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# **BBL IN ORAL SURGERY: A NEW ERA OF FAST & EFFECTIVE HEALING**

**Prof. Dr. Maher Atari**

MD, DDS, MSR, PhD

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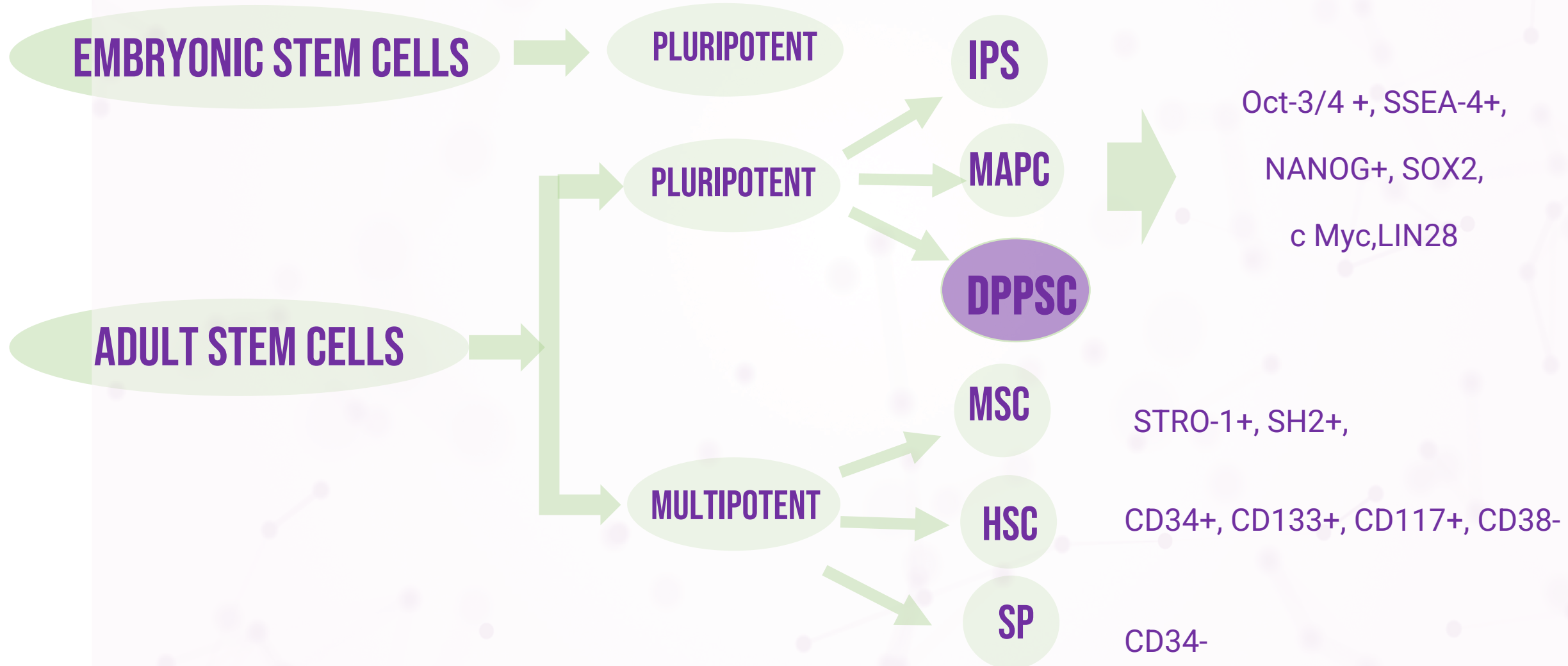
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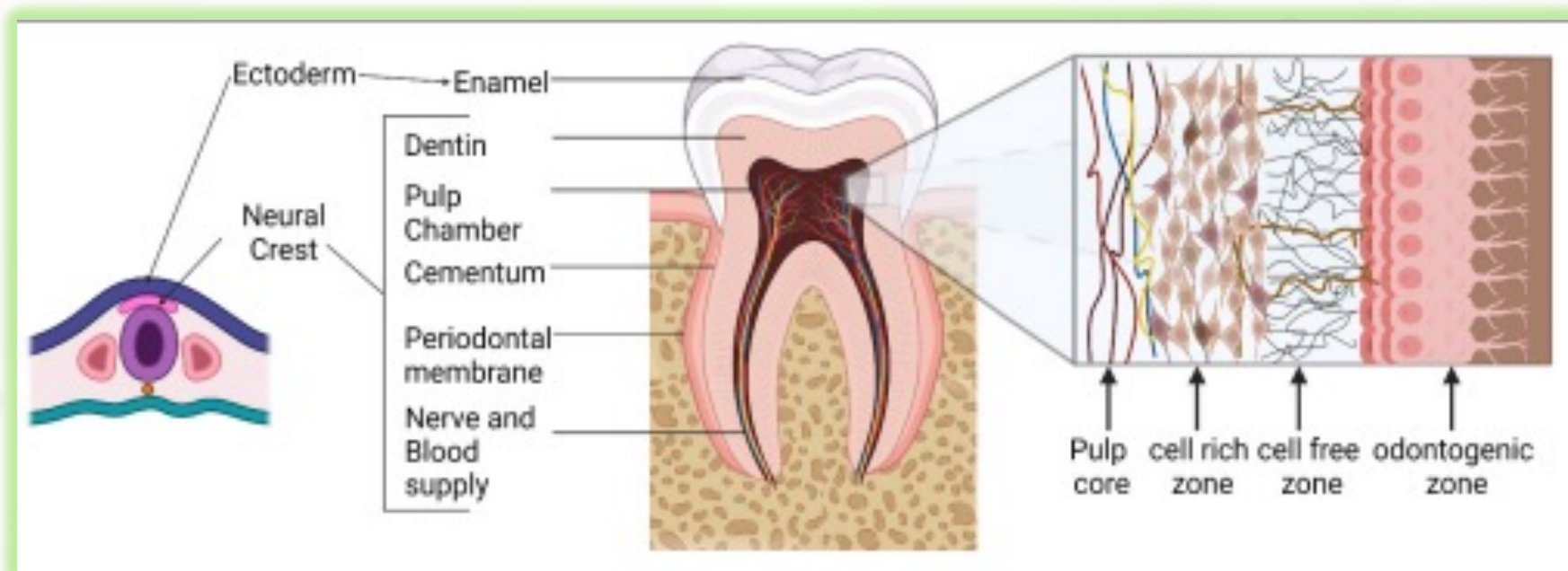
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# STEM CELLS



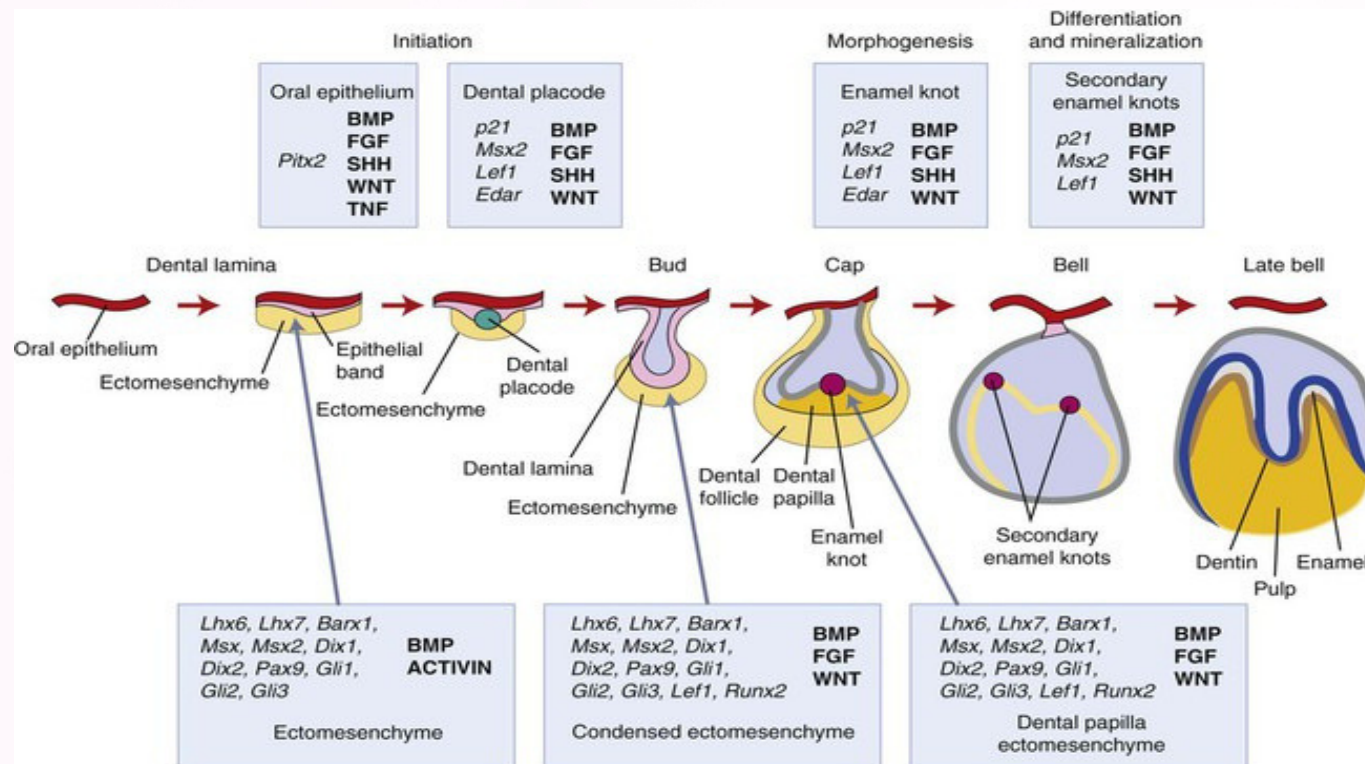
# STEM CELLS

Dental pulp of the third molar:  
a new source of pluripotent-like stem cells





# DPPSC ISOLATION



## Dental pulp of the third molar: a new source of pluripotent-like stem cells

Maher Atari<sup>1,2</sup>, Carlos Gil-Recio<sup>1</sup>, Marc Fabregat<sup>1</sup>, Dani García-Fernández<sup>1</sup>, Miguel Barajas<sup>3</sup>, Miguel A. Carrasco<sup>4</sup>, Han-Sung Jung<sup>5</sup>, F. Hernández Alfaro<sup>2</sup>, Nuria Casals<sup>6</sup>, Felipe Prosper<sup>3</sup>, Eduard Ferrés-Padró<sup>2</sup> and Luis Giner<sup>1,2,\*</sup>

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### Summary

Dental pulp is particularly interesting in regenerative medicine because of the accessibility and differentiation potential of the tissue. Dental pulp has an early developmental origin with multi-lineage differentiation potential as a result of its development during childhood and adolescence. However, no study has previously identified the presence of stem cell populations with embryonic-like phenotypes in human dental pulp from the third molar. In the present work, we describe a new population of dental pulp pluripotent-like stem cells (DPPSCs) that were isolated by culture in medium containing LIF, EGF and PDGF. These cells are SSEA4<sup>+</sup>, OCT3/4<sup>+</sup>, NANOG<sup>+</sup>, SOX2<sup>+</sup>, LIN28<sup>+</sup>, CD13<sup>+</sup>, CD105<sup>+</sup>, CD34<sup>+</sup>, CD45<sup>+</sup>, CD90<sup>+</sup>, CD29<sup>+</sup>, CD73<sup>+</sup>, STRO1<sup>+</sup> and CD146<sup>+</sup>, and they show genetic stability in vitro based on genomic analysis with a newly described CGH technique. Interestingly, DPPSCs were able to form both embryoid-body-like structures (EBs) in vitro and teratoma-like structures that contained tissues derived from all three embryonic germ layers when injected in nude mice. We examined the capacity of DPPSCs to differentiate in vitro into tissues that have similar characteristics to mesoderm, endoderm and ectoderm layers in both 2D and 3D cultures. We performed a comparative RT-PCR analysis of *GATA4*, *GATA6*, *MIXL1*, *NANOG*, *OCT3/4*, *SOX1* and *SOX2* to determine the degree of similarity between DPPSCs, EBs and human induced pluripotent stem cells (hiPSCs). Our analysis revealed that DPPSCs, hiPSC and EBs have the same gene expression profile. Because DPPSCs can be derived from healthy human molars from patients of different sexes and ages, they represent an easily accessible source of stem cells, which opens a range of new possibilities for regenerative medicine.

**Key words:** Dental pulp, DPPSC, Pluripotency, Teratoma formation, Embryonic markers, CGH technique

# BIOINTELLEGIENT PUBLICATIONS



Article

## Histologic and Histomorphometric Evaluation of a New Bioactive Liquid BBL on Implant Surface: A Preclinical Study in Foxhound Dogs

Eduard Ferrés-Amat <sup>1,†</sup>, Ashraf Al Madhoun <sup>2,†</sup>, Elvira Ferrés-Amat <sup>1,3</sup>, Saddam Al Demour <sup>4</sup>, Mera A. Ababneh <sup>5</sup>, Eduard Ferrés-Padró <sup>1,6</sup>, Carles Martí <sup>6,7</sup>, Neus Carrio <sup>3</sup>, Miguel Barajas <sup>6,8</sup> and Maher Atari <sup>6,9,\*</sup>



Brief Report

## The Effect of Commercially Available Endodontic Cements and Biomaterials on Osteogenic Differentiation of Dental Pulp Pluripotent-Like Stem Cells

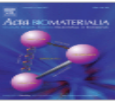
Atari Maher <sup>1,\*</sup>, Raquel Núñez-Toldrà <sup>1</sup>, Neus Carrio <sup>1</sup>, Eduard Ferrés-Padró <sup>2</sup>, Hamad Ali <sup>3</sup>, Sheyla Montori <sup>1</sup> and Ashraf Al Madhoun <sup>4,\*</sup>

## Dental pulp of the third molar: a new source of pluripotent-like stem cells

Maher Atari <sup>1,2</sup>, Carlos Gil-Recio <sup>1</sup>, Marc Fabregat <sup>1</sup>, Dani García-Fernández <sup>1</sup>, Miguel Barajas <sup>3</sup>, Miguel A. Carrasco <sup>4</sup>, Han-Sung Jung <sup>5</sup>, F. Hernández Alfaro <sup>2</sup>, Nuria Casals <sup>6</sup>, Felipe Prosper <sup>3</sup>, Eduard Ferrés-Padró <sup>2</sup> and Luis Giner <sup>1,2,\*</sup>



Acta Biomaterialia  
Volume 53, 15 April 2017, Pages 152-164



Full length article

## Improvement of osteogenesis in dental pulp pluripotent-like stem cells by oligopeptide-modified poly( $\beta$ -amino ester)s

Raquel Núñez-Toldrà <sup>a,1</sup>, Pere Dosta <sup>b,1</sup>, Sheyla Montori <sup>a</sup>, Víctor Ramos <sup>b</sup>, Maher Atari <sup>a</sup>, Salvador Borrós <sup>b,c</sup>

Research Article

## Chemically Defined Conditions Mediate an Efficient Induction of Dental Pulp Pluripotent-Like Stem Cells into Hepatocyte-Like Cells

Carlos Gil-Recio <sup>1</sup>, Sheyla Montori <sup>1</sup>, Saddam Al Demour <sup>2</sup>, Mera A. Ababneh <sup>3</sup>, Eduard Ferrés-Padró <sup>4</sup>, Carles Martí <sup>5</sup>, Elvira Ferrés-Amat <sup>6</sup>, Miguel Barajas <sup>7</sup>, Ashraf Al Madhoun <sup>8</sup> and Maher Atari <sup>1,9</sup>

Martínez-Sarrà et al. Stem Cell Research & Therapy (2017) 8:175  
DOI 10.1186/s13287-017-0621-3

Stem Cell Research & Therapy

RESEARCH

Open Access



## Human dental pulp pluripotent-like stem cells promote wound healing and muscle regeneration

Ester Martínez-Sarrà <sup>1,2</sup>, Sheyla Montori <sup>1</sup>, Carlos Gil-Recio <sup>1</sup>, Raquel Núñez-Toldrà <sup>1</sup>, Domiziana Costamagna <sup>2</sup>, Alessio Rotini <sup>2,3,4</sup>, Maher Atari <sup>1†</sup>, Aernout Luttun <sup>5†</sup> and Maurilio Sampaoli <sup>2,6†</sup>



# DPPS CELLULAR MORPHOLOGY CHARACTERISATION

Research Article

3343

## Dental pulp of the third molar: a new source of pluripotent-like stem cells

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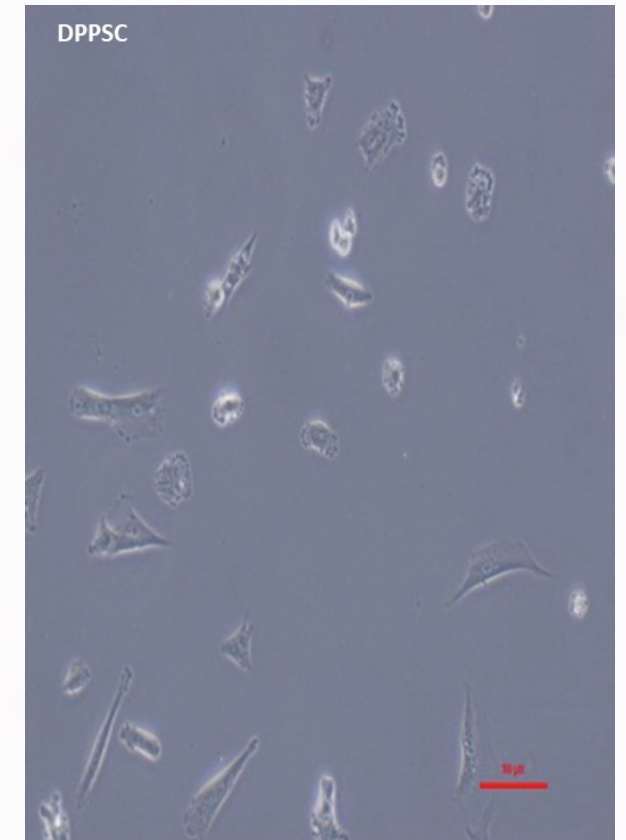
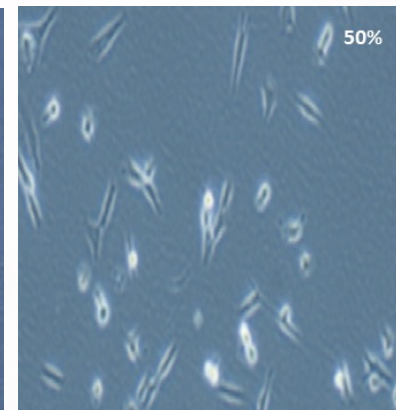
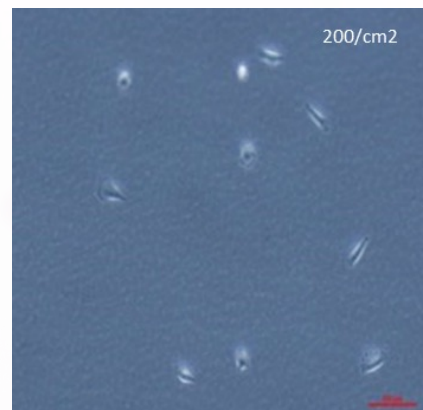
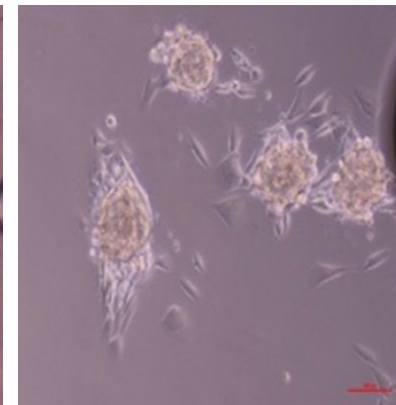
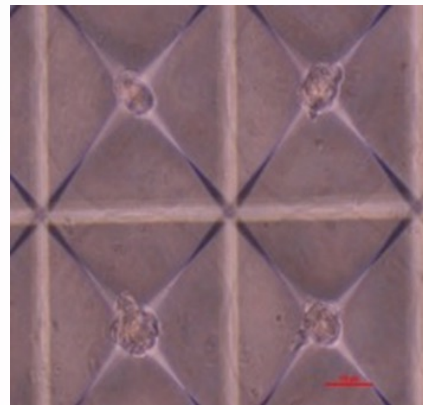
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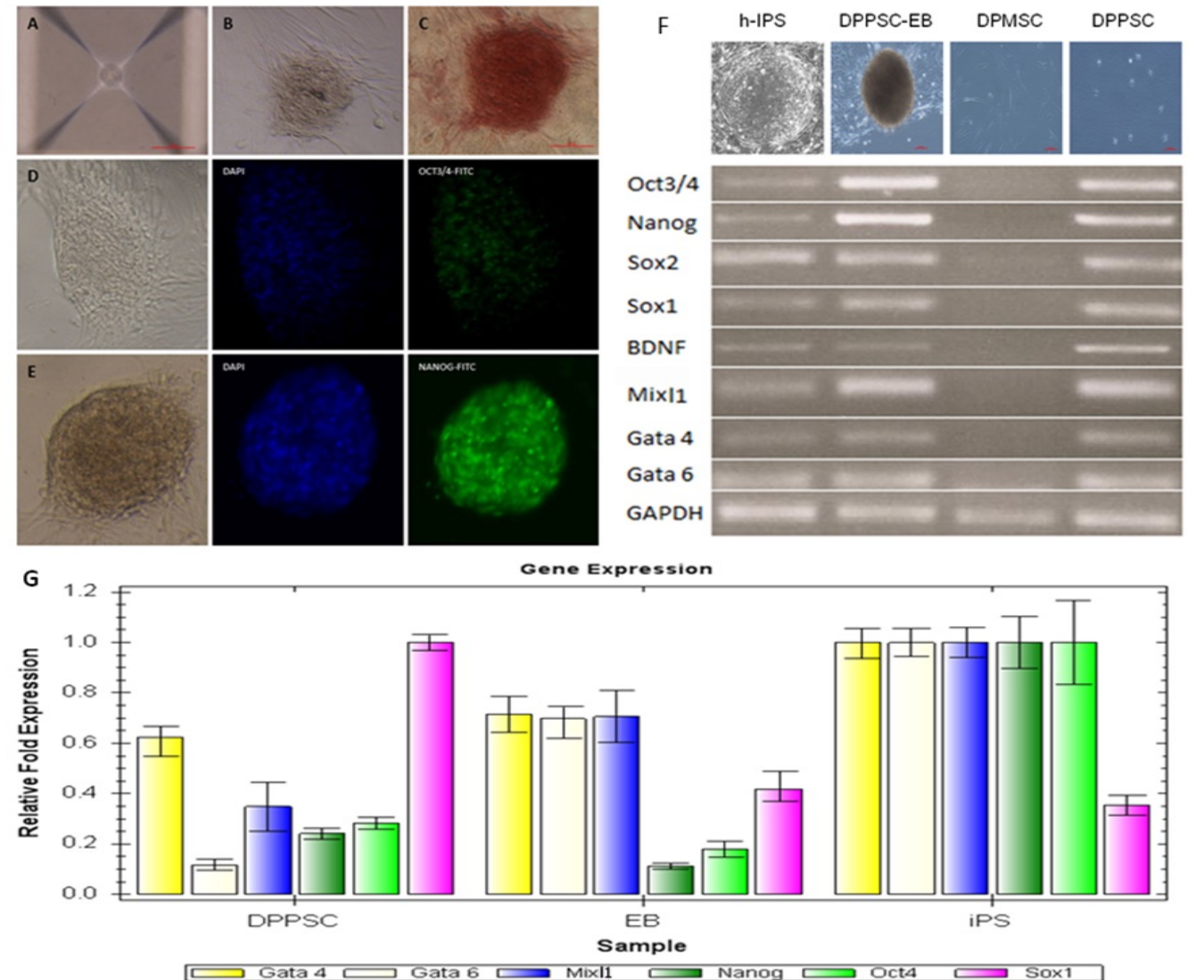
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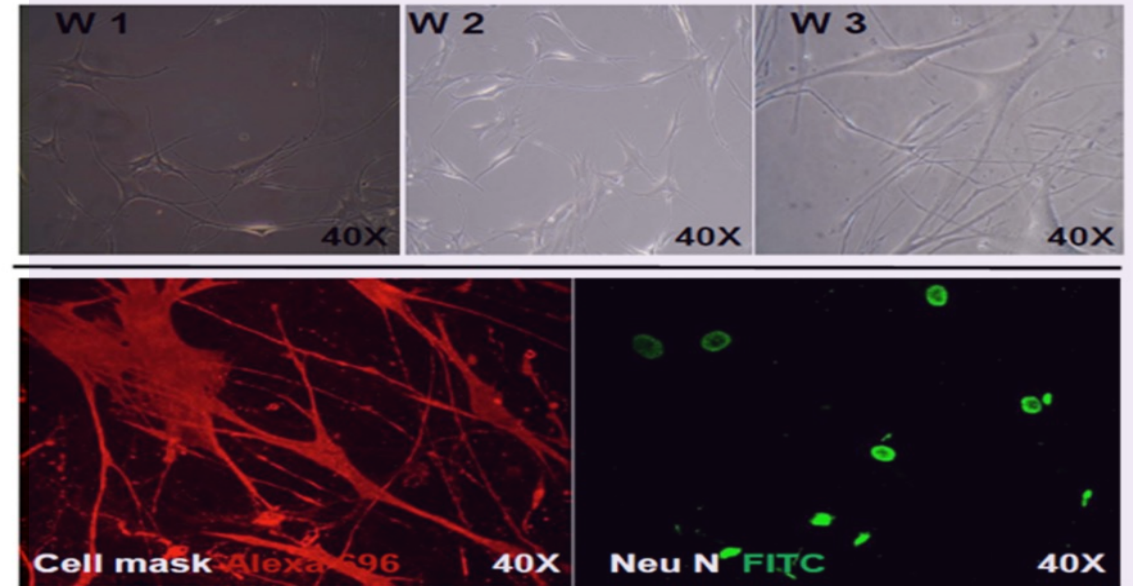
# COMPARISON OF PROFILES WITH ANOTHER STEM CELLS





