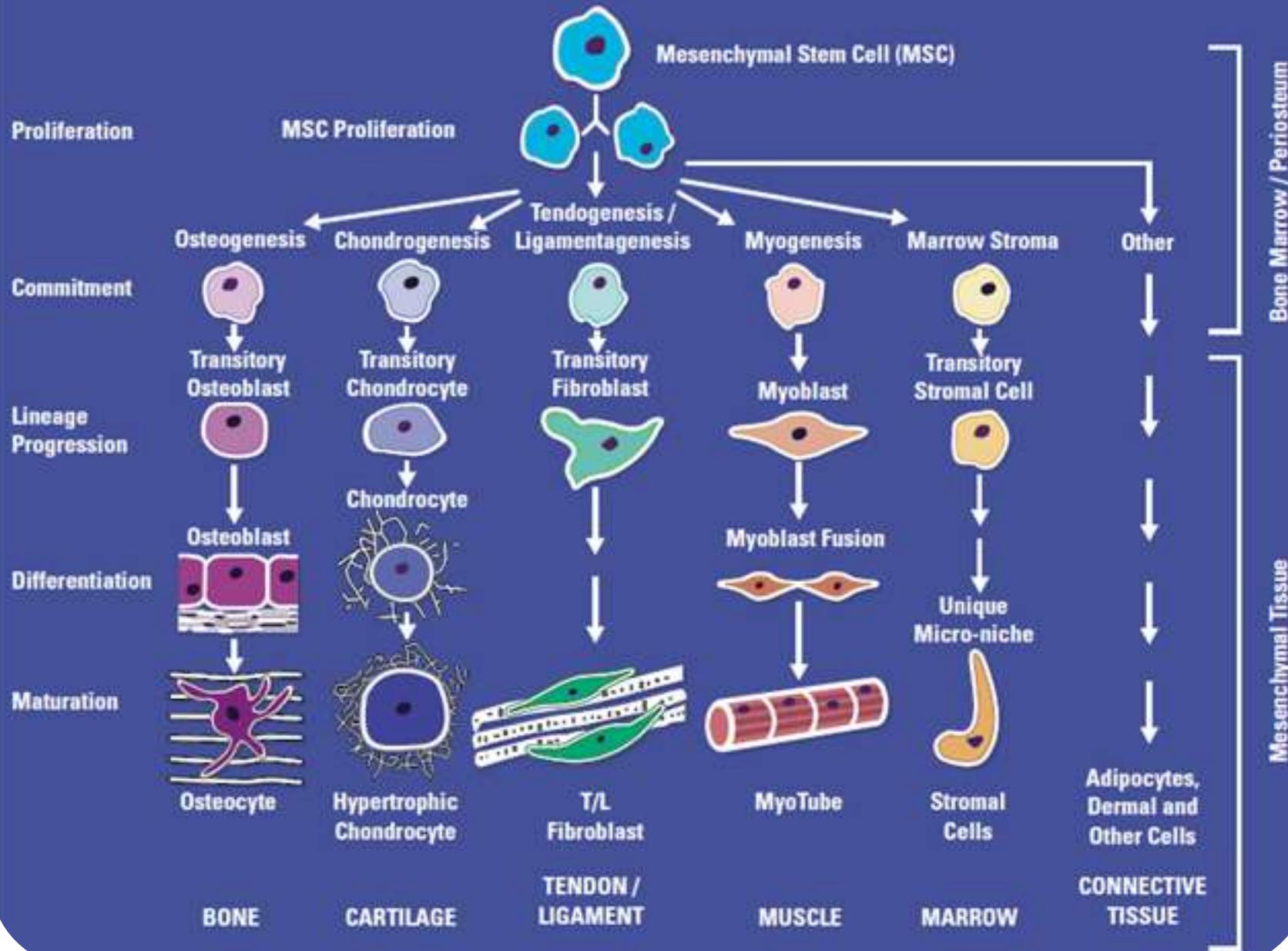
- Spontaneous tooth eruption after alveolar cleft osteoplasty using tissue-engineered bone: a case report

Oral Surg Oral Med OralPathol Oral Radiol Endod 2008;105:440-4)

Mesenchymal Stem Cell Therapy

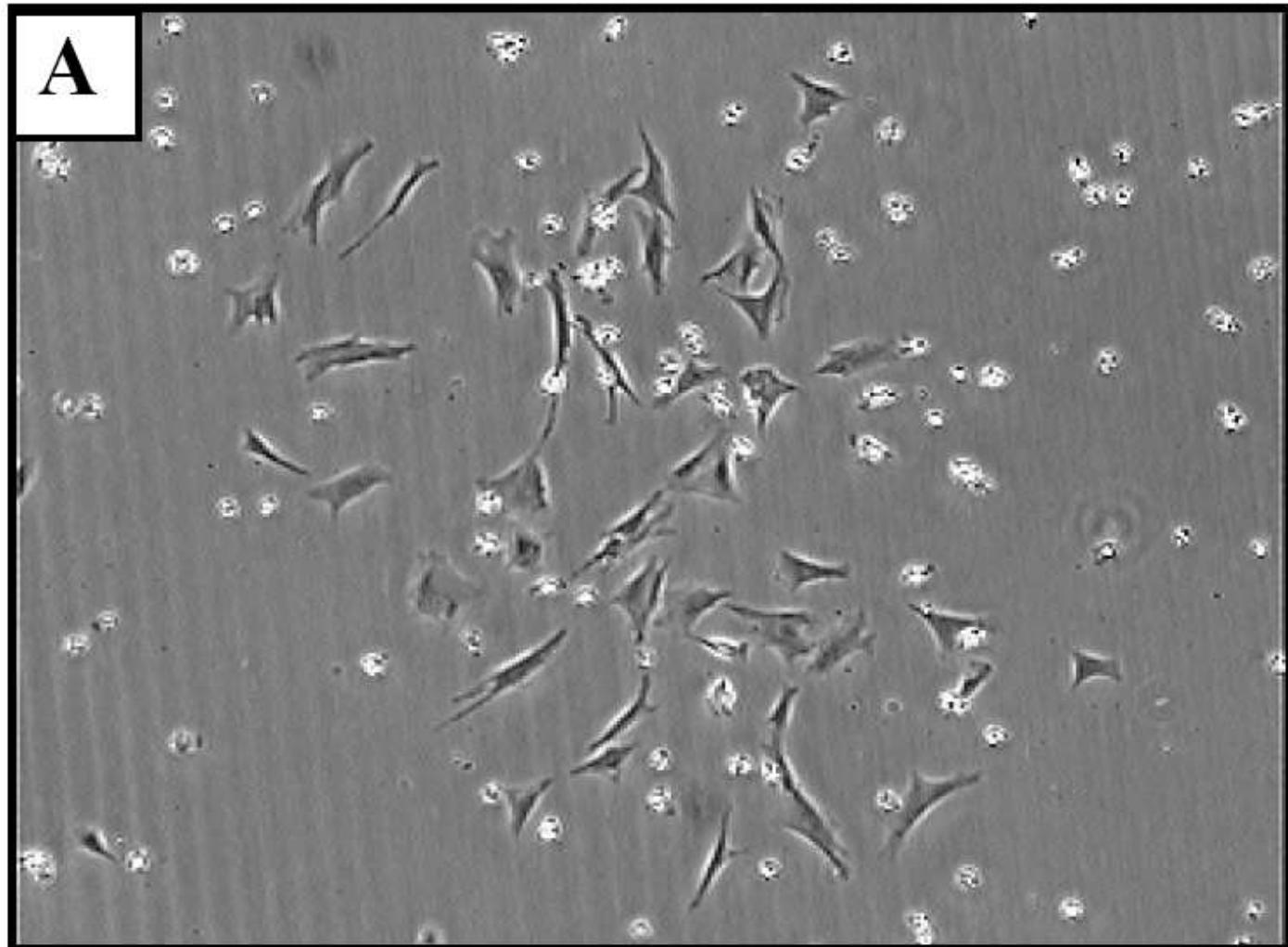
- Animal Studies
- Human Studies

THE MESENGENIC PROCESS

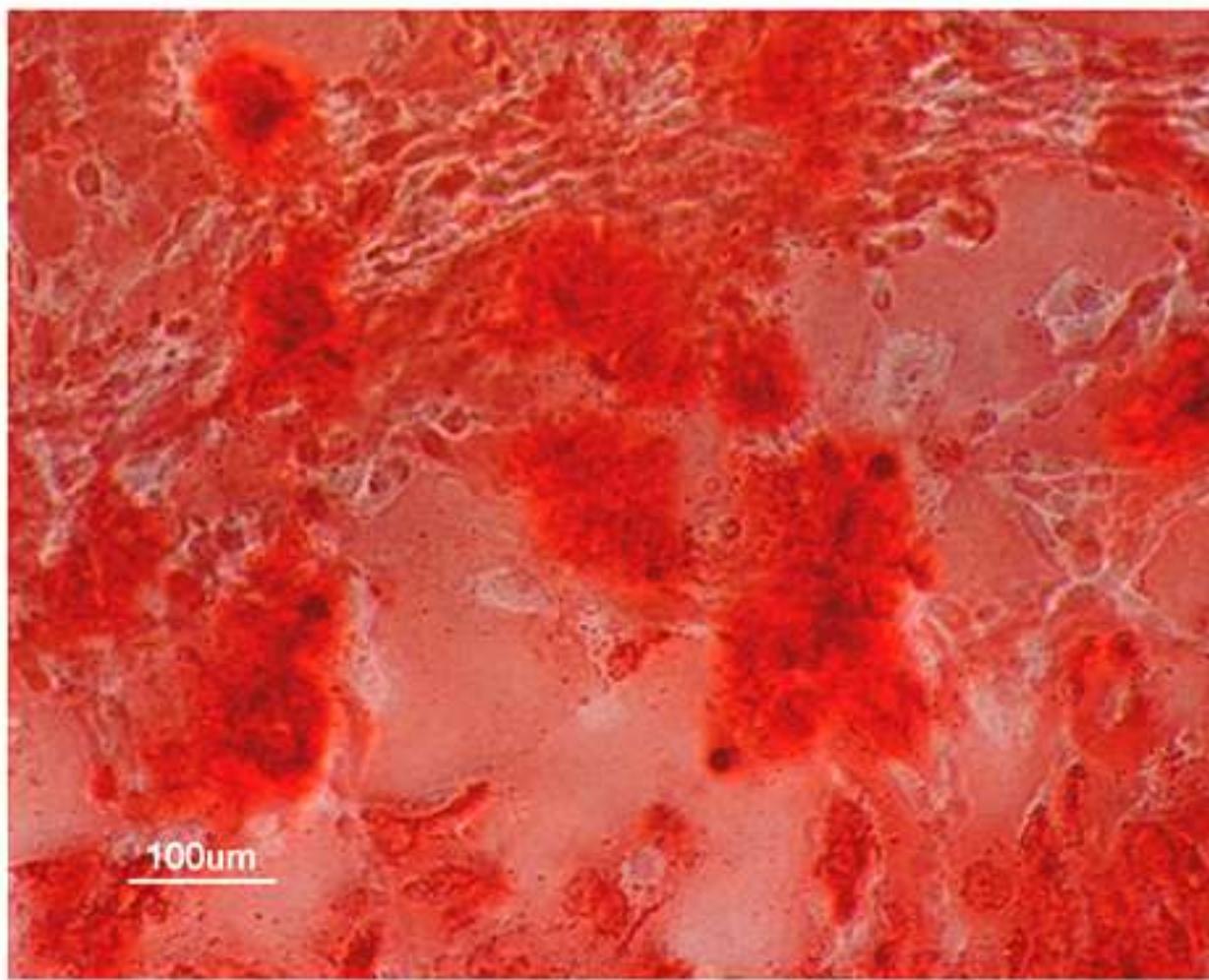




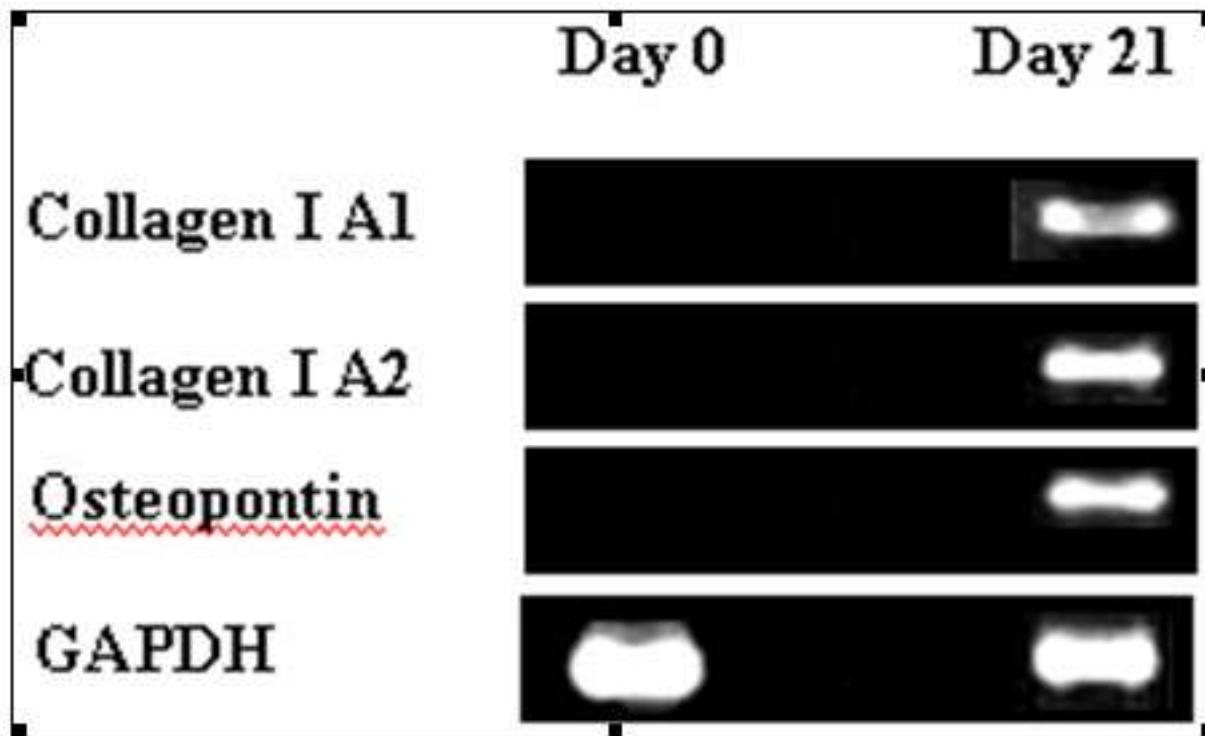
Culture



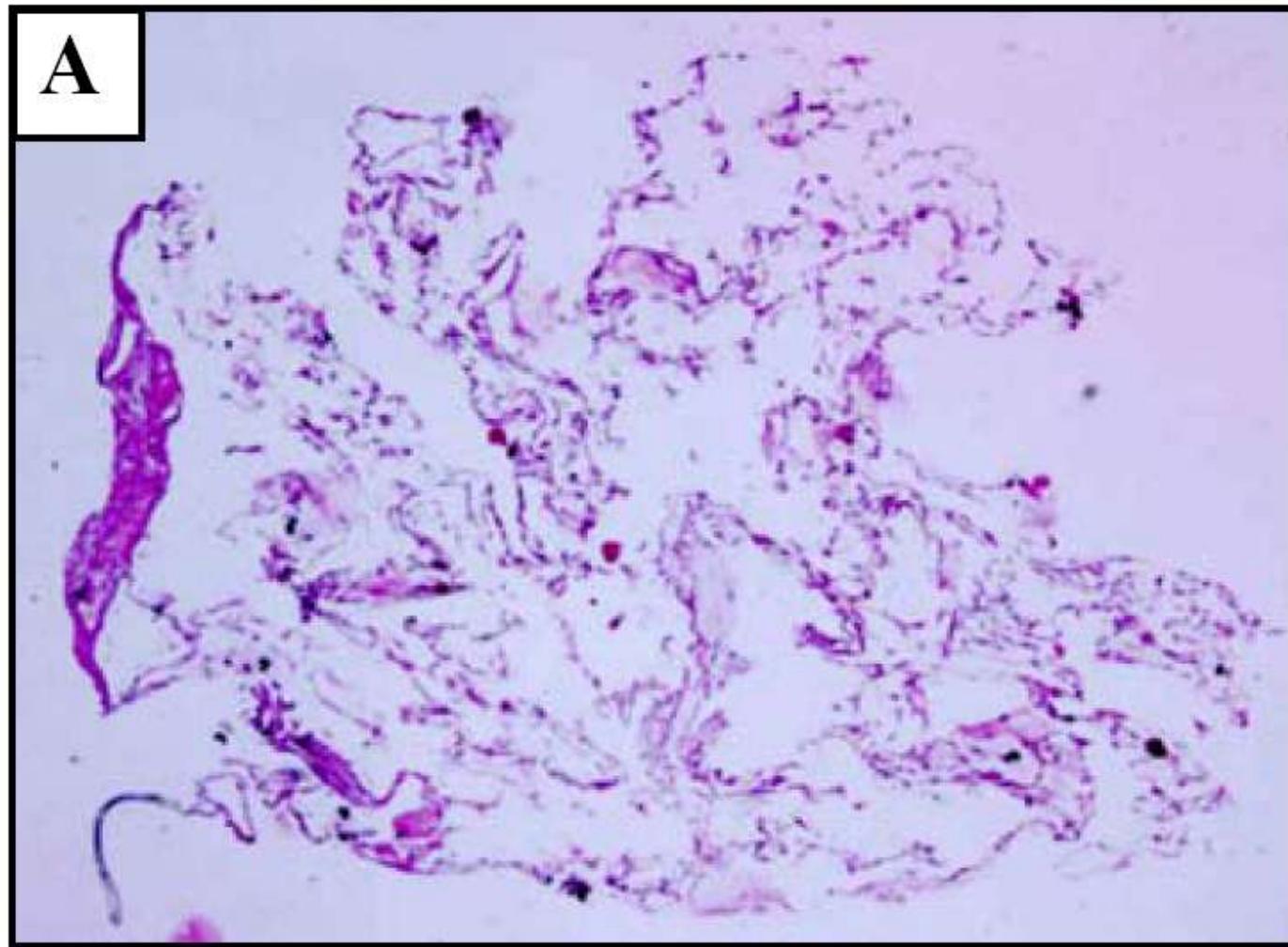
Alizarin Red Staining



RT-PCR



In vitro H&E Staining of Scaffold



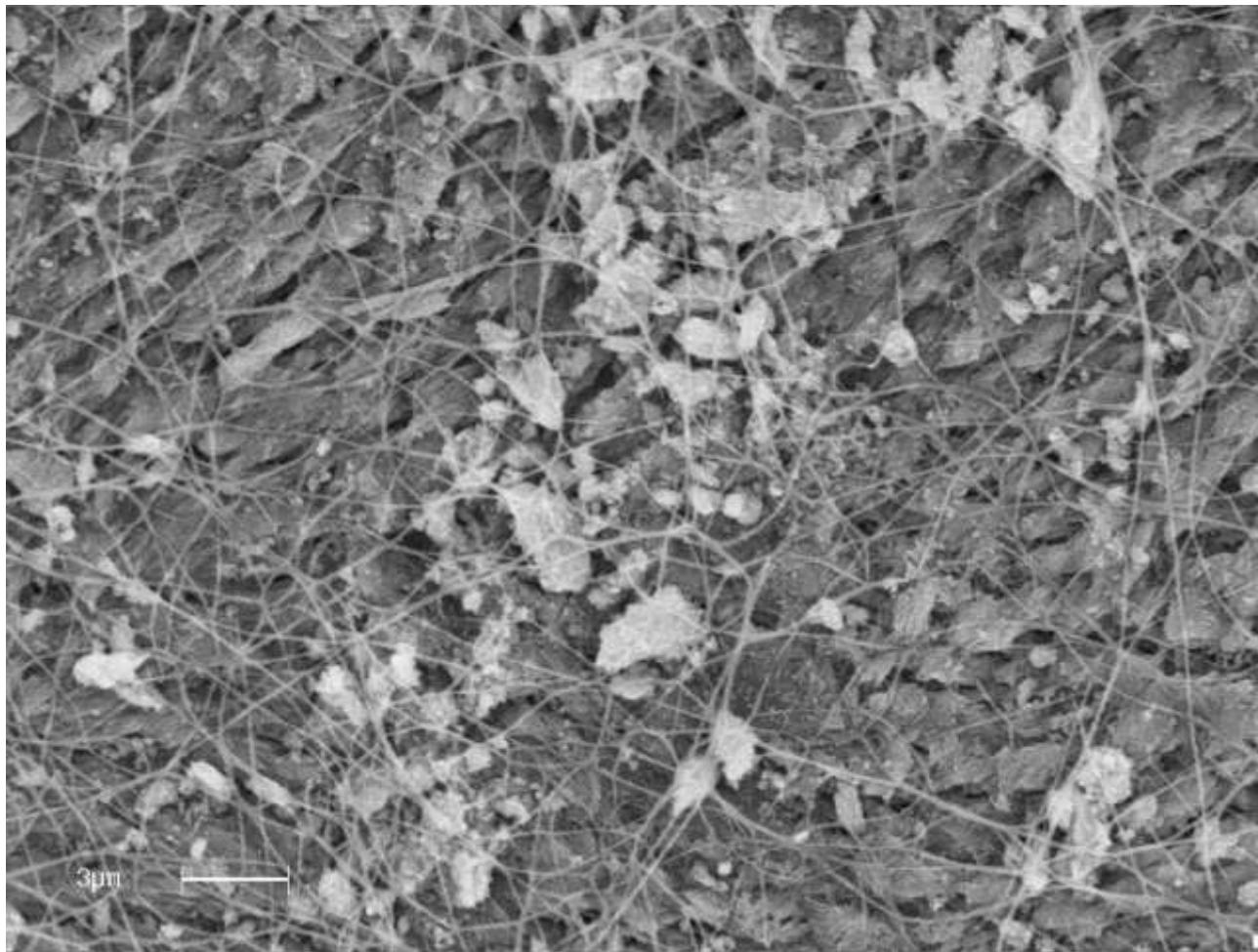
Scaffold Selection

Accelerated bone regeneration

SEM Analysis . HA/TCP



SEM Analysis: BioOss



Article

In vivo Bone Formation by Canine Mesenchymal Stem Cells Loaded onto HA/TCP Scaffolds: Qualitative and Quantitative Analysis

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Abstract

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Ectopic Bone Formation Investigation

Application of mesenchymal stem cells in dog masseter muscle

IRANIAN JOUR
VETERINARY SCI
(IJVS)
WWW.IVSA

Mesenchymal Stem Cells Loaded onto Natural Bovine Bone Minimally Enhance Ectopic Bone Formation in Canine Masseter Muscle

Mohamadreza Baghaban Eslaminejad^{1*}, PhD
Mohammad Jafarian², DMD, M.S

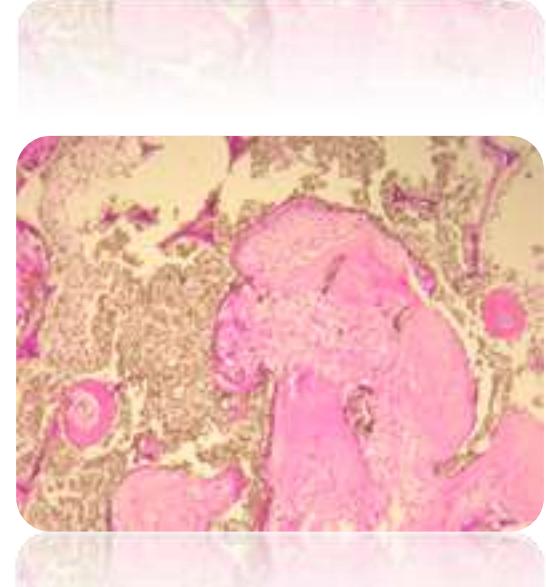
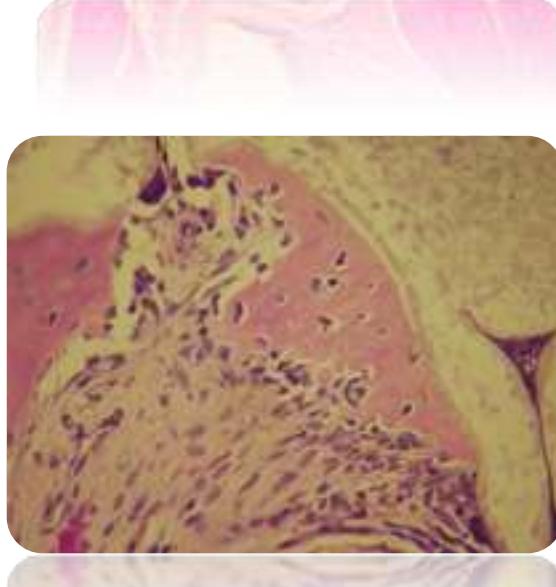
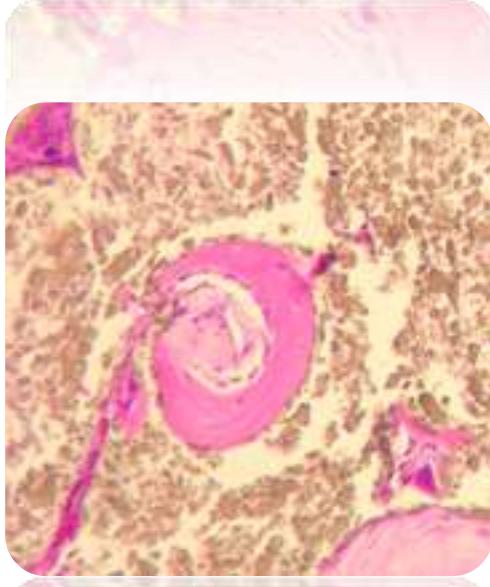
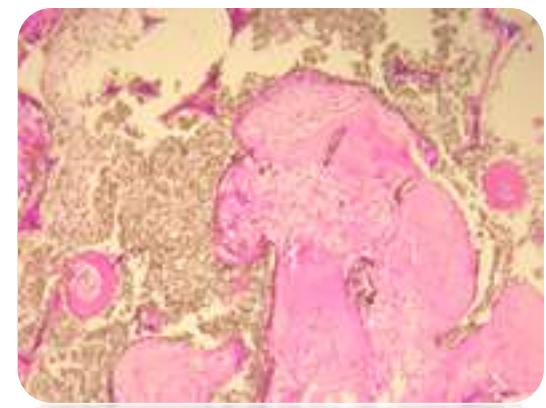
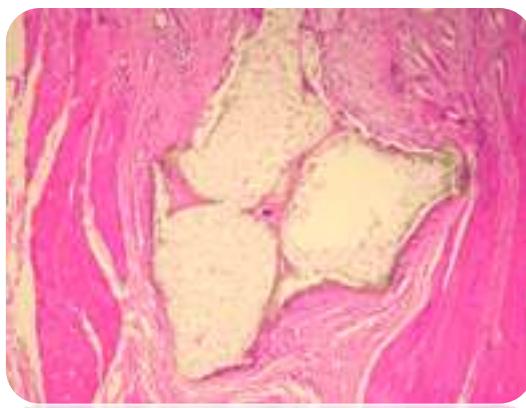
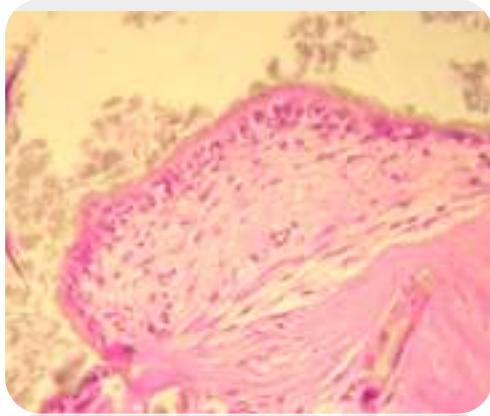
Arash Khojasteh², DMD

