



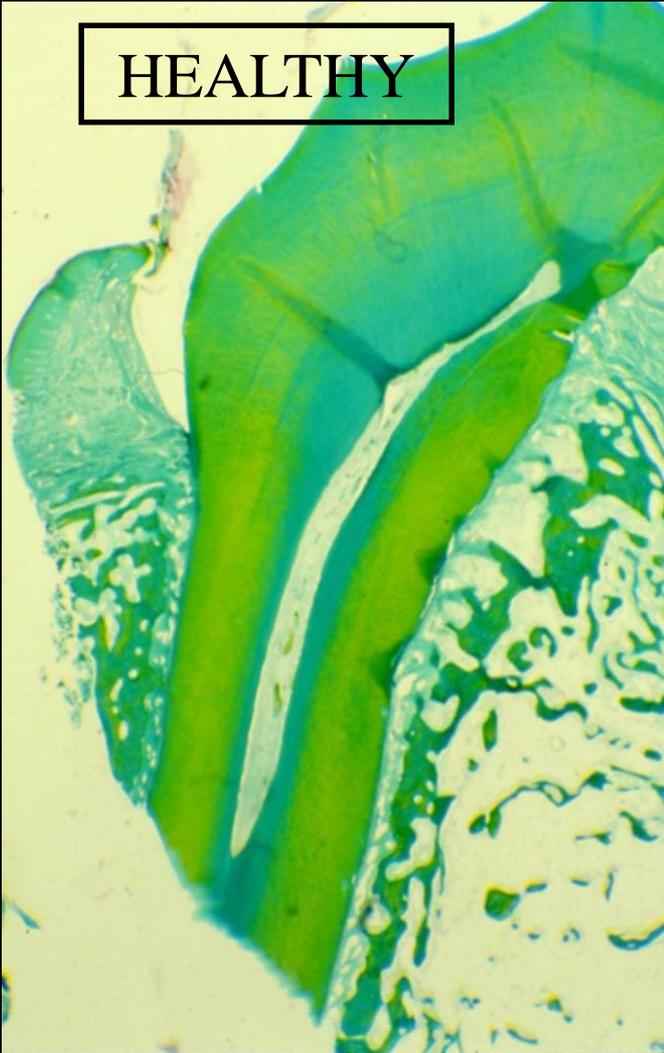
PERIODONTAL REGENERATION AND WOUND HEALING

Windisch Péter

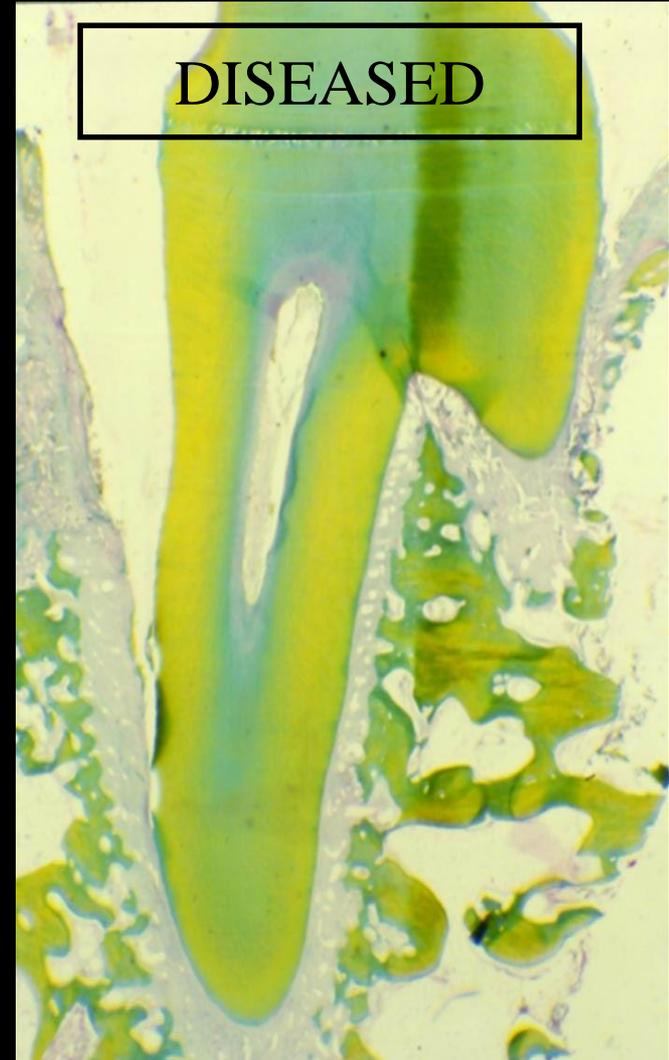
2016.

PERIODONTIUM

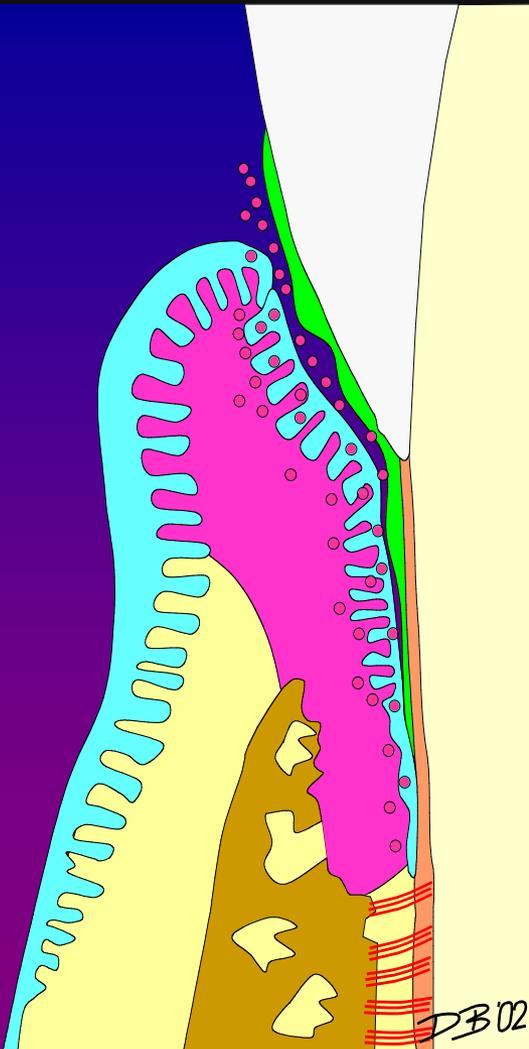
HEALTHY



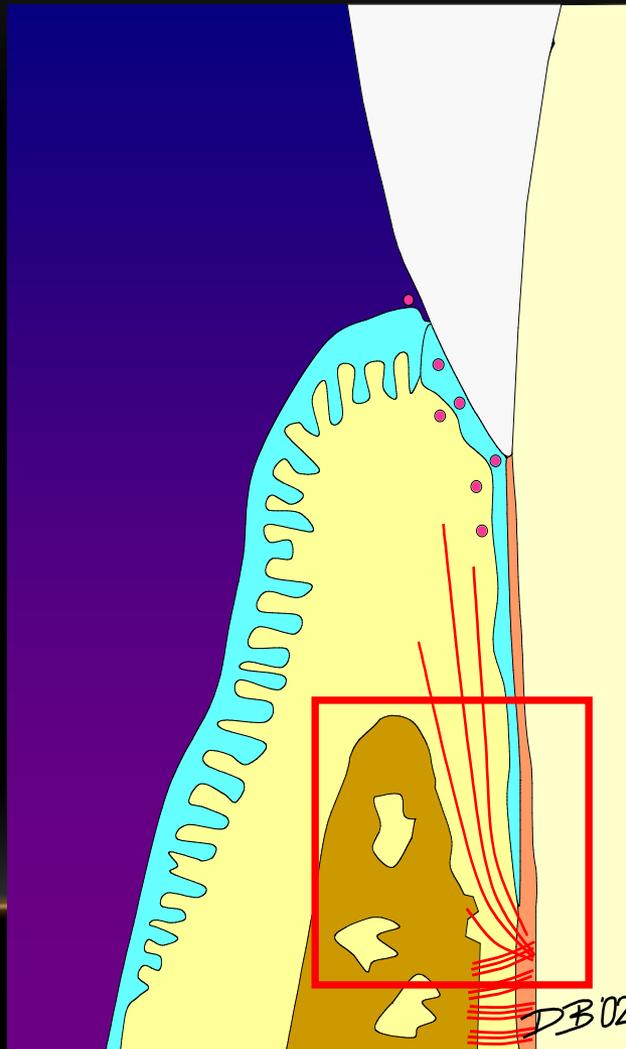
DISEASED



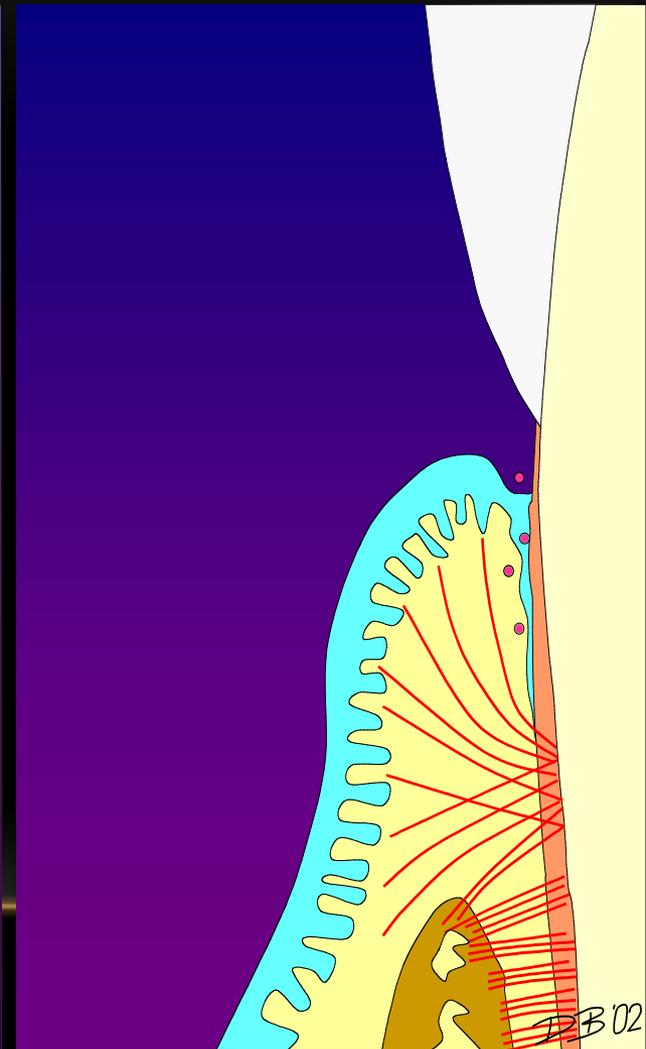
Periodontitis



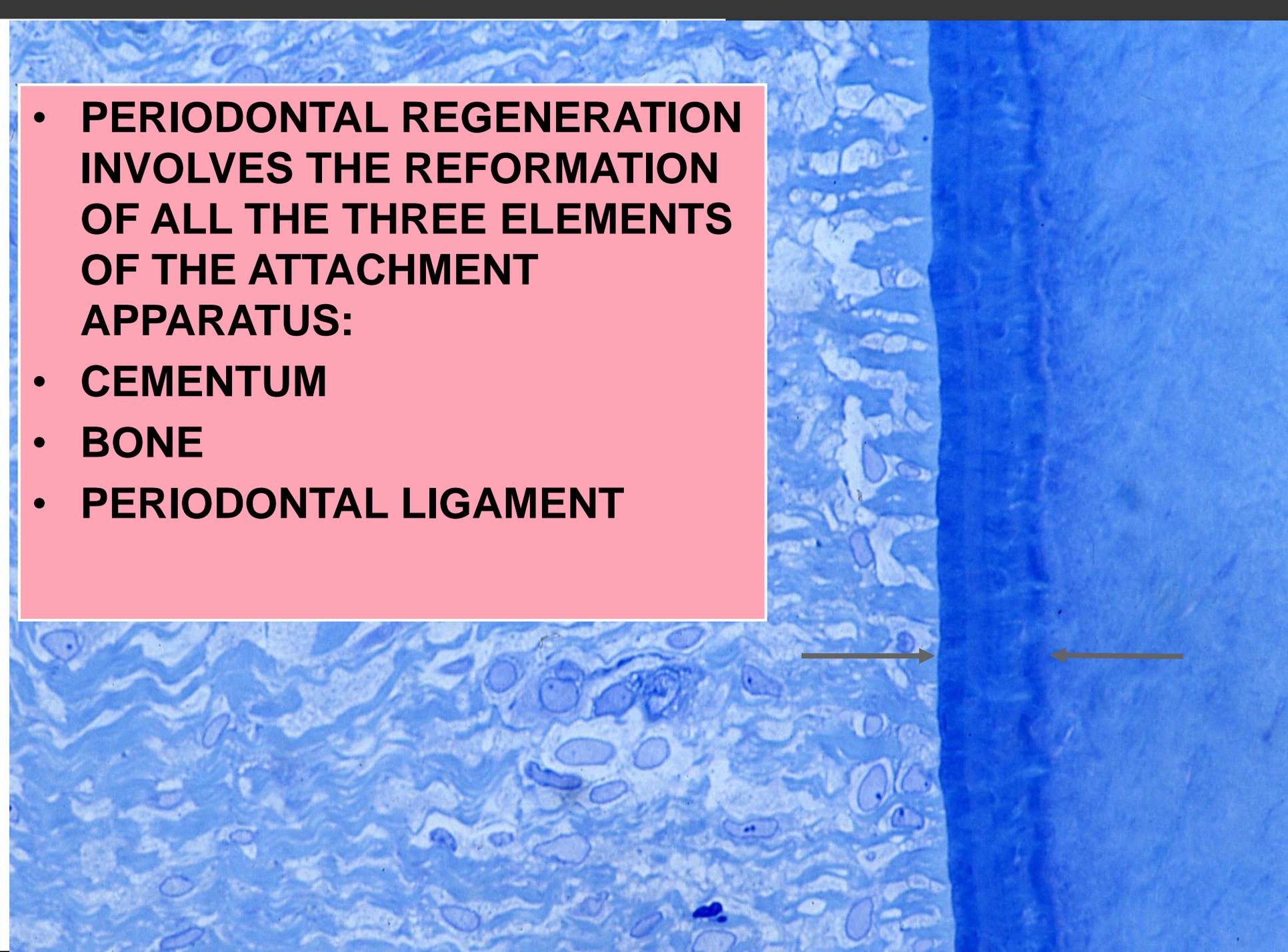
Reparation



Regeneration



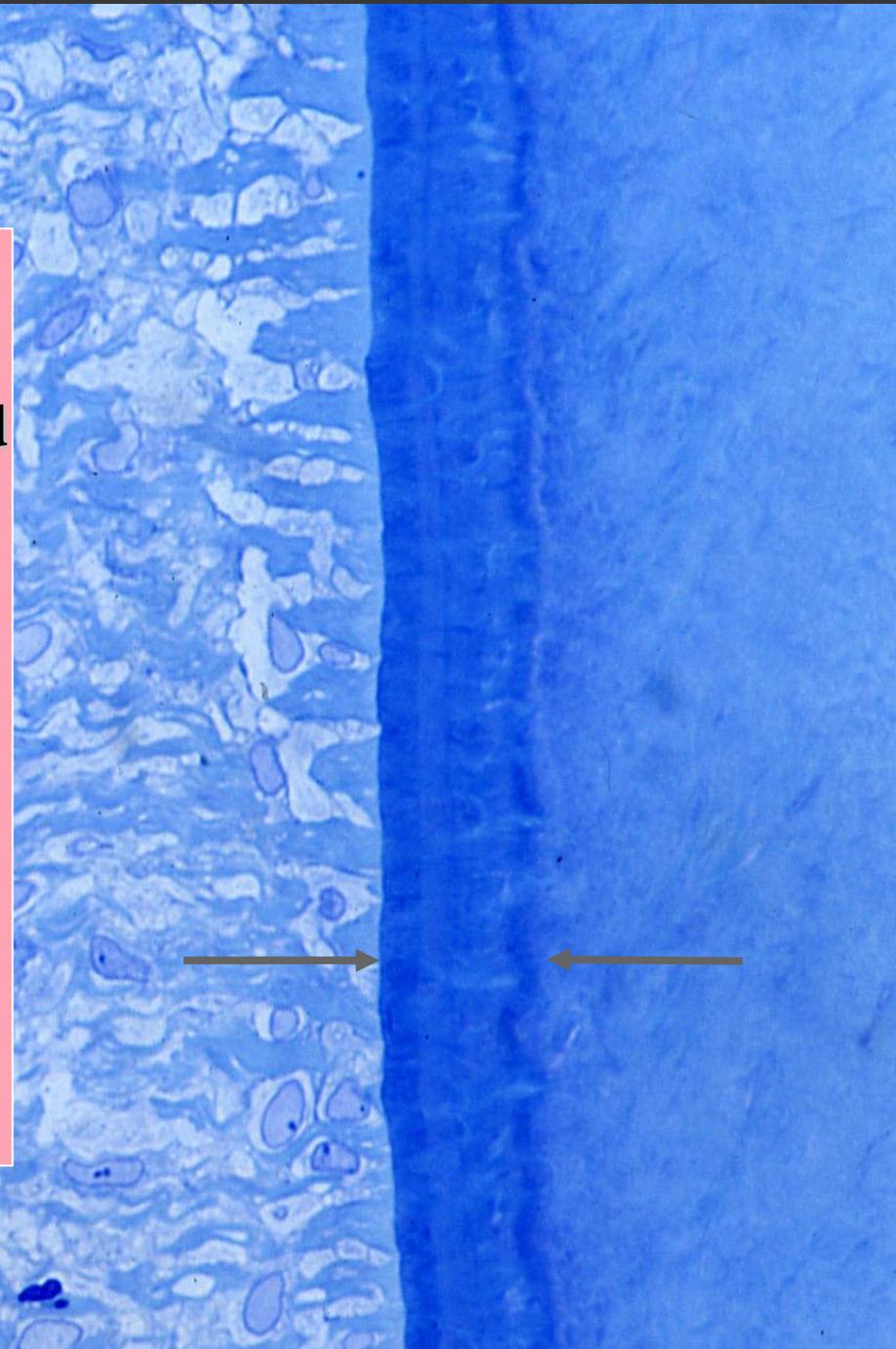
- **PERIODONTAL REGENERATION INVOLVES THE REFORMATION OF ALL THE THREE ELEMENTS OF THE ATTACHMENT APPARATUS:**
- **CEMENTUM**
- **BONE**
- **PERIODONTAL LIGAMENT**



This goal is attained by the presence of specific cell types, that occupy the defect area and form structures typical of the periodontal tissue during wound healing.

At the same time gingival cell types must be prevented from proliferating into the defect region

(Caton, 1976).



PERIODONTAL WOUND HEALING

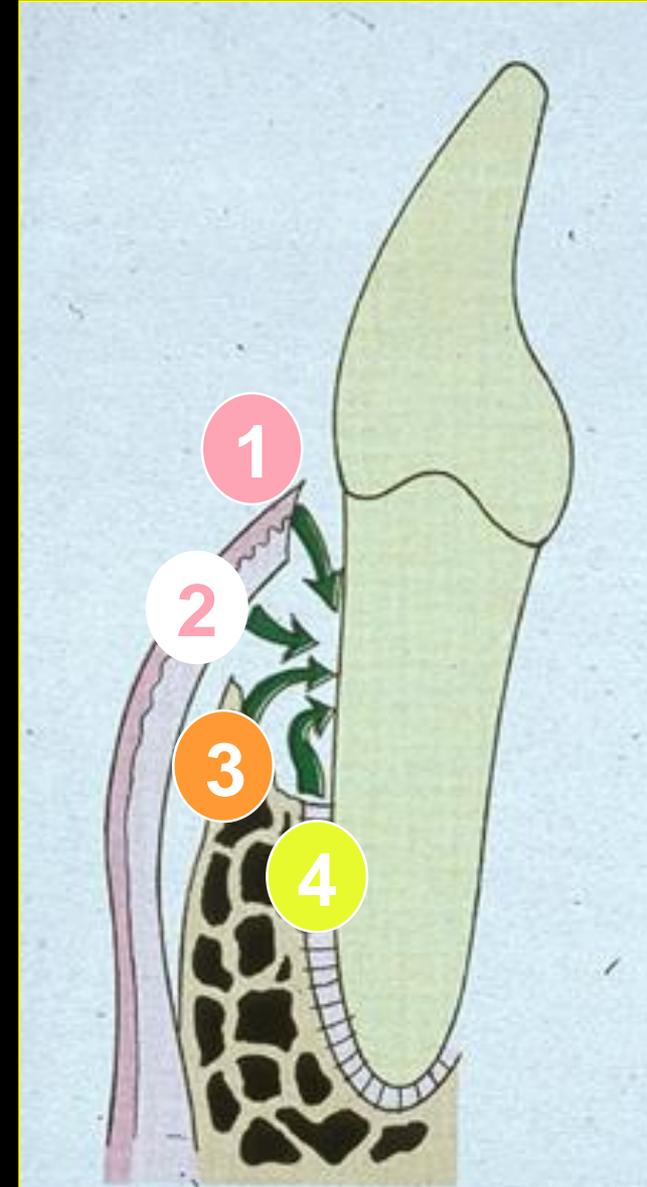
AFTER FLAP SURGERY THE WOUND CAN BE REPOPULATED BY FOUR GROUP OF CELLS:

Epithelial cells

Gingival connective tissue

Alveolar bone cells

Periodontal ligament cells



PERIODONTAL WOUND HEALING

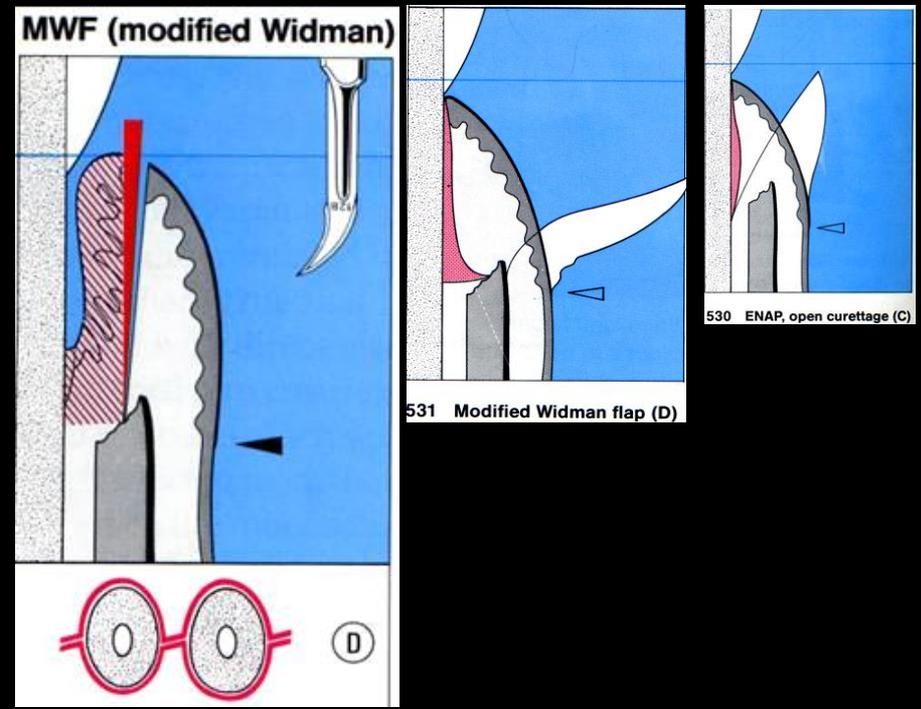
- Biological Problems
 - Open system (continuous bacterial contamination)
 - Scarce blood supply to the cementum and dentin

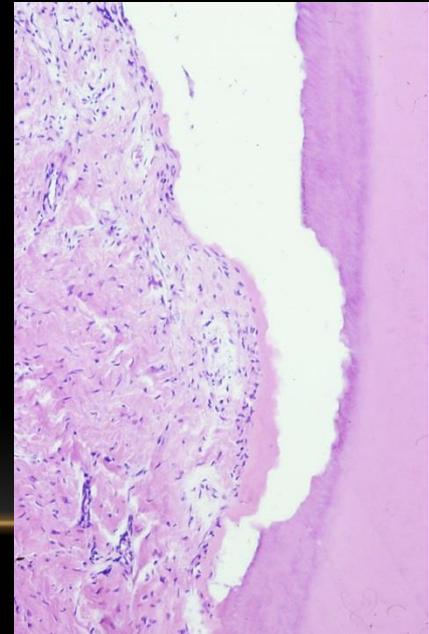
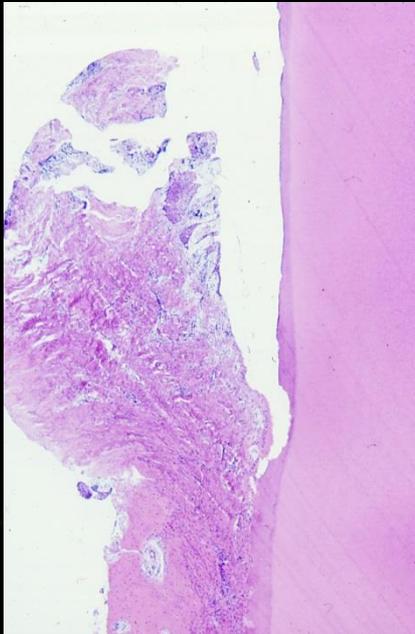
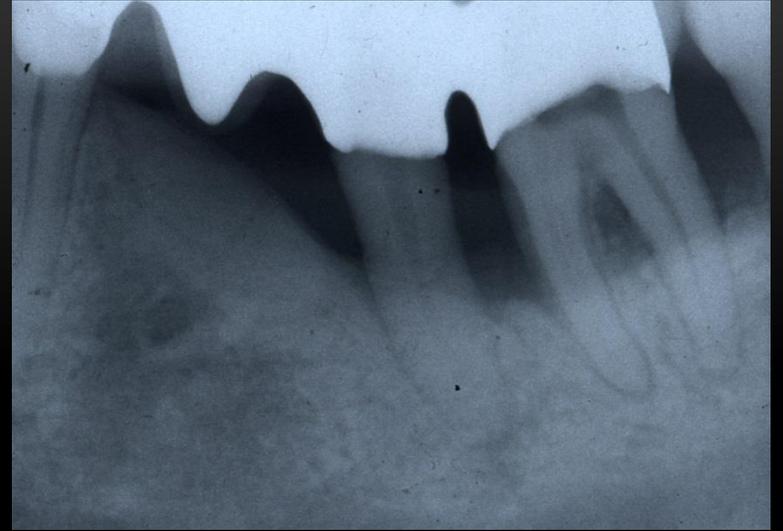
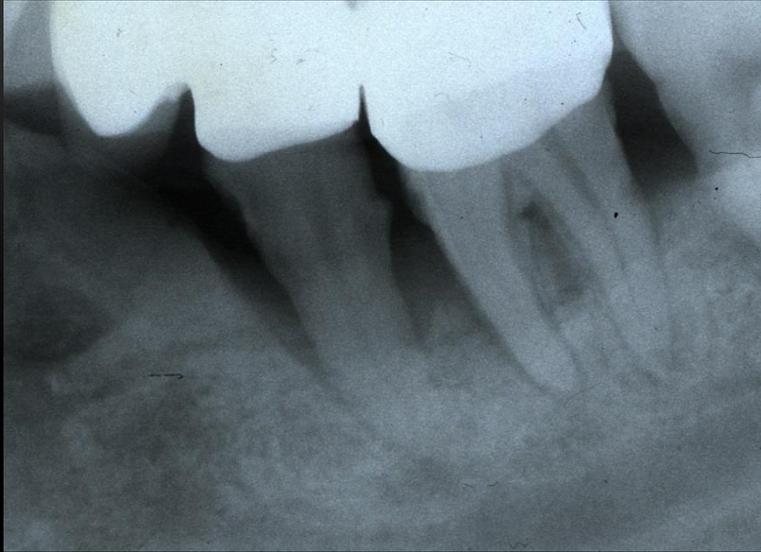
PERIODONTAL WOUND HEALING

- Reparation
 - LONG JUNCTIONAL EPITHELIUM (LJE)
 - CEMENTUM RESORPTION
 - ANKYLOSIS
- Regeneration
 - NEW CONNECTIVE TISSUE ATTACHMENT(CEMENTUM AND PDL)
 - COMPLETE PERIODONTAL REGENERATION (BONE, PDL, CEMENTUM)

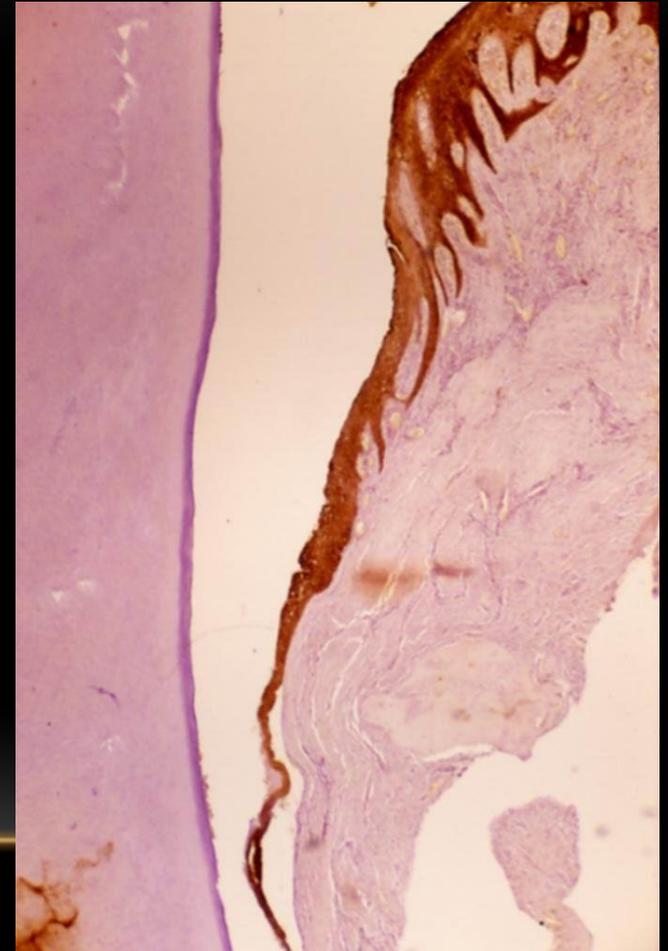
REPARATION

- AFTER CONVENTION PERIODONTAL SURGERY THE PERIODONTAL POCKET HEALS WITH LONG EPITHELIAL ATTACHMENT (LJE)

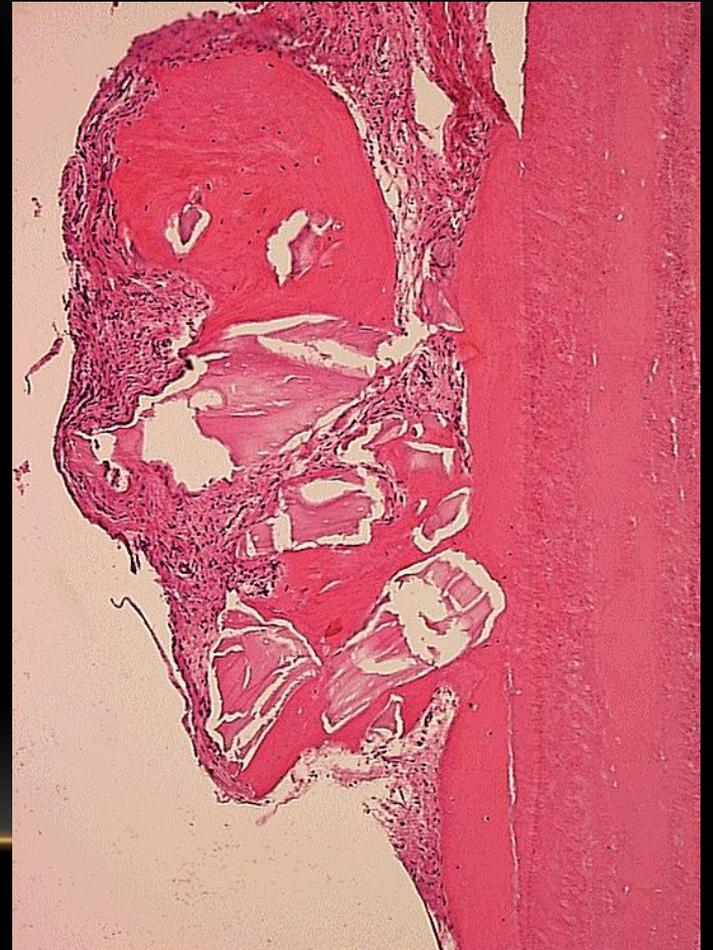




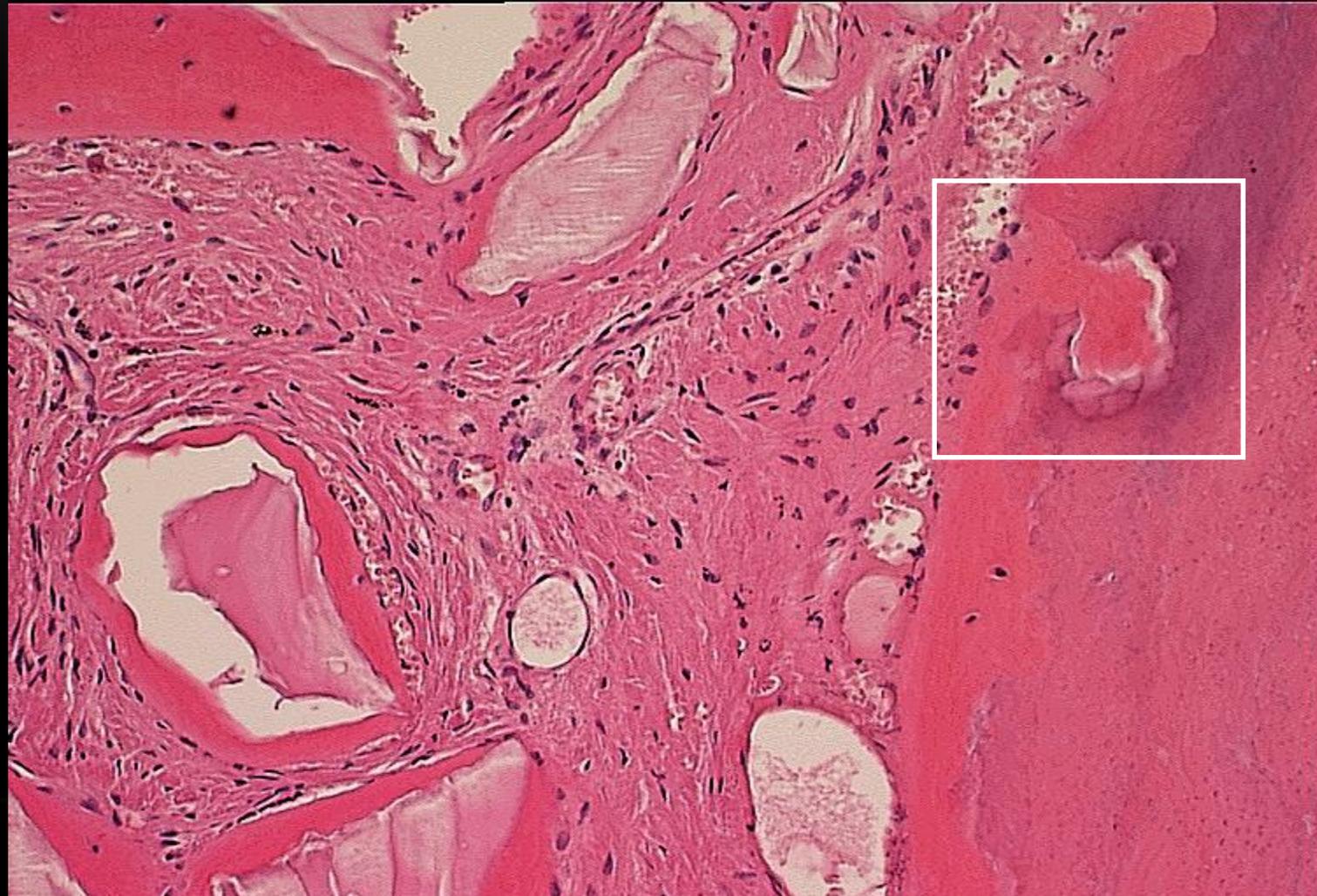
LONG JUNCTIONAL EPITHELIAL ATTACHMENT (LJE)



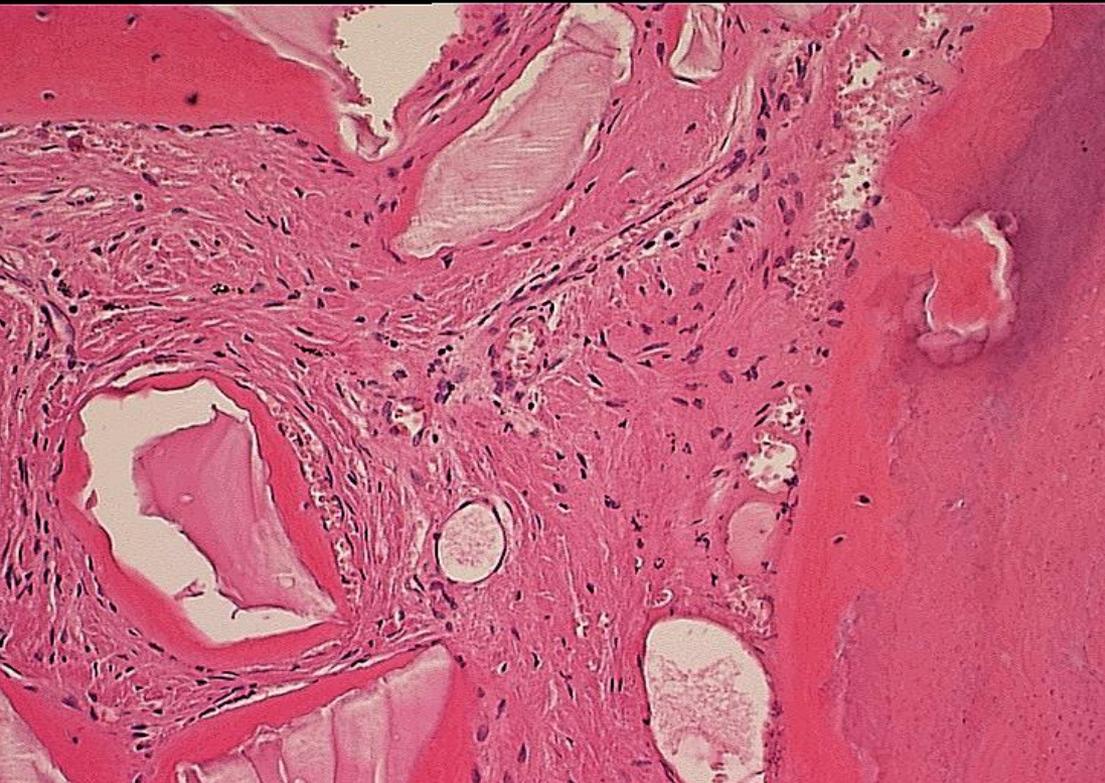
ANKYLOSIS

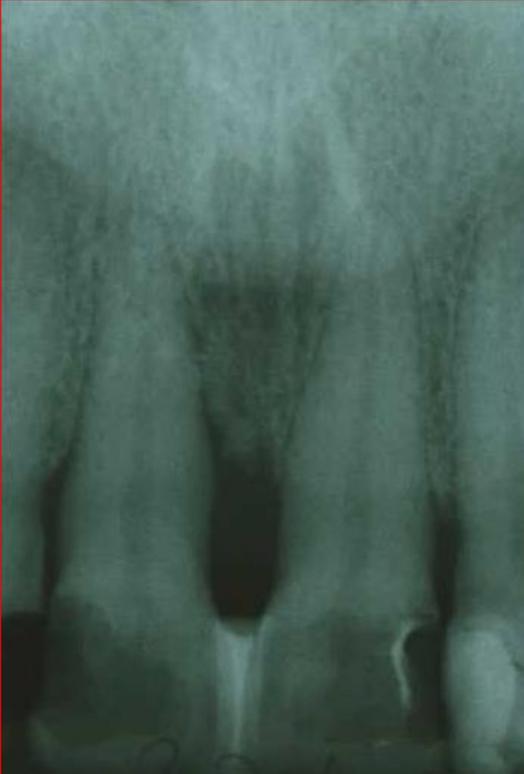
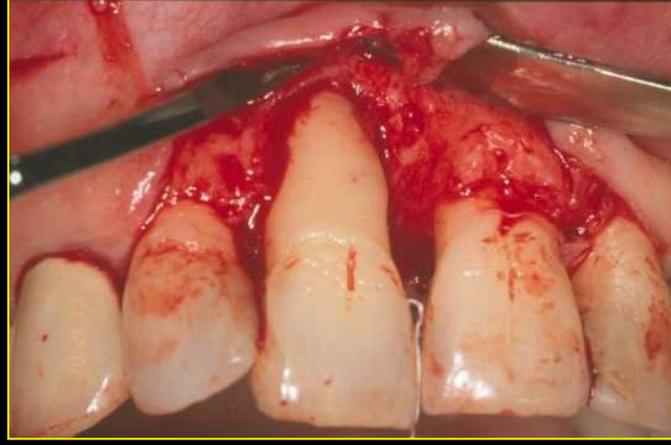


CEMENTUM RESORPTION

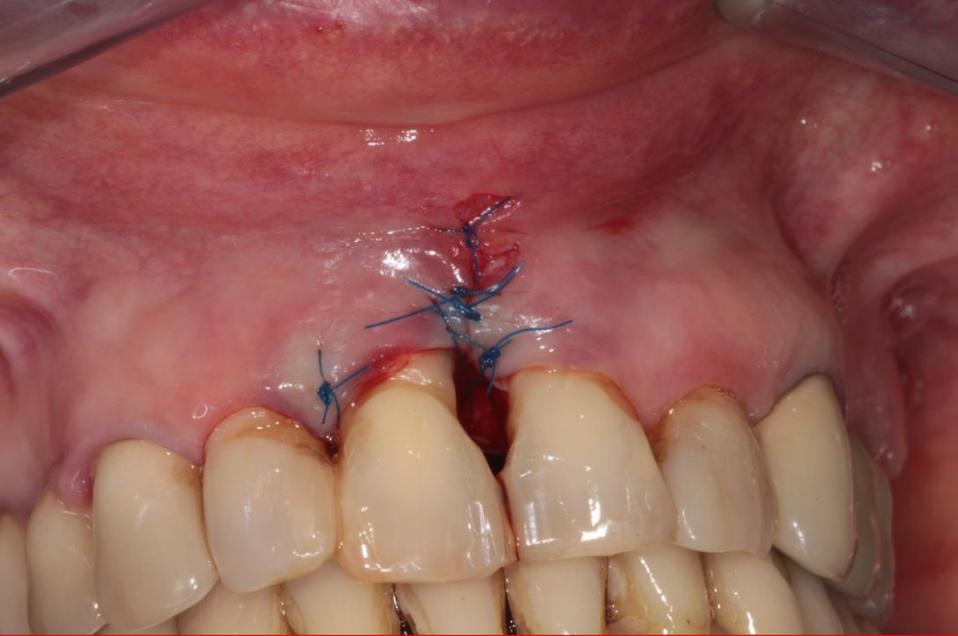


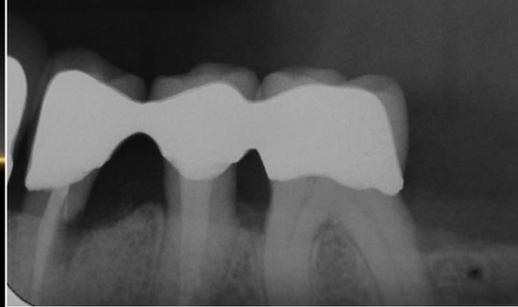
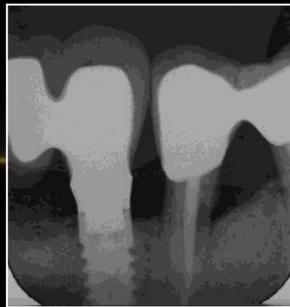
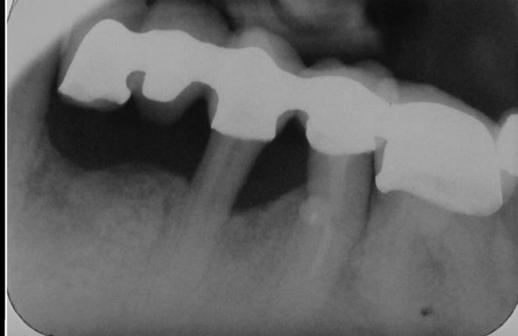
CEMENTUM RESORPTION







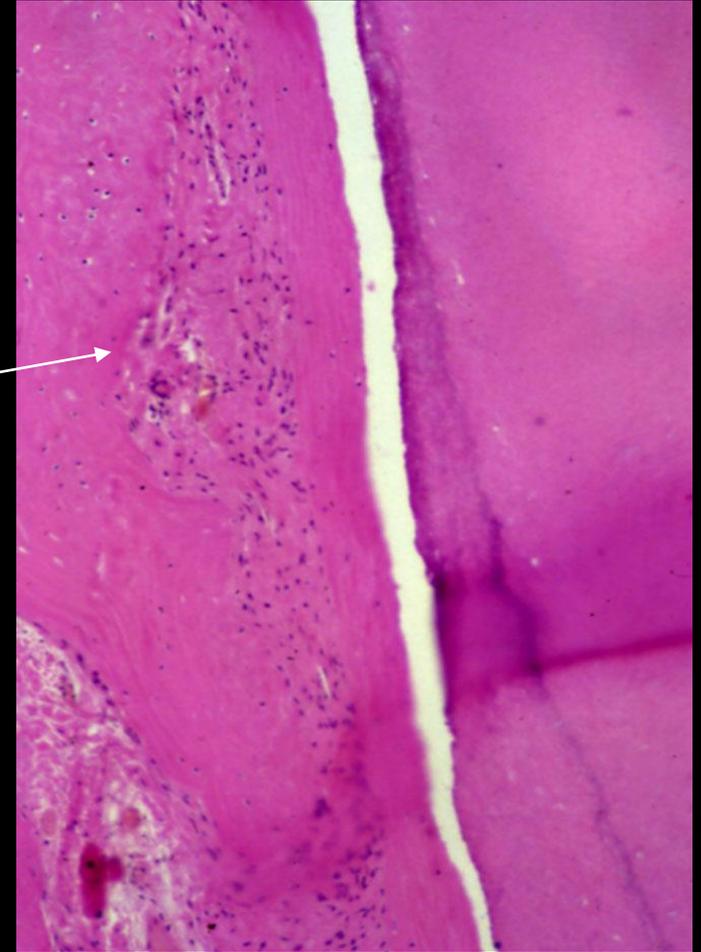
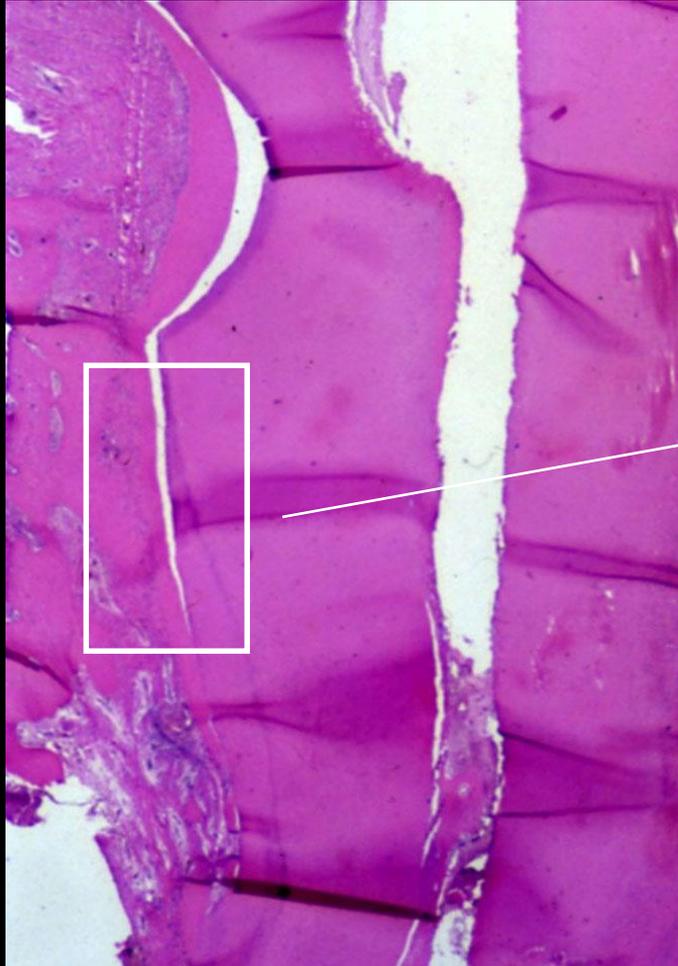




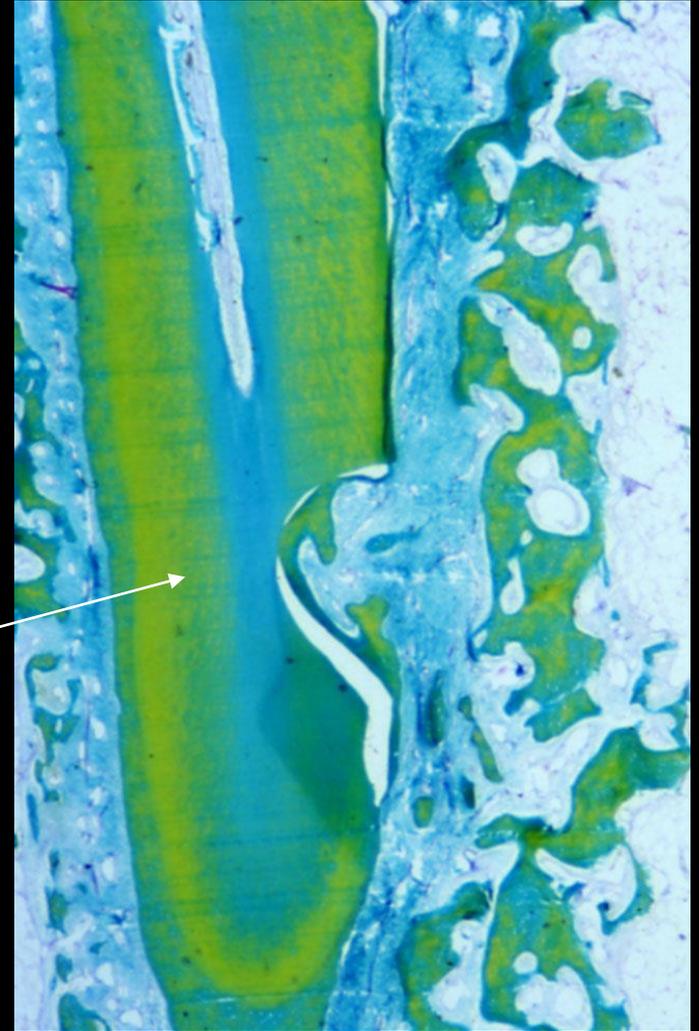
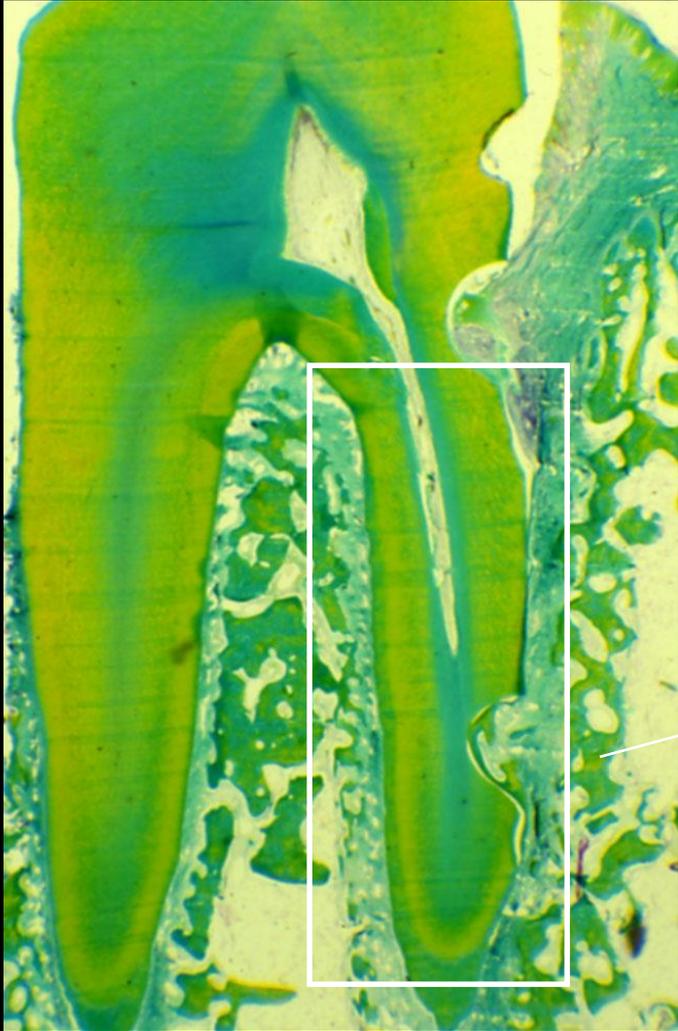
THE CHARACTERISTICS OF THE NEWLY FORMED REGENERATING ATTACHMENT (NEW ATTACHMENT PROCEDURES)

- NEW CEMENTUM FORMATION WITH MAINLY CELLULAR CEMENTUM
- NEW SHARPY'S FIBERS FORMATION
- REGENERATING OXYTALAN FIBERS
- NON REGENERATING MALASSEZ CELLS ?

REGENERATING PERIODONTAL ATTACHMENT (HUMAN)

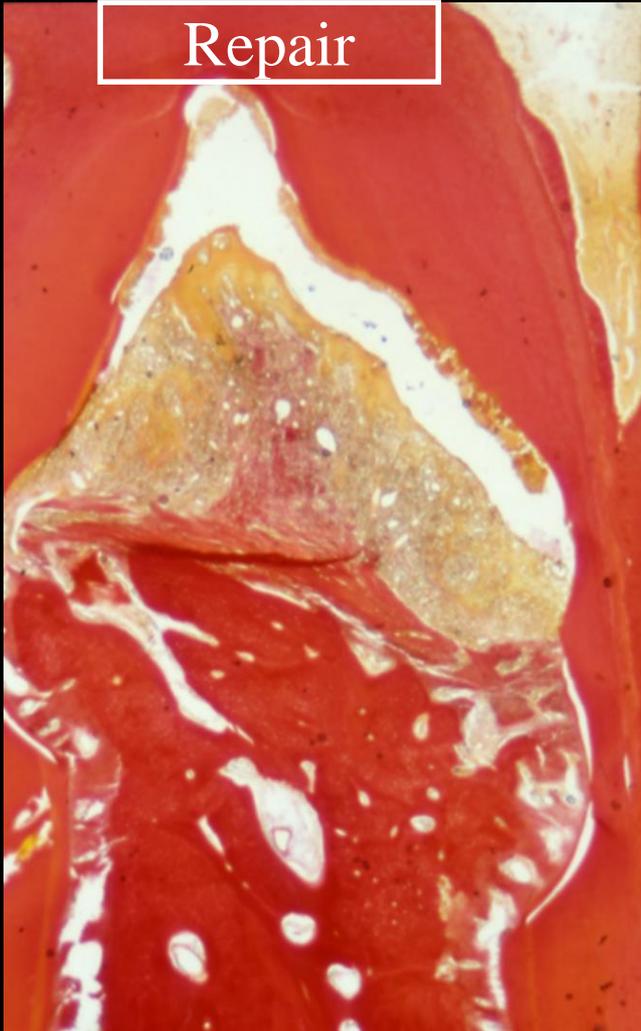


REGENERATING ROOT CEMENTUM (MONKEY)



WOUND HEALING

Repair



Regeneration



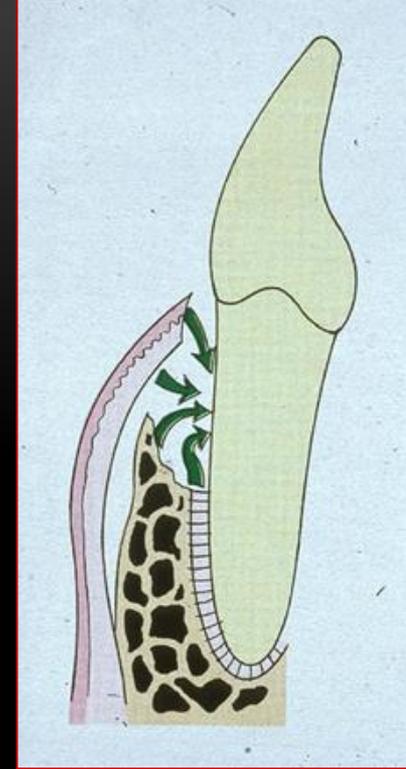
HISTORY

Regenerative potential of the periodontal structures

In 1976, Melcher postulated that, the cells which repopulate the root surface after surgery determine the nature of the attachment that will form.