# DPPSC ECTODERM DIFFERENTIATION

**A**

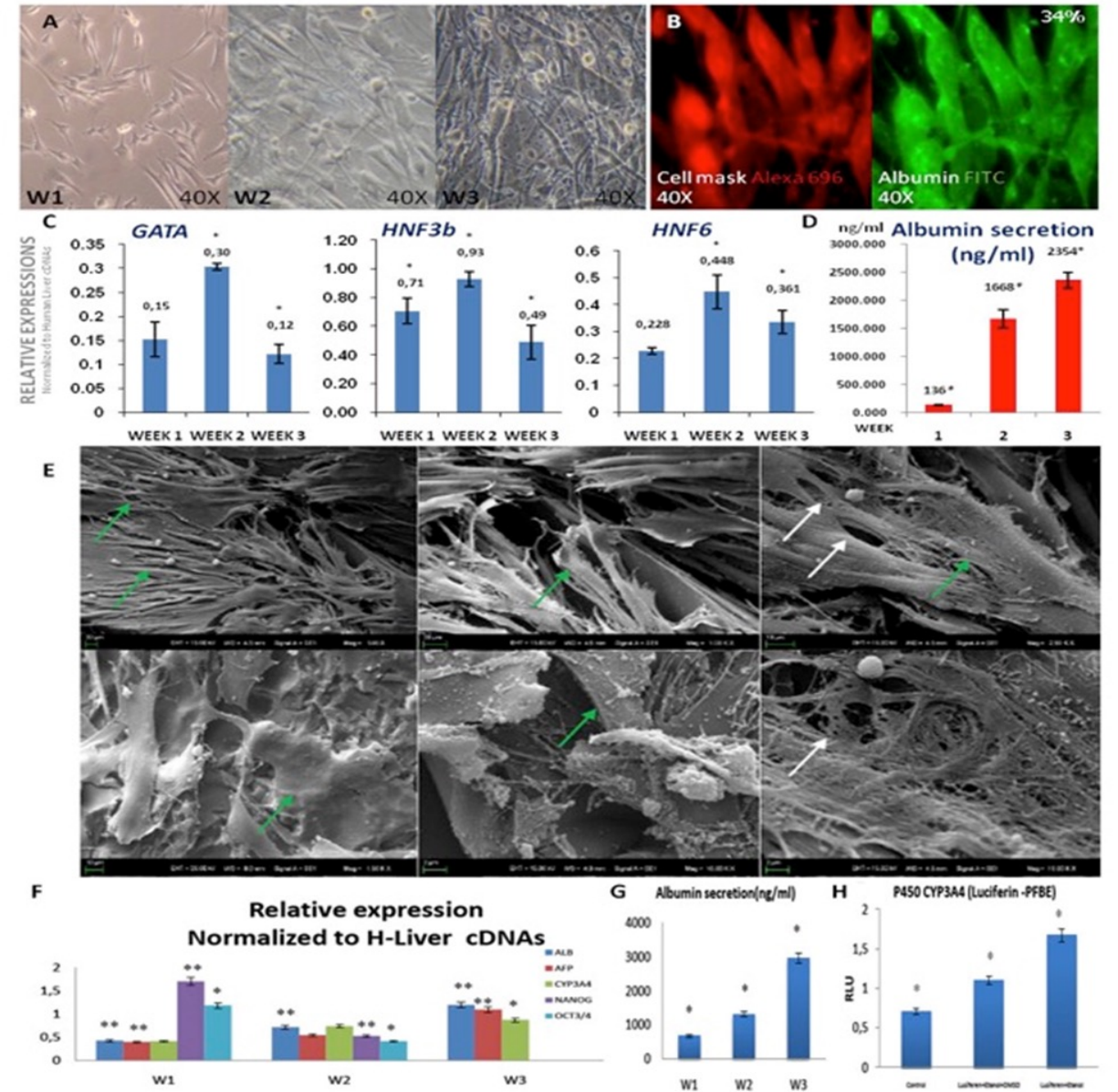


**B**

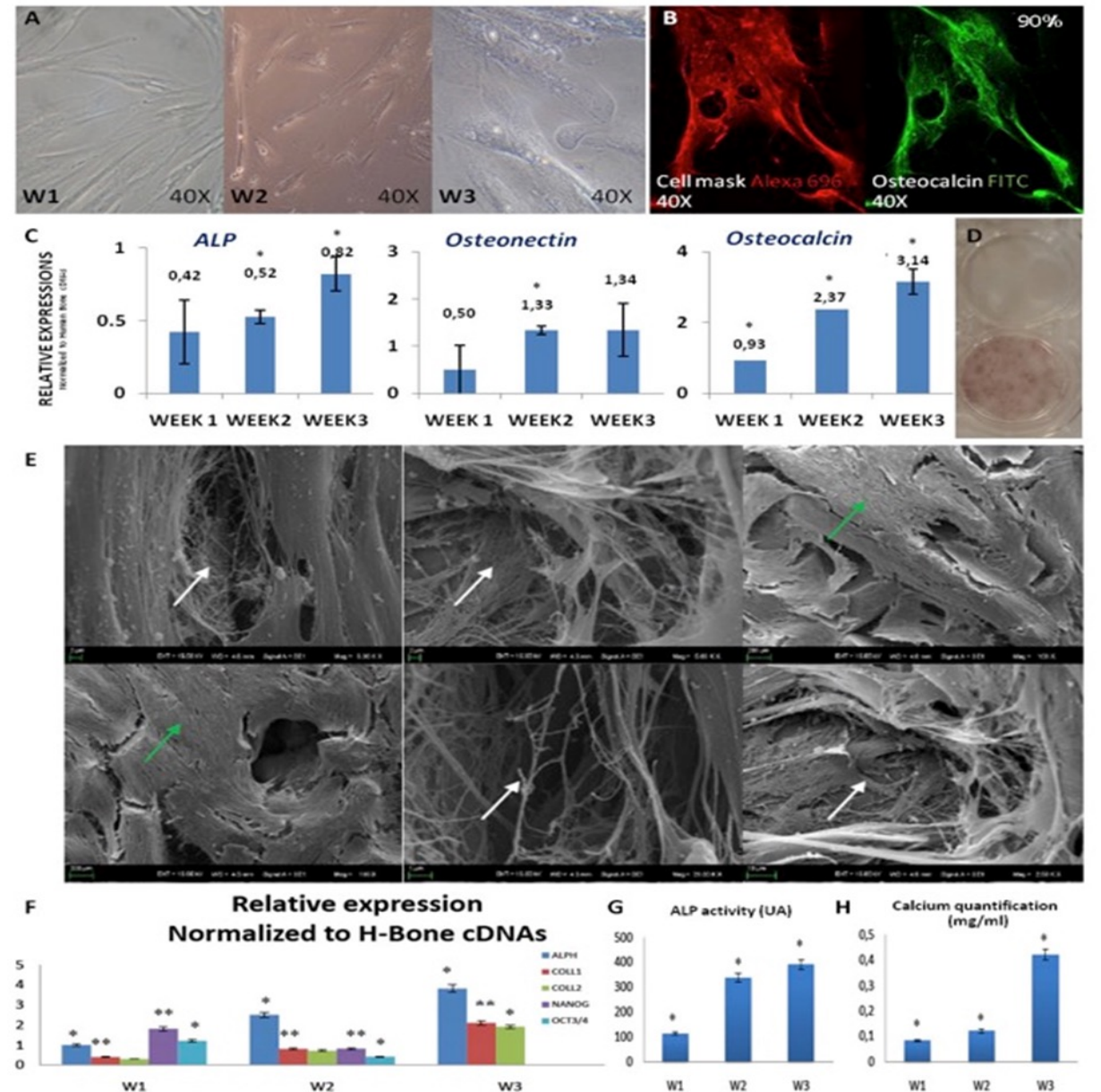
**RELATIVE EXPRESSIONS**  
Normalized to Human brain cDNAs



# DPPSC ENDODERM DIFFERENTIATION



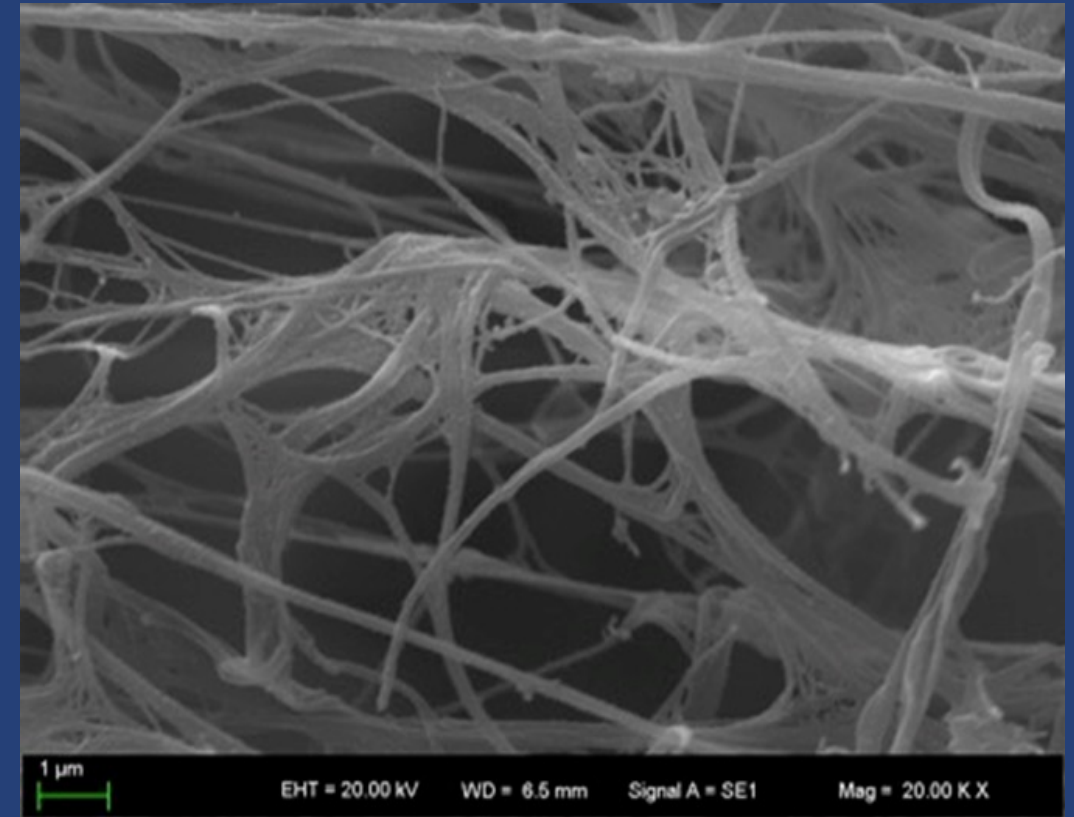
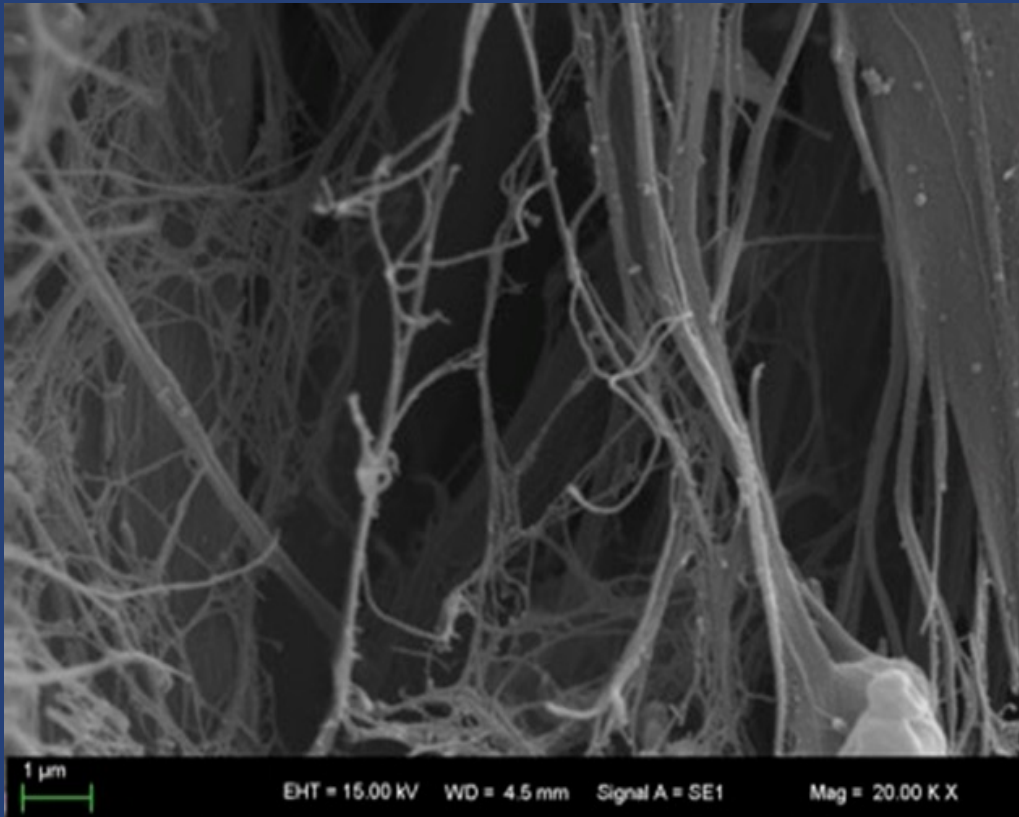
# DPPSC MESODERM DIFFERENTIATION





## DPPSC- BONE

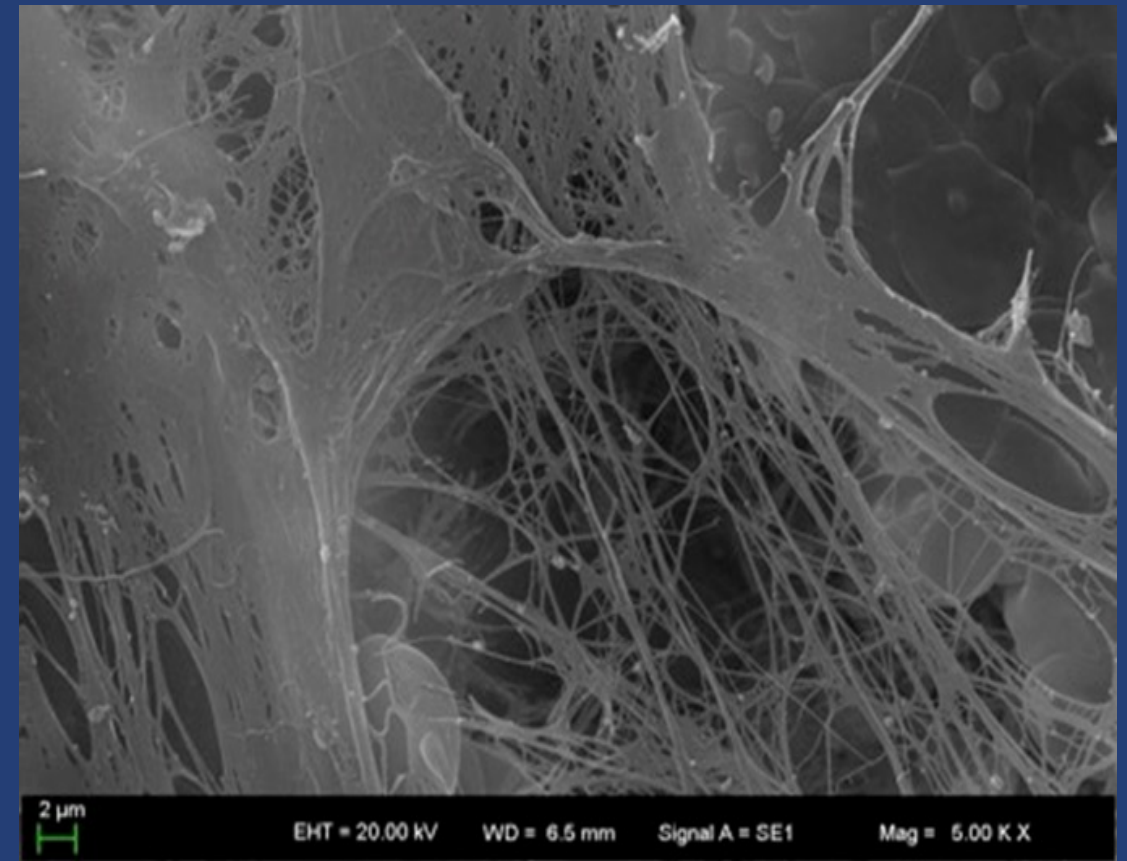
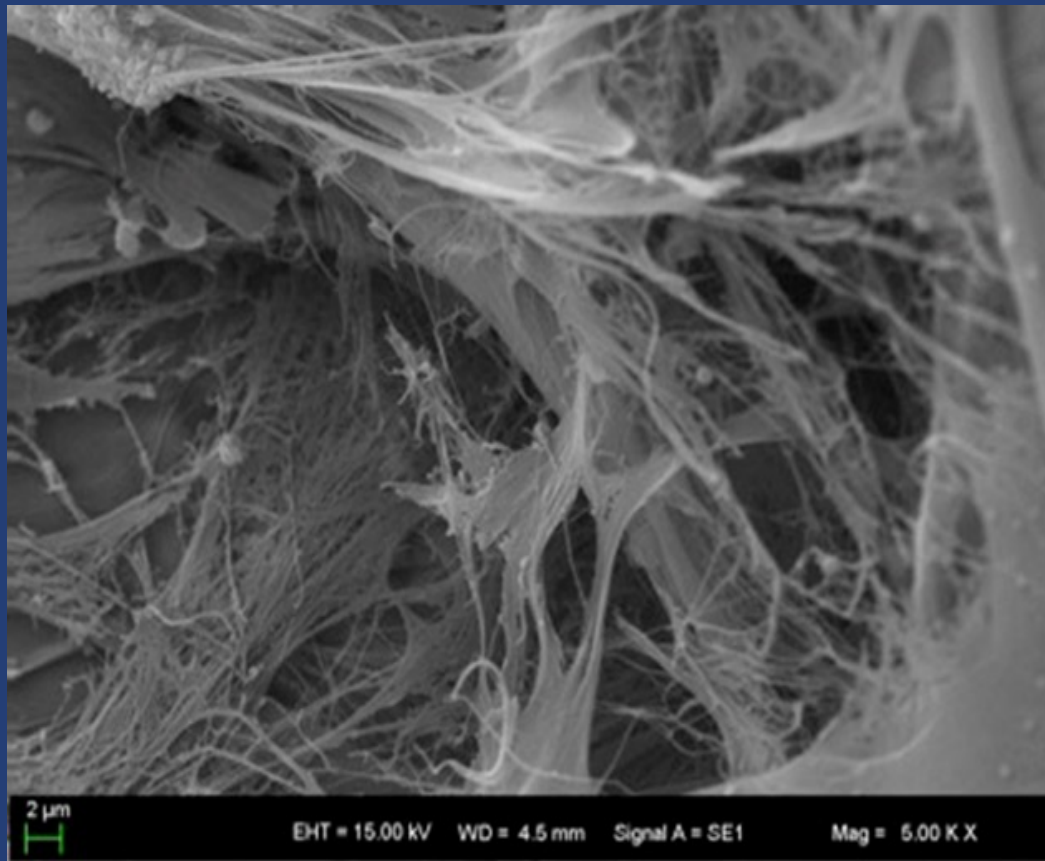
## HUMAN BONE