Fatemeh Mashhadi Abbas², DDS, MS

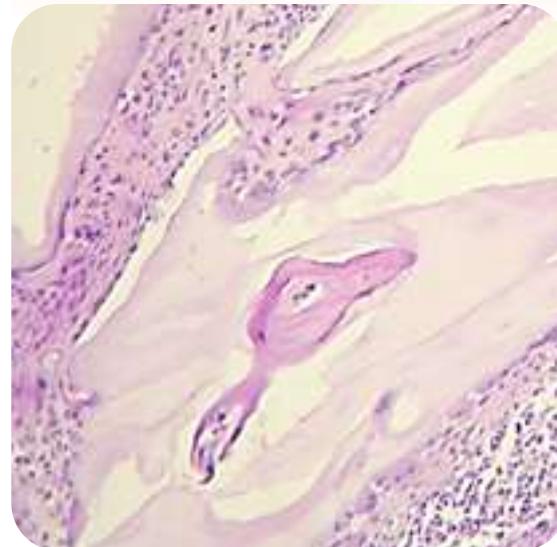
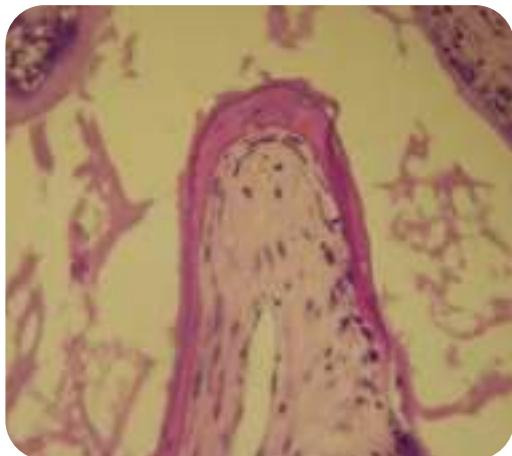
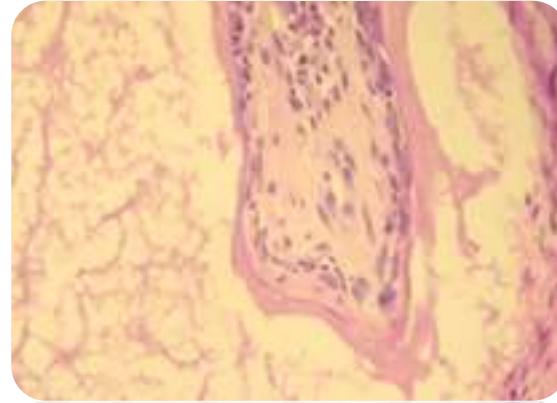
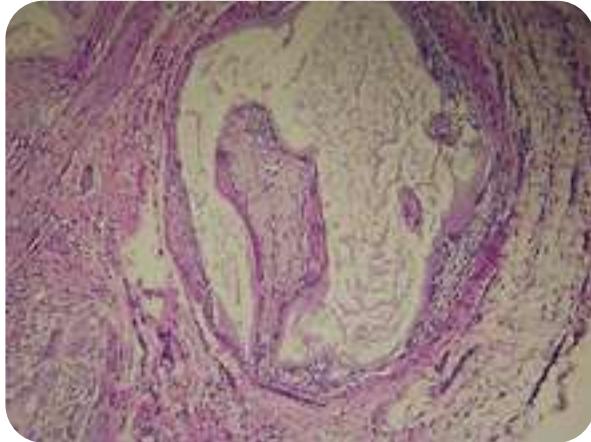
Mohammad Mehdi Dehghan³, DVSc

Bahar Houshmand⁴

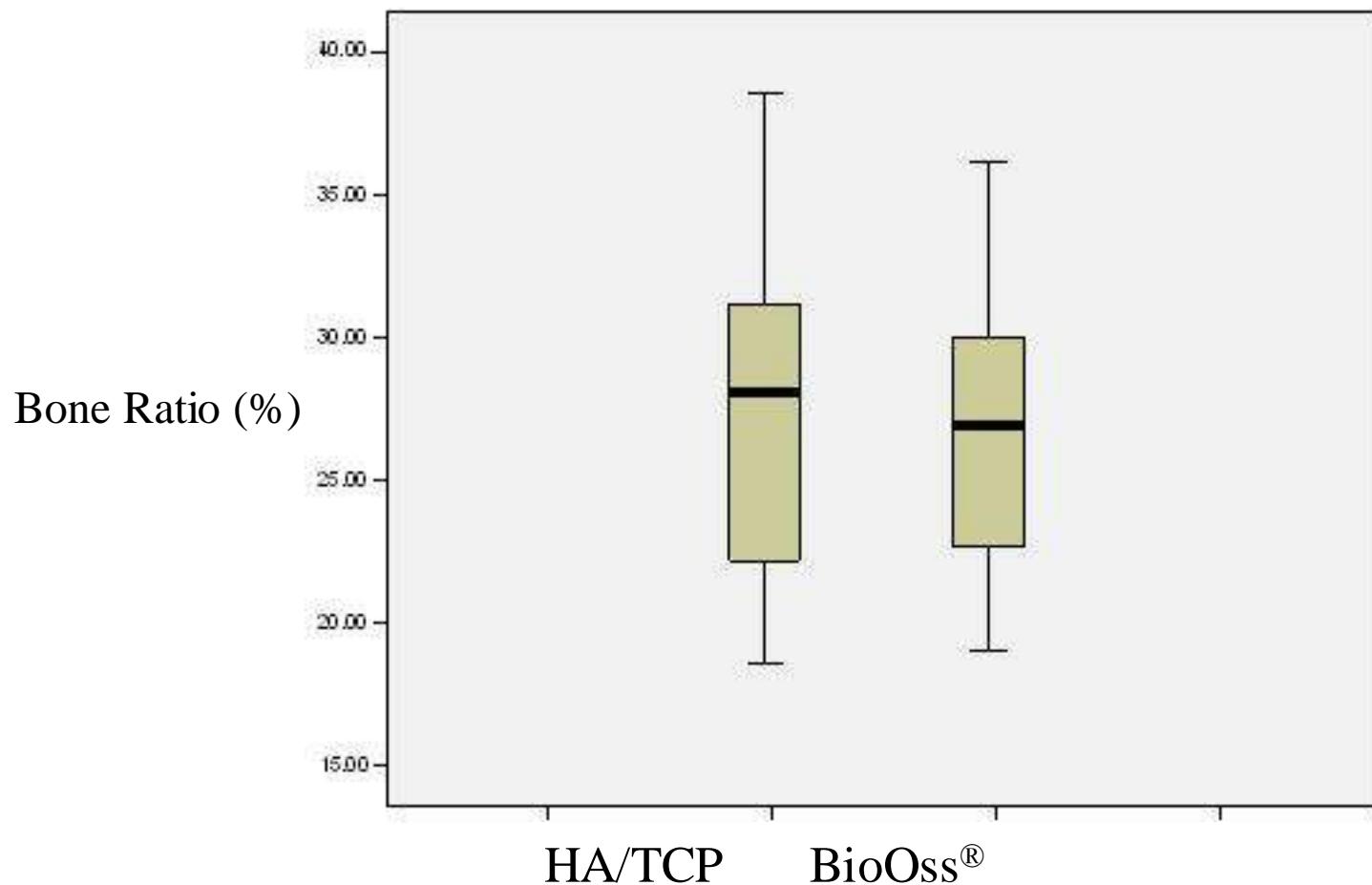
HA/TCP



BioOss®



Ectopic Bone formation in Masseter Muscle





Oral Surgery, Oral Medicine,
Oral Pathology, Oral Radiology, and
Endodontology

**mesenchymal stem cells-directed bone
formation in the dog mandible: a comparison between
calcium phosphate and natural bone mineral**

Rian, DMD, MS,^a Mohamadreza Baghaban Eslaminejad, PhD,^b
, DMD,^c Fatemeh Mashhadi Abbas, DDS, MS,^d
idi Dehghan, DVM, PhD,^e Rahele Hassanizadeh, DDS,^f and
id, DDS,^f Tehran, Iran
^a UNIVERSITY OF MEDICAL SCIENCES, ROYAN INSTITUTE, AND UNIVE

MSCs induced bone formation in Bony defects

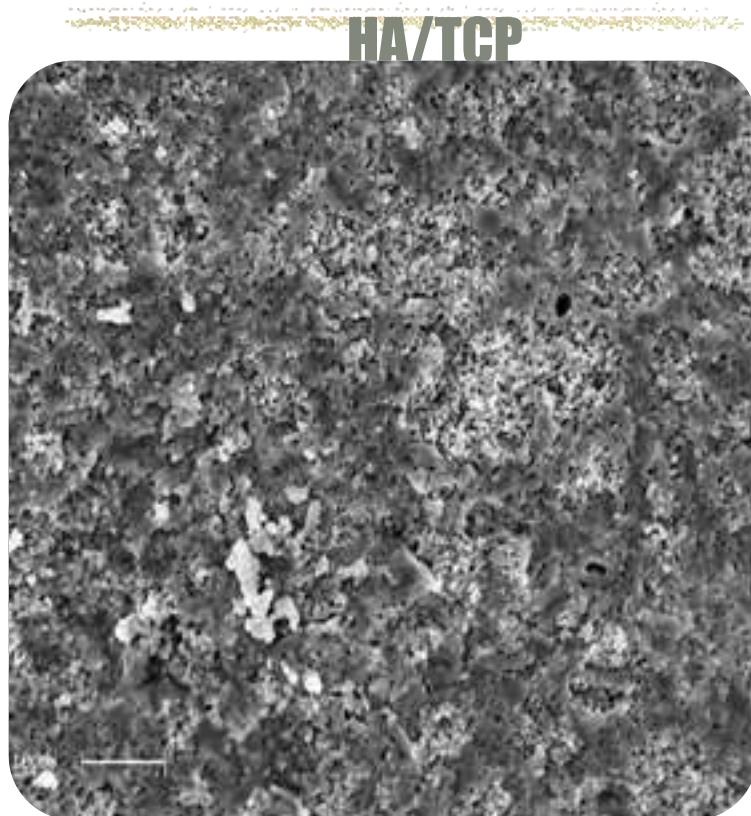
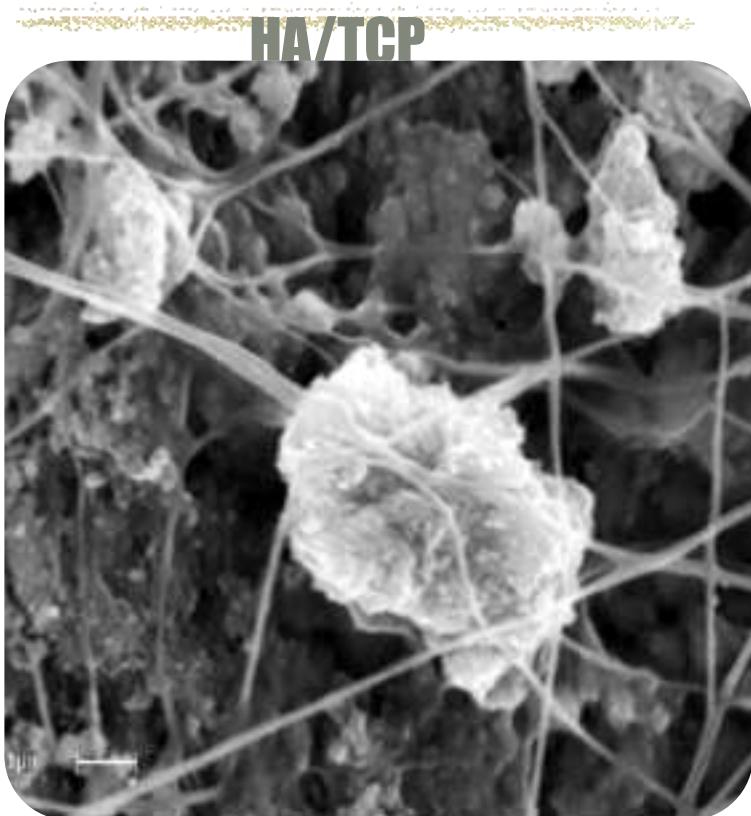
Application of MSCs in 10 mm through and Through Defects in dog mandible

Marrow-derived mesenchymal stem cells-directed bone regeneration in the dog mandible: A comparison between biphasic calcium phosphate and natural bone mineral

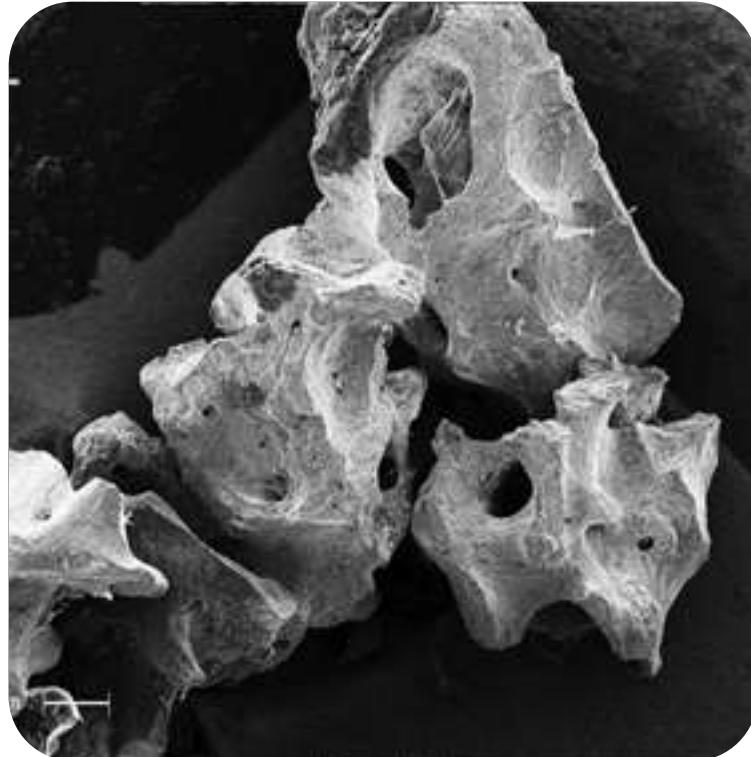
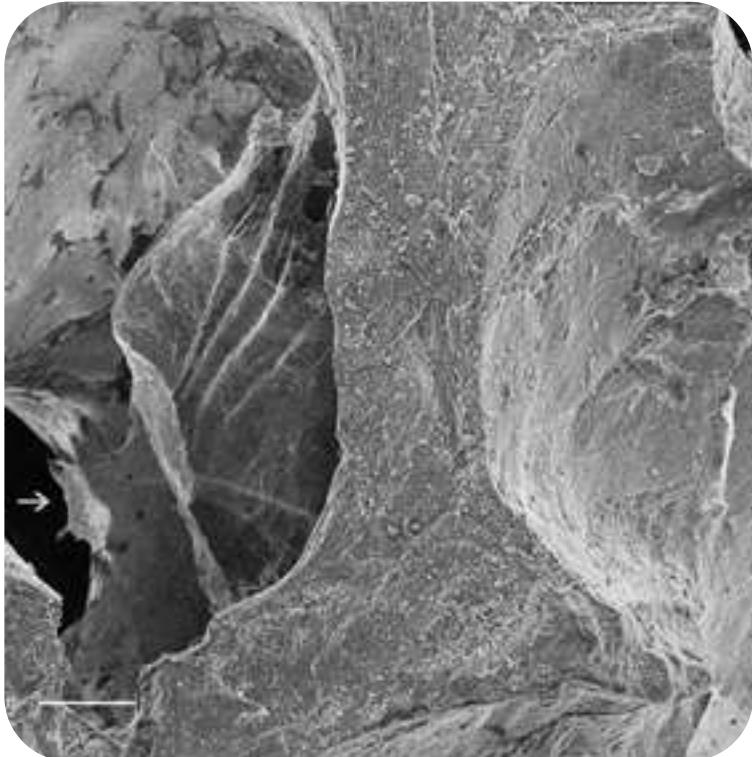
Jafarian M, Eslaminejad MB, Khojasteh A, Mashhadi Abbas F, Dehghan MM, Hassanizadeh R, Houshmand B.

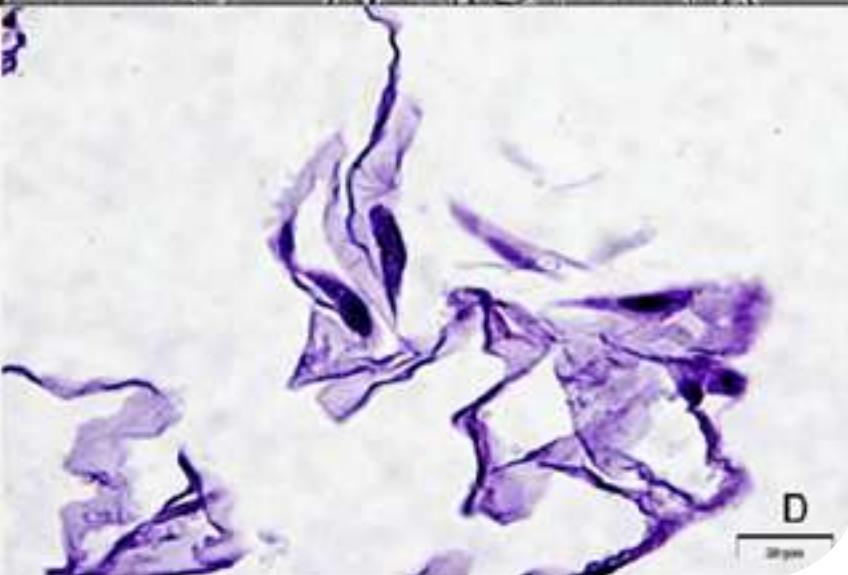
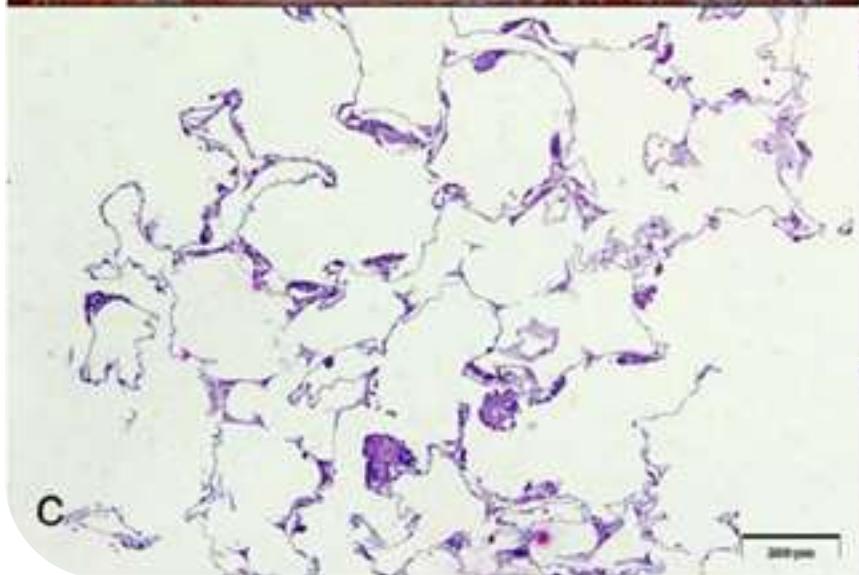
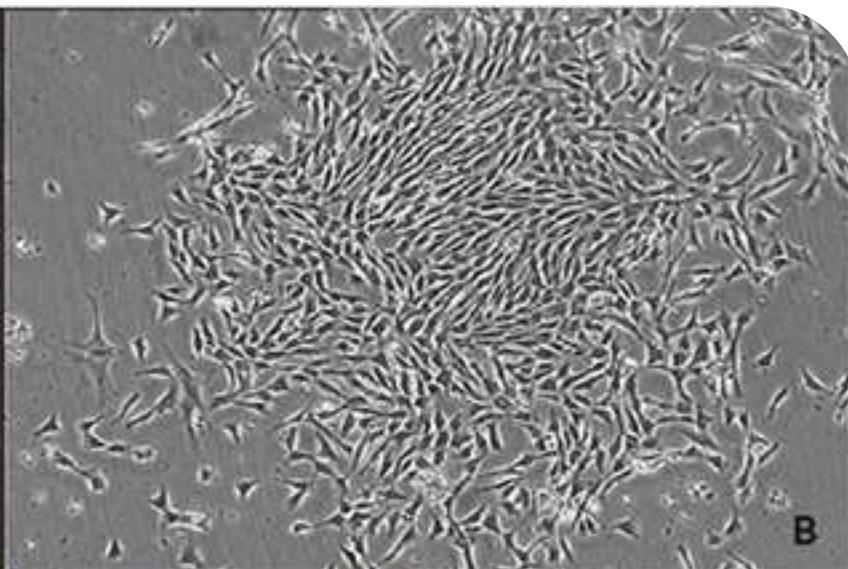
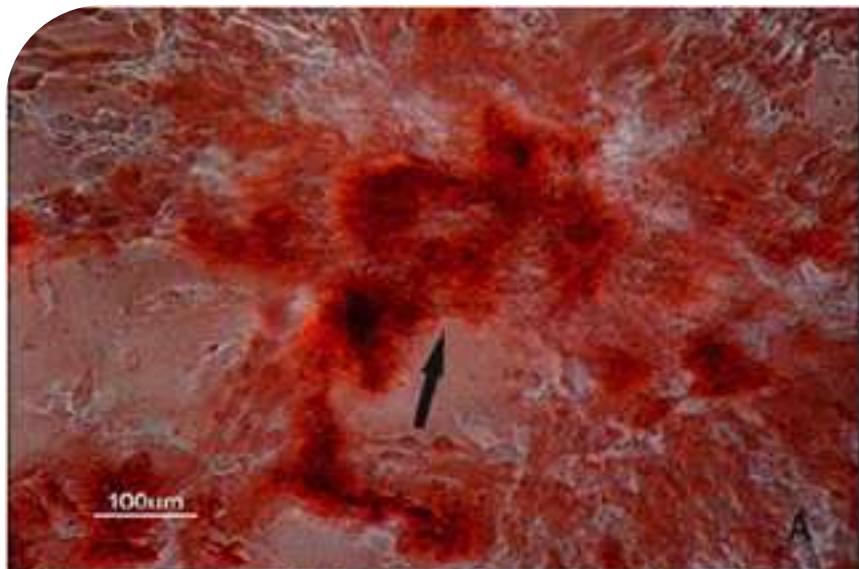
Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008 May;105(5):e14-24.

Scanning electron microscopy analysis



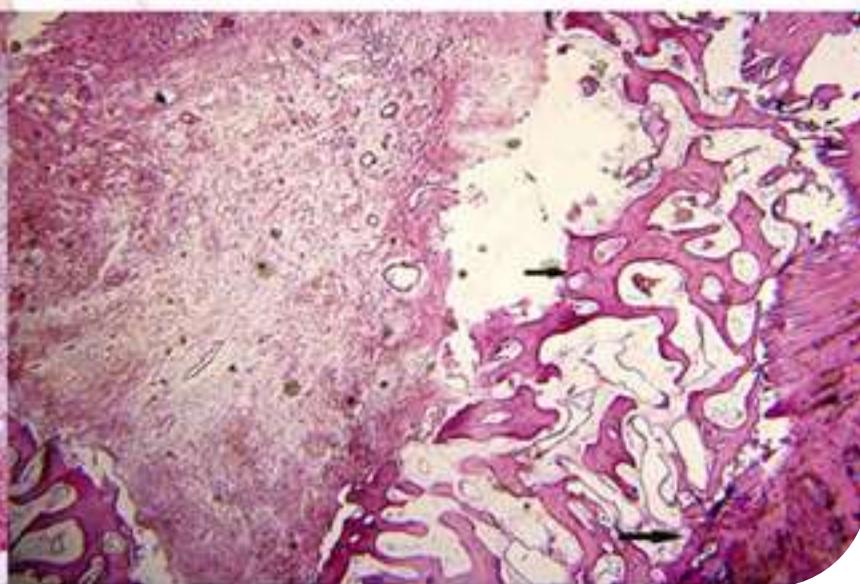
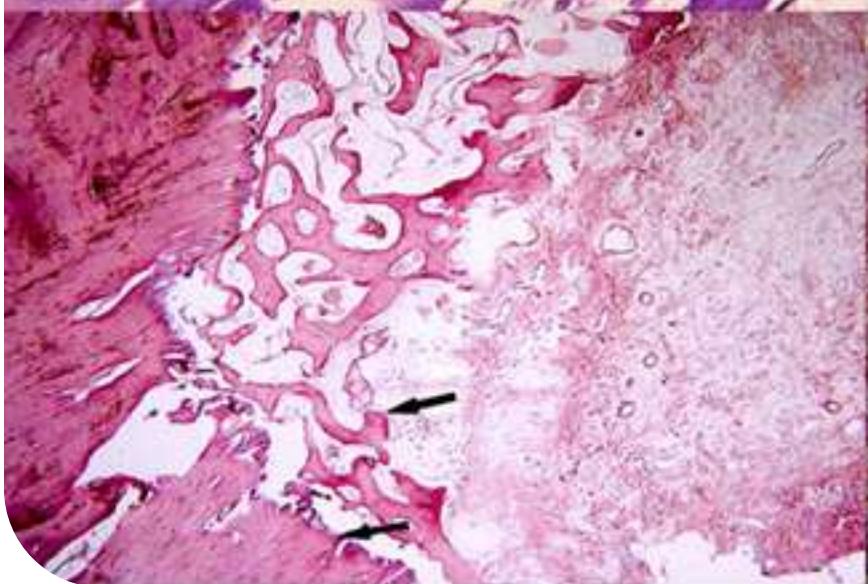
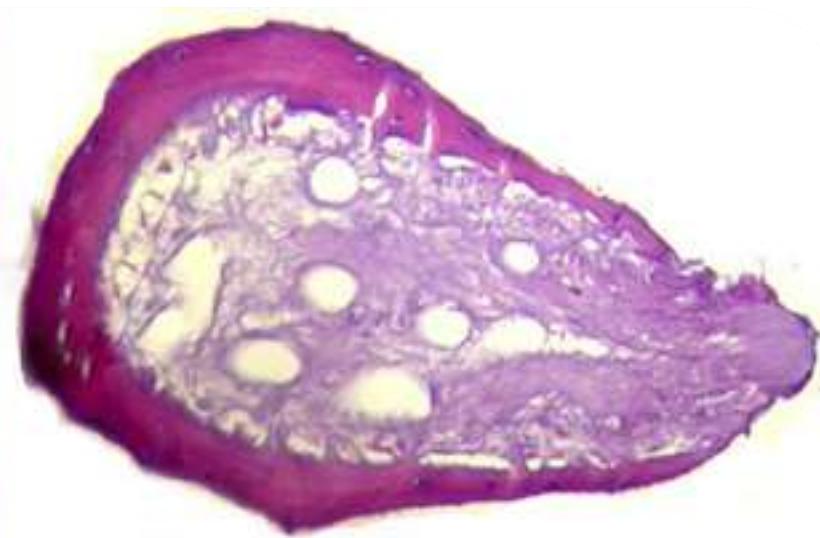
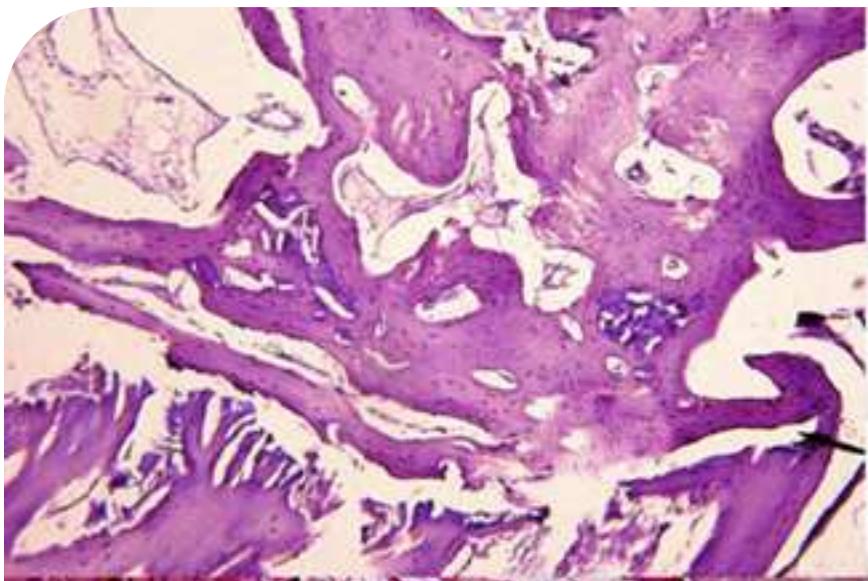
Scanning electron microscopy analysis