Root surface may be repopulated by 4 different types of cells:

1. Epithelial cells
2. Cells originating from the gingival connective tissue
3. Cells originating from the bone tissue
4. Cells originating from the periodontal ligament



Melcher, AH. On the repair potential of periodontal tissues. J Periodontol 1976;47:256-260.

CATON, J. & ZANDER, H. A.: OSSEOUS REPAIR OF AN INTRABONY POCKET WITHOUT NEW ATTACHMENT OF CONNECTIVE TISSUE. 1976. J. CLIN. PERIODONTOL. 3:54-58

- Aim: to study the healing of the periodontal structures after different modalities of periodontal therapy.
- „Monkey model”
 - 1. Periodic closed curettage
 - 2. Modified Widman flap operation without osseous surgery
 - 3. Modified Widman flap + autogenous cancellous bone
 - 4. Modified Widman flap + bone substitute (beta tricalcium phosphate)

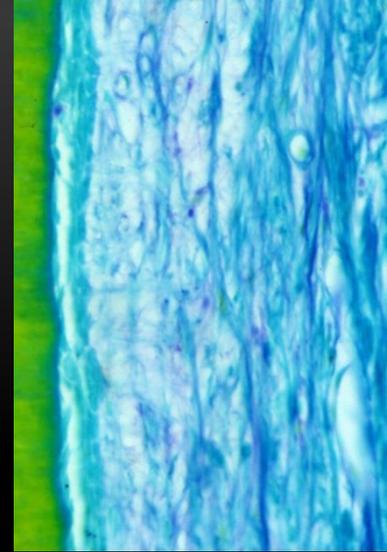
HISTOMETRIC ANALYSIS

- All the treatment procedures resulted in long junctional epithelium

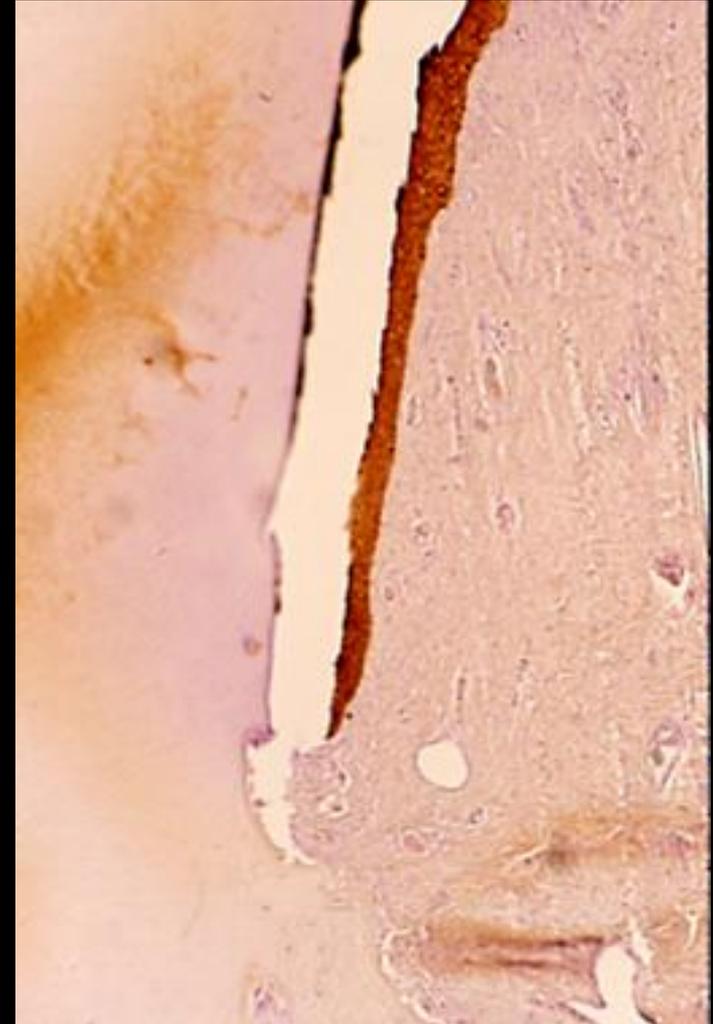
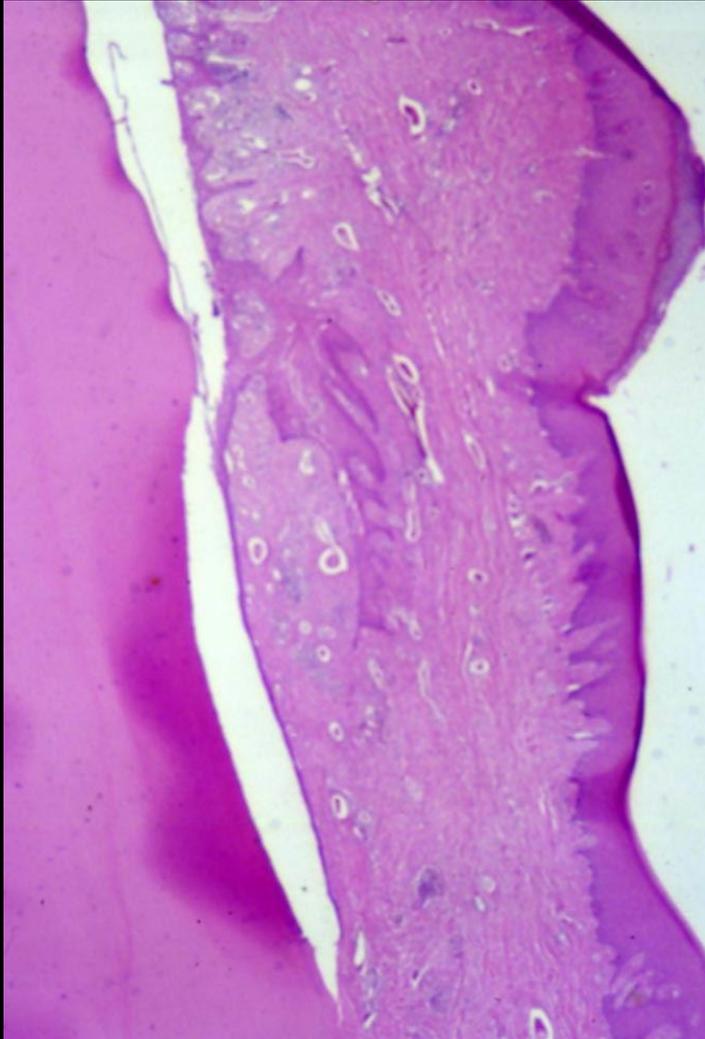
- Overall results of the studies:

New attachment formation is inhibited by the apically migrating dentogingival epithelium.

- The rapid proliferation of the epithelium prevent the gingival connective tissue from establishing a close contact with the root surface.
- An early contact between the gingival connective tissue and the root has been regarded as the prime prerequisite for the formation of a new connective tissue attachment.



LONG JUNCTIONAL EPITHELIAL ATTACHMENT (LJE)



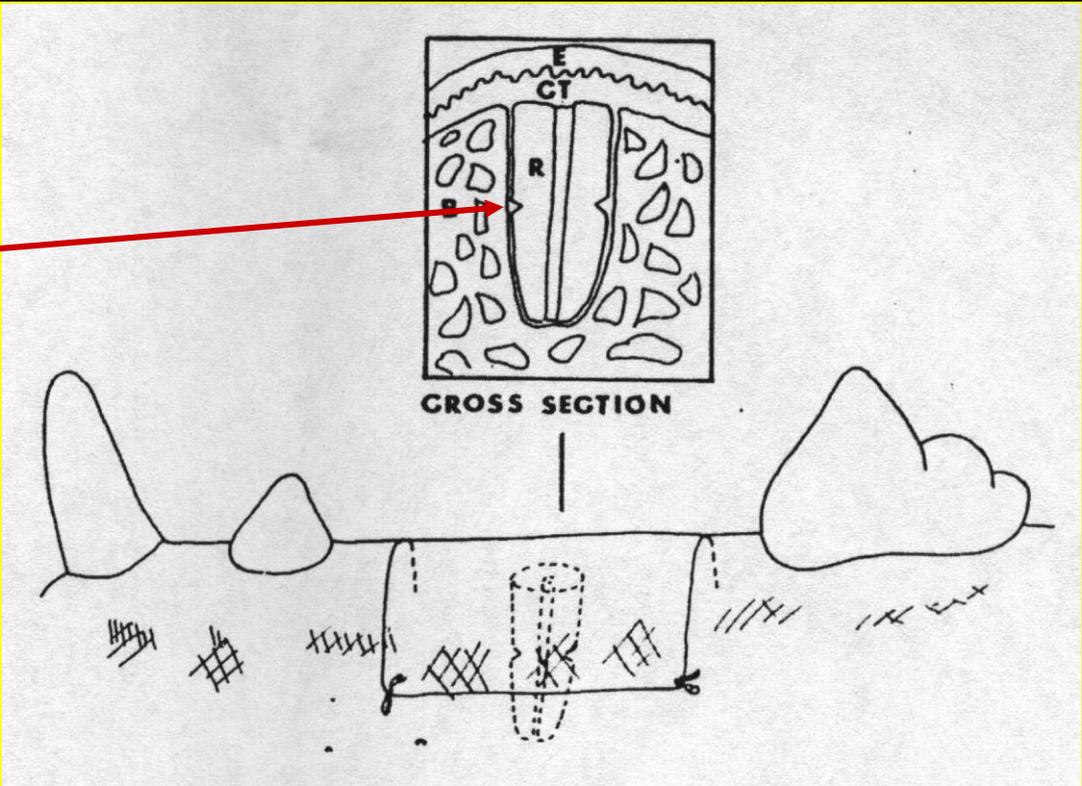
Karring T, Nyman S, Lindhe J. Healing following implantation of periodontitis affected roots into bone tissue. J Clin Periodontol 1980;7:96-105.

Experimental periodontitis in dogs

Periodontitis- affected teeth after rootplaning and total decoronation were reimplanted in artificial sockets prepared in the edentulous ridge

The gingival flap was tightly sutured to prevent the apical migration of the epithelium (totally submerged roots).

Bottom of pocket



Karring et al. (1980)

- **New connective tissue attachment could develop around decoronated roots if the gingival flap was tightly closed during the whole period of postoperative healing**
- **If the suture was not tight enough and the gingival flap opened up the gingival epithelium could migrate apically, new connective tissue attachment never occurred.**

conclusion:

The epithelial migration is the biggest obstacle of the connective tissue regeneration

Karring T, Nyman S, Lindhe J. Healing following implantation of periodontitis affected roots into bone tissue. J Clin Periodontol 1980;7:96-105

THE ROLE OF GINGIVAL CONNECTIVE TISSUE AND ALVEOLAR BONE

Periodontal tissue breakdown was produced around certain teeth (experimental teeth) in monkeys and dogs

according to

Caton and Zander (1975).

Caton J ,Zander HA. Primate model for testing periodontal treatment procedures: I. Histologic investigation of localized periodontal pockets produced by orthodontic elastics. J Periodontol 1975; 2:71-77.

EXPERIMENTAL PERIODONTITIS IN DOGS AND MONKEYS

50% ATTACHMENT LOSS

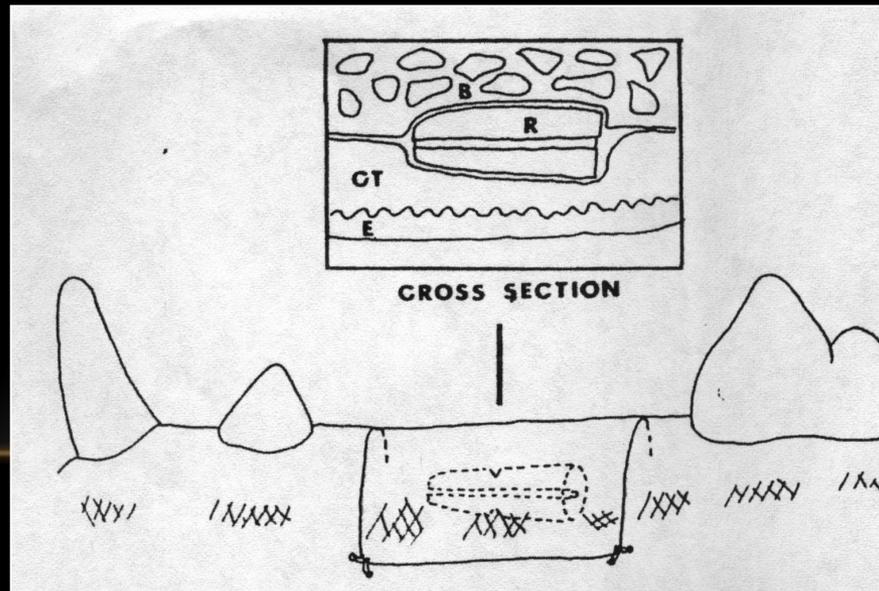
Recipient sites in the edentulous mandible for subsequent implantation of the diseased roots

Crowns of the experimental teeth were resected.

Nyman S, Karring T, Lindhe J, Planten S. Healing following implantation of periodontitis-affected roots into gingival connective tissue. J Clin Periodontol 1980;7:394-401

EXPERIMENTAL PERIODONTITIS IN DOGS AND MONKEYS

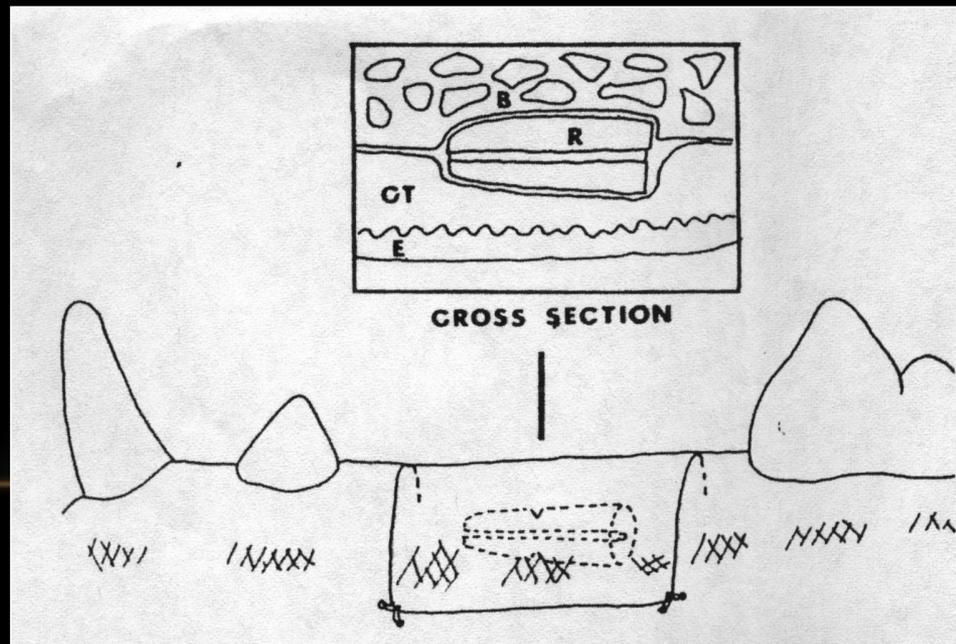
- Full thickness MW flaps
- The diseased parts of the root scaled and rootplaned
- Notches at the level of the marginal bone crest.
- Recipient site:
 - Full thickness flap
 - Horizontal grooves for roots to be implanted



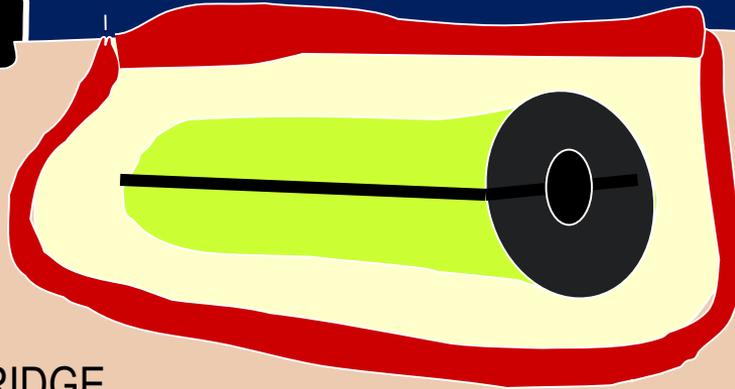
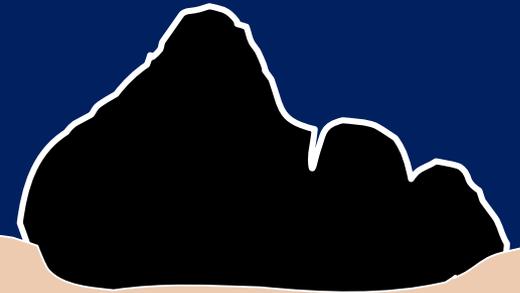
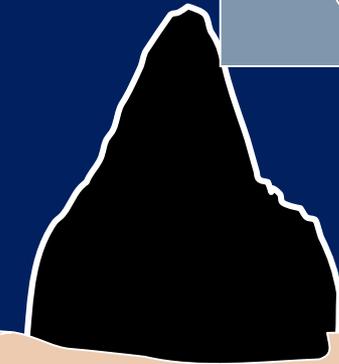
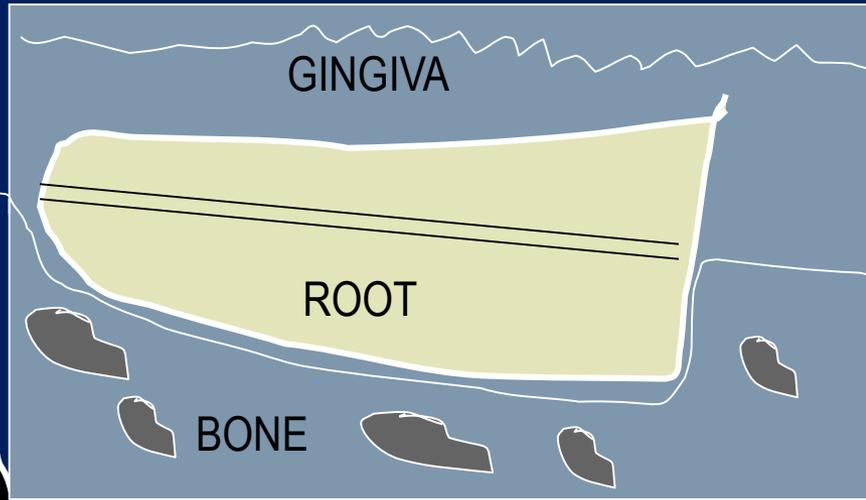
The roots of the experimental teeth were extracted and placed in an artificial socket in the alveolar bone.

The flaps were repositioned and sutured to completely cover the implanted root and the surrounding bone.

With this experimental design, the epithelium was prevented from migrating into the wound.



CROSS
SECTION

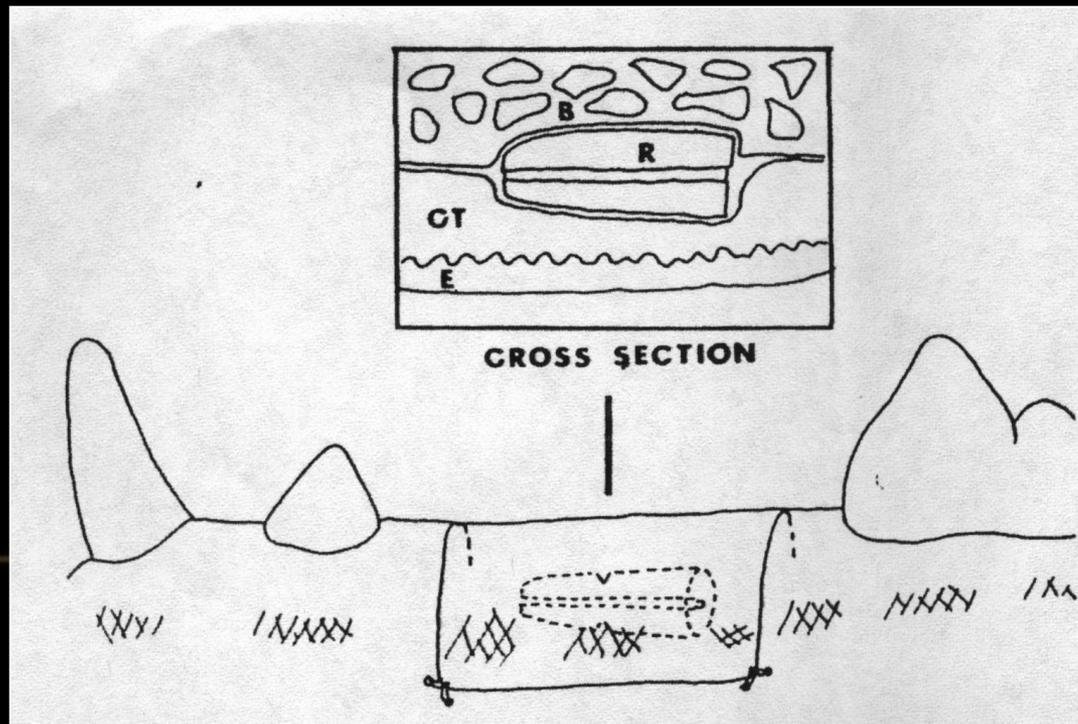


EDENTULOUS RIDGE

Nyman S, Karring T, Lindhe J, Planten S. Healing following implantation of periodontitis-affected roots into gingival connective tissue. *J Clin Periodontol* 1980;7:394-401.

Each implanted root was embedded to half its circumference into bone, and the remaining part was covered by the gingival connective tissue of the flap.

After 3 months of healing – histological examination



THE HISTOLOGICAL FINDINGS

- The diseased root faced the gingival connective tissue
- Collagen fibers parallel to the root surface.
- No de novo formation of root cementum
- Cementum resorption with multinucleated cells
- The diseased root facing the bone tissue
- Healing with extensive root resorption and ankylosis.

Granulation tissue derived from **gingival connective tissue** produced root resorption

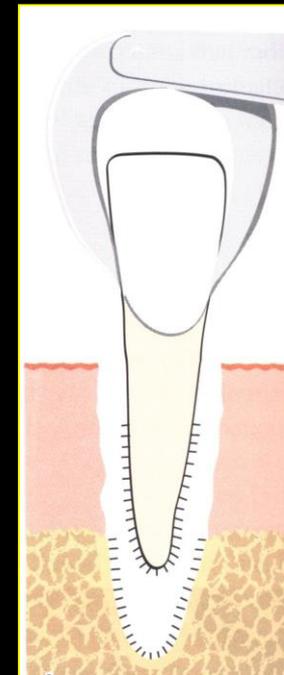
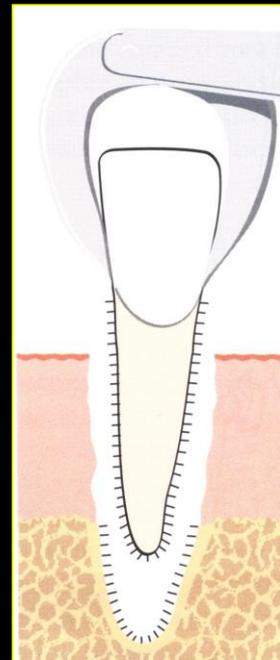
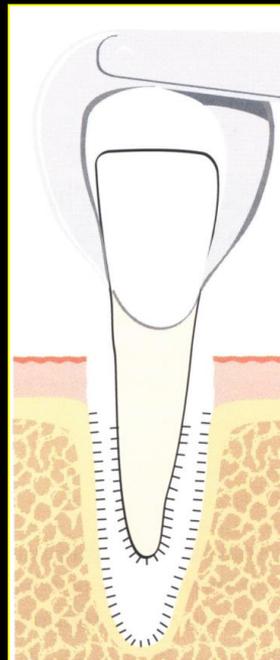
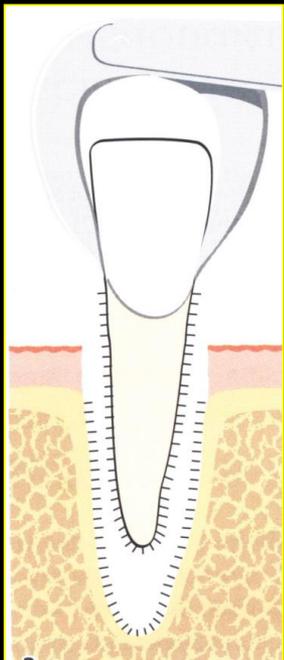
Granulation tissue derived from **bone** produced resorption and ankylosis.

This experiment revealed that granulation tissue originating from bone or gingival connective tissue lacks the ability to establish a new connective tissue attachment

Lindhe J, Nyman, S , Karring, T. Connective tissue attachment as related to presence or absence of alveolar bone. J Clin Periodontol 1984;11:33-40.

INCISORS WERE EXTRACTED AND LATER REIMPLANTED IN THEIR OWN SOCKET :

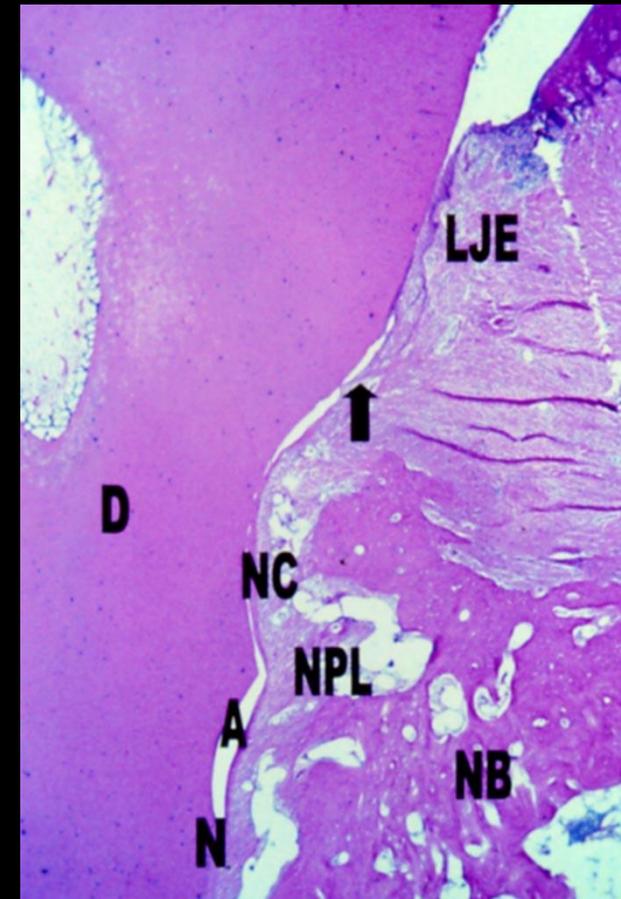
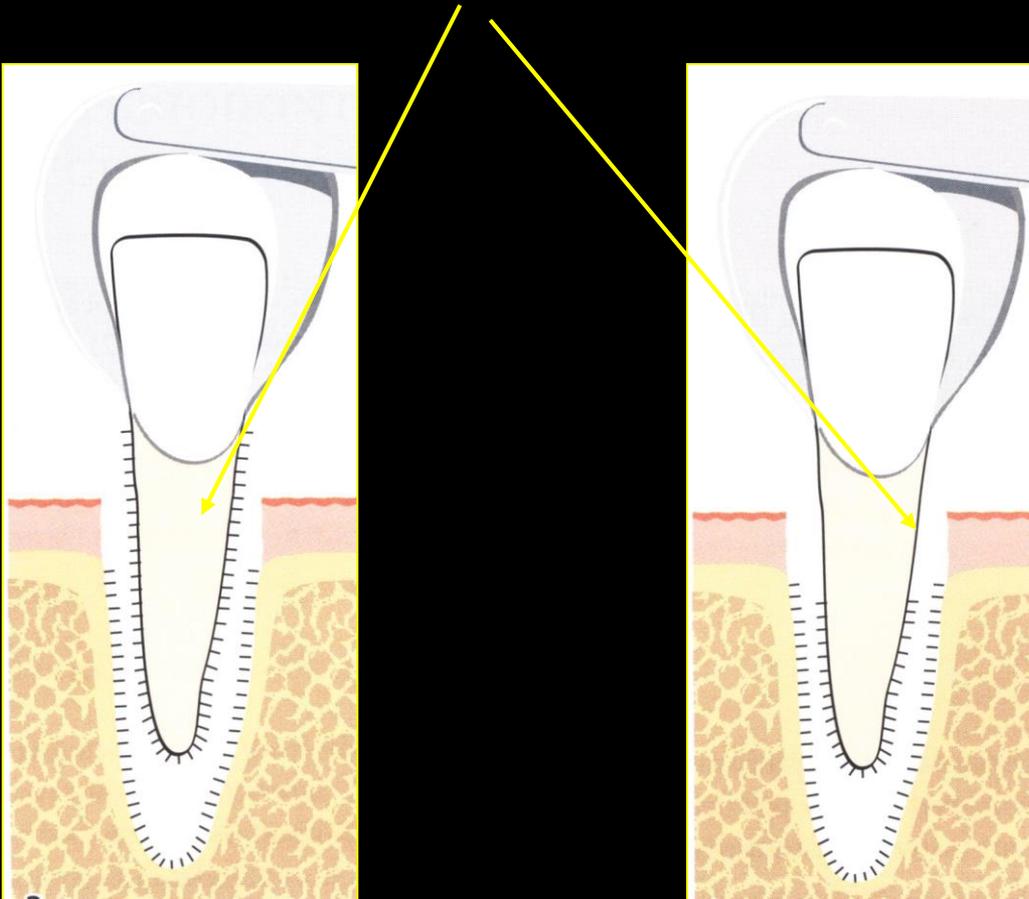
- Non- root planed teeth in sockets with normal bone height
- Root planed in the coronal third and reimplanted in sockets with normal bone height
- Non- root planed teeth in sockets with reduced bone height
- Root planed teeth reimplanted in sockets with reduced height



Histology after 6 months

fibrous reunion was established in areas where the original Sharpey fibers were preserved

In areas where the Sharpey fibers were destroyed only long epithelial attachment occurred



PERIODONTAL LIGAMENT CELLS

Monkey model

1. U shaped incision was made through the oral mucosa

2. A mucoperiosteal flap was raised on the coronal side of the incision to expose the buccal alveolar bone

3. Within the area 3 to 5mm buccal and approximal alveolar bone was resected and the root surface thoroughly planed to remove all cementum.

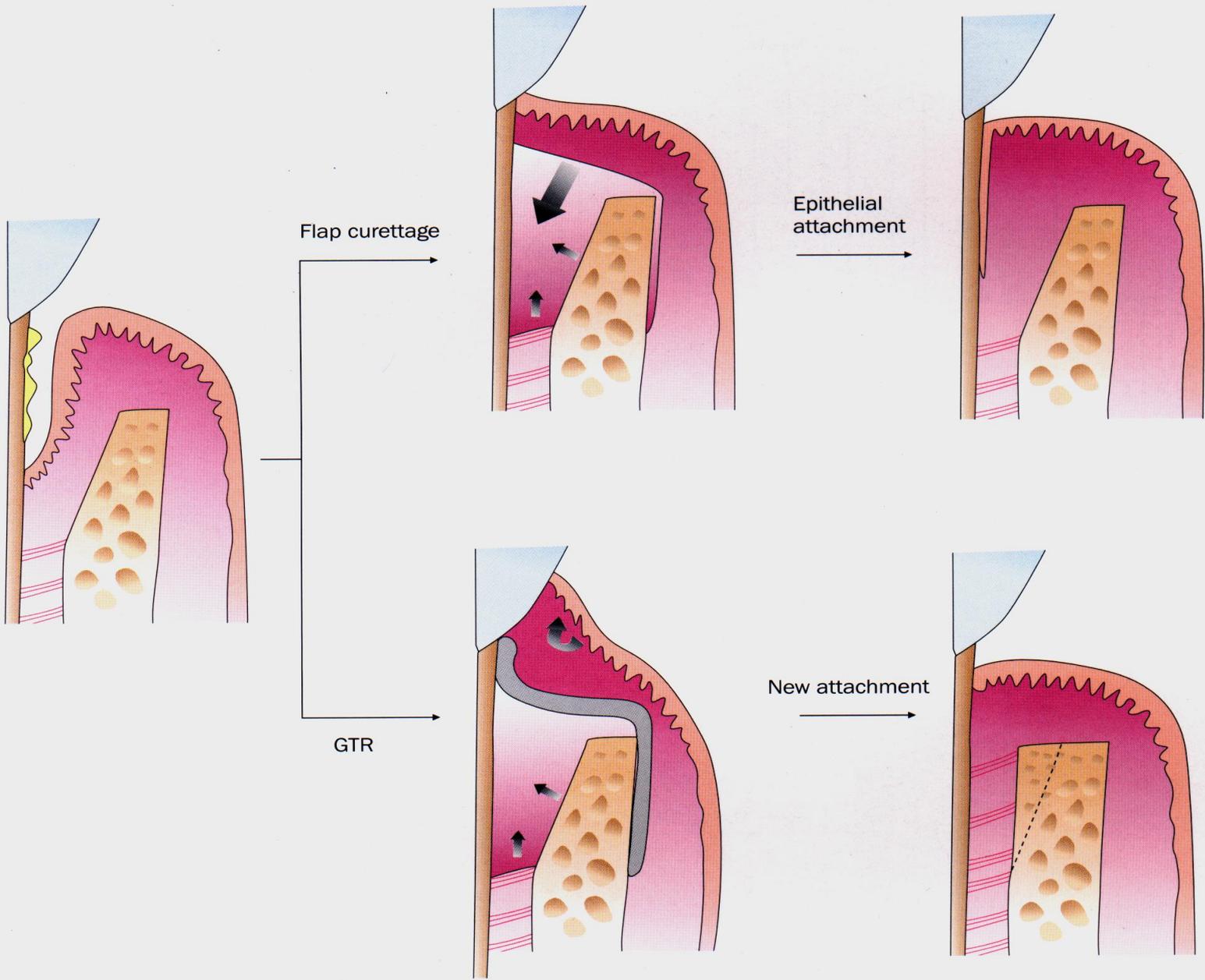
Gottlow, J., Nyman, S., Karring, T., Lindhe, J.
New attachment formation as the result of
controlled tissue regeneration.

J Clin Periodontol 1984; 11:494-503.



4. By preserving the most marginal portion of the periodontium, wound healing was allowed to occur without interference from an apically migrating dentogingival epithelium.
5. In order to prevent the gingival connective tissue from reaching contact with the root surface, a membrane was placed to cover the fenestration in the alveolar bone.
6. The flap was repositioned to the facial surface of the membrane and sutured.





The histological analysis of block sections representing 3 months of healing disclosed that:

New formation of attachment had occurred, including newly formed cementum with inserting collagen fibers and also supporting alveolar bone.

This finding demonstrates that periodontal ligament cells have a considerable potential for regeneration but only if the epithelium and the gingival connective tissue are prevented from occupying the wound area adjacent to the root.

In the study described, new attachment was obtained on the root surfaces, which were indeed previously deprived of their periodontal ligament and cementum but had not been exposed to plaque or to a periodontal pocket.

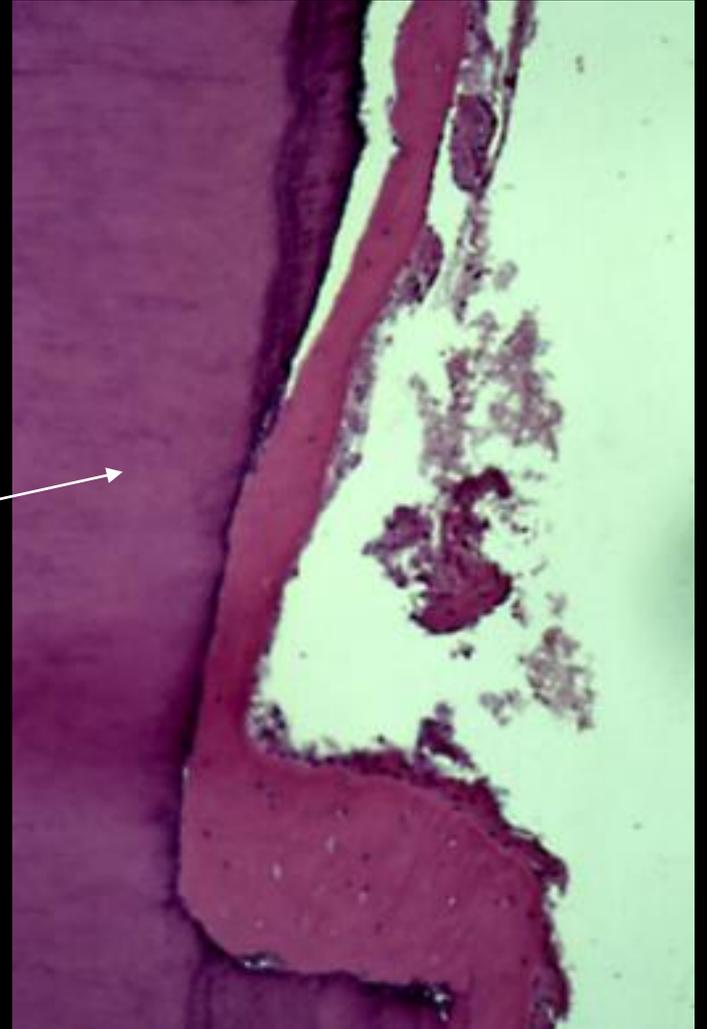
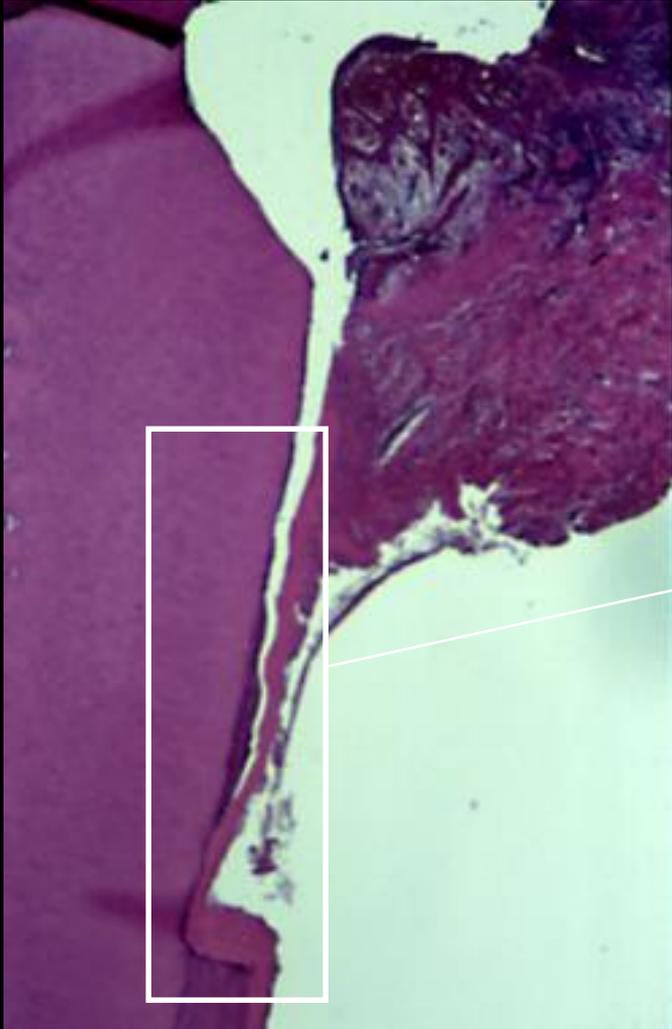
GUIDED TISSUE REGENERATION

GTR was developed based on a series of studies on periodontal wound healing performed in Scandinavia during the early 1980s by Nyman and coworkers.

The results of these studies, strongly suggested that the exclusion of epithelial and gingival connective tissue cells from the healing area by placing a physical barrier, between the periodontal defect and the gingival flap before suturing, may allow (guide) PDL cells to repopulate the detached root surface.

Their findings in animals were also histologically confirmed in humans.

NEW ATTACHMENT



SUMMARY

- The conventional non- surgical and surgical periodontal therapy result in not real periodontal regeneration
- The periodontal regeneration is a complex phenomenon followed by the reformation of new cementum, PDL and alveolar bone
- The condition of the remaining PDL and root cementum play critical role in the periodontal regenerative process

PERIODONTAL REGENERATION II.

Windisch Péter

2016

RELATED RESEARCH SUMMARY

- GTR TECHNIQUES HAVE BEEN USED AND STUDIED SINCE 1995 IN COOPERATION WITH PROF. SCULEAN AND HIS TEAM
- IN THE BEGINNING SHORT AND LONG TERM CLINICAL STUDIES WERE CONDUCTED WITH NON RESORBABLE AND RESORBABLE MEMBRANES
- LATER CLINICAL AND HISTOLOGICAL SHORT TERM STUDIES WERE DONE WITH NON RESORBABLE AND RESORBABLE MEMBRANES
- IN 1999 WE STARTED STUDYING THE HUMAN HISTOLOGY OF PERIODONTAL WOUND HEALING AFTER EMD THERAPY
- LATER GTR, EMD AND VARIOUS BONE SUBSTITUTES WERE USED IN COMBINATIONS - STUDIED CLINICALLY AND HISTOLOGICALLY
- IN THE PAST THREE YEARS THE EFFECTS OF PRP COMBINED WITH OTHER GTR TECHNIQUES ON PERIODONTAL WOUND HEALING WAS STUDIED .

CONCEPTUAL DEVELOPMENT

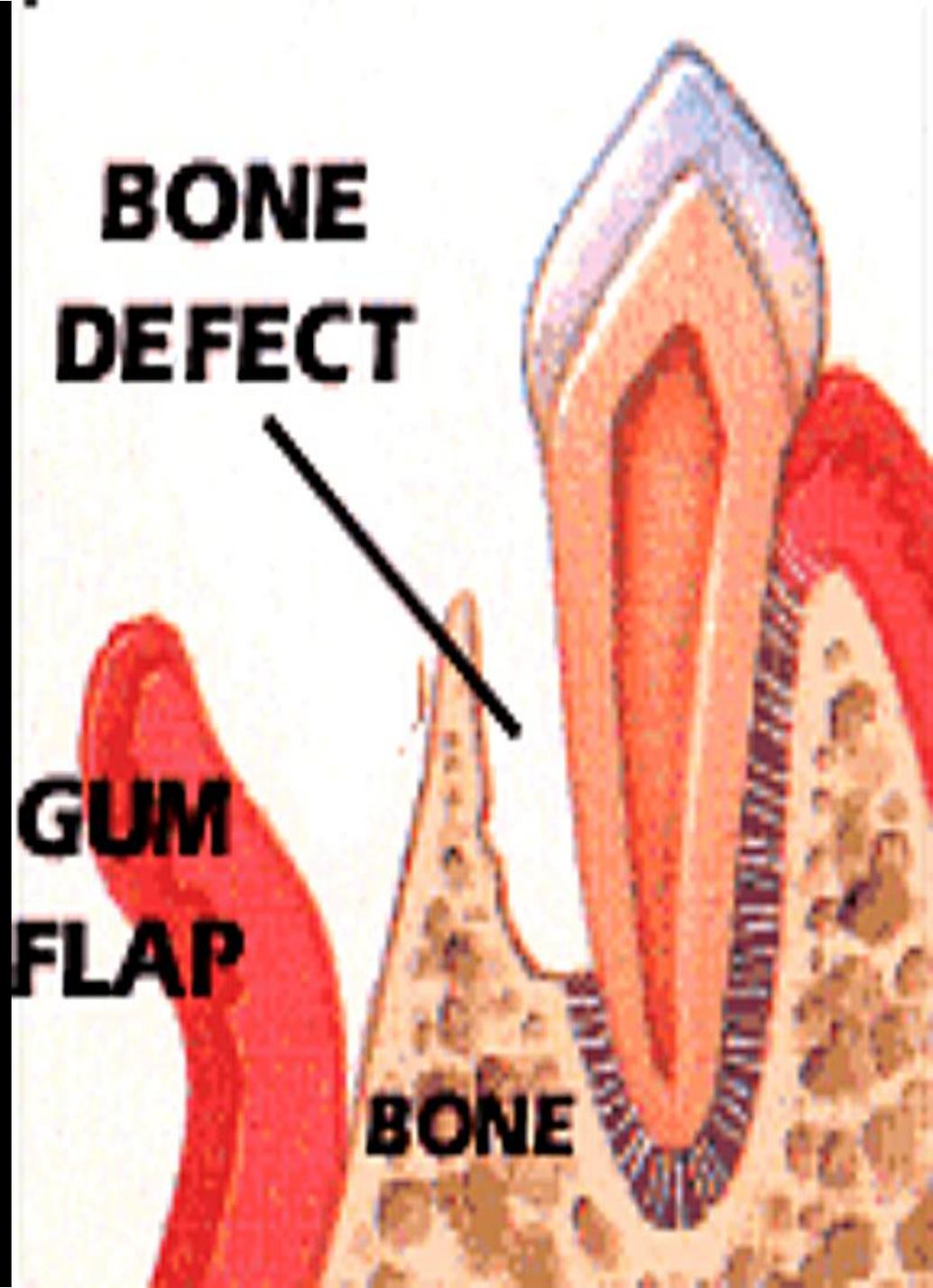
- **GTR**
- EMD
- GTR vs. EMD
- New treatment modalities using EMD
- EMD + bone substitutes
- GTR + bone substitutes
- Histological assessment of the regenerated periodontium
- Further therapeutic possibilities

GUIDED TISSUE REGENERATION

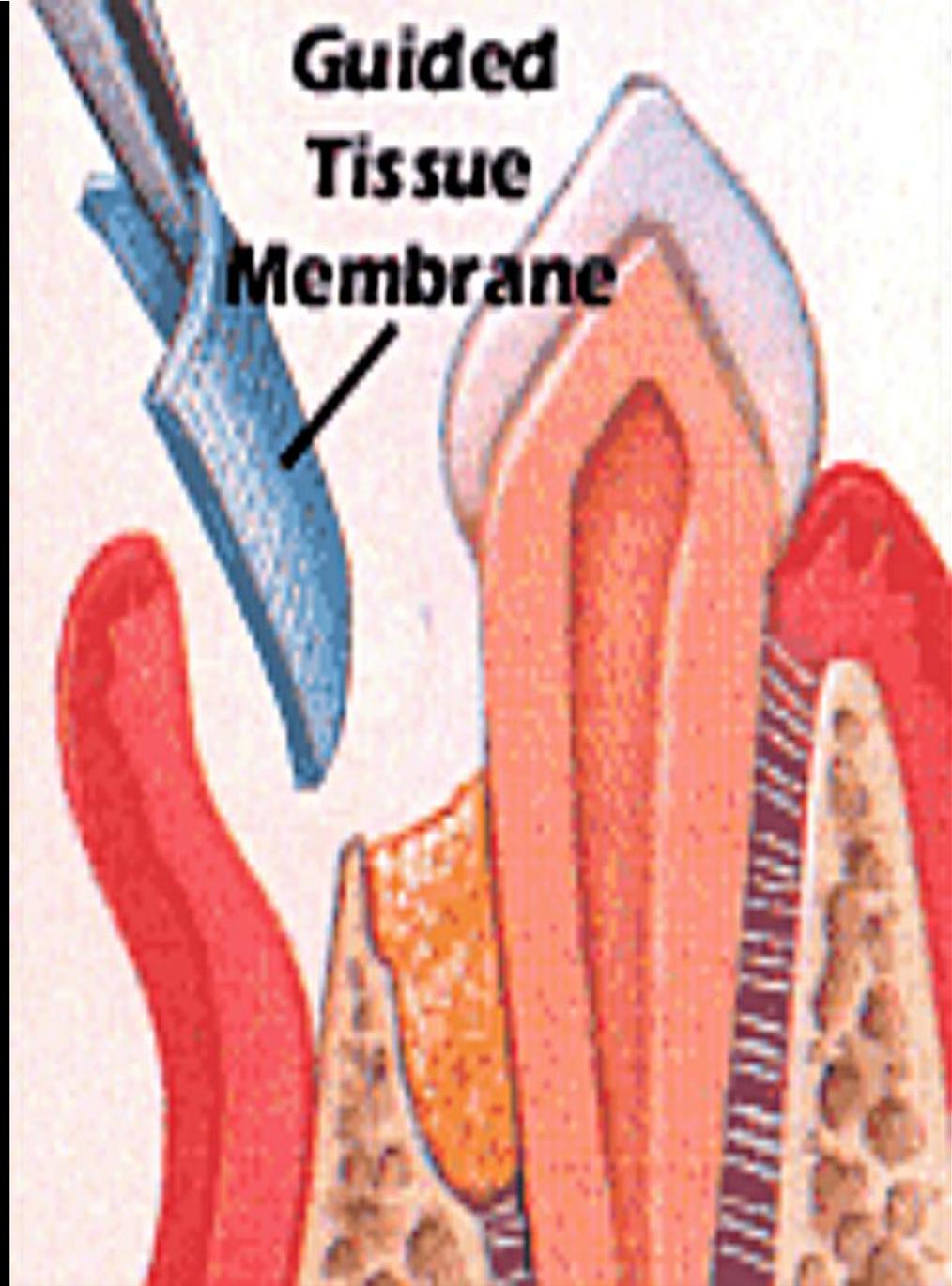
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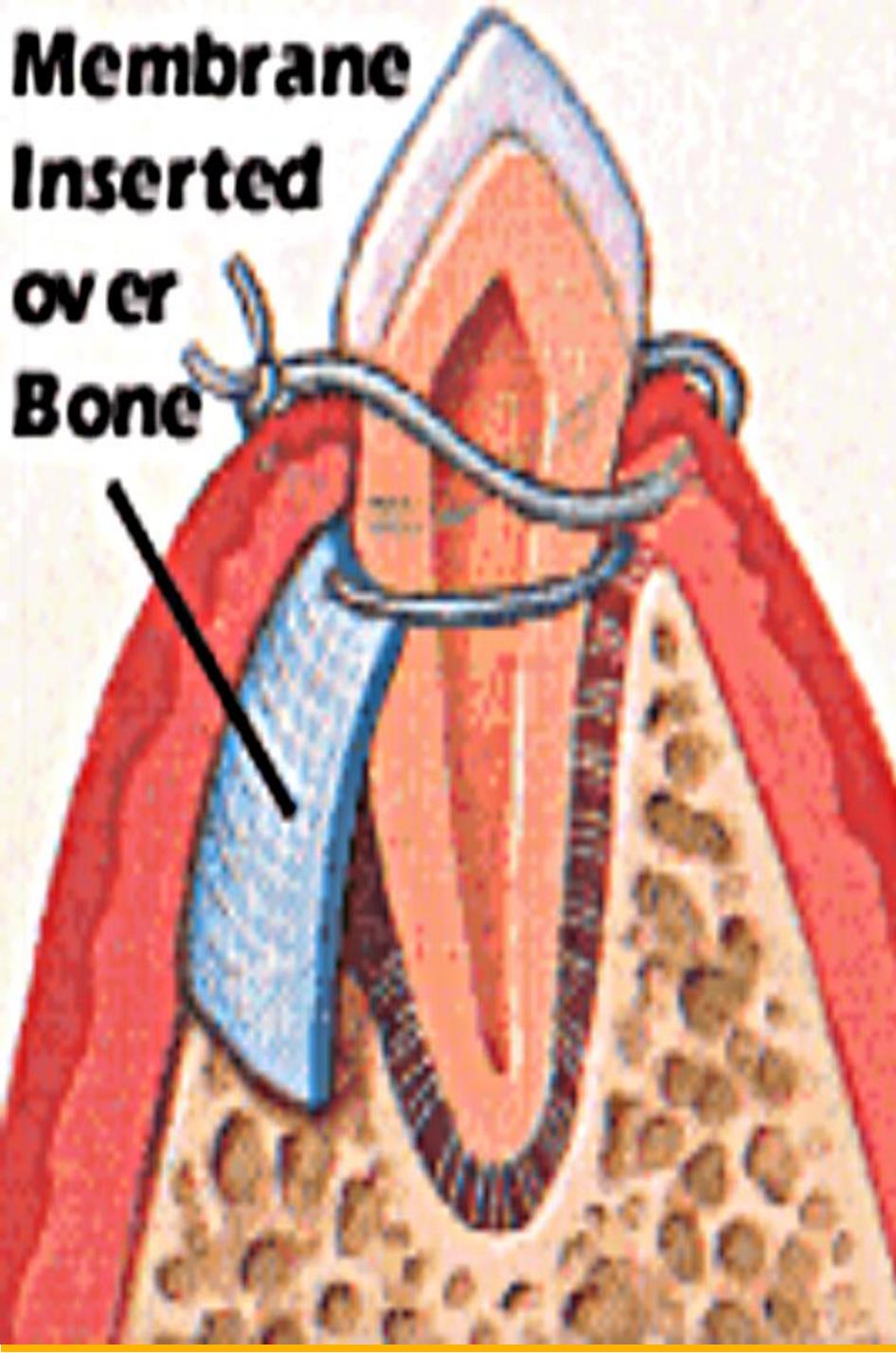
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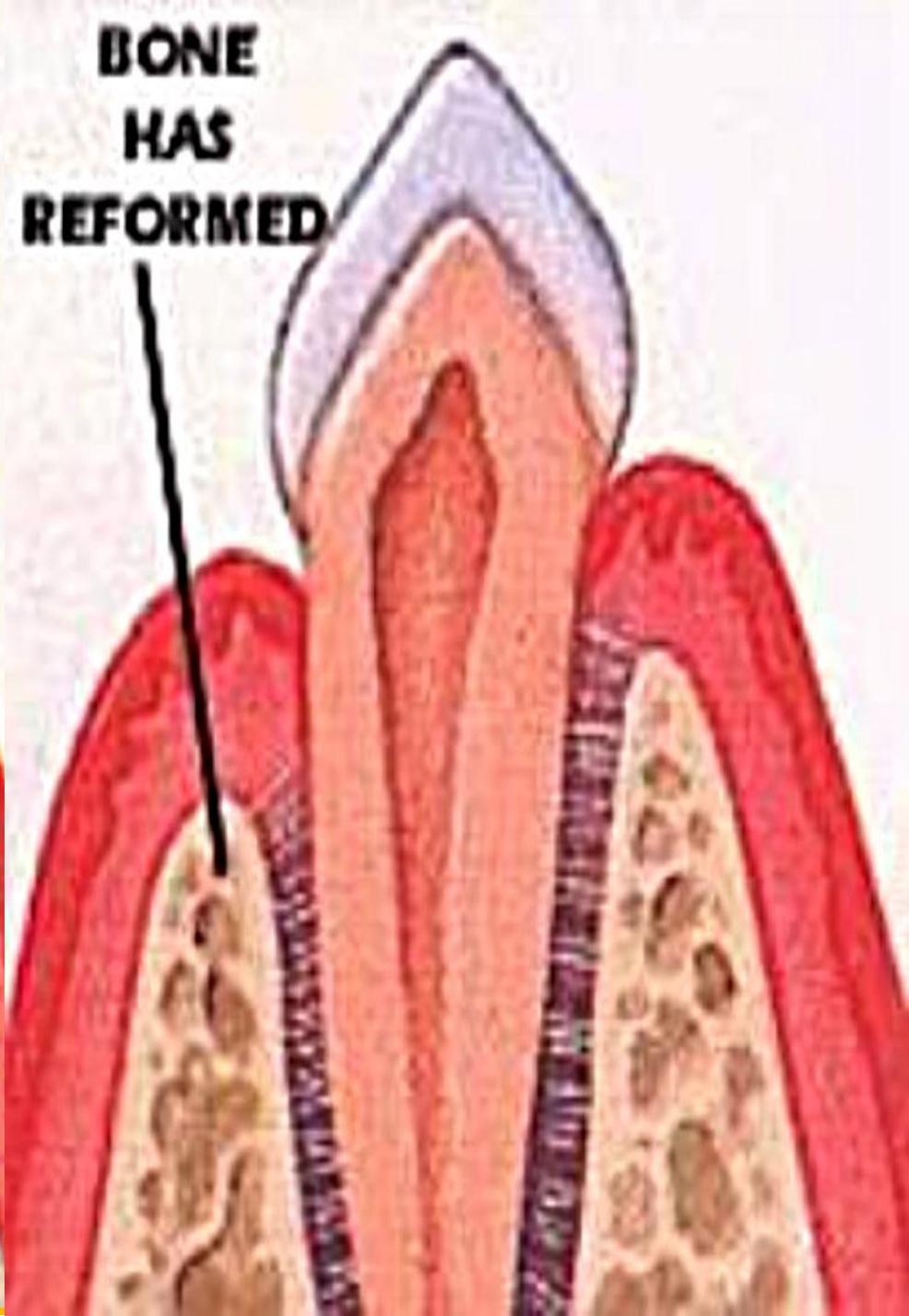
**Guided
Tissue
Membrane**