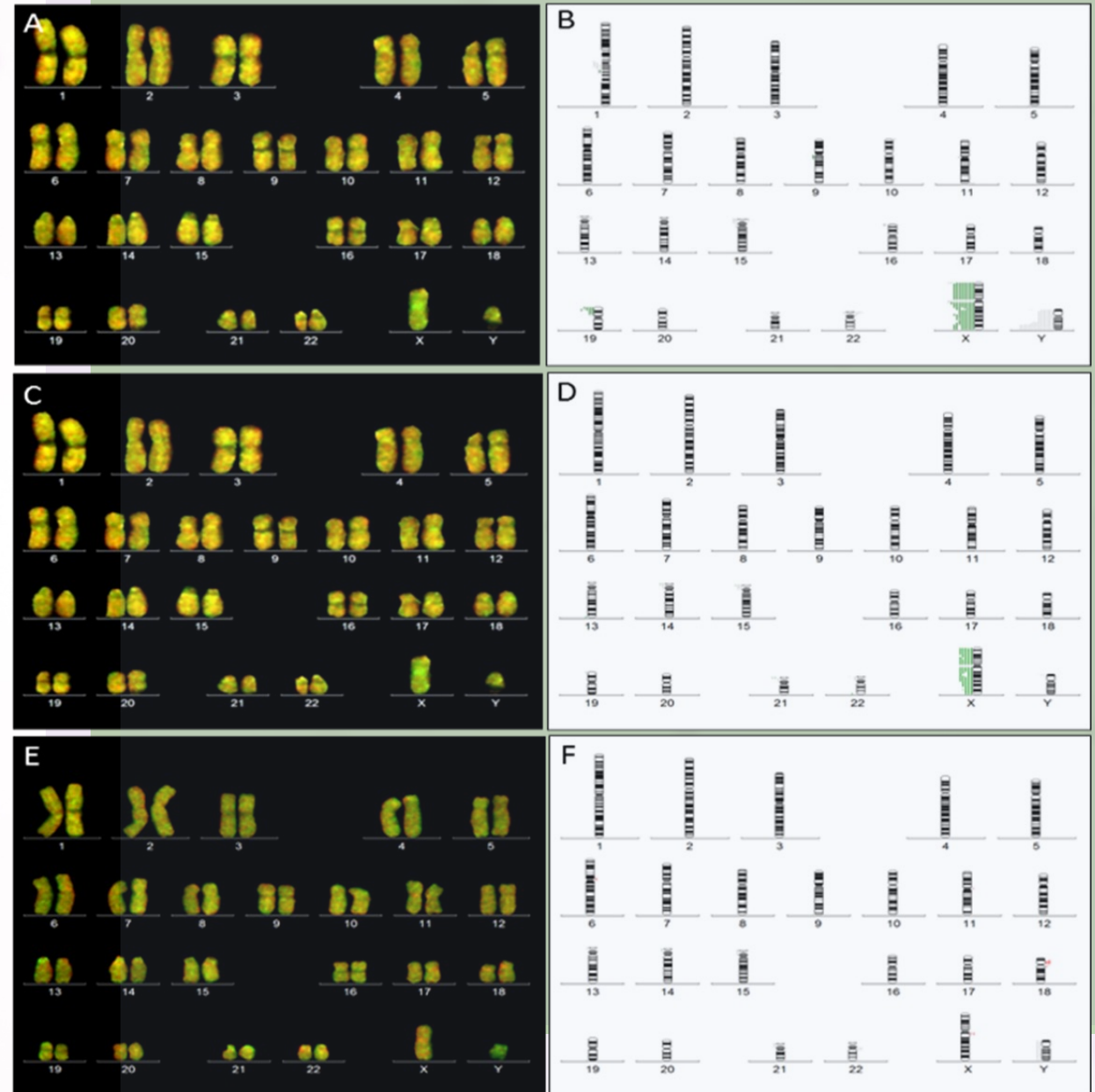


## DPPSC- BONE

## HUMAN BONE



# CHROMOSOMAL CHARACTERISATION



# PROTEIENS CHARACTERISATION

# FIBRONECTIN CD29, IL4, IL10, RANK

Protein name	Gene Names	LFQ Intensity	Protein name	Gene Names	LFQ Intensity	Protein name	Gene Names	LFQ Intensity
Brain acid soluble protein 1	BASP1	27696000	Adenylate kinase 2, mitochondrial	ADK2	912970	40S ribosomal protein S13	RPS13	480180
Galactose-specific lectin 3	LGALS3	9423700	8 kDa dynein light chain	DLC1	907720	Cootner subunit zeta-2	COPZ2	454430
Tubulin beta-3 chain	TUBB3	6822700	Heterogeneous nuclear ribonucleoprotein A0	HNRNP40	901440	DA2-associated protein 1	DAZAP1	452420
Myosin heavy chain, non-muscle Iib	MYH10	5975000	17-beta-hydroxysteroid dehydrogenase 4	EDH1B4	895890	Pyruvate-5-carboxylate reductase	PFYK1	451020
Defender against cell death 1	DIAD1	5353500	Protein transport protein Sec24D	KIAA0755	893120	Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3C variant	APOBEC1L	449760
Enhancer of rudimentary homolog	ERH	5054600	Asparagine-tRNA ligase	ASNS	882260	26S proteasome AAA-ATPase subunit RPT4	PSMC6	444410
Heat shock protein HSP 90-alpha	HSP90AA1	4651500	ATP synthase subunit delta, mitochondrial	ATP5D	878020	Citrate synthase	CS	432790
40S ribosomal protein S19	RPS19	4550700	DEAD box protein 6	DDX6	871660	5-AMP-activated protein kinase subunit gamma-1	PRKAG1	428130
60S ribosomal protein L38	RPL38	4404400	60S ribosomal protein L14	RPL14	866170	Fumarate hydratase, mitochondrial	FH	426070
Gamma-2-globin	HBB2	4021900	40S ribosomal protein S8	OK/SW-d.83	860510	c-Ki-ras	KRAS	422890
Myosin-Ic	MYO1C	3568600	Pyridoxal kinase	C21orf124	848420	Heme oxygenase 1	HMOX1	421930
Cystatin-B	CSTB	3418700	Proteasome subunit alpha type-3	PSMA3	846650	ES1 protein homolog, mitochondrial	C21orf33	418150
Hemoglobin alpha 1	HBA1/HBA2	2780000	Importin-7	IPO7	837730	Septin-8	KIAA0202	414550
Delta-sarcoglycan	SGCO	2608000	Guanine nucleotide-binding protein G(I)/G(S)/G(O) subunit gamma-12	GNG12	831500	Glioblastoma-amplified sequence	GBA5	394340
40S ribosomal protein S27-like	RPS27L	2473600	Mitochondrial 2-oxoglutarate/malate carrier protein	SLC20A4	821290	Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial	HADH	393310
Cootner subunit alpha	COPA	2241600	Small nuclear ribonucleoprotein Sm D3	SNRPD3	816520	Dynactin complex subunit 22 kDa subunit	DCTN22	390810
60S ribosomal protein L36	RPL36	2220900	60S ribosomal protein L22	RPL22	810130	Protein kinase C and casein kinase substrate in neurons protein 2	PACSN2	386110
Septin-2	KIAA0202	2167200	Malectin	MLEC	804740	2,3-cyclic-nucleotide 3-phosphodiesterase	CNP	378640
Putative uncharacterized protein ALDOC	ALDOC	2116900	ATP-specific succinyl-CoA synthetase subunit beta	SUCLA2	800330	C-terminal-binding protein 2	CTBP2	375770
Up-regulated during skeletal muscle growth protein 5	HCVTP2	2051200	Major prion protein	PRNP	784470	Methionine adenosyltransferase 2	MAT2A	371860
Coagulation factor XIII A chain	F13A	2049900	MAP1 light chain LC2	MAP1A	781630	Interferon-induced transmembrane protein 3	IFITM3	371360
60S ribosomal protein L18a	RPL18A	2016900	Integrin beta-5	ITGB5	751840	Vasodilator-stimulated phosphoprotein	VASP	370070
Apolipoprotein H	APOH	1945300	SH3 domain-binding glutamic acid-rich-like protein	SH3BGRL	748820	Isolevucine-tRNA ligase	IARS	347000
C-C chemokine receptor type 8	CCR8	1906900	60S ribosomal protein L6	RPL6	745740	Ornithine aminotransferase, hepatic form	OAT	334300
Membrane-associated progesterone receptor component 2	PGRM2	1898100	p30 DBC	KIAA1967	736270	Leprecan-like protein 2	LEPREL2	332270
Histone H2A.2	H2AF2	1884200	Lissencephaly-1 protein	LIS1	731180	Glycine hydroxymethyltransferase	SHMT2	319110
Axonemal beta dynein heavy chain 7	DNAH7	1804300	Four and a half LIM domains protein 3	FHL3	724840	Oncogene FUS	FUS	311850
Protein transport protein Sec61 subunit beta	SEC61B	1756200	Macropain subunit C7-4	PSM82	720440	Androgen-regulated short-chain dehydrogenase/reductase 1	ARSOR1	311180
G gamma-I	GNG2	1666700	Microtubule-associated proteins 1A/1B light chain 3 beta 2	MAP1LC3B2	717490	Acetyl-CoA acetyltransferase, cytosolic	ACAT2	310430
Elongation factor Tii, mitochondrial	TUFM	1642900	DEAD box polypeptide 17 isoform p82 variant	DDX17	713810	Vacuolar ATPase isoform VA68	ATP6A1	310360
Phosphoserine aminotransferase	PSA	1634500	Macropain epsilon chain	LMPX	709880	60S ribosomal protein L12	RPL12	308390
70 kDa subunit of Ku antigen	XRCC6	1634000	Pre-mRNA-splicing factor SF3b1 130 kDa subunit	KIAA0017	699460	ADP-ribosylation factor-like protein 1	ARL1	305820
Eukaryotic initiation factor 4A-II	EIF4A2	1489000	Leucine-tRNA ligase	KIAA1352	695650	Endoplasmic reticulum-Golgi intermediate compartment protein 1	ERGIC1	302740
60S ribosomal protein L30	RPL30	1471300	40S ribosomal protein S5	RPS5	691660	Vacuolar protein sorting-associated protein 26A	VPS26A	297080
9.55 alpha-1-glycoprotein	APCS	1410300	Tetratricopeptide repeat protein 35	KIAA0103	687970	Chap1	HRHF82157	278040
ICP-2	TOM22	1394200	DORGG domain-containing protein 1	DORGG1	687570	Protein 40-6-3	SUGT1	276970
Actin-related protein 2/3 complex subunit 5	ARC16	1360700	Cytochrome c	CYC	682870	p120GAP	RASA	266070
Adenylate kinase 1	AK1	1342200	Opa-interacting protein 1	OIP1	676250	Baboon M7 virus receptor	ASCT2	252180
FK506-binding protein 1A	FKBP1A	1331600	Cyclocoxygenase-1	COX1	669280	Mitogen-activated protein kinase 1-interacting protein 1-like	MAPK1P1L	223430
CD49 antigen-like family member B	CD49B	1289300	CD63 antigen	CD63	660080	Complex 1-POSW	NDUF810	215470
Eukaryotic initiation factor 4A-III	EIF4A3	1265400	PEP11 homolog	DC15	657420	ATP synthase subunit g, mitochondrial	ATP5L	215200
CD49 antigen-like family member F	ITGA6	1229600	Malic enzyme 2	ME2	648290	Importin subunit beta-3	IPO5	200740
Chromosome 14 open reading frame 166	C14orf166	1173800	Ubiquitin cross-reactive protein	USP15	645570	Beta-actin-like protein 2	ACTBL2	195870
60S acidic ribosomal protein P2	D11S2243E	1167200	Prostaglandin reductase 1	PTGRL1	627690	Collagen alpha-1(VI) chain	COL4A1	181310
17-beta-hydroxysteroid dehydrogenase 10	ERAB	1162100	Neural precursor cell expressed developmentally down-regulated protein 6	NEDD6	619140	D1039P13.2.2 (Acidic calponin 3)	CNN3	165600
Apolipoprotein C3	APOC3	1143000	SH3 and PX domain-containing protein 3B	SH3PX3B3B	599160	Calcineurin-like phosphoesterase domain-containing protein 1	CPPED1	165420
ATP synthase subunit O, mitochondrial	ATP5O	1126800	Thioredoxin domain-containing protein 1	TMX	599030	Sorting nexin-5	SNX5	163330
Splicing factor U2AF 65 kDa subunit	U2AF2	1104400	Histidine-tRNA ligase	HARS	591600	3D3/LYRIC	AEQ1	162090
40S ribosomal protein S25	RPS25	1090300	33 kDa VAMP-associated protein	VAPB3	589310	Membrane component chromosome 3 surface marker 1	TM4SF1	160190
VH3 protein	VH3	1086000	60S ribosomal protein L35	RPL35	571500	Fibrillin-1	FBN1	155200
Dienosine tetraphosphate synthetase	GARS	1080500	Casein kinase 2 beta polypeptide	CSNK2B	568020	Vasorin	VASN	151290
Ribosomal protein L15	RPL15	1077600	Oxoglutarate (Alpha-ketoglutarate) dehydrogenase	OGDH	563800	Small nuclear ribonucleoprotein F	SNRPF	141150
60S ribosomal protein L7a	RPL7A	1036700	Protein FAM120A	FAM120A	559680	Nucleoside diphosphate kinase A	NME1	141060
Inhibitor of nuclear factor kappa-B kinase-interacting protein	IKBIP	1034500	26S proteasome non-ATPase regulatory subunit 7	PSM07	558850	Membrane-associated protein HEM-2	HEM2	136100
Lon protease homolog, mitochondrial	LONP1	1003500	Eukaryotic translation initiation factor 2 subunit 3	EIF2G	556780	Biliverdin reductase A	BLVR	131340
HLA-DR-associated protein II	SET	997090	26S proteasome AAA-ATPase subunit RPT5	PSMC3	553220	Oncogene c-mel	MEL	118320
Transmembrane protein 205	TMEM205	990230	Endoplasmic oxidoreductin-1-like protein	ERO1L	549700	A-kinase anchor protein 12	AKAP12	106320
Barrier-to-autointegration factor	BAF	985230	Neuron cytoplasmic protein 9.5	UCHL1	540420	17-beta-hydroxysteroid dehydrogenase 12	HSD17B12	104420
XP-C repair-complementing complex 58 kDa protein	RAD23B	983200	NEDD8 carrier protein	UBC12	531740	Integrin beta-3	ITGB3	83297
Arsenical pump-driving ATPase	ASNA1	982310	Docking protein alpha	SRPR	528950	MEX-binding partner 1	MAP2K3IP1	80713
EH domain-containing protein 3	EH03	975500	Archain 1, isoform CRA_a	ARCNA1	528220	Nodal modulator 2	NOMOD2	76571
60S ribosomal protein L11	RPL11	966430	40S ribosomal protein S23	RPS23	525930	Complex 5-S140	NDUFPV1	72738
Kinase-related protein	MLCK	955770	Clathrin light chain B	CLTB	520450	Alpha-2-antiplasmin	AAP	72124
Leucine-rich repeat-containing protein 15	LRRCL15	954900	N-acetylglucosaminidase, alpha-	NAGA	518890	Proteasome inhibitor P31 subunit	PSMF1	61442
Catenin delta-1	CTNND1	928760	Profilin II	PFN2	492890	Fas ligand-associated factor 1	FAPL1	20033
26 kDa prosomal protein	PROS26	923350	B5	ITM1	469390	Complex 1-19K0	NDUFAB	12750
Eukaryotic translation initiation factor 3 subunit A	EIF3A	923340	Ubiquitin carboxyl-terminal hydrolase 14	USP14	460270	BRG1-associated factor 170	BAF170	11516





**STEM CELLS**

**DAY 1**

**DAY 7**

**BONE TISSUE**

**DAY 21**





# Bone Bioactive Liquid Ingredients

Aqua

Net Negative  
Charge

**Biosalts** : Calcium chloride, Disodium phosphate, Magnesium chloride, Potassium chloride, Potassium phosphate, Sodium chloride

# Bone Bioactive Liquid Mechanism Of Action

SIGNALING PATHWAYS ACTIVATION  
STIMULATE FIBRONECTIN ,CD29, IL4, IL10, RANK

MAINTAIN THE  
SUITABLE PH FOR  
STEM CELL

FACIALITATE THE  
CELL-CELL  
COMMUNICATION

STEM CELL  
ATTRACTION

BALANCE OF THE  
INFLAMMATORY  
FACTORS

## TISSUE REPAIR

STOP BLEEDING

Promote Angiogenesis  
Increasing Nutrients To  
Wound Area

Soft & Hard Tissue  
Regeneration

Promote  
Ossteointegration

Accelerate  
wound healing



# BIOINTELLIGENT PRODUCTS

**THERAVE**  
Oral **PLUS**



**THERAVE**  
Tissue Care **PLUS**



**THERAVE**  
Tissue Care **Spray**



**THERAVE**  
Nasal **Spray**





# BONE BIOACTIVE LIQUID

## THERAVEX TOTAL ORAL CARE PLUS

**THERAVE**   
Oral **PLUS**



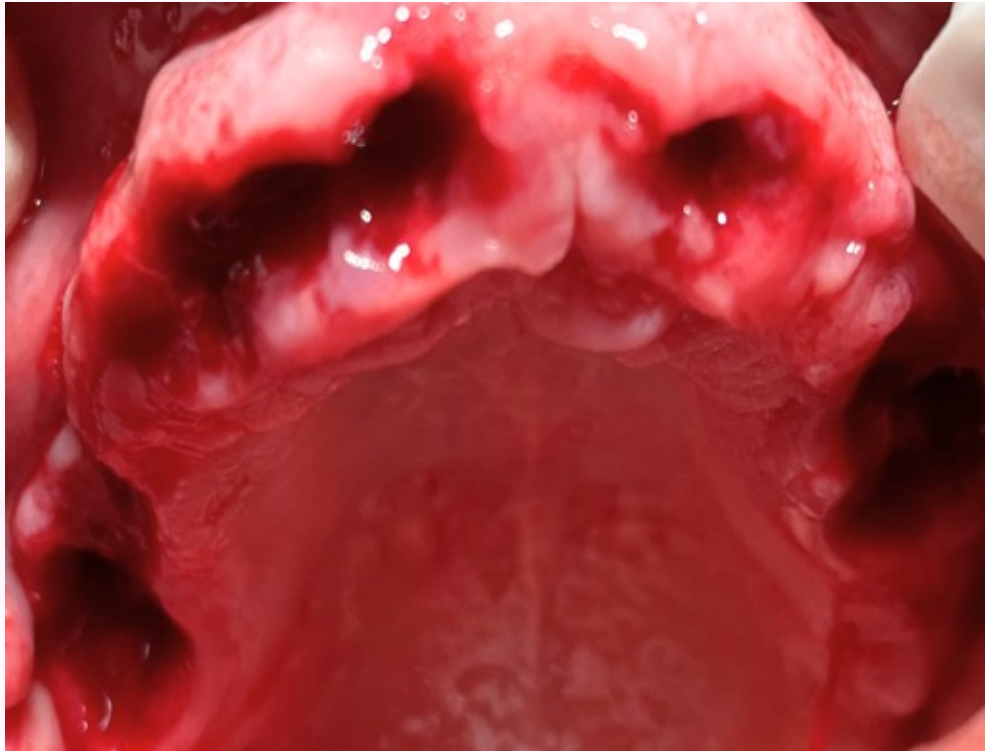
### *INDICATION FOR USE*

**Immediately after surgery, 2-3 time a day for one week**

Post-operative care following any oral surgery

- Post tooth extractions
- Dental implant replacement
- Managing pathologies of the oral mucosa (e.g., thrush, ulcers)
- Post dry socket treatment
- Post necrotic tissue treatment

## THE POWER OF BBL TECHNOLOGY IN HEALING



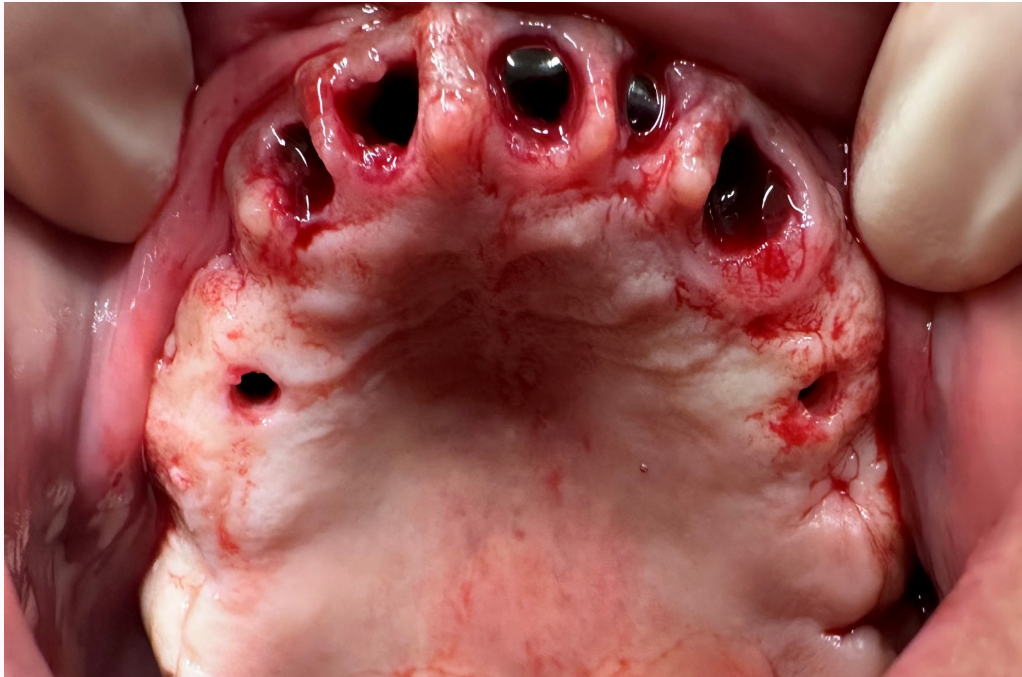
**0 DAYS**



**7 DAYS**



## THE POWER OF BBL TECHNOLOGY IN HEALING



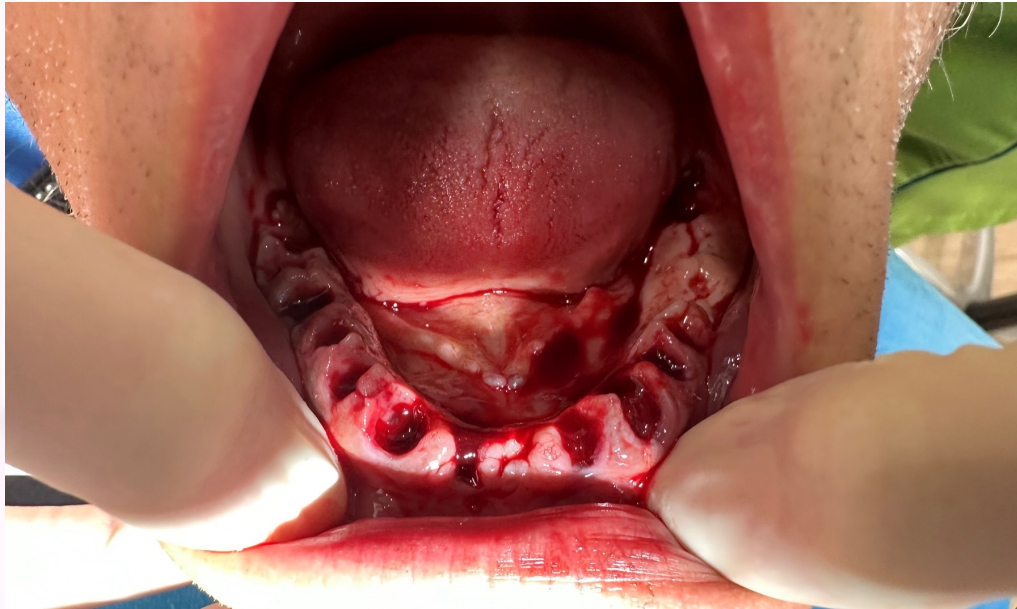
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**7 DAYS**