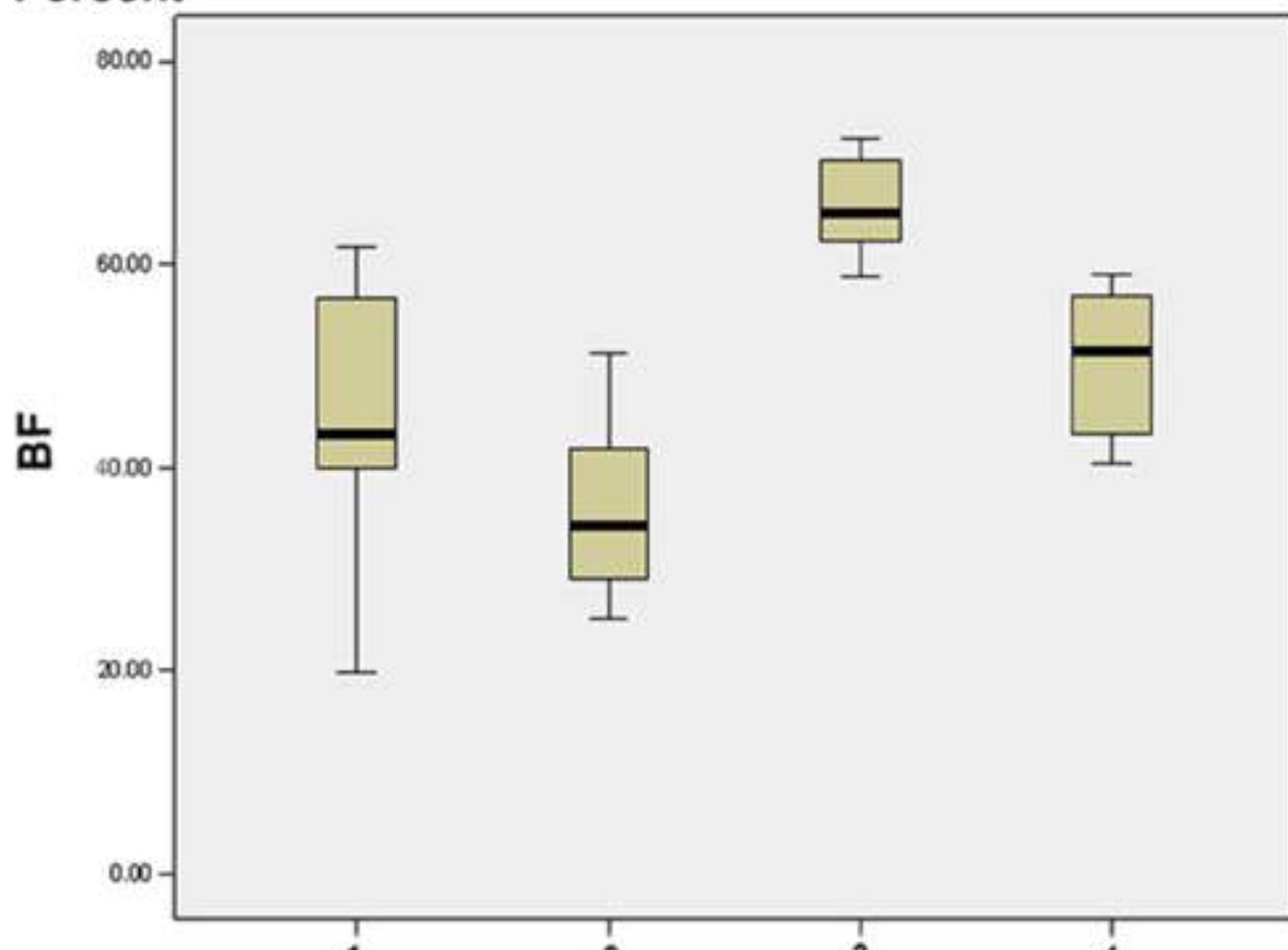




Dr Jafarian, Dr Khojasteh, Dr Hassanzadeh

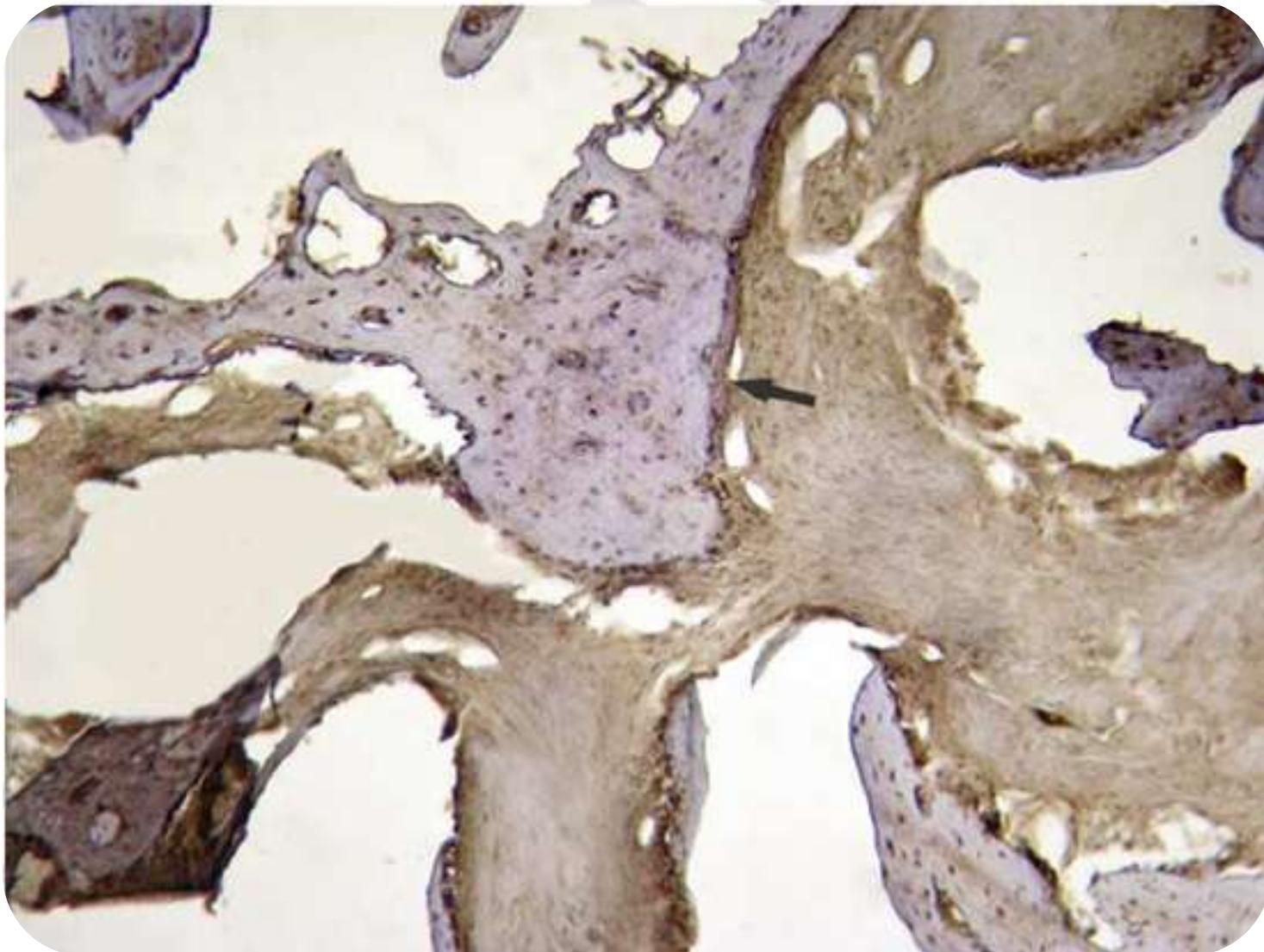


Percent



Groups

Groups





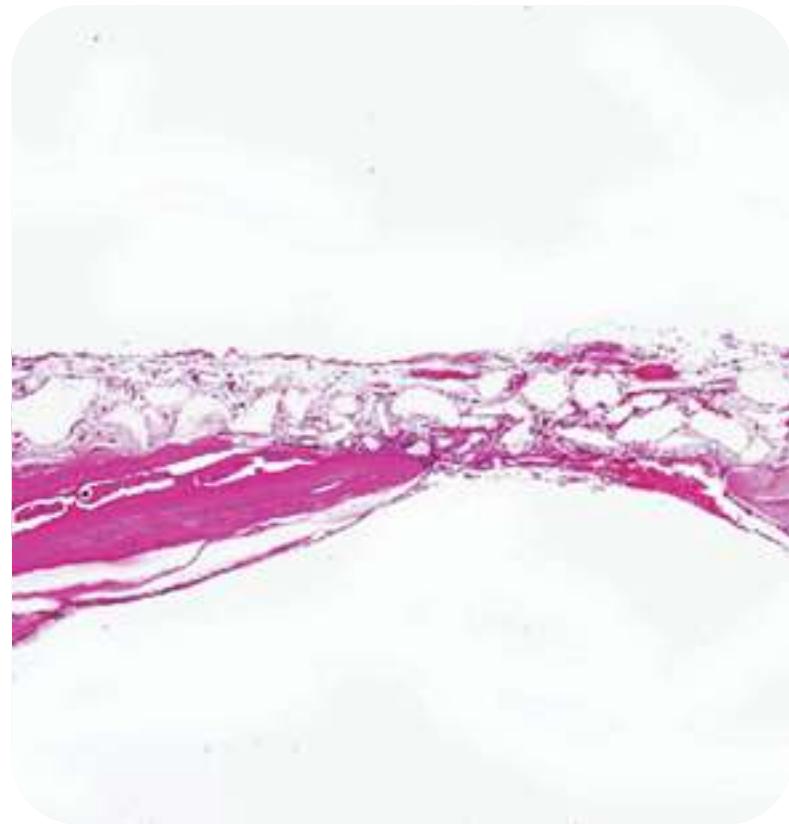
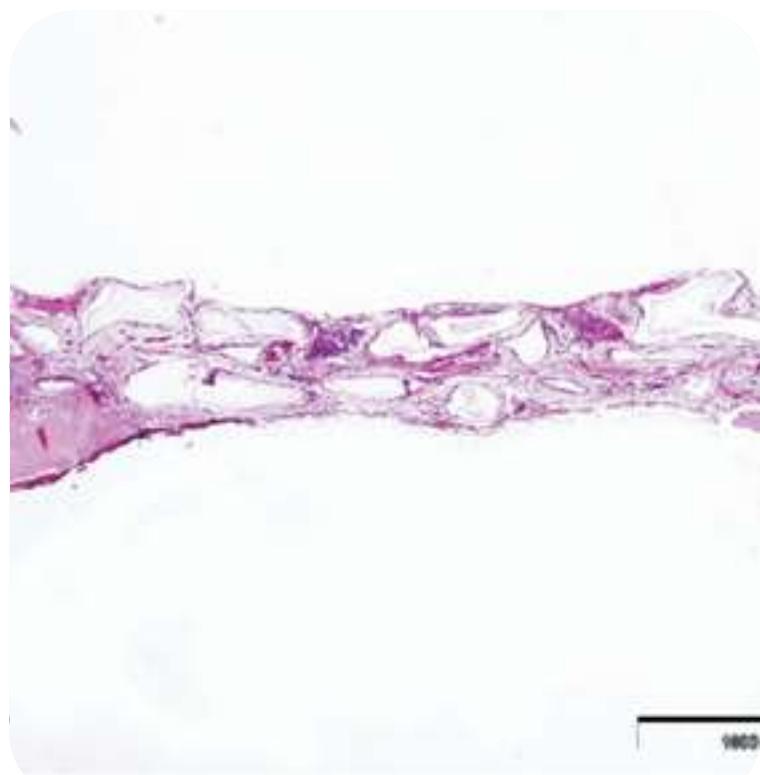
Oral Surgery, Oral Medicine,
Oral Pathology, Oral Radiology, and
Endodontology

Mesenchymal stem cells enhance bone regeneration in rat calvarial critical size defects more than platelete-rich plasma
Arash Khojasteh, DMD,^a Mohammadreza Baghban Eslaminejad, PhD,^a Hamid Nazarian, MSc,^b
Tehran, Iran
SHAHID BEHESHTI UNIVERSITY OF MEDICAL SCIENCES AND ROYAN INSTITUTE

Mesenchymal stem cells enhance bone regeneration in rat calvarial critical size defects more than platelete-rich plasma

Arash Khojasteh, Mohammad reza Baghban Eslaminejad, Hamid Nazarian,

Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008 Sep;106(3):356-62;



MSCs more than PRP

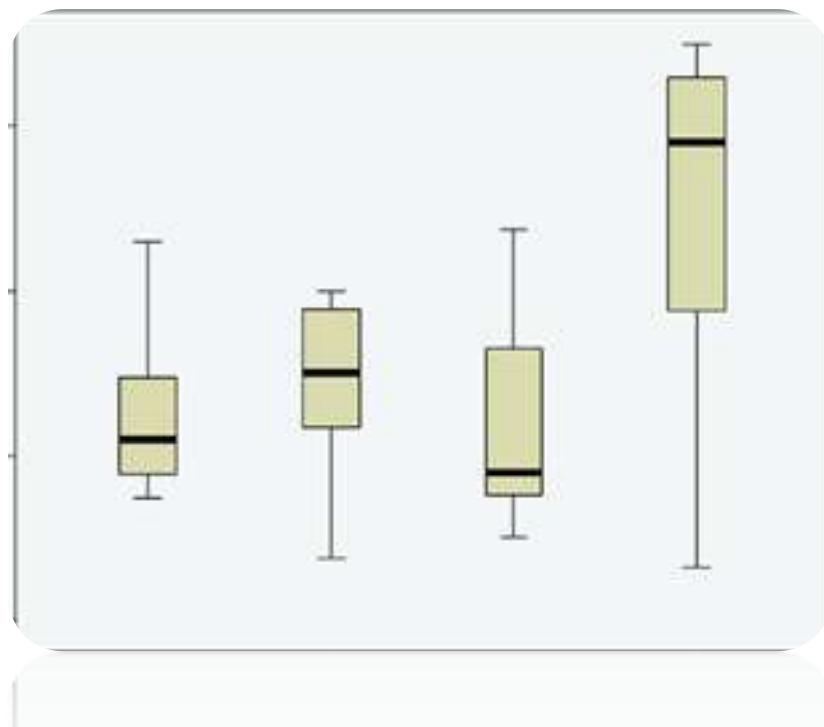


Table I. Mean of the bone length in the rat calvaria

<i>Group</i>	<i>Mean, mm</i>	<i>Standard Deviation</i>
Bio-Oss + PRP	1.27	0.56
Bio-Oss + MSCs	1.44	0.55
Kasios + PRP	1.21	0.7
Kasios + MSCs	2.53	1.02

Sinus augmentation using human mesenchymal stem cells loaded into a beta tricalcium phosphate/hydroxyapatite scaffold

Shayesteh YS, Khojasteh A,
Soleimani M, Alikhasi M,
Khoshzaban A, Ahmadbeigi N

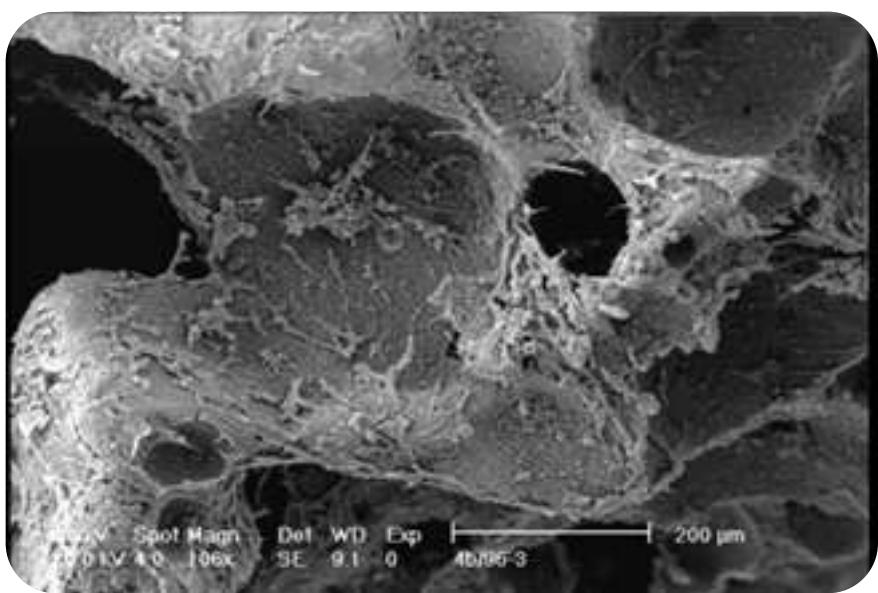
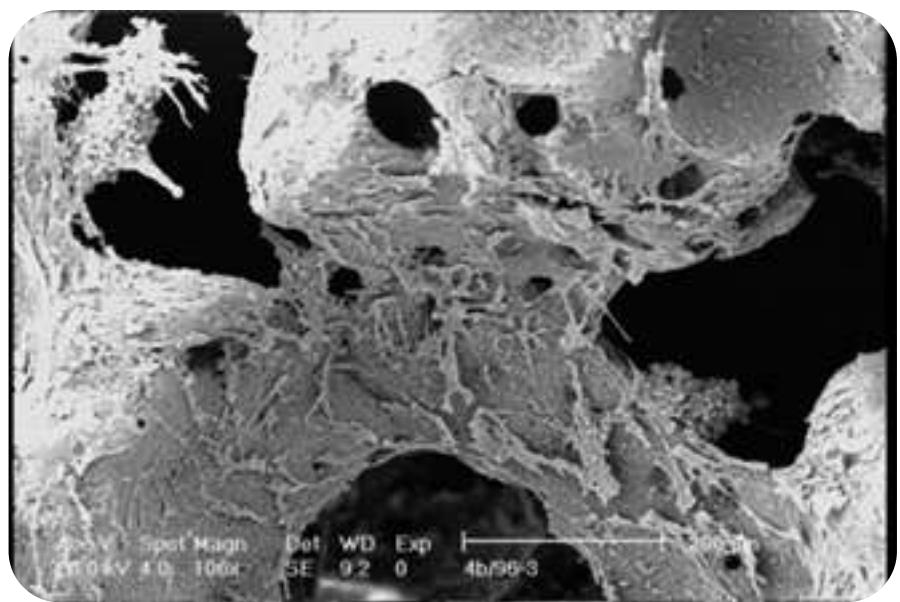
Oral Surgery, Oral Medicine,
Oral Radiology, and
Oral Pathology. Oral
Pathology
Oral Radiology
Endodontontology
ORAL AND MAXILLOFACIAL IMPLANTS

Vol. 106 No. 2 August 2008

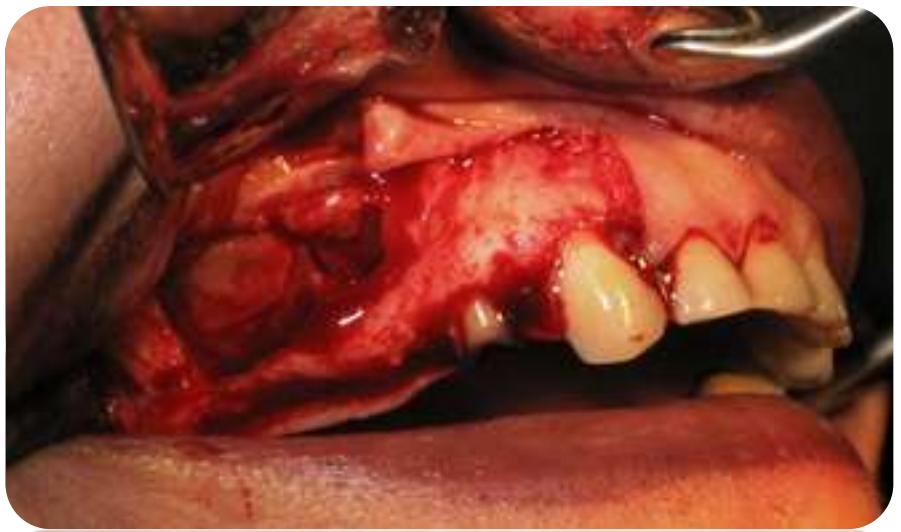
Oral augmentation using human mesenchymal stem cells loaded
into a β -tricalcium phosphate/hydroxyapatite scaffold

Sinus augmentation using human mesenchymal stem cells loaded
into a β -tricalcium phosphate/hydroxyapatite scaffold

Yadollah Soleimani, DDS,^a Arash Khojasteh, DMD,^b Masoud Soleimani, PhD,^c Shahrooz Khoshzaban, DDS,^d and Naser Ahmadbeigi, PhD,^e TEHRAN MOADERES UNIVERSITY, AND STEM CELL TECHNOLOGY CENTER, TEHRAN, IRAN

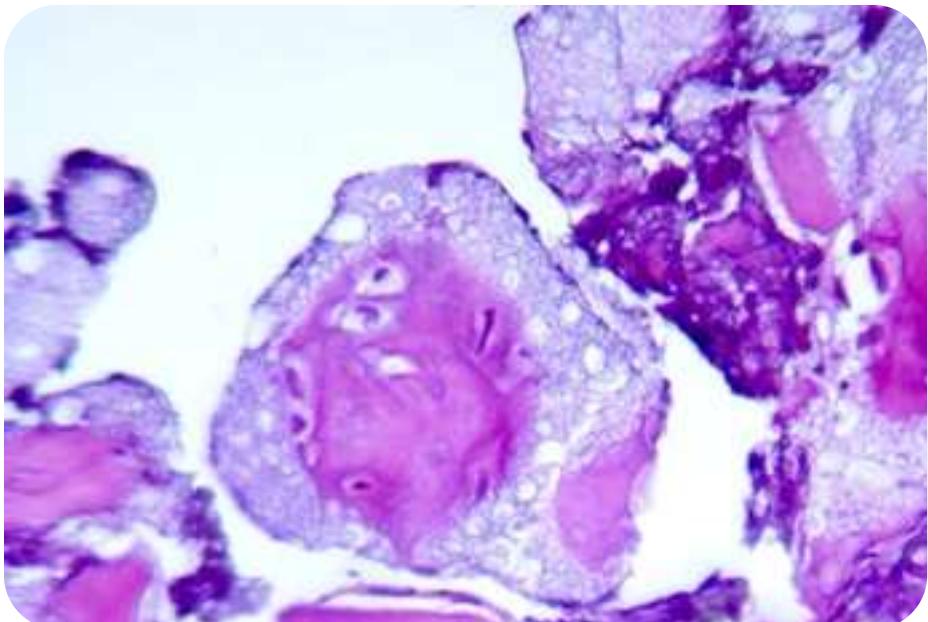










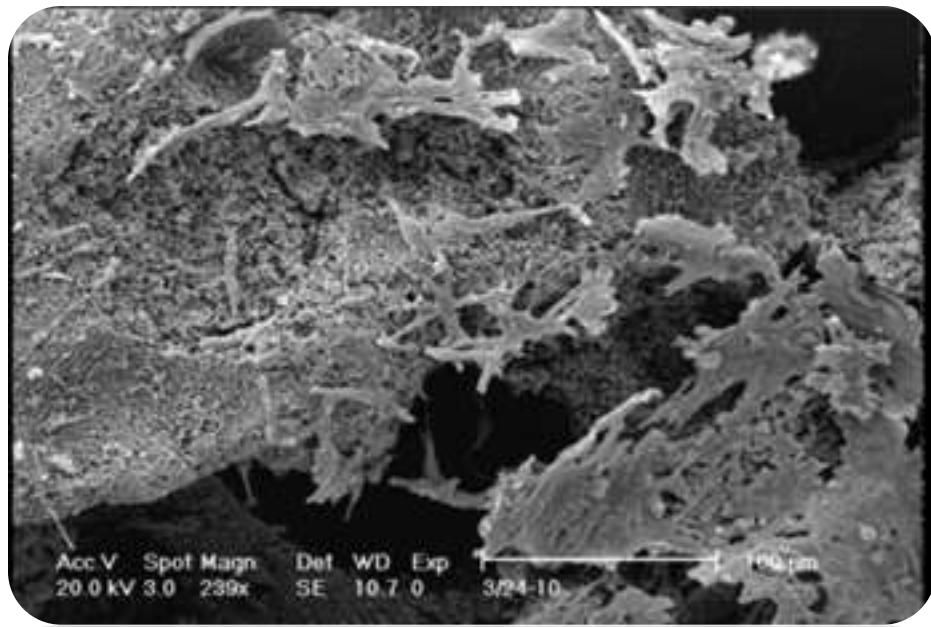
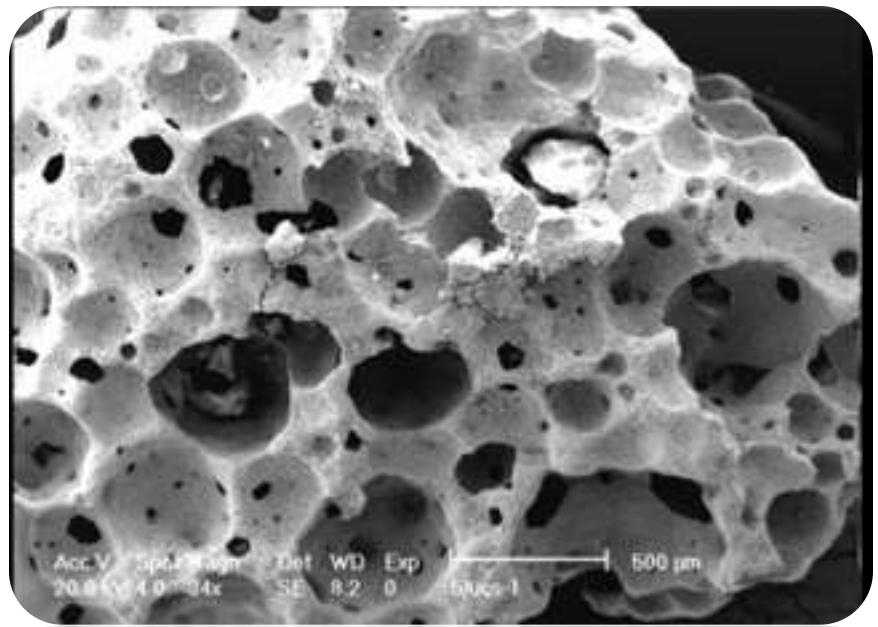


Secondary repair of alveolar clefts using human mesenchymal stem cells

Hossein Behnia, Arash
Khojasteh, Masoud Soleimani,
Azita Tehranchi,
Ahad Khoshzaban, Saeed Hidari
Keshel, Reza Atashi, PhD