**Membrane
Inserted
over
Bone**



**BONE
HAS
REFORMED**



GTR MEMBRANES

- Synthetic, non-resorbable
 - Synthetic, resorbable
 - Natural, biologically resorbable
-

GTR

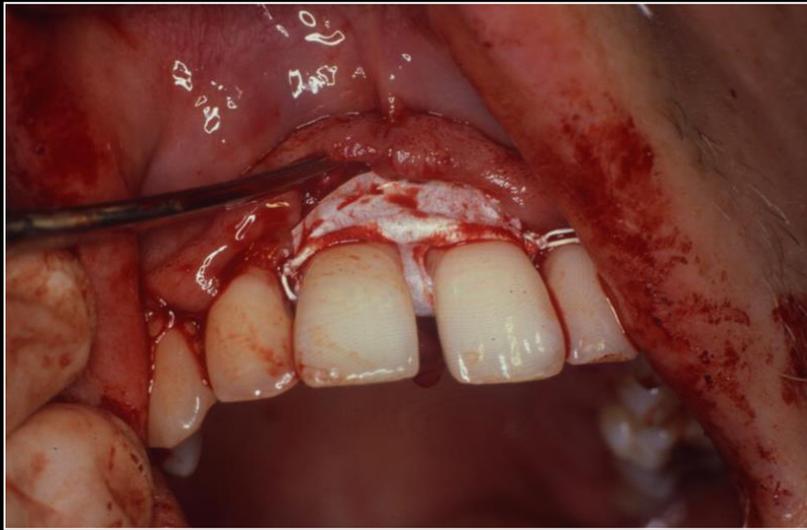
Nonresorbable vs. resorbable membranes

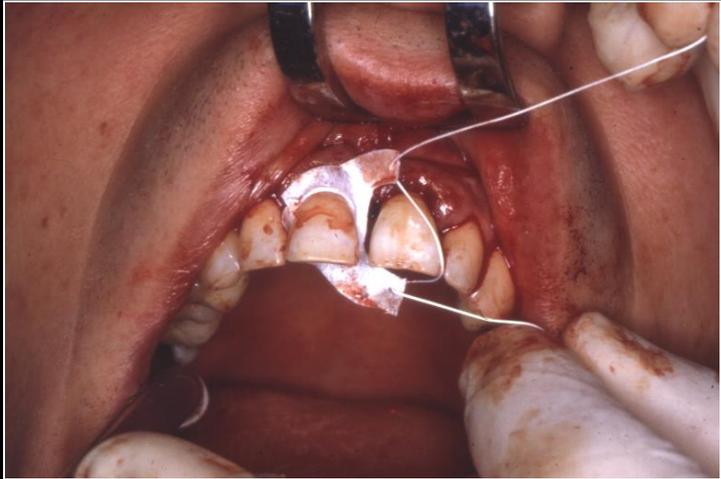
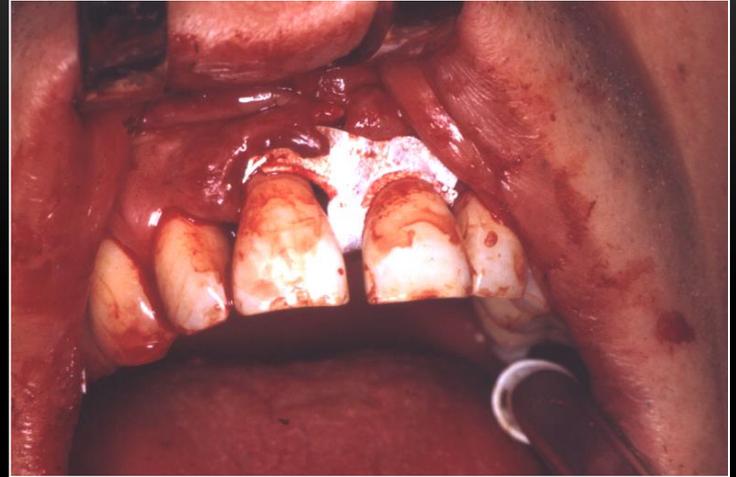
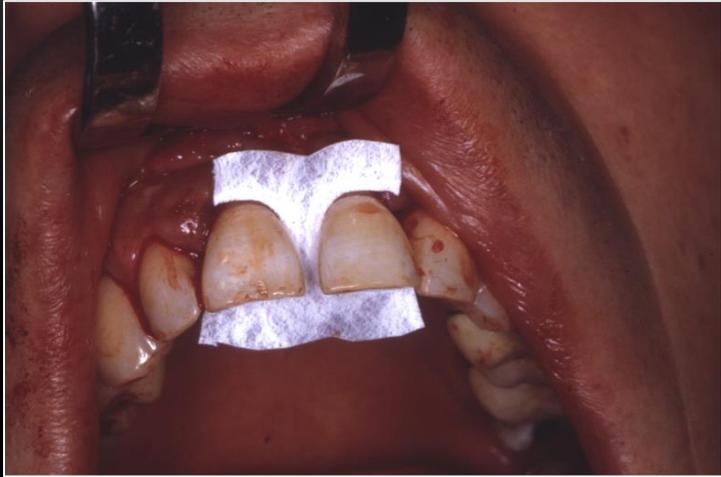
Materials and methods: three years follow-up clinical study

Three groups including 20 patients each: Gore Resolut, titanium-reinforced Gore-Tex membrane and Gore-Tex membrane

Results: No significant differences in changes of PPD, GR and CAL between groups at year one and three

Conclusion: no benefit of non-resorbable membranes

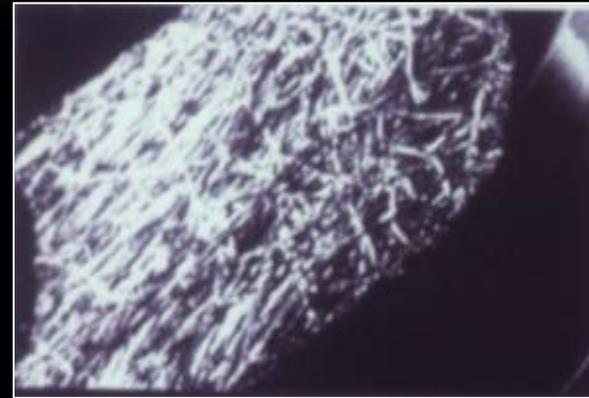






RESORBABLE MEMBRANES I

The surface of the resolut membrane:

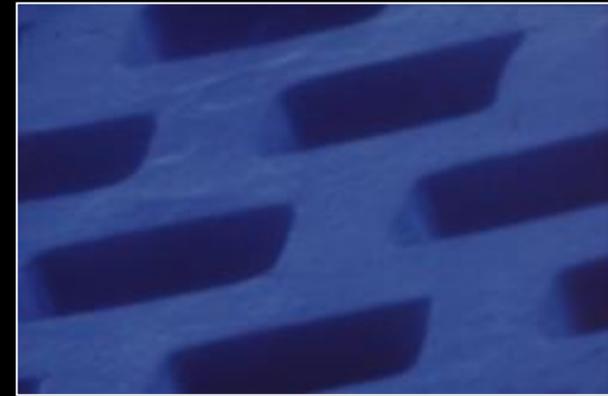
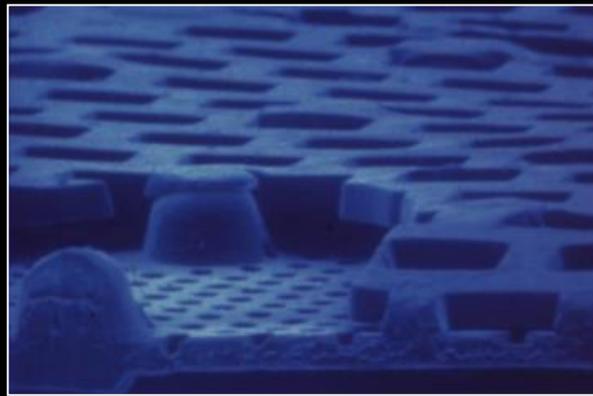
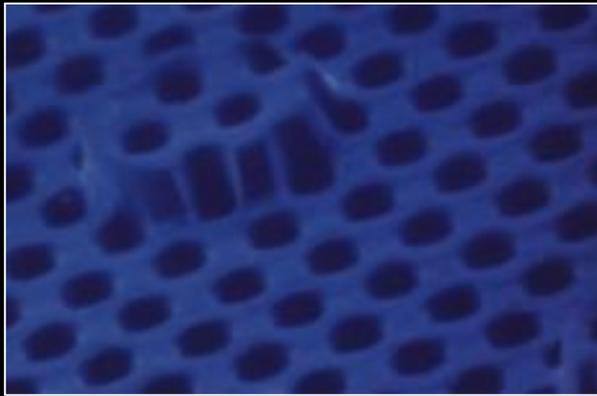


Advantages of resorbable membranes:

- Second surgery is unnecessary
- Surface character is able to achieve not only the connective tissue integration, but
- favourable contact with the epithel cell layer

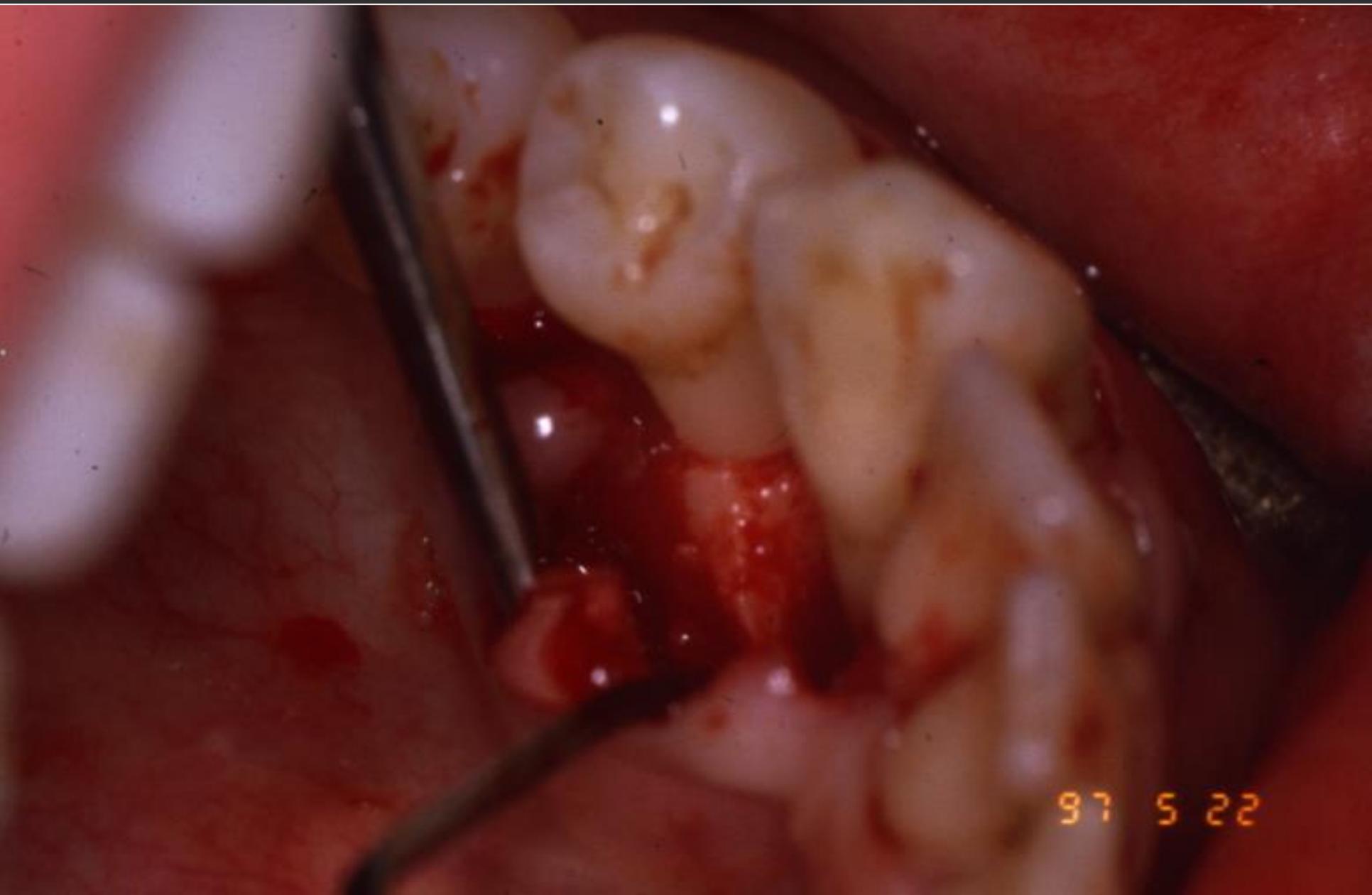
RESORBABLE MEMBRANES II

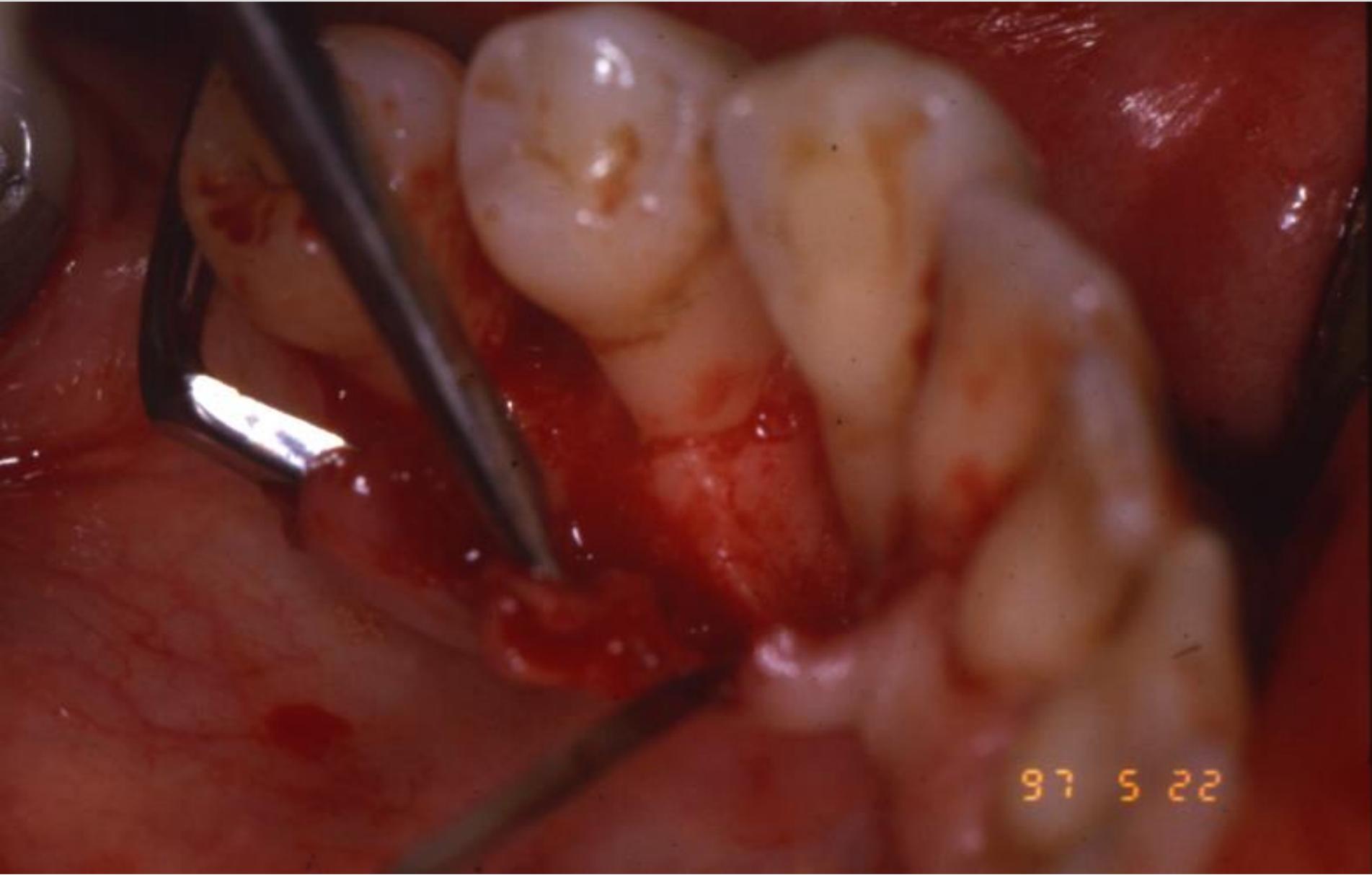
The surface of the Guidor membrane:



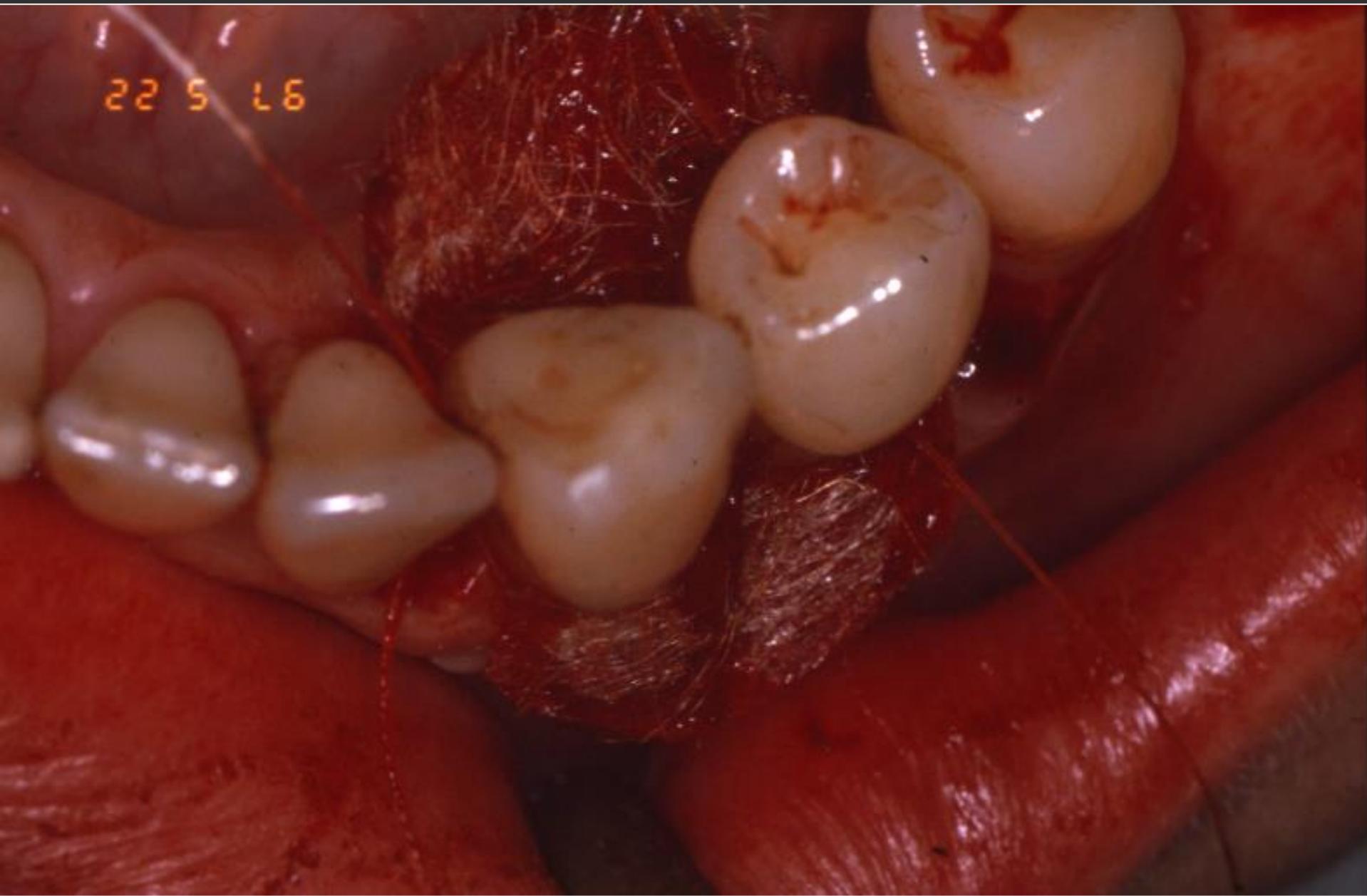


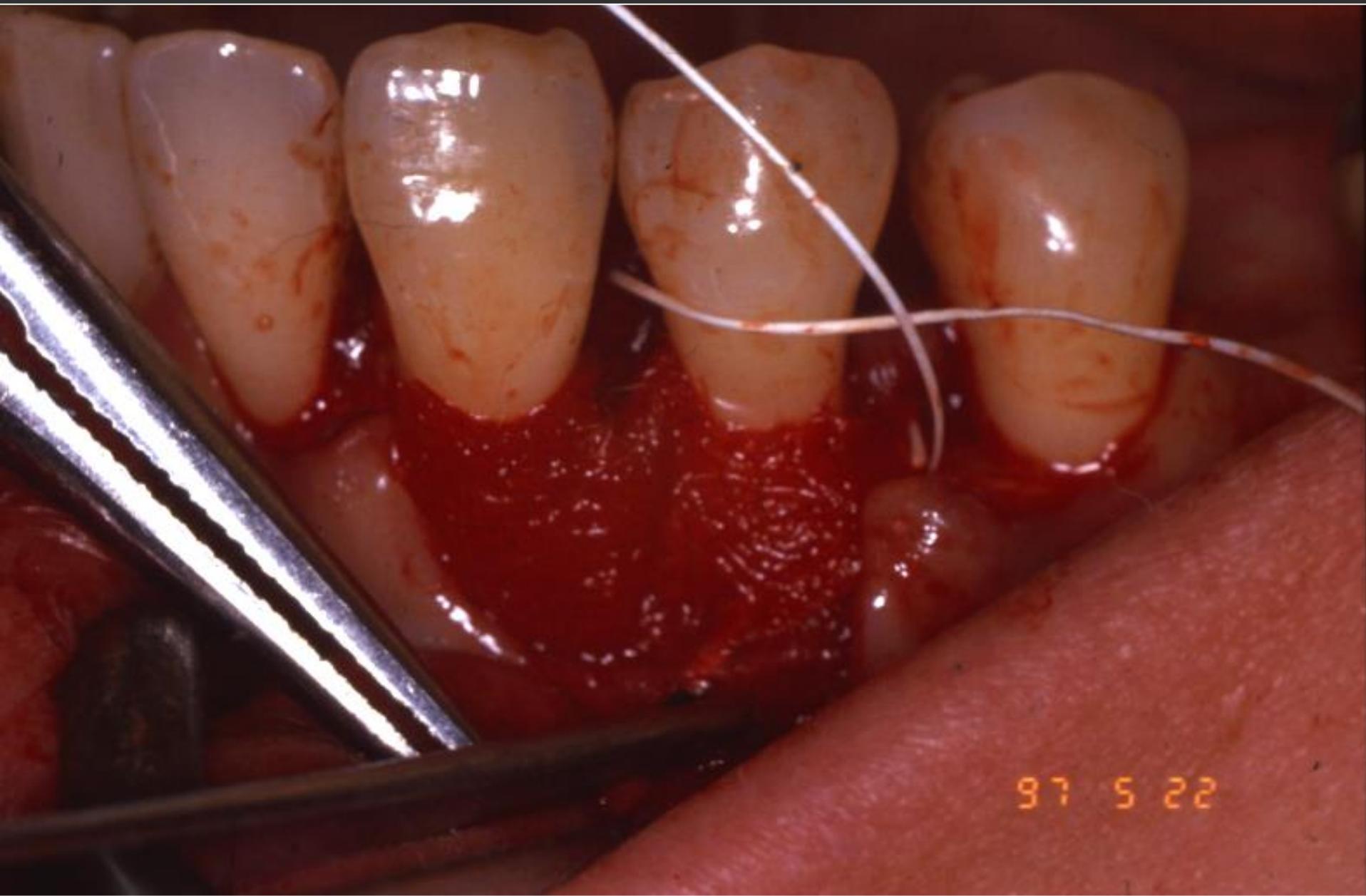
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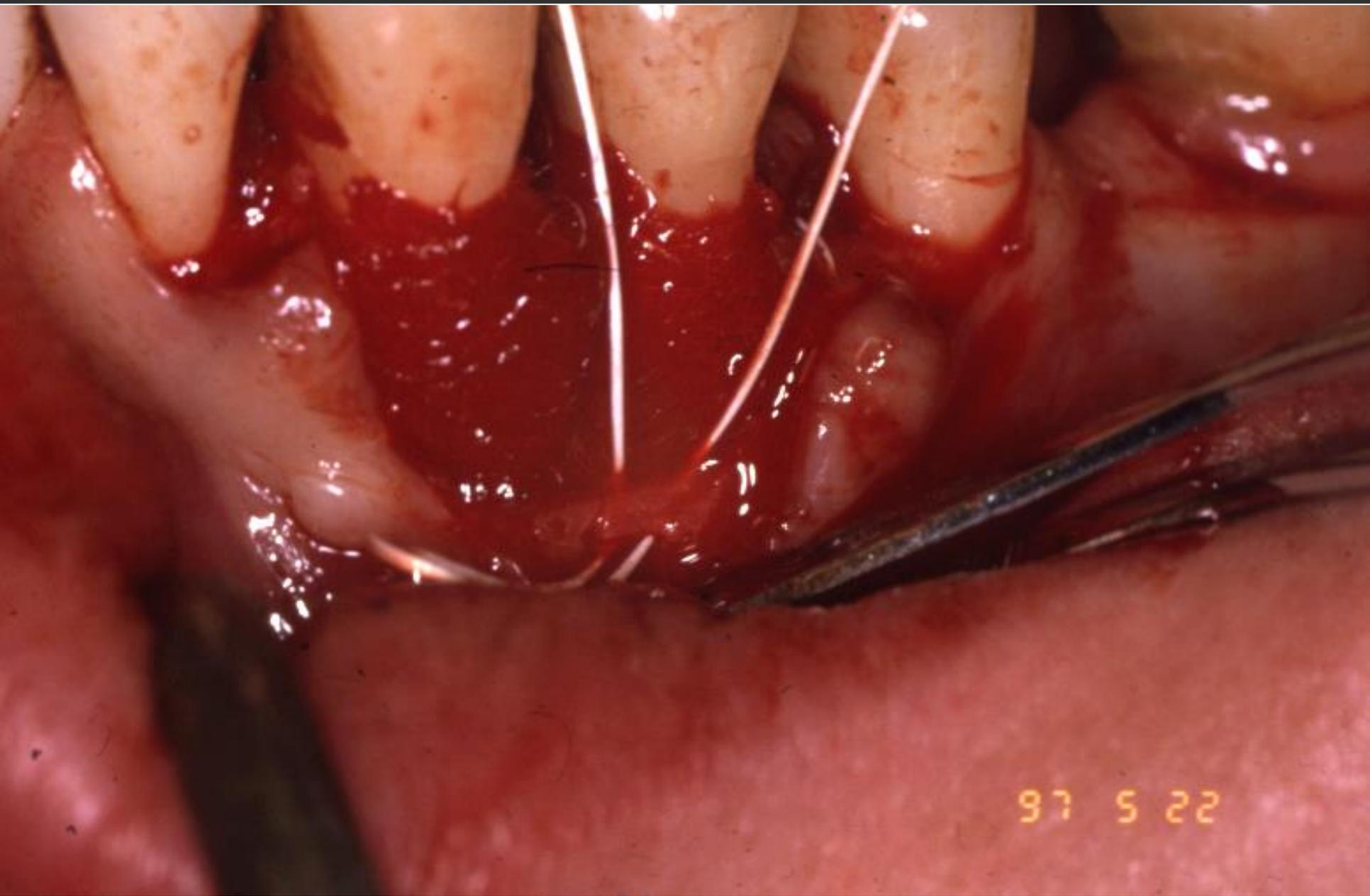




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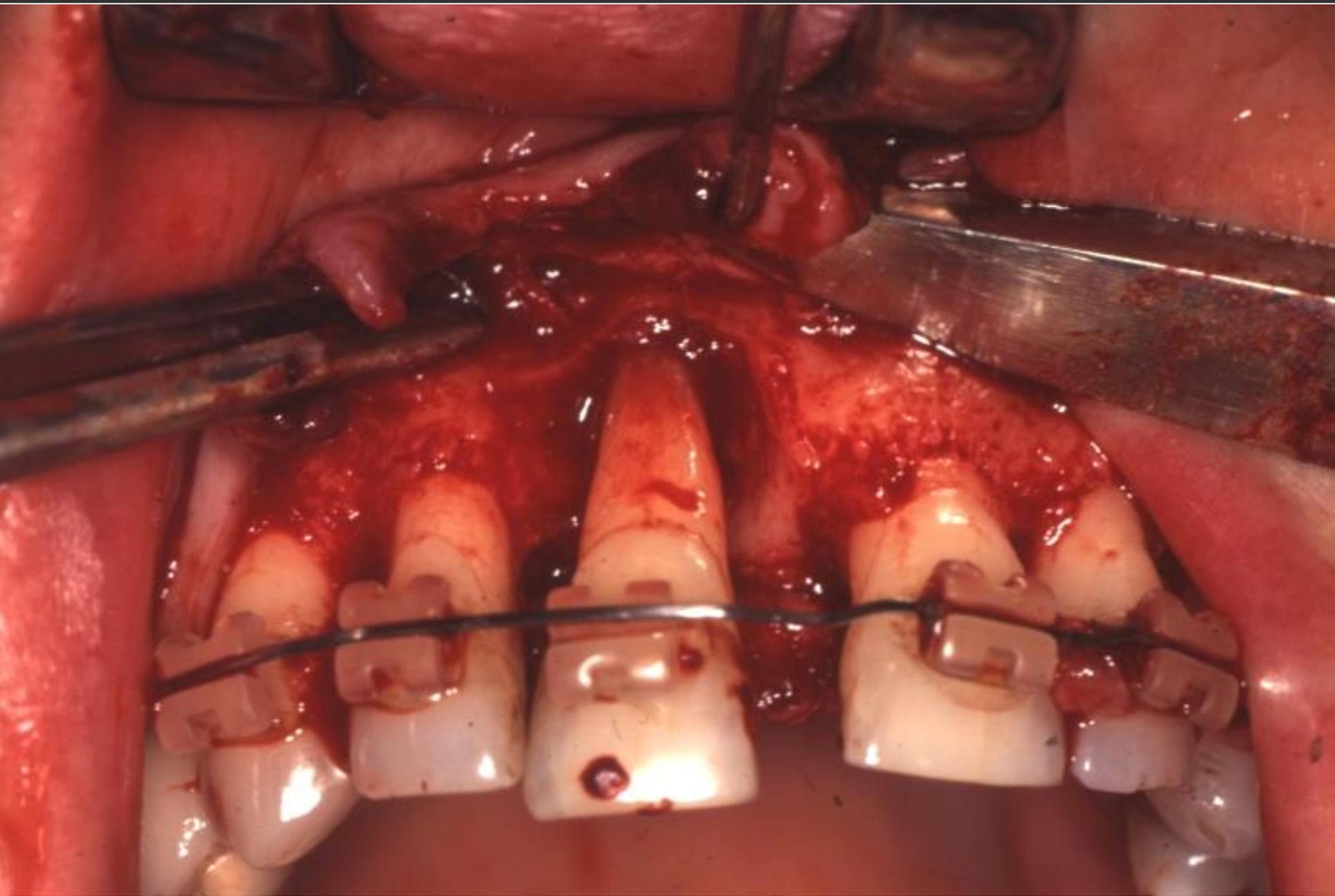
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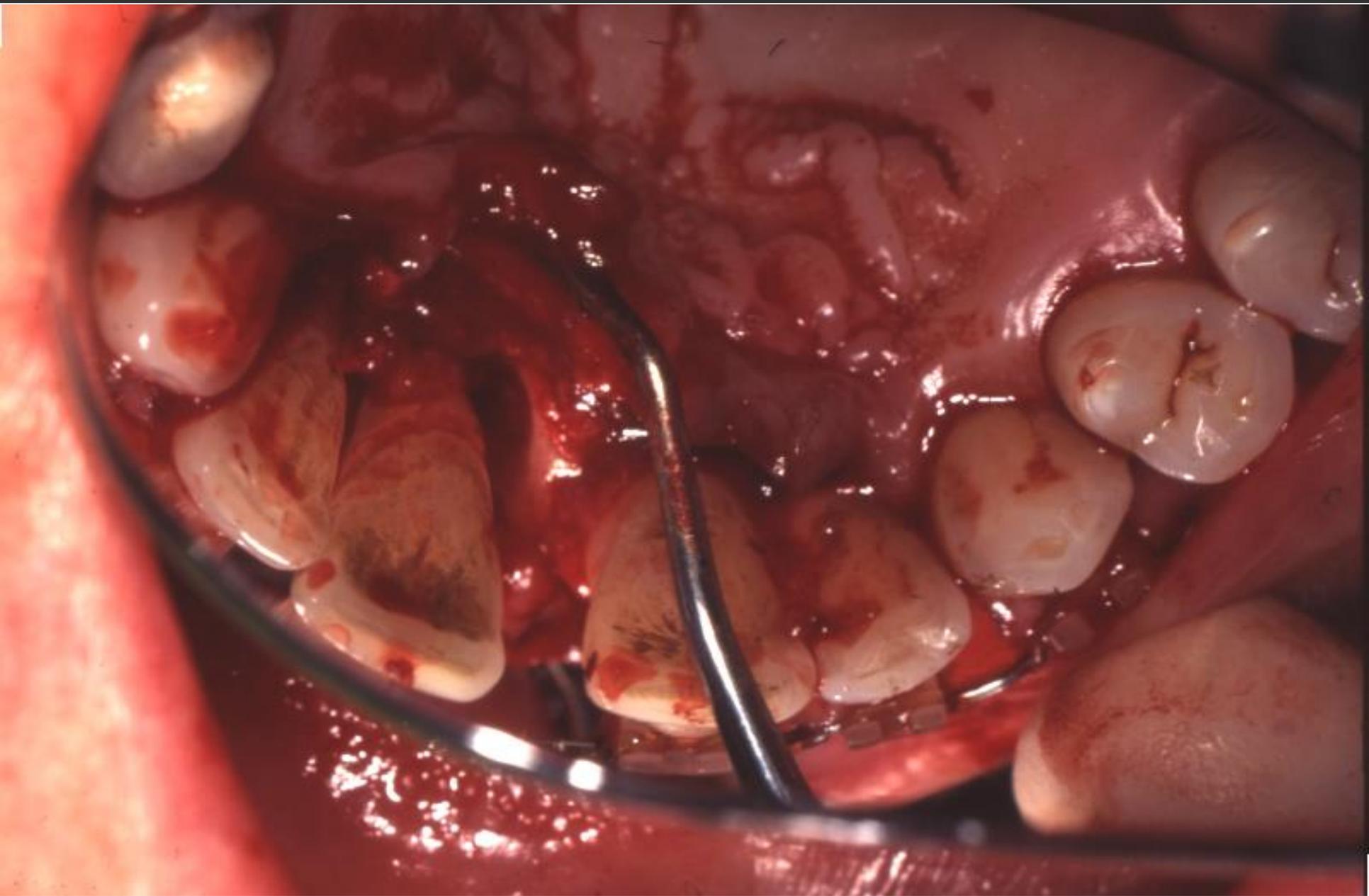




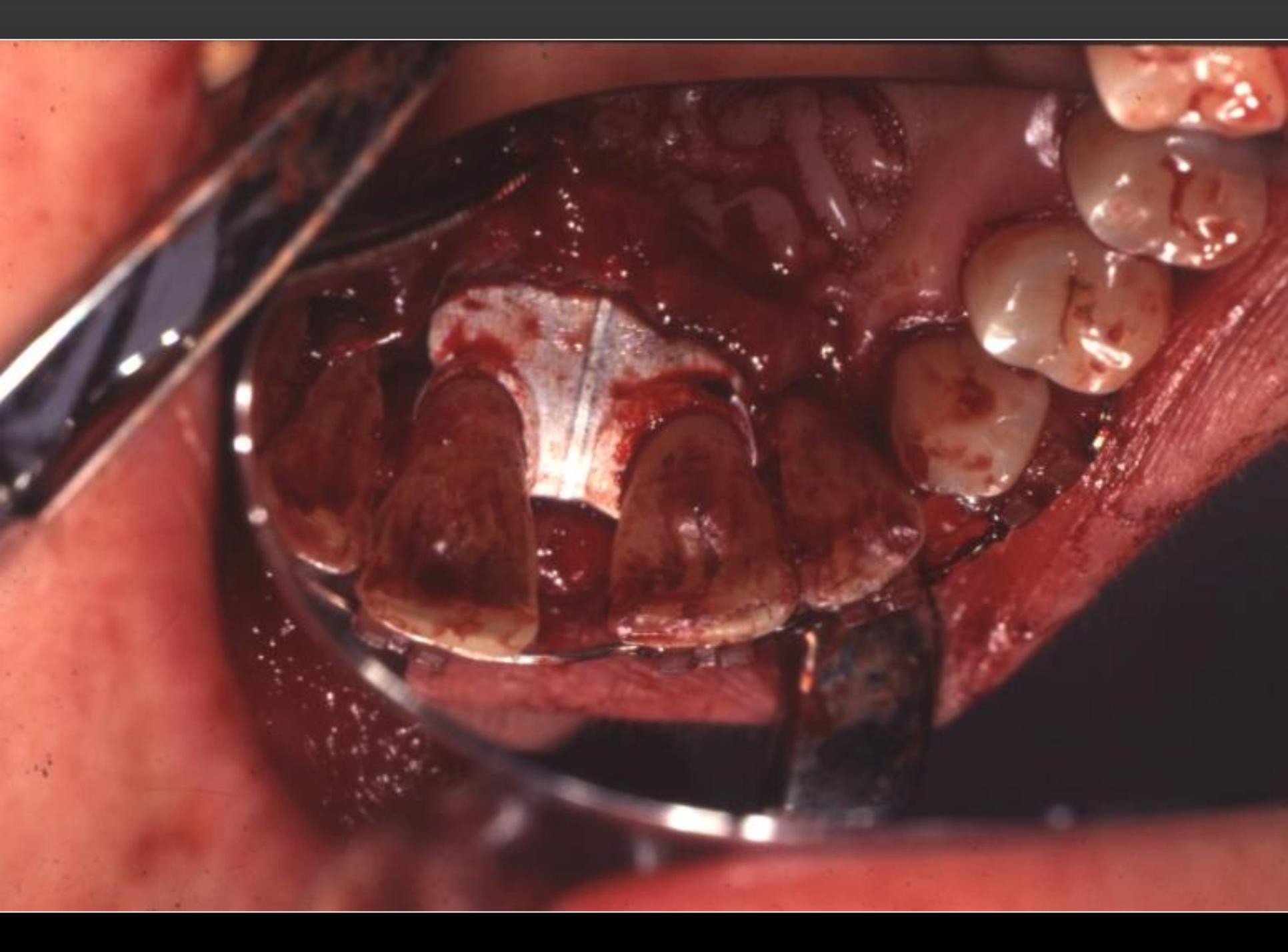
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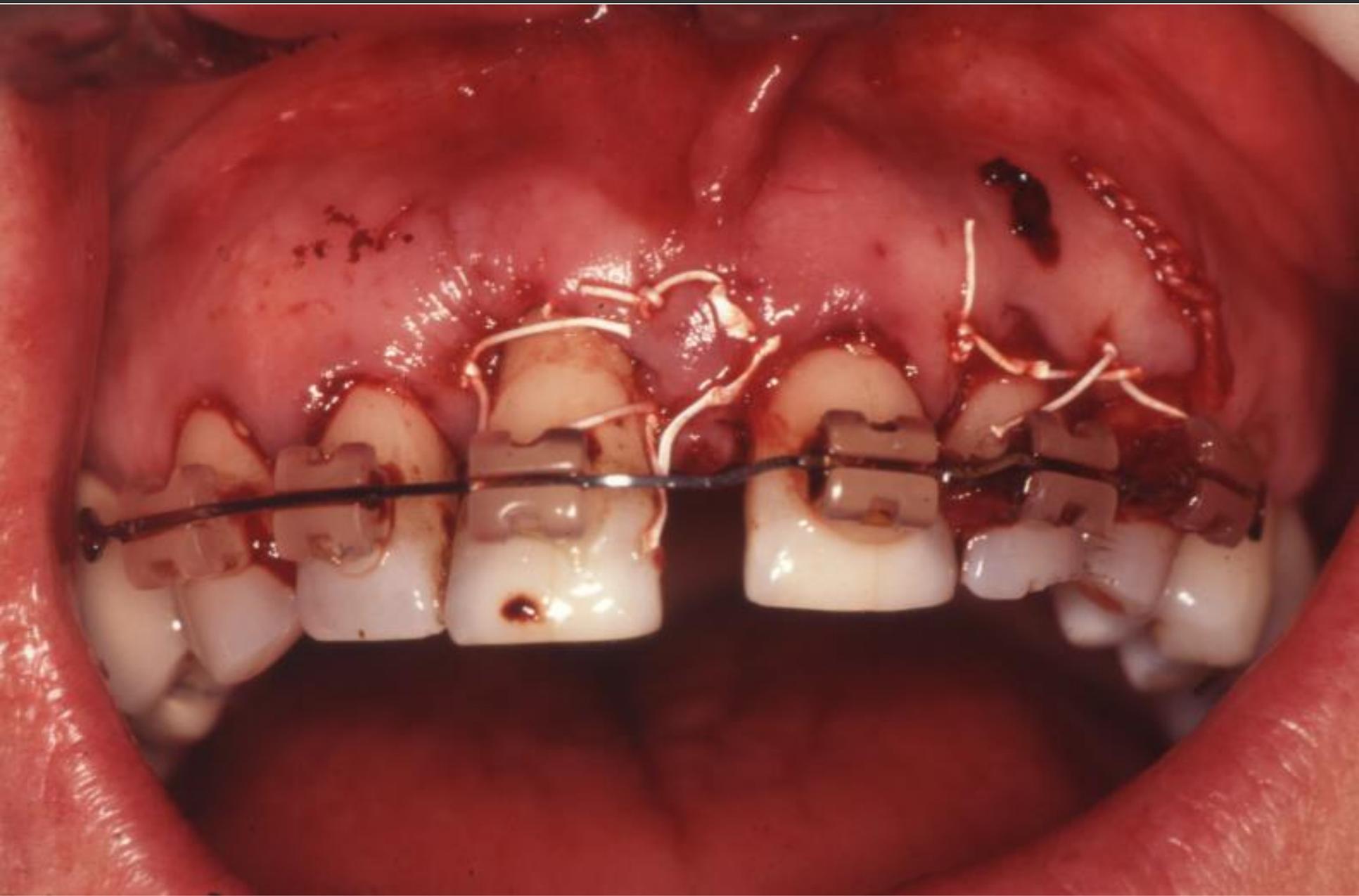


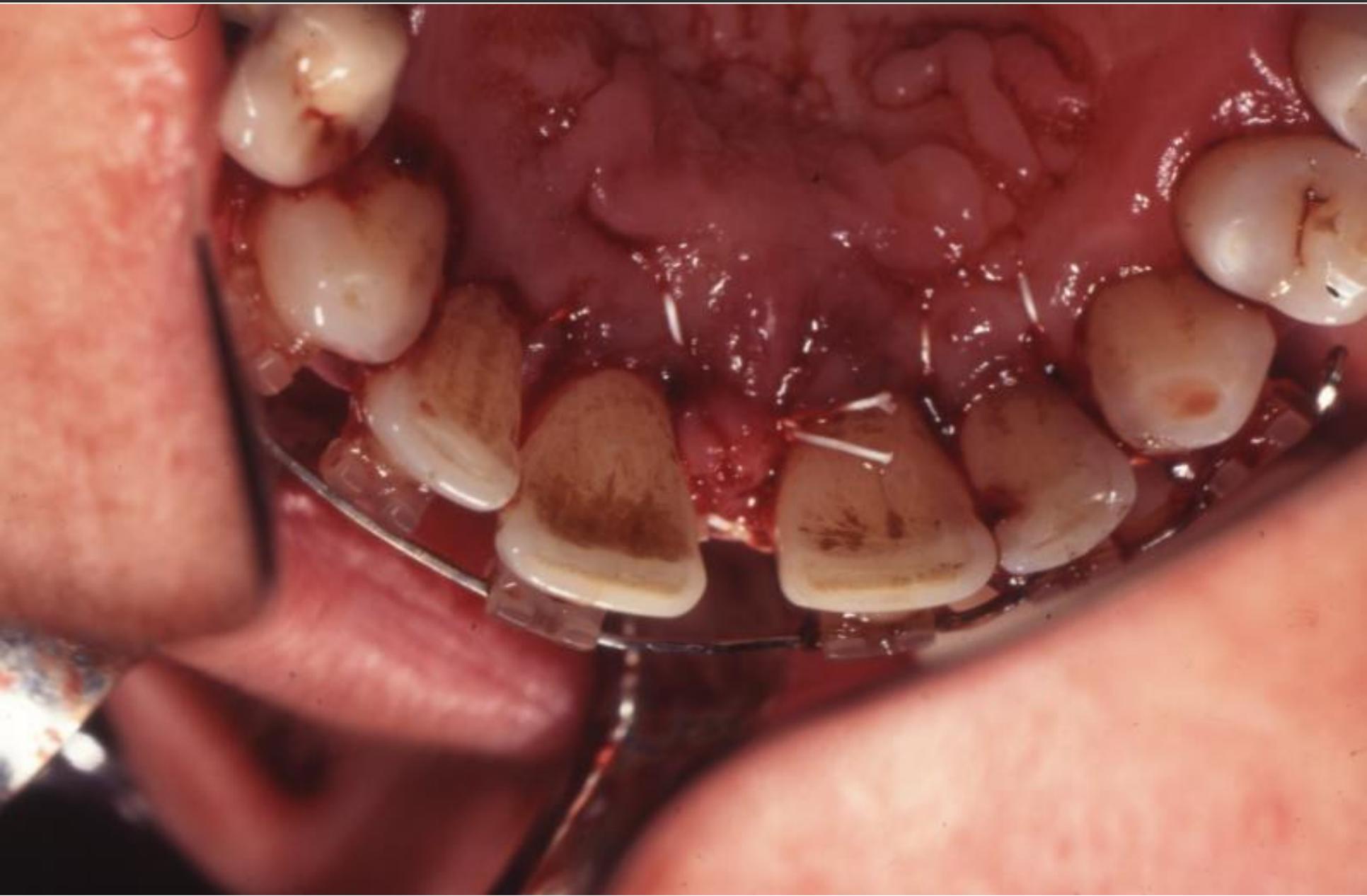


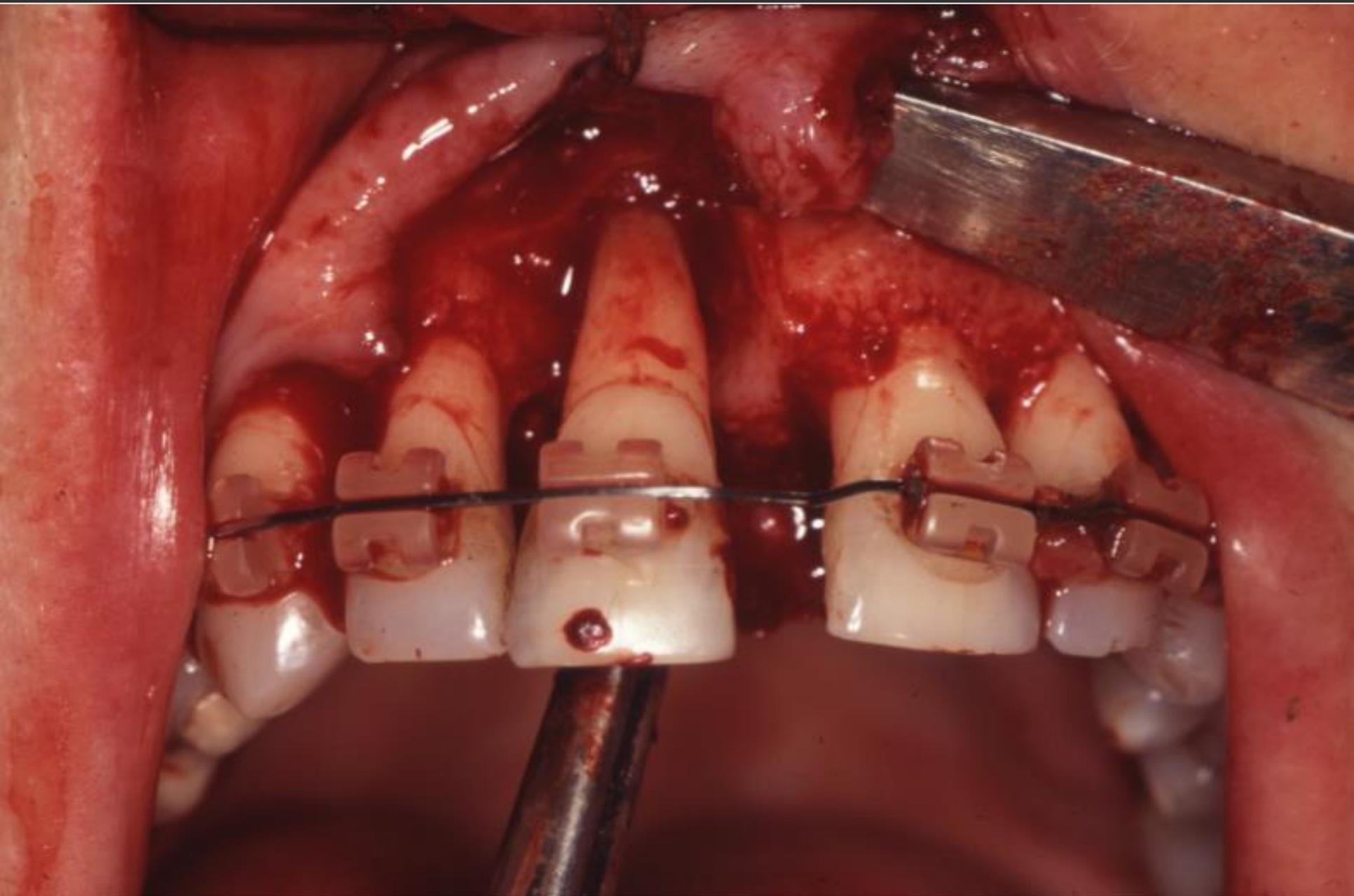


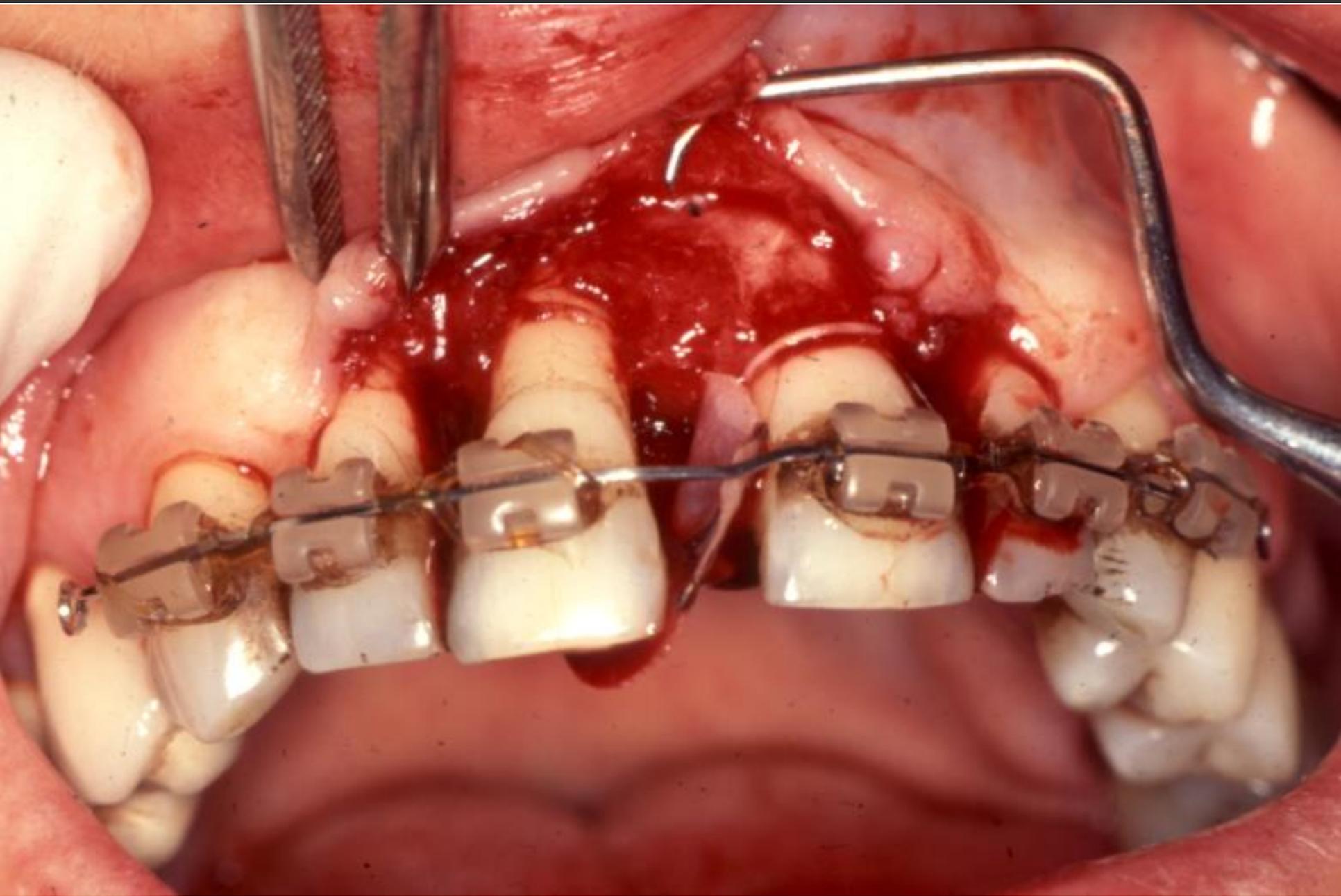














96 7 9





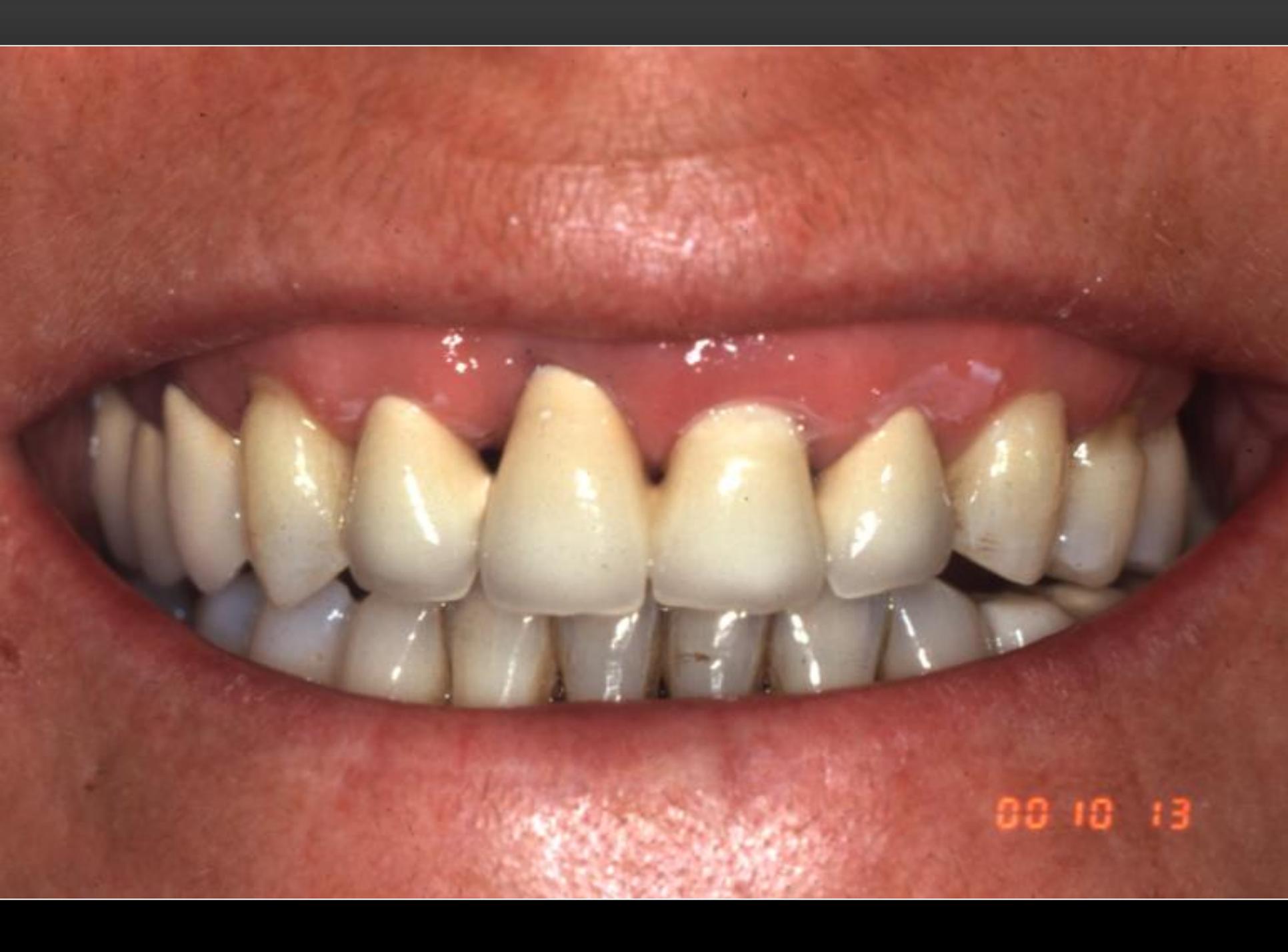


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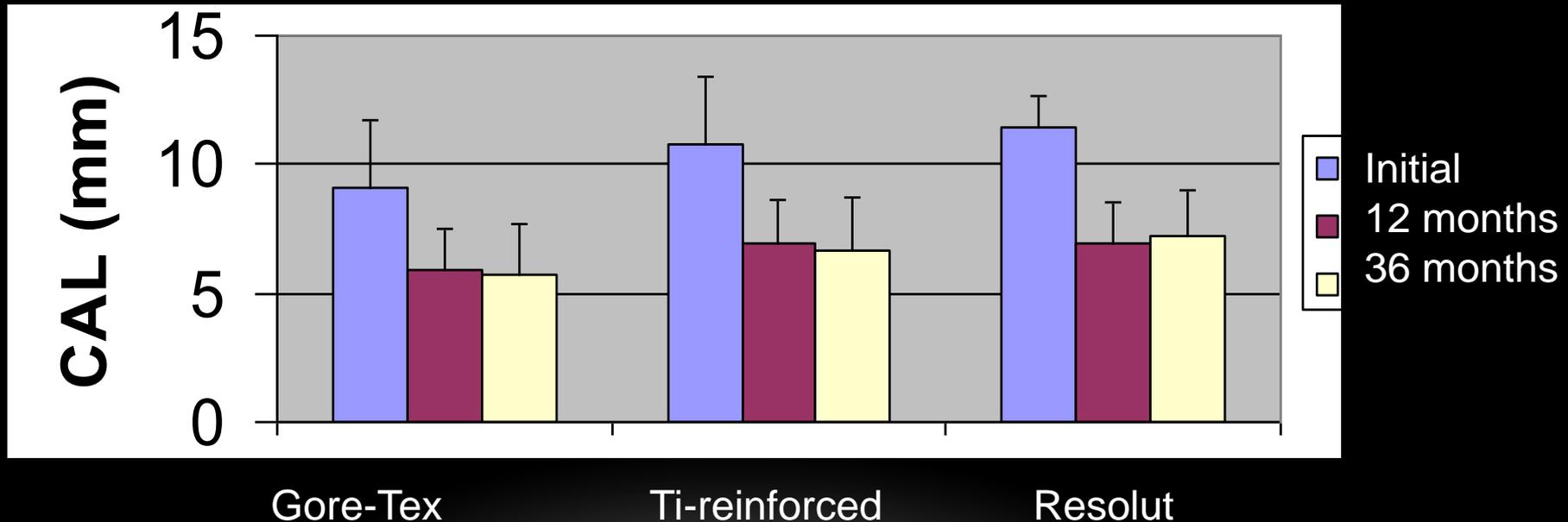