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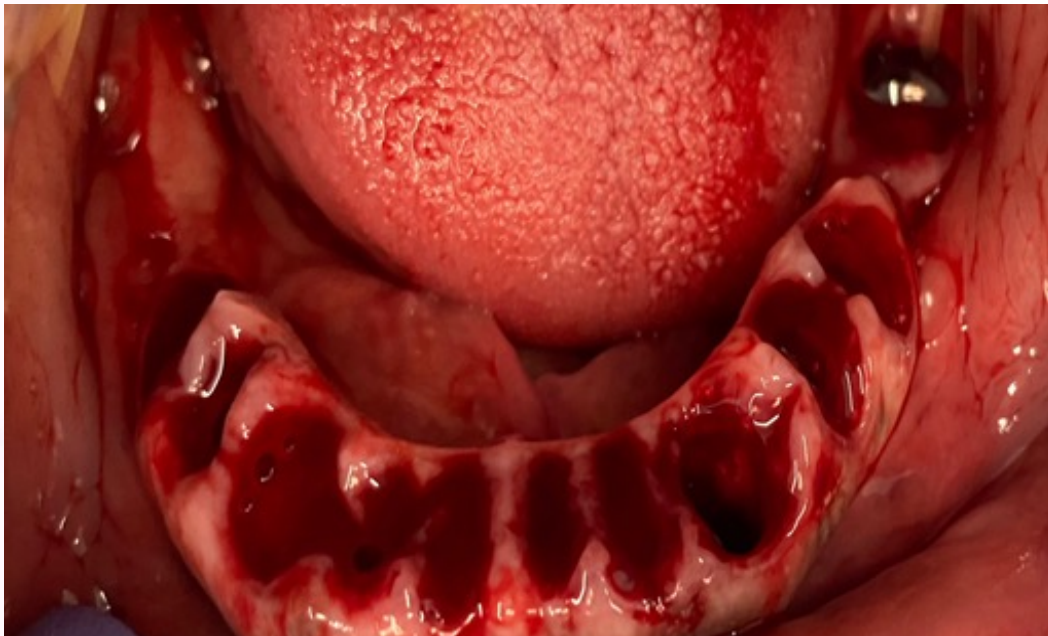


**0 DAYS**



**7 DAYS**

## THE POWER OF BBL TECHNOLOGY IN HEALING



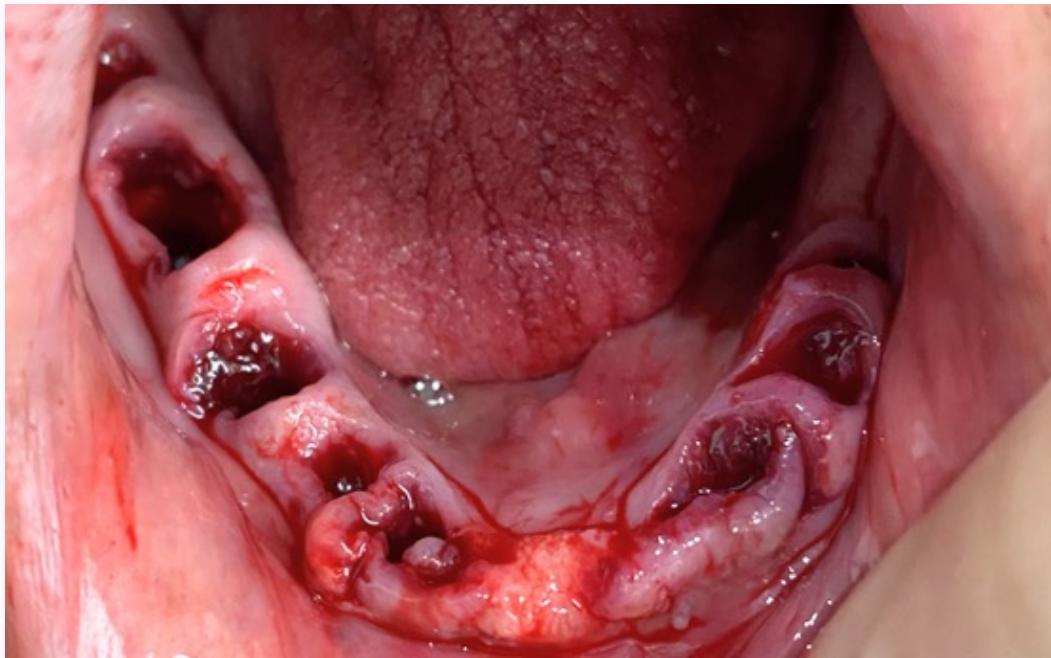
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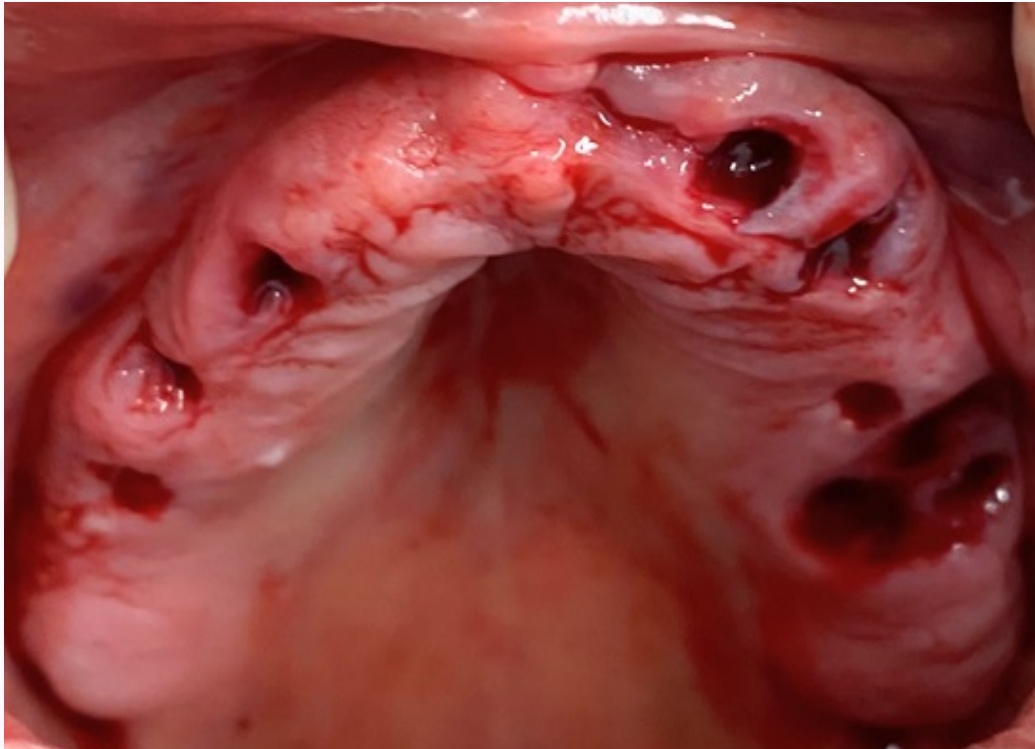
**0 DAYS**



**7 DAYS**



## THE POWER OF BBL TECHNOLOGY IN HEALING



**0 DAYS**



**7 DAYS**

## THE POWER OF BBL TECHNOLOGY IN HEALING



**0 DAYS**



**7 DAYS**

## THE POWER OF BBL TECHNOLOGY IN HEALING



**0 DAYS**



**7 DAYS**



## THE POWER OF BBL TECHNOLOGY IN HEALING



**0 DAYS**



**7 DAYS**

## THE POWER OF BBL TECHNOLOGY IN HEALING



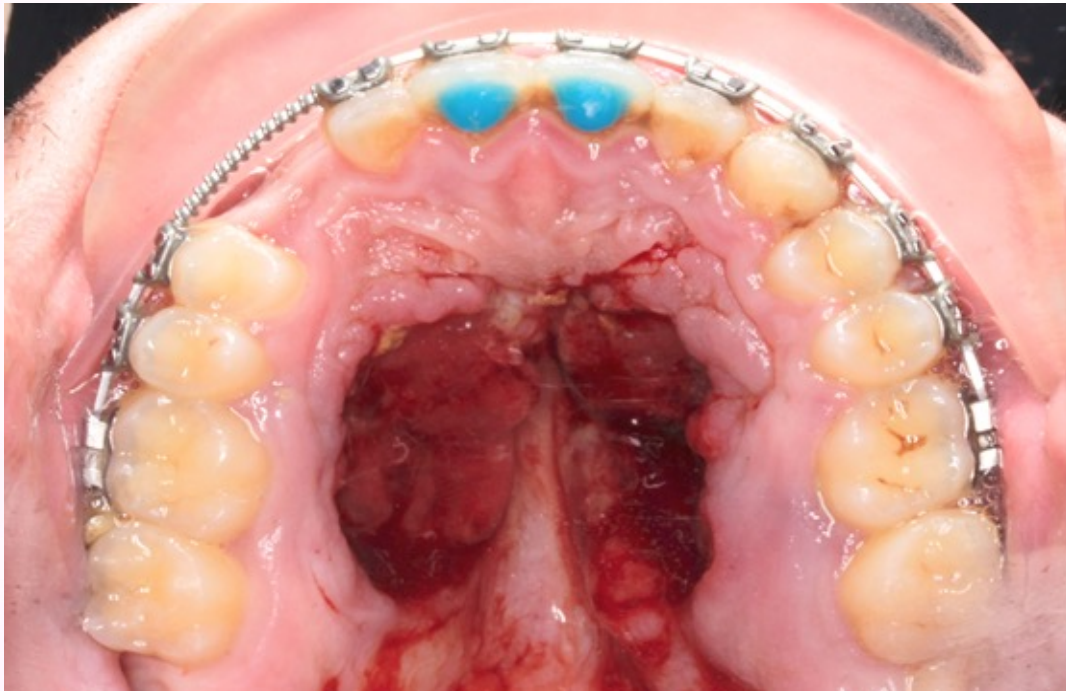
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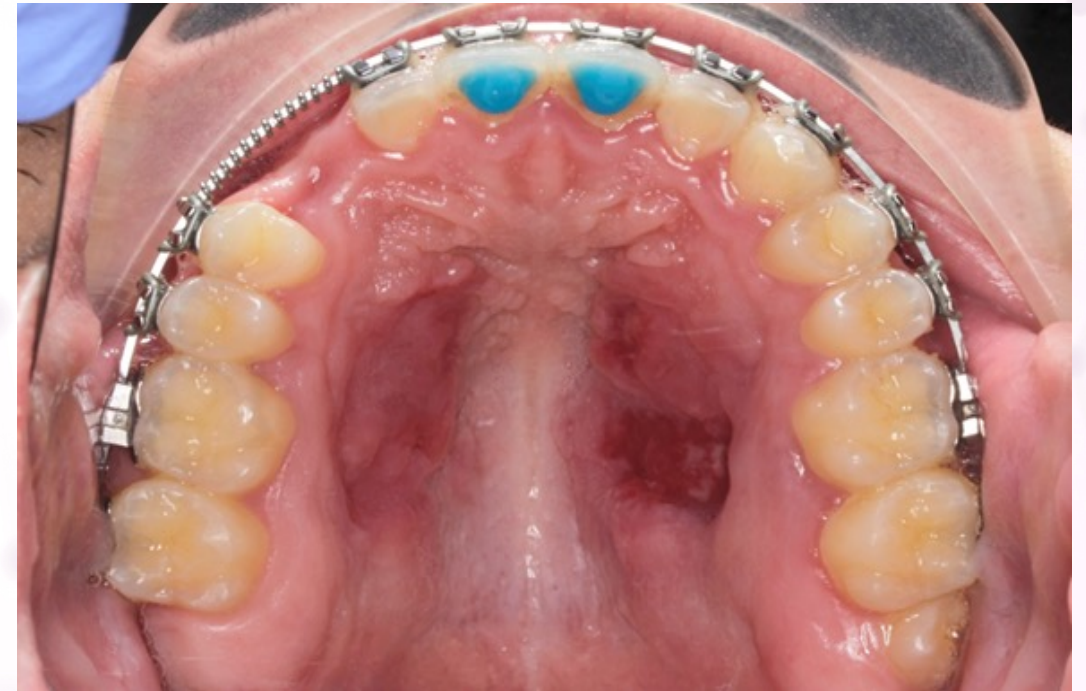
**7 DAYS**



# THE POWER OF BBL TECHNOLOGY IN HEALING



**0 DAYS**



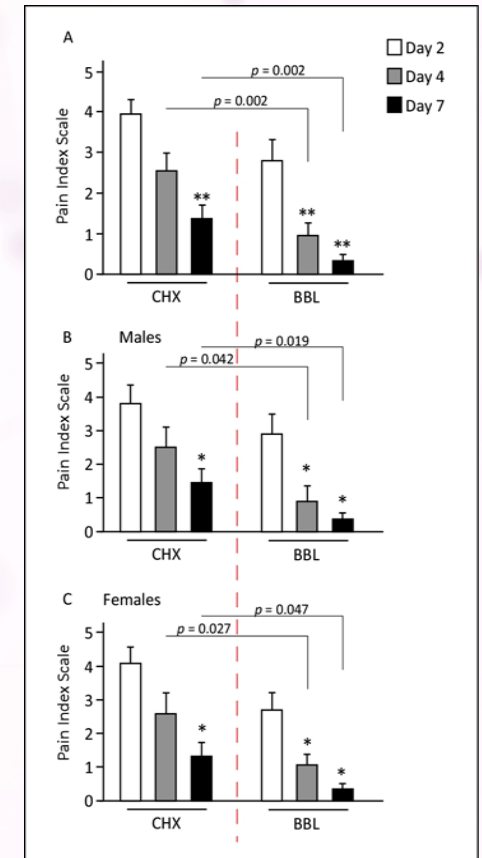
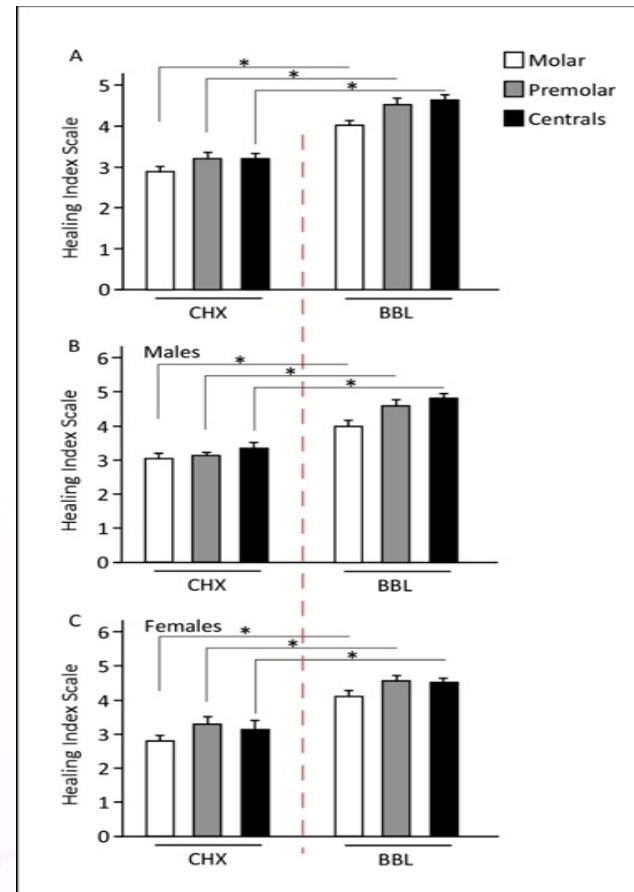
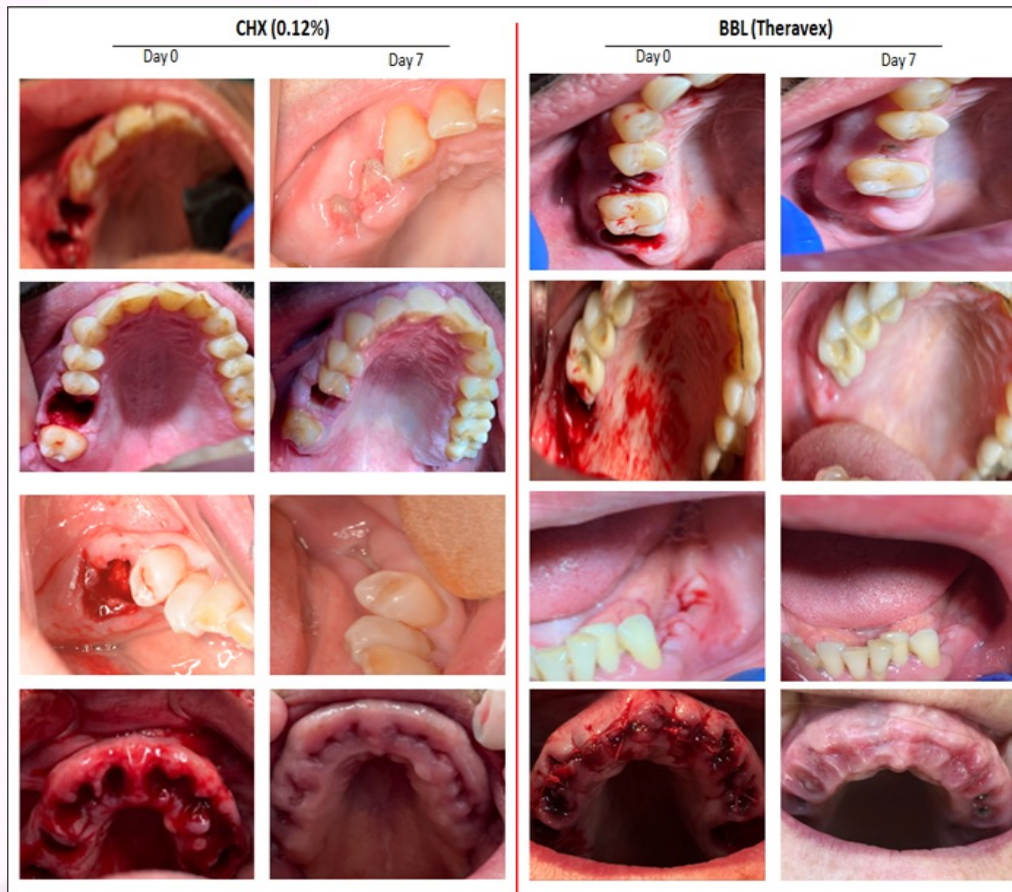
**7 DAYS**



Brief Report

# Comparison of 0.12% Chlorhexidine and a New Bone Bioactive Liquid, BBL, in Mouthwash for Oral Wound Healing: A Randomized, Double Blind Clinical Human Trial

Eduard Ferrés-Amat <sup>1,2,†</sup>, Ashraf Al Madhoun <sup>3,†</sup>, Elvira Ferrés-Amat <sup>1,2</sup>, Neus Carrió <sup>4</sup>, Miguel Barajas <sup>5,6</sup>, Areej Said Al-Madhoun <sup>6</sup>, Eduard Ferrés-Padró <sup>1,6</sup>, Carles Martí <sup>6,7</sup> and Maher Atari <sup>6,8,9,\*</sup>

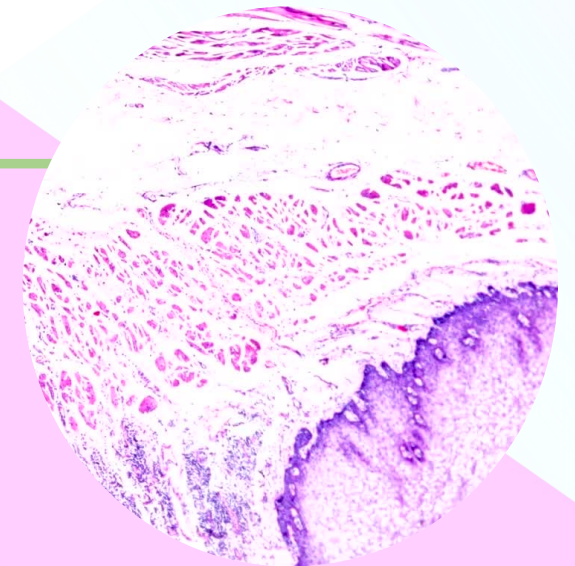


# BONE BIOACTIVE LIQUID TECHNOLOGY THERAVEX TISSUE CARE PLUS



**THERAVE**  
Tissue Care **PLUS**

## BBL TECHNOLOGY







# BONE BIOACTIVE LIQUID THERAVEX TISSUE CARE PLUS DENTISTRY



## Dental Implantology

Dental implant placement  
Periimplantitis



## Periodontology

Periodontitis  
Mucogingival surgery



## Root Canal Treatment

Reversible pulpitis  
Pediatric pulpitis



## Oral Surgery Bone Regeneration

Bone graft  
maxillofacial surgery



## TITANIUM BONE BIOACTIVE LIQUID

GROUP A



SURFACE TREATMENT

**GROUP A**

No treatment

**GROUP B**

Bone bioactive liquid

GROUP B



## STUDY IN RABBITS OF A BBL NEW SURFACE

**DAY 0**

**SURGERY**

**MEDICIÓN  
DE ISQ**

Radiografías

**DAY 15**

**5 RABBITS**

**MEDICIÓN  
DE ISQ**

**RESISTENCIA AL  
TORQUE REVERSO**

Radiografías

**HISTOLOGIA**

**DAY 30**

**5 RABBITS**

**MEDICIÓN  
DE ISQ**

**RESISTENCIA AL  
TORQUE REVERSO**

Radiografías

**HISTOLOGIA**

**DAY 45**

**5 RABBITS**

**MEDICIÓN  
DE ISQ**

**RESISTENCIA AL  
TORQUE REVERSO**

Radiografías

**HISTOLOGIA**

**DAY 60**

**5 RABBITS**

**MEDICIÓN  
DE ISQ**

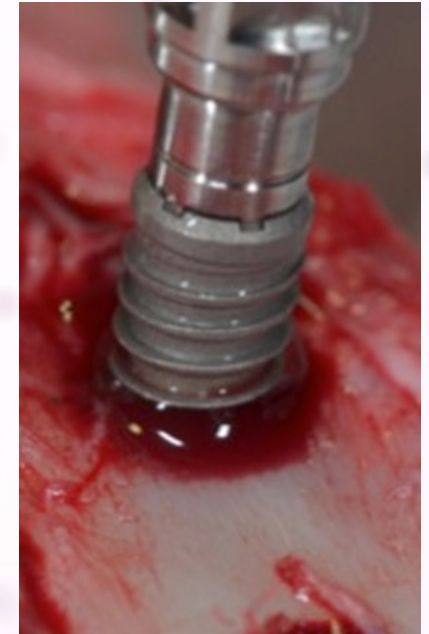
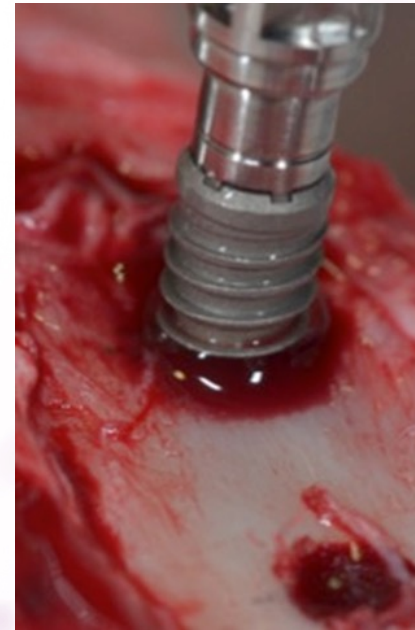
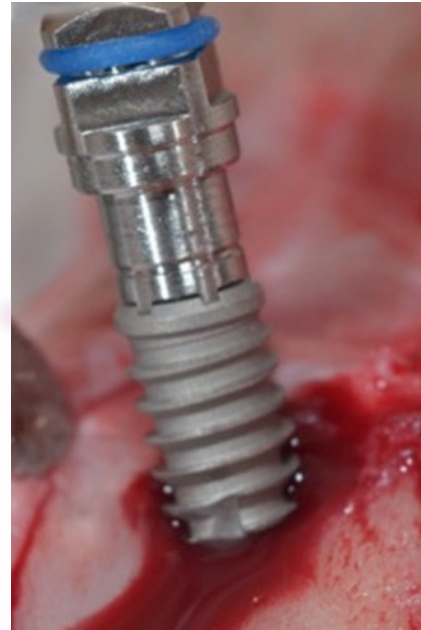
**RESISTENCIA AL  
TORQUE REVERSO**