Secondary repair of alveolar clefts using human mesenchymal stem cells

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A

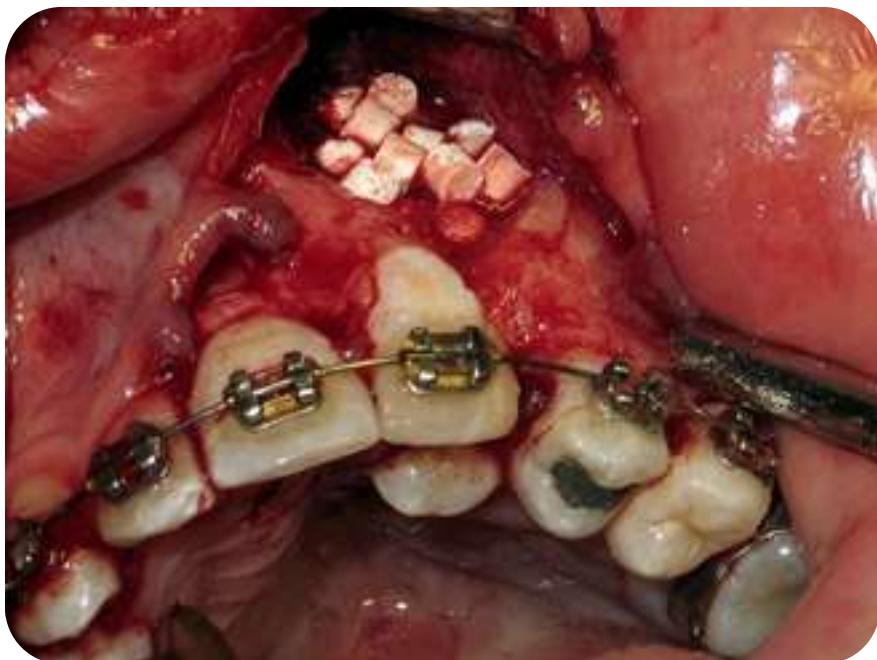


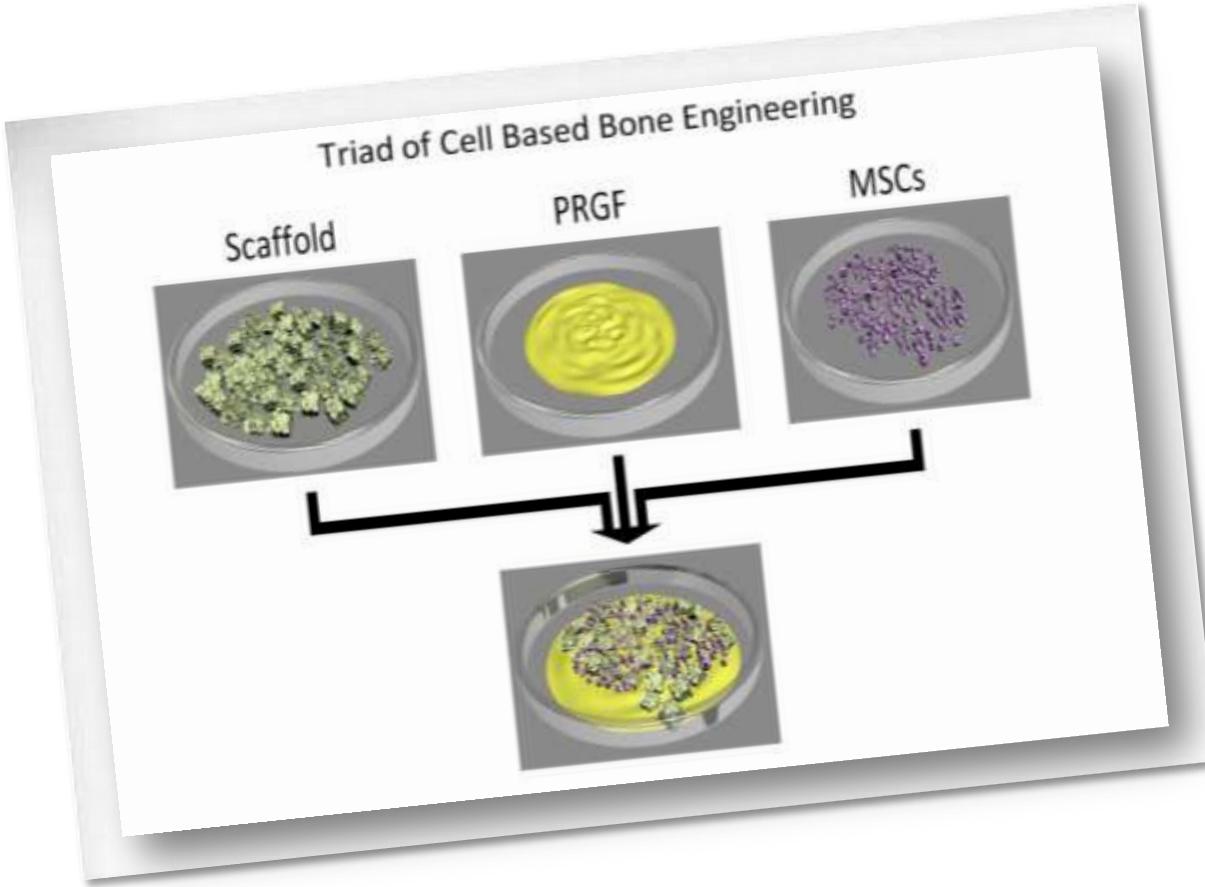
B



C

25%-34% Bone fill



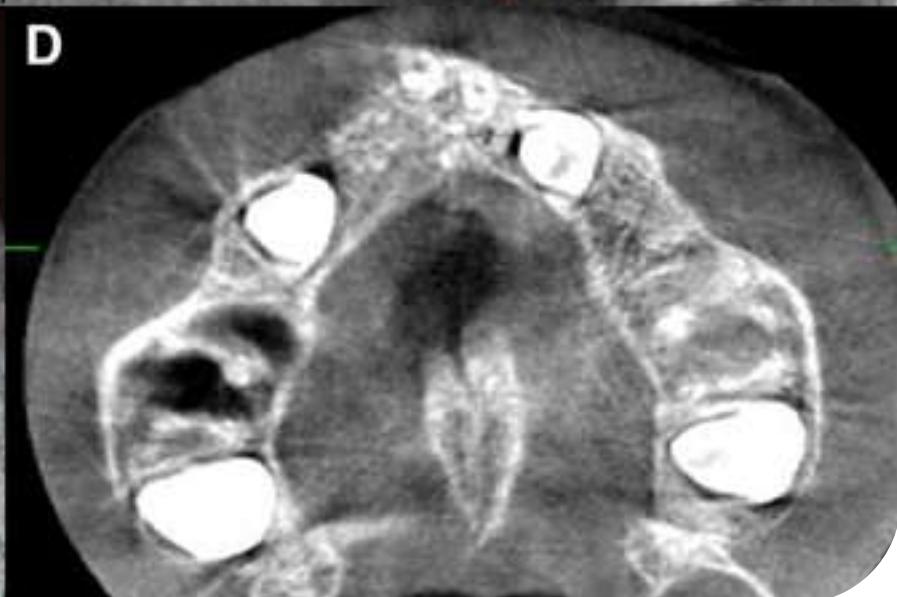
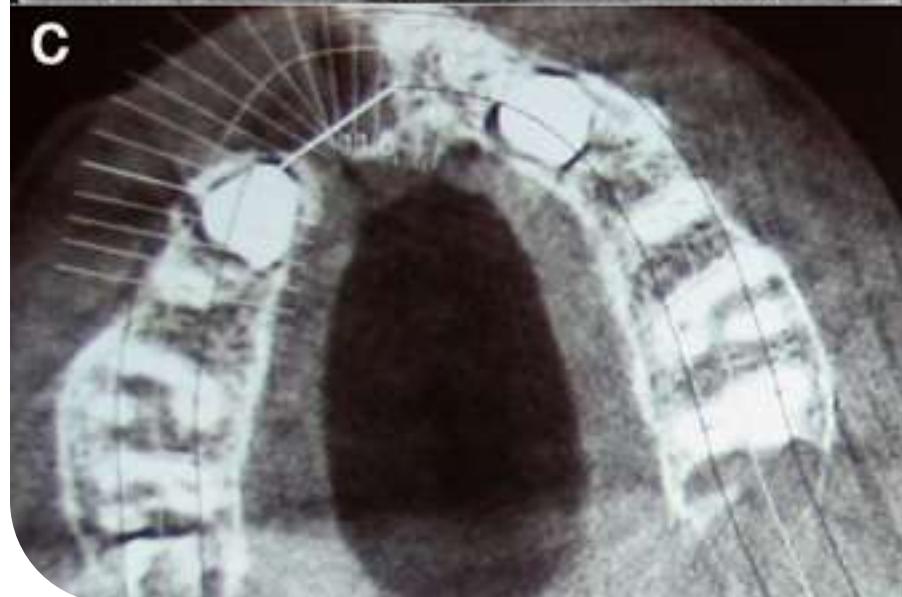


Triad of Tissue Engineering

JCMF, 2011





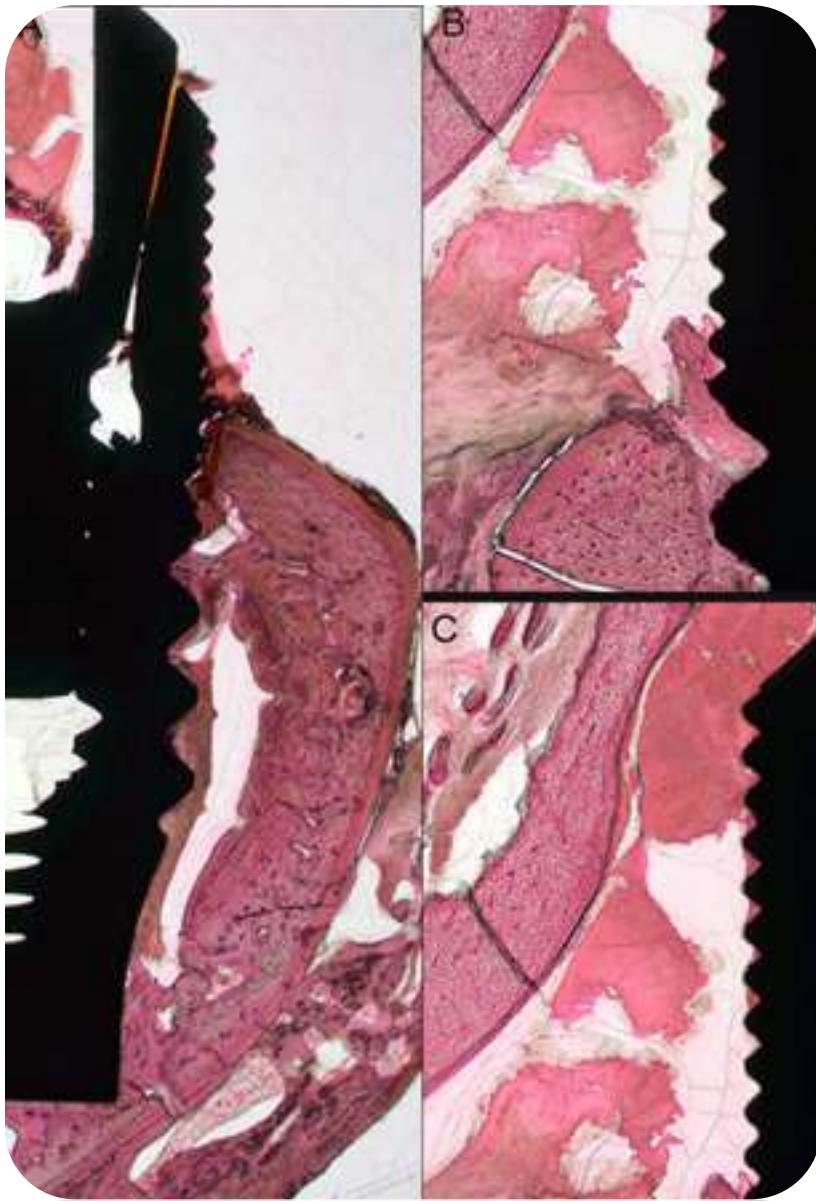


Gender	Defect Type	Age at surgery (Y.O)	3 months postoperative bone volume (%)
F	Right PMC	13	54.8
F	Right PMC	8	50.8
	Left PMC		48.3
M	Right PMC	9	51.2
		10 (Mean)	51.3 (Mean)

J.Oral Implantology 2011



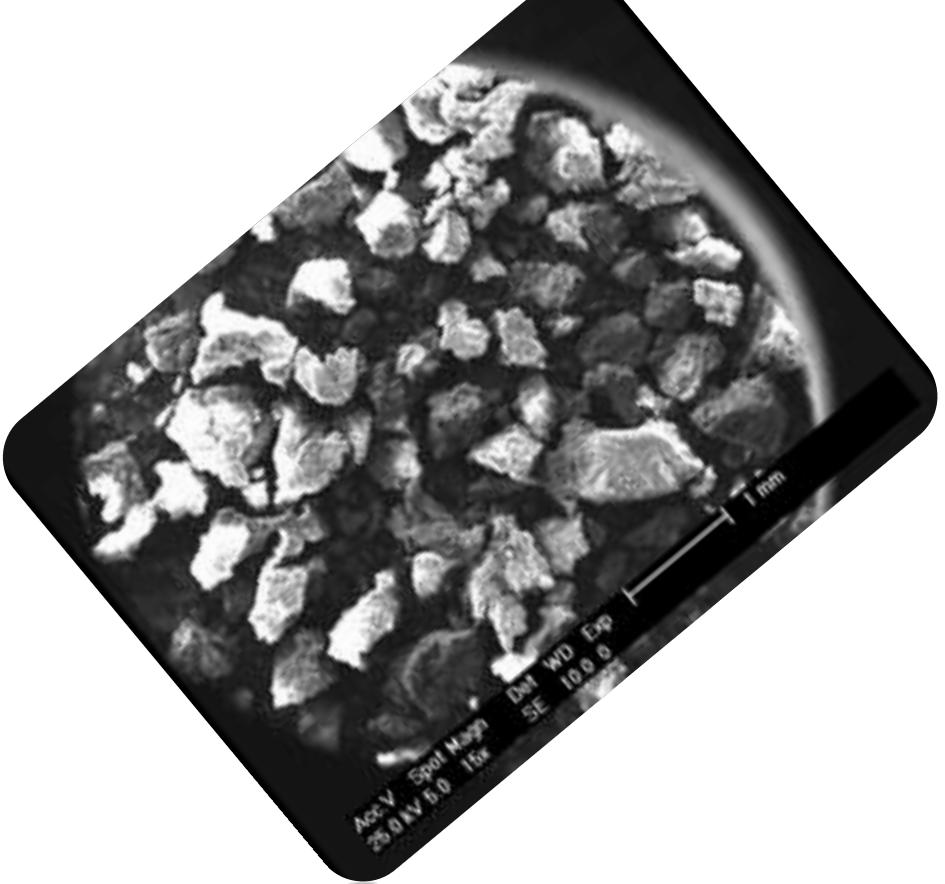




	Group 1(Test)	Group2 (control)	P Value
VBL (mm)	2.09	1.03	P<0.05
BF(8 weeks)%	28.5±4.5	4.3%±1.8	P<0.05

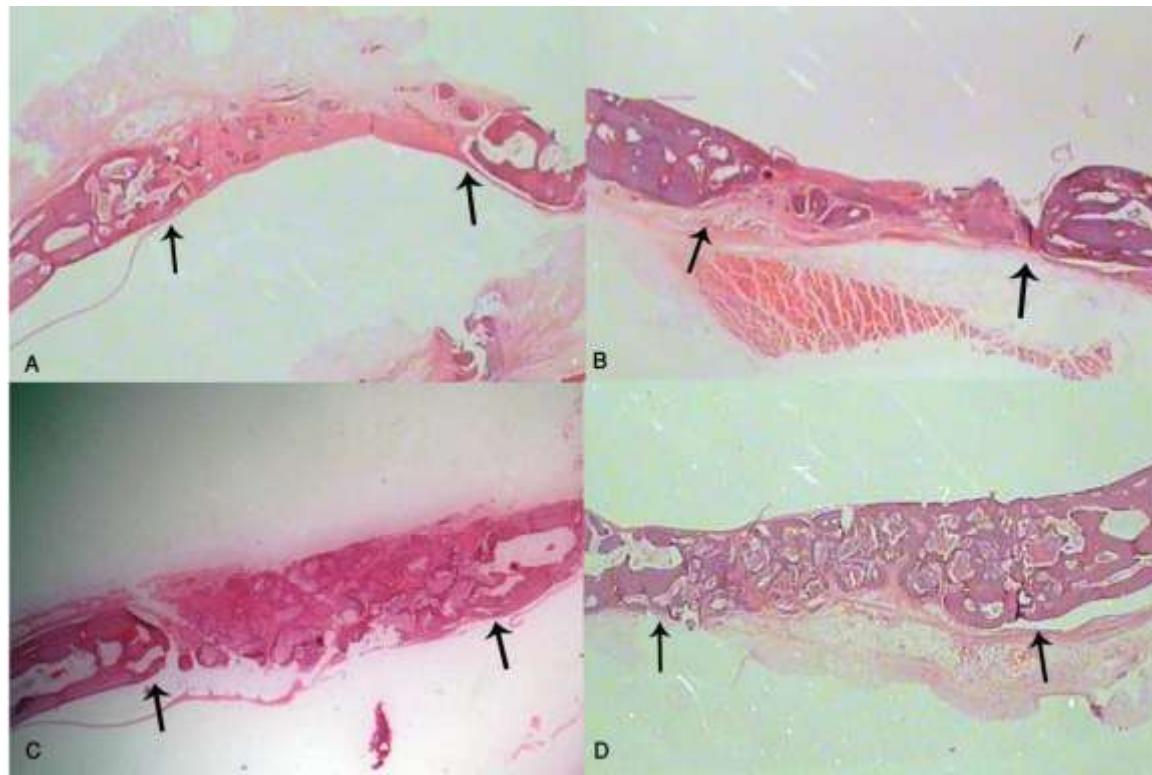
Insitu Osteogenesis

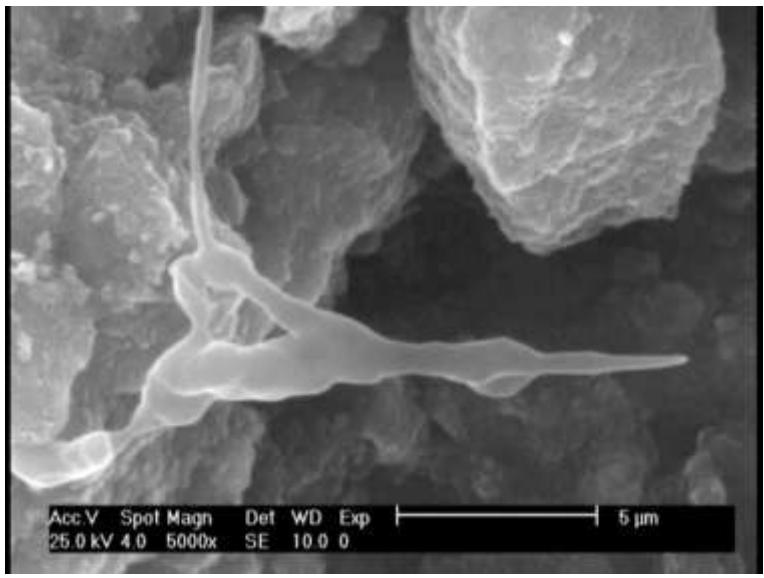
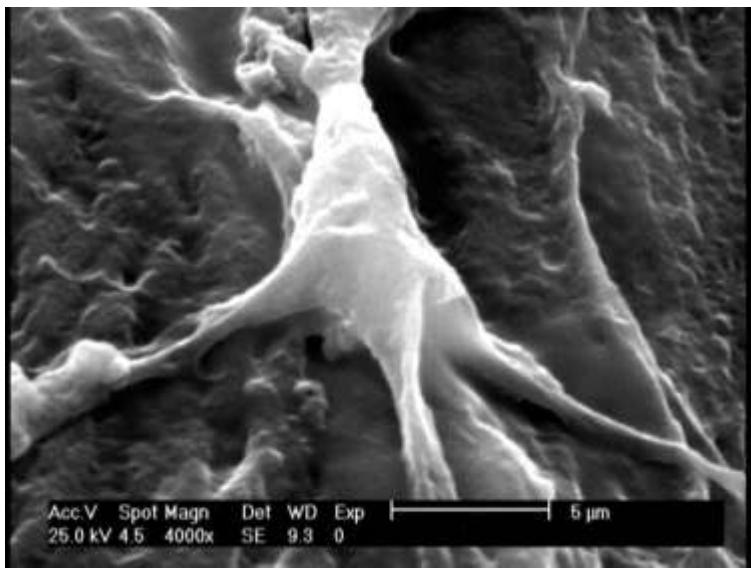
- Autogenous bone is the gold standard

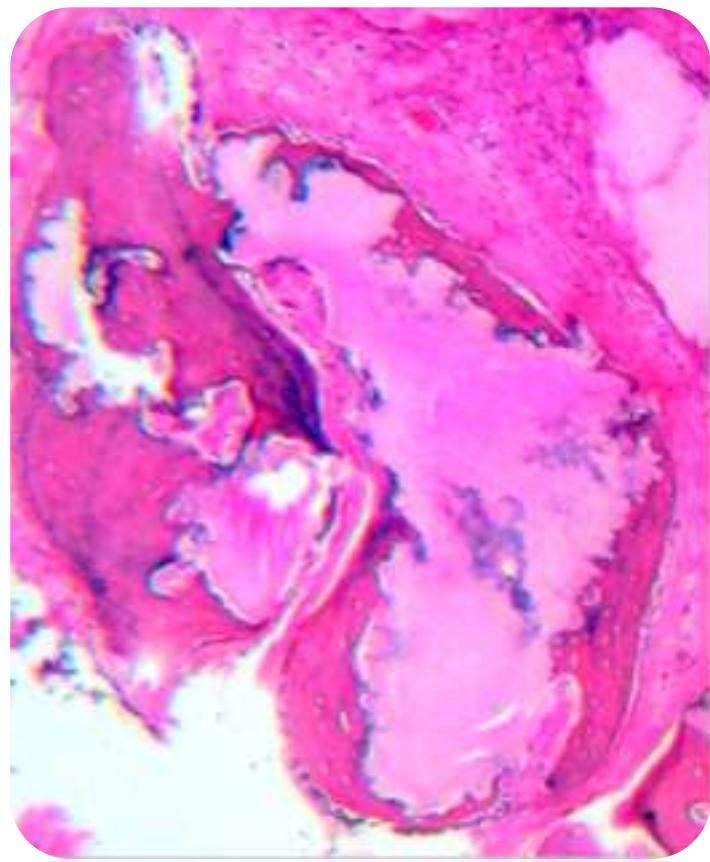


Nano scaffolds

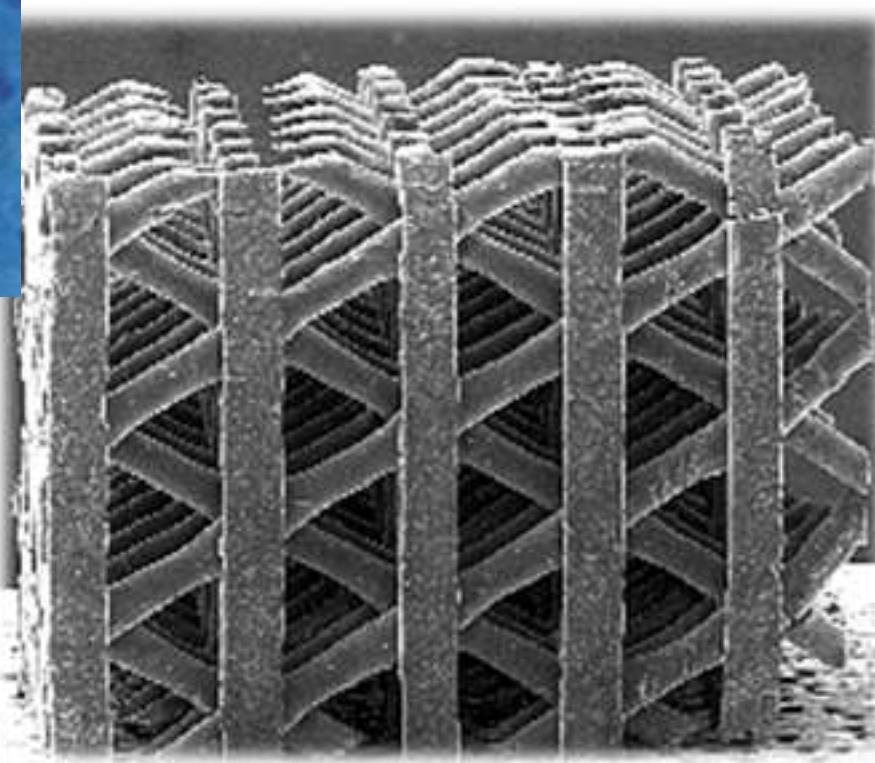
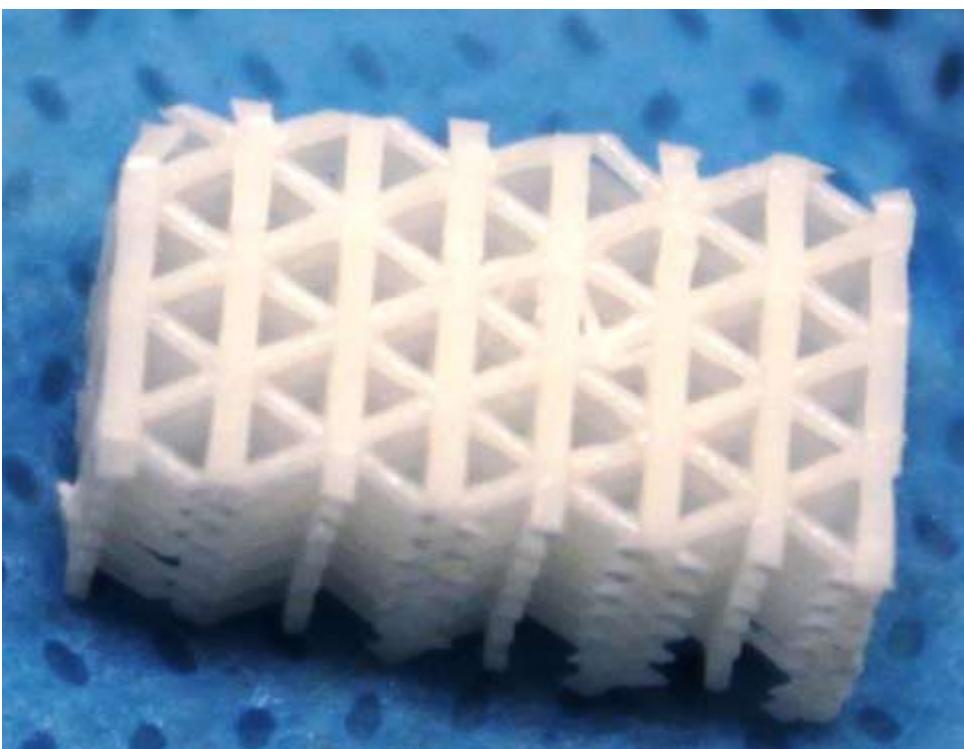
Nanosilica HA

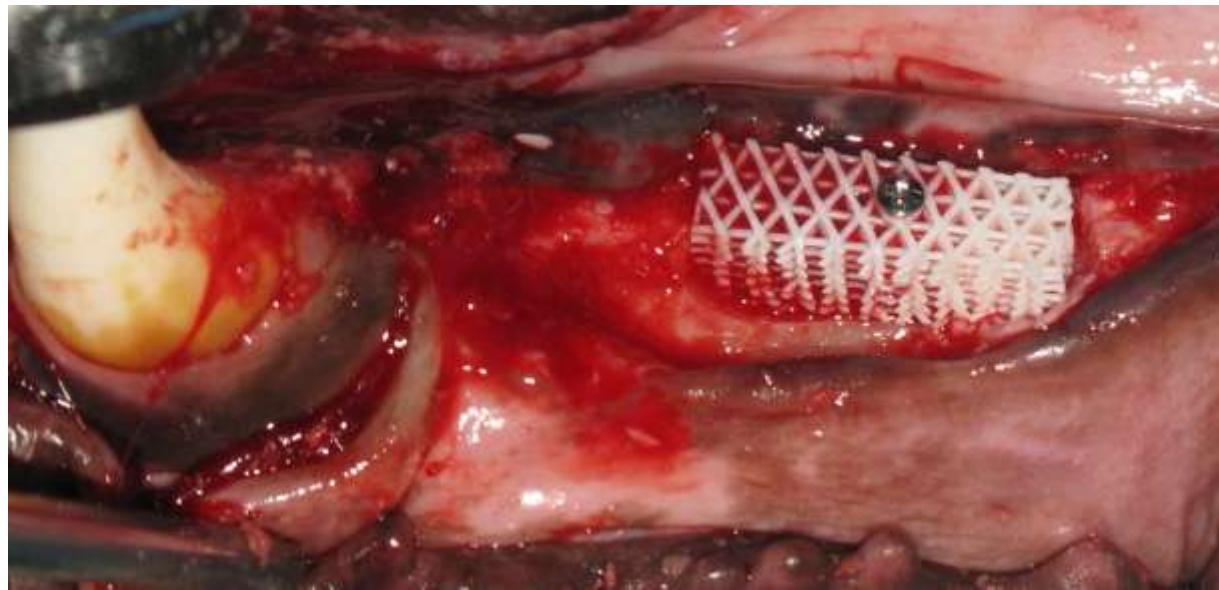




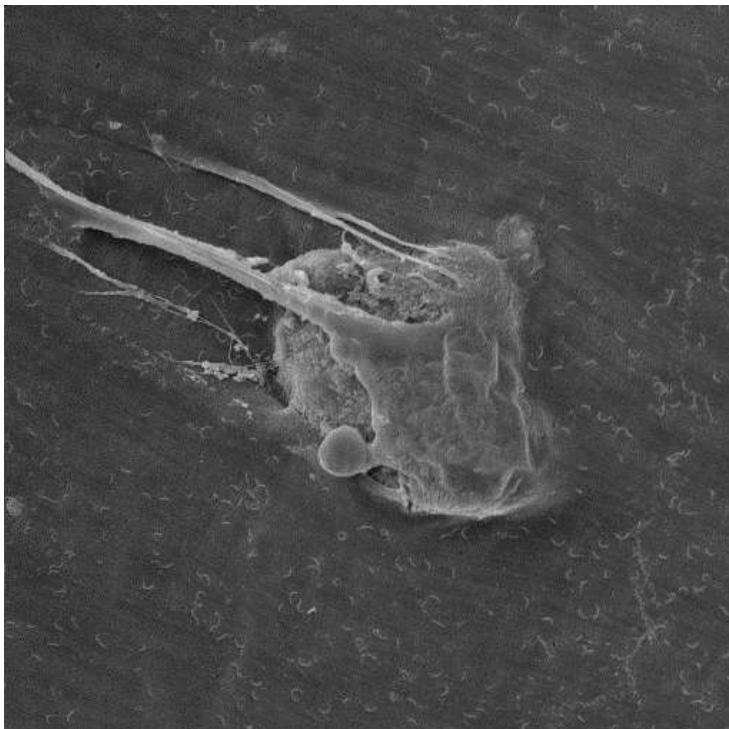
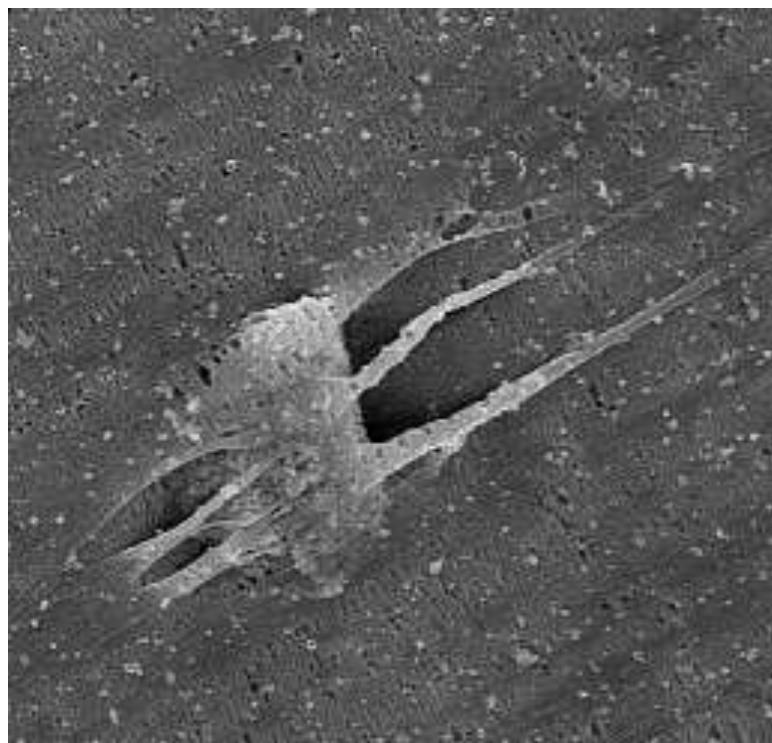


Groups	Duration	6 Weeks	12 Weeks
Group 1		11.35	32.53
Group 2		29.10	39.74
Group 3		25.82	39.11
Group 4		29.45	44.55