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GTR

Changes in clinical attachment levels



GTR

Resorbable membranes

Materials and methods: two years follow-up clinical study

52 intrabony defects with 1, 2 or 3 walls treated with Resolut membranes, two additional histological samples

Results:

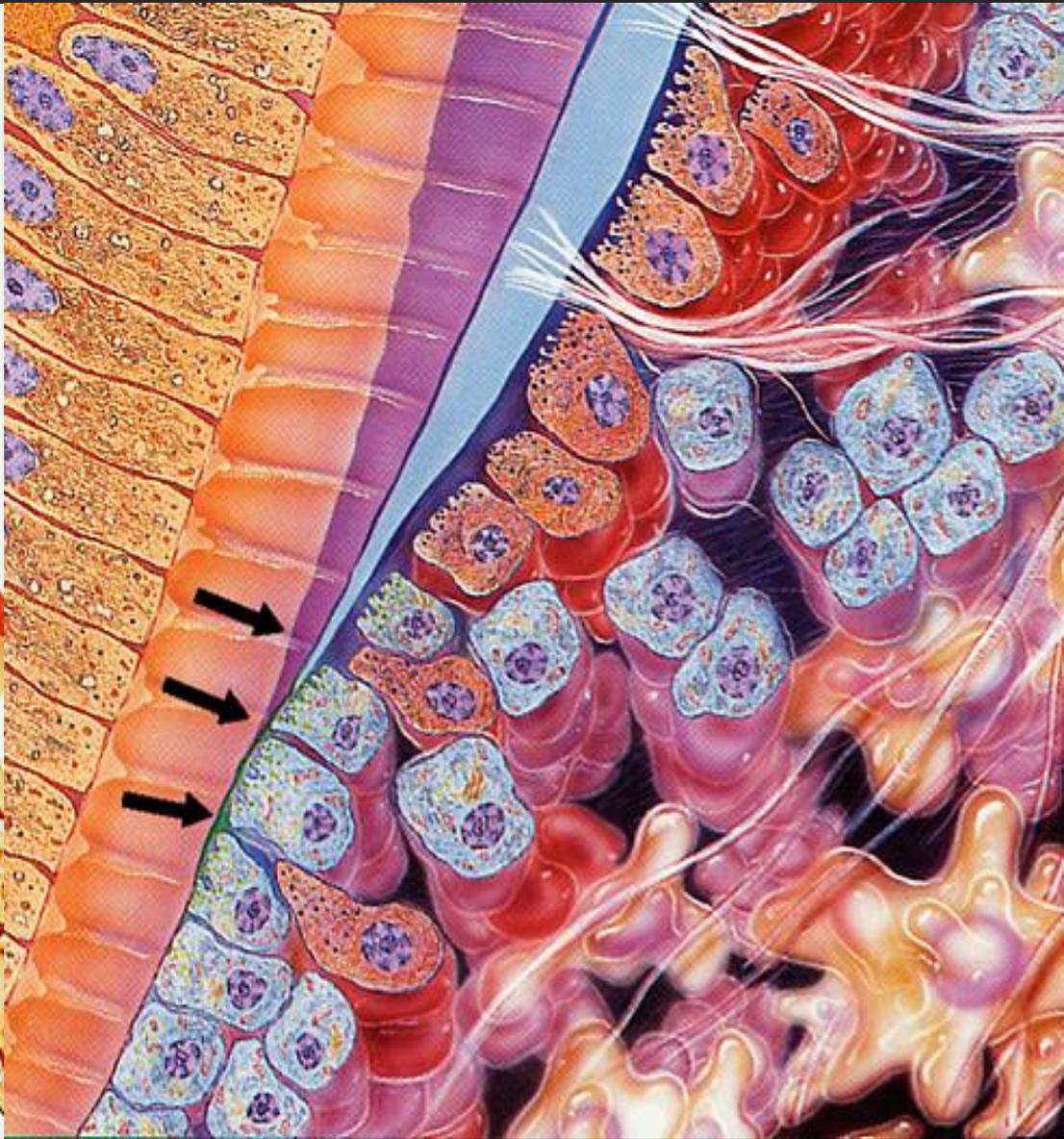
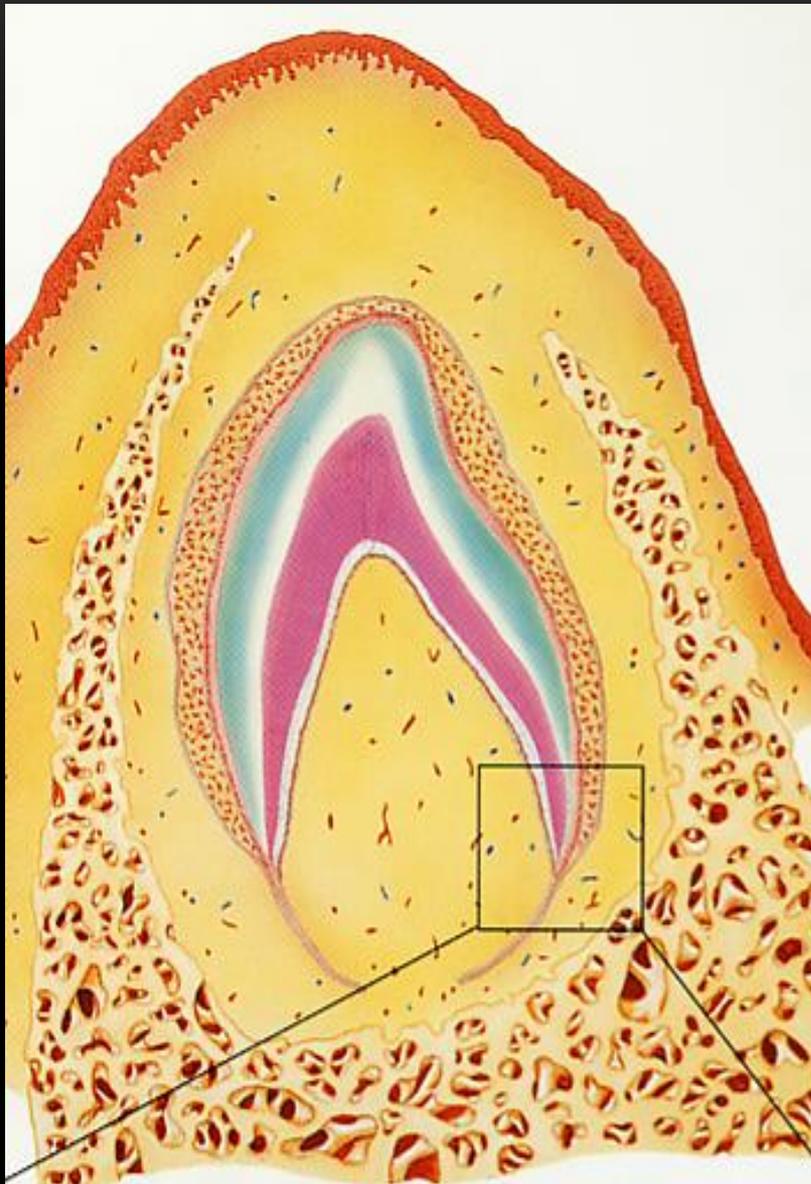
a) mean reduction of CAL from 9.9 ± 1.3 mm to 6.5 ± 1.6 mm after year one, no further differences thereafter

b) human histology revealed neof ormation of a connective tissue attachment and new alveolar bone

CONCEPTUAL DEVELOPMENT

- GTR
 - **EMD**
 - GTR vs. EMD
 - New treatment modalities using EMD
 - EMD + bone substitutes
 - GTR + bone substitutes
 - Histological assessment of the regenerated periodontium
 - Further therapeutic possibilities
-

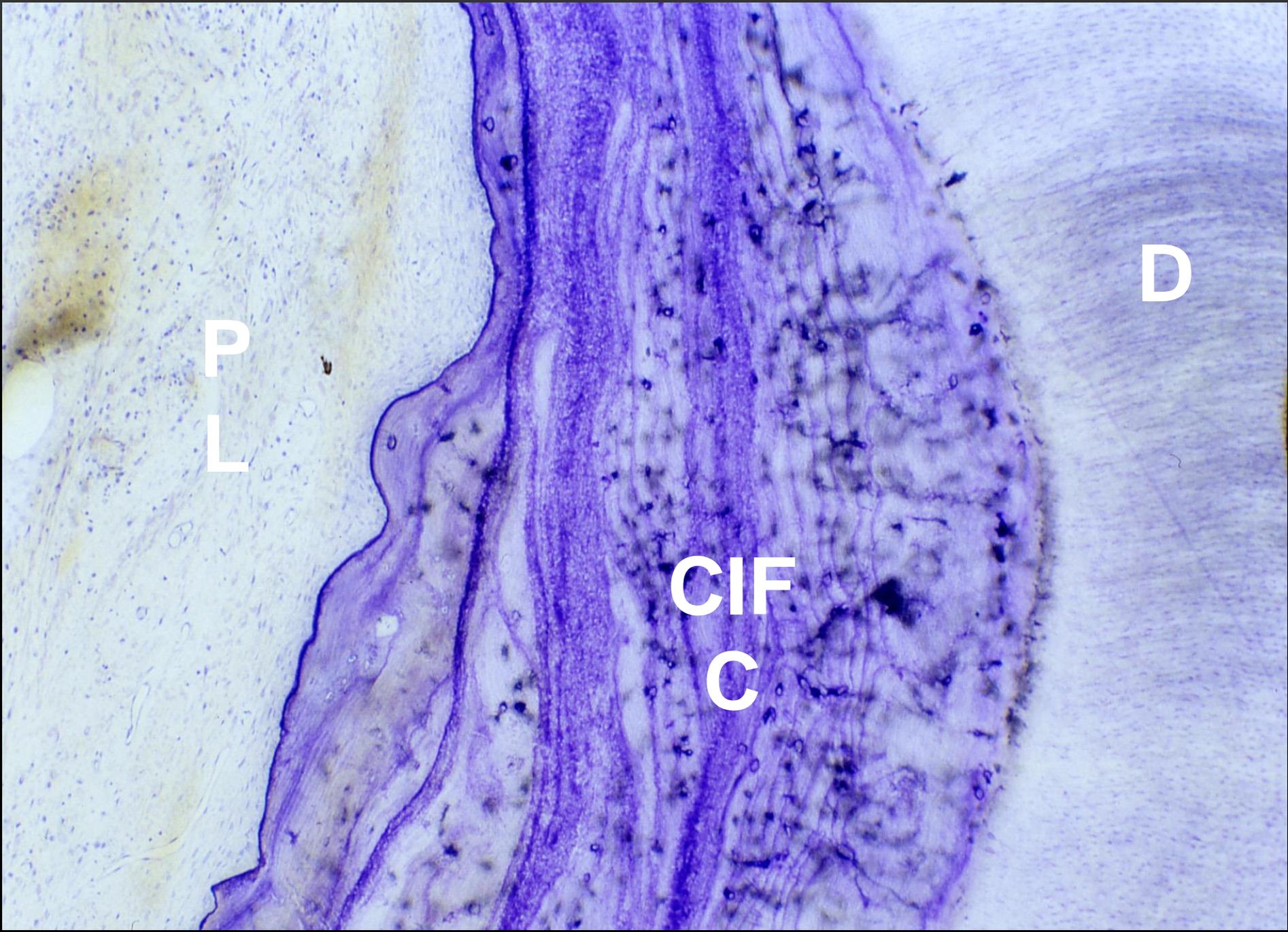
Supposed mechanism of action

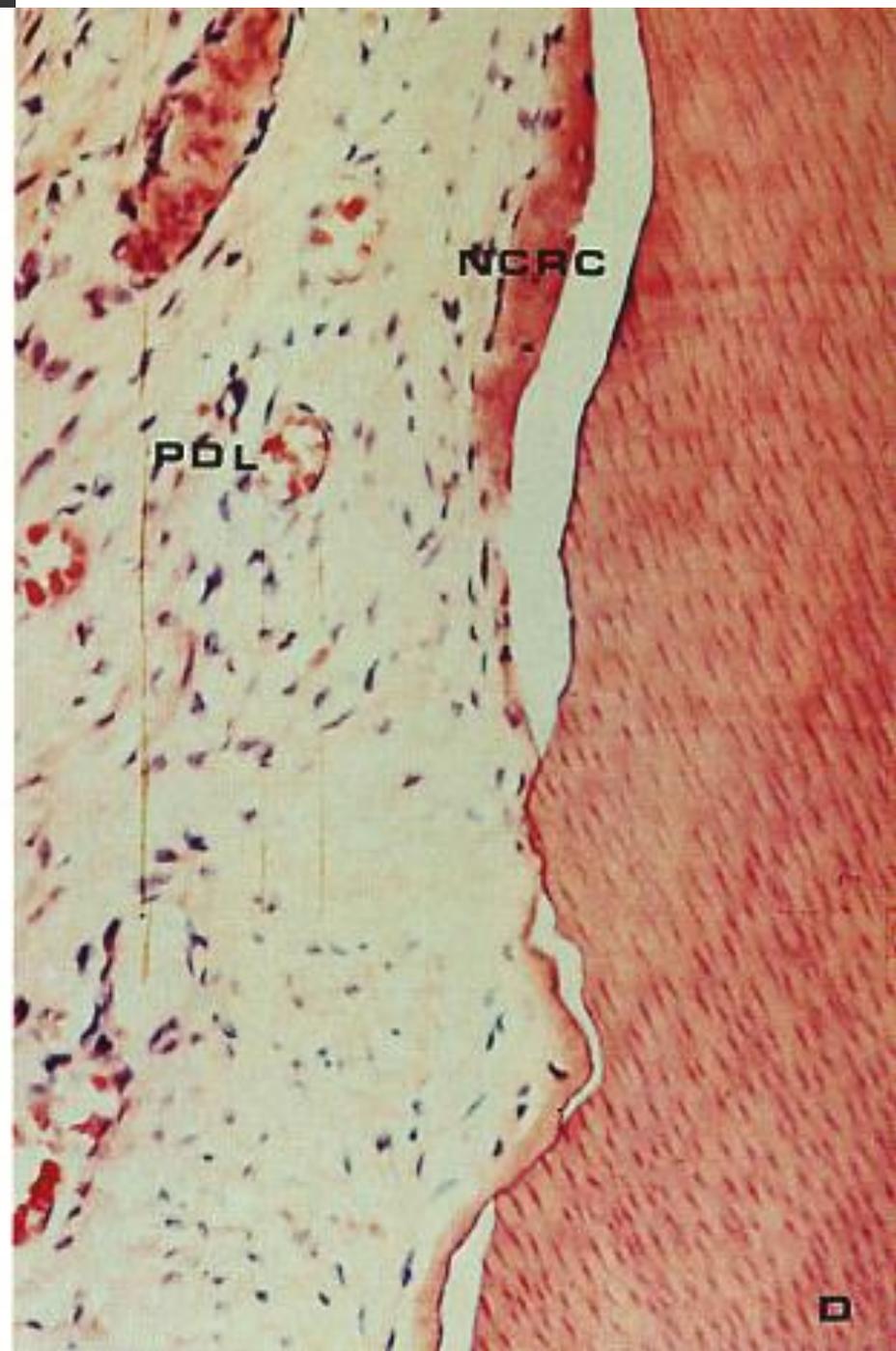
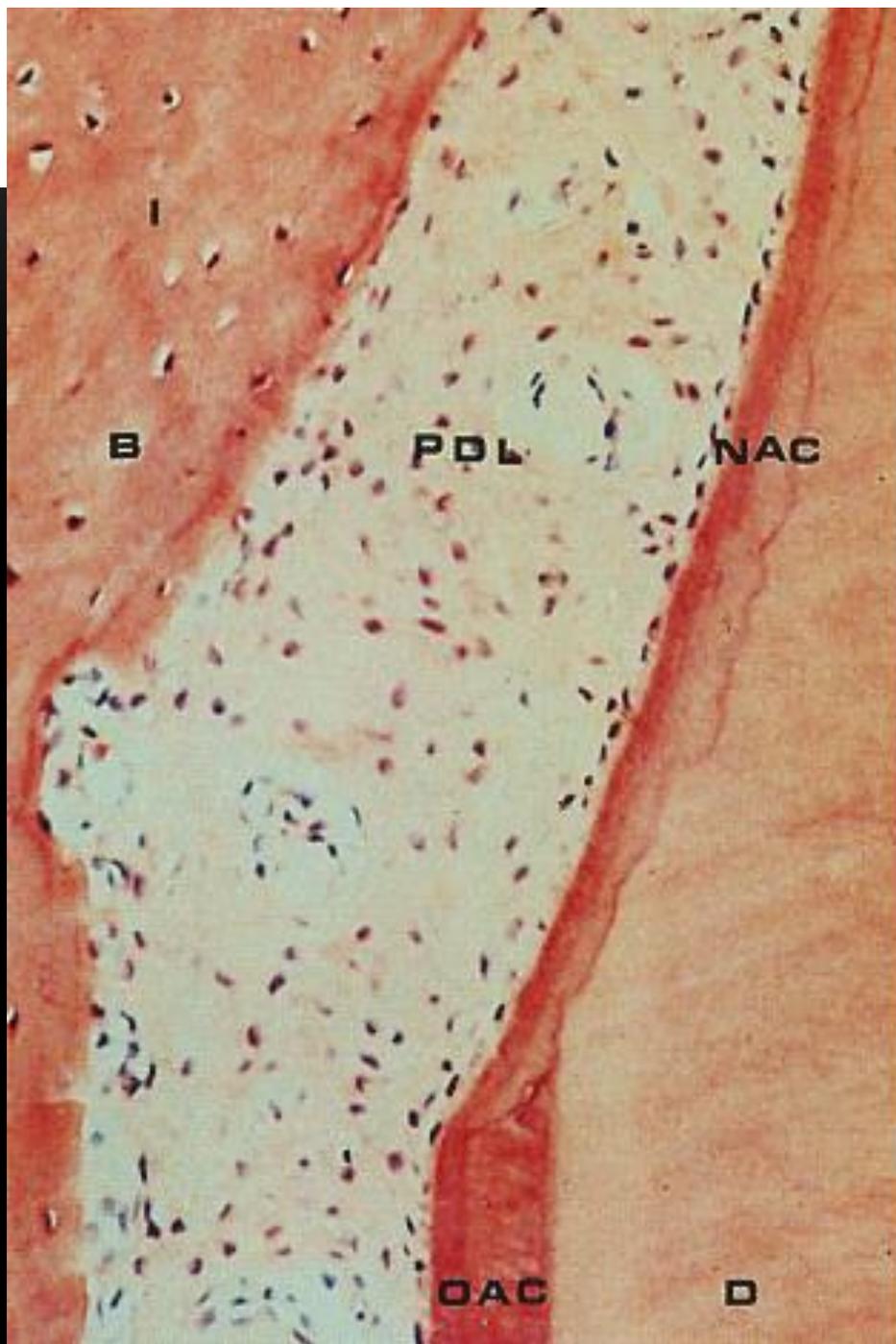


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Different effects of EMD-EMP have been verified in the following cells:

- cementogenic cells
- fibroblast cells (desmodontium + gingiva)
- osteogenic and chondrogenic cells
- epithelial cells
- Wound healing and answer of immune system
- bacteria

Effect of EMD (I.)

- **EMD *in vitro* influences (among other things):**
 - **Cell proliferation**
 - **Cell migration**
 - **Cell adhesion**
 - **Cell differentiation**
 - **Cell metabolism**

Effects of EMD-EMP (II.)

- EMD-EMP influences (among other things):
 - steps of protein synthesis from nucleic acid (ALP, TGF- β , IL-6, PDGF-AB, OPN)
 - **Mineralisation** *in vitro* and ectopic bone formation
 - **wound healing** (cell proliferation, cell migration, MMP, TIMP)
 - **Microorganisms** (antibacterial effect)

Effects of EMD(III.)

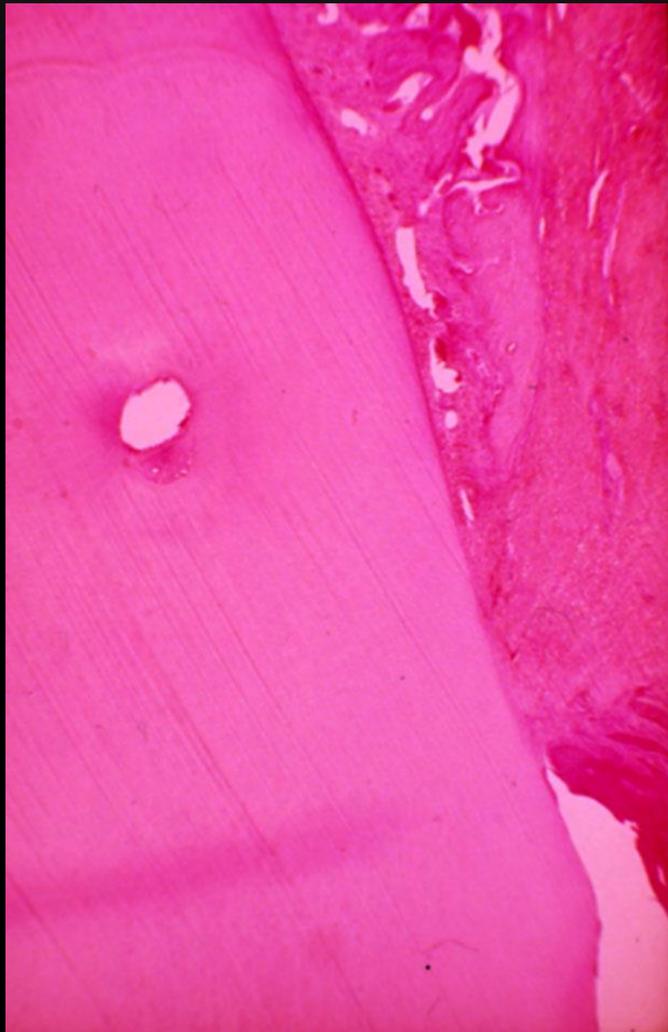
- It is still a question to answer what are the really effective ingredients of EMD
- **Amelogenins may play the main role**
- **Random infections like BSP or TGF- β still could not be excluded**

- **Gestrelus et al. 1997**
- **Suzuki et al. 2001**
- **Kawase et al. 2001**
- **Iwata et al. 2002**

ENAMEL-MATRIX-PROTEIN



ENAMEL-MATRIX-PROTEIN



EMD

Preliminary case reports and additional human histology

Materials and methods: clinical study (periodontal defects treated with EMD) supplemented with two human histological investigations

Results: newly formed cementum with inserting collagen fibers was found in both specimens, new bone in one sample

Conclusion: EMD stimulates new connective tissue attachment formation

However no predictable bone formation!

GTR vs. EMD



CONCEPTUAL DEVELOPMENT

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- EMD
- **GTR vs. EMD**
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- GTR + bone substitutes
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- Further therapeutic possibilities

GTR VS. EMD

Human histological study

Materials and methods: 8 patients Resolut vs. 6 patients EMD; 1 circular or combined 1- and 2-wall defect each

Results: more favorable **wound healing** with **EMD**, in 12 cases signs of radiological bone fill. Histologically newly formed cementum with predominantly **cellular** character in both groups. Except for the formation of new bone, no statistically significant differences between both therapies could be seen.

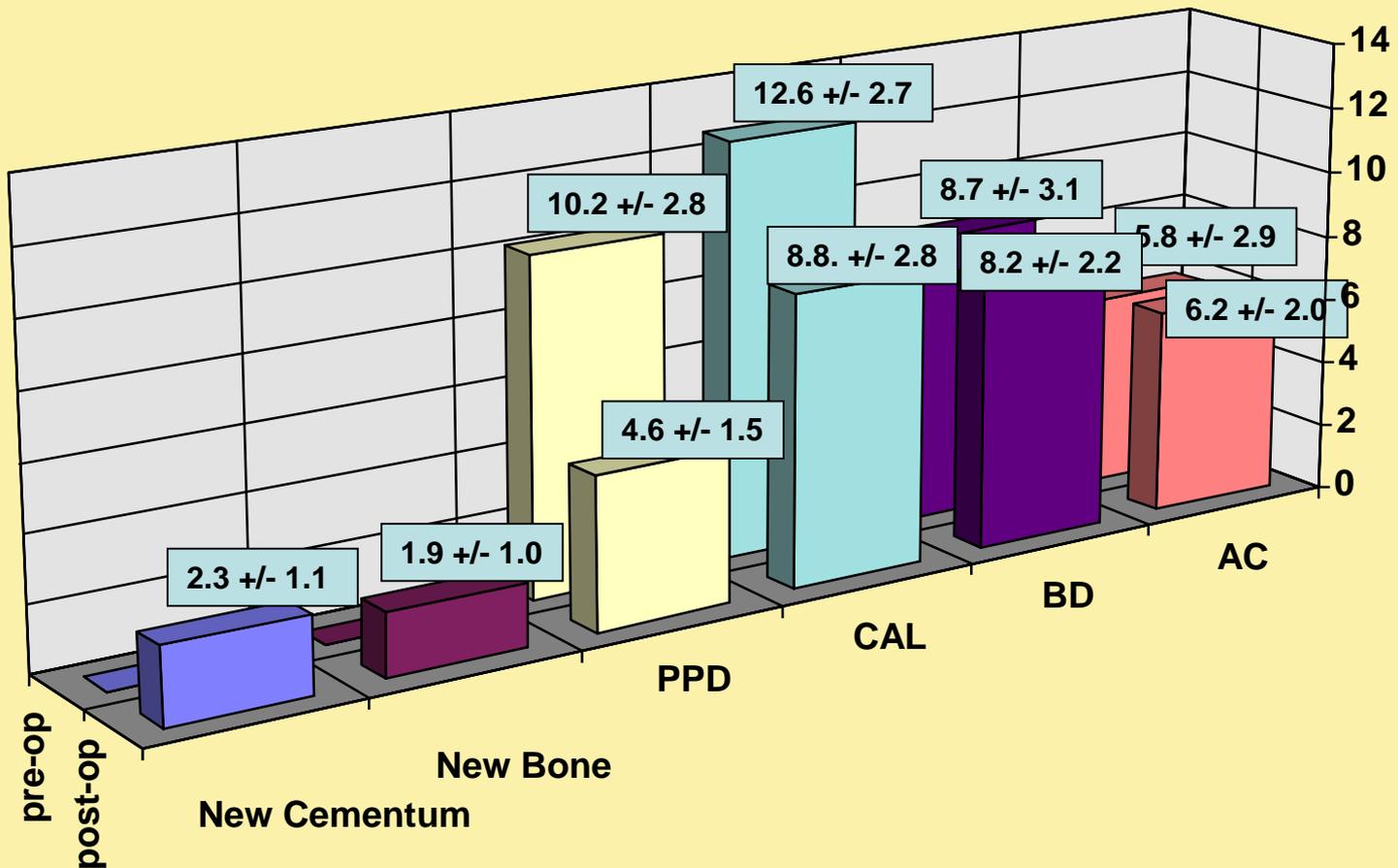
Conclusion: formation of new connective tissue with both techniques BUT less bone formation with EMD

Sculean A, Donos N, Windisch P, Brex M., Gera I, Reich E, T. Karring J. Healing of human intrabony defects following treatment with enamel matrix proteins or guided tissue regeneration. *J Periodont Res.* 1999; 34: 310-322

Windisch P, Sculean A, Klein F., Toth V., Eickholz P, Reich E, Gera I : Comparison of clinical, radiographic and histometric measurements following treatment with guided tissue regeneration or with enamel matrix proteins in human periodontal defects. *J. Periodontol* 2002;73: 409-417

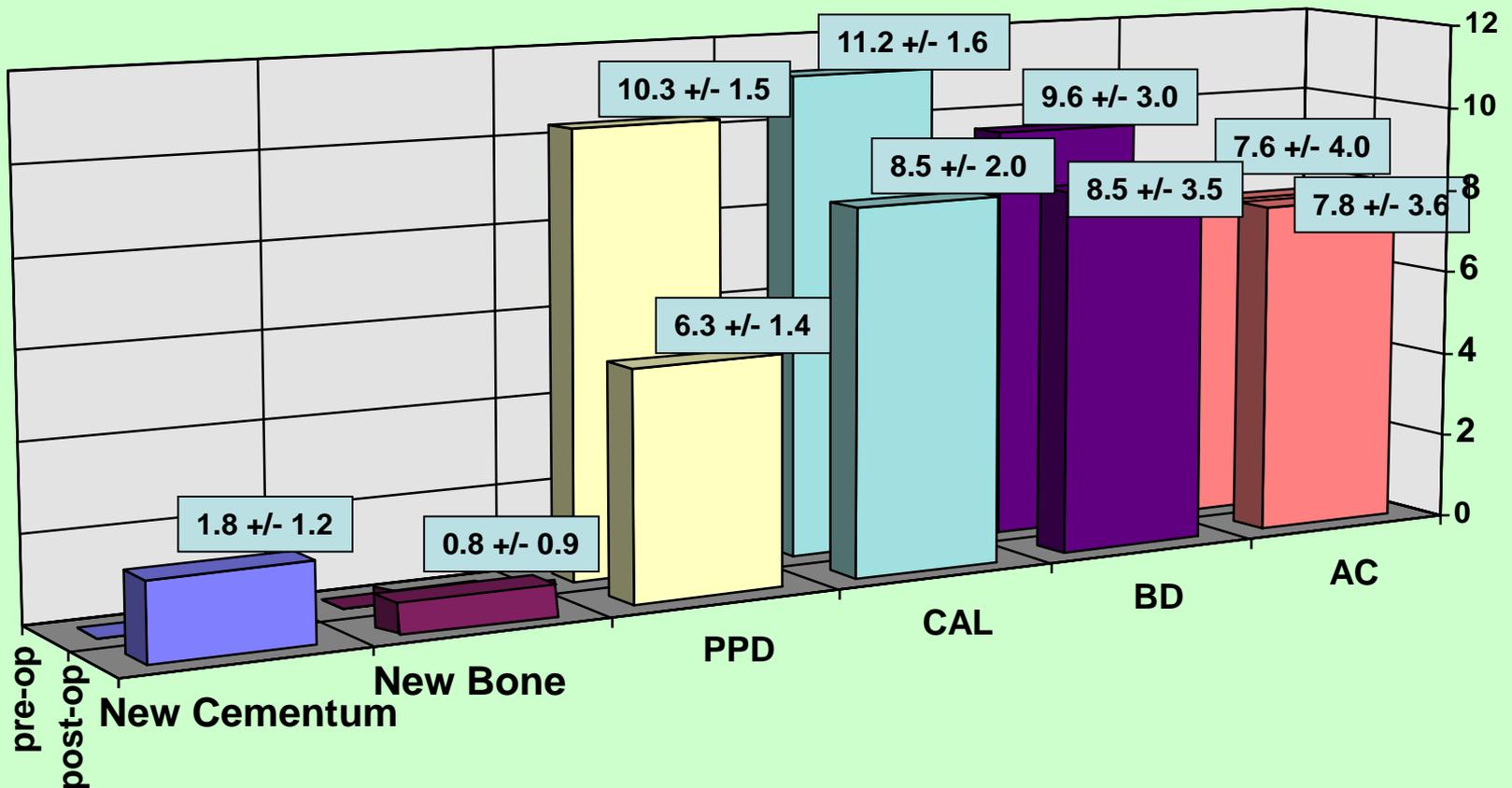
GTR vs. EMD

Therapeutical effect (RESOLUT) n=8



GTR vs. EMD

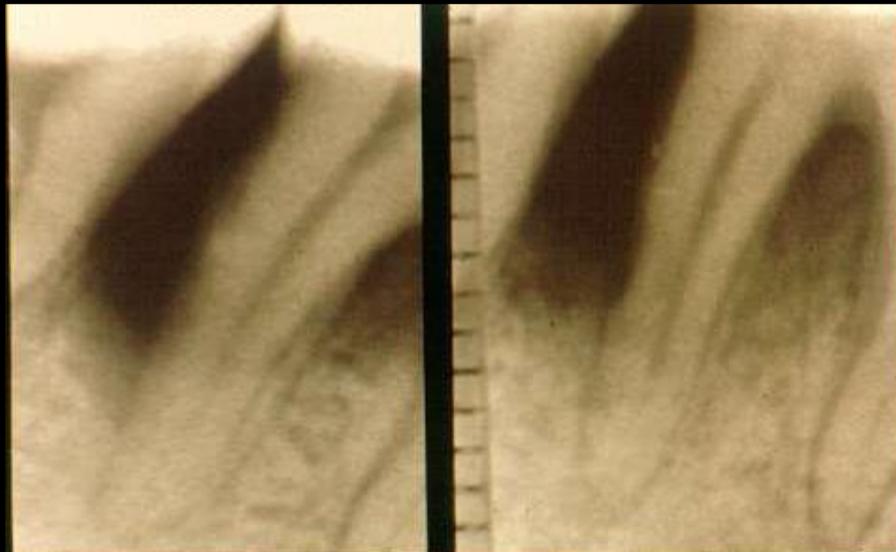
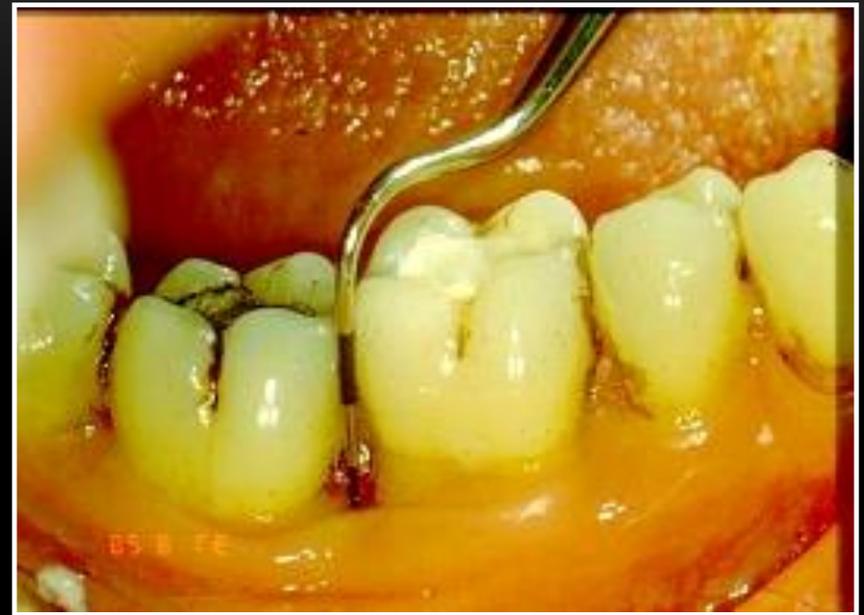
Therapeutical effect (EMDOGAIN) n=6



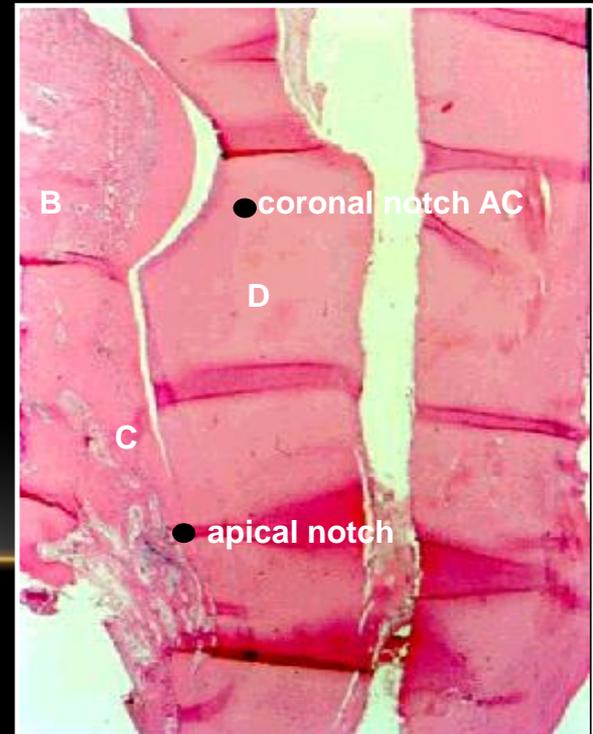
GTR vs. EMD



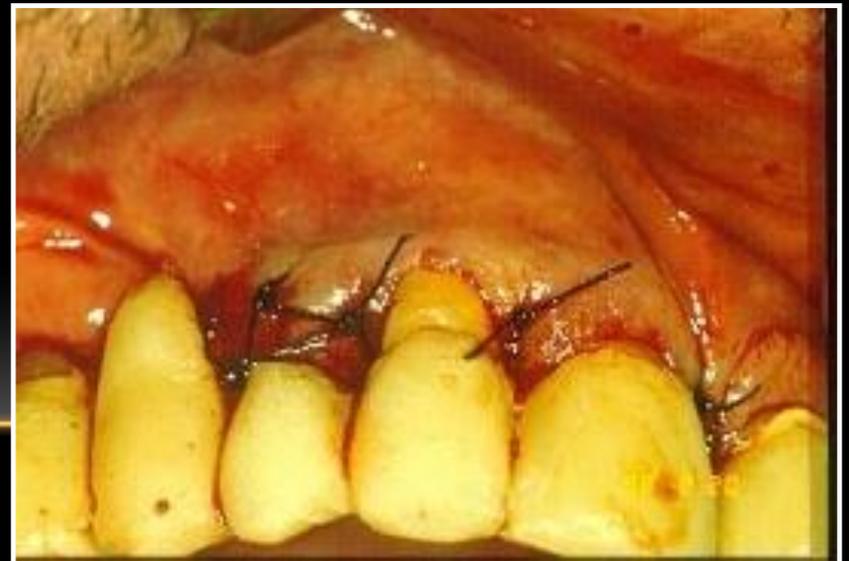
GTR vs. EMD



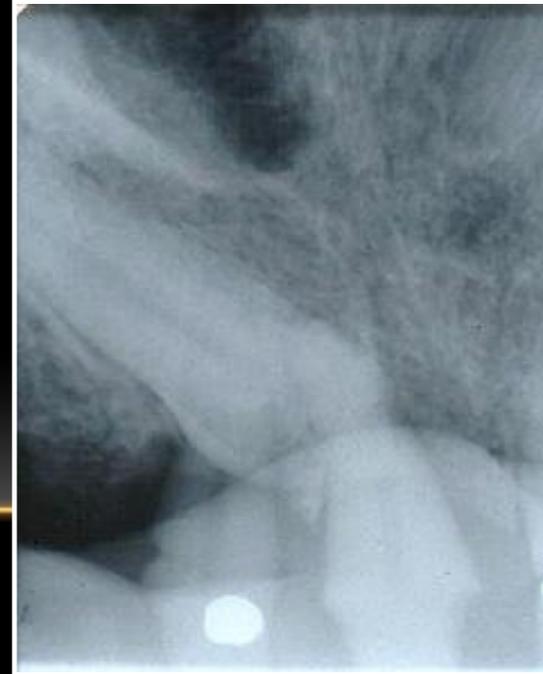
GTR vs. EMD



GTR vs. EMD



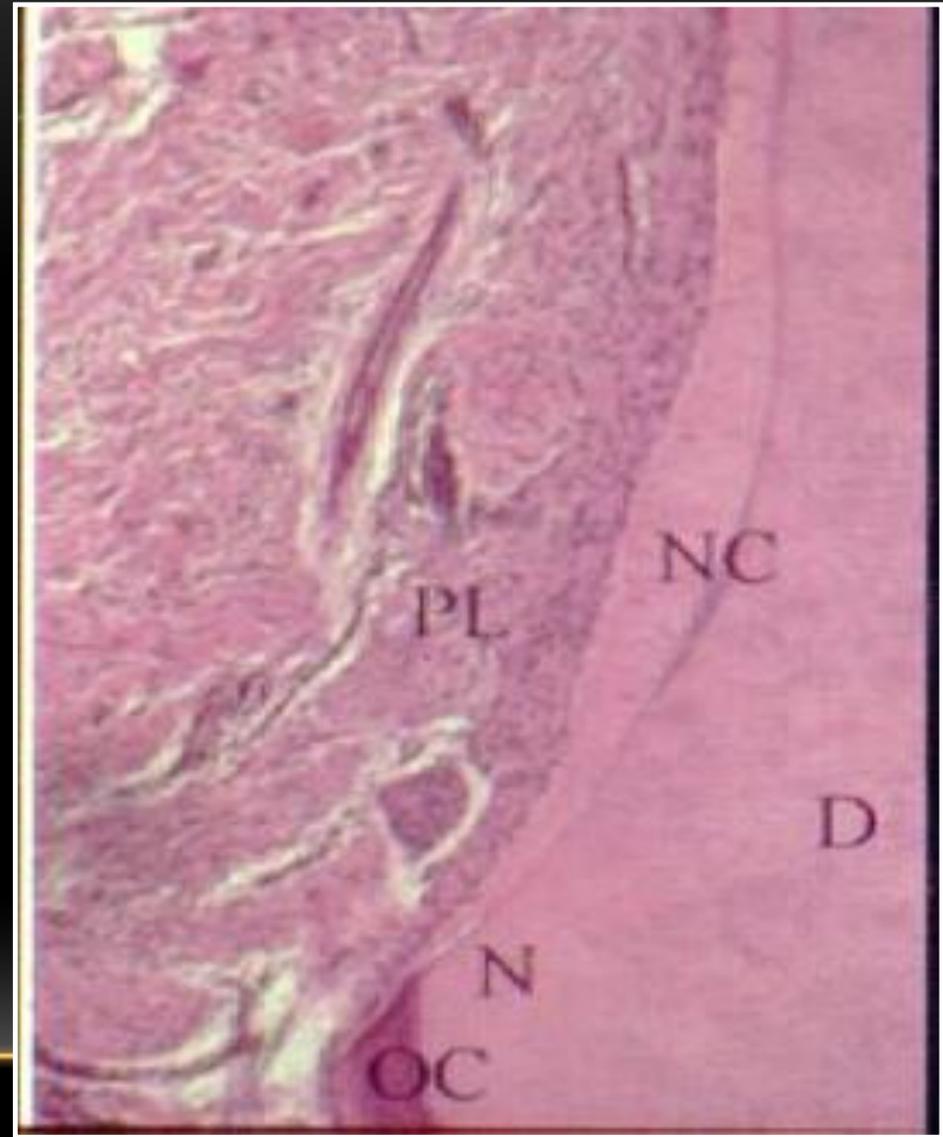
GTR vs. EMD



GTR vs. EMD

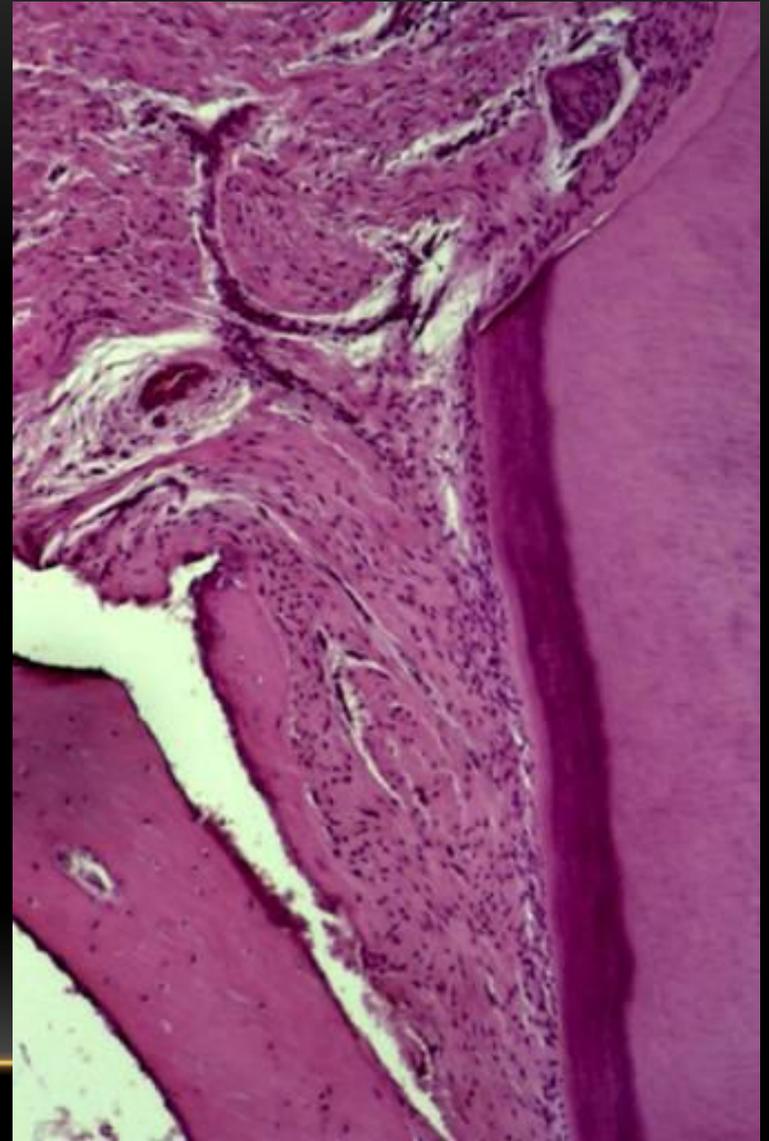
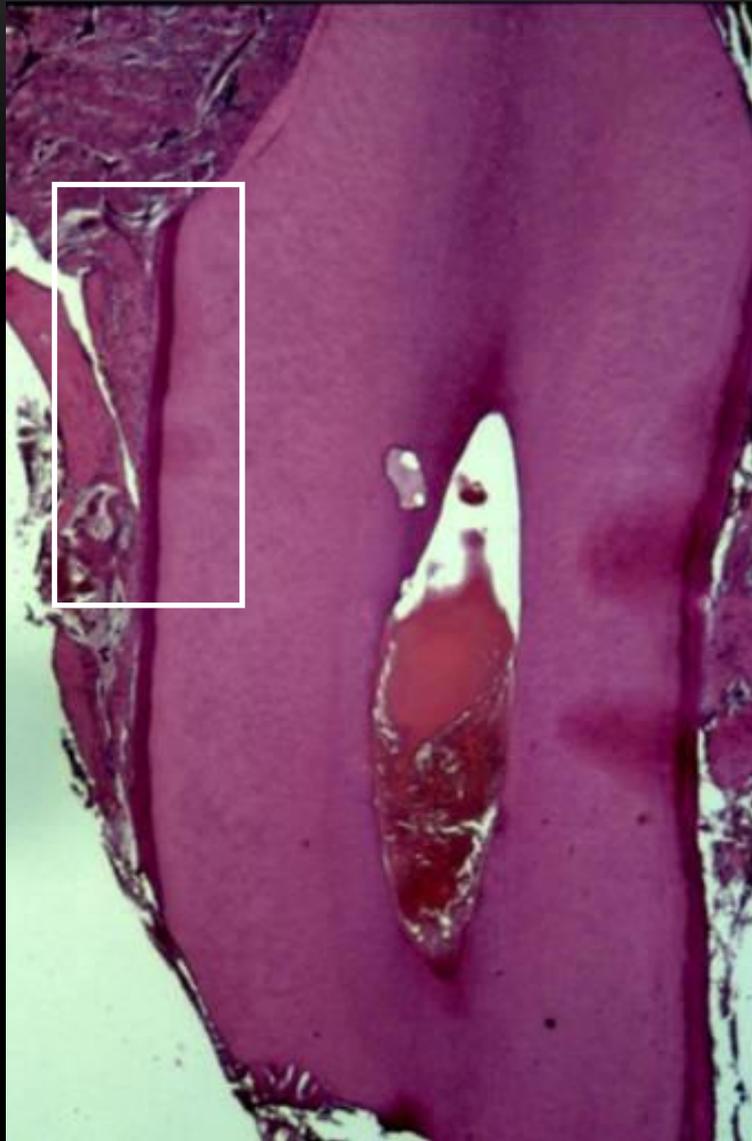


GTR vs. EMD



Windisch P, Sculean A, Klein F, Toth V, Eickholz P, Reich E, Gera I : Comparison of clinical, radiographic and histometric measurements following treatment with guided tissue regeneration or with enamel matrix proteins in human periodontal defects. *J. Periodontol* 2002;73: 409-417

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CONCEPTUAL DEVELOPMENT

- GTR
- EMD
- GTR vs. EMD
- **New treatment modalities using EMD**
- EMD + bone substitutes
- GTR + bone substitutes
- Histological assessment of the regenerated periodontium
- Further therapeutic possibilities

NEW TREATMENT MODALITIES USING EMD I

Non-surgical treatment of human intrabony defects

Materials and methods: 6 months follow-up and histology

EMD with subgingival scaling and root planing in 4 defects, Vector + EMD in 6 defects, Vector in 6 defects /control/

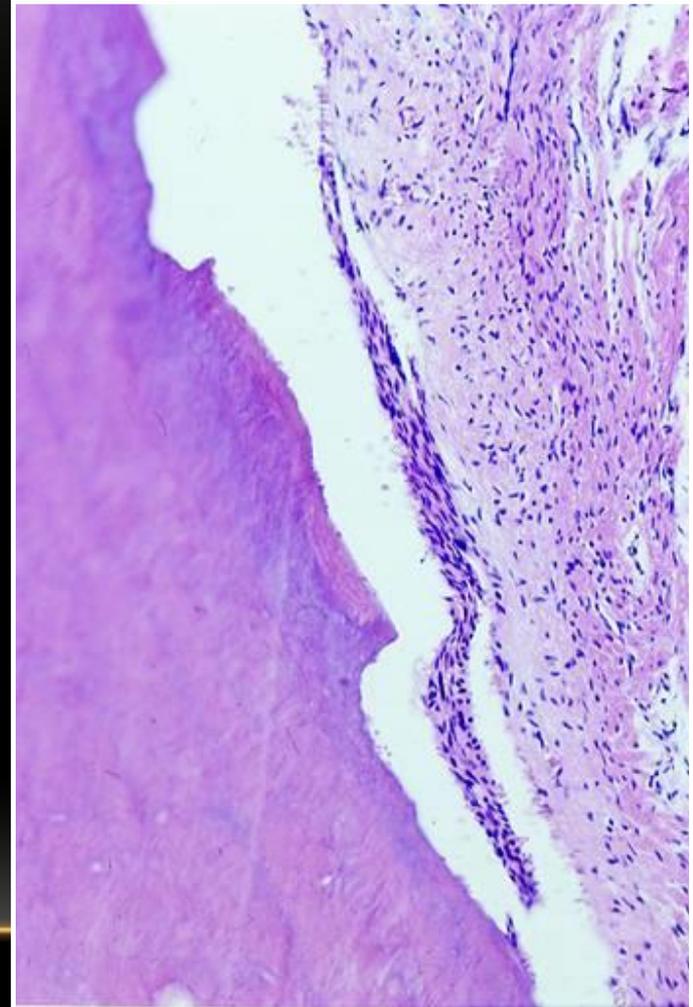
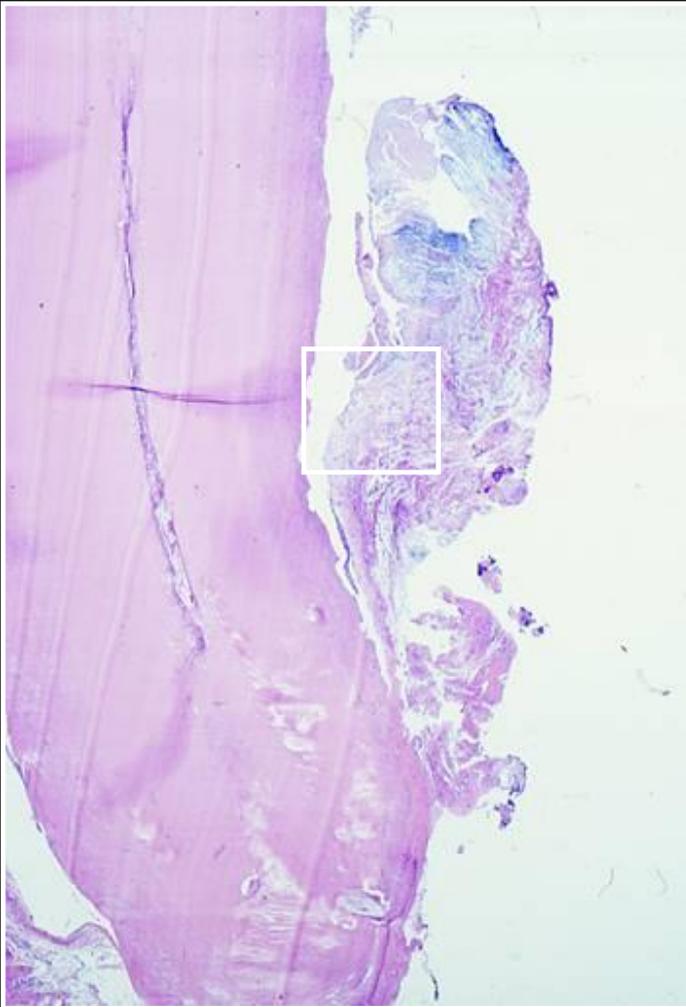
Results: Formation of **long junctional epithelium** with all three techniques along the instrumented root surface, no predictable regeneration of attachment apparatus.