Radiografías

**HISTOLOGIA**

# TITANIUM BONE BIOACTIVE LIQUID THERAVEX TISSUE CARE PLUS SURGICAL PROCEDURE

**THERAVE**  
Tissue Care PLUS





# TITANIUM BONE BIOACTIVE LIQUID THERAVEX TISSUE CARE PLUS

**THERAVE**  
Tissue Care **PLUS**

15 DAYS

**GROUP A**

**NO TREATED SURFACE**



**GROUP B**

**BBL TREATED SURFACE**



60 DAYS

**GROUP A**

**NO TREATED SURFACE**



**GROUP B**

**BBL TREATED SURFACE**

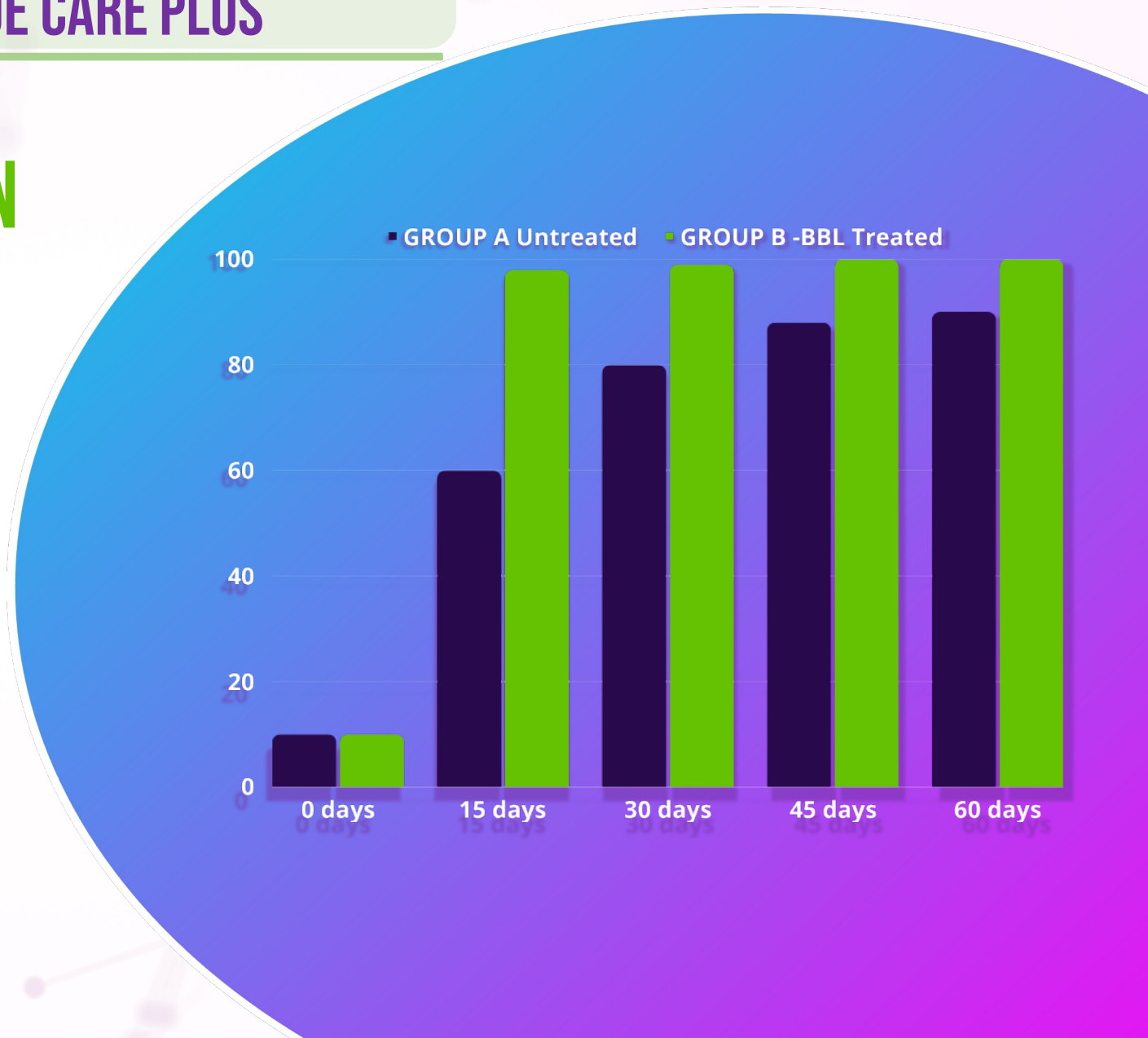


# TITANIUM BONE BIOACTIVE LIQUID THERAVEX TISSUE CARE PLUS



## NEW BONE FORMATION

TIME OF MEASUREMENT	GROUP A UNTREATED SURFACE (CONTROL)  mean $\pm$ SD	GROUP B TREATED SURFACE (BBL)  mean $\pm$ SD
15 Days	33,7 $\pm$ 2,3 %	68.92 $\pm$ 0.3 %*
30 Days	35,8 $\pm$ 1,8%	69,35 $\pm$ 2,2%*
45 Days	37,9 $\pm$ 1,2%	70,34 $\pm$ 1,1%*
60 Days	41,2 $\pm$ 0,8%	73,89 $\pm$ 1,9%*





Article

# Histologic and Histomorphometric Evaluation of a New Bioactive Liquid BBL on Implant Surface: A Preclinical Study in Foxhound Dogs

Eduard Ferrés-Amat <sup>1,†</sup>, Ashraf Al Madhoun <sup>2,†</sup>, Elvira Ferrés-Amat <sup>1,3</sup>, Saddam Al Demour <sup>4</sup>, Mera A. Ababneh <sup>5</sup>, Eduard Ferrés-Padró <sup>1,6</sup>, Carles Martí <sup>6,7</sup>, Neus Carrio <sup>3</sup>, Miguel Barajas <sup>6,8</sup> and Maher Atari <sup>6,9,\*</sup>

- <sup>1</sup> Oral and Maxillofacial Surgery Service, Hospital HM Nens, HM Hospitales, 08009 Barcelona, Spain; eduard.fa@institutferresamat.com (E.F.-A.); elvira.fa@institutferresamat.com (E.F.-A.); eduard.fp@institutferresamat.com (E.F.-P.)
- <sup>2</sup> Department of Animal and Imaging Core Facilities, Dasman Diabetes Institute, Dasman 15462, Kuwait; ashraf.madhoun@dasmaninstitute.org
- <sup>3</sup> Oral and Maxillofacial Surgery Department, Universitat Internacional de Catalunya, St Josep Trueta s/n, Sant Cugat del Valles, 08195 Barcelona, Spain; neuscarrioer@gmail.com
- <sup>4</sup> Department of Special Surgery/Division of Urology, School of Medicine, The University of Jordan, Amman 11942, Jordan; saldemour@ju.edu.jo
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- <sup>6</sup> BioIntelligent Technology Systems SL, Diputacion 316, 3D, 08009 Barcelona, Spain; martipages.c@gmail.com (C.M.); miguelbarajas@unavarra.es (M.B.)
- <sup>7</sup> Oral and Maxillofacial Surgery Department, Hospital Clínic de Barcelona, 08036 Barcelona, Spain
- <sup>8</sup> Biochemistry Area, Department of Health Science, Public University of Navarre, 31008 Pamplona, Spain
- <sup>9</sup> Zicom Medical SL, C. Buhos, 2, 28320 Madrid, Spain

\* Correspondence: matari@biointelligentsl.com

† Eduard Ferrés-Amat and Ashraf Al Madhoun should be considered joint first author.



**Citation:** Ferrés-Amat, E.; Al Madhoun, A.; Ferrés-Amat, E.; Al Demour, S.; Ababneh, M.A.; Ferrés-Padró, E.; Martí, C.; Carrio, N.; Barajas, M.; Atari, M. Histologic and Histomorphometric Evaluation of a New Bioactive Liquid BBL on Implant Surface: A Preclinical Study in Foxhound Dogs. *Materials* **2021**, *14*, 6217. <https://doi.org/10.3390/ma14206217>

Academic Editors: Gianmario Schierano and Giuliana Muzio

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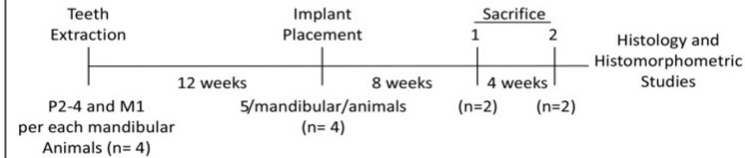


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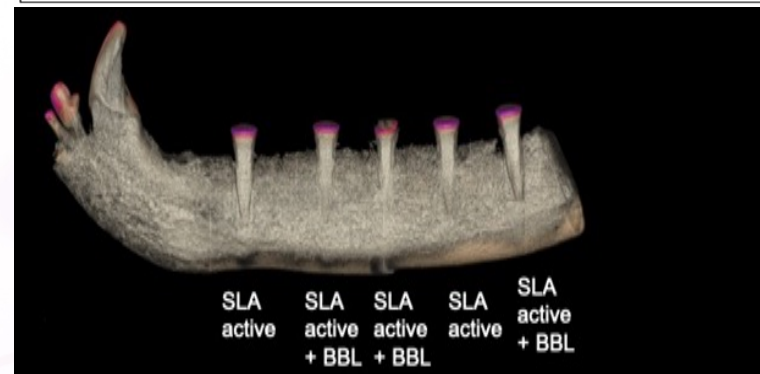
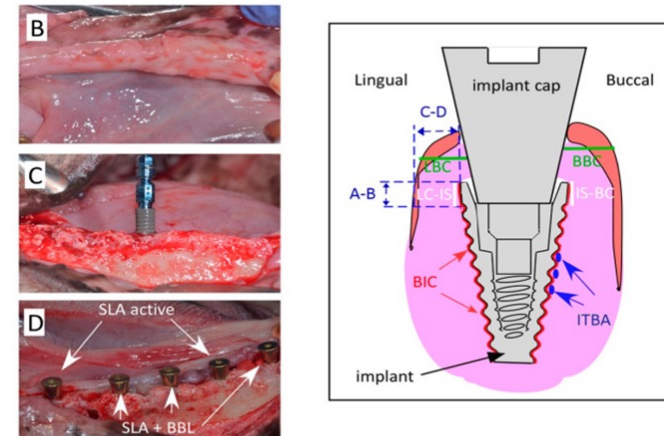
**Abstract:** Background: Bioactive chemical surface modifications improve the wettability and osseointegration properties of titanium implants in both animals and humans. The objective of this animal study was to investigate and compare the bioactivity characteristics of titanium implants (BLT) pre-treated with a novel bone bioactive liquid (BBL) and the commercially available BLT-SLA active. Methods: Forty BLT-SLA titanium implants were placed in in four foxhound dogs. Animals were divided into two groups (n = 20): test (BLT-SLA pre-treated with BBL) and control (BLT-SLA active) implants. The implants were inserted in the post extraction sockets. After 8 and 12 weeks, the animals were sacrificed, and mandibles were extracted, containing the implants and the surrounding soft and hard tissues. Bone-to-implant contact (BIC), inter-thread bone area percentage (ITBA), soft tissue, and crestal bone loss were evaluated by histology and histomorphometry. Results: All animals were healthy with no implant loss or inflammation symptoms. All implants were clinically and histologically osseointegrated. Relative to control groups, test implants demonstrated a significant 1.5- and 1.7-fold increase in BIC and ITBA values, respectively, at both assessment intervals. Crestal bone loss was also significantly reduced in the test group, as compared with controls, at week 8 in both the buccal crests ( $0.47 \pm 0.32$  vs  $0.98 \pm 0.51$  mm,  $p < 0.05$ ) and lingual crests ( $0.39 \pm 0.3$  vs  $0.89 \pm 0.41$  mm,  $p < 0.05$ ). At week 12, a pronounced crestal bone loss improvement was observed in the test group (buccal,  $0.41 \pm 0.29$  mm and lingual,  $0.54 \pm 0.23$  mm). Tissue thickness showed comparable values at both the buccal and lingual regions and was significantly improved in the studied groups ( $0.82$ – $0.92$  mm vs.  $33$ – $48$  mm in the control group). Conclusions: Relative to the commercially available BLT-SLA active implants, BLT-SLA pre-treated with BBL showed improved histological and histomorphometric characteristics indicating a reduced titanium surface roughness and improved wettability, promoting healing and soft and hard tissue regeneration at the implant site.

**Keywords:** BLT-SLA active; BBL; dental implant; osseo integration dental implantation

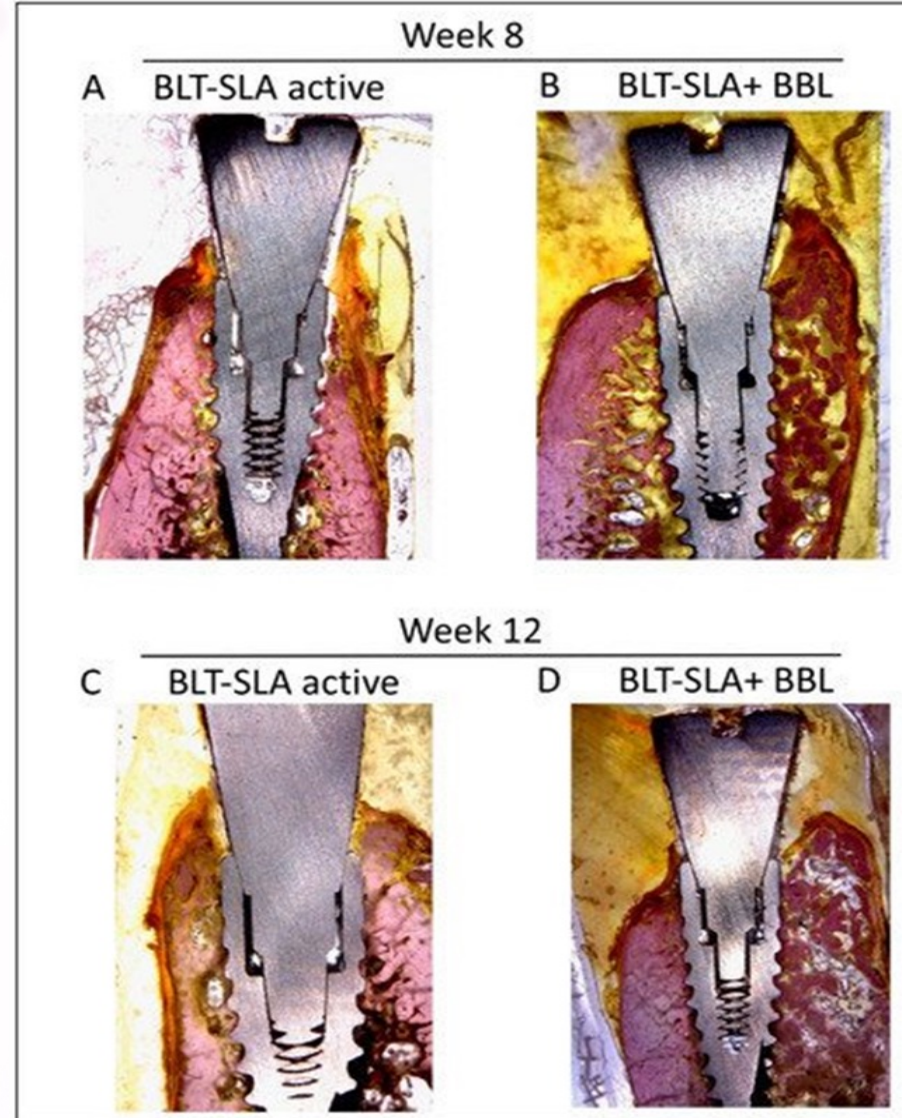
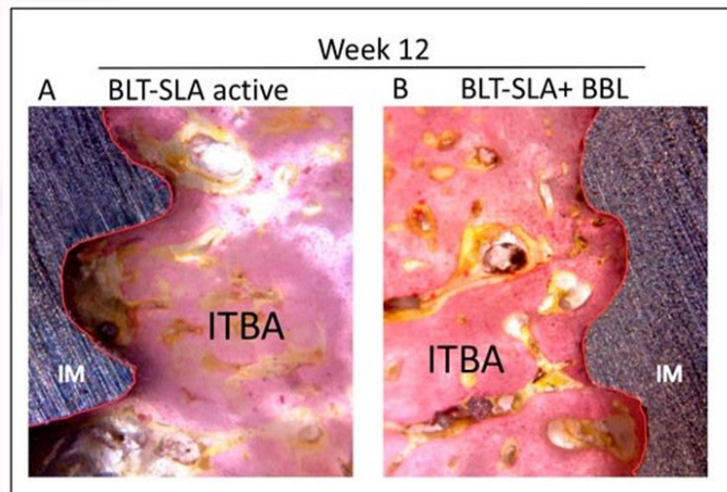
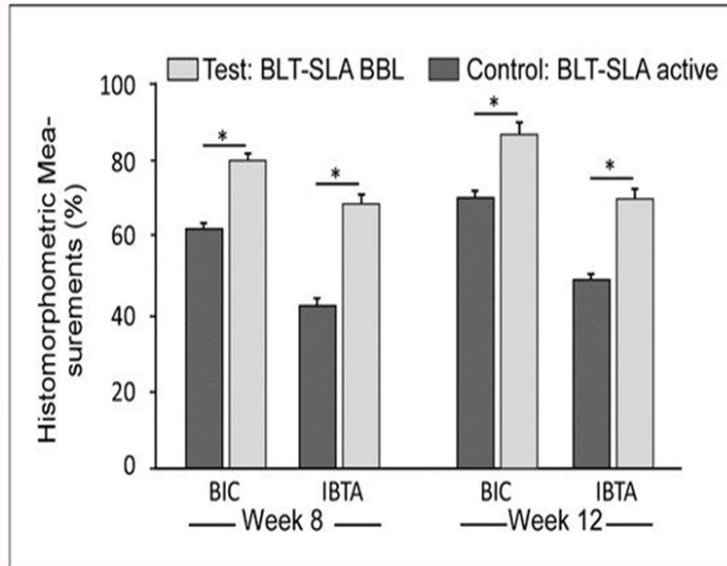
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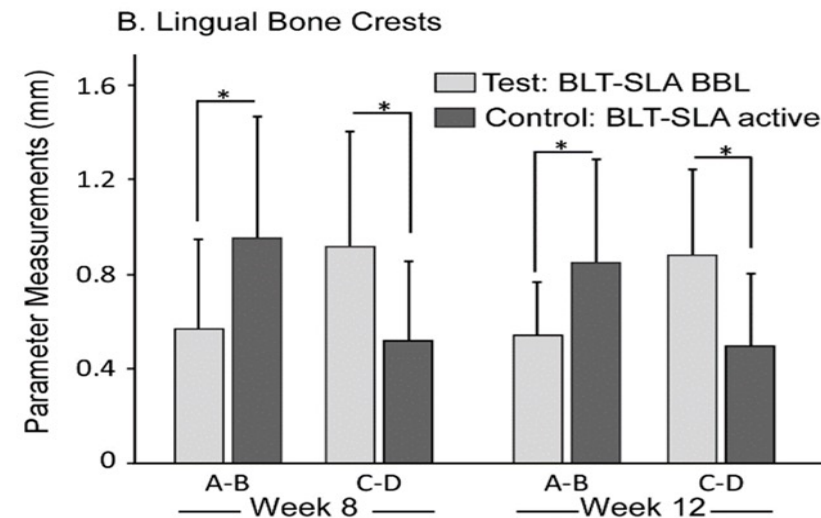
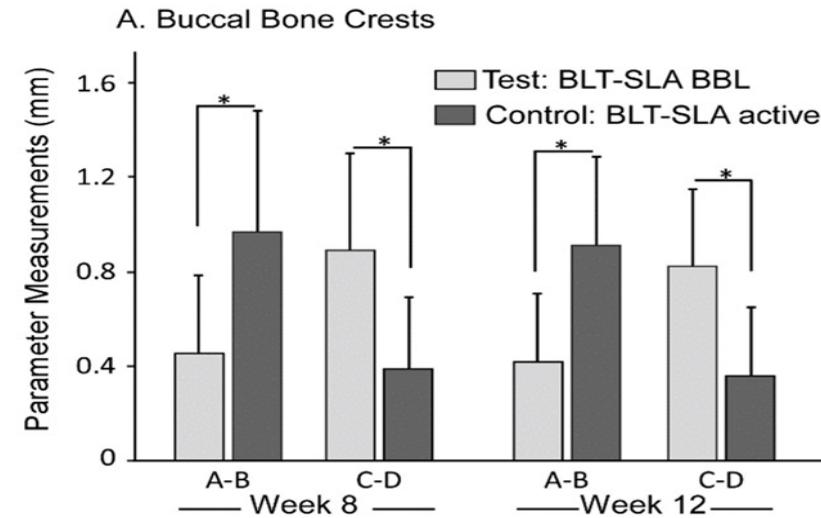
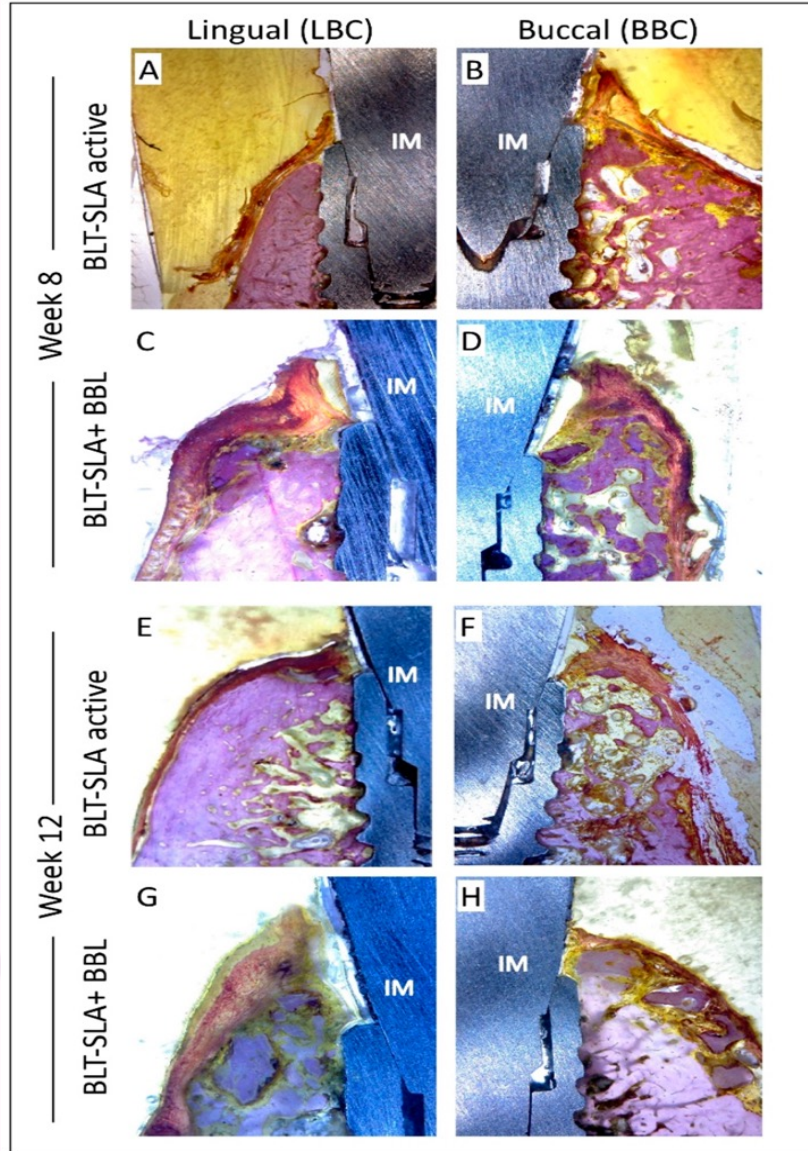