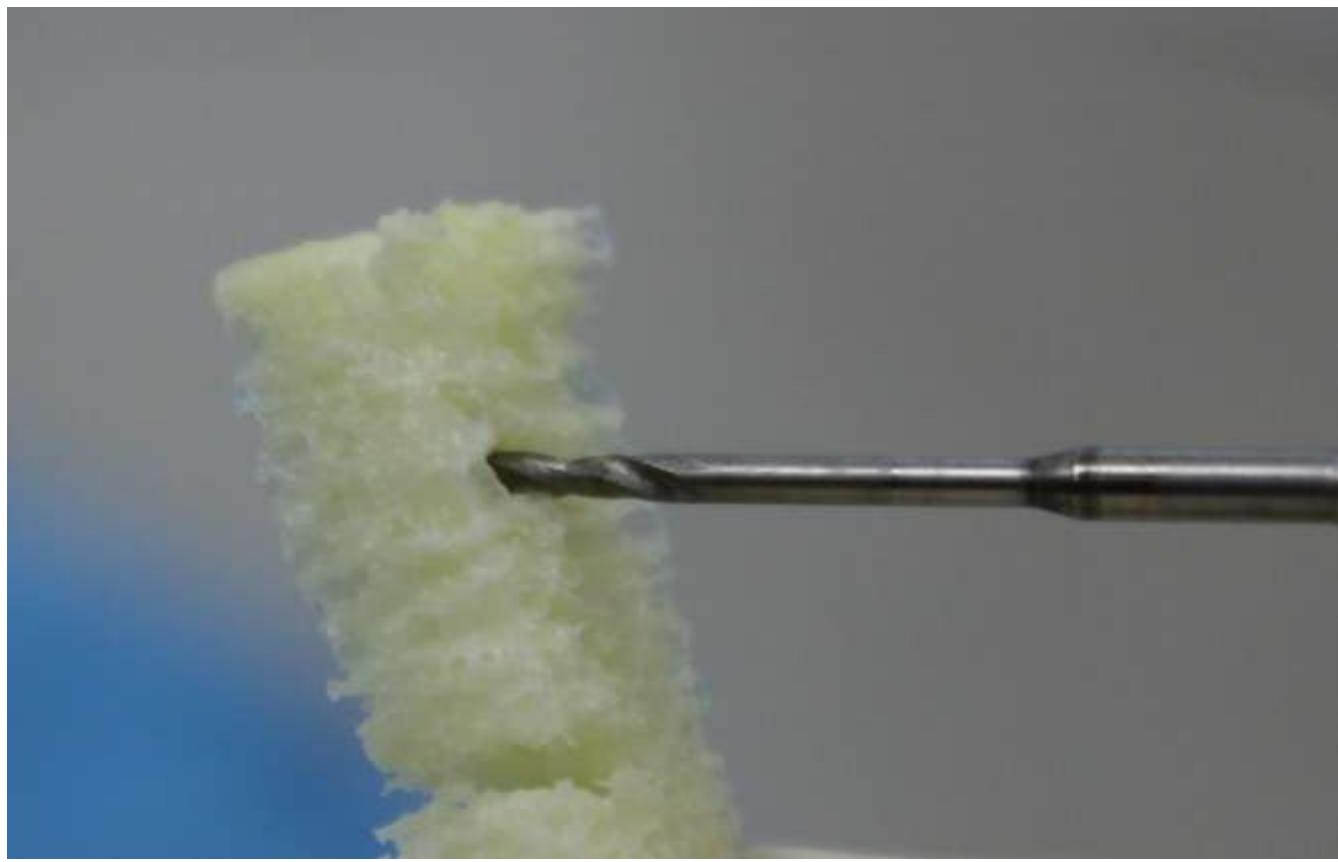


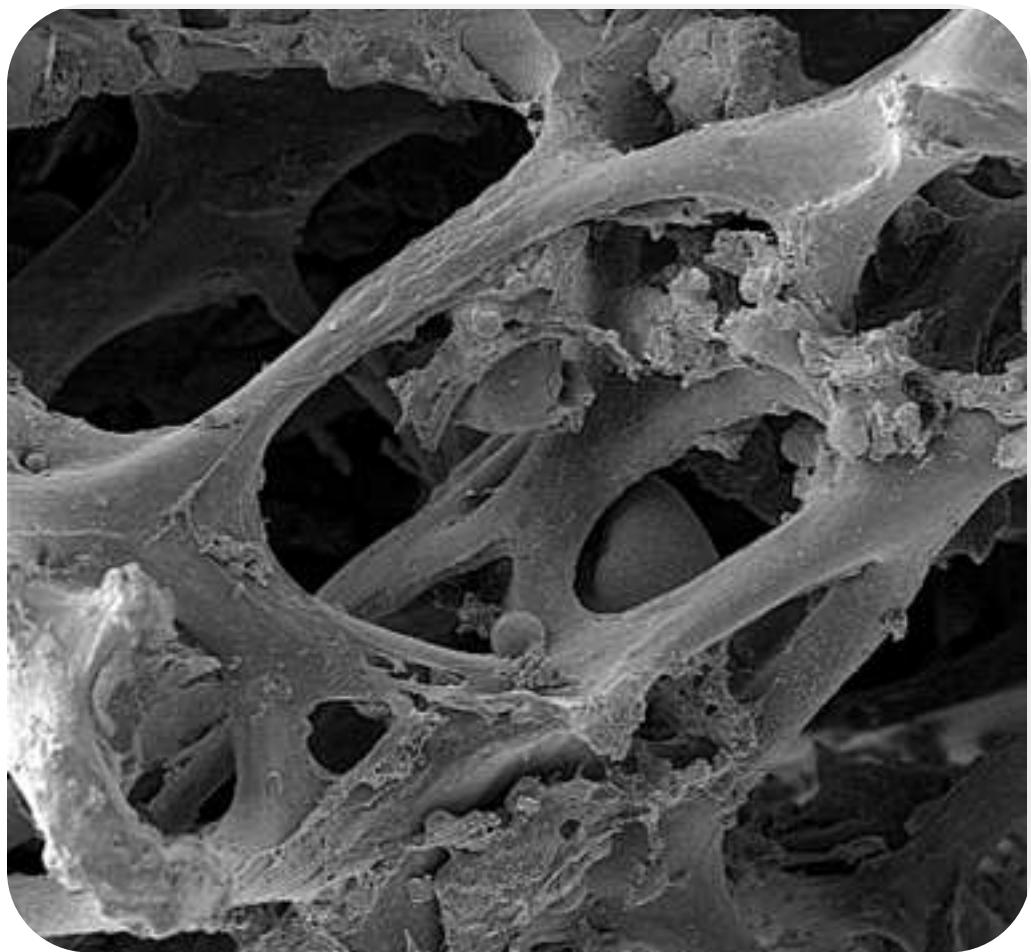
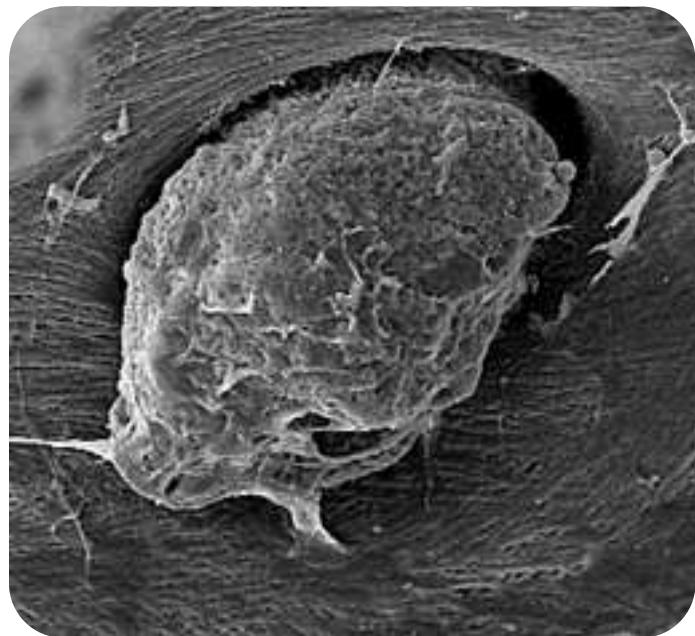
SEM MAG: 1.00 kx Det: SE Detector
SEM HV: 15.00 kV WD: 14.0870 mm 20 μ m
Date(m/d/y): 01/01/02 Vac: HiVac

VEGA TESCAN
RAZI

GEM 21s

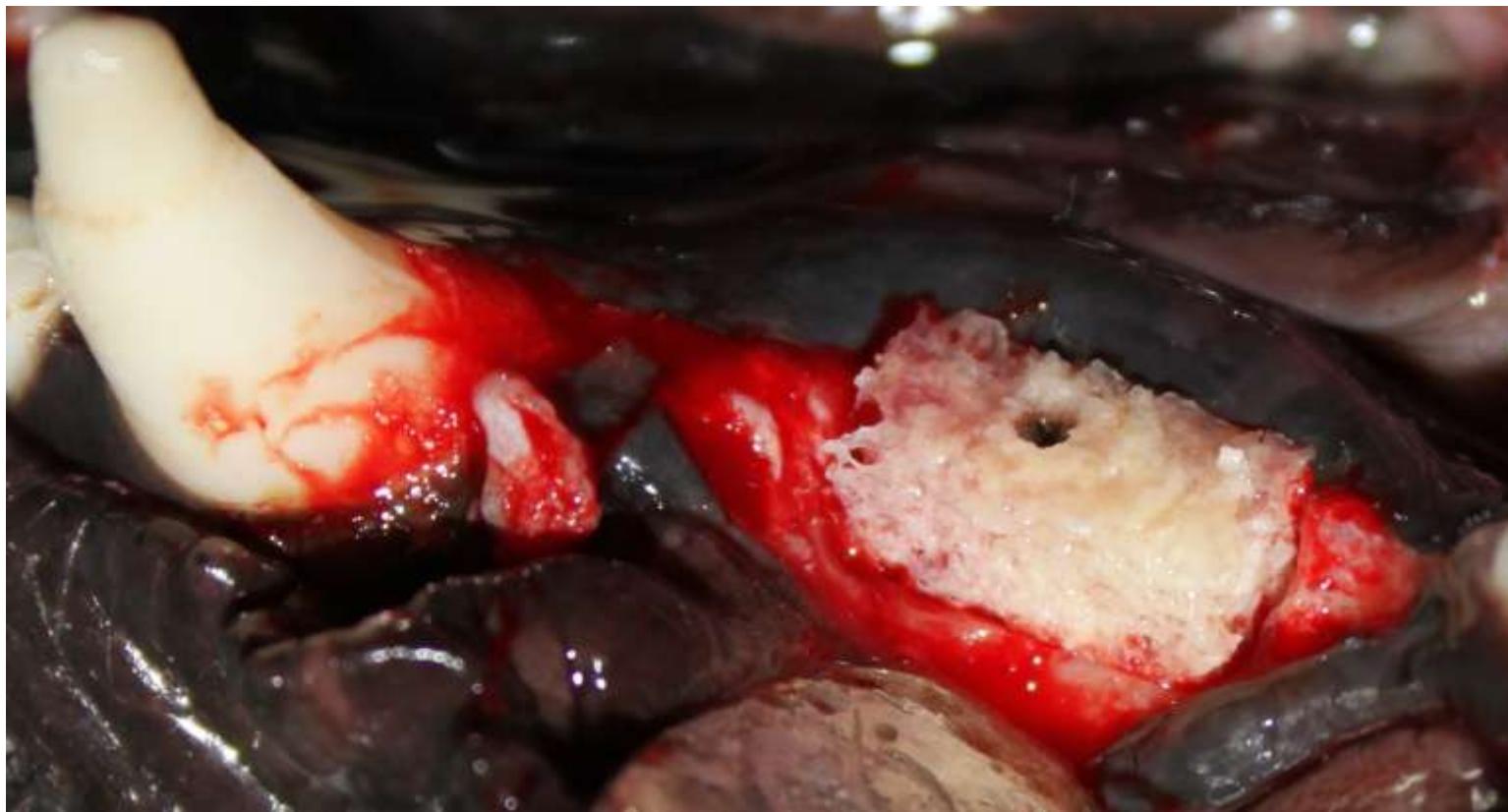


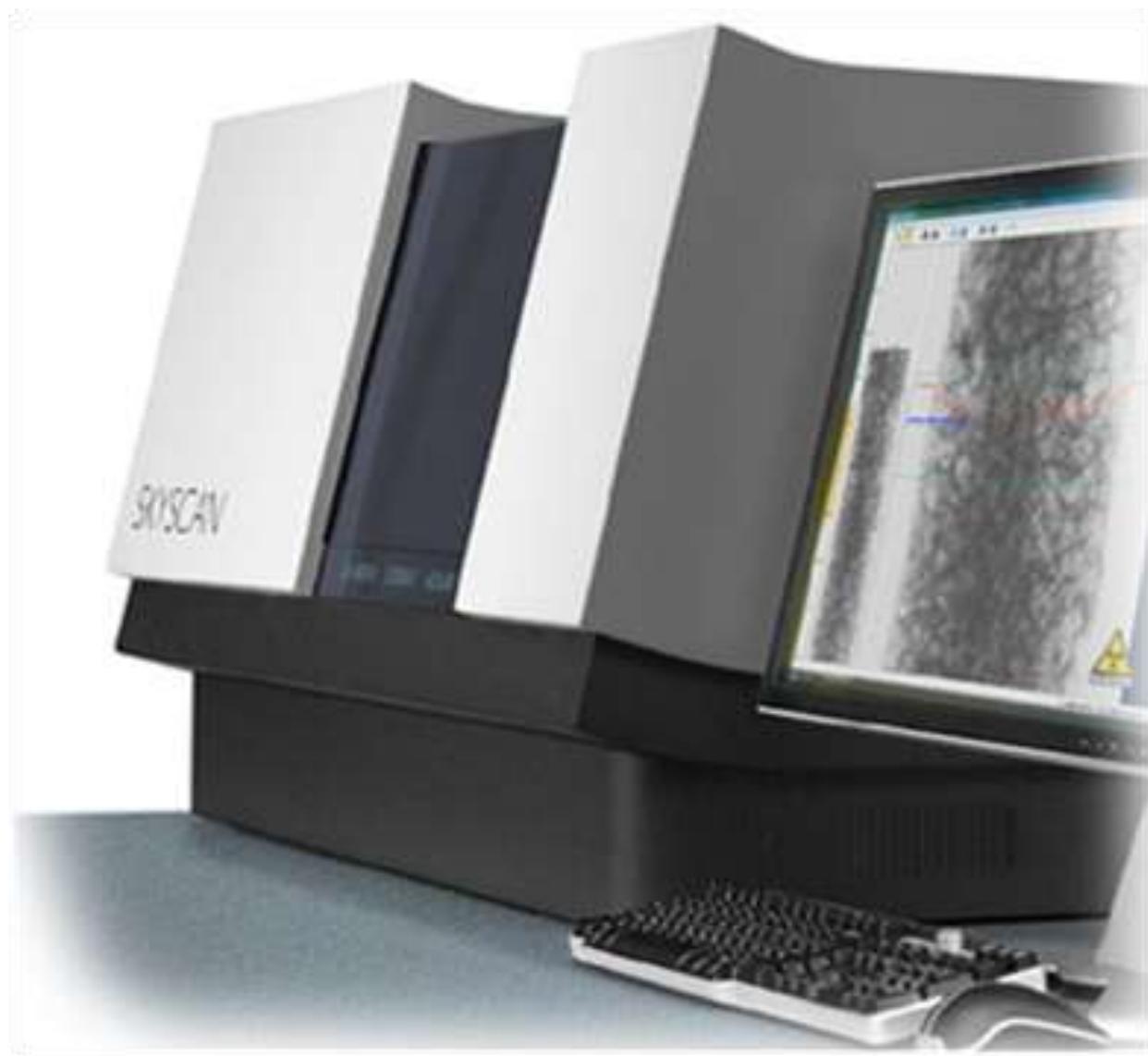


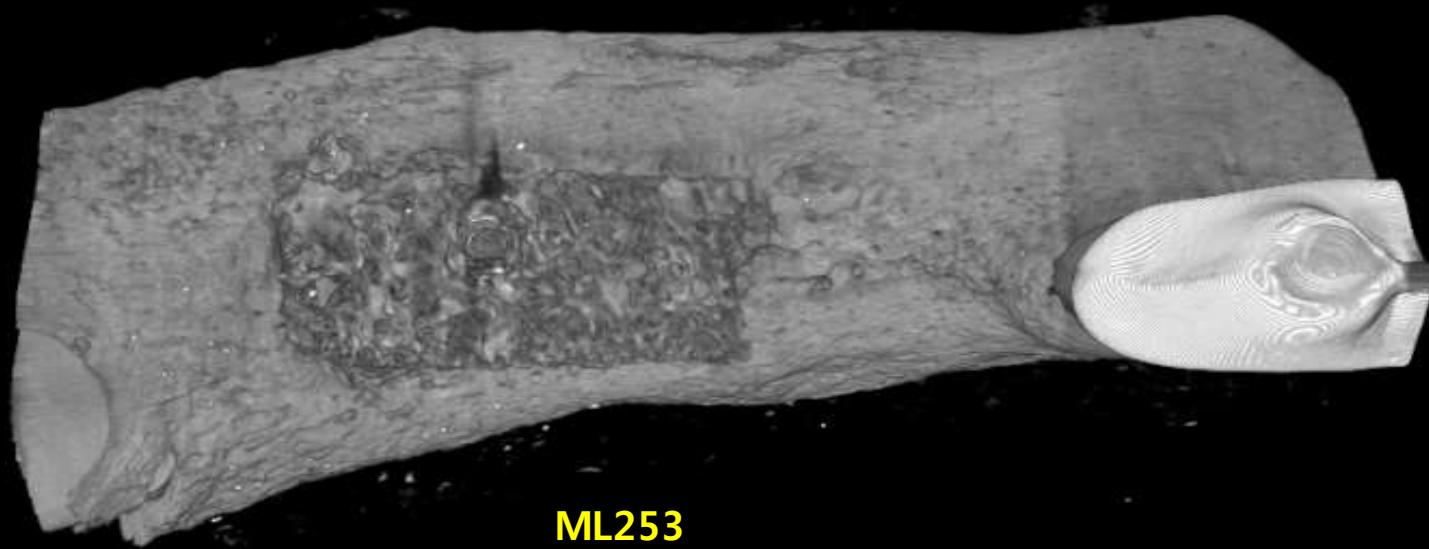












ML253

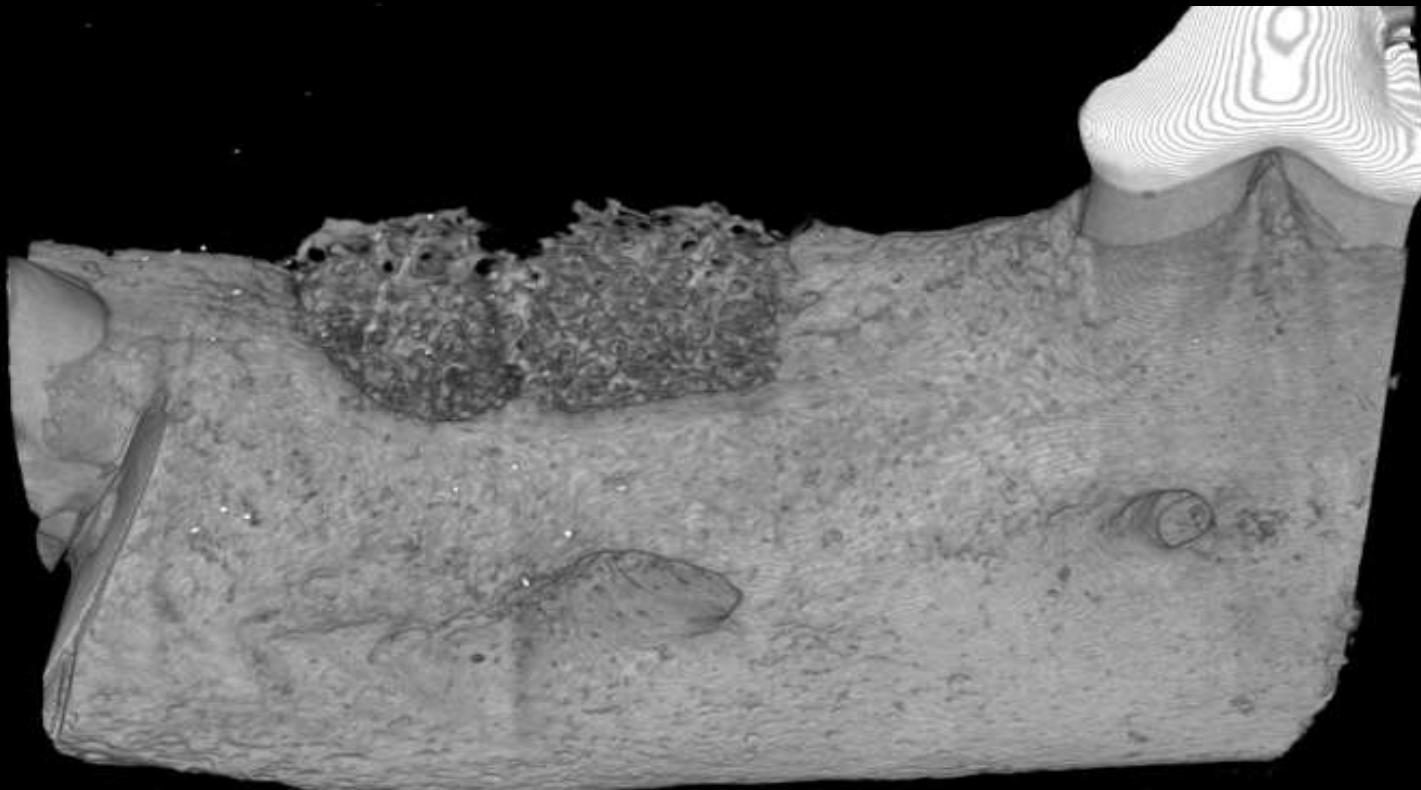
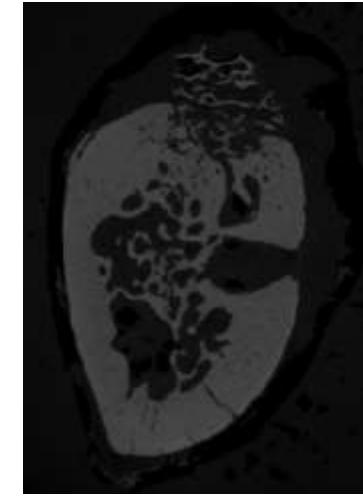
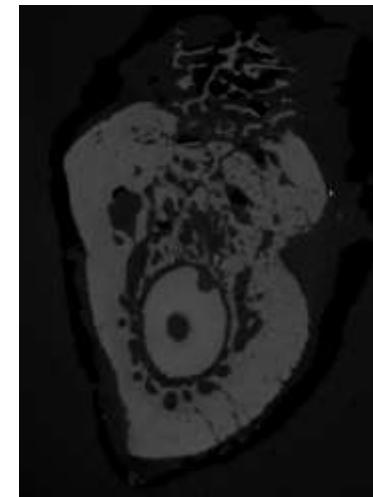
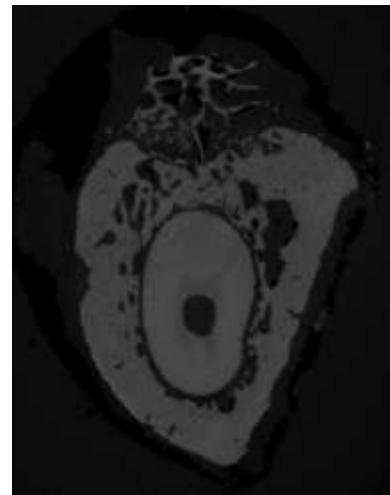
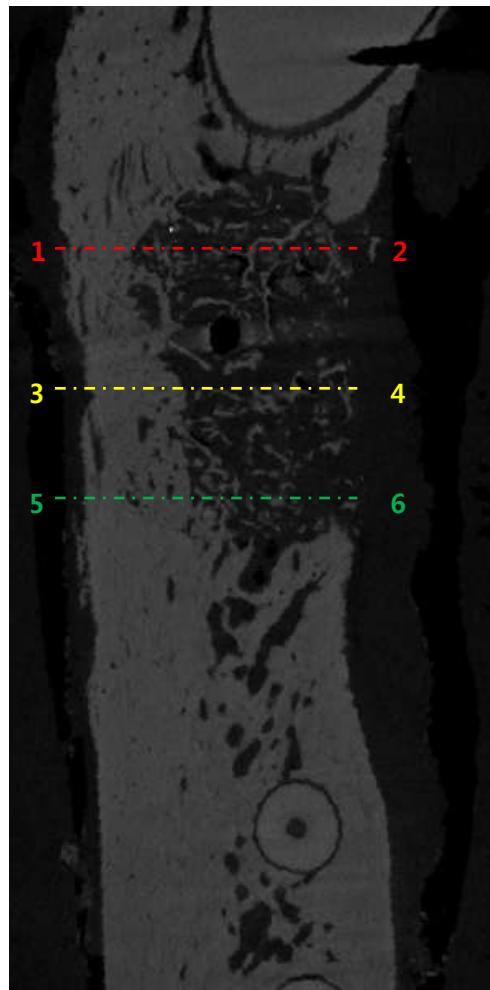
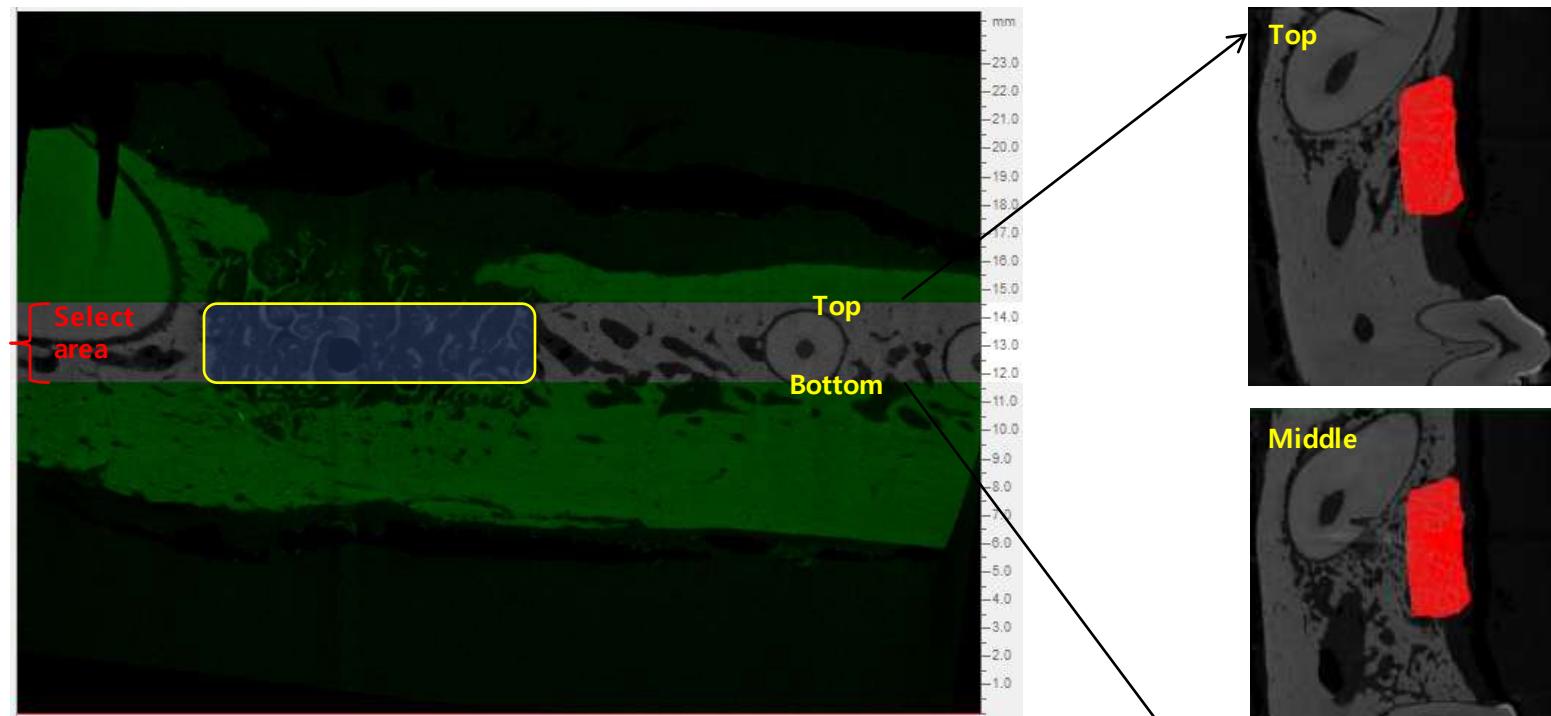


Image analysis(Cross-section)



Region of Interest

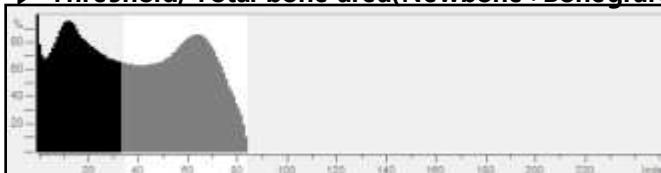


► Threshold: New bone area



About : 5.6%

► Threshold: Total bone area(Newbone + Bonegraft)