Conclusion: no periodontal regeneration following non-surgical treatment with subgingival application of EMD

New treatment modalities using EMD

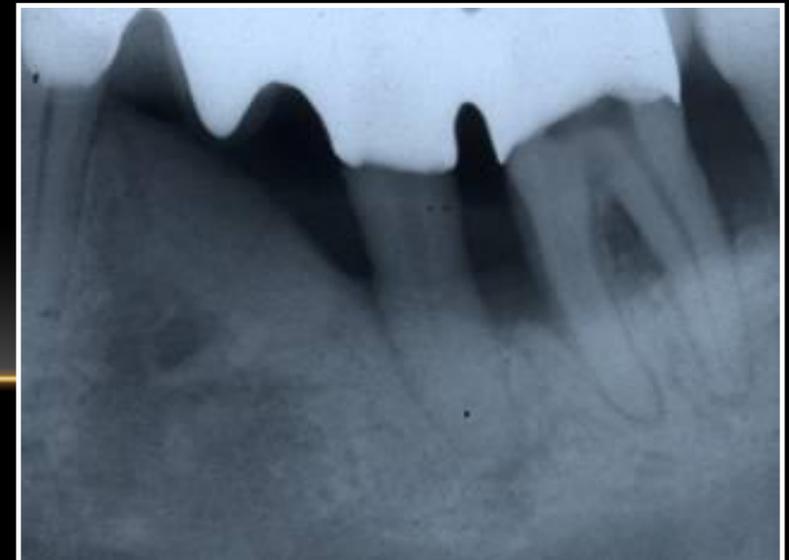


New treatment modalities using EMD

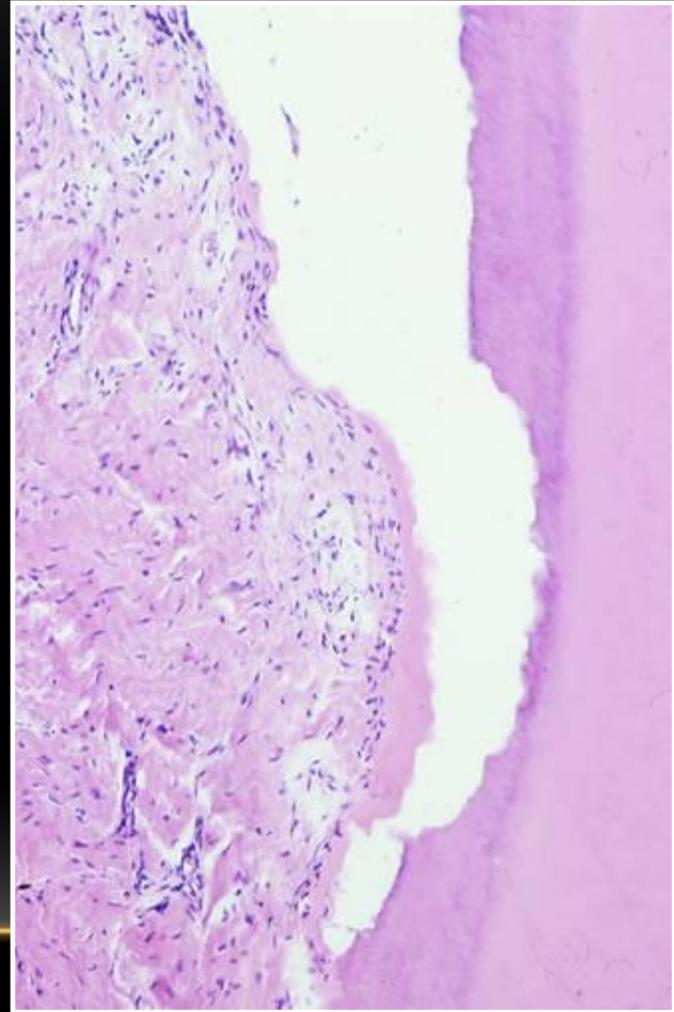
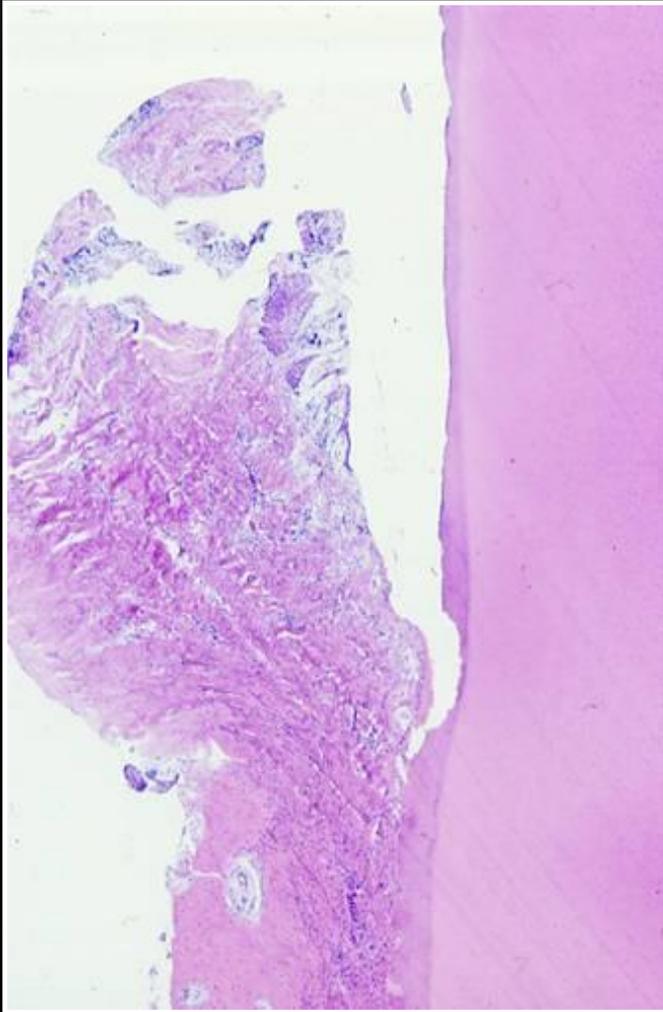


Sculean A, Windisch P, Keglevich T, Gera I. Histologic evaluation of human intrabony defects following non-surgical periodontal therapy with and without application of an enamel matrix Protein derivativ *J. Periodontol* 2003;74: 153-160

New treatment modalities using EMD



New treatment modalities using EMD



Sculean A, Windisch P, Keglevich T, Gera I. Histologic evaluation of human intrabony defects following non-surgical periodontal therapy with and without application of an enamel matrix Protein derivativ *J. Periodontol* 2003;74: 153-160

NEW TREATMENT MODALITIES USING EMD II

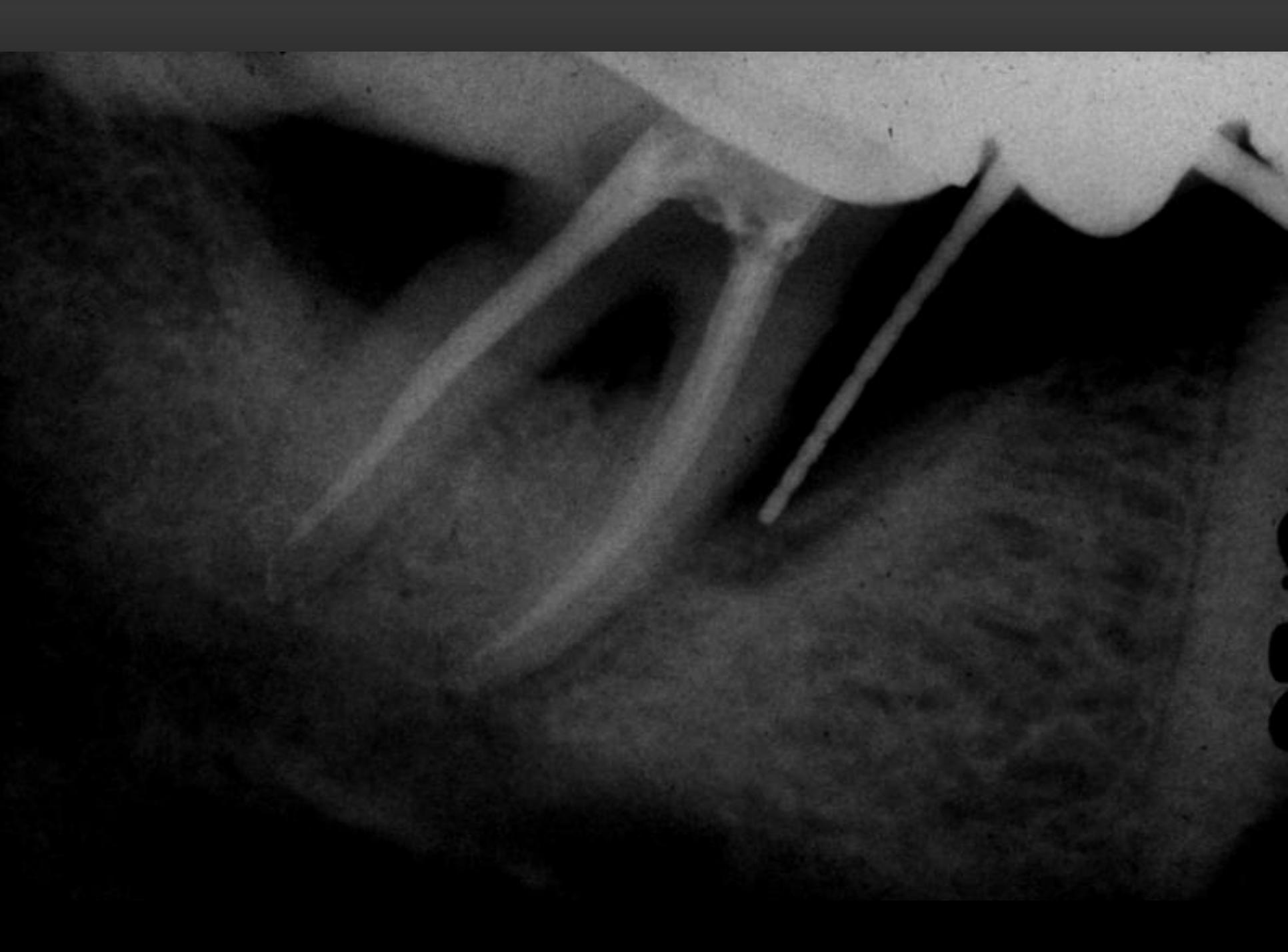
GTR + EMD combined treatment

Materials and methods: 6 months follow-up and histology

56 patients in 4 groups /14 patients each/: EMD + Resolut compared with: Resolut alone, EMD alone and MWF as controls

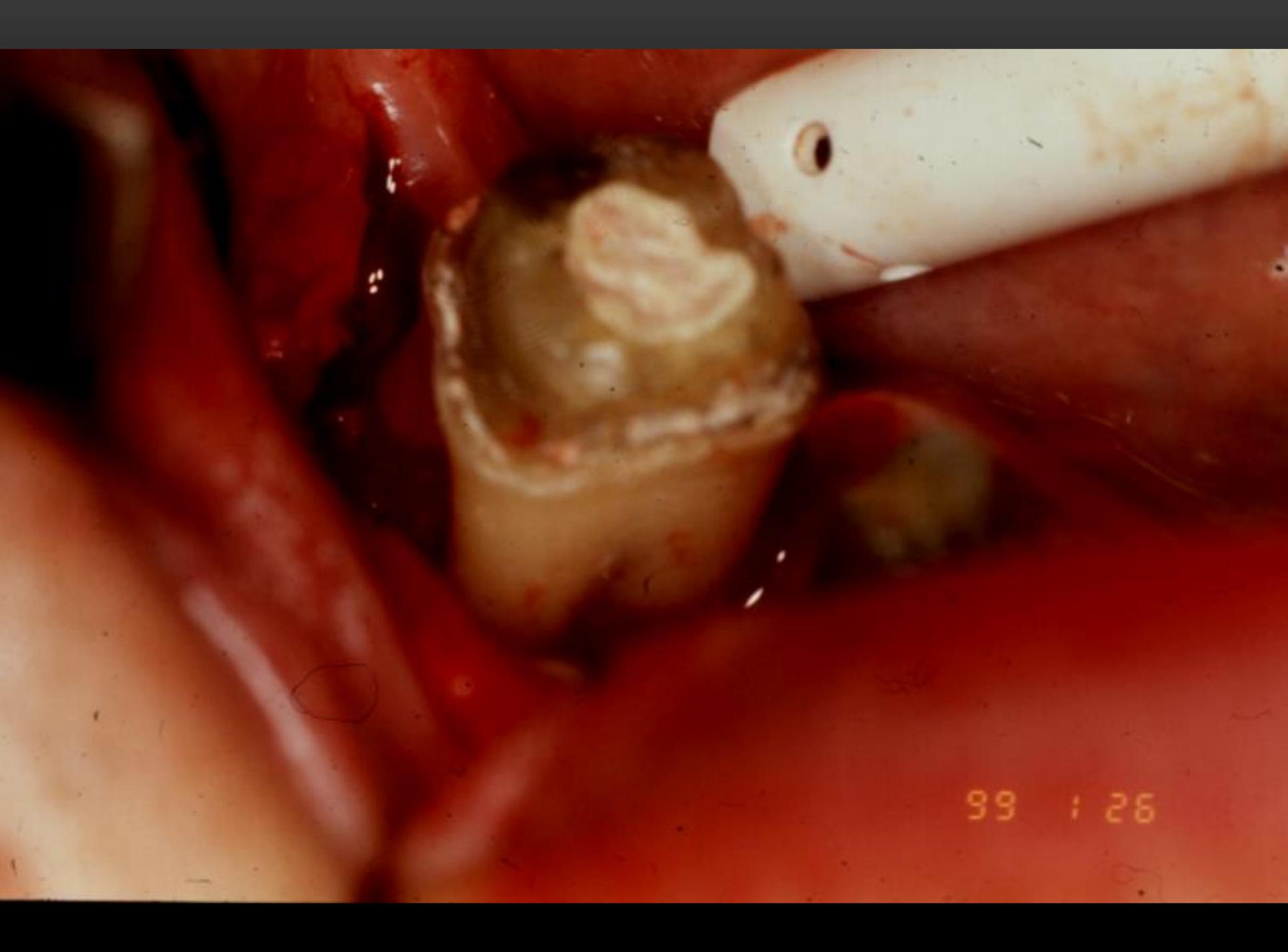
Results: CAL gain of 3.2-3.4 mm /no significant difference between Resolut, EMD and Resolut + EMD/, CAL gain of only 1.7 mm with MWF

Conclusion: combined treatment does not carry any additional benefit over different single regenerative procedures

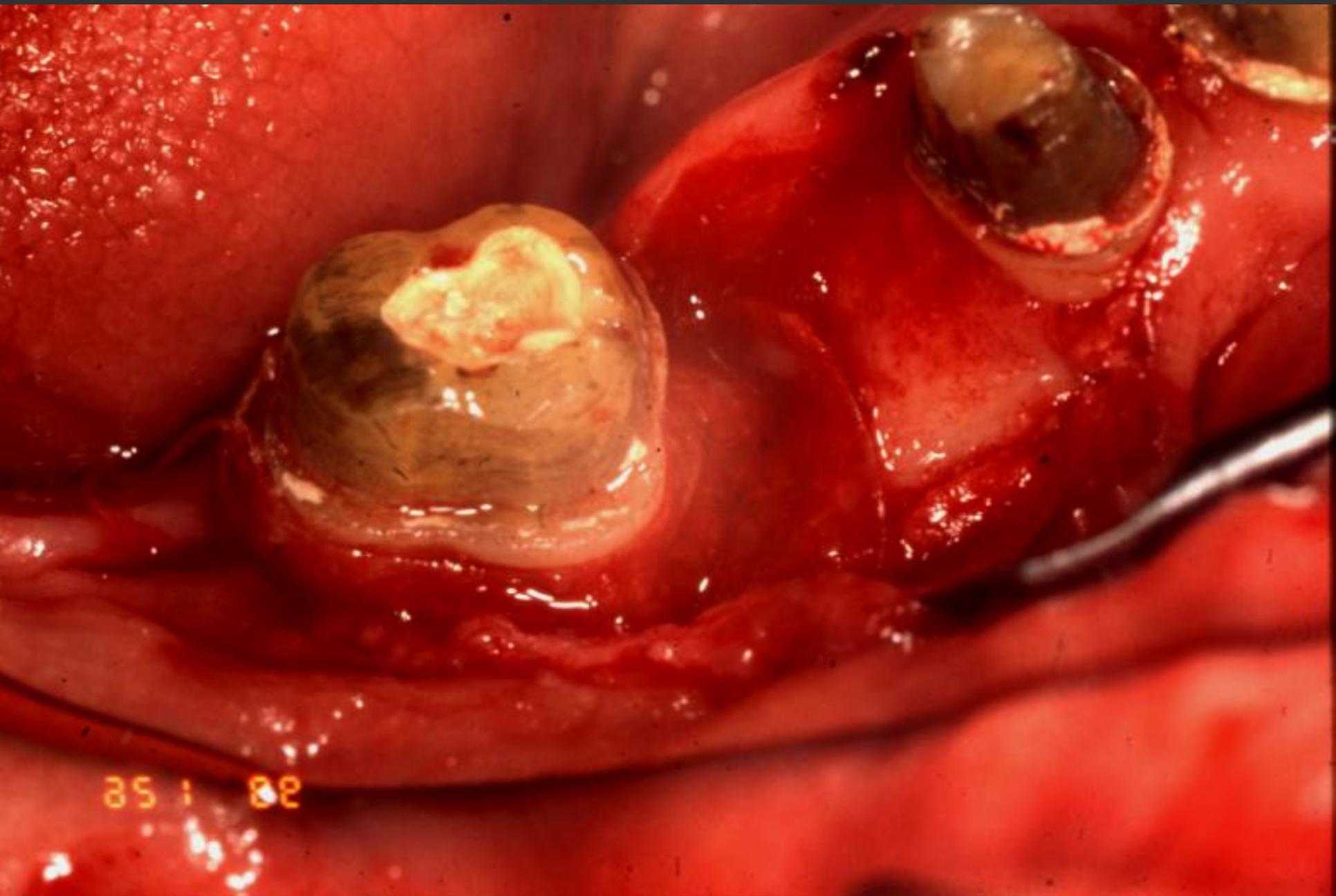


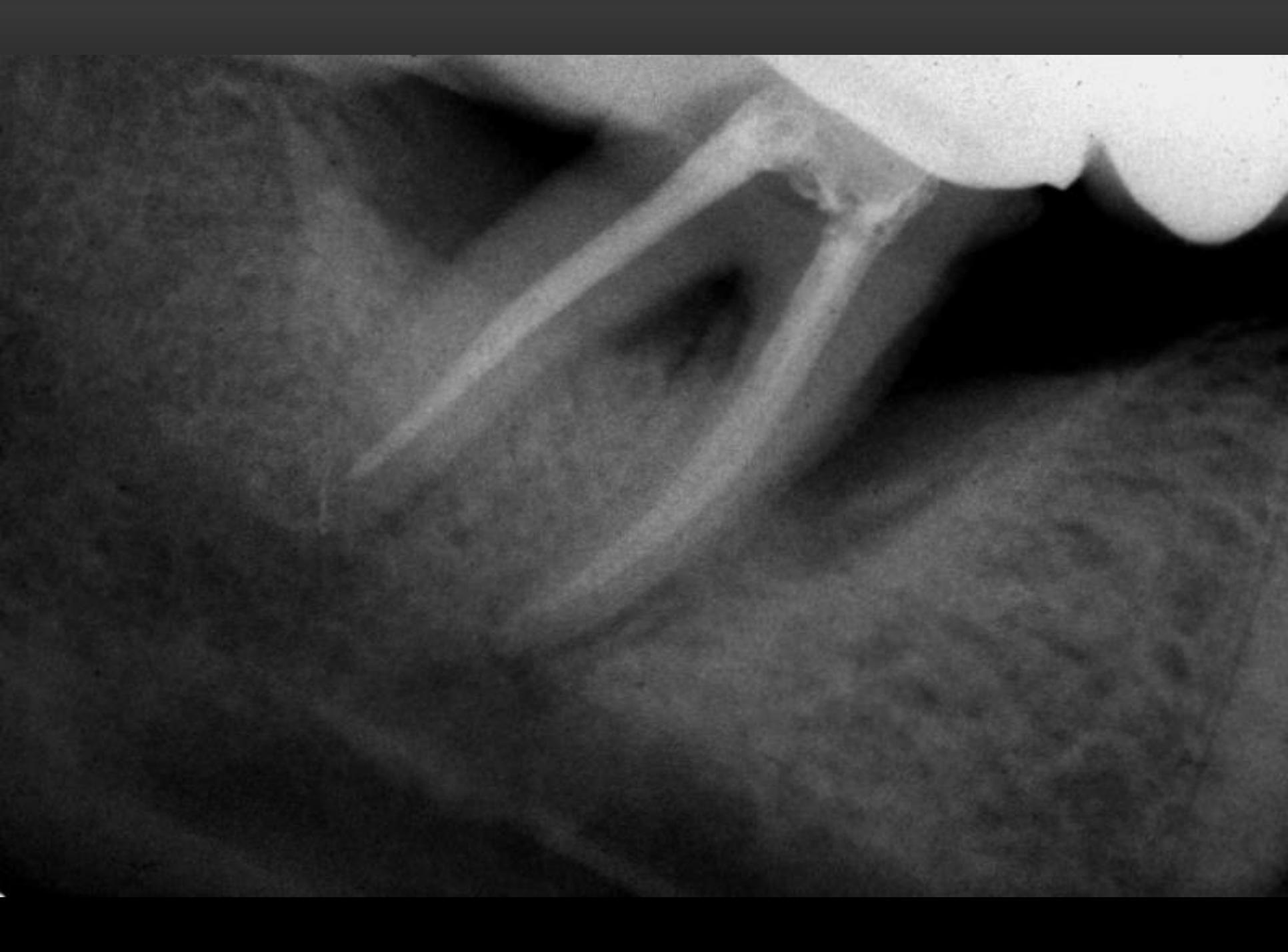


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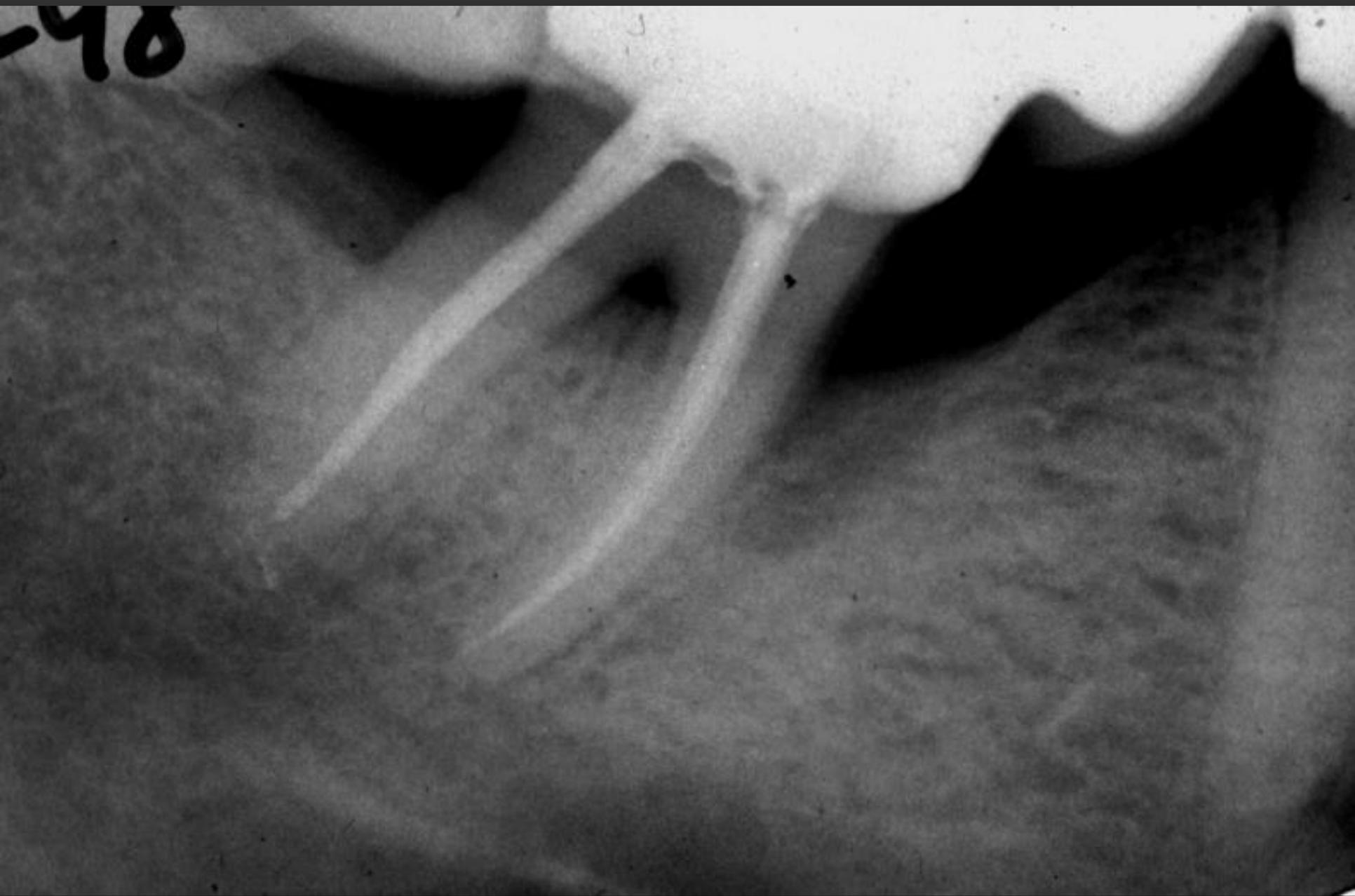


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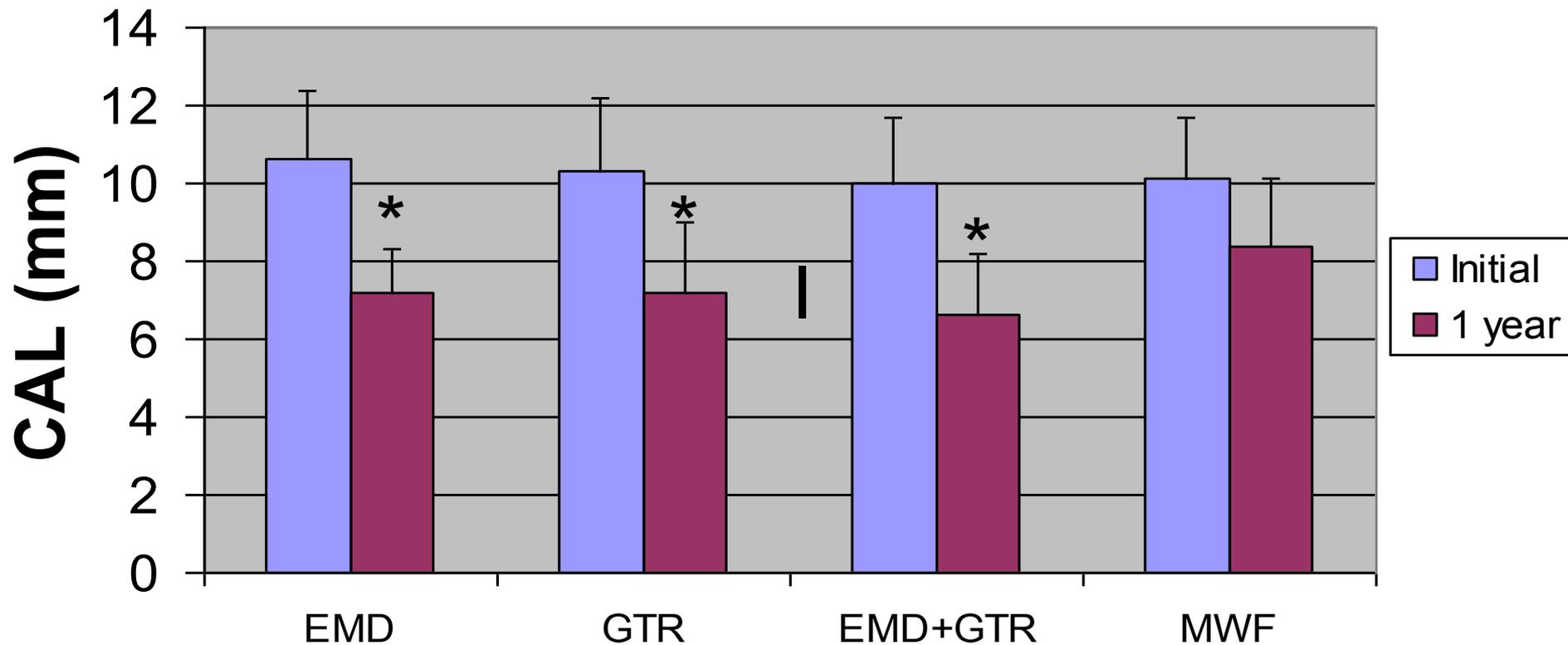


98



New treatment modalities using EMD

Changes in clinical attachment level



CONCEPTUAL DEVELOPMENT

- GTR
- EMD
- GTR vs. EMD
- New treatment modalities using EMD
- **EMD + bone substitutes**
- GTR + bone substitutes
- Histological assessment of the regenerated periodontium
- Further therapeutic possibilities

EMD+BONE SUBSTITUTES

Materials and methods: one year follow-up clinical study with intrabony defects, group 1 /EMD + BDX, 12 patients/, group 2 /BDX alone, 12 patients/

Results: Group 1 showed a CAL gain of 4.7 mm, group 2 showed a CAL gain of 4.9 mm /NS/. Radiographical **bone fill (?)**.

Conclusion: adding EMD to BDX does not improve clinical outcome

EMD+BONE SUBSTITUTES

Human histological studies

Materials and methods:

Intrabony defects were treated 1) EMD + BDX /two defects/, 2) BDX alone /one defect/, 3) EMD + BDX + GTR /one horizonto-vertical defect/, 4) EMD + BG, /three intrabony defects /, 5) BG alone /three intrabony defects/. Six months after surgery, histologic evaluation was performed.

Results: in the intrabony component, all therapeutical options resulted in new connective tissue formation, except for BG alone (long epithelial downgrowth). No direct contact between BG or BDX particles and the root surface was observed. Bone substitute particles were embedded in a bone-like tissue. Healing in the suprabony part epithelial downgrowth to the coronal notch and encapsulation of bone substitute particles in dense connective tissue occurred.

Conclusion: all techniques but BG alone were regenerative in the intrabony component, however no regeneration occurred in the suprabony component.

Sculean A, Windisch P, Keglevich T, Chiantella GC, Gera I, Donos N. Clinical and histological evaluation of human intrabony defects treated with an enamel matrix protein combined with a bovine derived xenograft. *Int J Periodontics Restorative Dent* 2003; 23: 47-55

Sculean A, Windisch P, Chiantella GC. Human histologic evaluation of an intrabony defect treated with enamel matrix derivative, xenograft, and GTR. *Int J Periodontics Restorative Dent*. 2004 Aug;24(4):326-33.

Sculean A, Windisch P, Keglevich T, Gera I. Clinical and histologic evaluation of an enamel matrix protein derivative combined with a bioactive glass for the treatment of intrabony periodontal defects in humans. *Int J Periodontics Restorative Dent*. 2005 Apr;25(2):139-47.

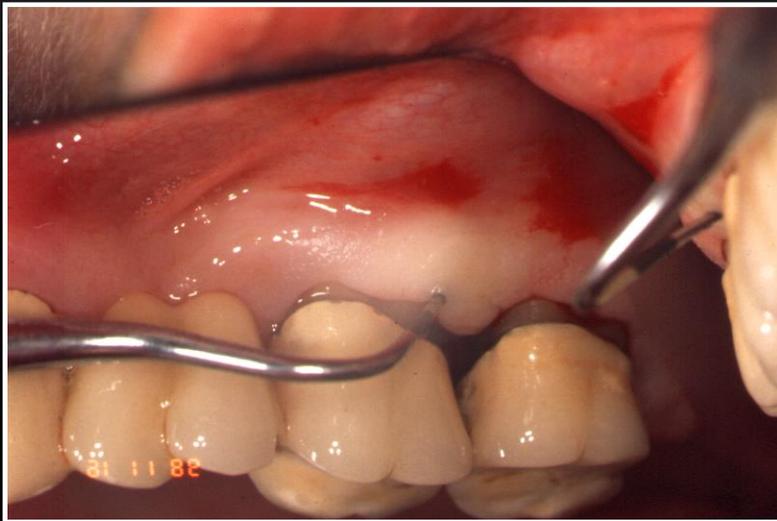
EMD+BONE SUBSTITUTES

Further related publications:

- Sculean A, Stavropoulos A, Berakdar M, Windisch P, Karring T, Brex M. Formation of human cementum following different modalities of regenerative therapy. Clin Oral Investig. 2005 Mar;9(1):58-64. Epub 2005 Jan 6
- Döri F, Arweiler N, Gera I, Sculean A : Clinical evaluation of an enamel matrix protein derivative combined with either a natural bone mineral or beta-tricalcium phosphate. J. Periodontol. 2005 Dec;76(12):2236-43.
- Gera I, Dori F, Keglevich T, Anton S, Szilagy E, Windisch P. Experience with the clinical use of beta-tri-calcium phosphate (Cerasorb) as a bone replacement graft material in human periodontal osseous defects Fogorv Sz. 2002 Aug;95(4):143-7. Hungarian]
- Döri F, Arweiler N, Gera I, Sculean A : Clinical evaluation of an enamel matrix protein derivative combined with either a natural bone mineral or beta-tricalcium phosphate. J. Periodontol. 2005 Dec;76(12):2236-43.

EMD + bone substitutes

preoperative

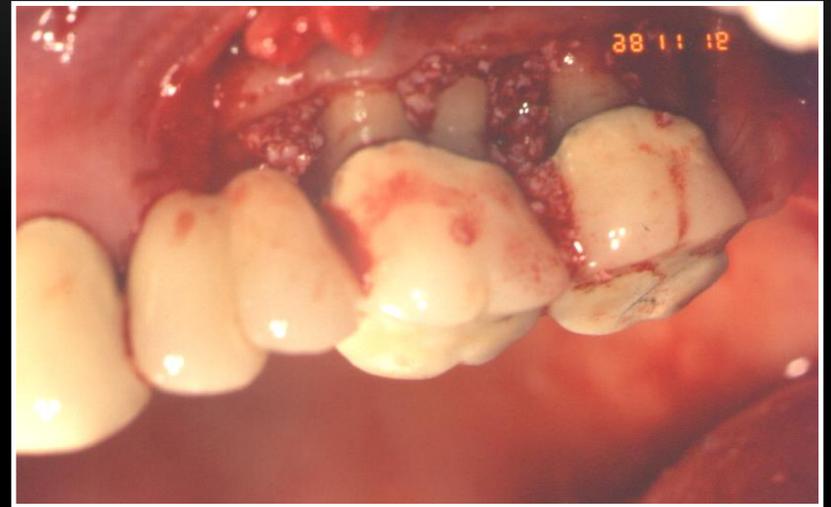


posztoperative



EMD + bone substitutes

preoperative



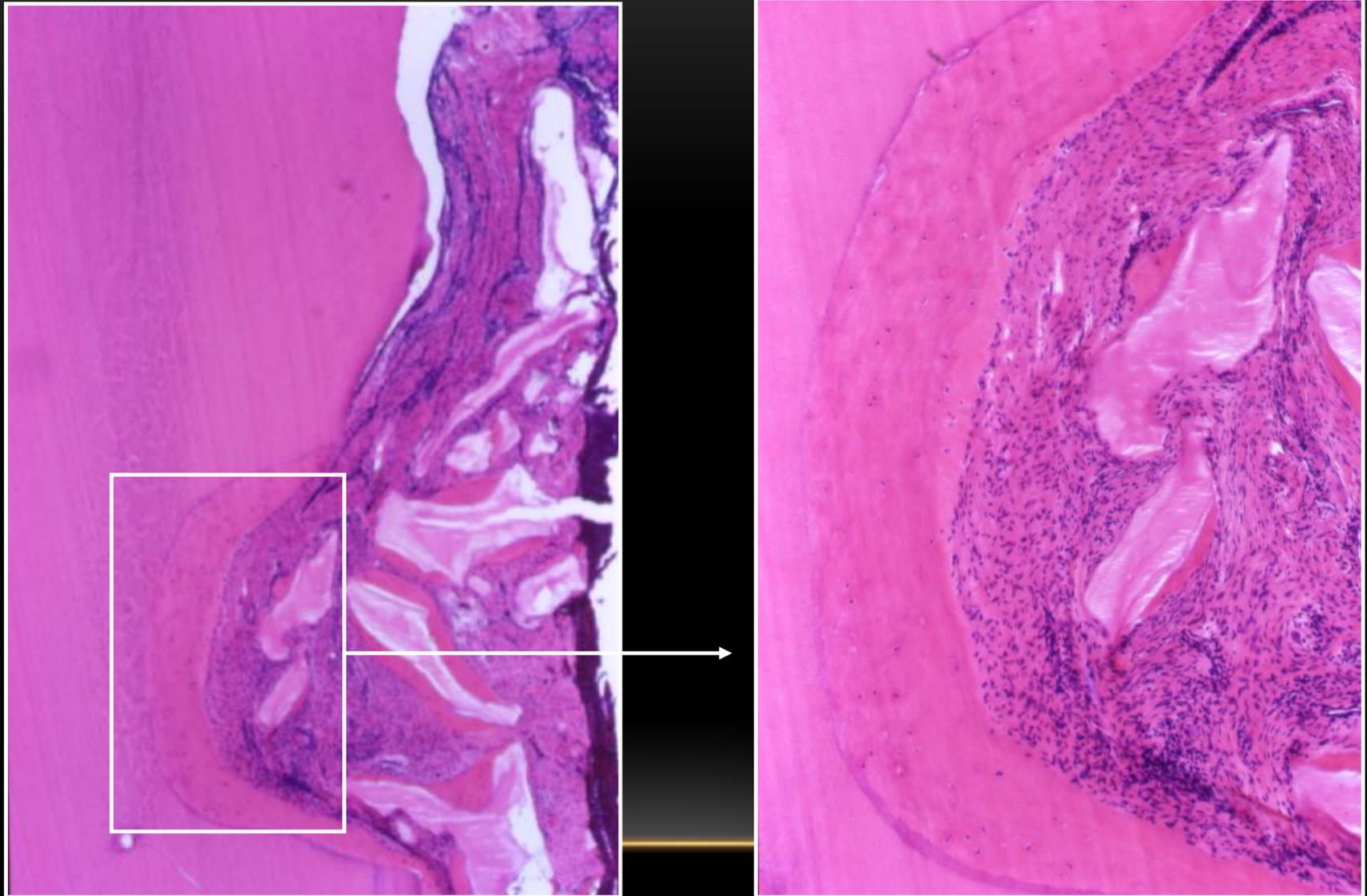
posztoperative



posztoperative

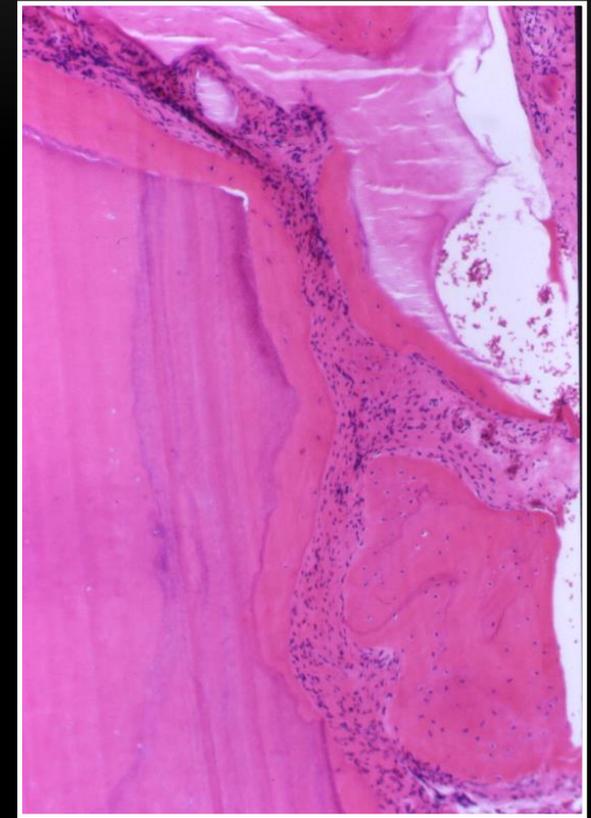
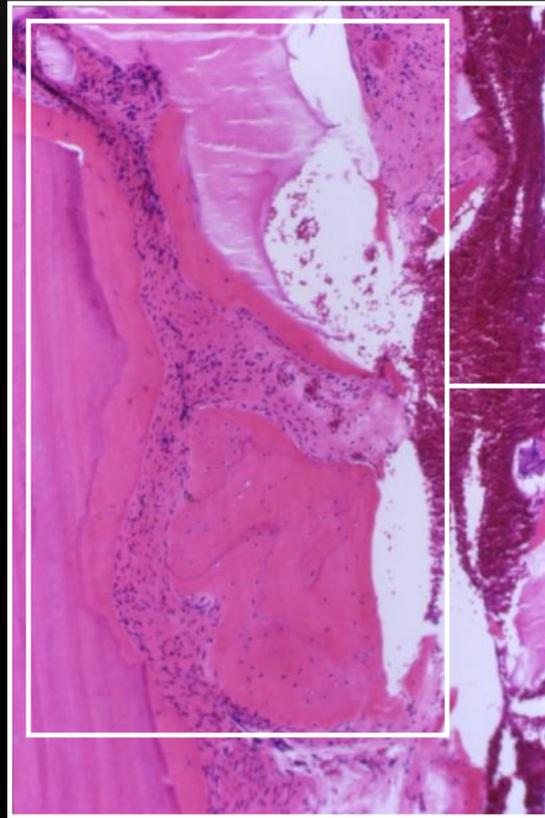
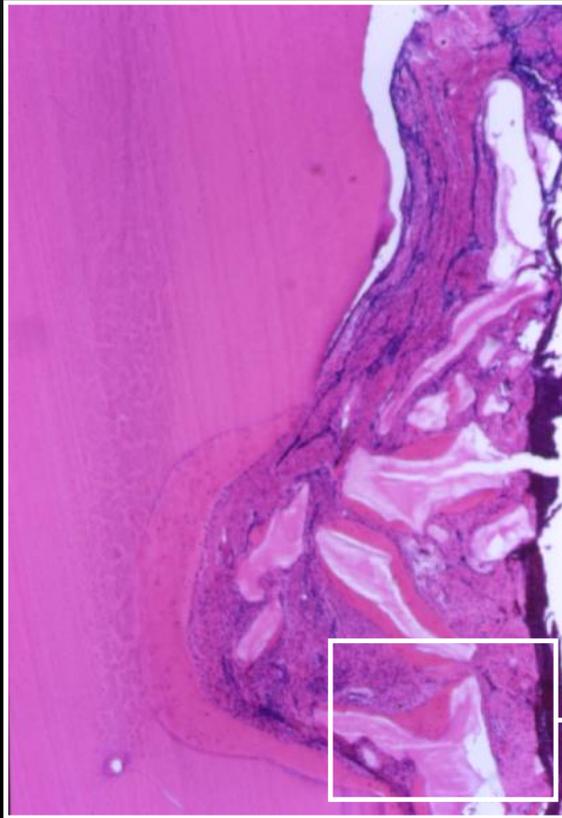


EMD + bone substitutes



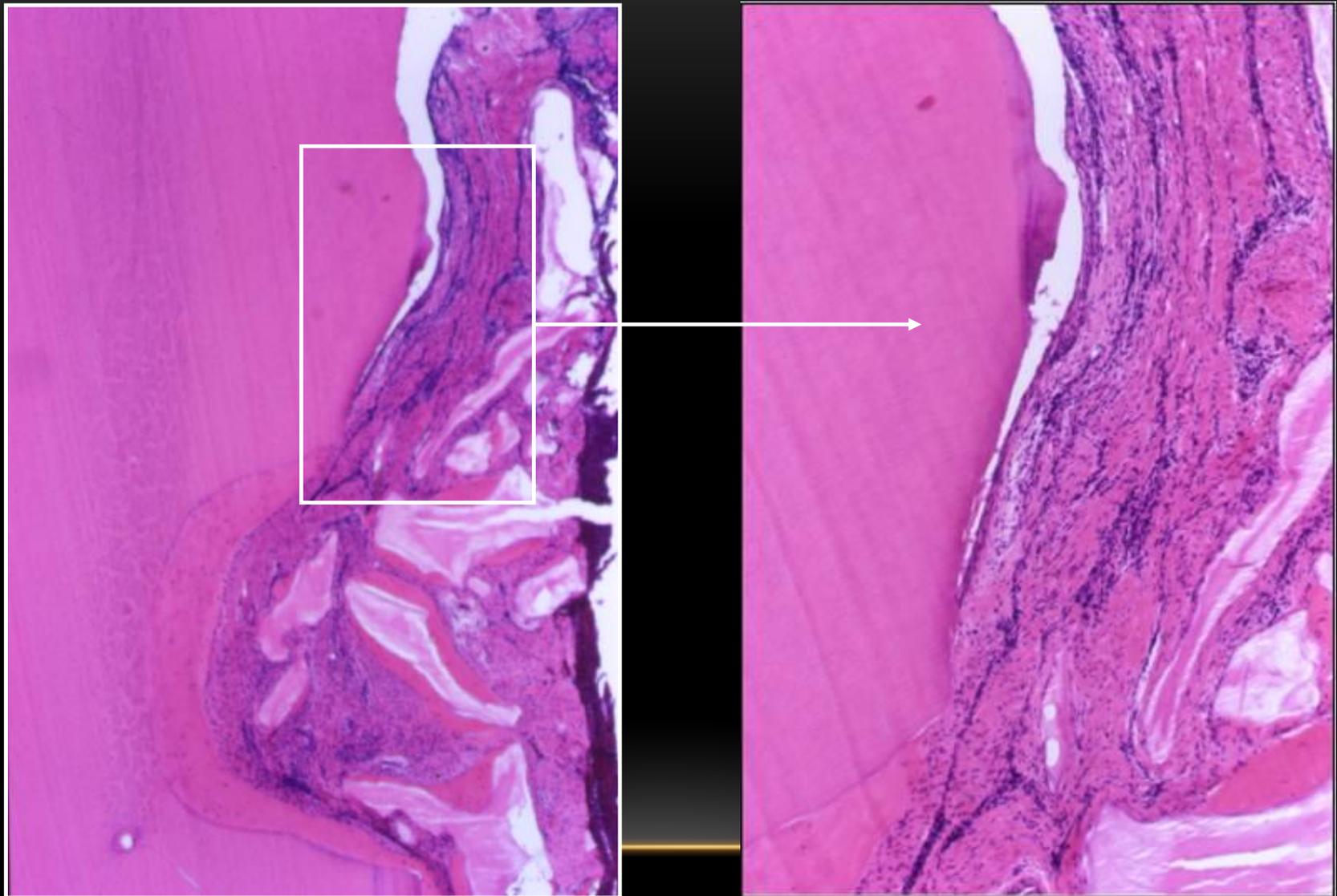
Sculean A, Windisch P, Keglevich T, Chiantella GC, Gera I, Donos N. Clinical and histological evaluation of human intrabony defects treated with an enamel matrix protein combined with a bovine derived xenograft. *Int J Periodontics Restorative Dent* 2003; 23: 47-55

EMD + bone substitutes



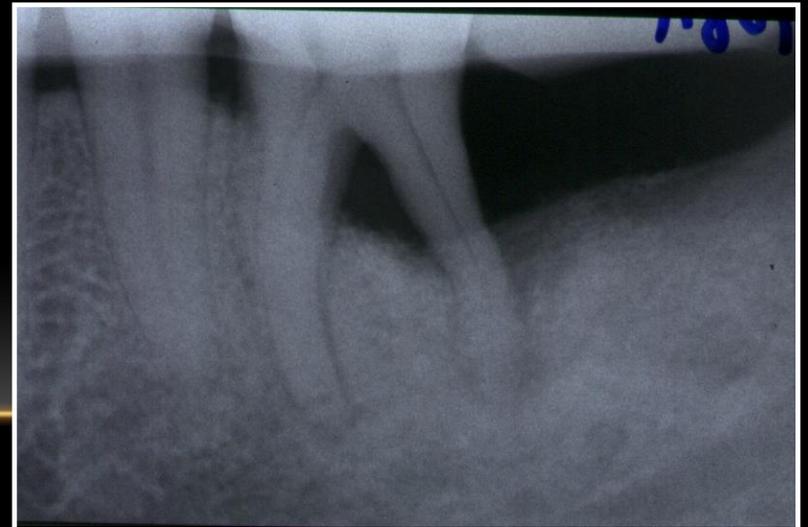
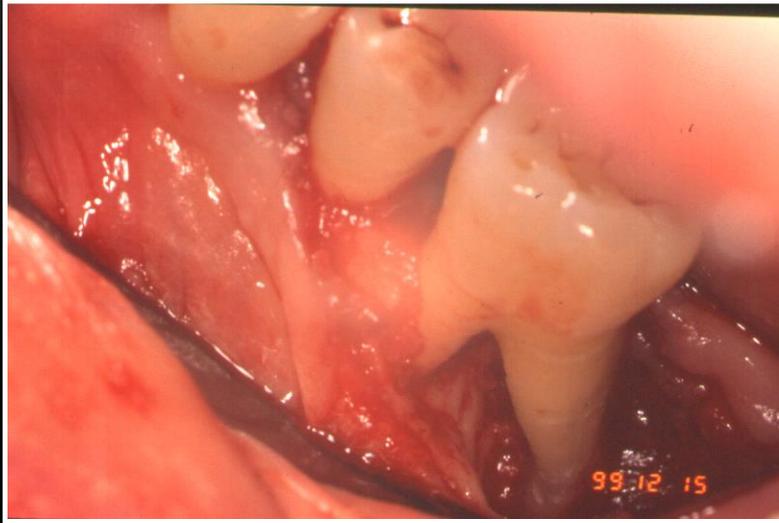
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EMD + bone substitutes

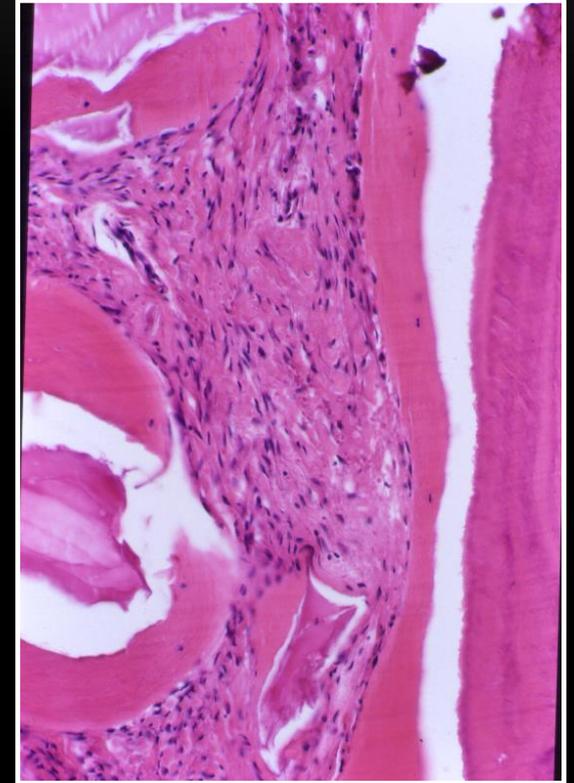
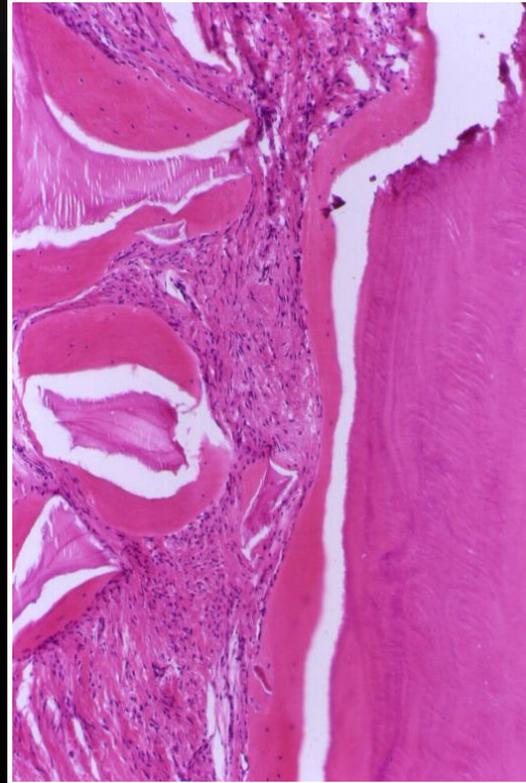
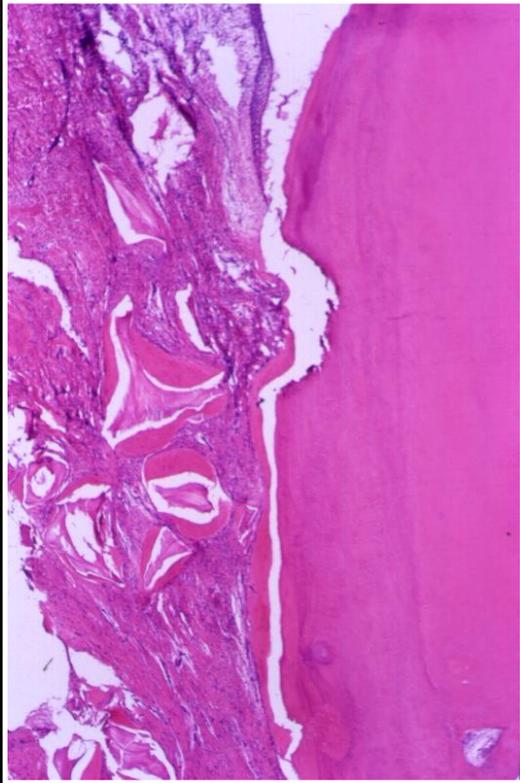


