30 Years of
Leadership and Credibility

Periodontal regenerative procedures in the era of implant dentistry

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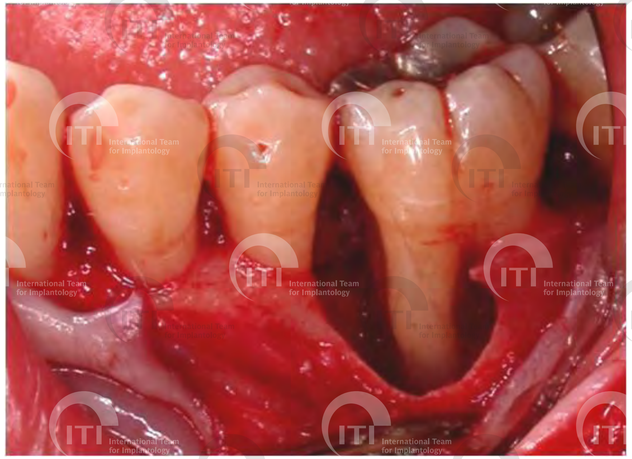
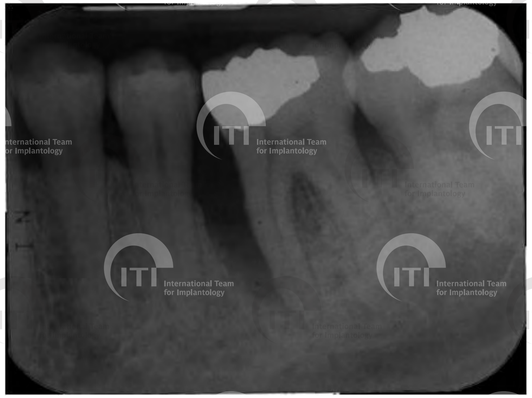
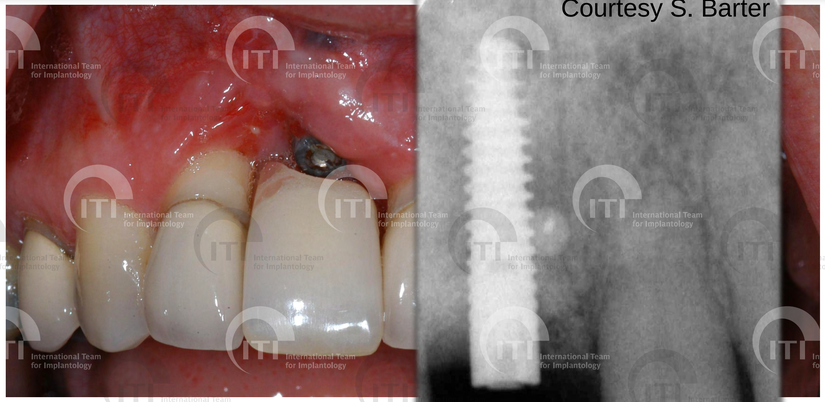
To save/regenerate or to extract? Are implants the best alternative & do implants perform better than treated periodontal teeth ?



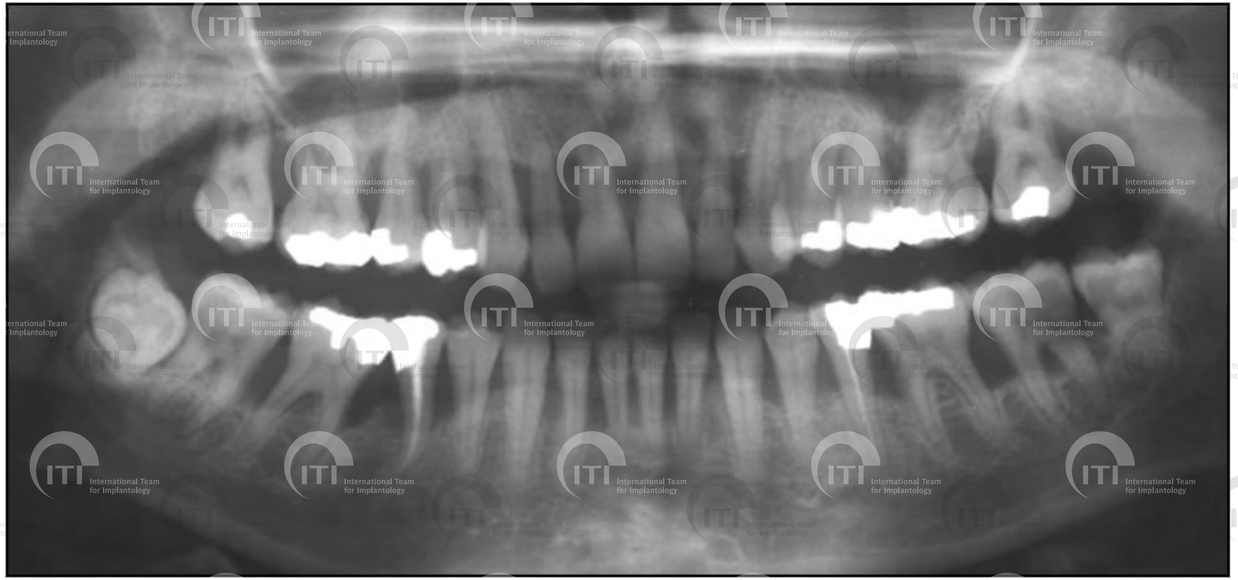


Is this condition better in function and aesthetics than a saved natural tooth?