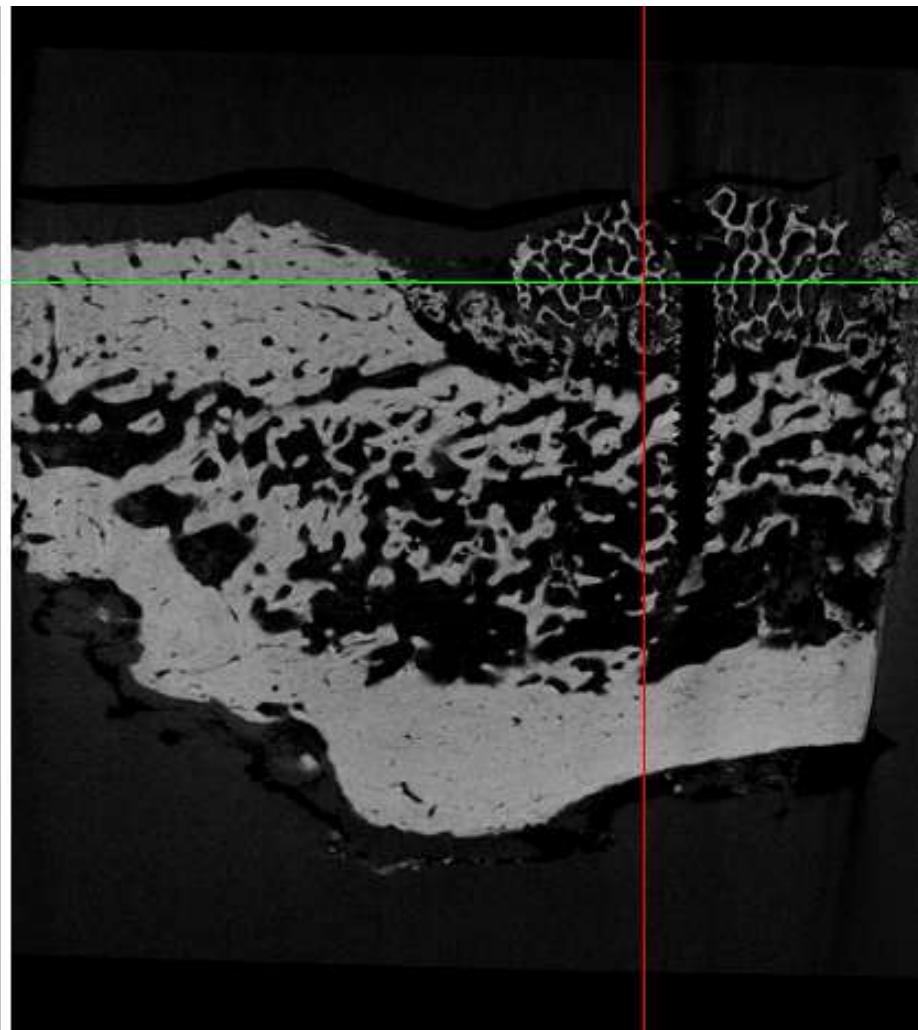
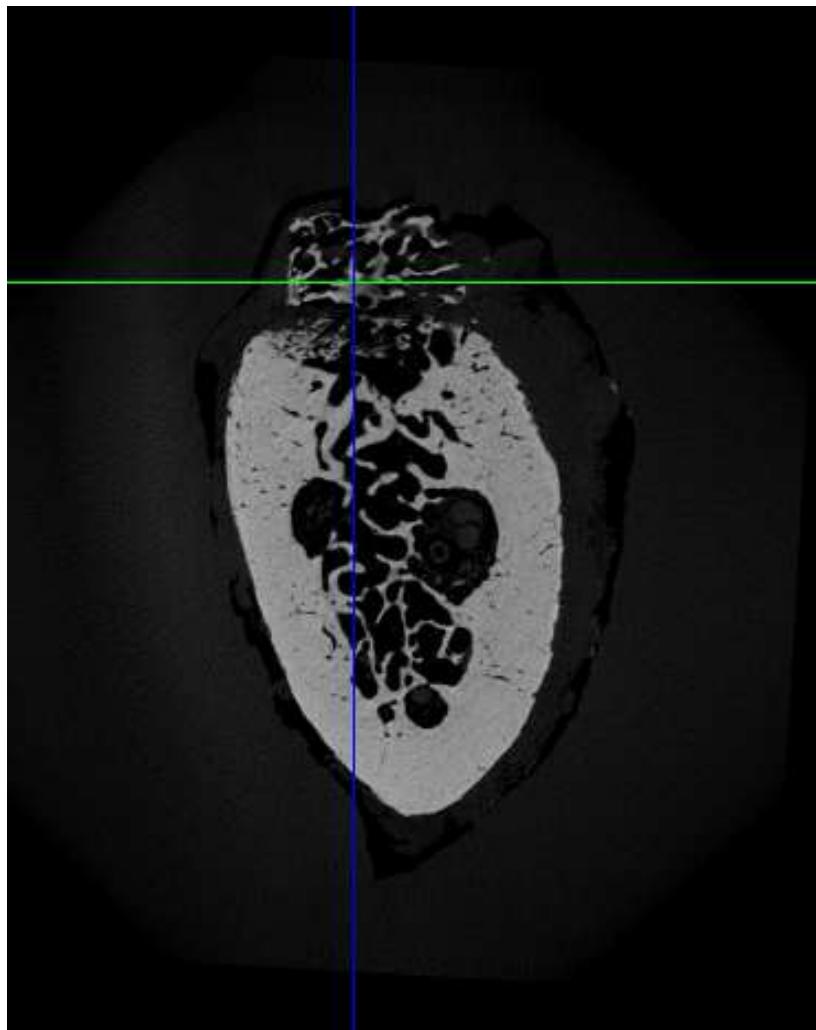


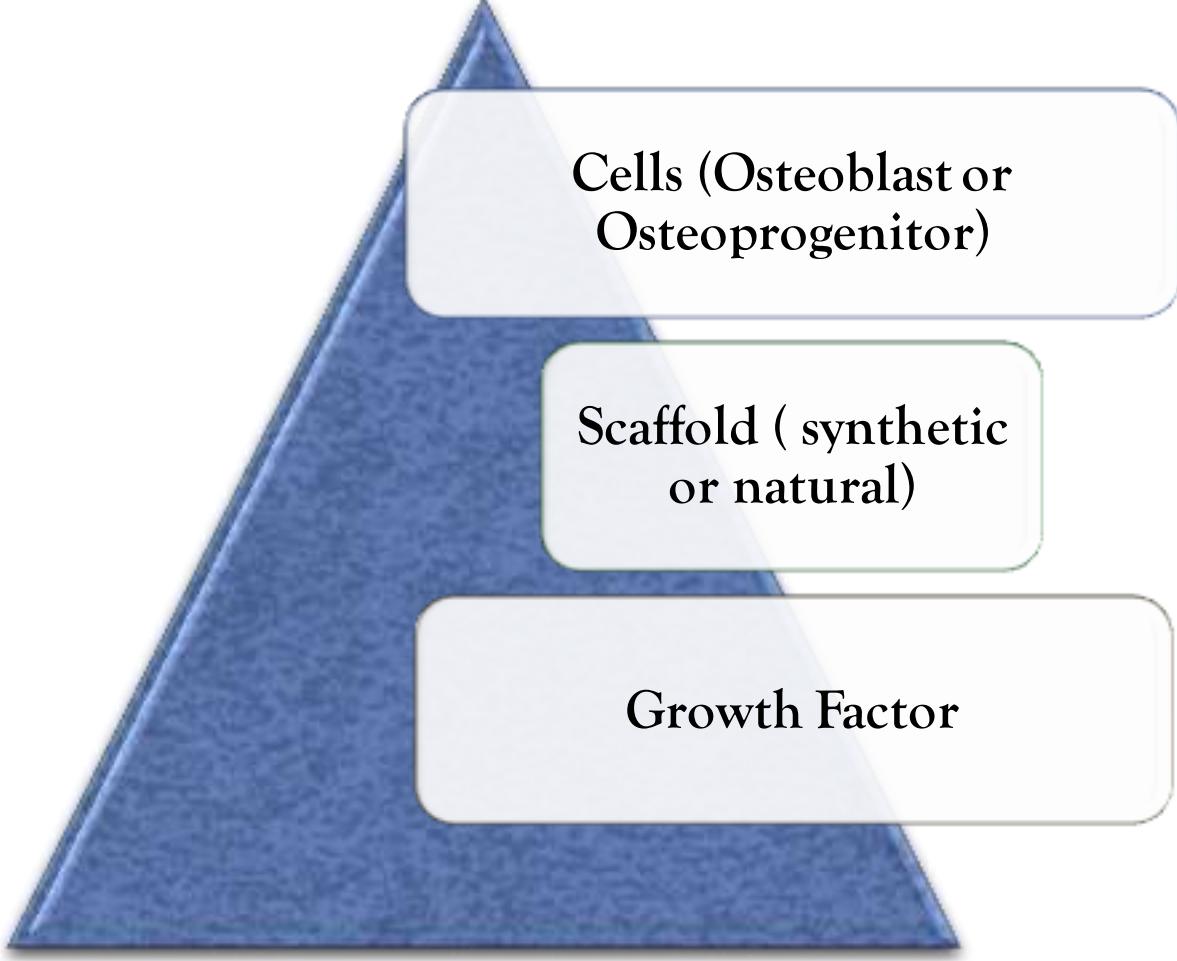
About : 27.4%

=> "Bone volume ratio" depends on the area(ROI).

Cross-section image

3D axis Image

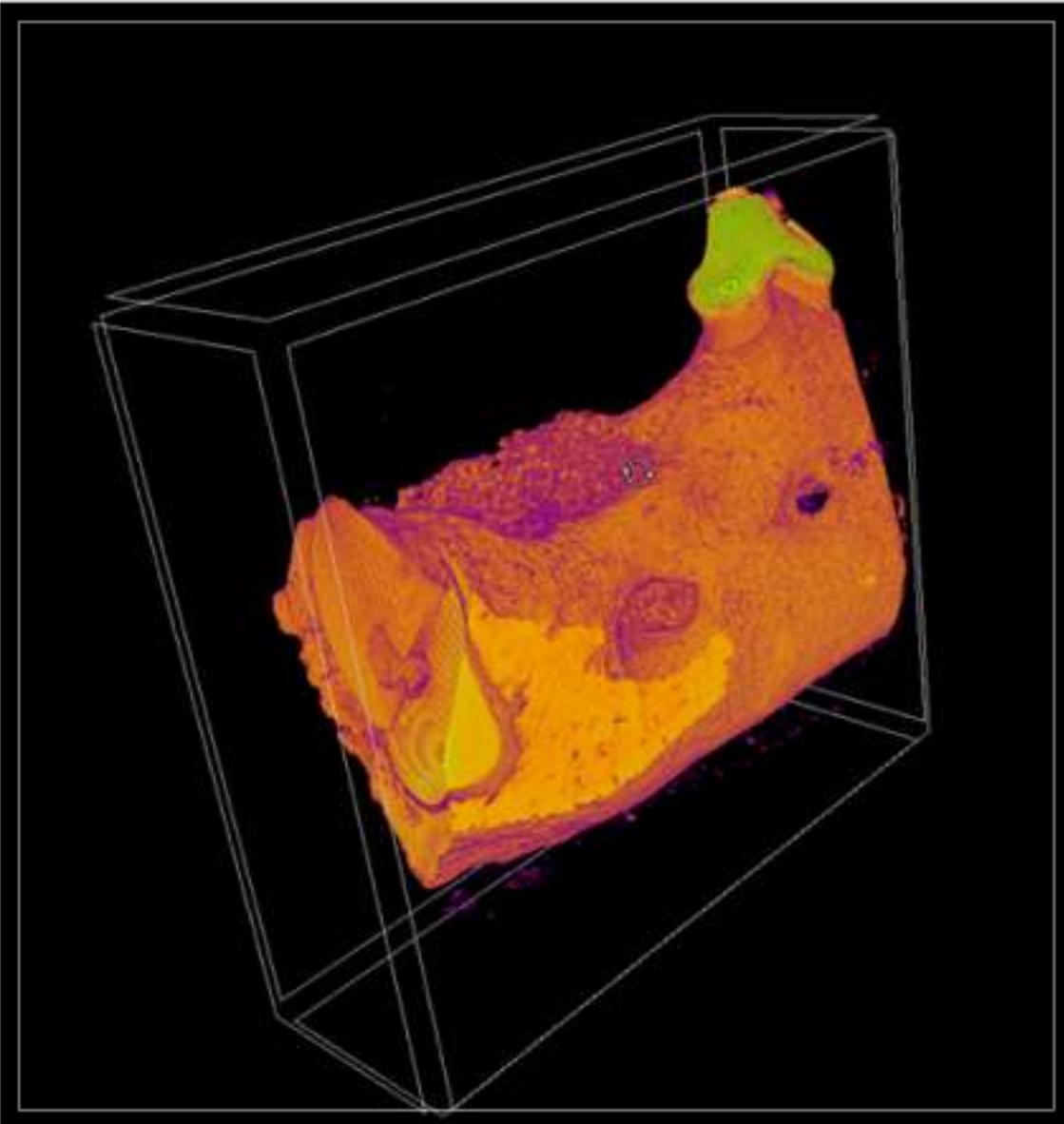


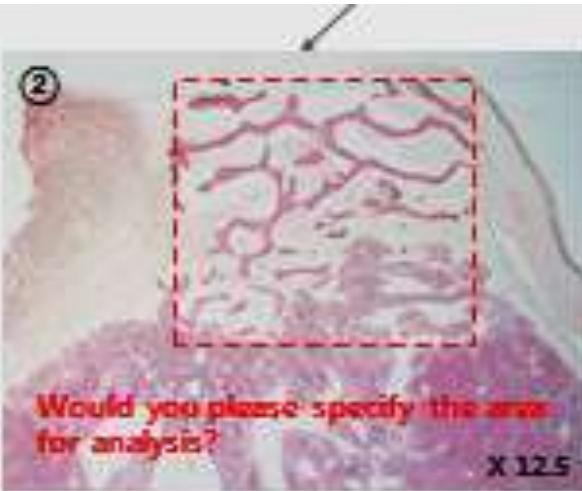


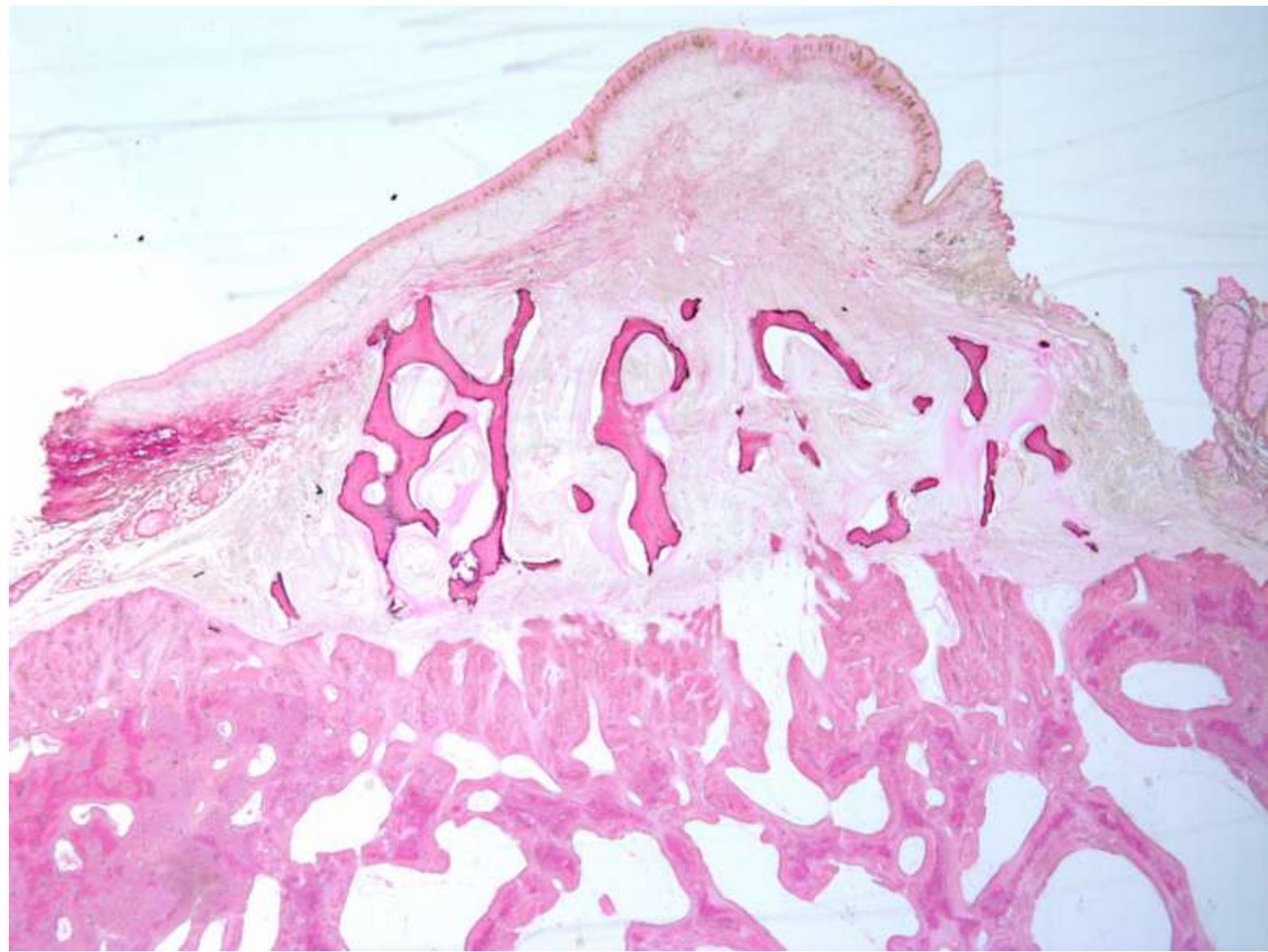
**Cells (Osteoblast or
Osteoprogenitor)**

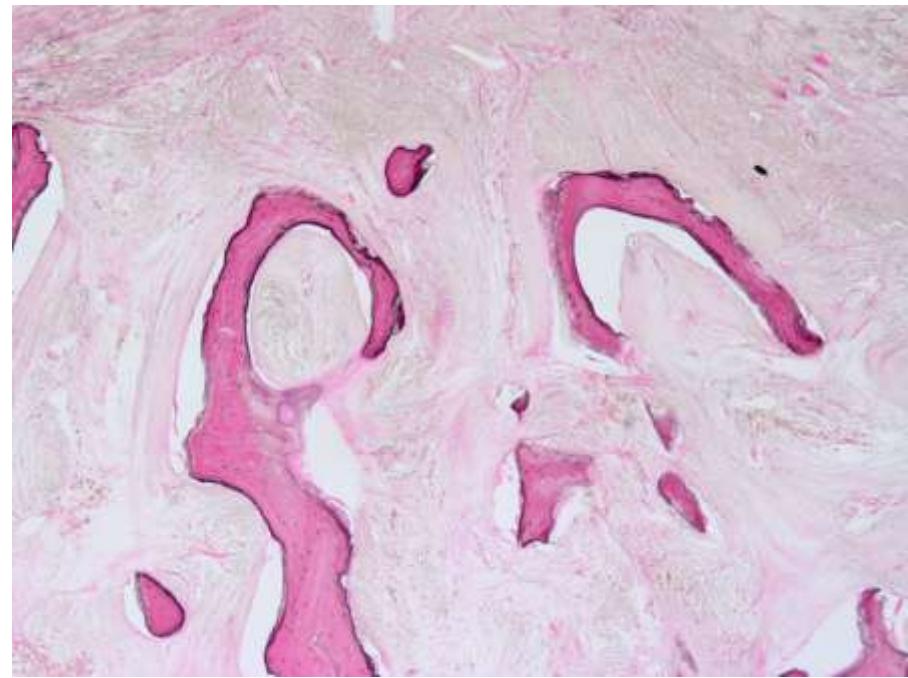
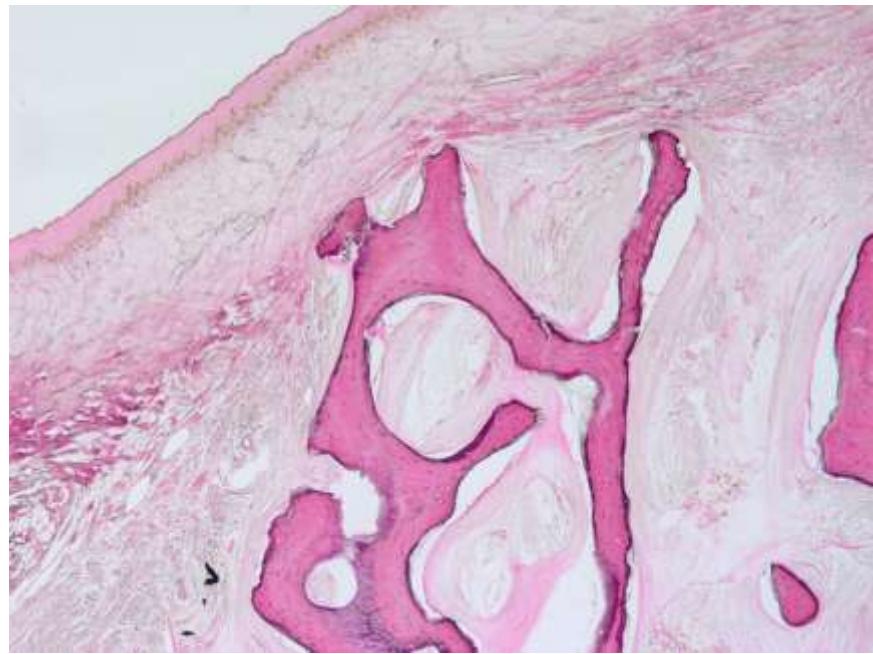
**Scaffold (synthetic
or natural)**

Growth Factor

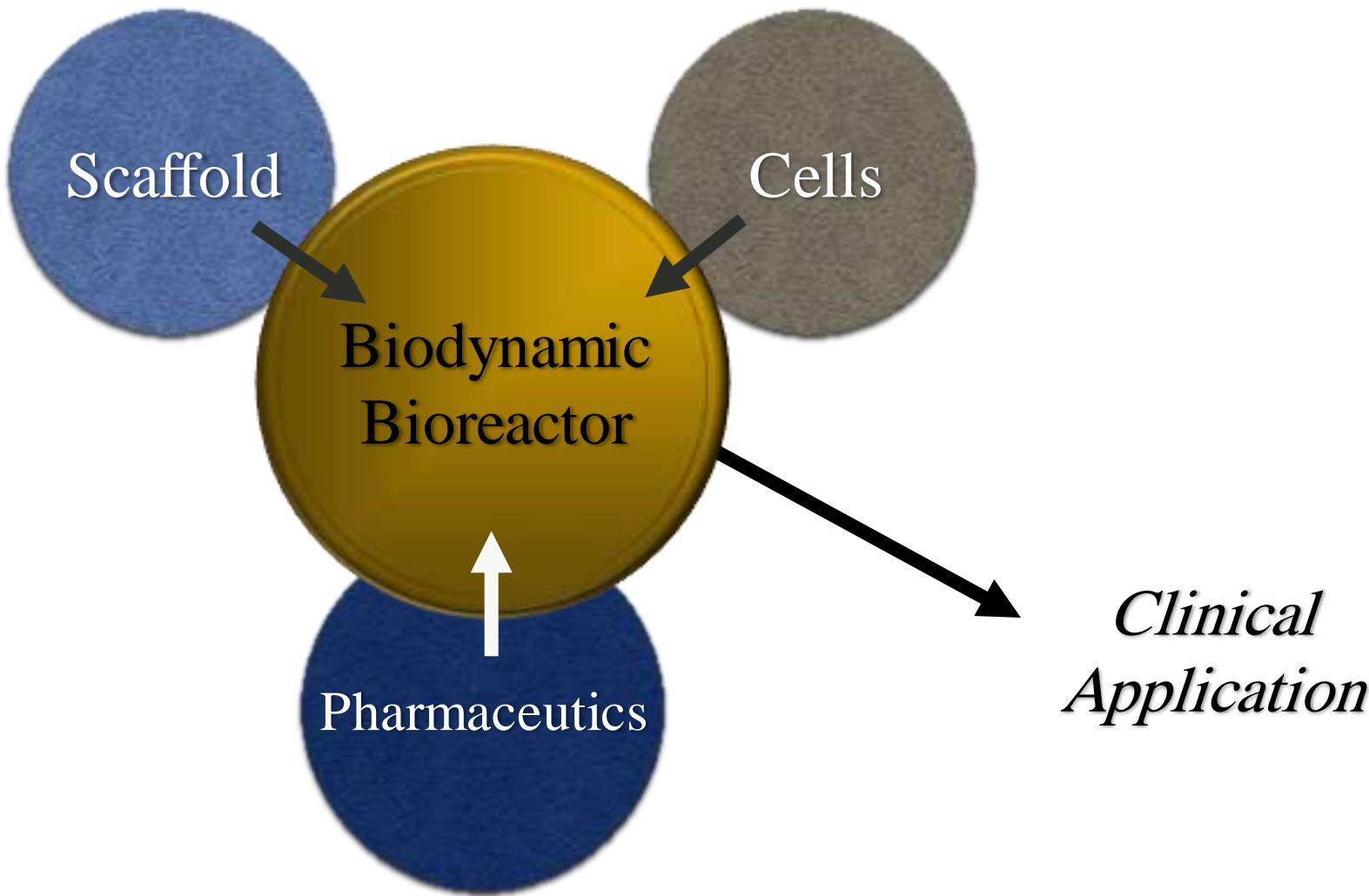






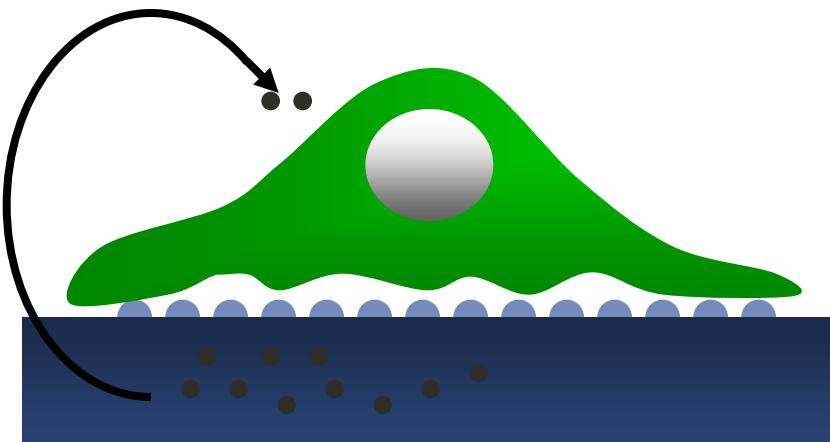


Strategy for Engineered Bone



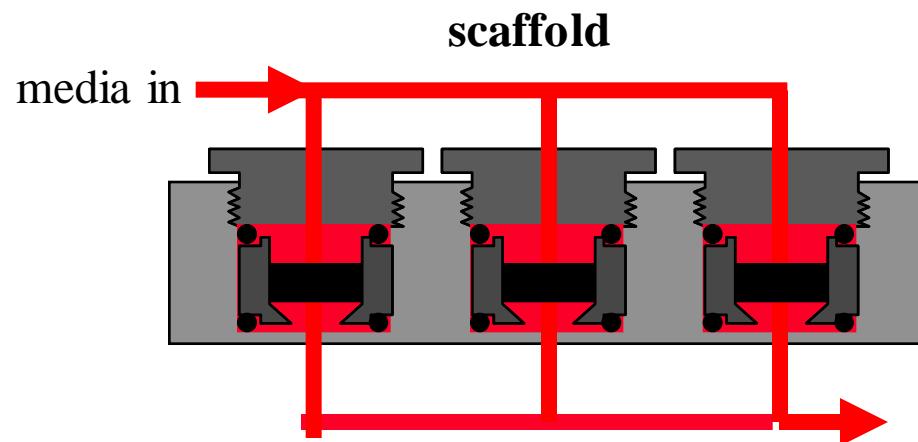
Scaffold

- Key issues
 - Stimulate cell function: bioactive factors on material surface, drug/gene in material compliance/degradation matching