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BDX alone

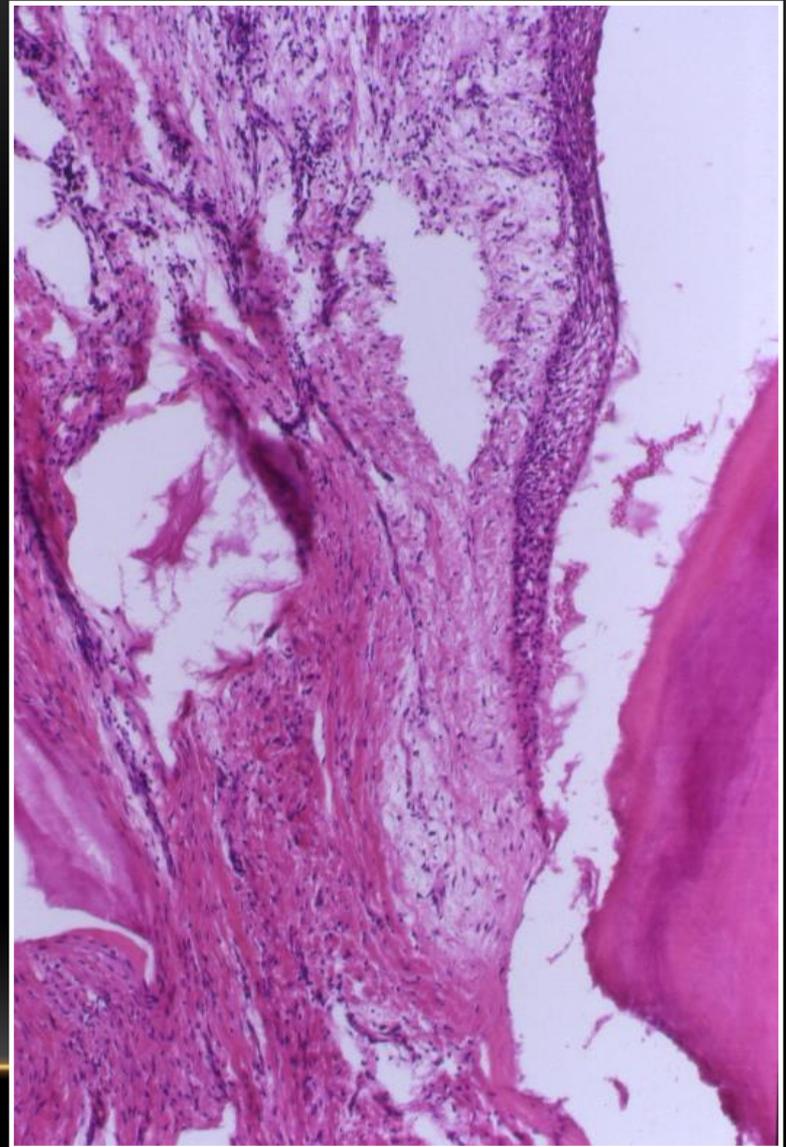
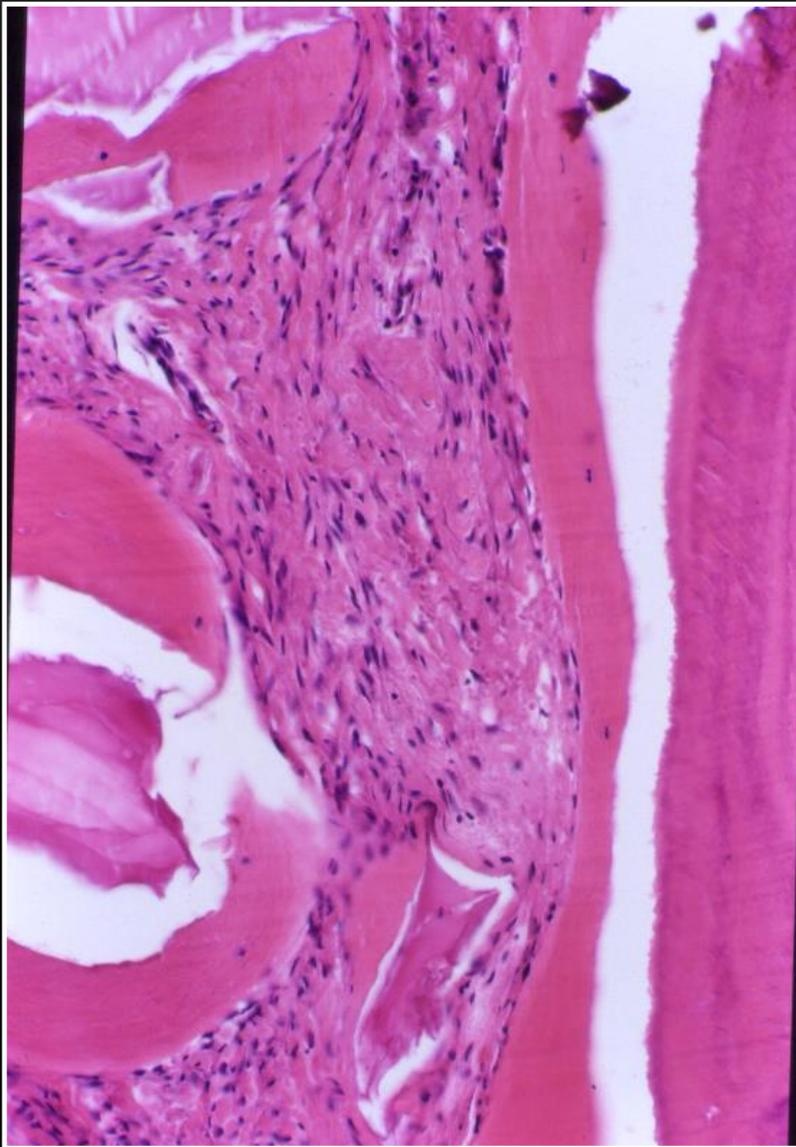


BDX alone



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BDX alone



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- EMD + bone substitutes
- **GTR + bone substitutes**
- Histological assessment of the regenerated periodontium
- Further therapeutic possibilities

GTR + BONE SUBSTITUTES

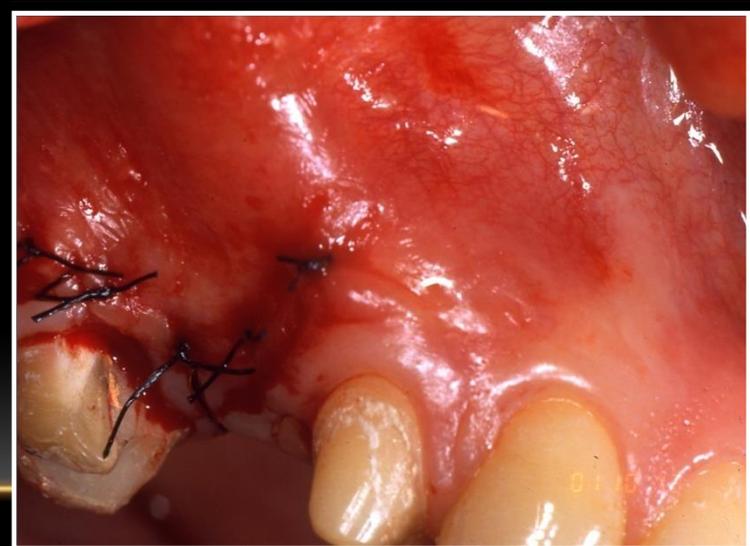
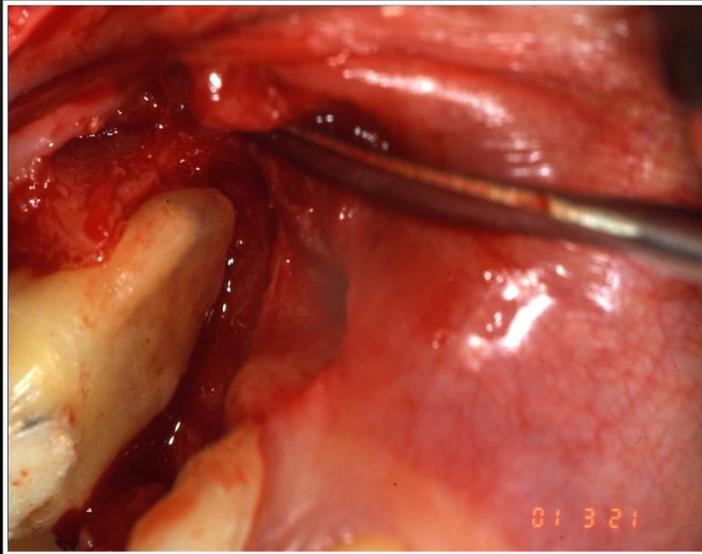
Materials and methods: human histological study

Group 1: GTR + BDX /5 patients/, Group 2: BDX-collagen + GTR /3 patients/, one defect each

Results: New cellular cementum with PDL, in most biopsies new bone formation around BDX particles in both groups

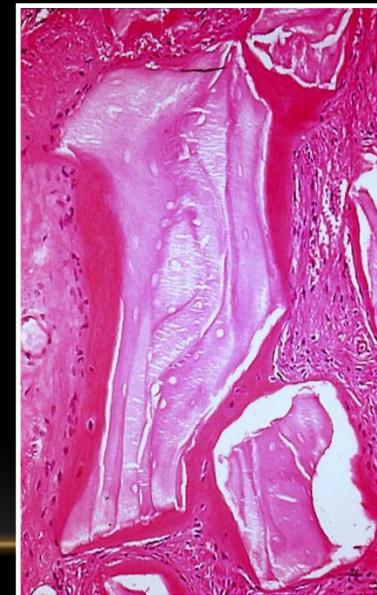
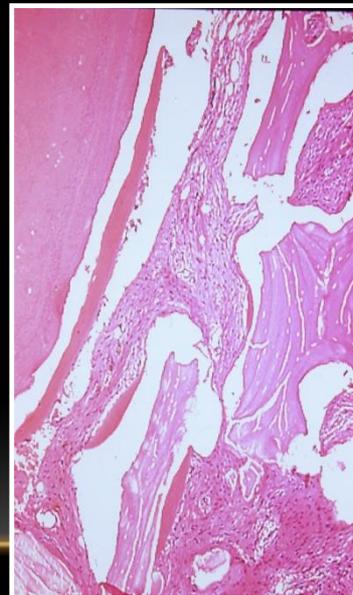
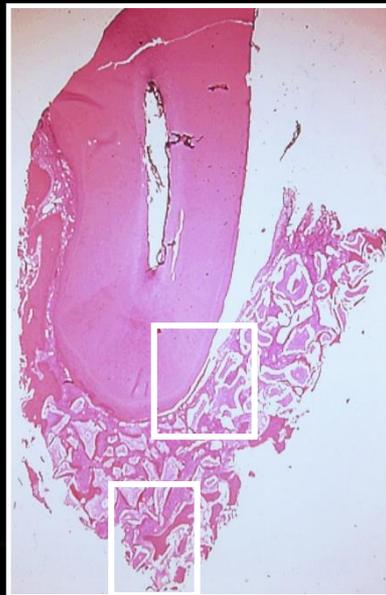
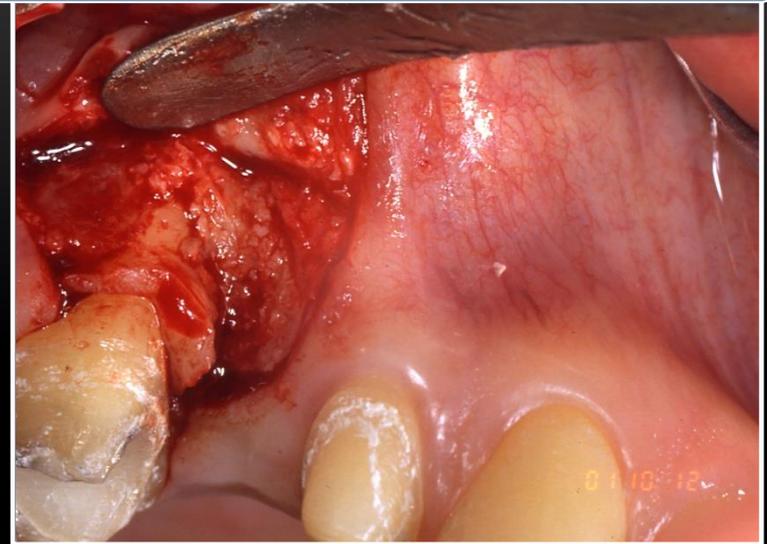
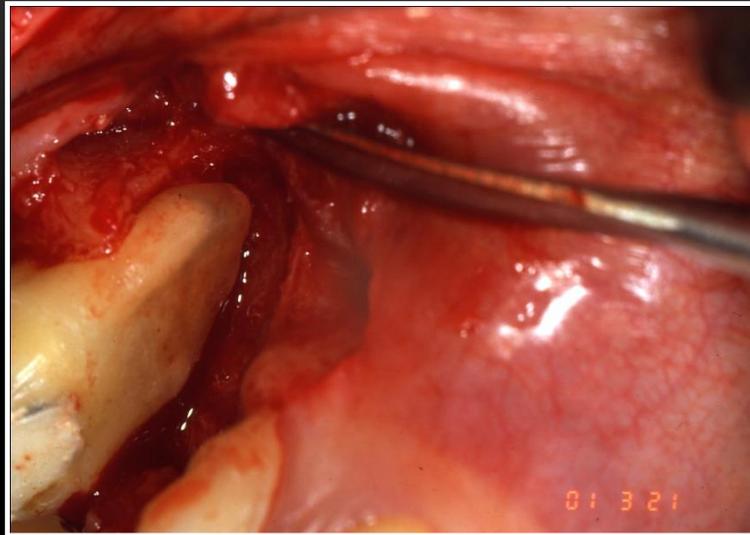
Conclusion: additional collagen-sponge matrix does not improve clinical outcome

GTR + bone substitutes



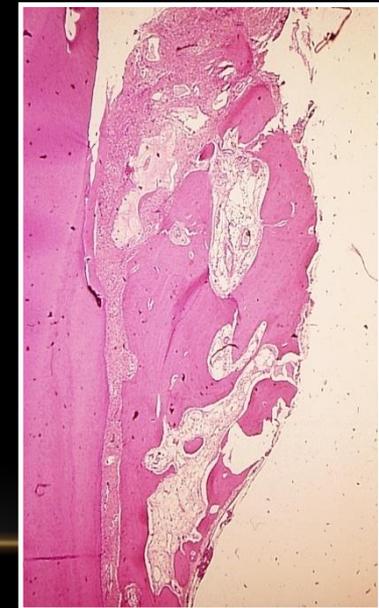
Sculean A, Stavropoulos A, Windisch P, Keglevich T, Karring T, Gera I. Healing of human intrabony defects following regenerative periodontal therapy with a bovine-derived xenograft and guided tissue regeneration. *Clin Oral Investig* 2004; 8: 70-74.

GTR + bone substitutes



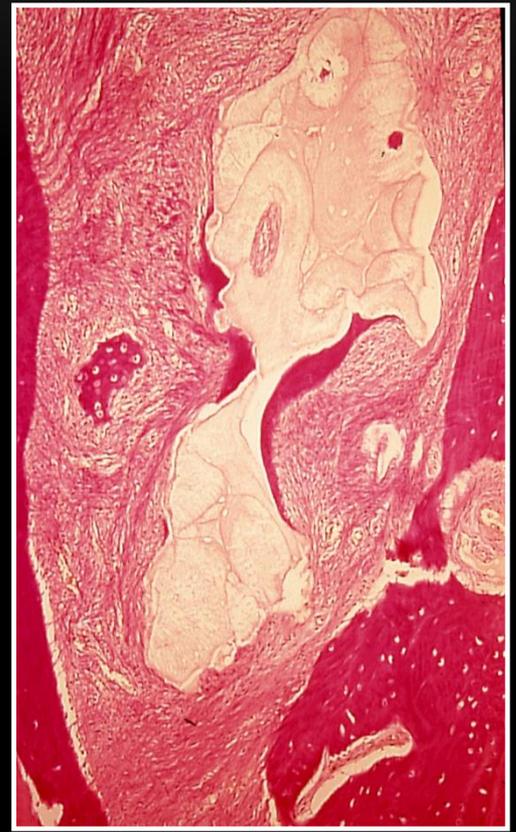
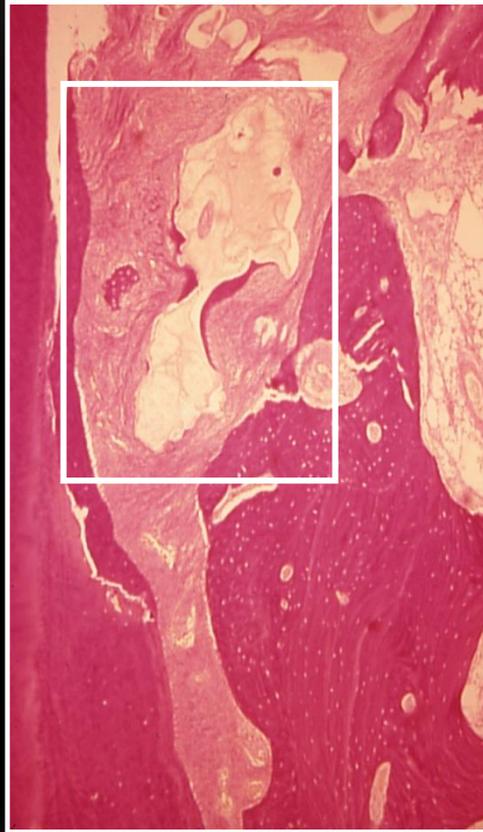
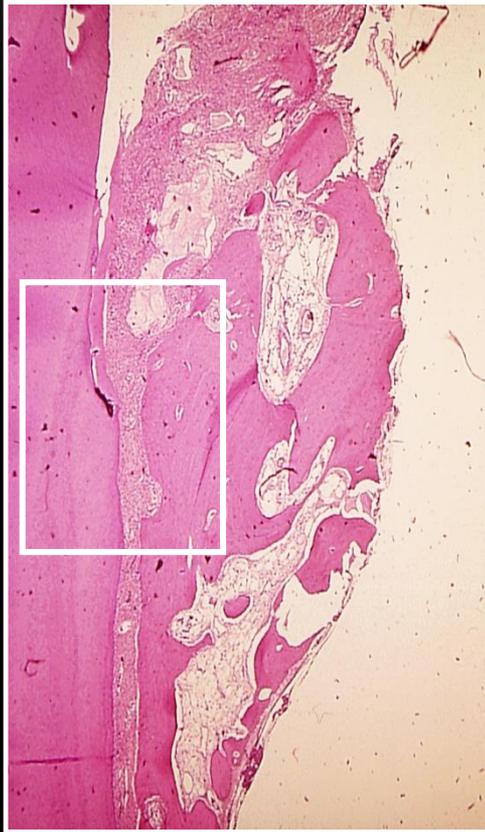
Sculean A, Stavropoulos A, Windisch P, Keglevich T, Karring T, Gera I. Healing of human intrabony defects following regenerative periodontal therapy with a bovine-derived xenograft and guided tissue regeneration. *Clin Oral Investig* 2004; 8: 70-74.

GTR + bone substitutes



Sculean A, Stavropoulos A, Windisch P, Keglevich T, Karring T, Gera I. Healing of human intrabony defects following regenerative periodontal therapy with a bovine-derived xenograft and guided tissue regeneration. *Clin Oral Investig* 2004; 8: 70-74.

GTR + bone substitutes



Sculean A, Stavropoulos A, Windisch P, Keglevich T, Karring T, Gera I. Healing of human intrabony defects following regenerative periodontal therapy with a bovine-derived xenograft and guided tissue regeneration. *Clin Oral Investig* 2004; 8: 70-74.

CONCEPTUAL DEVELOPMENT

- GTR
- EMD
- GTR vs. EMD
- New treatment modalities using EMD
- EMD + bone substitutes
- GTR + bone substitutes
- **Histological assessment of the regenerated periodontium**
- Further therapeutic possibilities

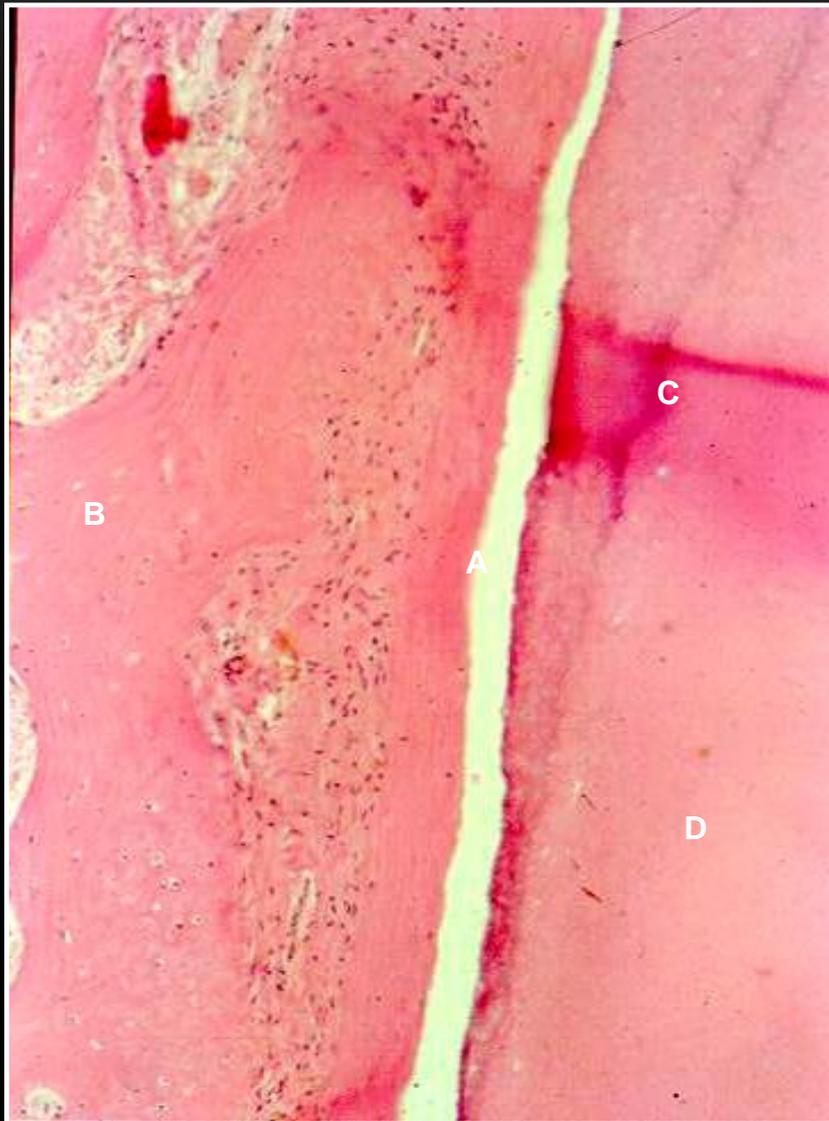
HISTOLOGICAL ASSESSMENT OF THE REGENERATED PERIODONTIUM

Tissue differentiating staining

A regenerated periodontal ligament containing **newly formed oxytalan fibers** was observed in all specimens. Many of them **inserted into the newly formed cementum** on the root surface. It is concluded that oxytalan fibers are formed **de novo** in human regenerated periodontal ligament tissue.

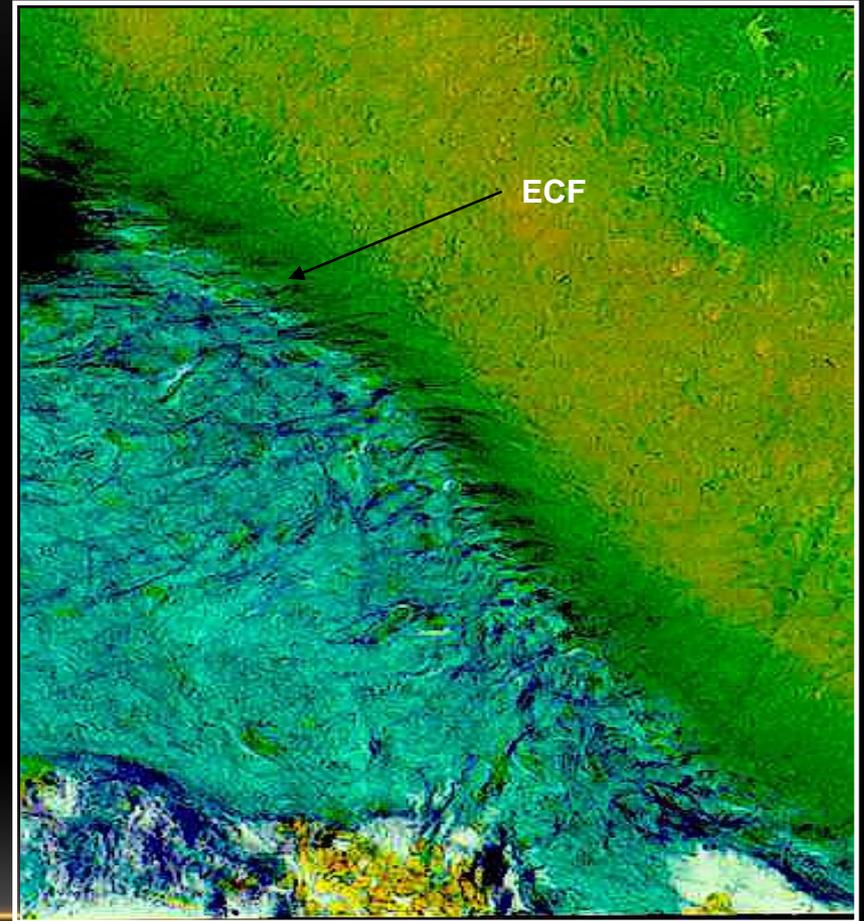
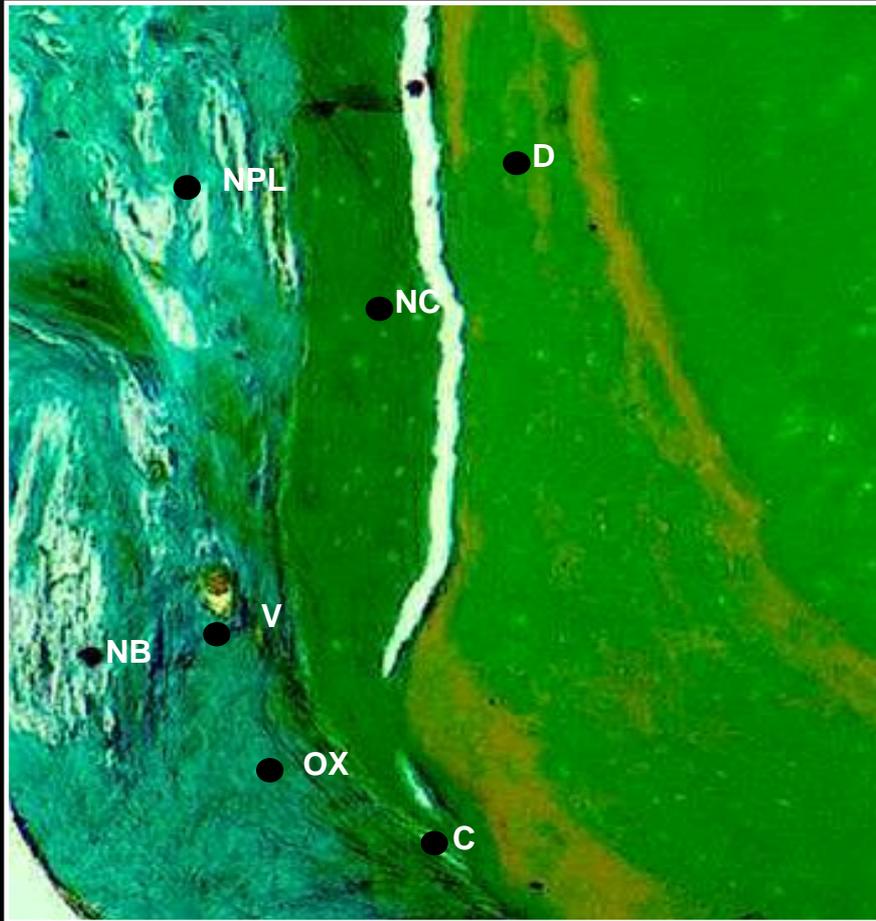
Sculean, A., Donos, N., Windisch P., Reich E., Gera I., Brex M., Karring T.: Presence of oxytalan fibers in human regenerated periodontal ligament. *J. Clin Periodontol* 1999;26: 318-321.

Histological assessment of the regenerated periodontium

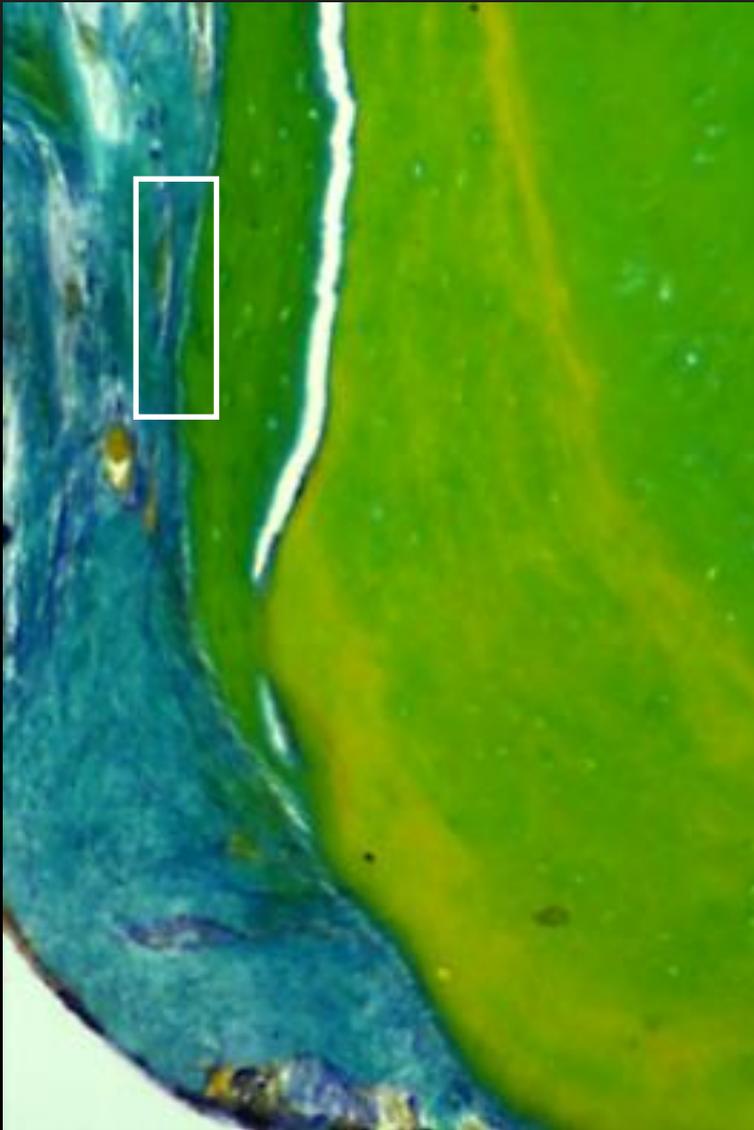


Sculean, A., Donos, N., Windisch P., Reich E., Gera I., Brex M., Karing T.: Presence of oxytalan fibers in human regenerated periodontal ligament. *J. Clin Periodontol* 1999;26: 318-321.

Histological assessment of the regenerated periodontium



Histological assessment of the regenerated periodontium



Sculean, A., Donos, N., Windisch P., Reich E., Gera I., Brex M., Karing T.: Presence of oxytalan fibers in human regenerated periodontal ligament. *J. Clin Periodontol* 1999;26: 318-321.

Histological assessment of the regenerated periodontium

Immunohistochemistry I

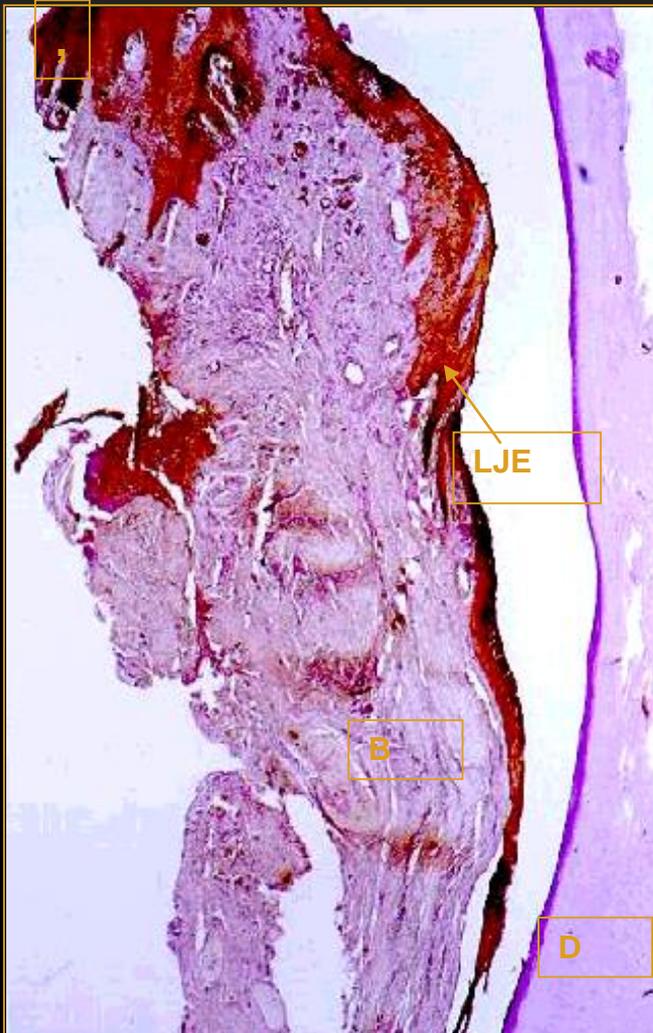
- a) The **reformed junctional epithelium**, following any type of surgical procedure, displays a **similar pattern of cytokeratin expression to the original junctional epithelium**
- b) In the **newly formed periodontal ligament**, **no expression of cytokeratins** is present
- c) The epithelial **rests of Malassez do not seem to reform** after regenerative periodontal surgery

Immunohistochemistry II

The presented findings indicated that

- a) the reformed PDL displayed a similar expression of vimentin to the intact (original) PDL,
- b) the cells capable of regenerating new PDL and new cementum appear to be of mesenchymal origin and their source may be in the intact PDL.

Histological assessment of the regenerated periodontium



Broad spectrum monoclonal antibodies against cytokeratin 1, 2, 5, 6, 7, 8, 10, 11, 16 and 19. LJE - long junctional epithelium, B - bone, D - dentin. /25x magnification/



LJE - long junctional epithelium, B - bone, D: dentin, A: artefact. /25x magnification/

Histological assessment of the regenerated periodontium

A1, A2 – artefacts

**GCT – gingival
connective tissue**

**LJE -long junctional
epithelium**

OC – old cementum

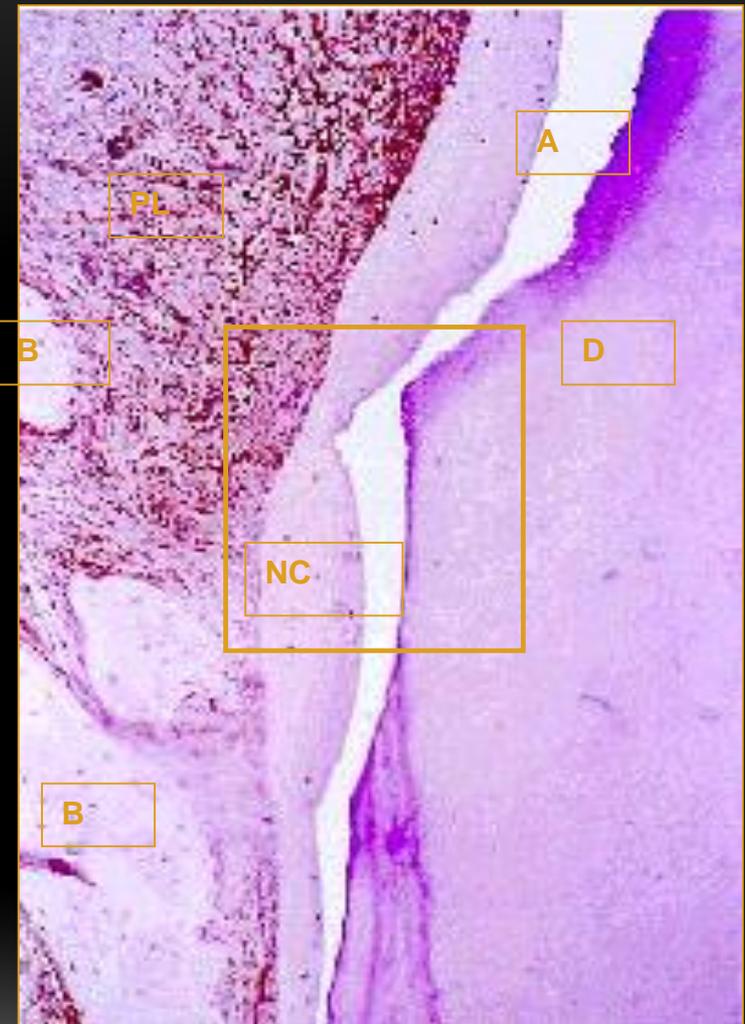
/150 x magnification/



Histological assessment of the regenerated periodontium



Antibodies against cytokeratin
NC–new cementum, PL– periodontal ligaments, B – alveolar bone, D - dentin, A – artefact. /50 x magnification/



Antibodies against Vimentin
NC –new cementum, PL – periodontal ligaments, B – alveolar bone, D - dentin, A – artefact . /50 x magnification/

Histological assessment of the regenerated periodontium

NC – new cementum

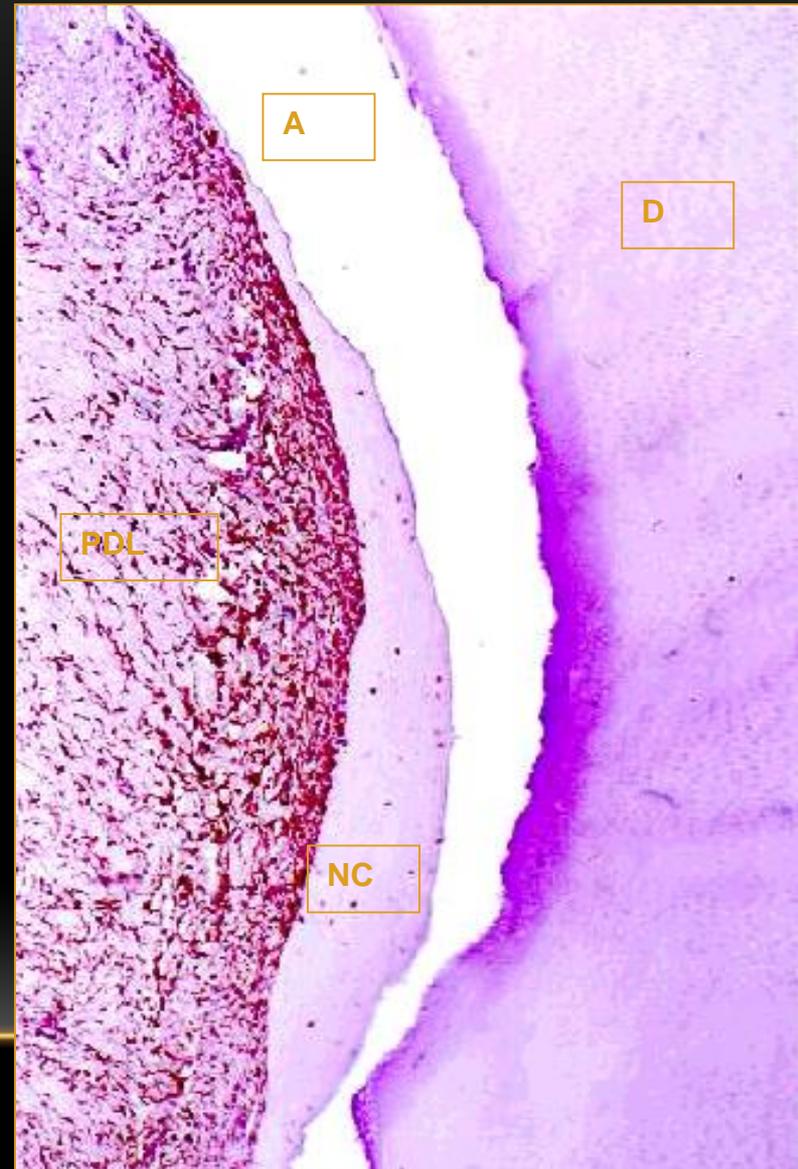
PDL – periodontal ligaments

B – alveolar bone

D - dentin

**A – artefact, vimentin antibody
against connective tissue**

/150 x magnification/



Histological assessment of the regenerated periodontium

Immunohistochemistry III

Immunohistochemical evaluation demonstrated the **presence of EMD** on all test root surfaces during the entire **observation period of 4 weeks**. No EMD was detected on any of the control roots. The results demonstrate for the first time in humans that **EMD is present** on treated root surfaces for **up to 4 weeks following periodontal surgery**.

Sculean A, Windisch P, Keglevich T, Fabi B, Lundgren E, Lyngstadaas PS. Presence of an enamel matrix protein derivative on human teeth following periodontal surgery. Clin Oral Investig. 2002 Sep;6(3):183-7.

Histological assessment of the regenerated periodontium

Immunohistochemistry IV

This study investigated immunohistochemically in humans the expression of matrix molecules associated with periodontal tissues reformed after treatment with EMD.

Osteopontin expression was most intense at the border **near the newly formed cementum and bone**.

In the regenerated periodontal ligament, **collagen I and III** were localized throughout the **entire periodontal ligament** connective tissue.

Within the newly formed PDL connective tissue the immunohistochemical staining was **stronger for collagen III than for collagen I**

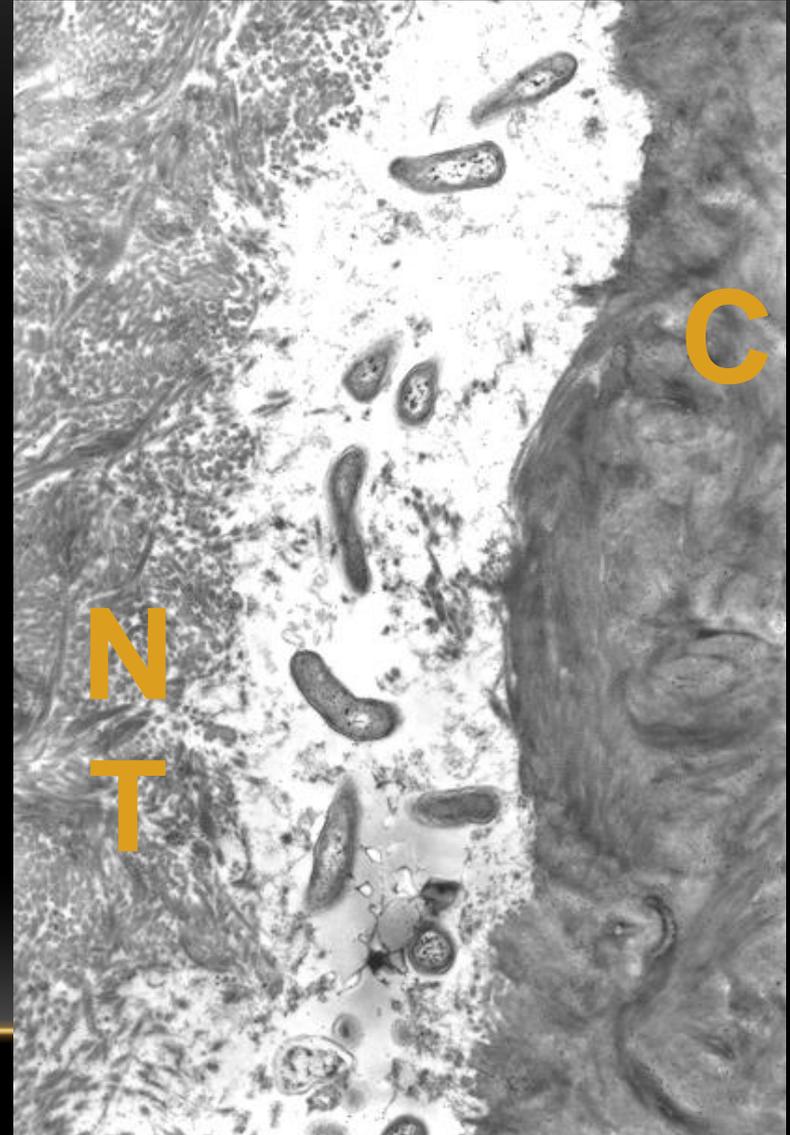
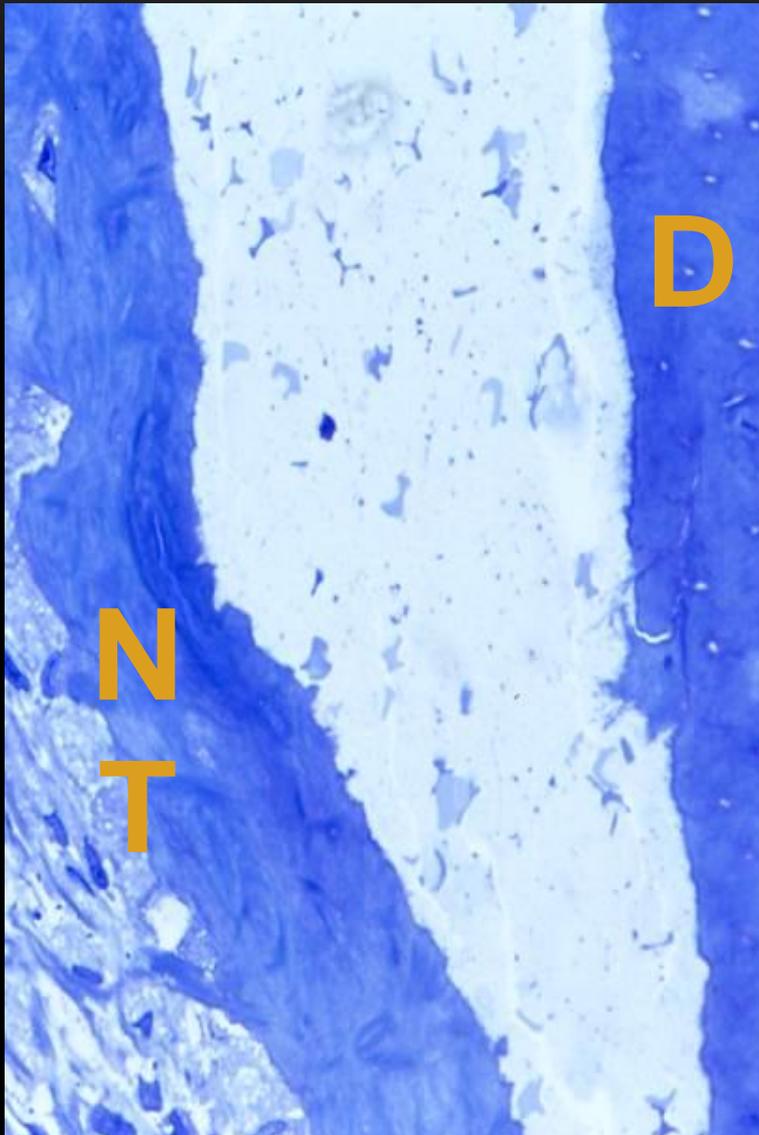
Histological assessment of the regenerated periodontium

Electronmicroscopy

Tissues developing on the root surface following application of EMD within the first month could be characterized as follows :

- a) bone-like tissue resembling **cellular intrinsic fibres** cementum may develop on the root surfaces, instead of AEFC.
- b) EMD may both induce **de novo** formation of a mineralized **connective tissue** on scaled root surfaces and stimulate matrix deposition on old native cementum.
- c) Interfacial bonding appeared to be weak after 6 weeks of healing.

Histological assessment of the regenerated periodontium

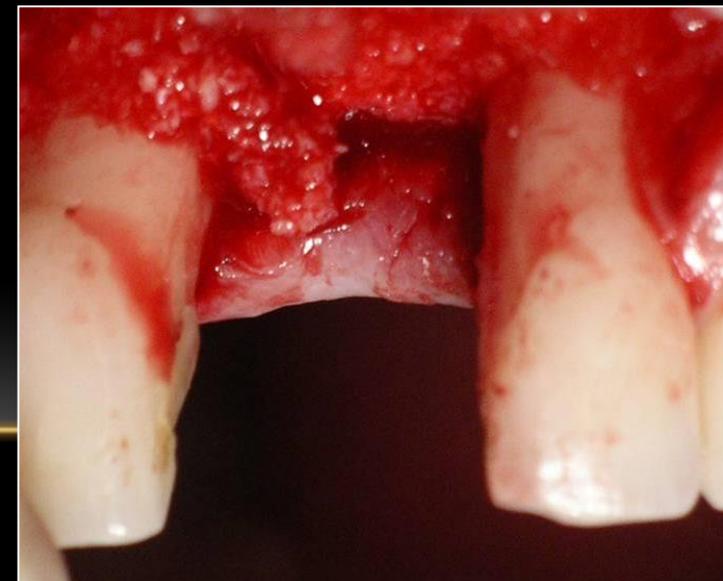
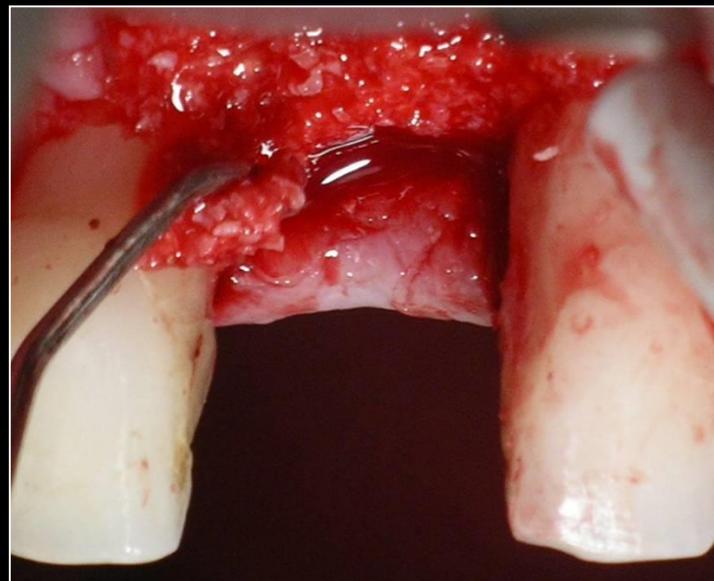
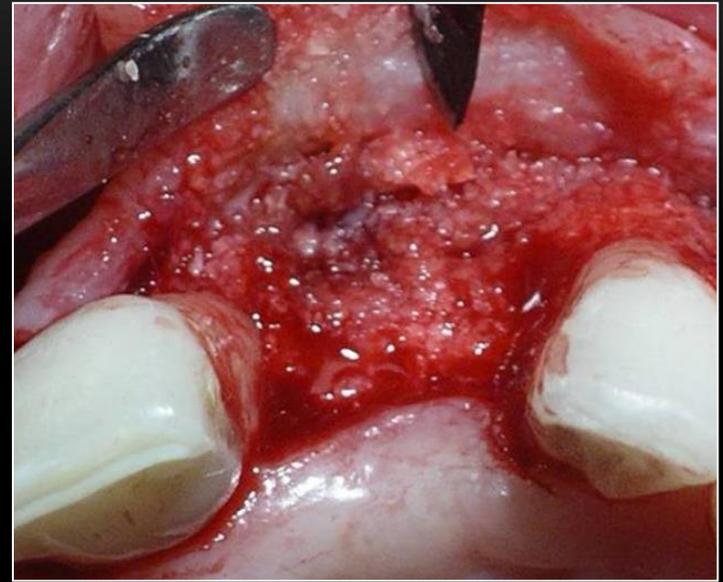
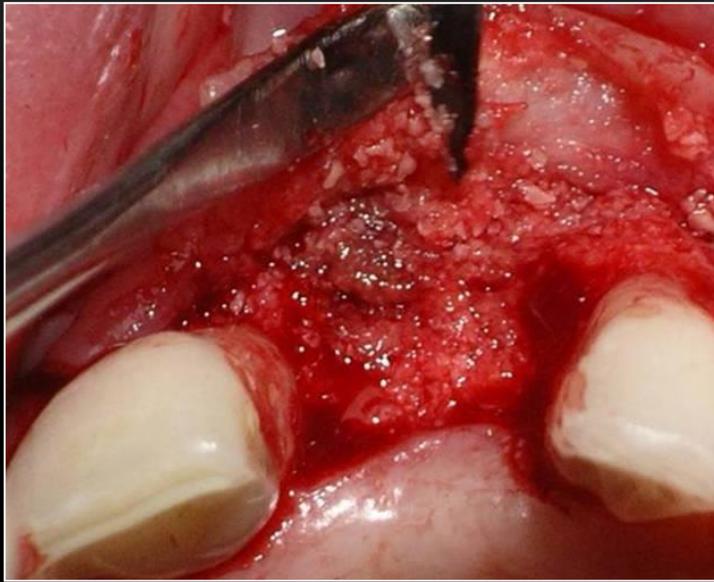


Bosshardt DD, Sculean A, Windisch P, Pjetursson BE, Lang NP. Effects of enamel matrix proteins on tissue formation along the roots of human teeth. *J Periodontol Res.* 2005 Apr;40(2):158-67.