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# STUDY TITLE: THE IMPACT OF TITAN SUREACTIVE IN VIVO

## TEST PRODUCT: GALAXY IMPLANTS TITAN SURE ACTIVE

- INDICATION STUDIED: DENTAL EXTRACTION, DENTAL IMPLANT REPLACEMENT
- STUDY DESIGN: SPELT MOUTH.
- PROTOCOL IDENTIFICATION: 01/2021
- STUDY INITIATION DATE: 2/01/2022
- STUDY COMPLETION DATE: 10/04/2022

## INVESTIGATORS:






### PRINCIPAL INVESTIGATOR: MAHER ATARI

- INVESTIGATORS INVOLVED: FERRÉSPADRÓ, EDUARD  
FERRÉSAMAT, ELVIRA  
FERRÉS AMAT, EDUARD  
CARLES MARTIN  
JAVIER MAREQUE



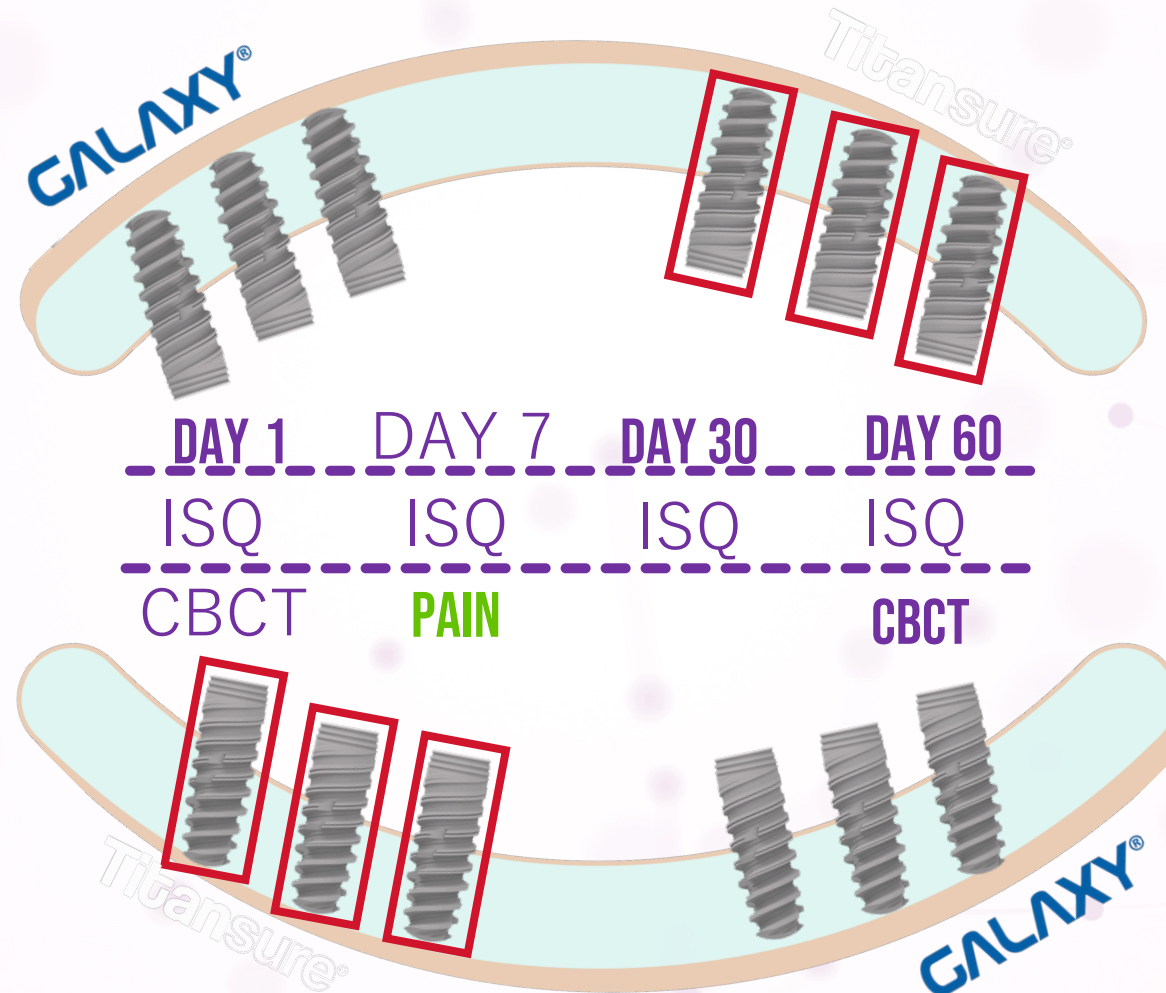
#### Article

### Randomized Clinical Trial: Bone Bioactive Liquid Improves Implant Stability and Osseointegration

Ashraf Al Madhoun <sup>1,†</sup>, Khaled Meshal <sup>2,†</sup>, Neus Carrió <sup>3</sup>, Eduard Ferrés-Amat <sup>2,4</sup>, Elvira Ferrés-Amat <sup>5</sup>, Miguel Barajas <sup>2,6</sup>, Ana Leticia Jiménez-Escobar <sup>7</sup>, Areej Said Al-Madhoun <sup>2</sup>, Alaa Saber <sup>2</sup>, Yazan Abou Alsamen <sup>2</sup>, Carles Martí <sup>2,8</sup> and Maher Atari <sup>2,\*</sup>



# THE IMPACT OF TITAN SUREACTIVE IN VIVO



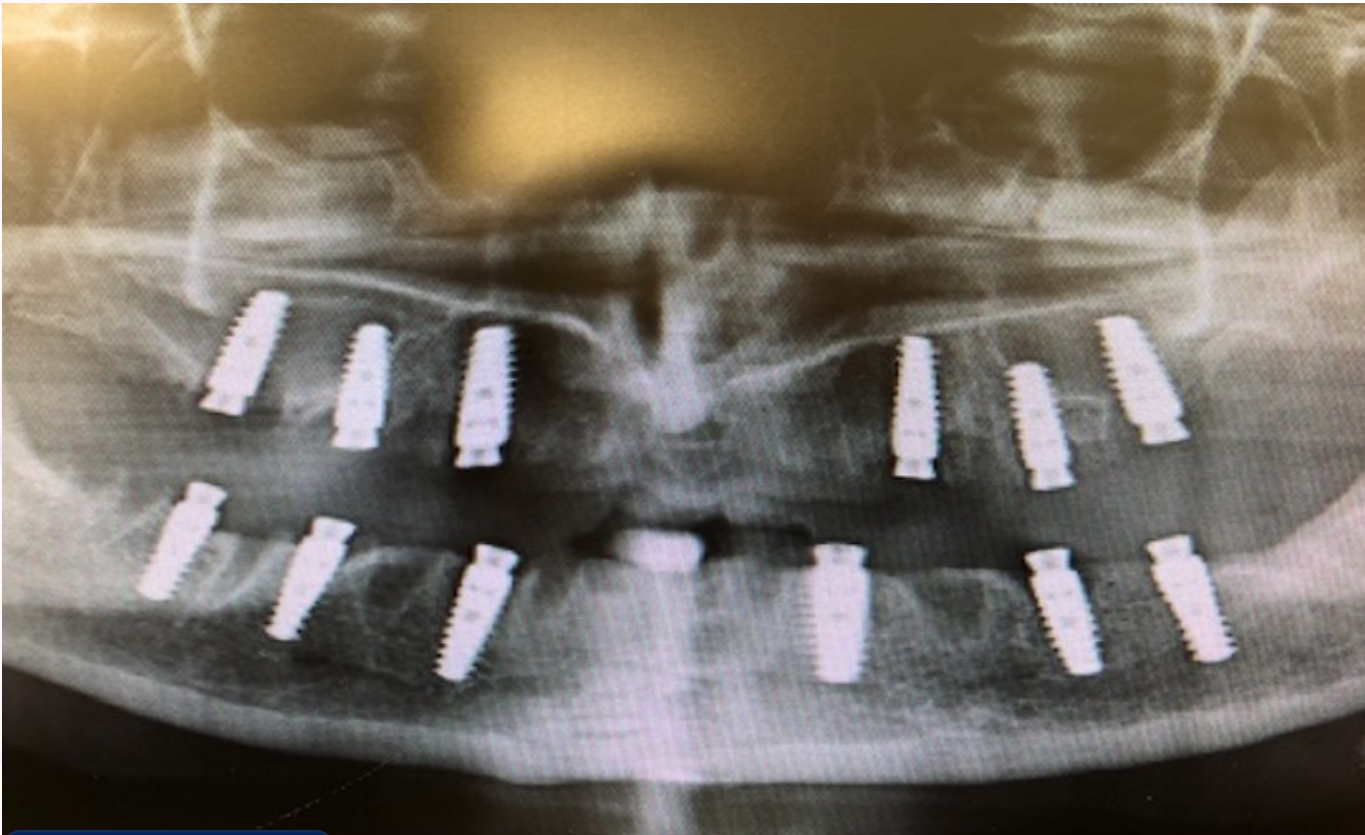
N Imp = 640

N pac = 80



# THE IMPACT OF TITAN SUREACTIVE IN VIVO

**GALAXY®**



**Titan**sure®

**GALAXY®**



$N_{Imp} = 640$

$N_{pac} = 80$



# THE IMPACT OF TITAN SUREACTIVE IN VIVO

**Titan**sure®



**DAY 1**



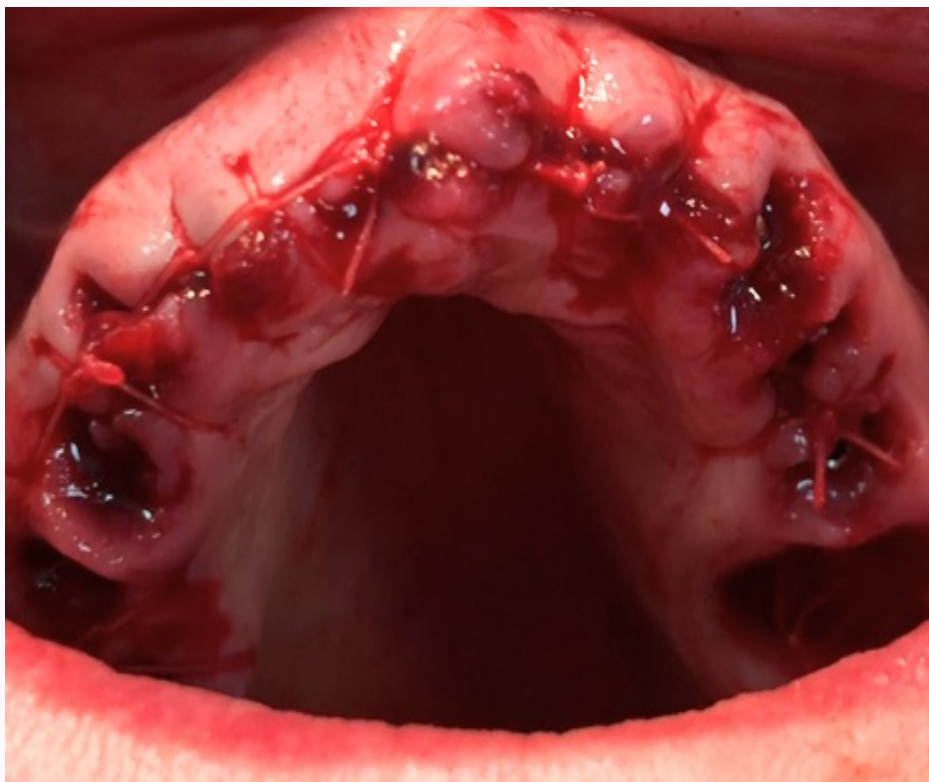
**DAY 7**





## THE IMPACT OF TITAN SUREACTIVE IN VIVO

**Titan**sure®



**DAY 1**



**DAY 7**



# THE IMPACT OF TITAN SUREACTIVE IN VIVO

**Titan**sure®



**DAY 1**



**DAY 7**





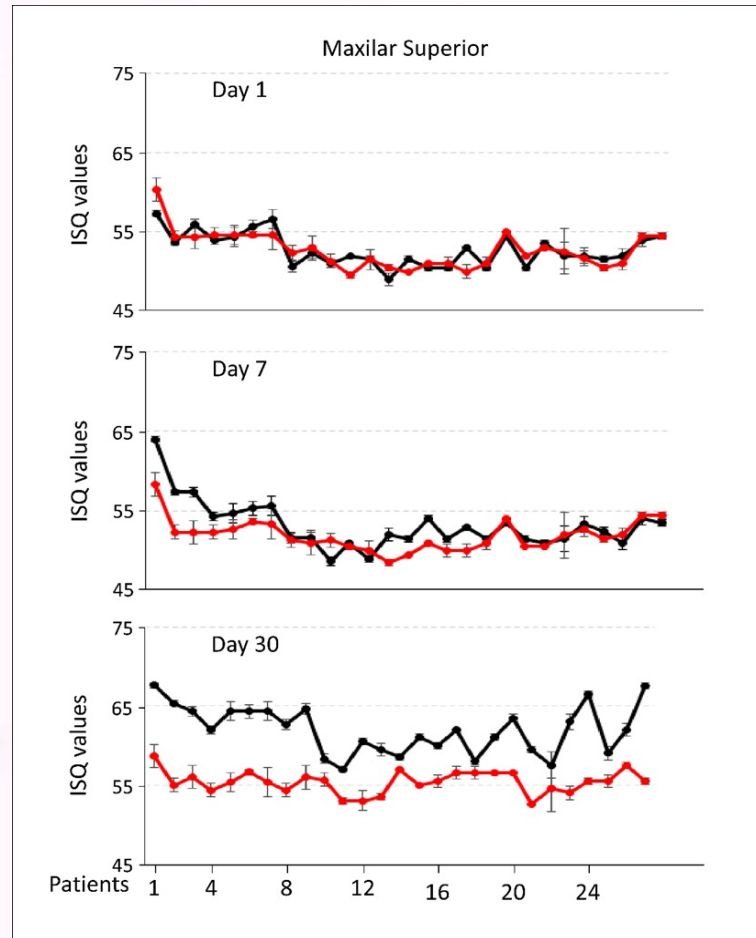


Figure 1: The mean implant stability quotient (ISQ) values at Maxilar Superior for each individual patient measured at days 1, 7, and 30 post-surgeries. The evaluation of implant stability was measured by resonance frequency analysis. Each dot represents a patient. Implants treated with BBL are in red, without BBL are in Black. The values are means  $\pm$  standard error of the mean for 4 readings.

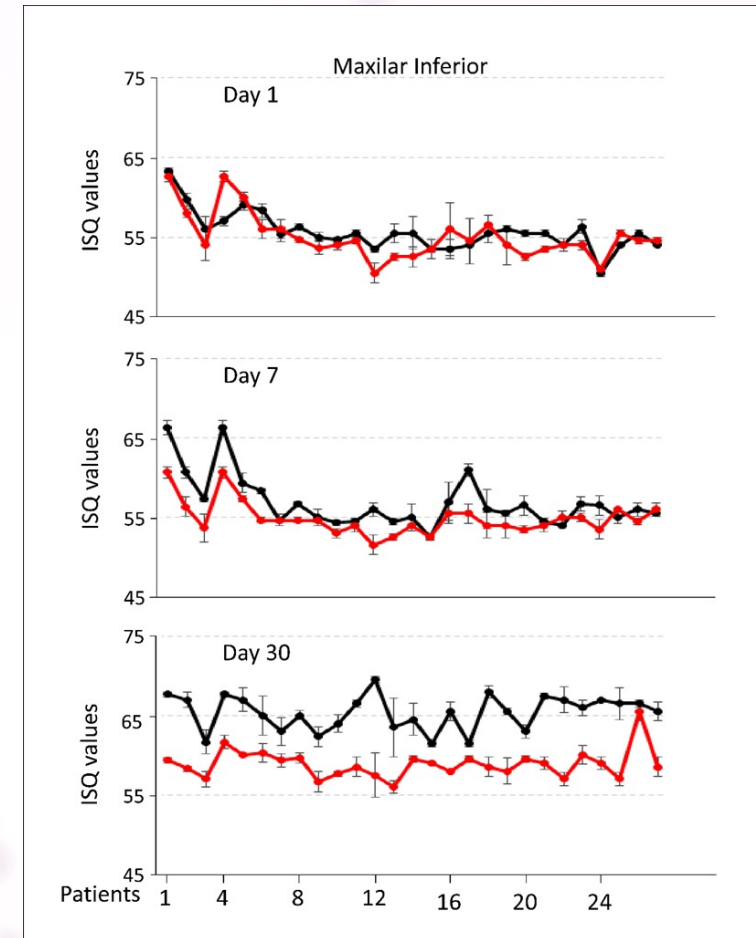


Figure 2: The mean implant stability quotient (ISQ) values at Maxilar Inferior of each individual patient measured at days 1, 7, and 30 post-surgeries. The evaluation of implant stability was measured by resonance frequency analysis. Each dot represents a patient. Implants treated with BBL are in red, without BBL are in Black. The values are means  $\pm$  standard error of the mean for 4 readings