Biodynamic Bioreactor

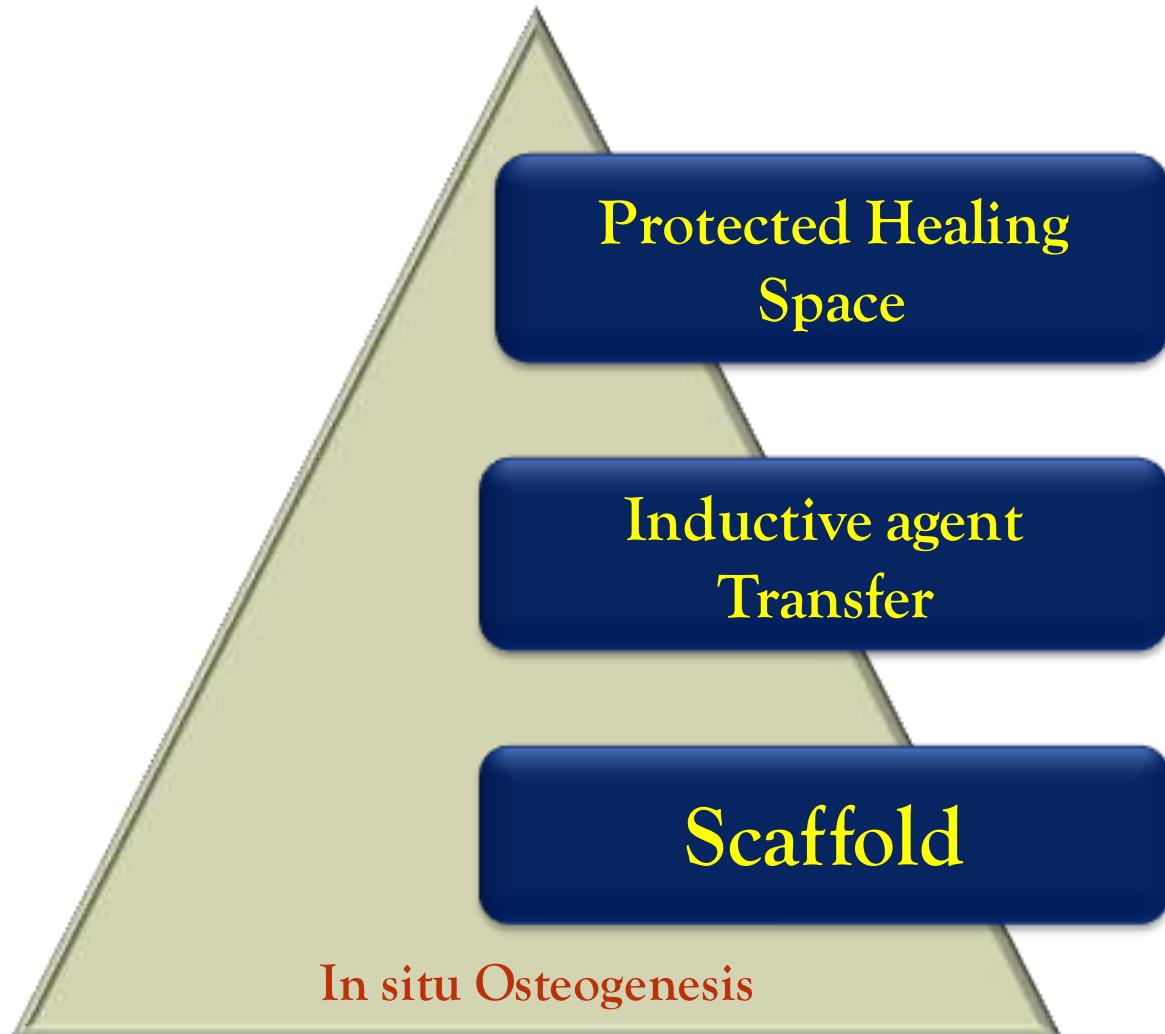
Deliver nutrients and oxygen to maintain cell viability throughout scaffold



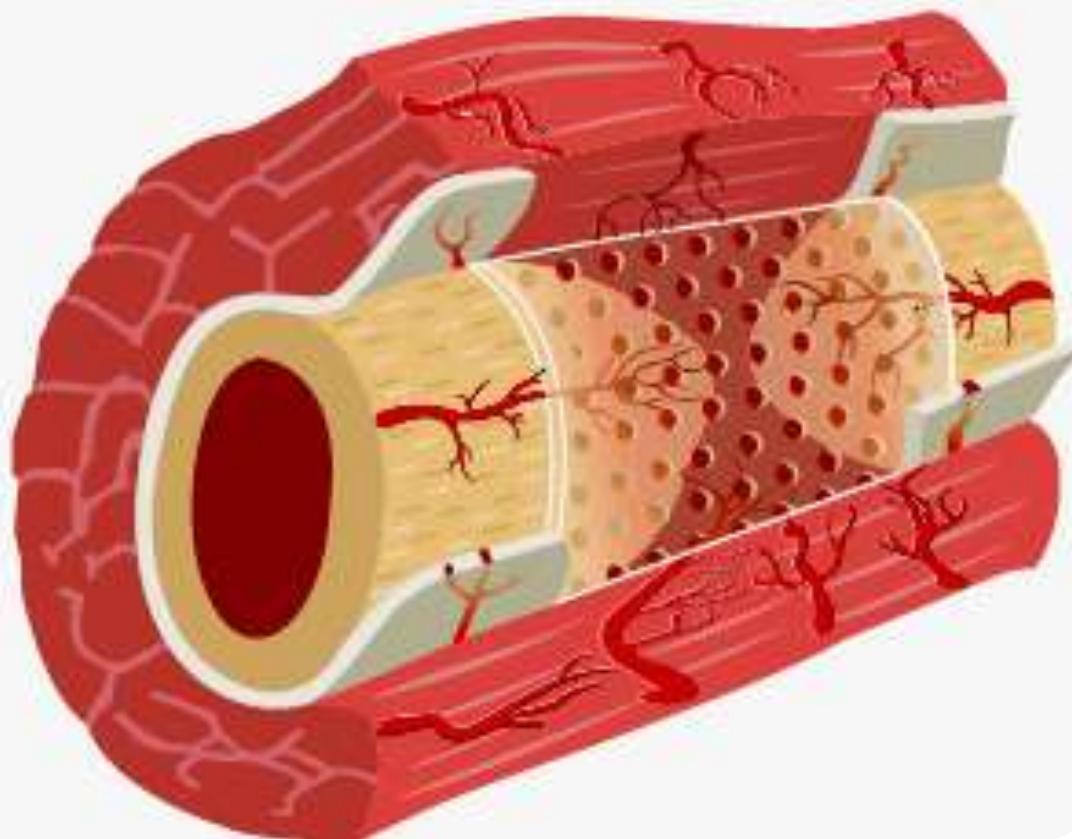
Goldstein et al *Biomaterials* 22:1279, 2001

Perfusion System

In situ Osteogenesis



Protected Healing Space









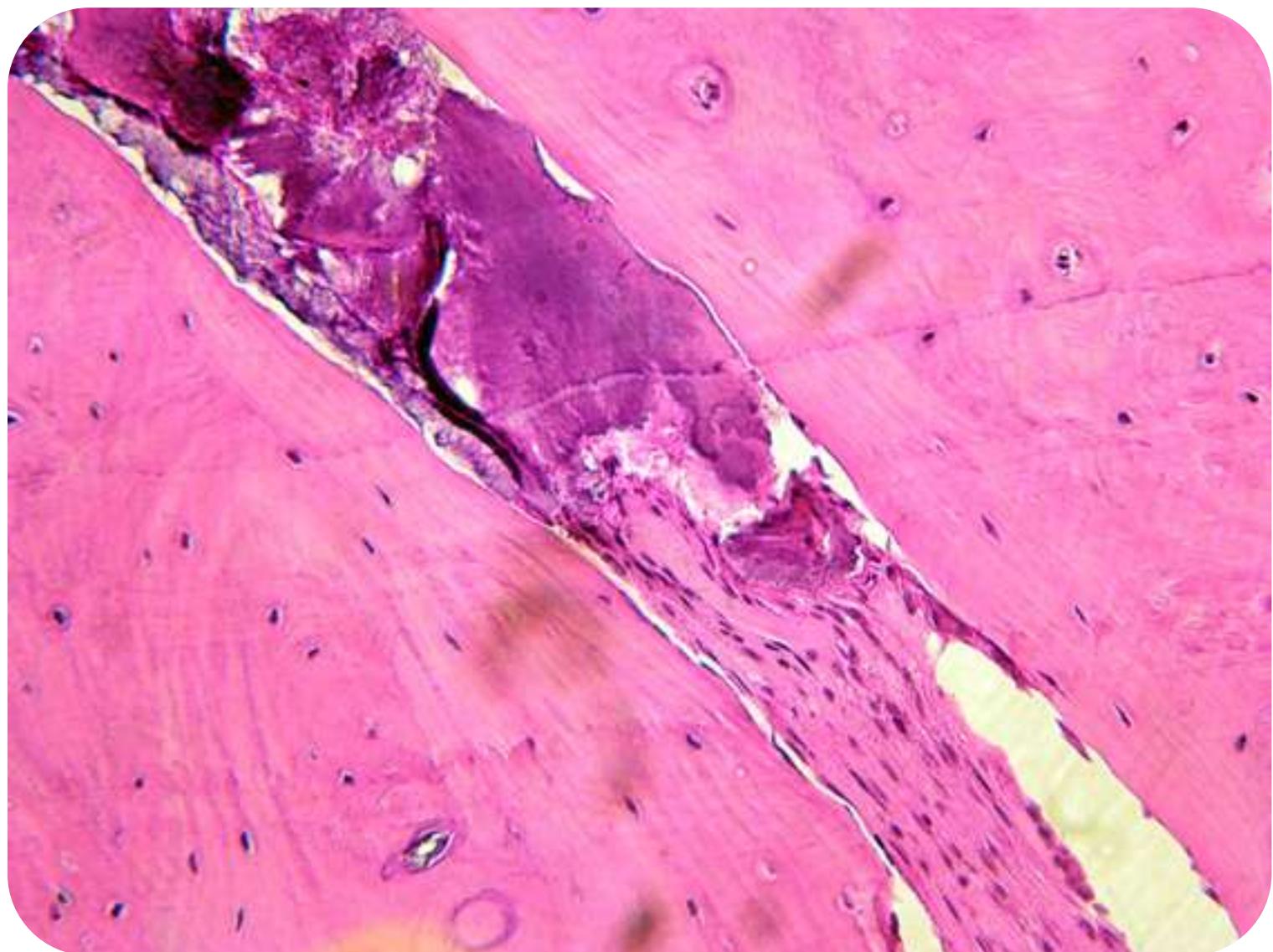
A



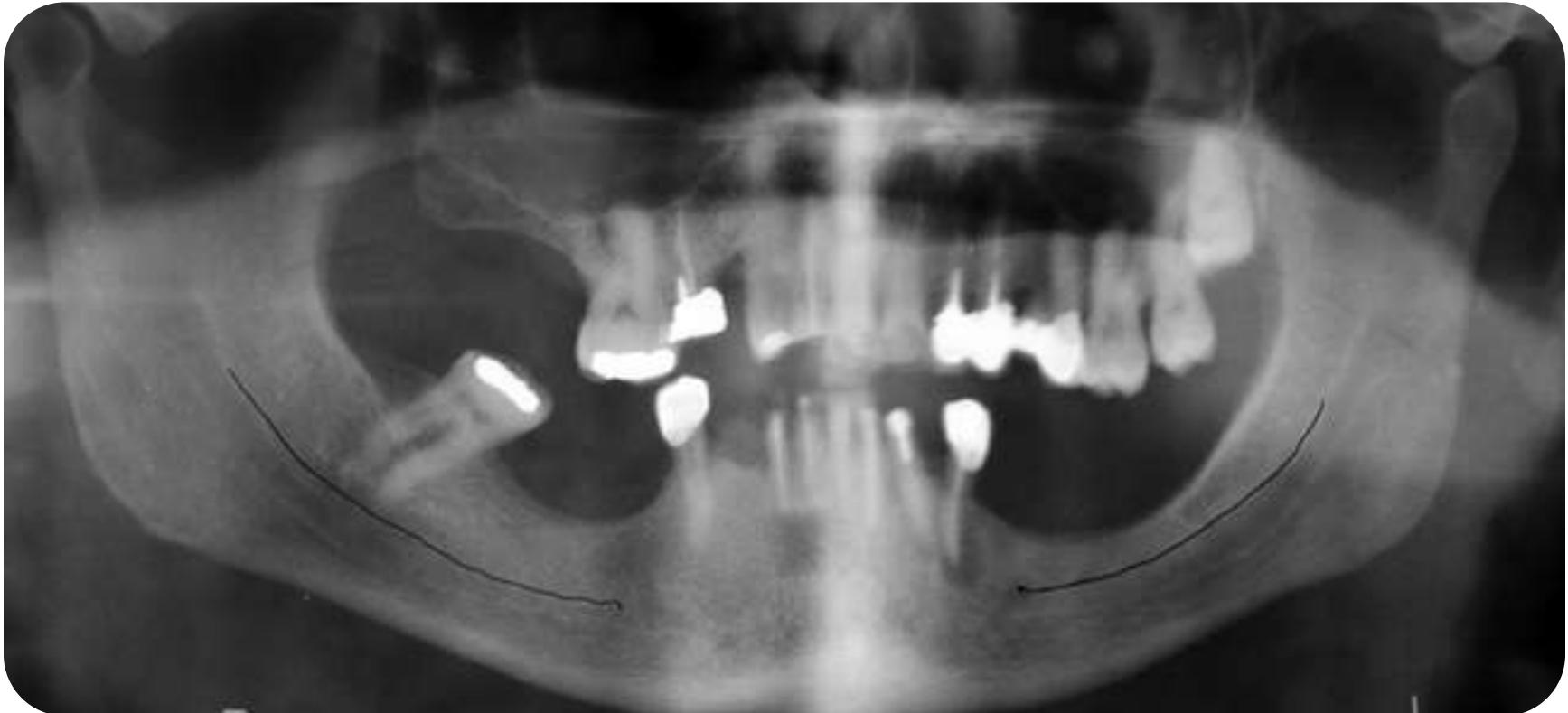
B



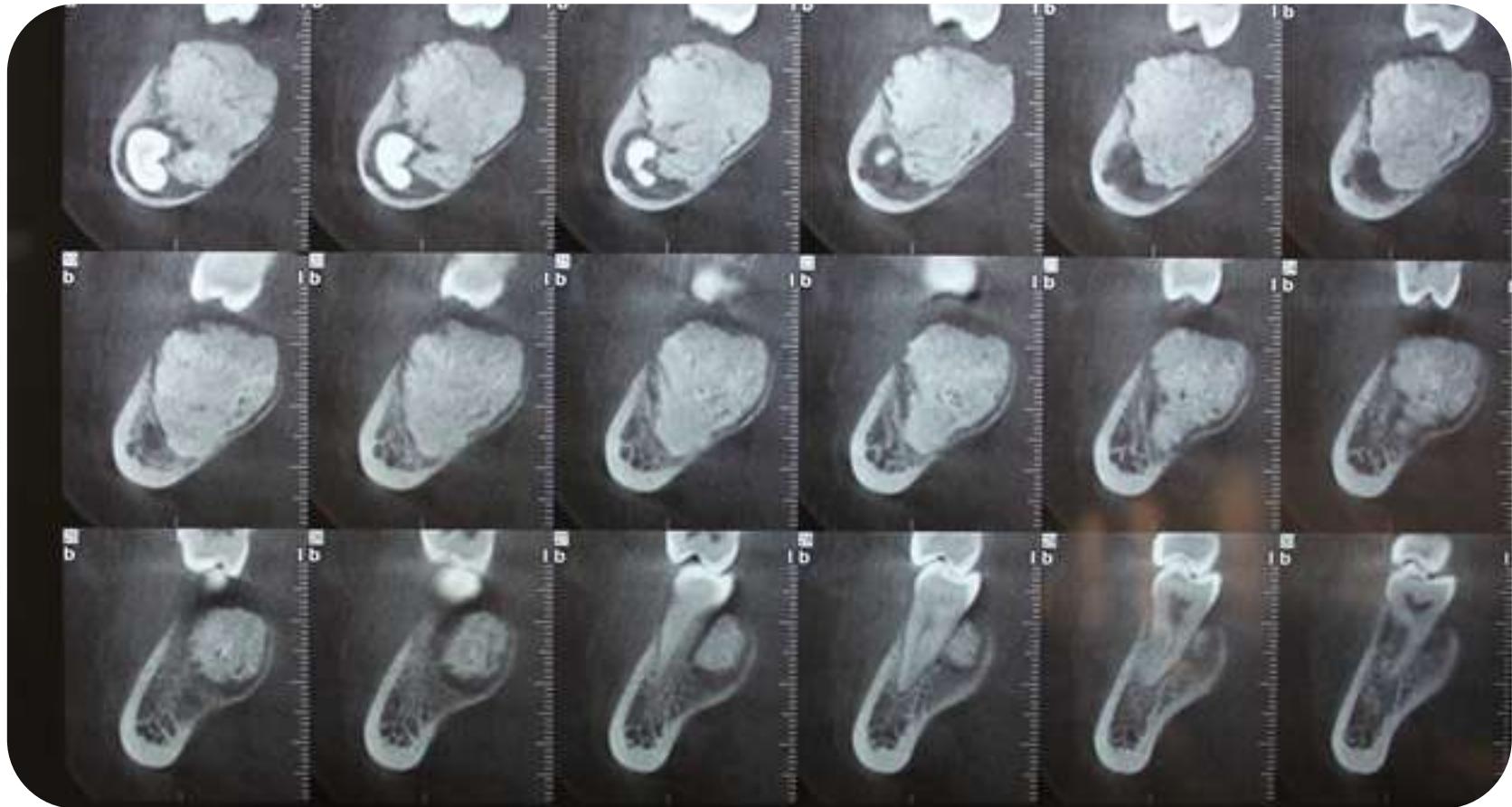
C

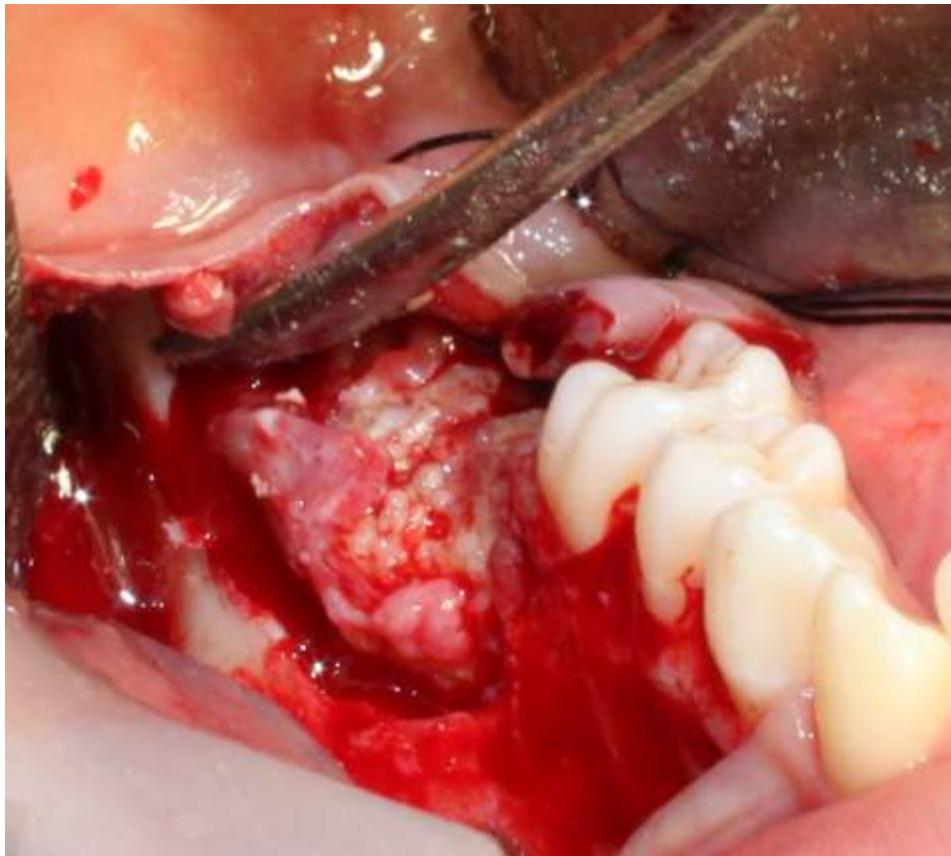


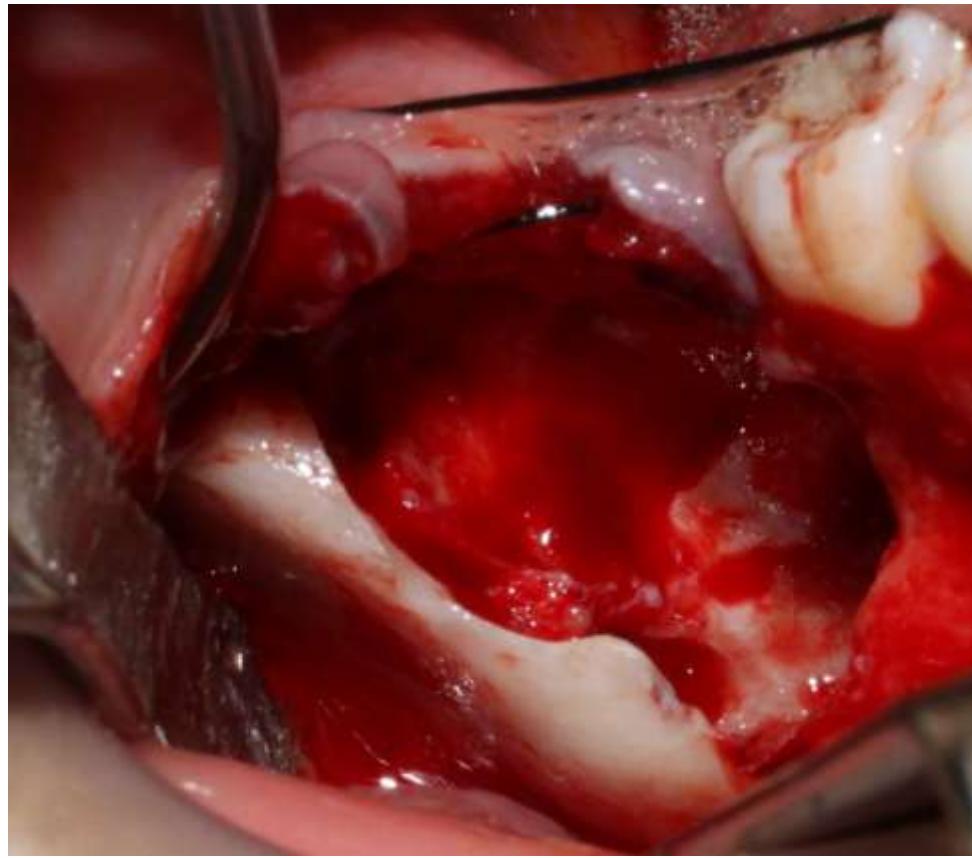
Biphasic Synthetic Material As an occlusive resorptive membrane