LIMITATIONS OF EXISTING PROCEDURES

- Limited periodontal bone regeneration
- No predictable hard tissue formation around bone substitutes
- Residual pockets
- No regeneration in the suprabony component of horizonto-vertical defects /particular difficulties with adjacent edentulous ridge/
- Postoperative gingival recession

Limitations of existing procedures



CONCEPTUAL DEVELOPMENT

- GTR
- EMD
- GTR vs. EMD
- New treatment modalities using EMD
- EMD + bone substitutes
- GTR + bone substitutes
- Histological assessment of the regenerated periodontium
- **Further therapeutic possibilities**

FURTHER THERAPEUTIC POSSIBILITIES I

GTR+BDX+CTG

Indication: Edentulous ridge with periodontal defects at adjacent teeth

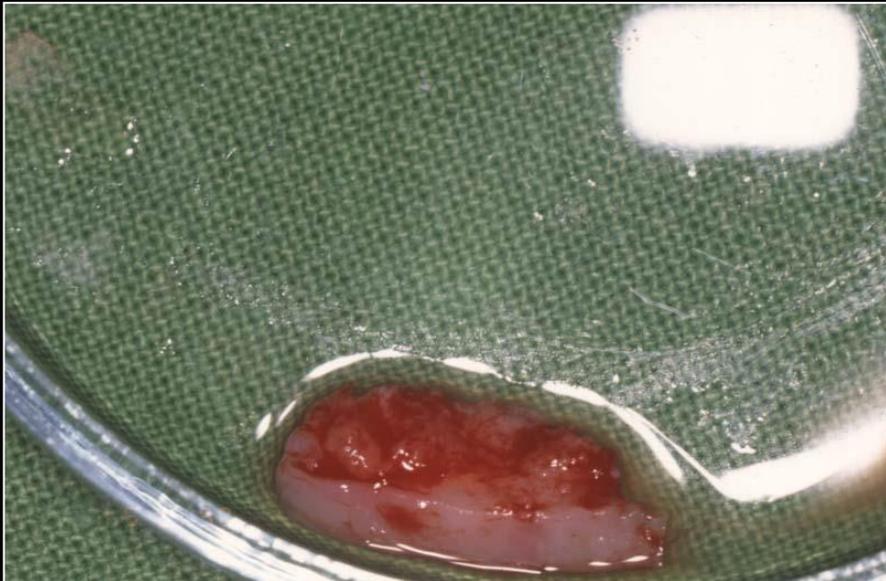
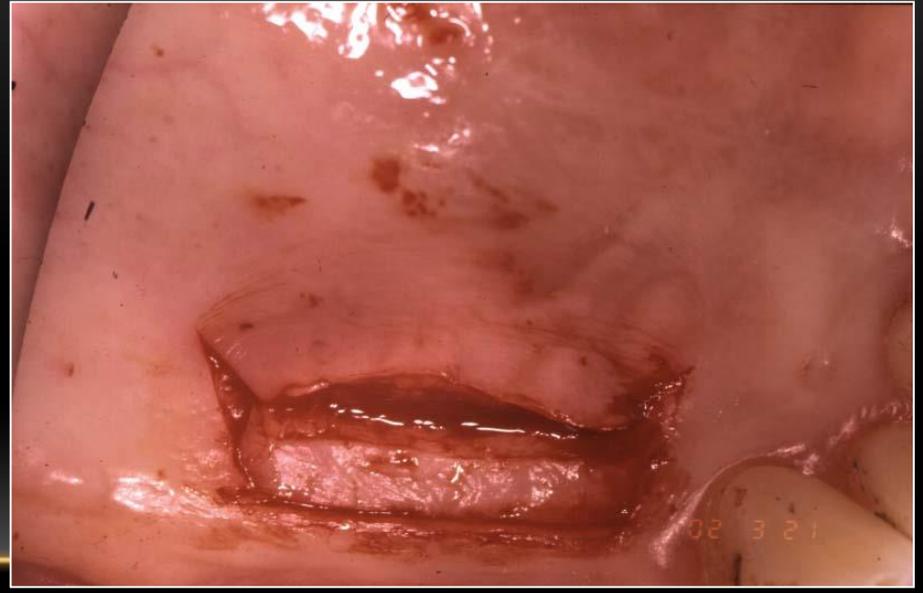
Proposed procedure:

Stage 1: GTR+BDX+connective tissue graft harvested from the palate for enlarging the keratinized tissue

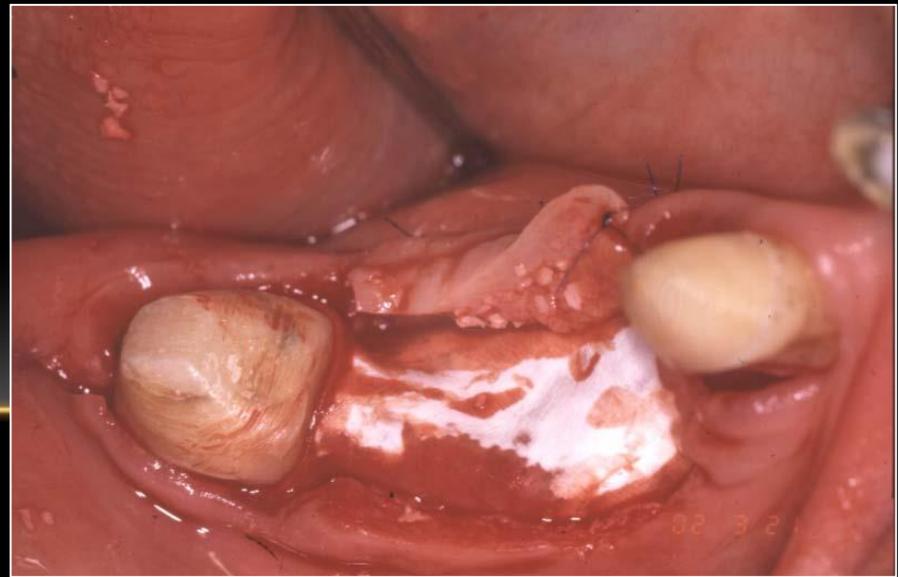
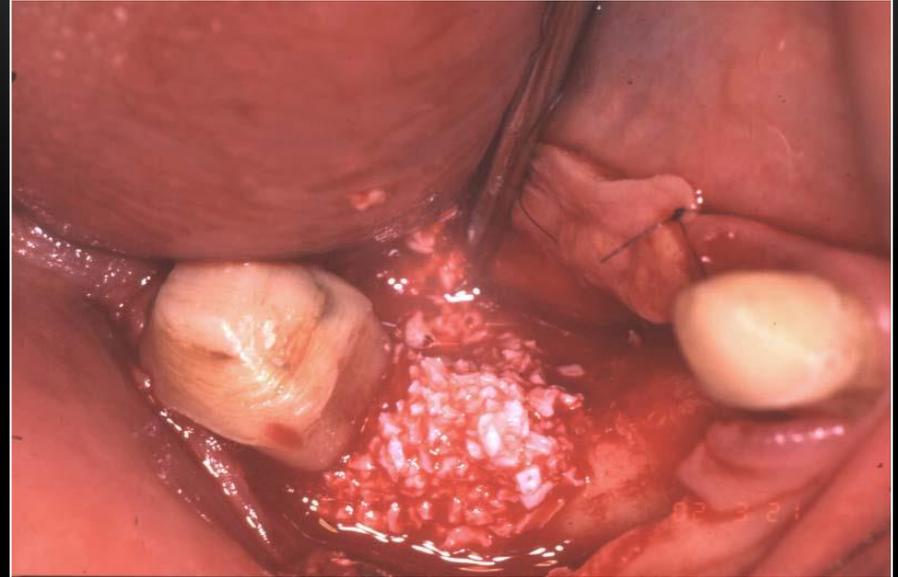
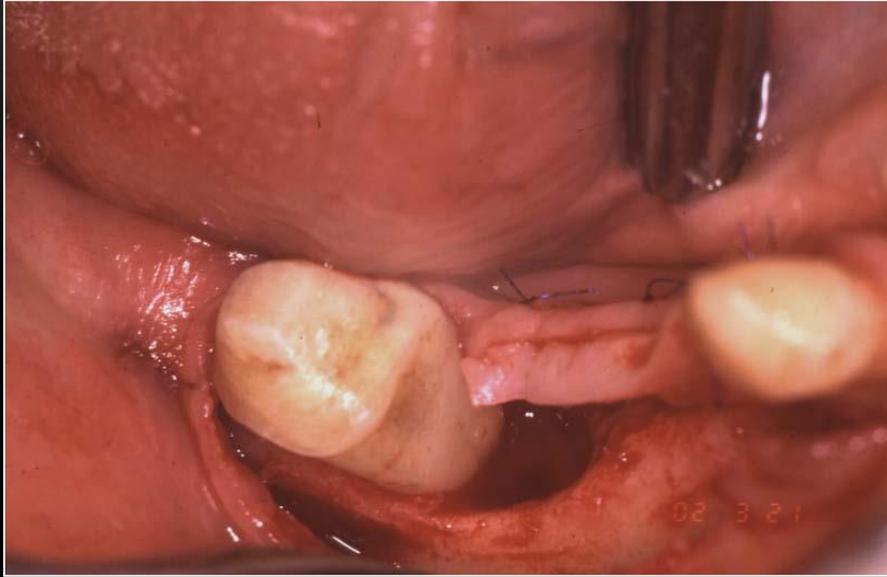
Stage 2: reentry, implant installation

Expected benefits: Ridge augmentation combined with periodontal regeneration

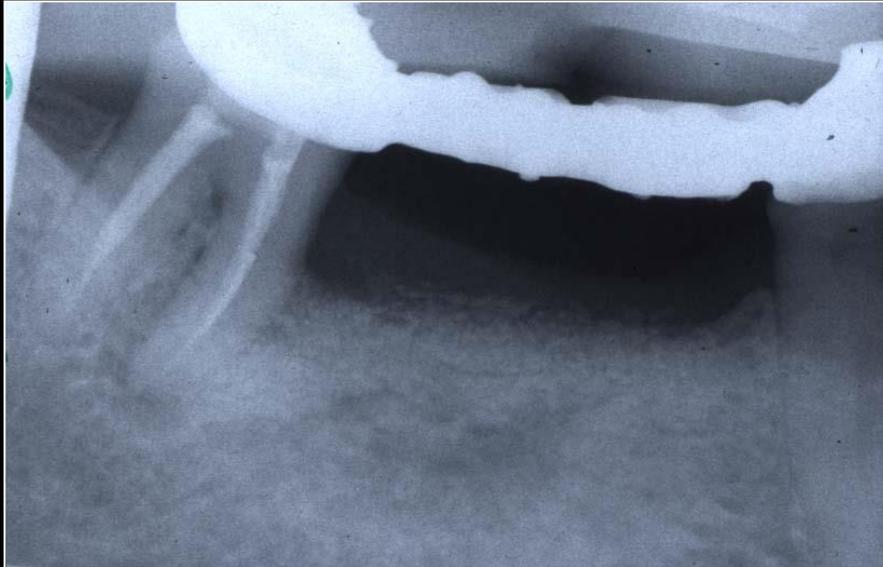
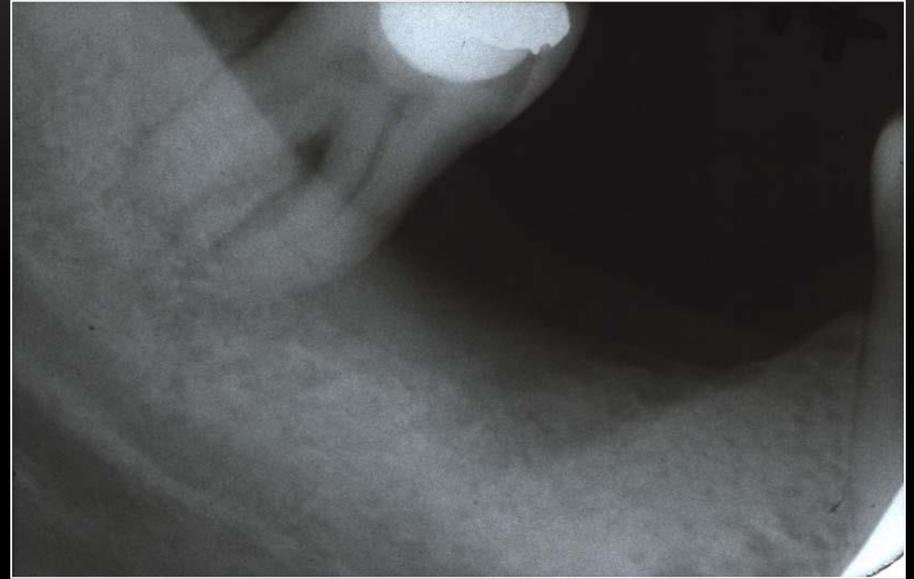
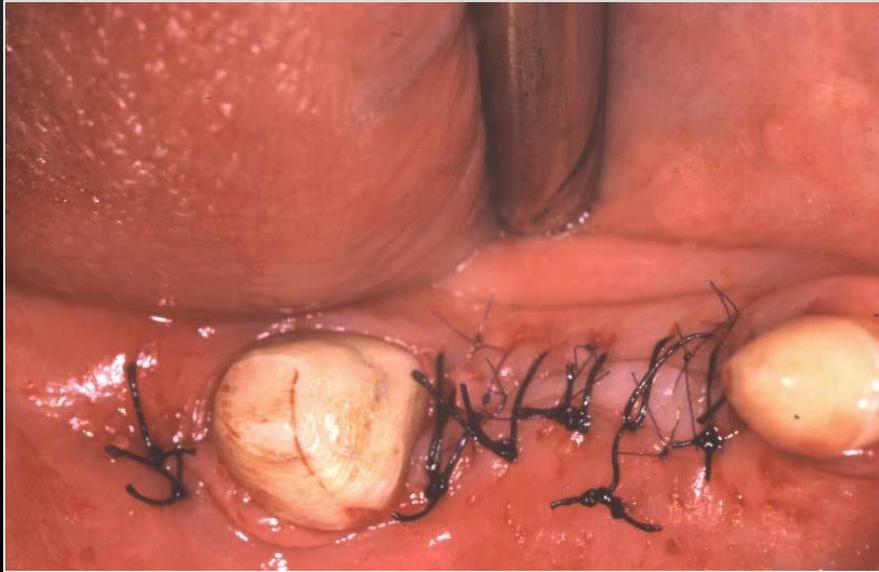
GTR+BDX+CTG



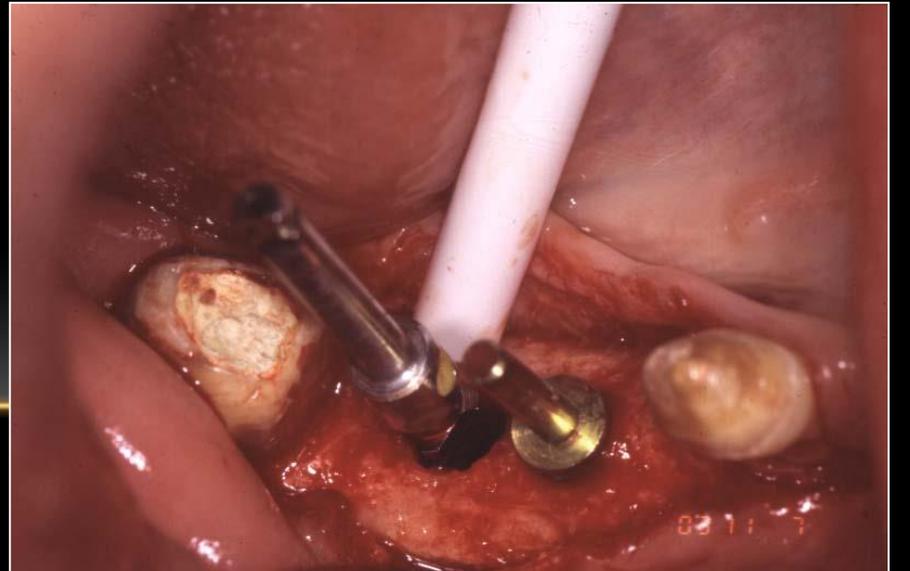
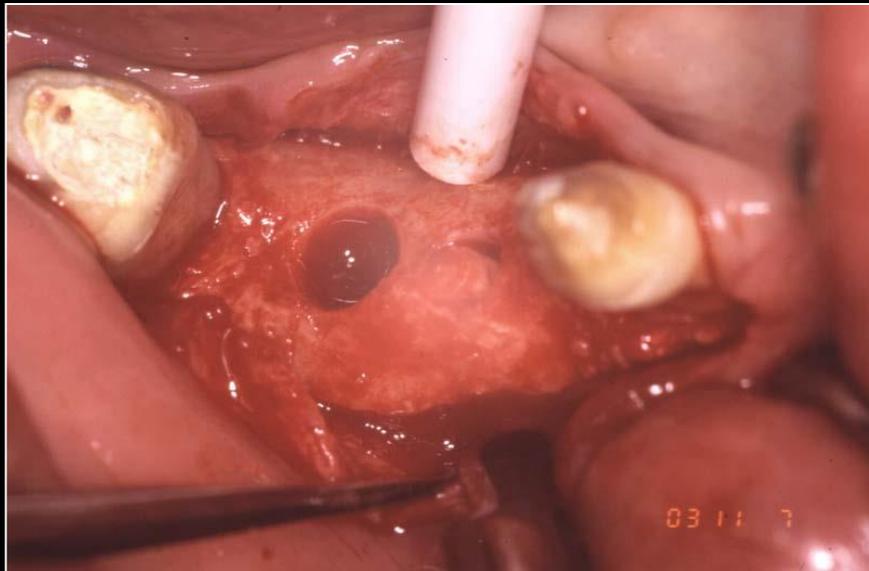
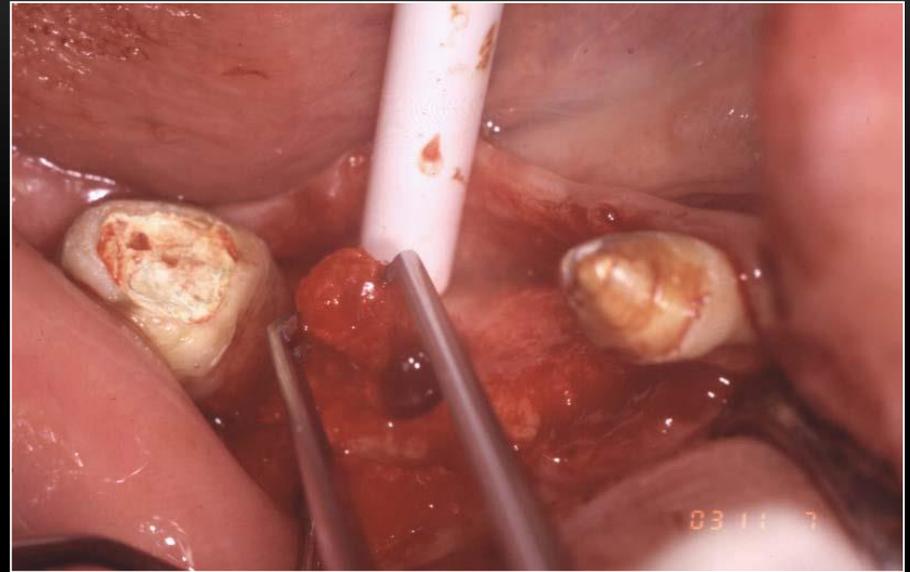
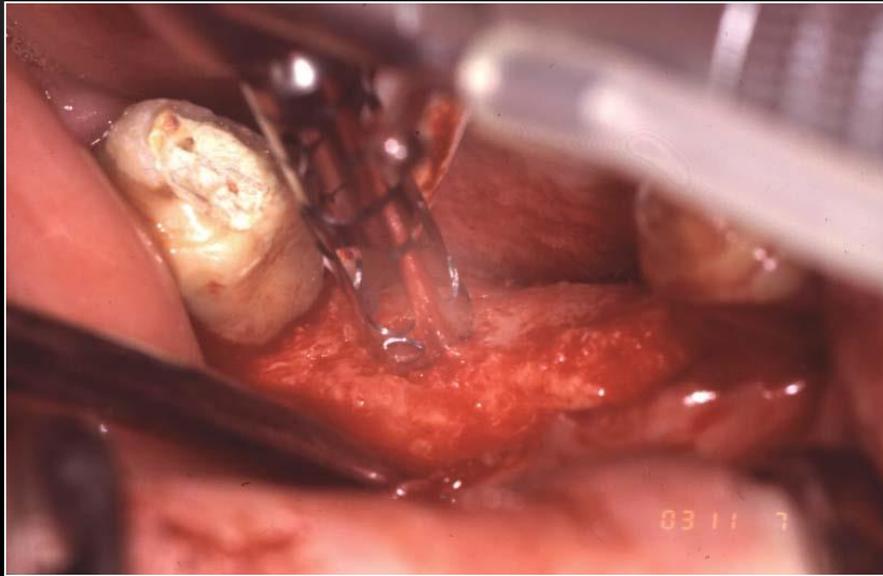
GTR+BDX+CTG



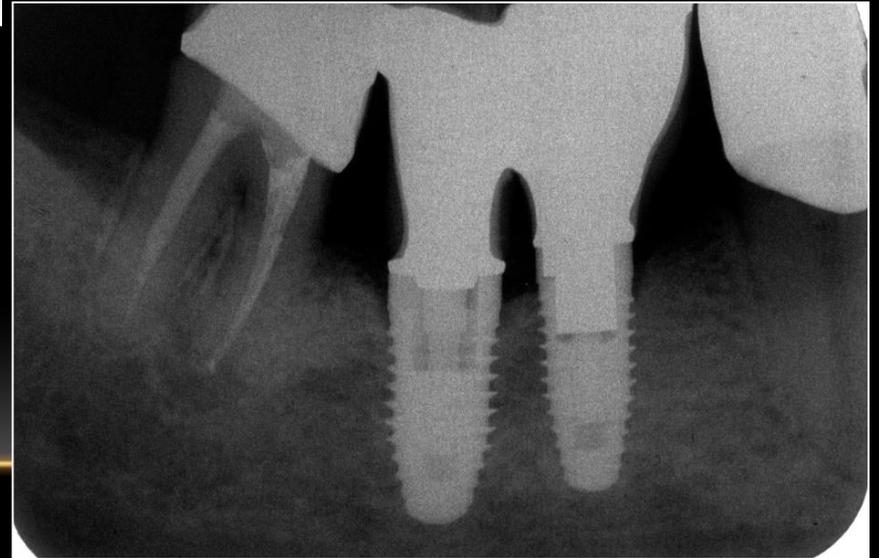
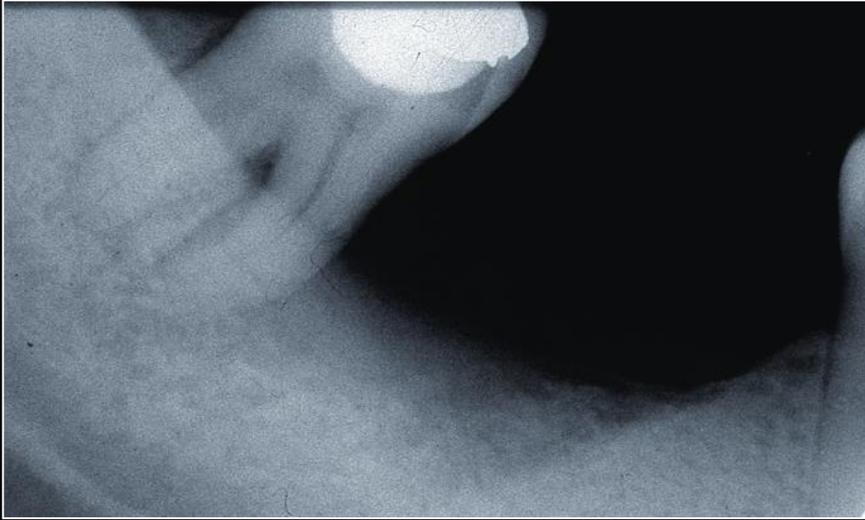
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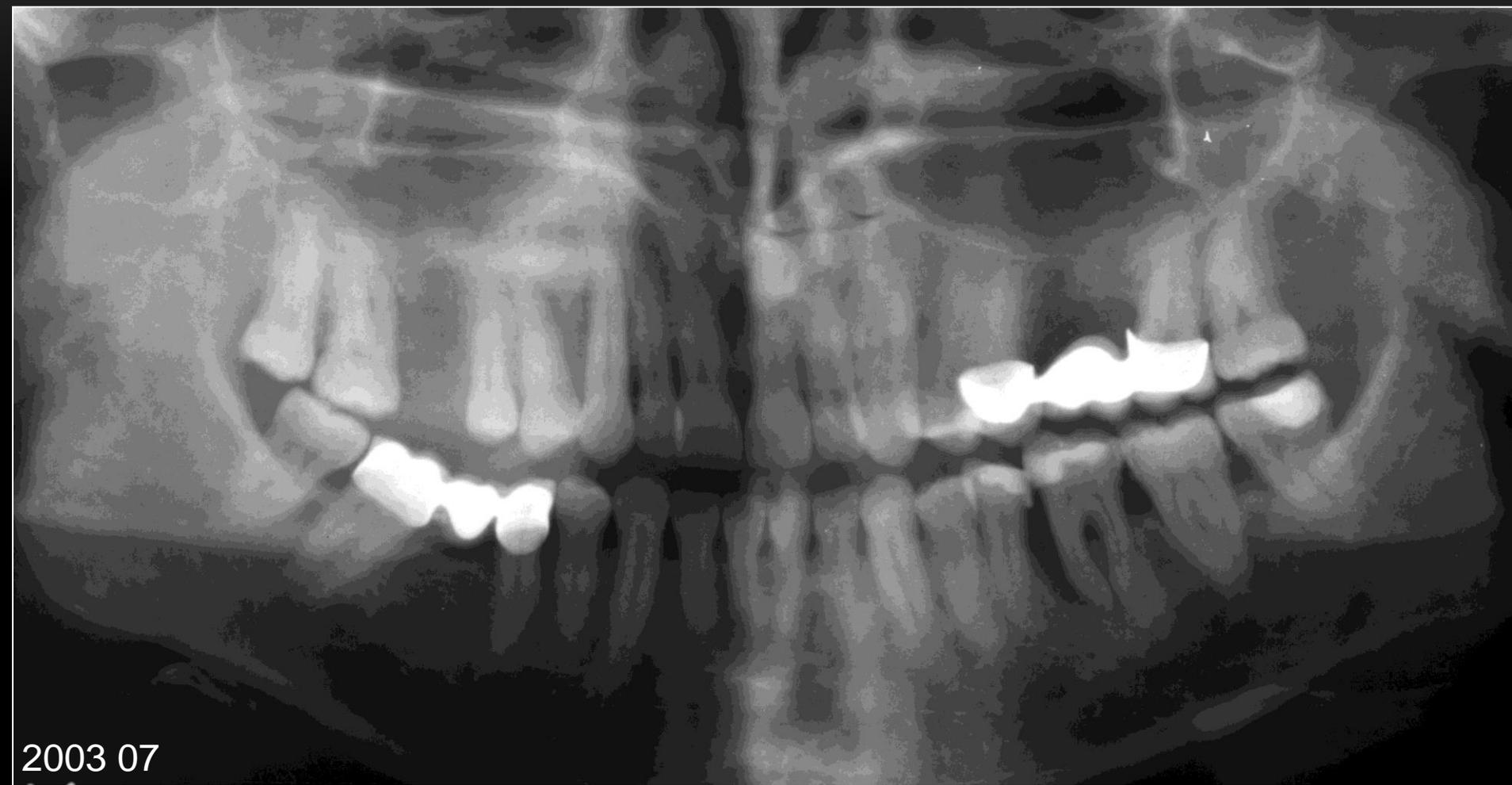


GTR+BDX+CTG



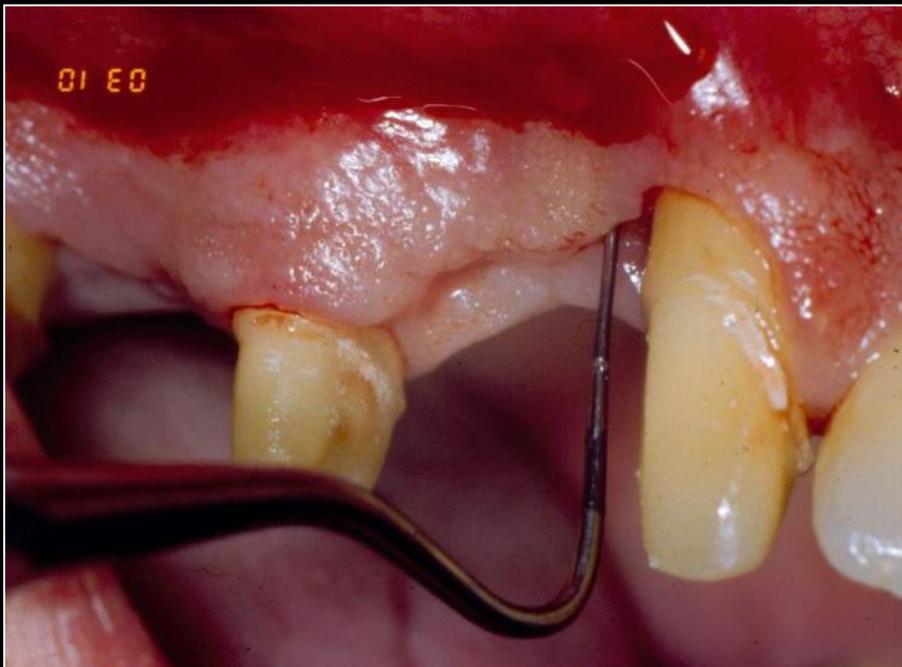
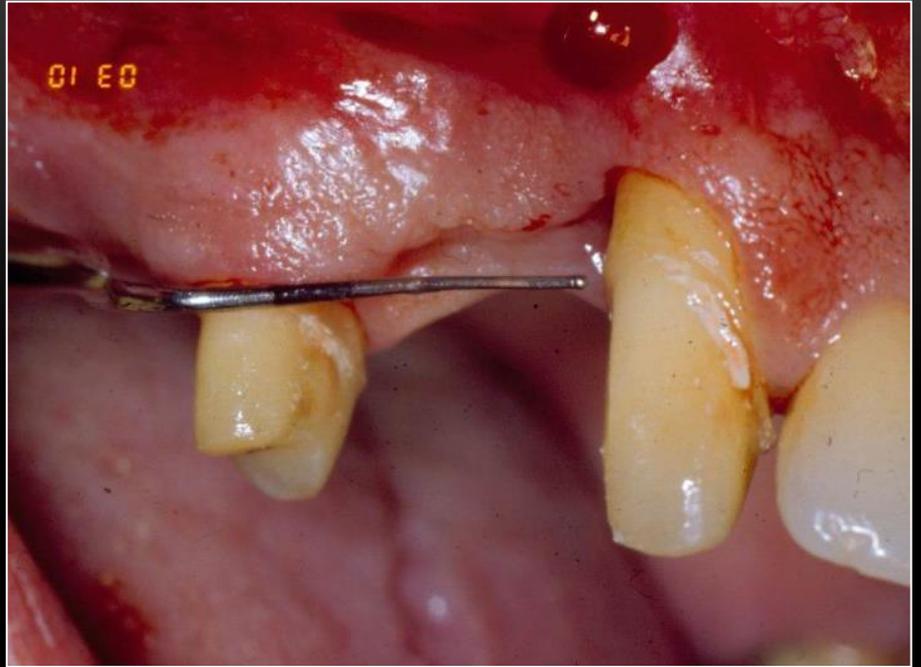
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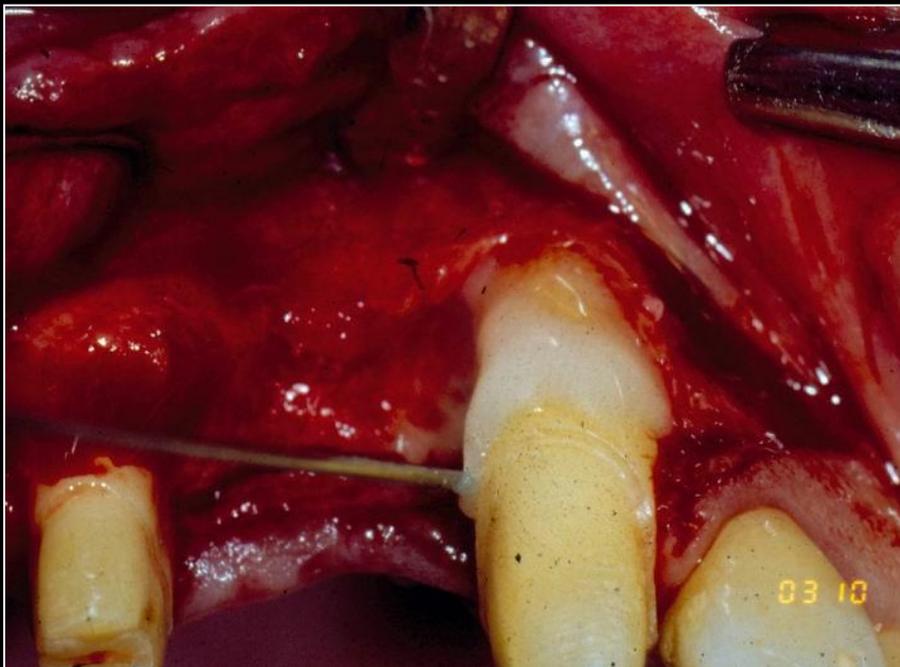
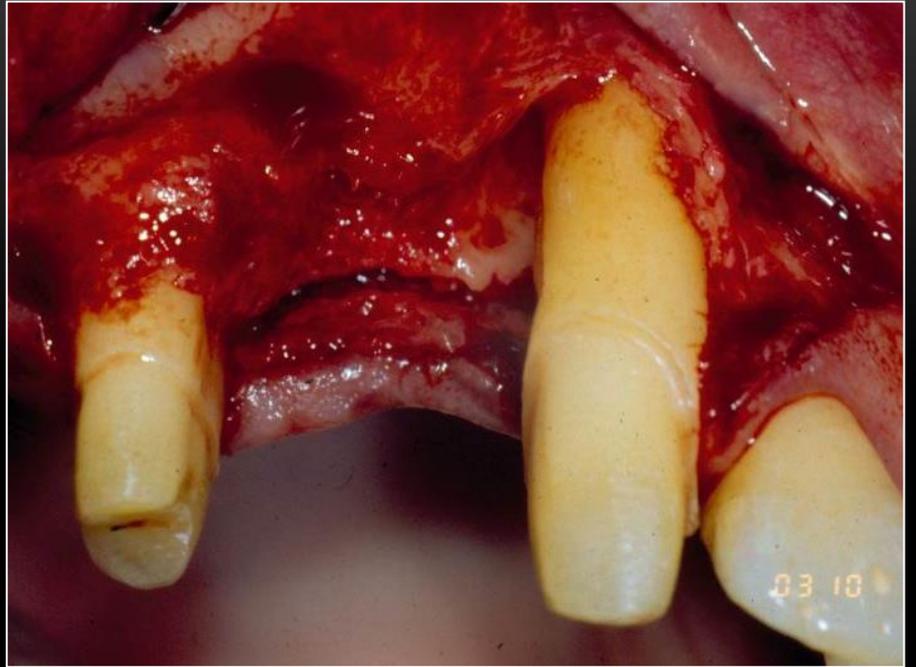
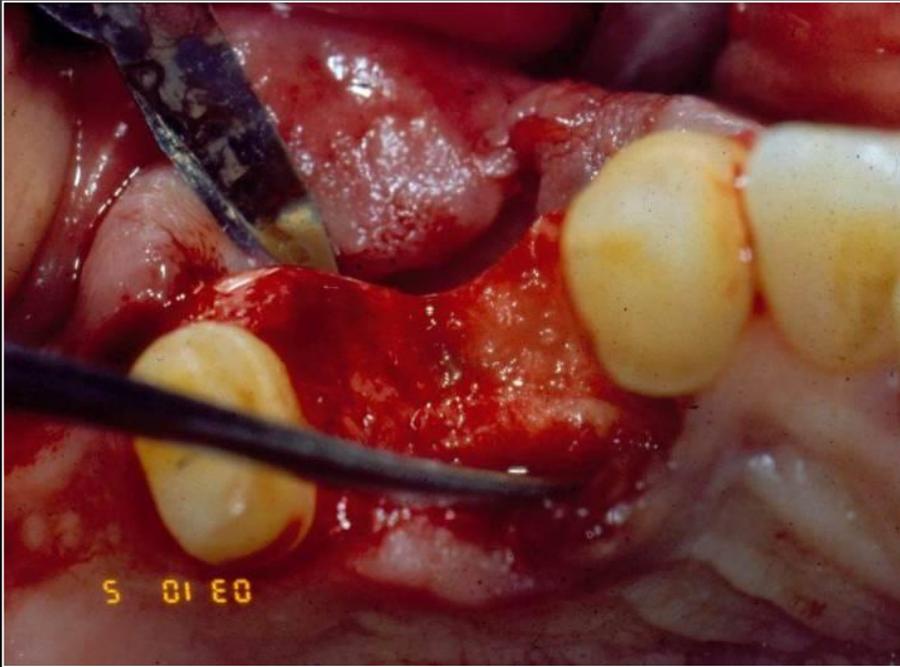


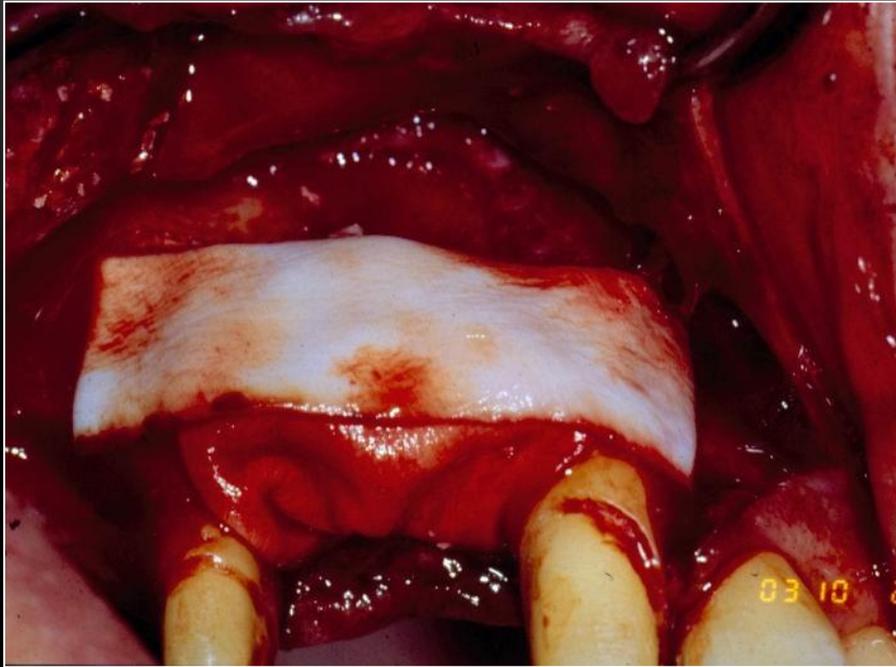


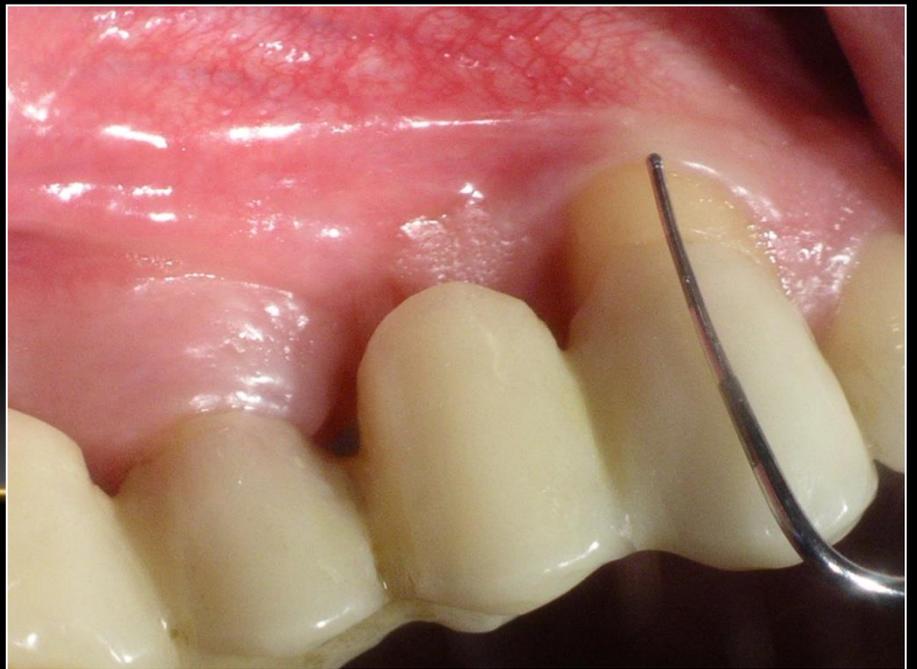
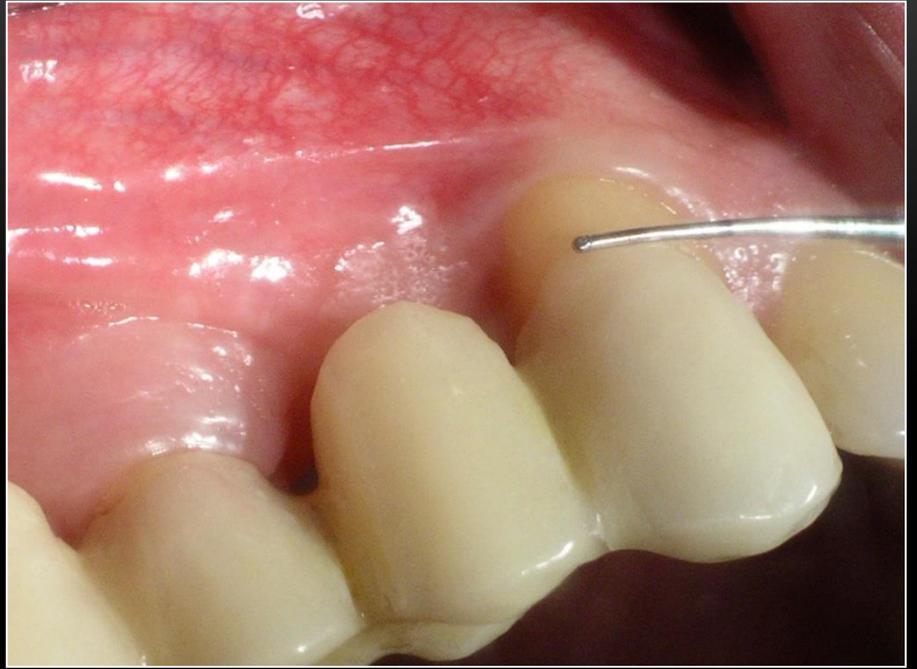
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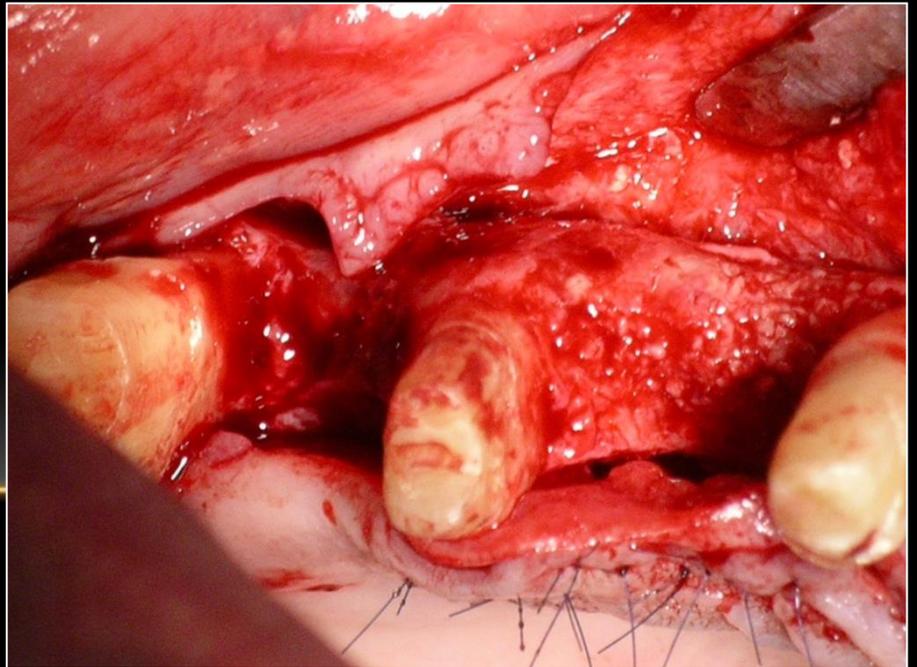
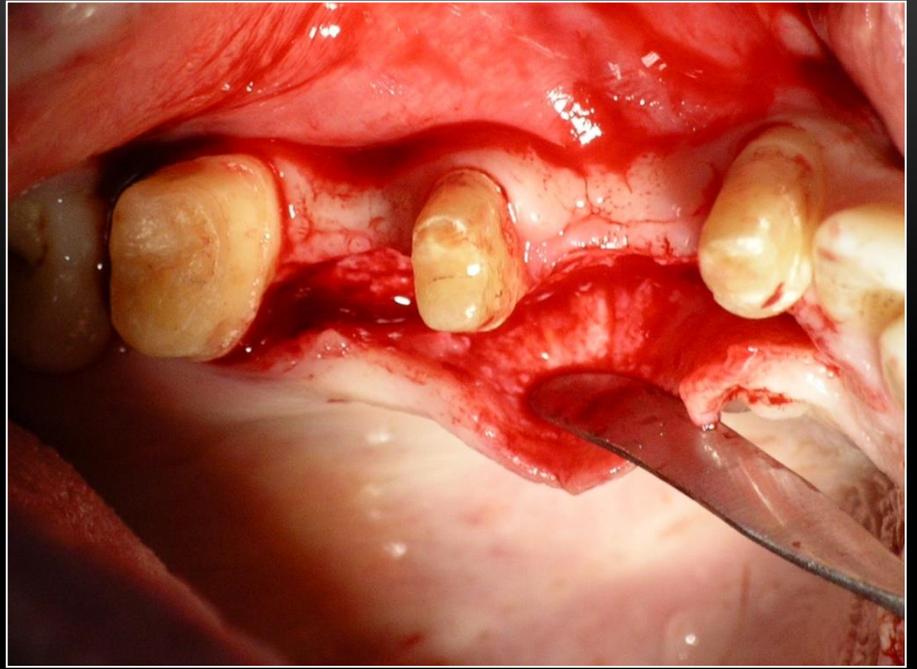
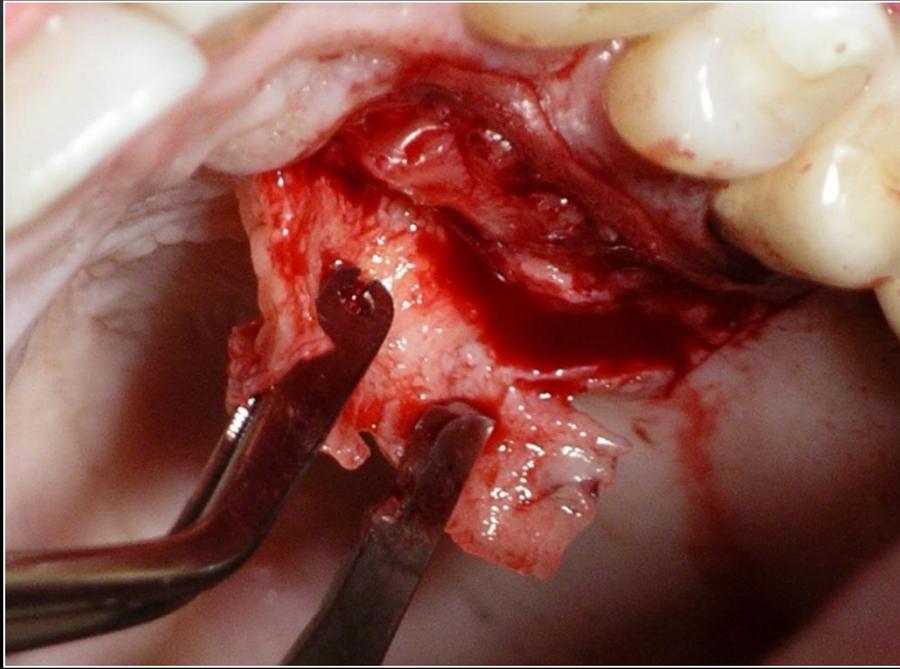
Windisch Péter, Szendrői-Kiss Dóra, Horváth Attila, Suba Zsuzsanna, Gera István, Anton Sculean
Reconstructive periodontal therapy with simultaneous ridge augmentation. A clinical and histological case series report
Clin Oral Invest DOI 10.1007/s00784-008-0194-8

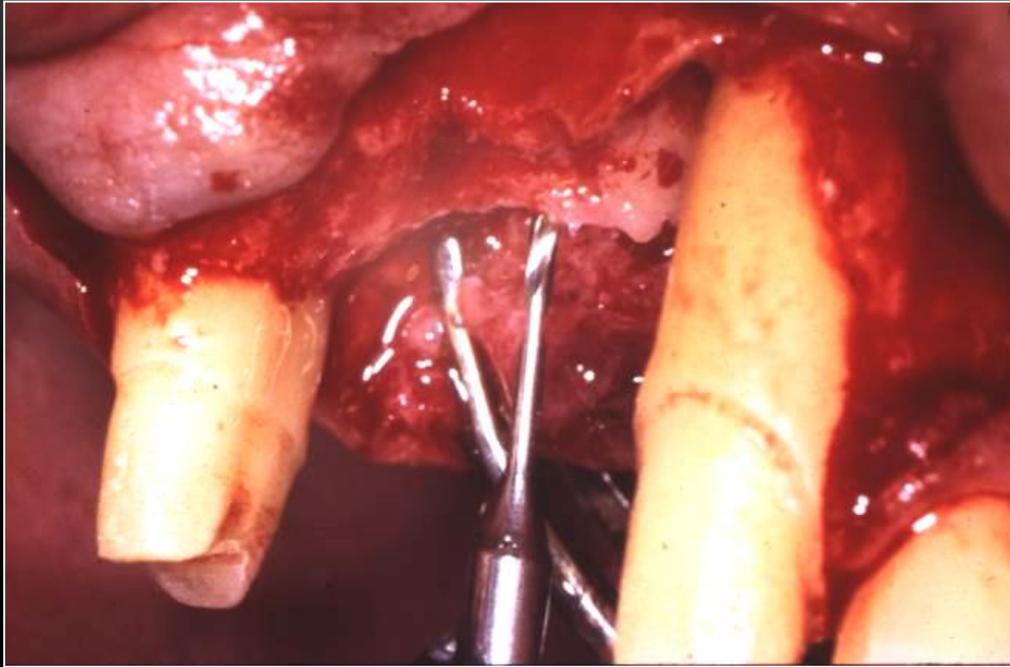








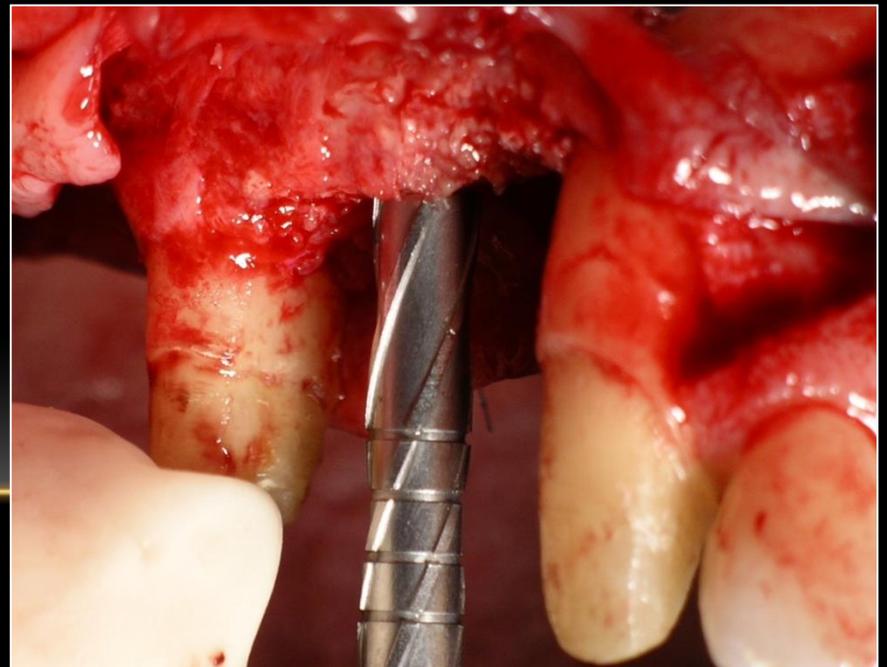


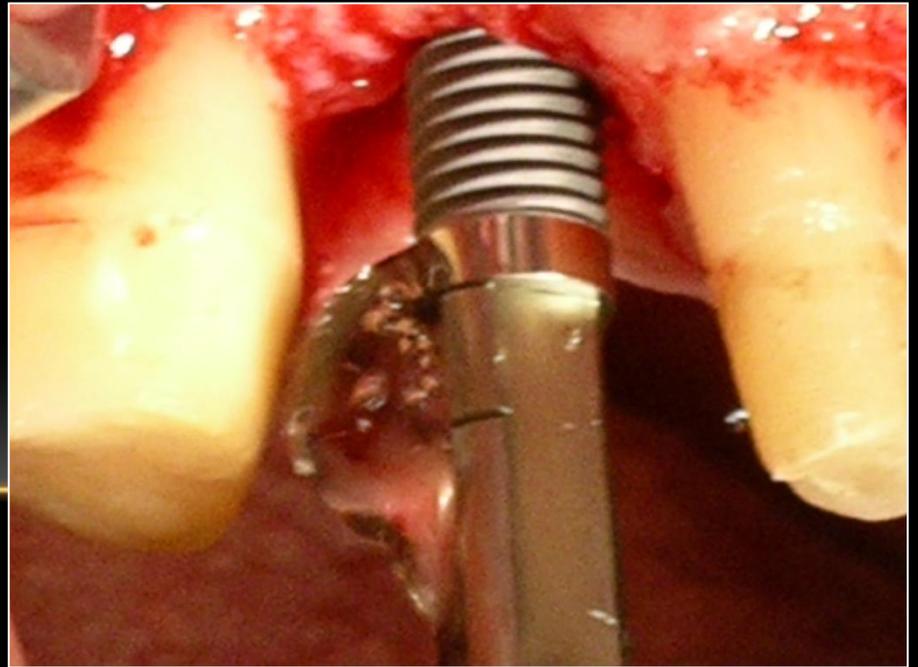
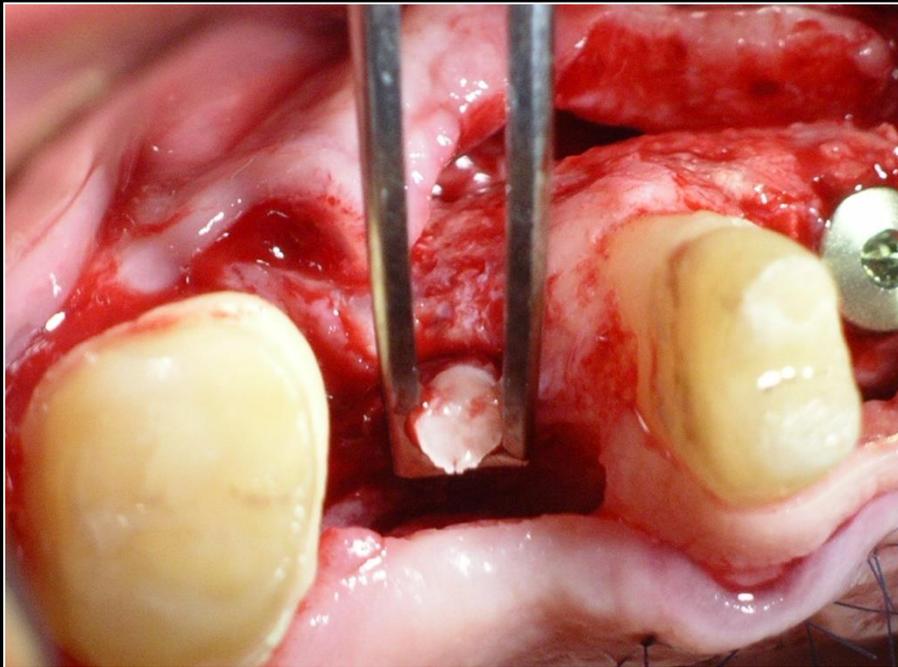
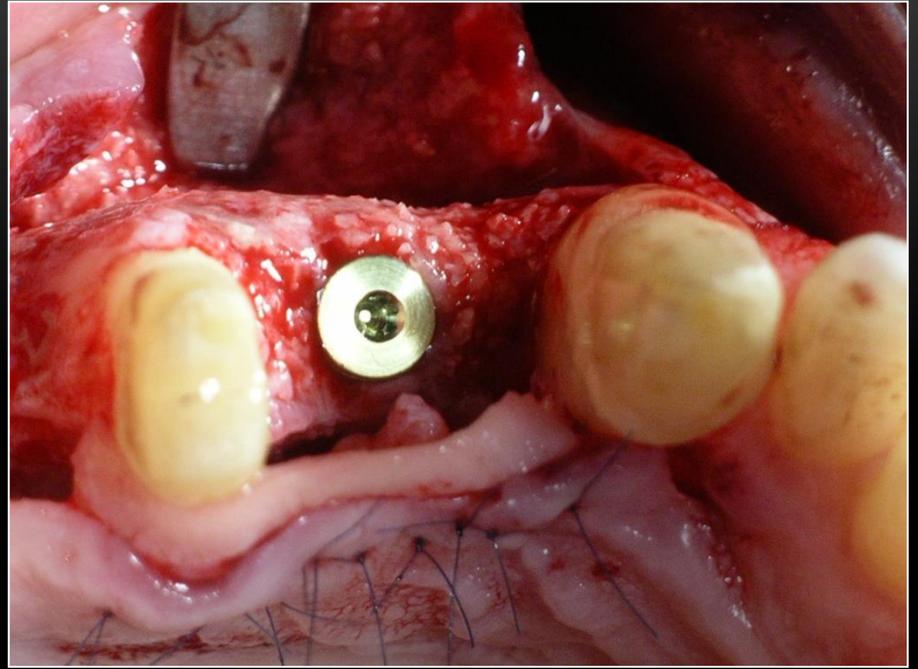
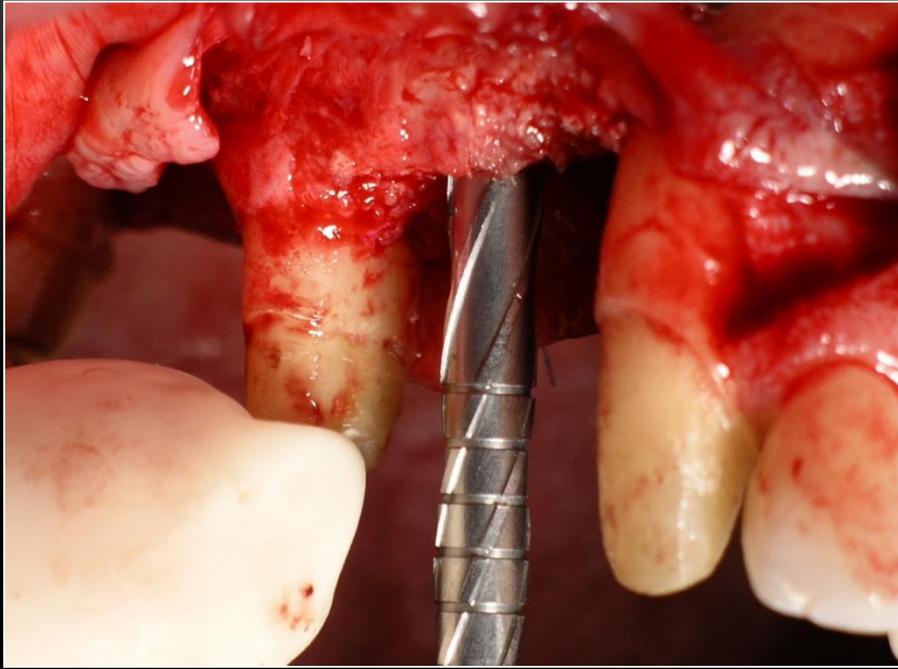