# BONE BIOACTIVE LIQUID THERAVEX TISSUE CARE PLUS

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## BIOMATERIAL & HEALING

# STRAUMANN-BBL STUDY MARCH 2017

## PRELIMINARY PILOT STUDY IN DOGS

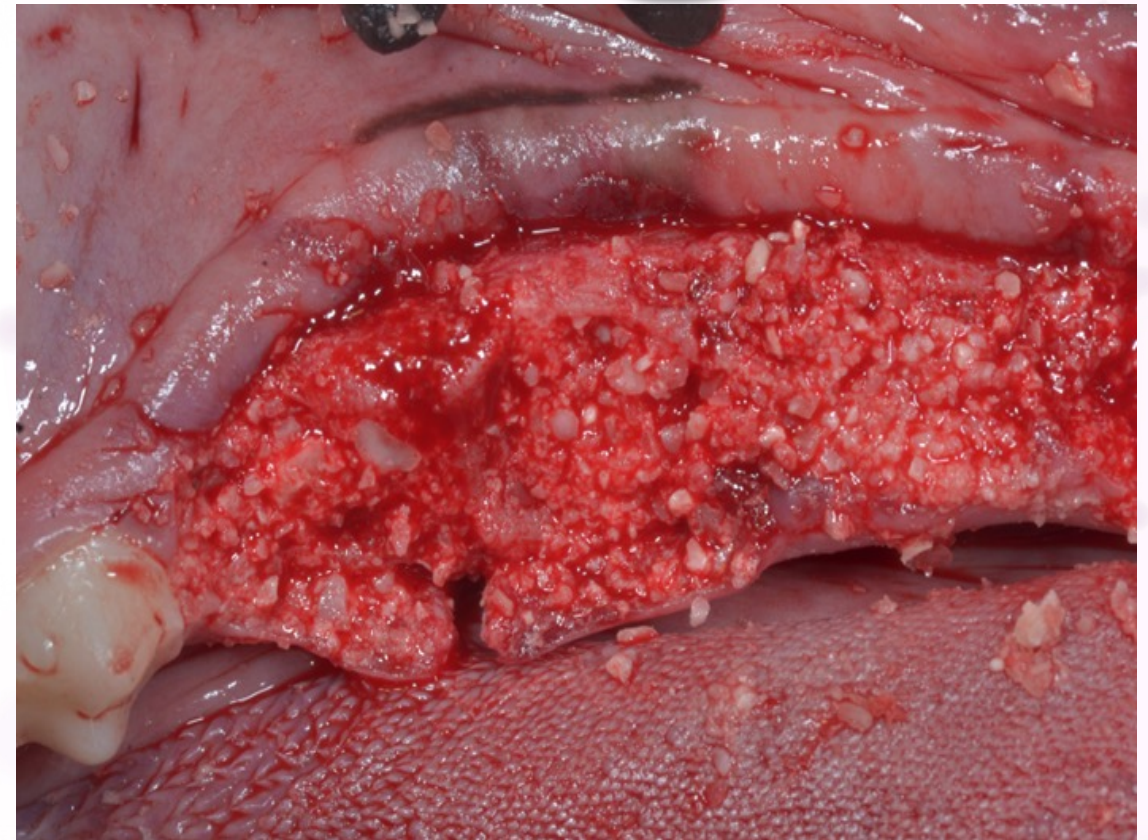
### BIOMATERIALS



**XENOGRAFT**



**XENOGRAFT + BBL**

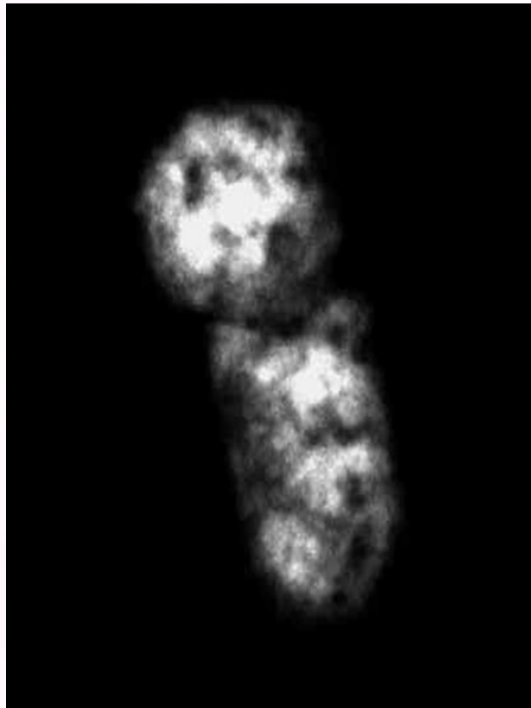




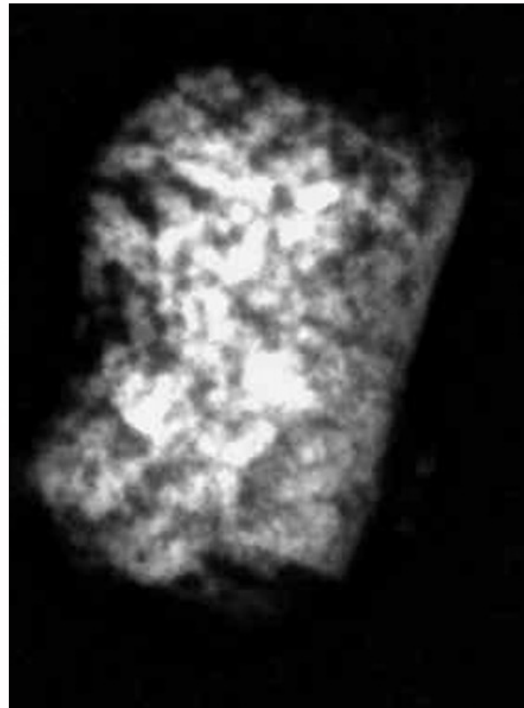
# STRAUMANN-BBL STUDY MARCH 2017

## PRELIMINARY PILOT STUDY IN DOGS

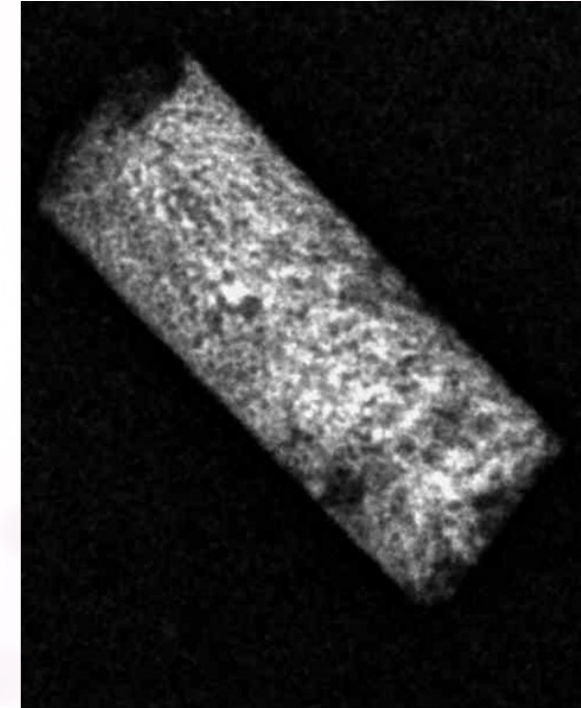
### BIOMATERIALS



CONTROL



XENOGRAFT



XENOGRAFT + BBL

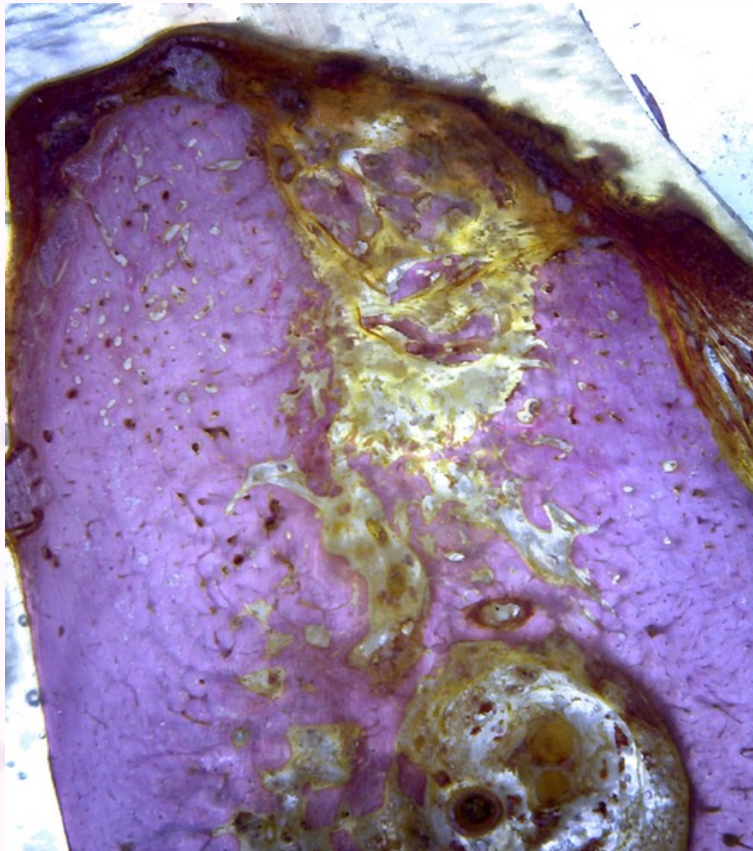
**BBL AFTER 1 MONTH**



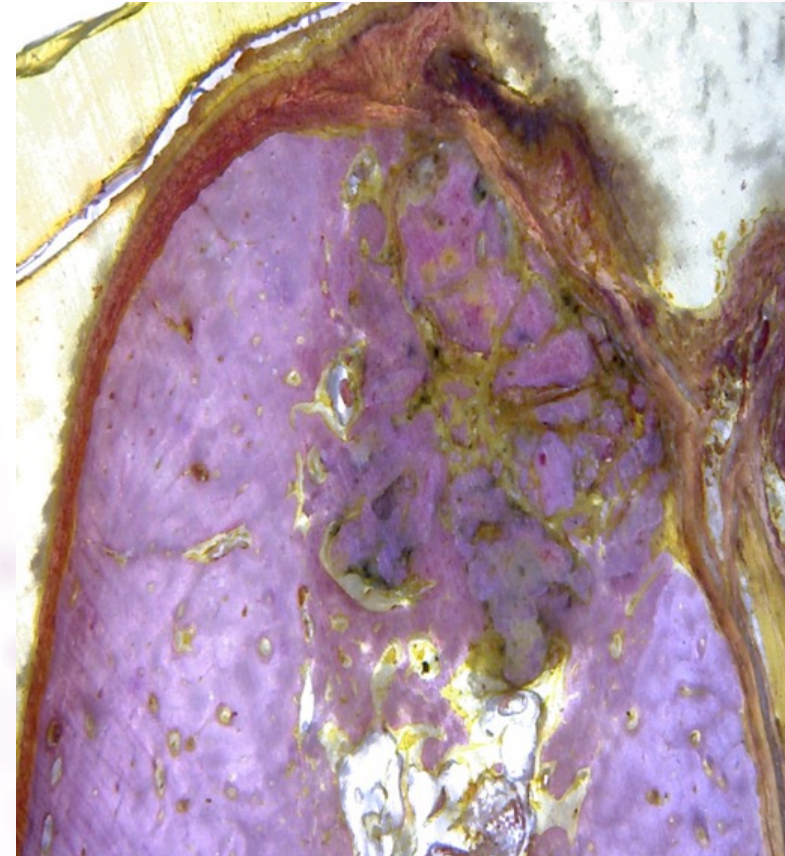
# STRAUMANN-BBL STUDY MARCH 2017

## PRELIMINARY PILOT STUDY IN DOGS

### BIOMATERIALS



XENOGRAPH BIOMATERIALS **WITHOUT** BBL 1 MONTH



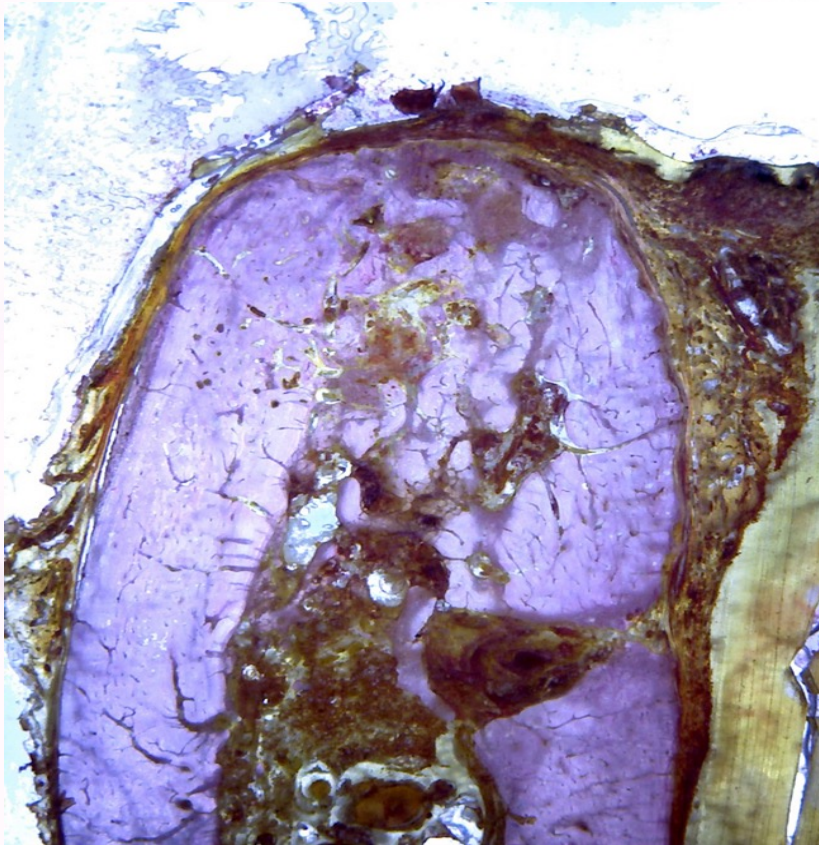
XENOGRAPH BIOMATERIALS **WITH** BBL 1 MONTH



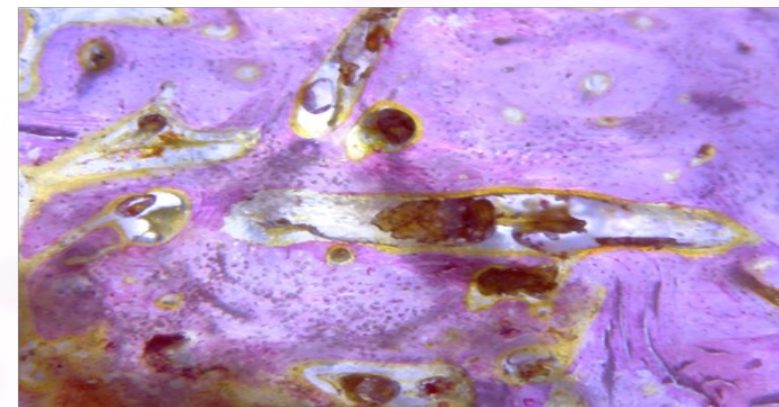
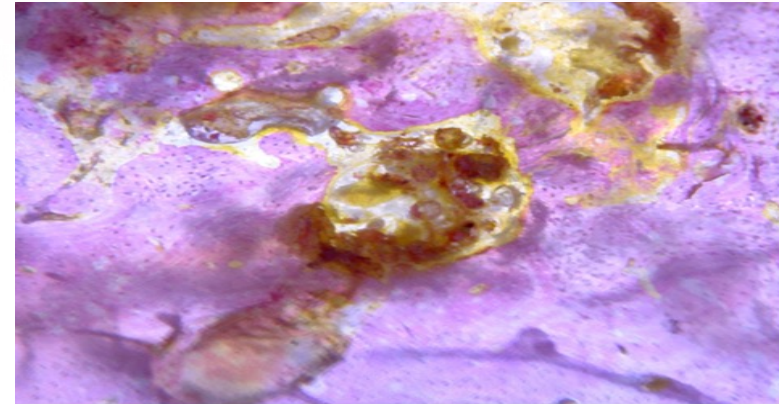
# STRAUMANN-BBL STUDY MARCH 2017

## PRELIMINARY PILOT STUDY IN DOGS

### BIOMATERIALS



XENOGRAFT WITH BBL 2 MONTH



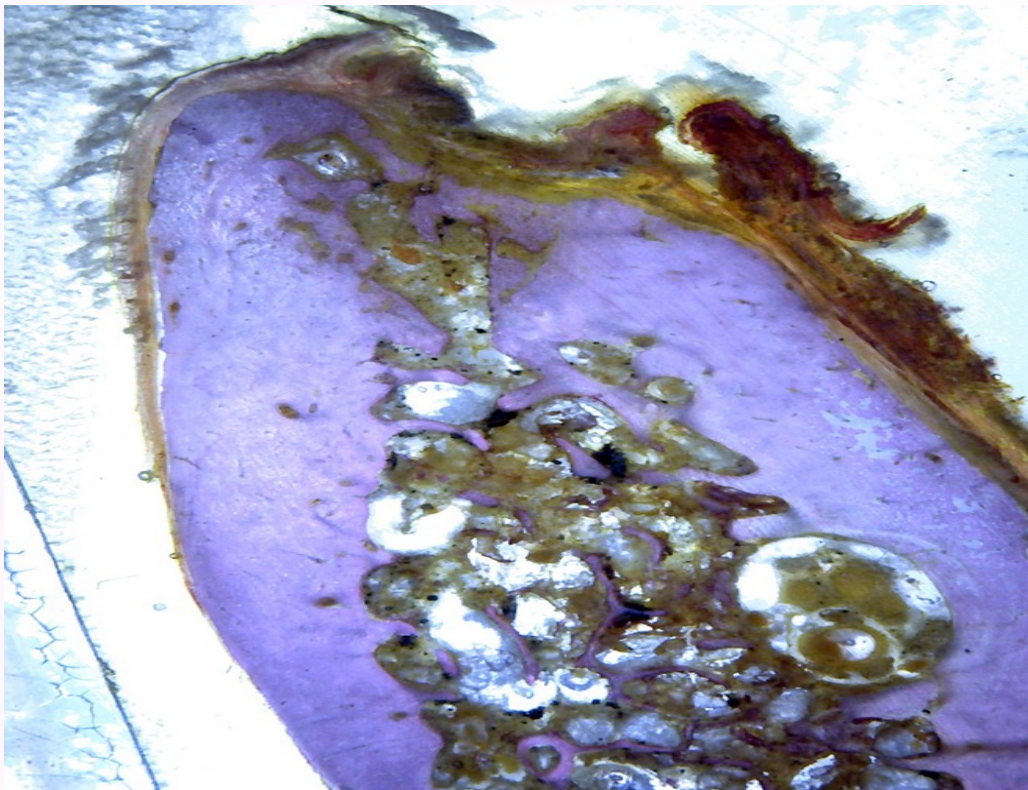
COMPLETE BONE FORMATION ON THE CORTICAL AREA



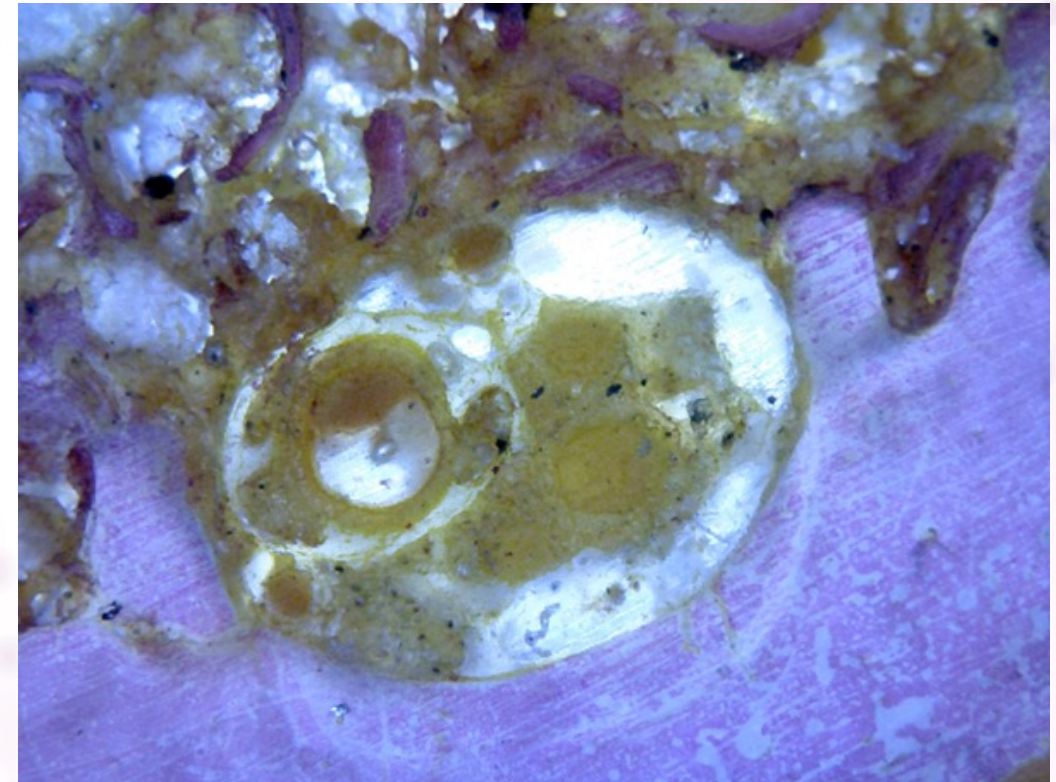
# STRAUMANN-BBL STUDY MARCH 2017

## PRELIMINARY PILOT STUDY IN DOGS

### BIOMATERIALS



XENOGRAPH **WITHOUT** BBL 2 MONTH



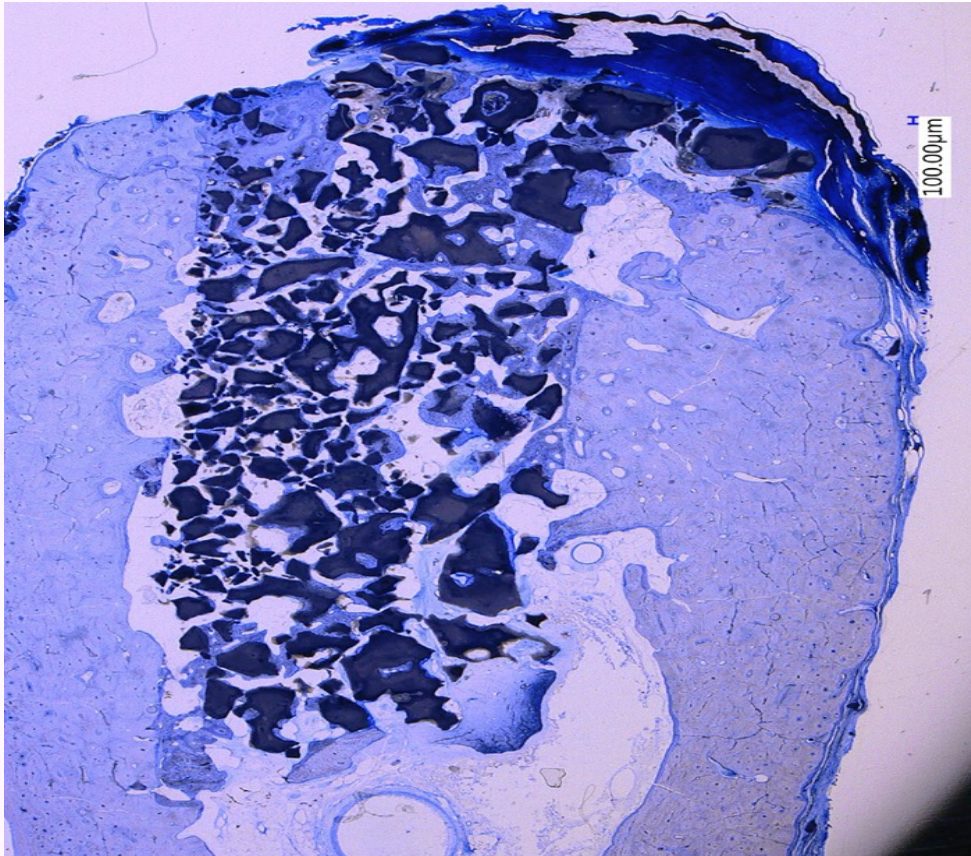
HIGHLY BONE FOMATION INSIDE THE ALVEOLUS  
LIGHTLY CRESTAL BONE RESOPTION



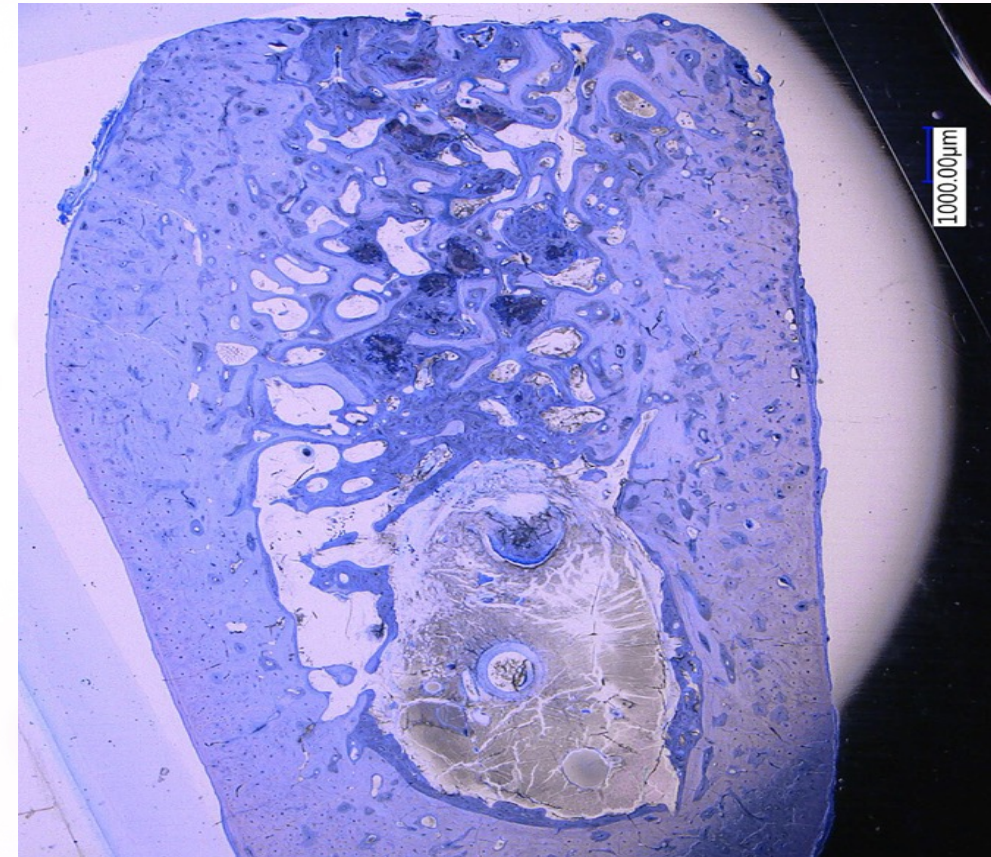
# STRAUMANN-BBL STUDY MARCH 2017

## PRELIMINARY PILOT STUDY IN DOGS

### BIOMATERIALS



XENOGRAPH **WITHOUT** BBL 3 MONTH



XENOGRAPH **WITH** BBL 3 MONTH





# BONE BIOACTIVE LIQUID THERAVEX TISSUE CARE PLUS

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## PERIODONTAL SURGERY



# BONE BIOACTIVE LIQUID THERAVEX TISSUE CARE PLUS

## PERIODONTAL SURGERY

**DAY 1**



**1. Preparation and Debridement:**  
Remove infected tissue using periodontal scaling curettes, ensuring thorough cleaning of the root surface.