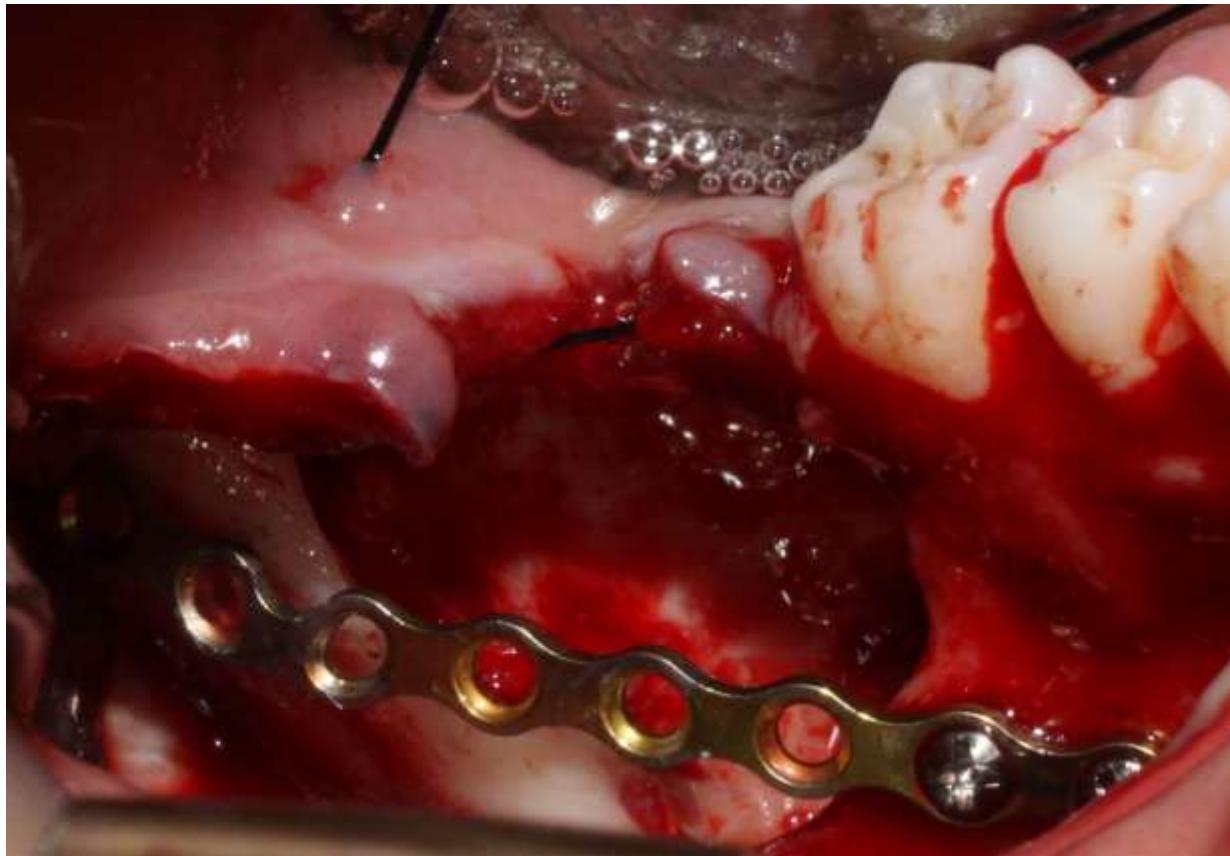


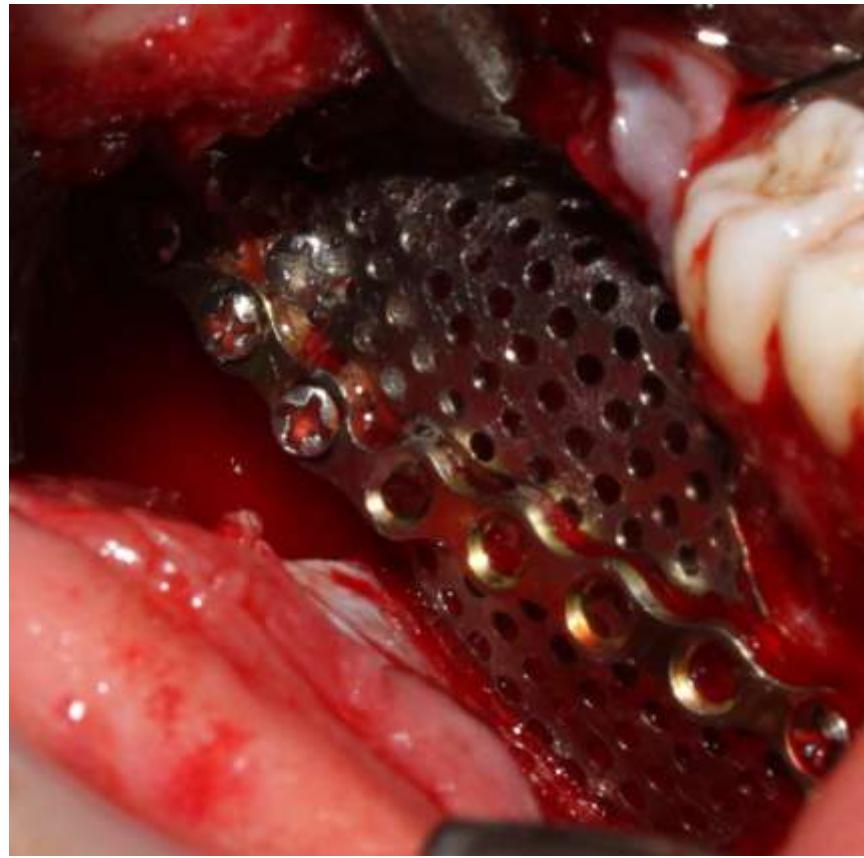




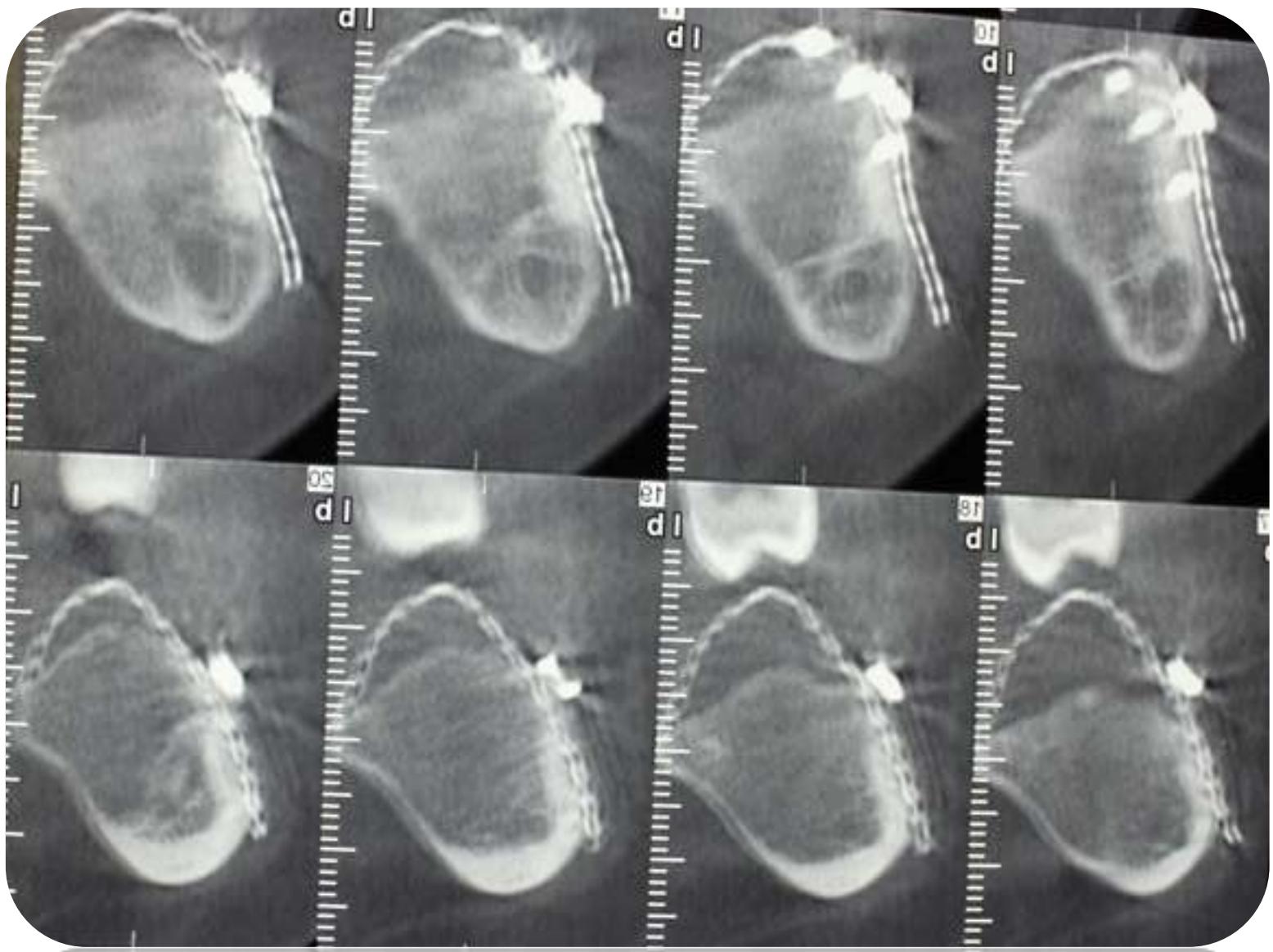




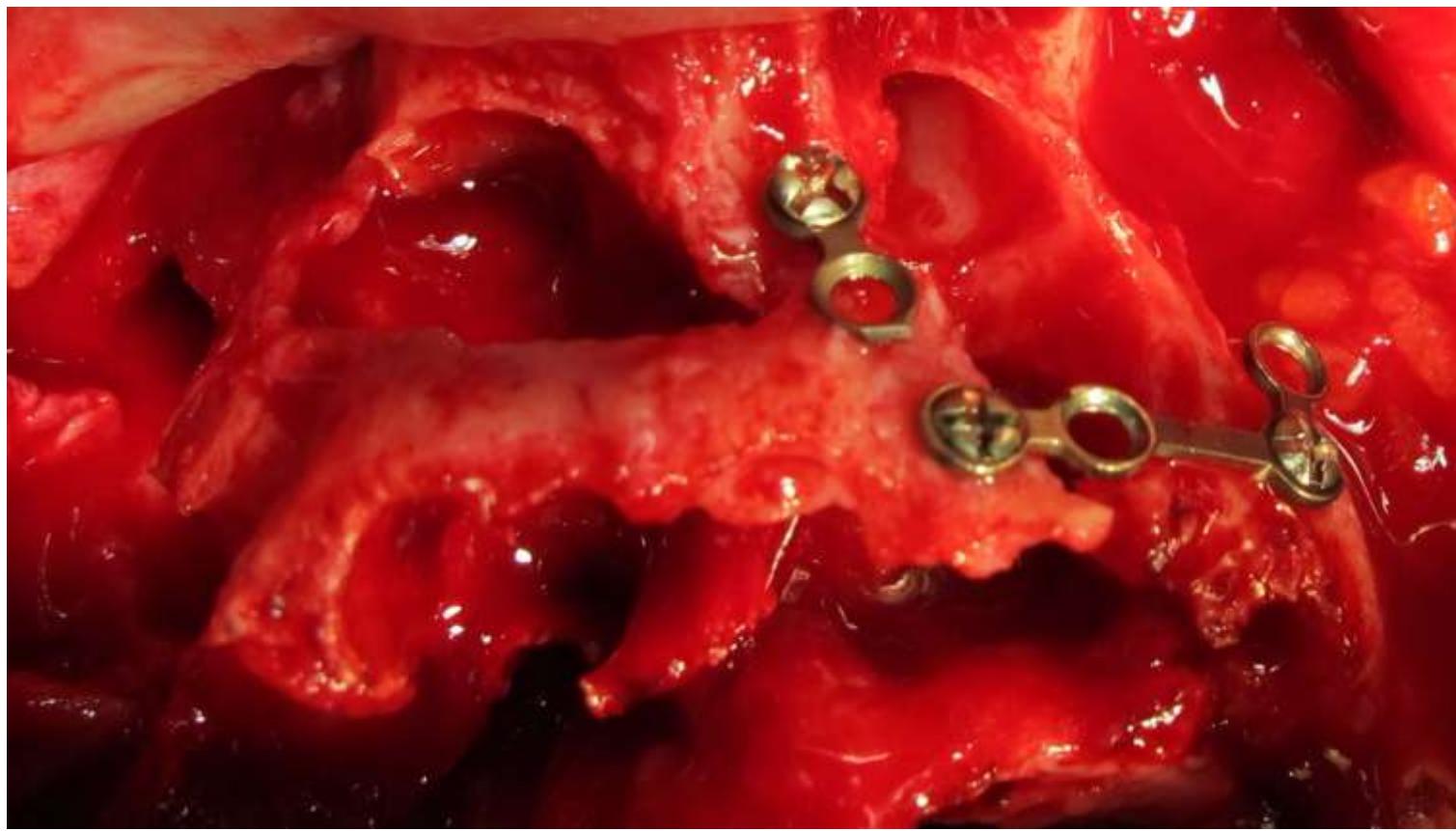


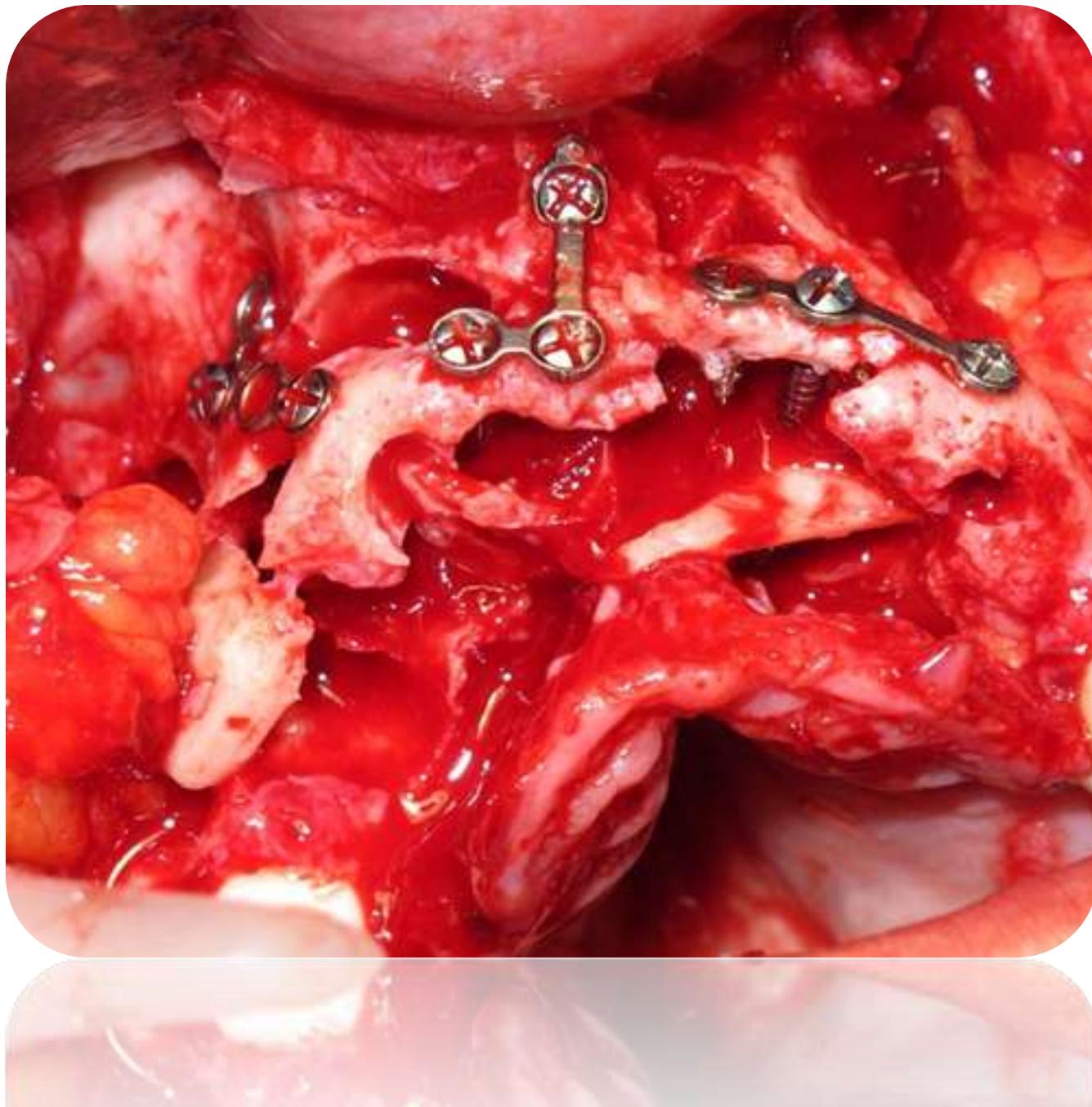


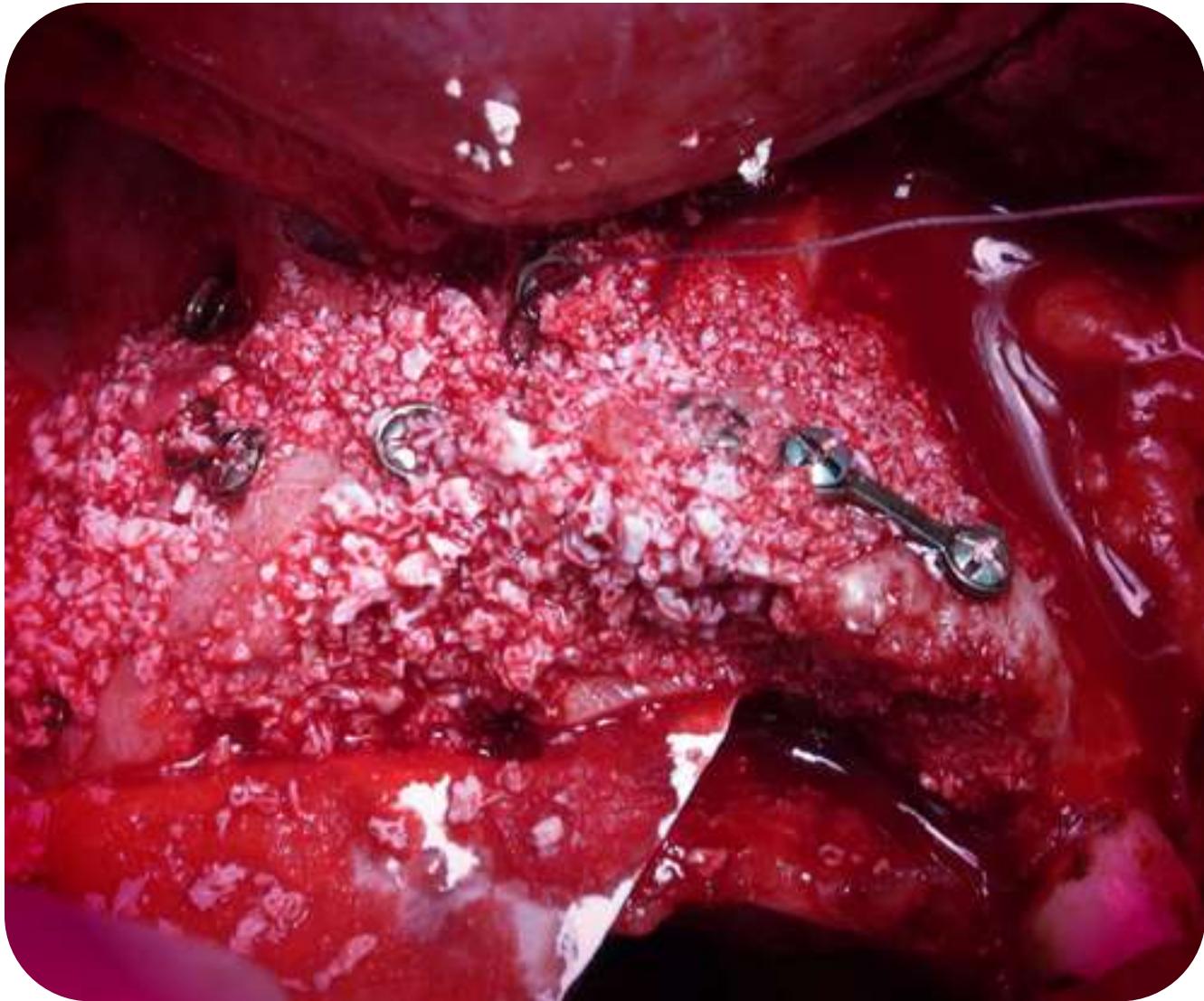


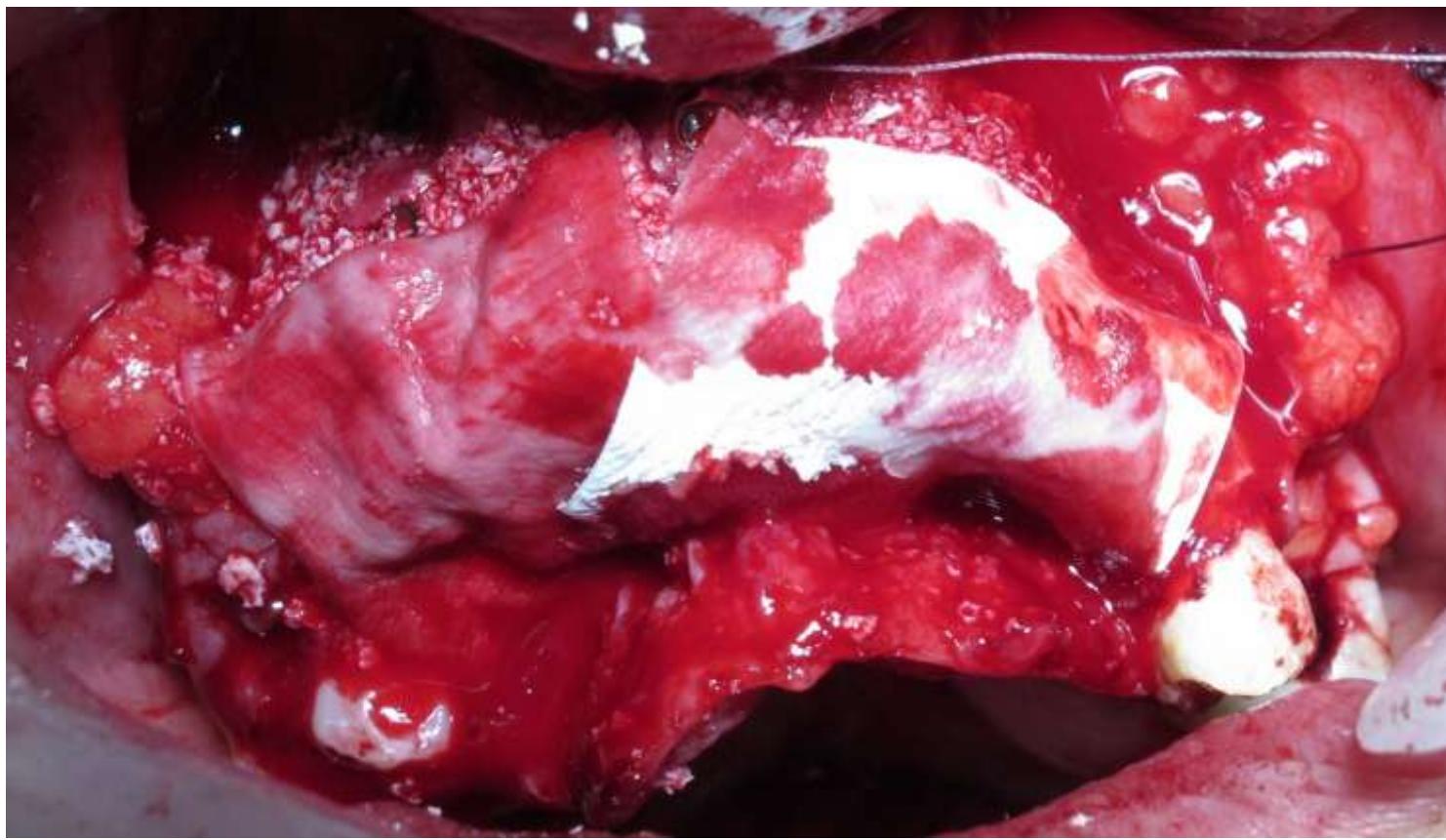


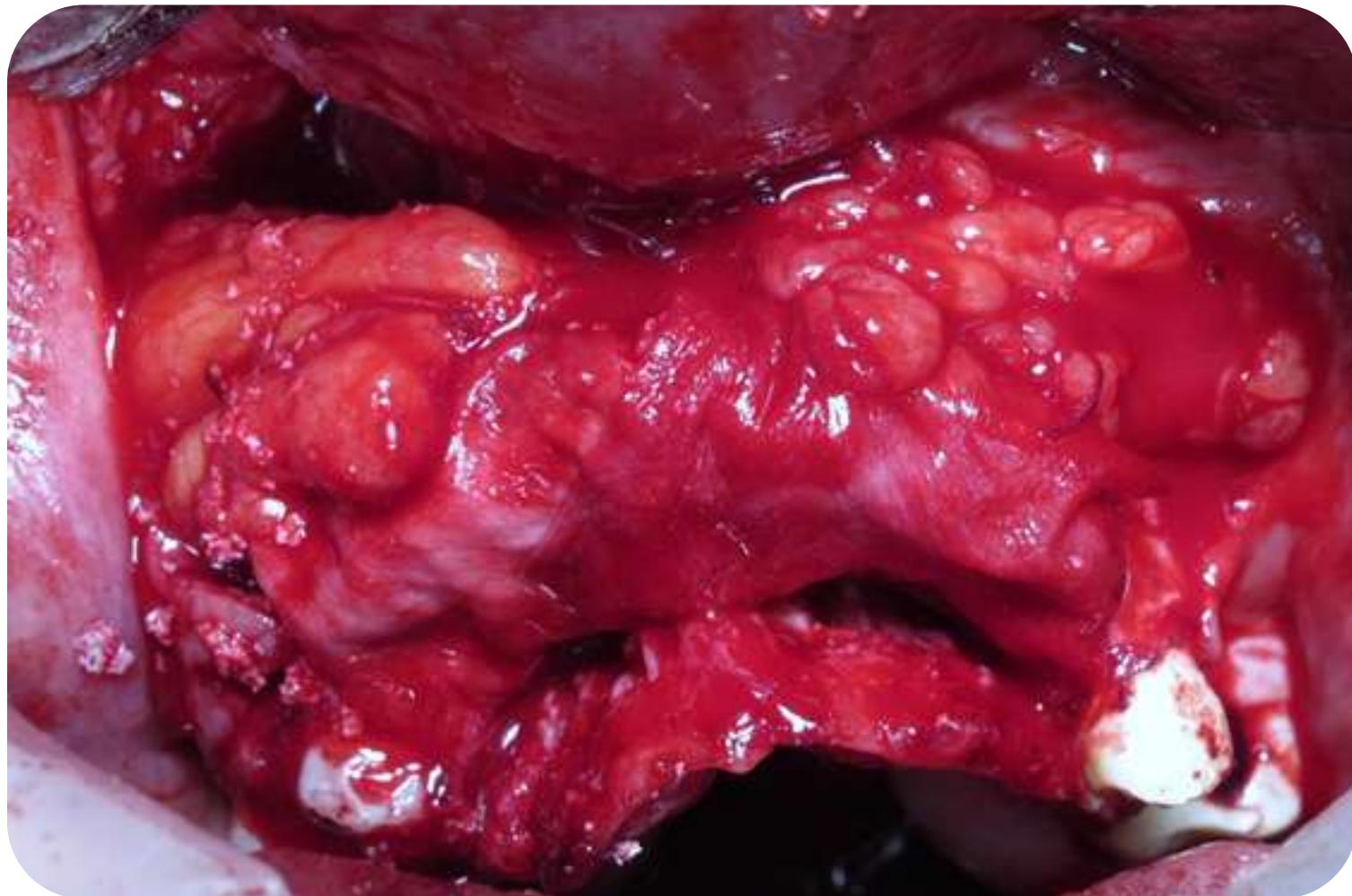


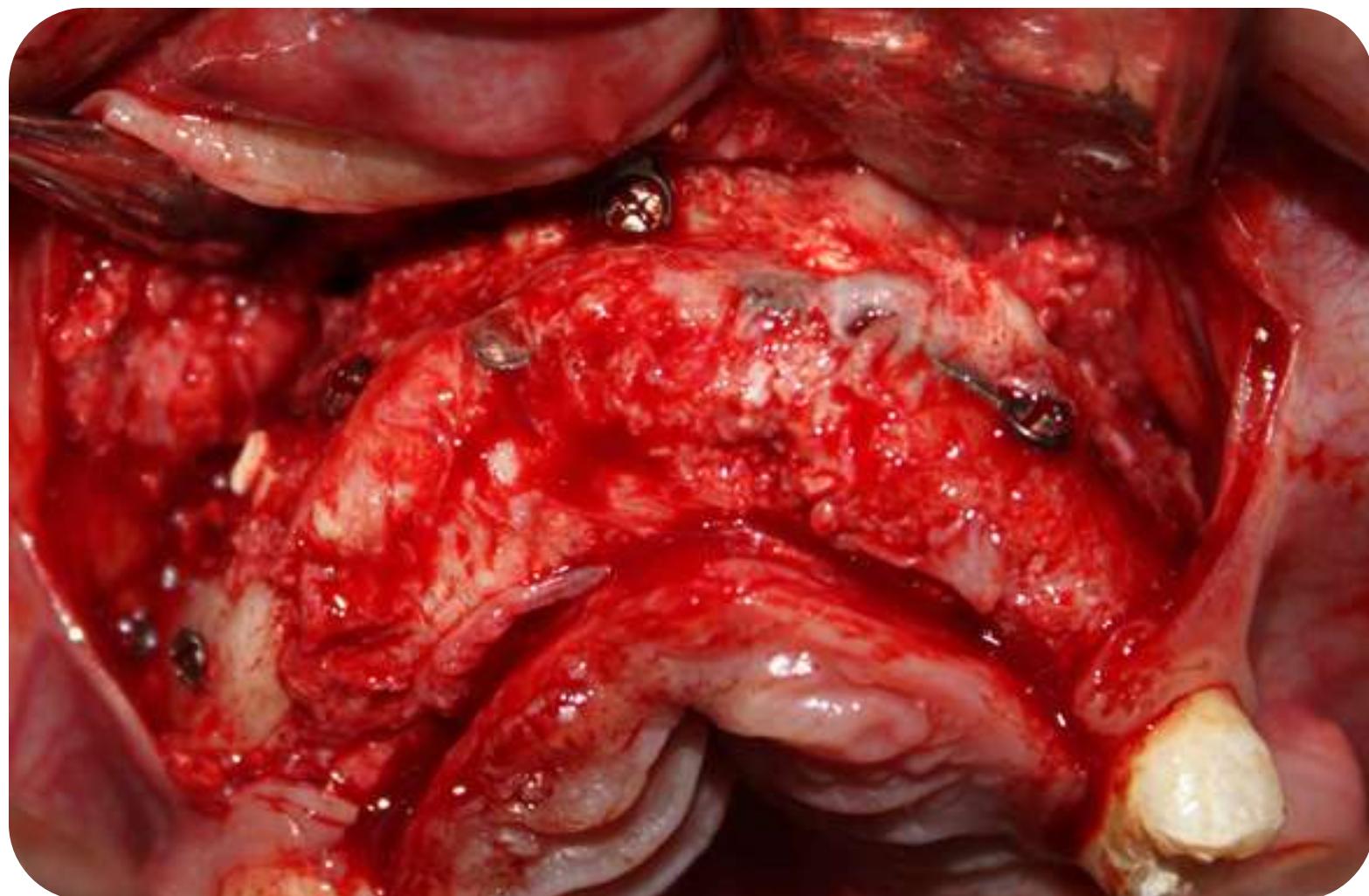




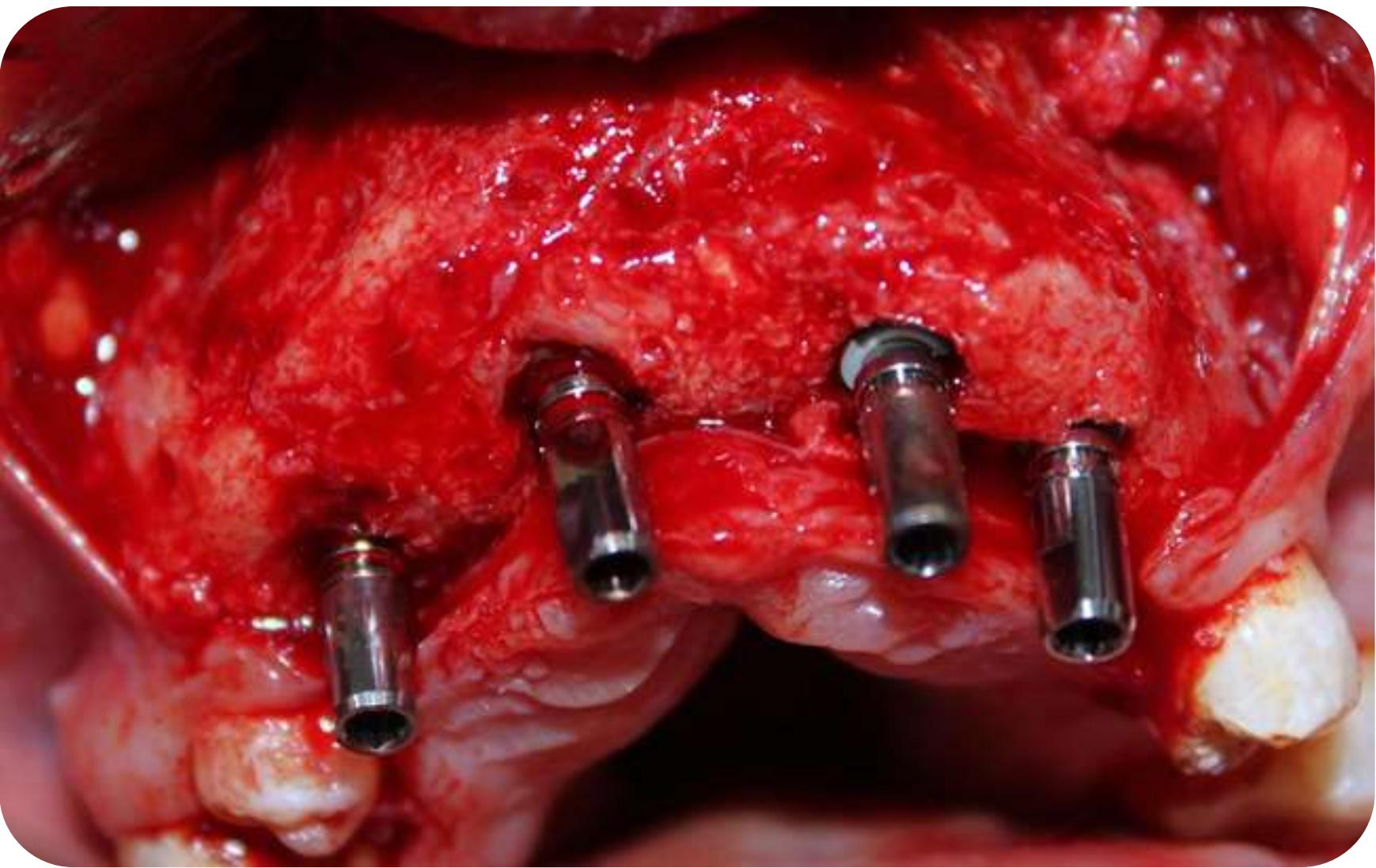














Dr Jafarian, Dr Khojasteh,
Dr Hassanzadeh

Arash Khojasteh
Thank you for your
Consideration