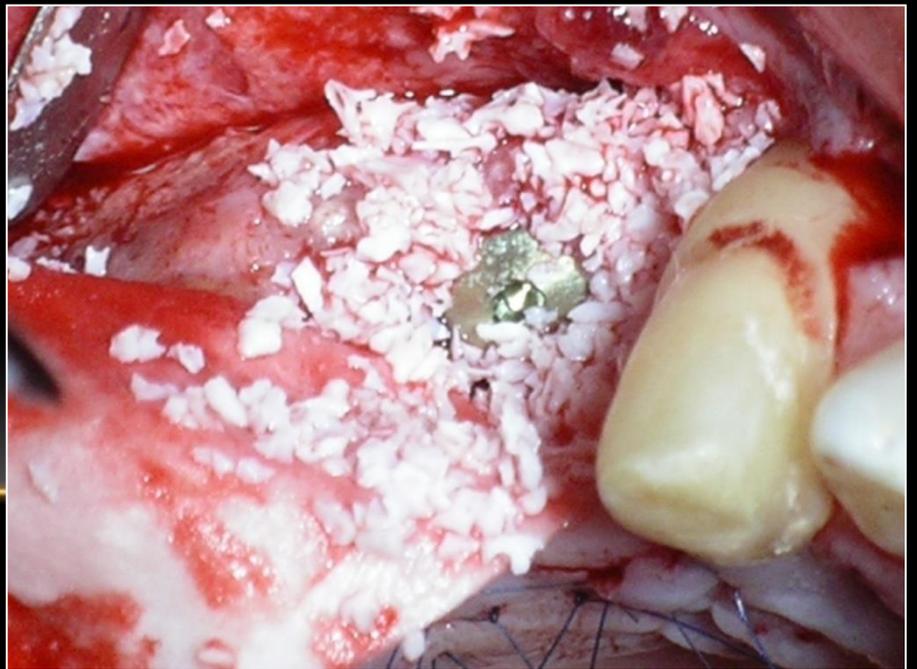
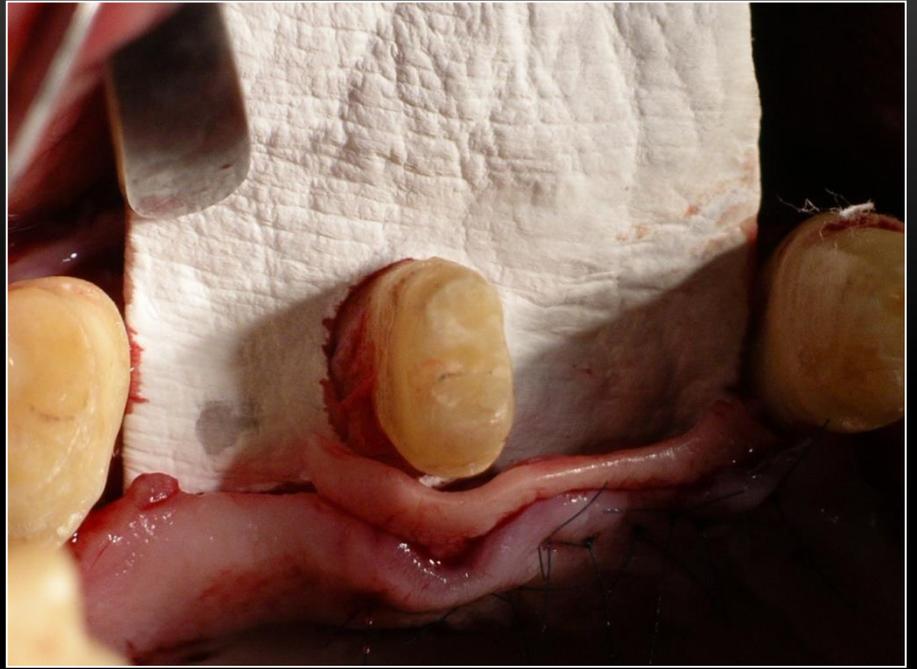
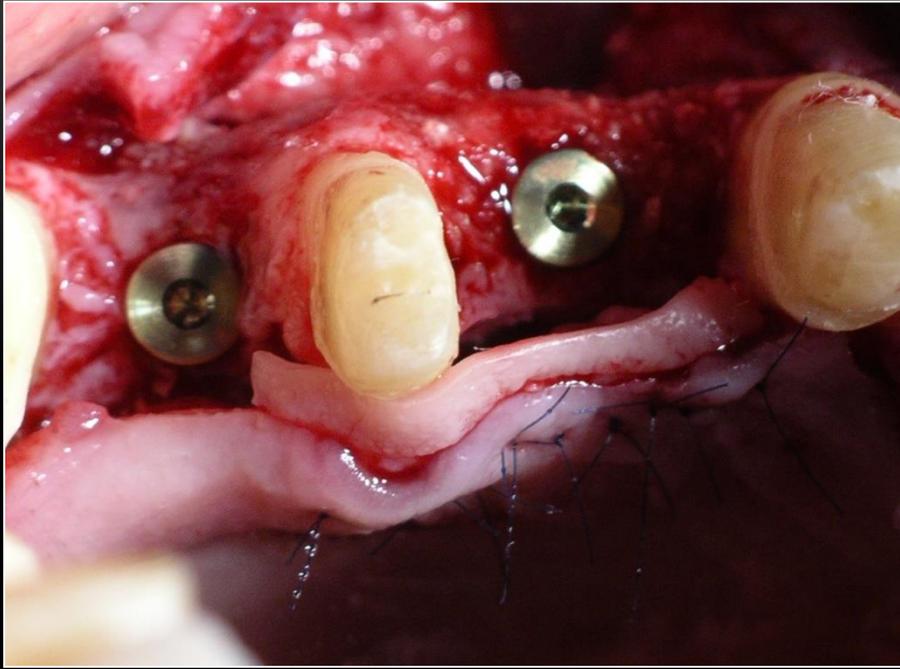
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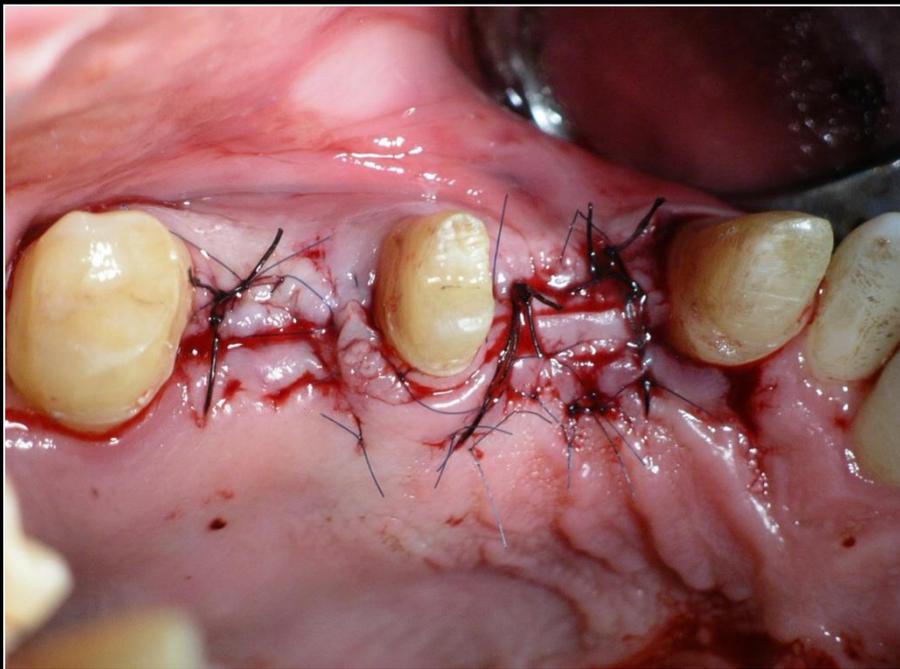
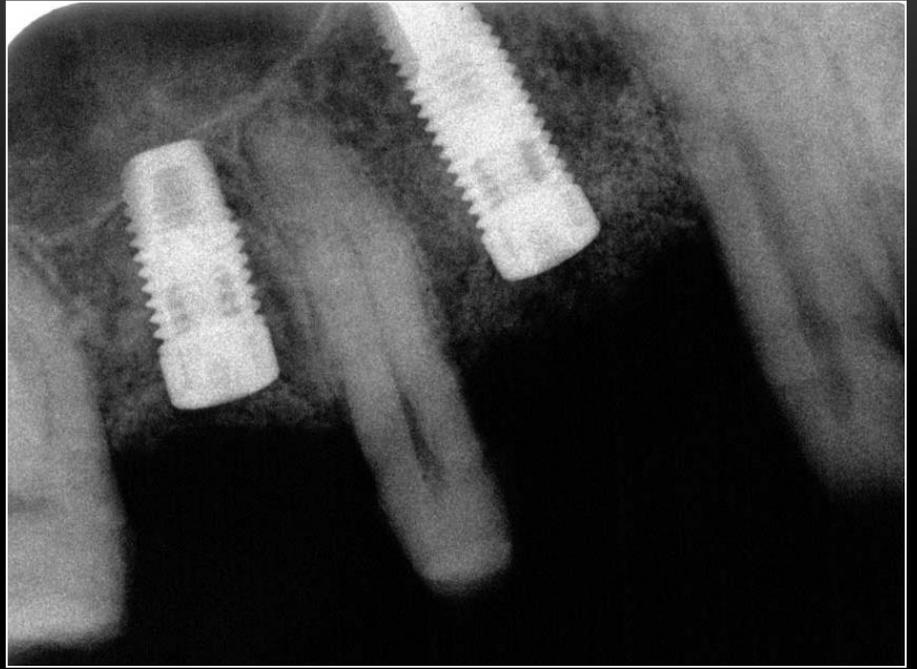
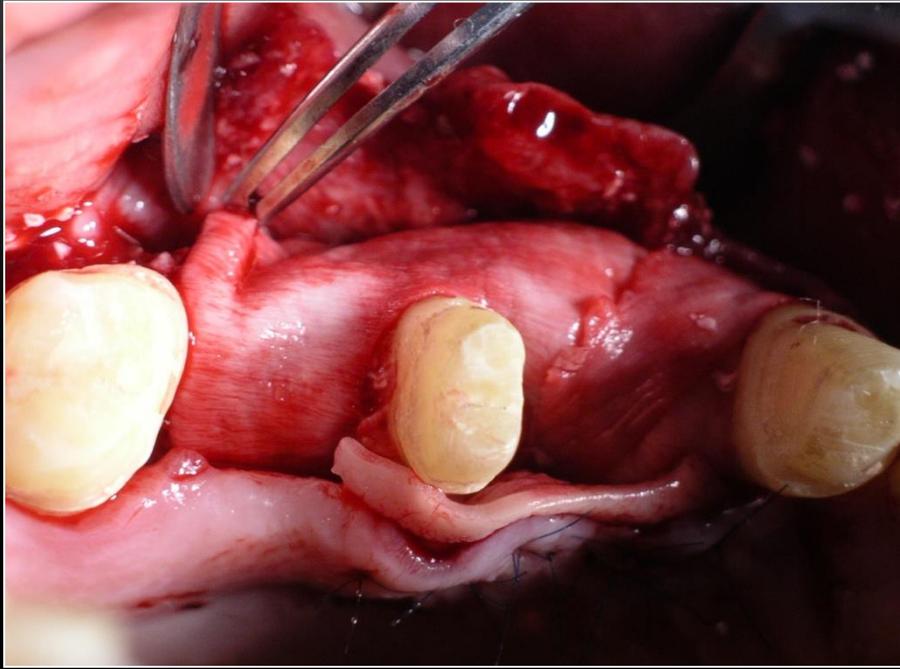


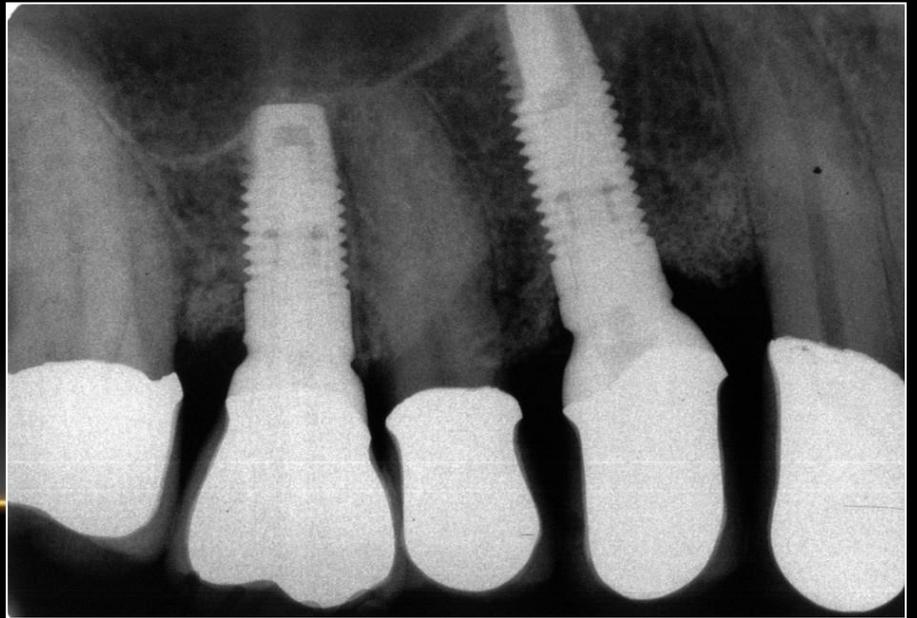
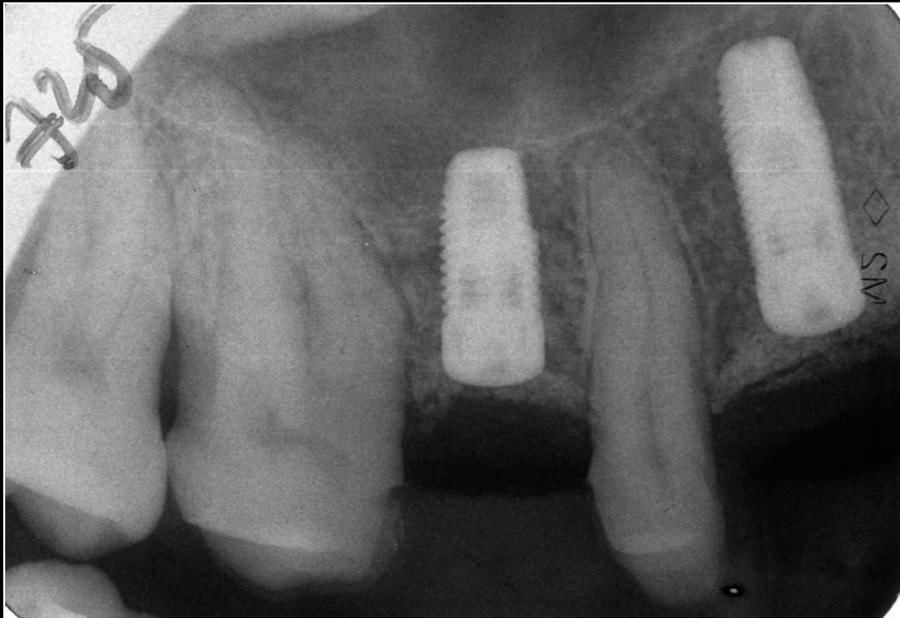
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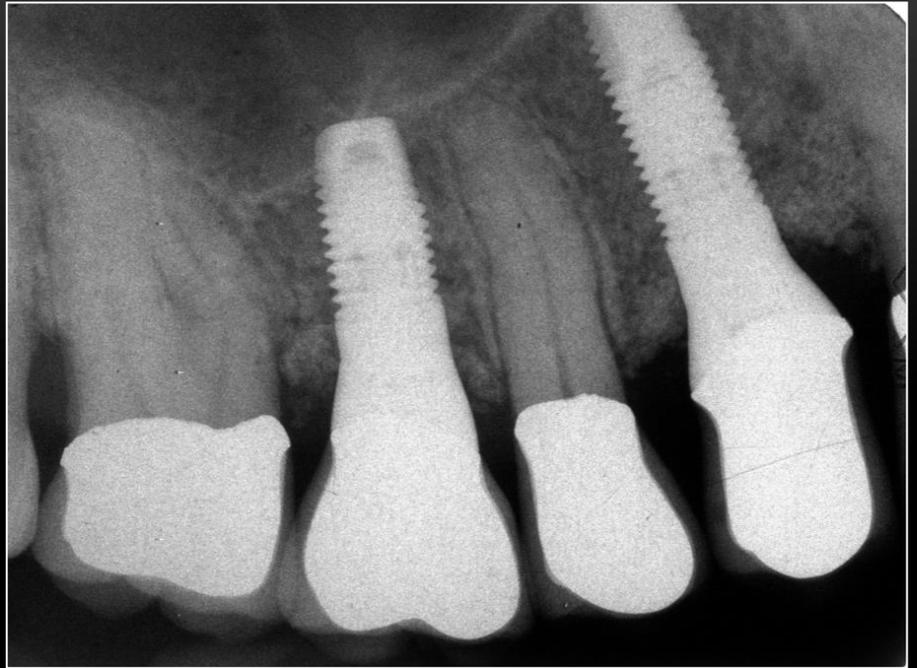












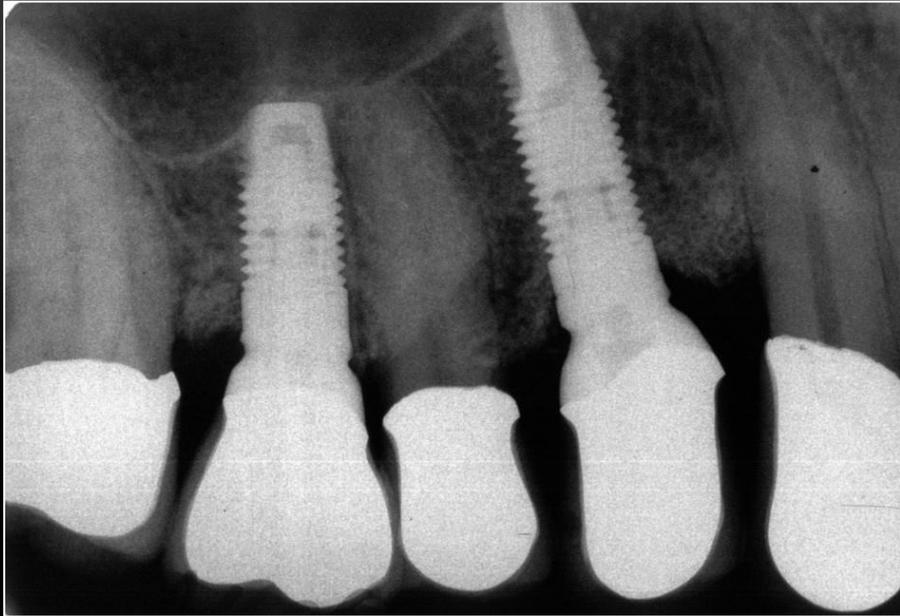


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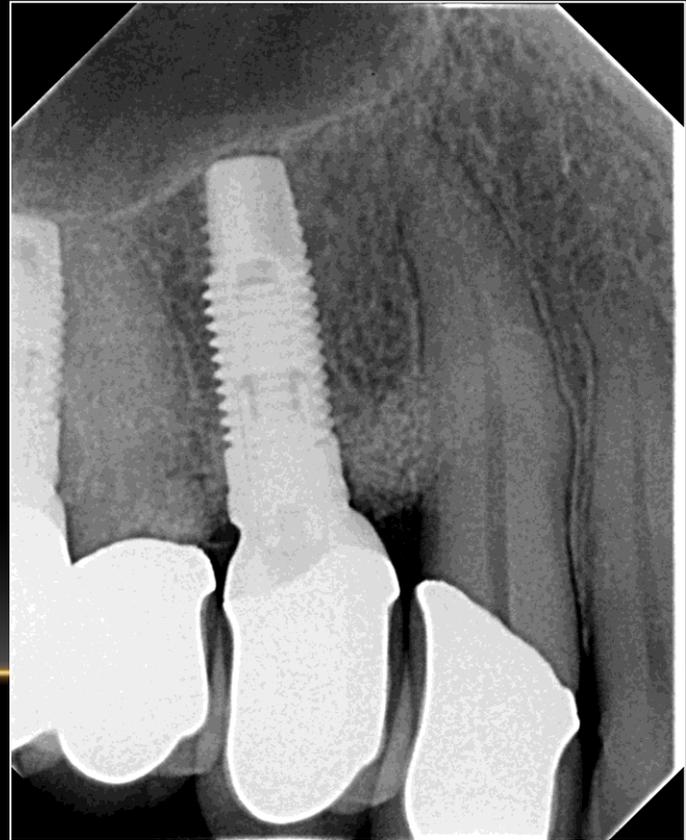
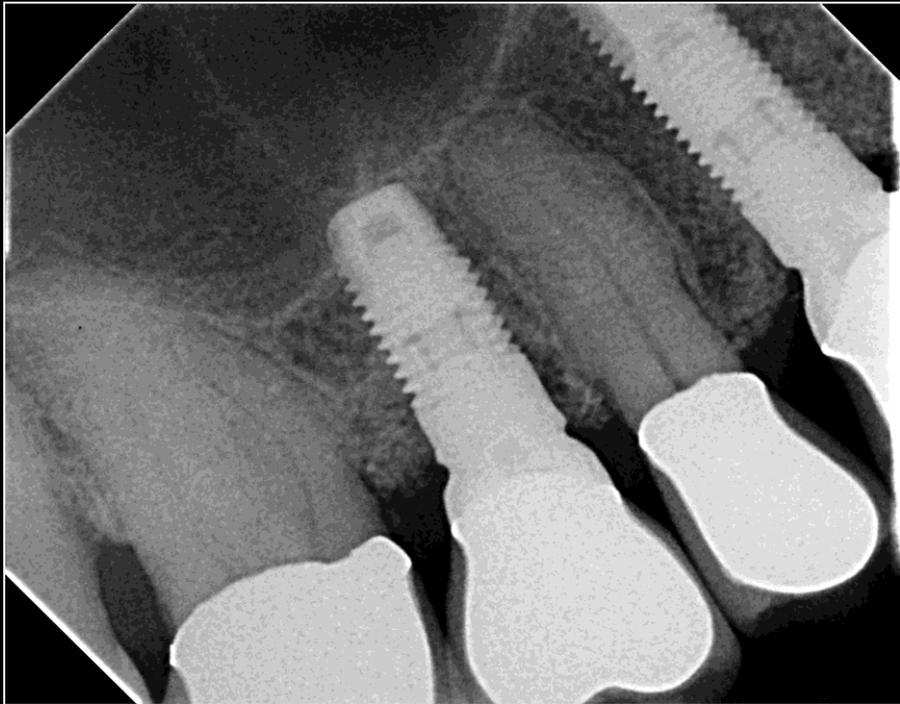


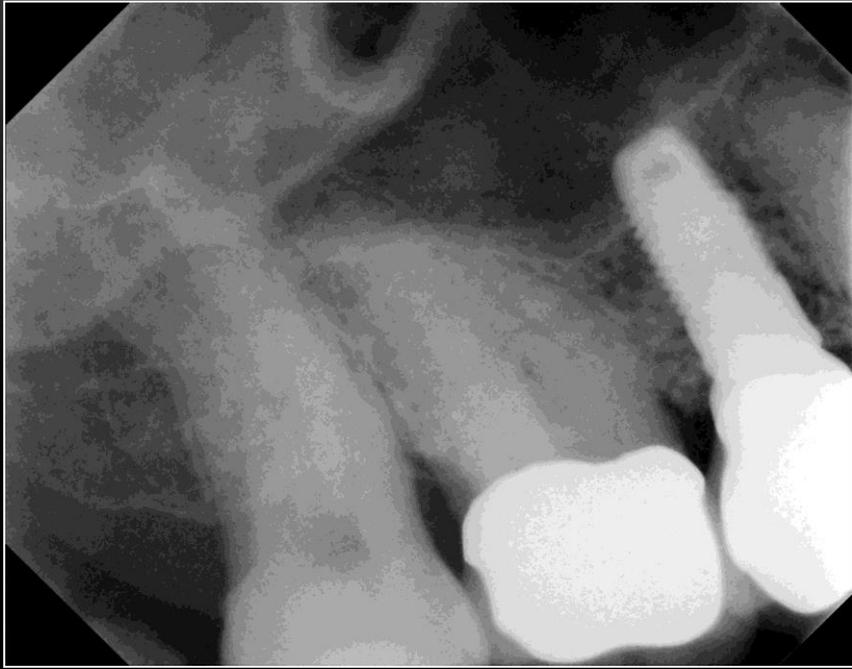
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1,5 ys control





3 ys control



FURTHER THERAPEUTIC POSSIBILITIES II

EMD + autogenous bone

Indication: Edentulous ridge with periodontal defects at adjacent teeth

Proposed procedure:

Stage 1: before fixture placement trephine core bone retrieval – defect filled with EMD + particulated bone.

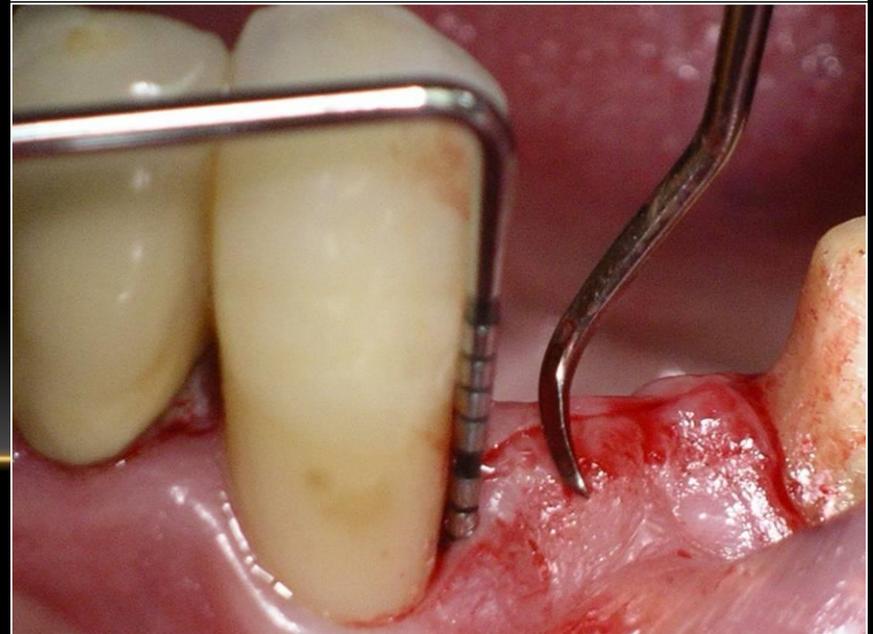
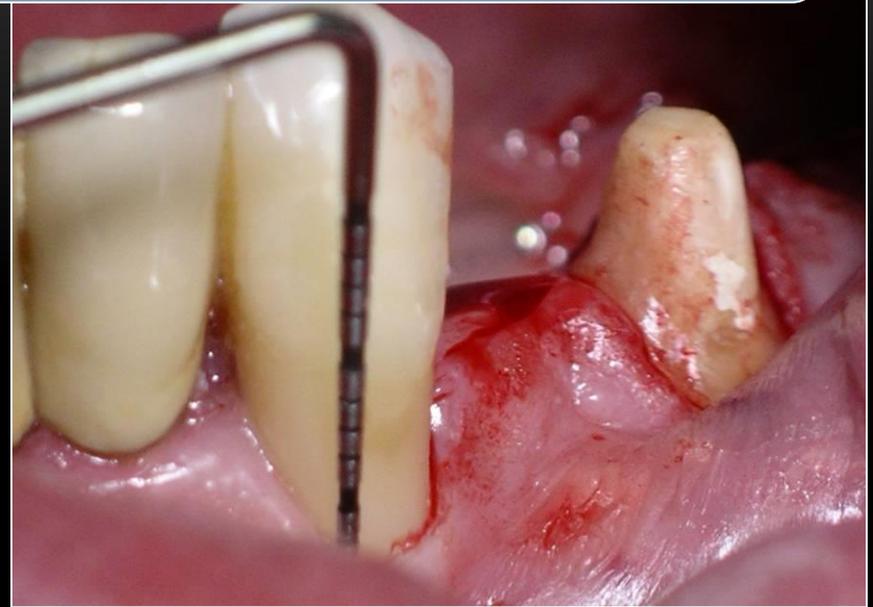
Stage 2: Reentry - abutment connection

Expected benefits: More predictable new bone formation in periodontal defects

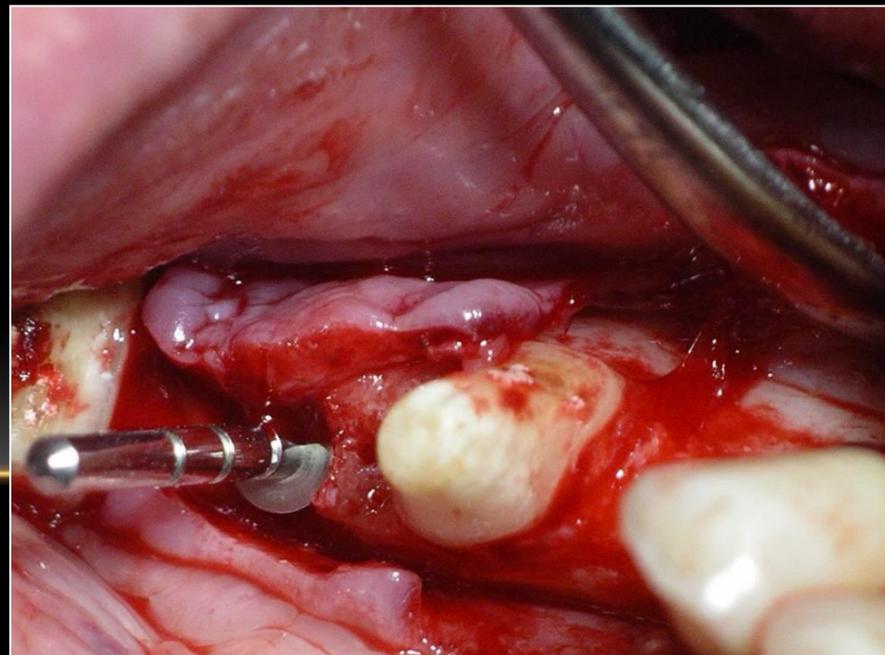
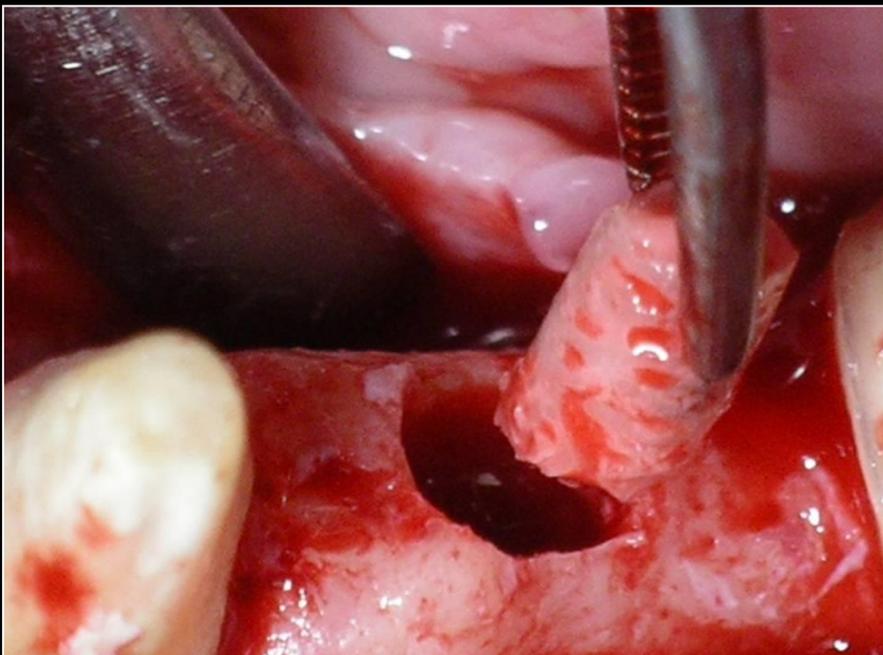
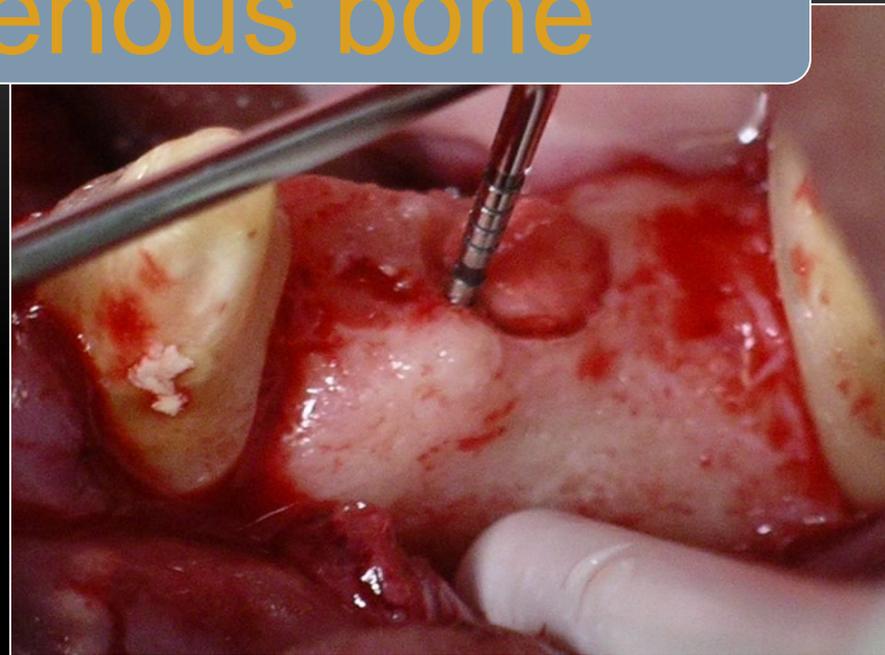
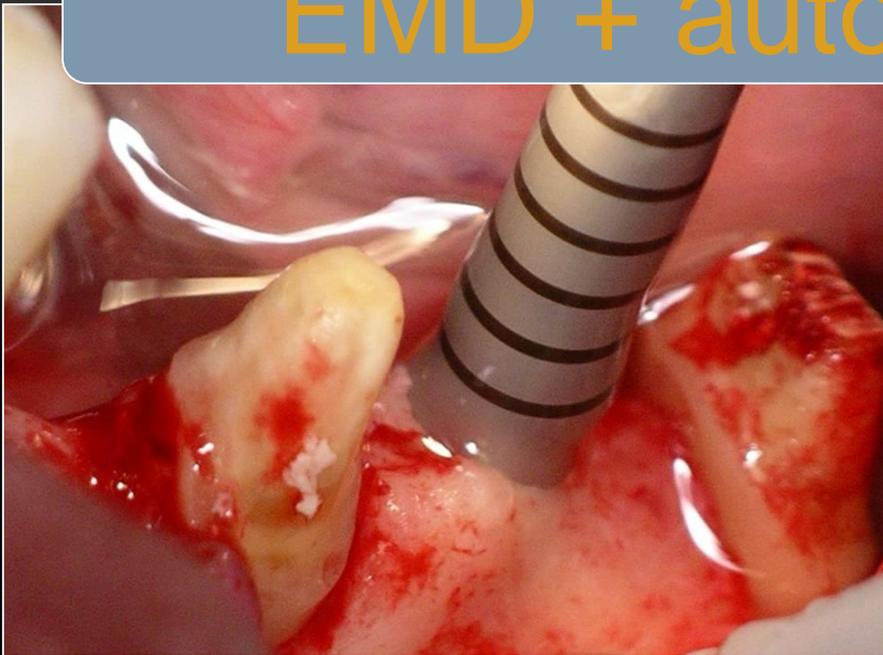
Cochran DL, Jones A, Heijl L, Mellonig JT, Schoolfield J, King GN. Periodontal regeneration with a combination of enamel matrix proteins and autogenous bone grafting. J Periodontol. 2003 Sep;74(9):1269-81

Leung G, Lin L. A combined approach of enamel matrix derivative gel and autogenous bone grafts in treatment of intrabony periodontal

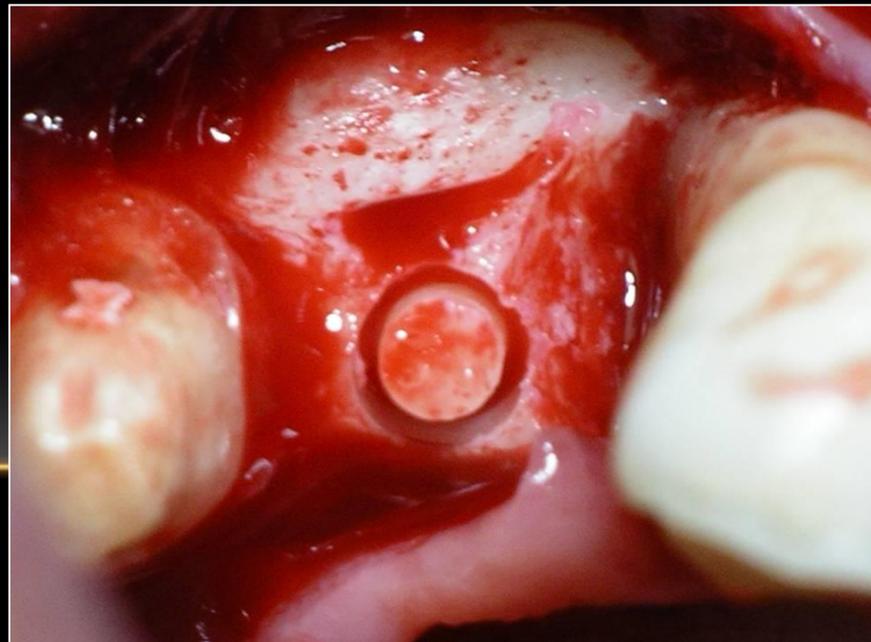
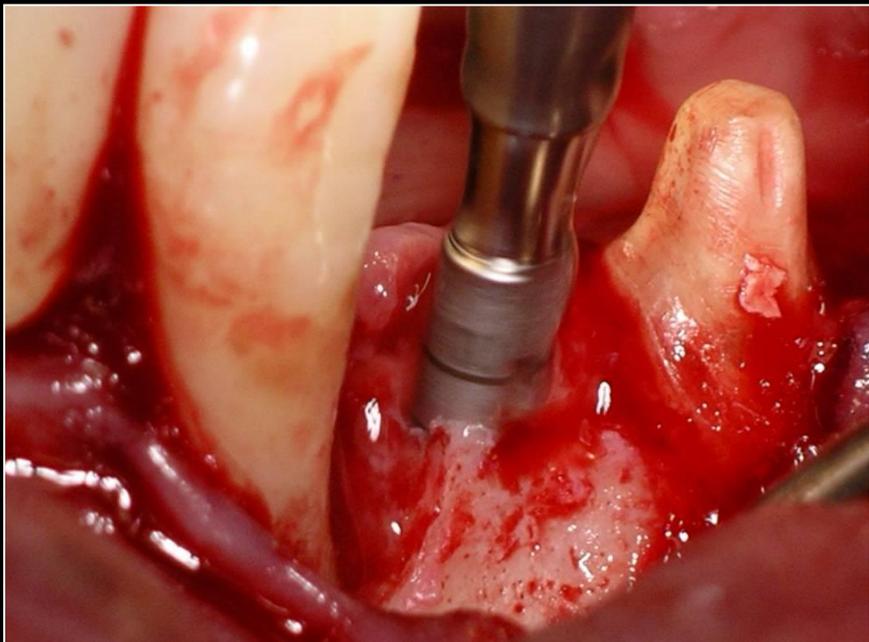
EMD + autogenous bone



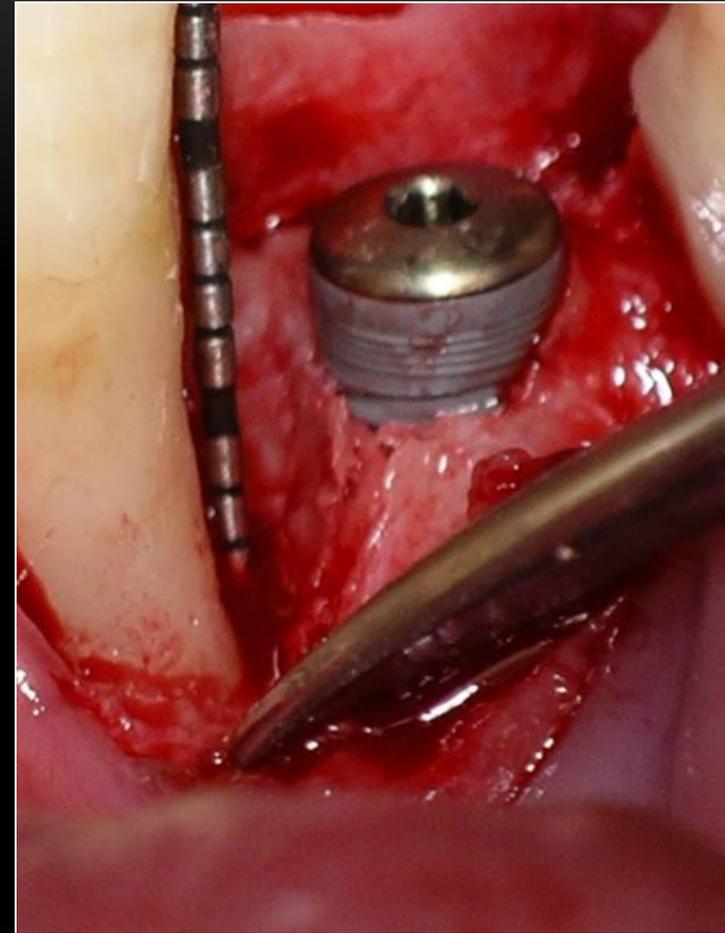
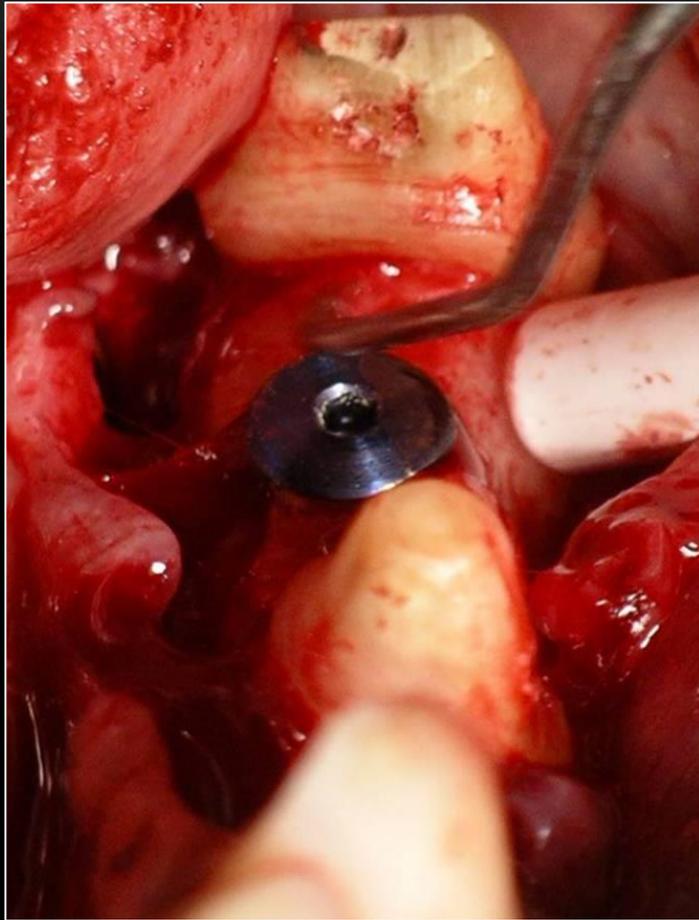
EMD + autogenous bone



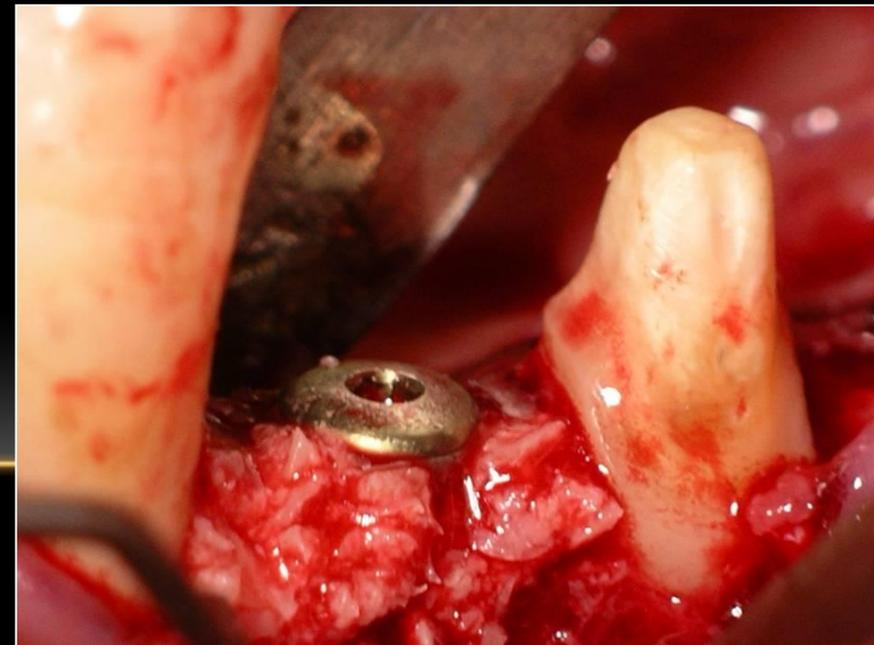
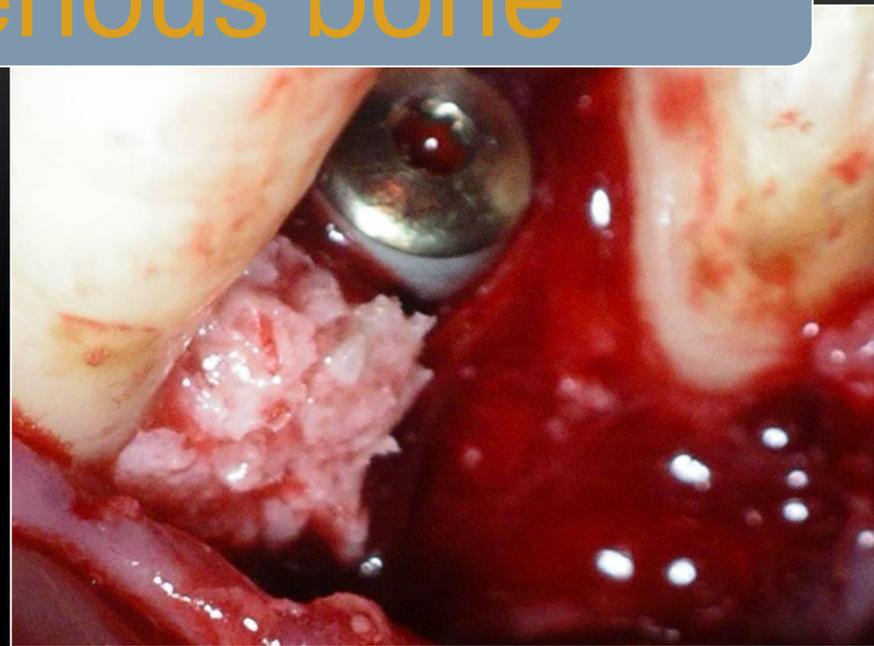
EMD+autogenous bone



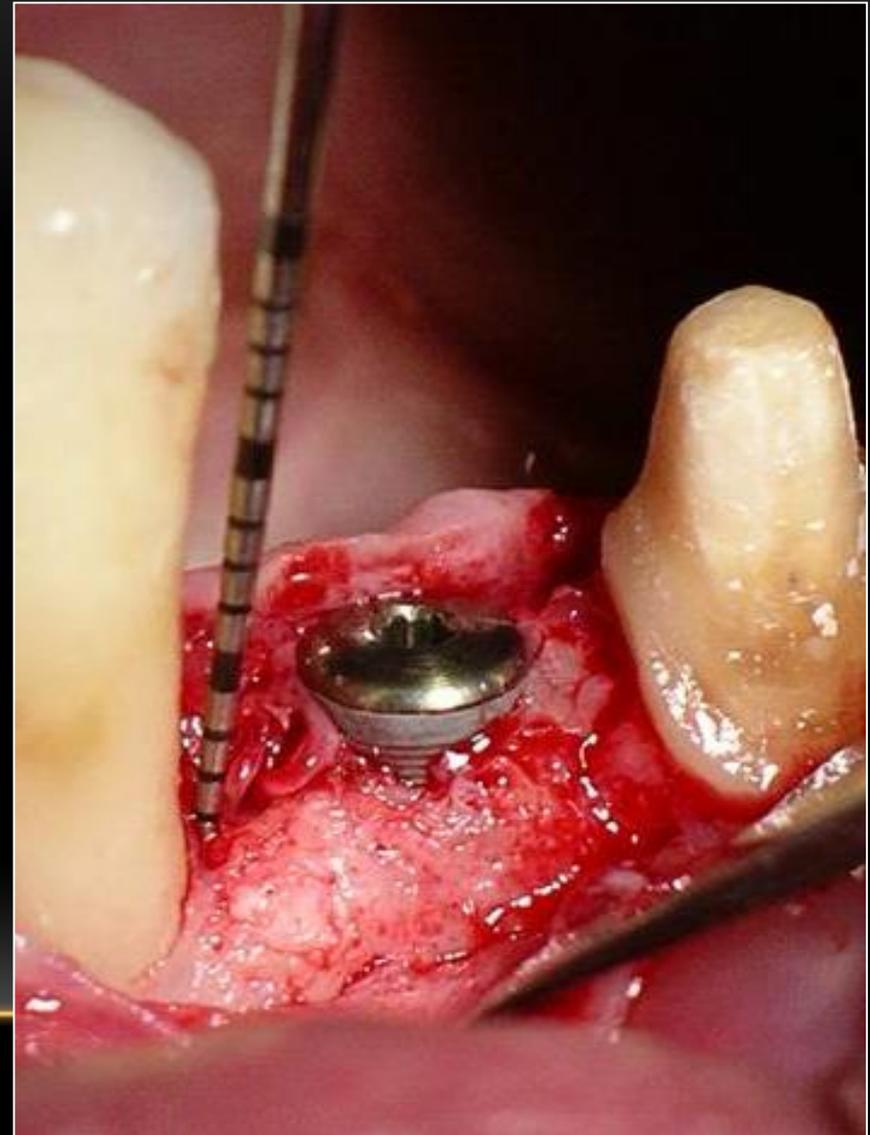
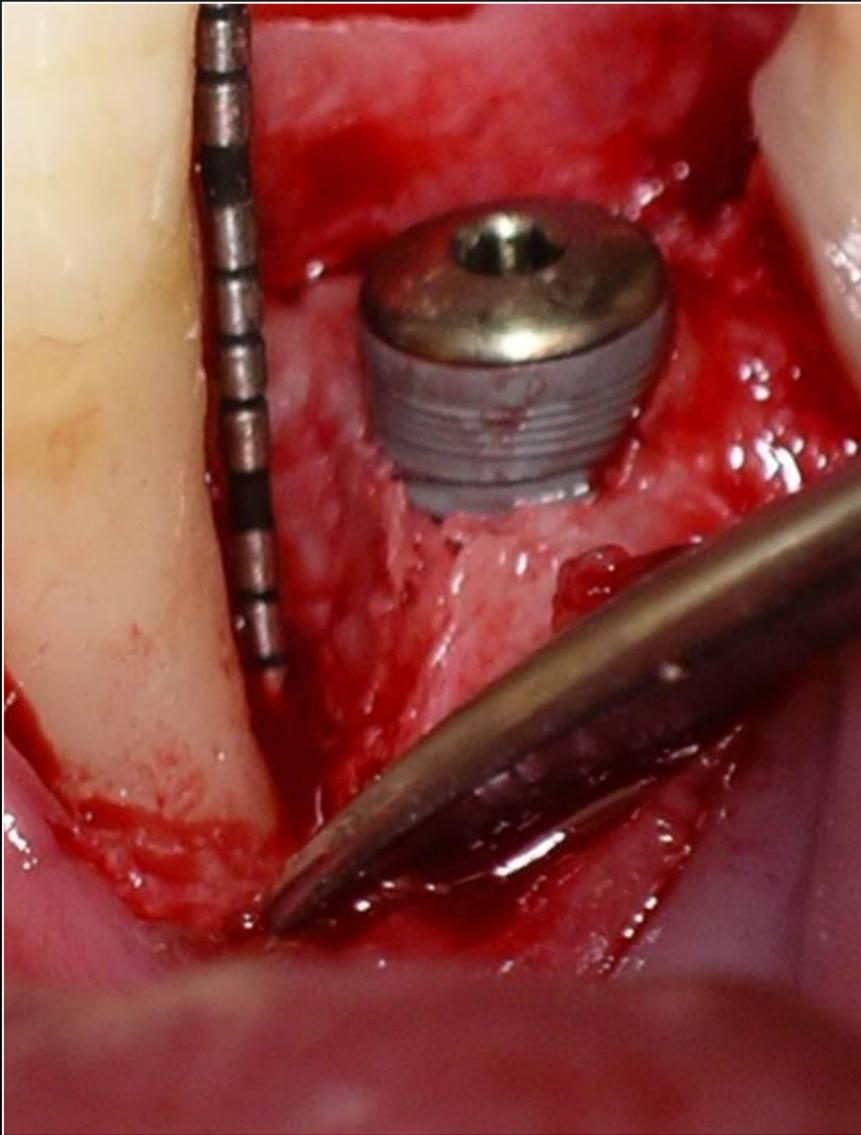
EMD+autogenous bone



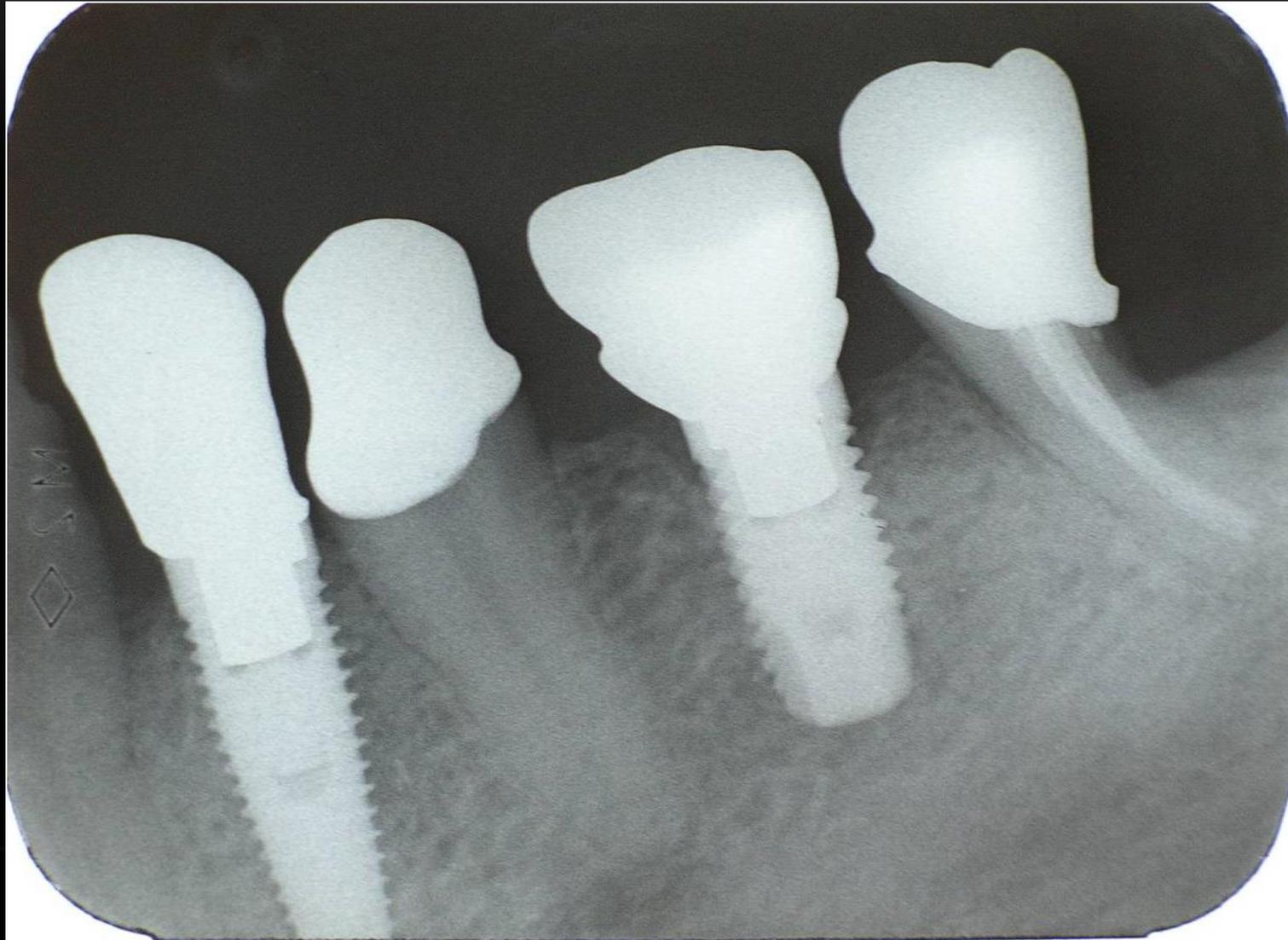
EMD+autogenous bone



EMD+autogenous bone



EMD+AUTOGENOUS BONE



**THANK YOU FOR YOUR
ATTENTION!**