**2. Application of Theravex Tissue Care Plus:**

- Apply 2 ml of Theravex Tissue Care Plus directly to the root surface, ensuring comprehensive coverage.
- Allow Theravex Tissue Care Plus to remain in contact with the root surface for one minute to facilitate tissue regeneration and promote healing.

**3. Treatment of Gingival Graft:**  
Submerge the prepared gingival graft in 2 ml of Theravex Tissue Care Plus for 2 minutes to enhance graft viability and promote optimal integration.

**DAY 10**



**4. Surgical Closure:**  
Close the surgical site with primary closure using sutures, ensuring proper alignment and stabilization of the graft and surrounding tissues.

**5. Post-operative Care:**  
Complete the treatment regimen by prescribing Theravex Total Oral Care to enhance tissue regeneration and support post-operative healing.



# BONE BIOACTIVE LIQUID THERAVEX TISSUE CARE PLUS

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## ROOT CANAL TREATMENT



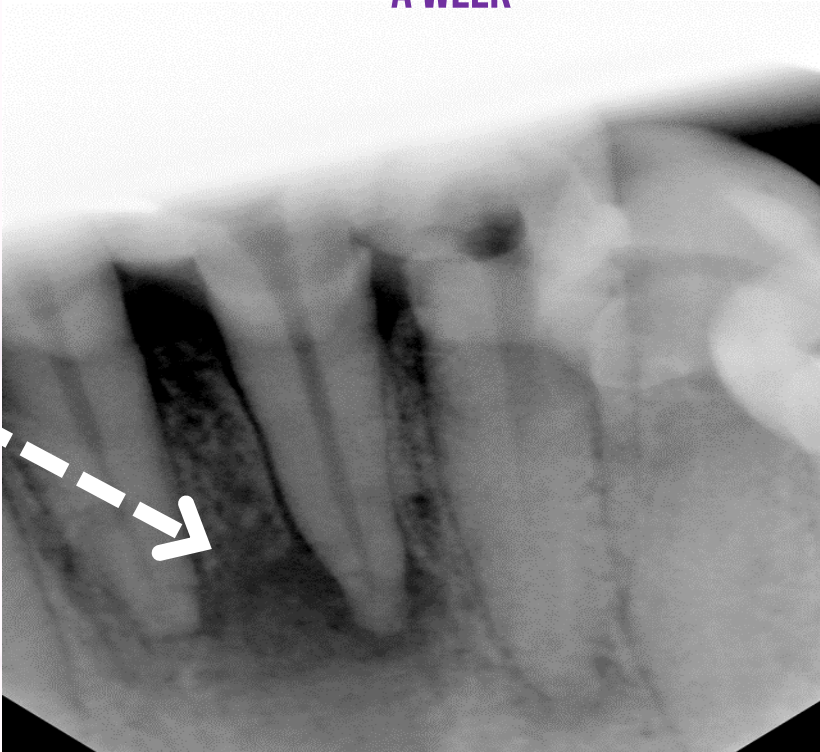
## ENDODONTICS ROOT CANAL TREATMENTS

**THERAVE**  
Tissue Care PLUS



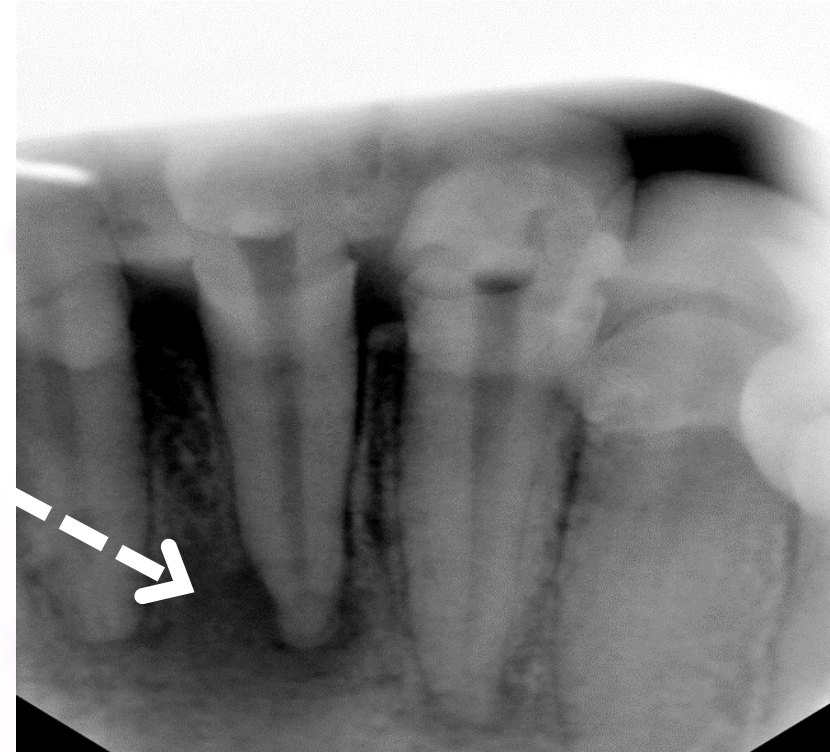
IRRIGATION WITH 1ML OF BBL 100% ONCE

A WEEK



WEEK 1

CLASSIFICATION OF ROOT LATERAL CANALS



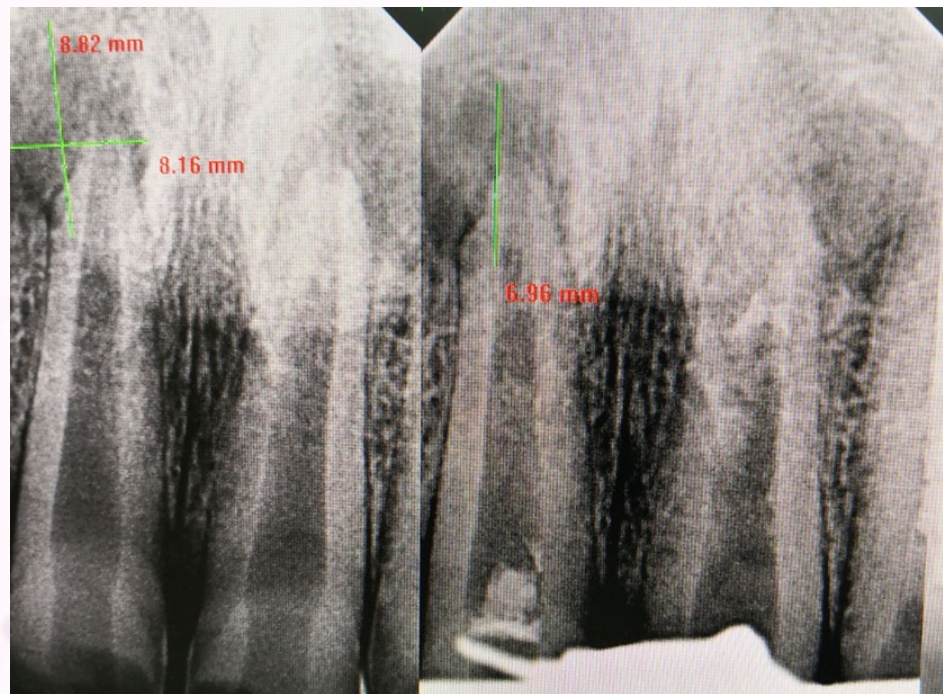
WEEK 3

## ENDODONTICS ROOT CANAL TREATMENTS

**THERAVE**  
Tissue Care PLUS



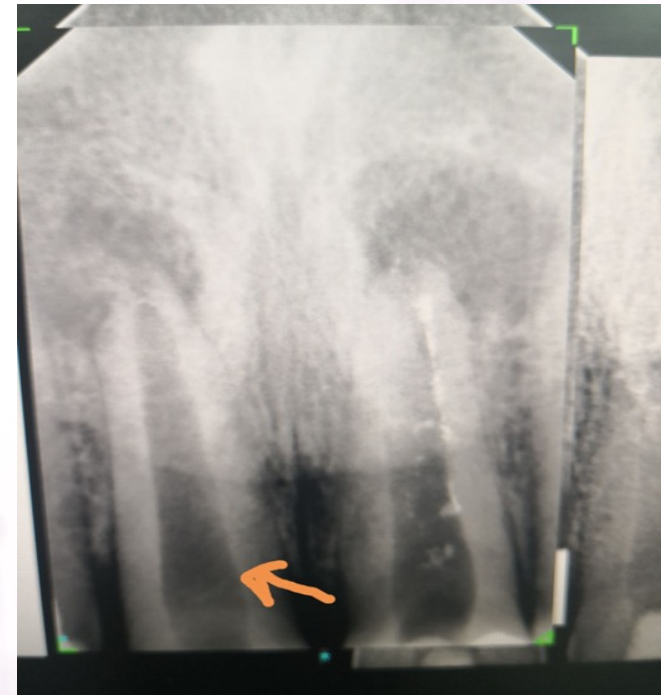
IRRIGATION WITH 1ML OF BBL 100% ONCE A WEEK



**DAY 1**

**WEEK 1**

REDUCTION OF CYST SIZE AND  
CALCIFICATION OF THE ROOT



**WEEK 3**



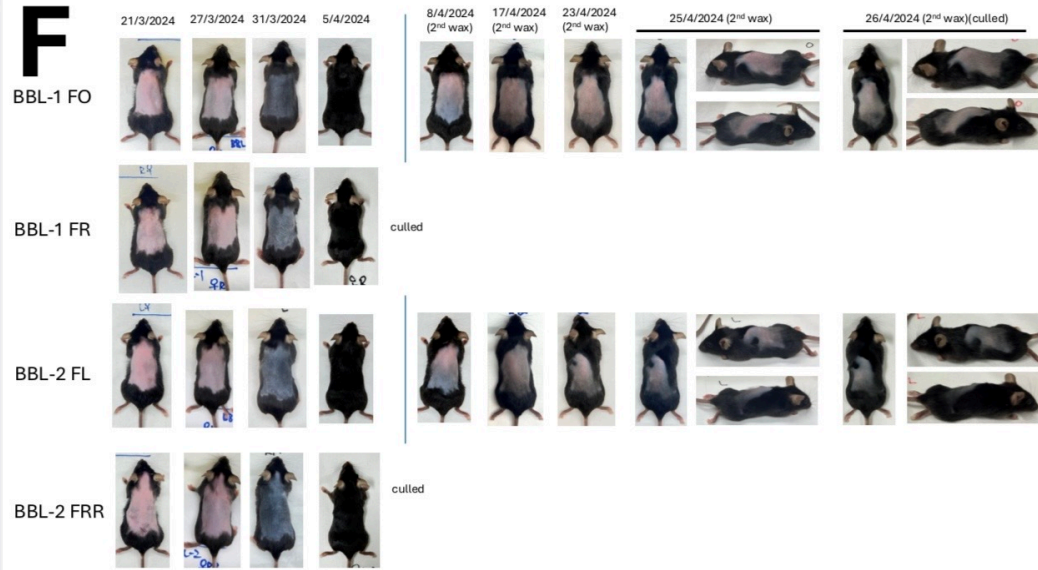


# BONE BIOACTIVE LIQUID THERAVEX TISSUE CARE PLUS

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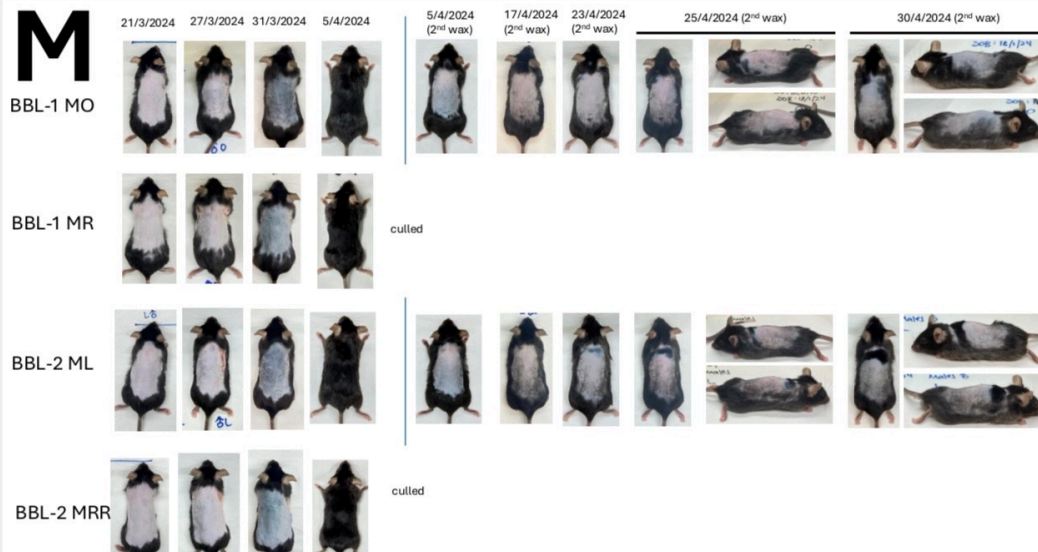
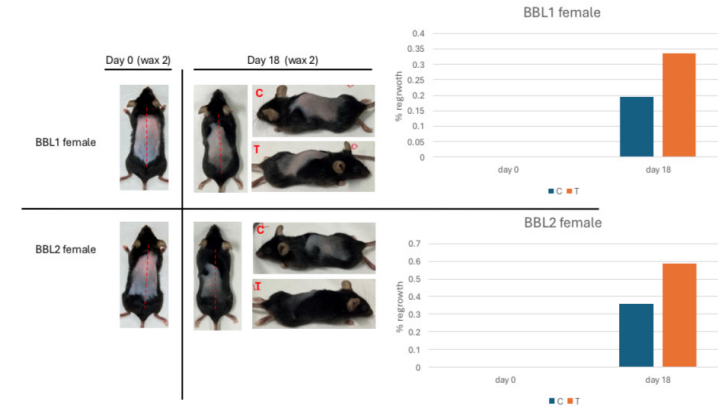
## HAIR TRANSPLANT

# HAIR TRANSPLANT



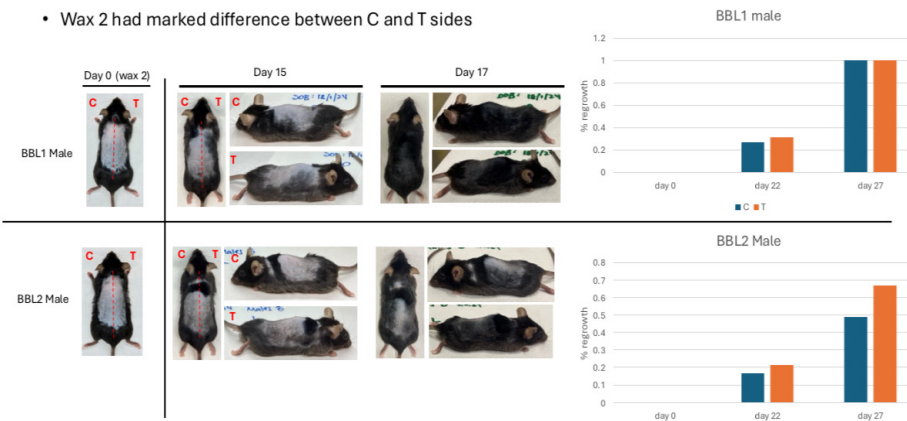
## Females

- Wax 1 observations: hair grew back uniformly, did not notice any major differences in the C and T sides
- Wax 2 had marked difference between C and T sides



## Males

- Wax 1 observations: hair grew back uniformly, did not notice any major differences in the C and T sides
- Wax 2 had marked difference between C and T sides





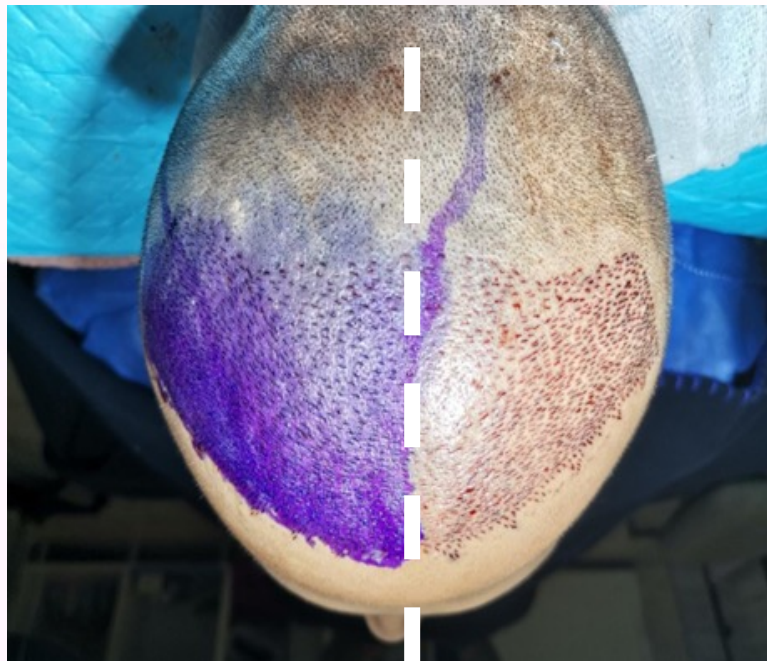
# HAIR TRANSPLANT

**THERAVE**  
Tissue Care PLUS



TRANSPLANTATION OF FOLLICLES FROM THE OCCIPITAL TO THE FRONTAL AREA WAS PERFORMED BY WETTING THE HAIR FOLLICLES WITH THE BBL. IN THE RIGHT FRONTAL AREA OF THE PATIENT WITH THE BBL AND THE LEFT AREA WITH THE USUAL TECHNIQUE.

DAY 0



Theravex tissue  
care plus

DAY 1



Theravex tissue  
care plus

1 YEAR



Theravex tissue  
care plus

# HAIR TRANSPLANT

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**1 YEAR**



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**DAY 1**



**1 YEAR**



Theravex tissue care plus





# BONE BIOACTIVE LIQUID THERAVEX TISSUE CARE PLUS

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## FACIAL APPLICATION

# FACIAL APPLICATION

**THERAVE**  
Tissue Care PLUS



**DAY 1**



**3 WEEKS**





# FACIAL APPLICATION

**THERAVE**  
Tissue Care PLUS



**DAY 1**



**3 WEEKS**



# FACIAL APPLICATION

**THERAVE**  
Tissue Care PLUS



**DAY 1**



**3 WEEKS**







**BONE BIOACTIVE LIQUID  
THERAVEX CARE SPRAY**

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**WOUND HEALING  
SKIN REGENERATION**

# SKIN BURN GRADE II



**DAY 0**



**DAY 7**



**DAY 15**



**DAY 20**



# SKIN BURN GRADE III DIABETIC FOOT



DAY 0



DAY 15



DAY 20



DAY 0



DAY 15



DAY 25



# SKIN ULCERS



DAY 0



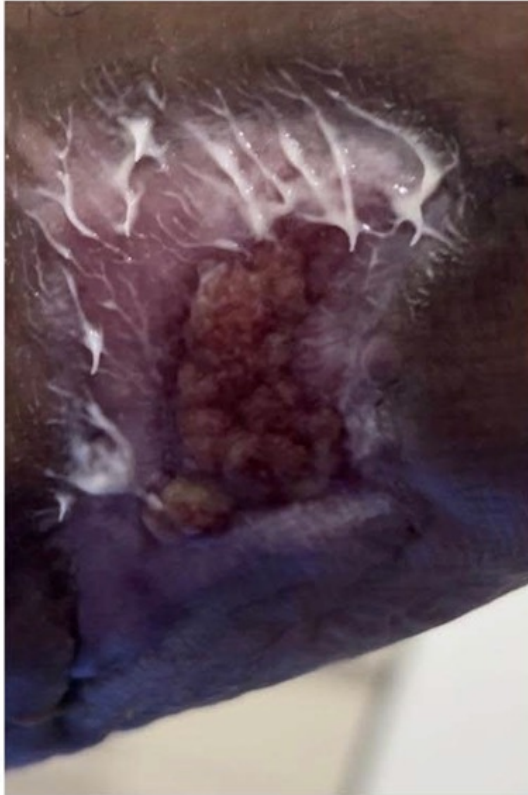
DAY 20



DAY 25



# DIABETIC FOOT



**DAY 0**



**DAY 7**



**DAY 14**

# DIABETIC FOOT



**THERAVE**  
Tissue Care Spray



**DAY 0**



**DAY 7**



**DAY 14**



# DIABETIC FOOT



**THERAVE**  
Tissue Care Spray



**DAY 0**



**DAY 7**



**DAY 14**

# DIABETIC FOOT



**DAY 0**



**DAY 7**



**DAY 14**



# BIOINTELLIGENT'S COLLABORATION WITH UNIVERSITIES

**UIC**  
barcelona

Universitat Internacional de Catalunya



UNIVERSITAT DE  
BARCELONA



**JUST**

**upna**

Universidad Pública de Navarra  
Nafarroako Unibertsitate Publikoa



**NANYANG  
TECHNOLOGICAL  
UNIVERSITY**  
**SINGAPORE**





**Prof. Dr. Maher Atari**  
MD, DDS, PhD

**THANK YOU**