Courtesy S. Barter

Are implants more resistant to patient's susceptibility to periodontal disease (AgP)? Why would implants have a better prognosis in such patients?



Estimated number of implants placed 2008 (http:www.implant-warning.com/definition.html)

- USA: 300,000-400,000/year
- France: 120,000/year
- Spain: 185,000/year
- Italy: 410,000/year
- Germany: 420,000/year
- U.K.: >100,000/year

67,000 implant failures/year in Europe only

Definition and prevalence of peri-implant diseases

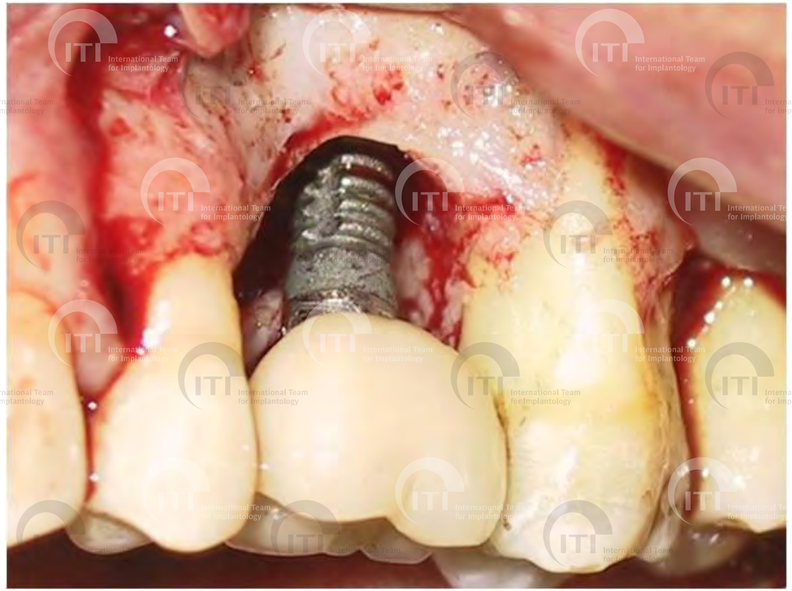
Zitzmann N., Berglundh T. Journal of Clinical Periodontology 2008

- Cross sectional and longitudinal studies
- Implants in function 5 years
- Study excluded if <50 patients
- 2 studies: Roos-Jansaker et al. 2006; Fransson et al. 2008

Peri-implant mucositis (BoP and no bone loss): 79% of subjects and 50% of implants (R-J. 2006) & >90% of implants (Fransson 2008)

Peri-implantitis in 28% and >56% of subjects and in 12% and 43% of implants respectively

Definitions (van Steenberghe et al 1999)

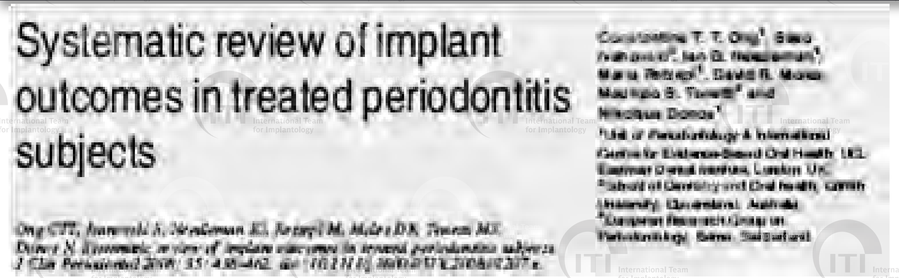


Is this success?

- Survival rate: proportion of implants still in place at a certain time, even if they are of no clinical value or even cause side effects

- Success (dogmatic): focused on stability of marginal bone as a surrogate measurement for long-term success

Is implant success independent of periodontitis?



Systematic review of implant outcomes in treated periodontitis subjects

Aim: To determine implant outcomes in partially dentate patients who have been treated for periodontitis vs. periodontally healthy patients

Study	Design	Yrs	Survival treated-perio	Survival non-perio	Statistical tests
Karoussis et al. 2003	Cohort	10	90.5% SE: 0.064	96.5% SE: 0.020	Not significant (imp)
Watson et al. 1990	Cohort (subgp)	4	100%	100%	No analysis
Evian et al. 2004	Case series	> 10	79.22%	91.67%	Statistically significant (pt) Cox's regression, P= 0.0122; Log-rank test, P= 0.0213
Hardt et al. 2002	Case series	5	92%	96.7%	Not reported
Roos-Jansåker et al. 2006a	Case series	9-14	16 events (94 pts)	2 events (62 pts)	Statistically significant (pt) Log-rank test (& Cox's regression analyses), P= 0.01

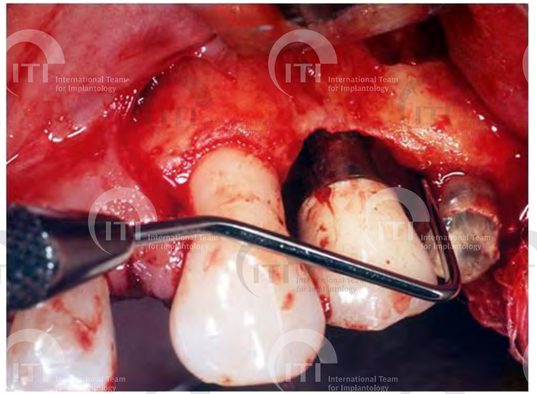
Studies evaluating the success of implants from patient's perspective are few

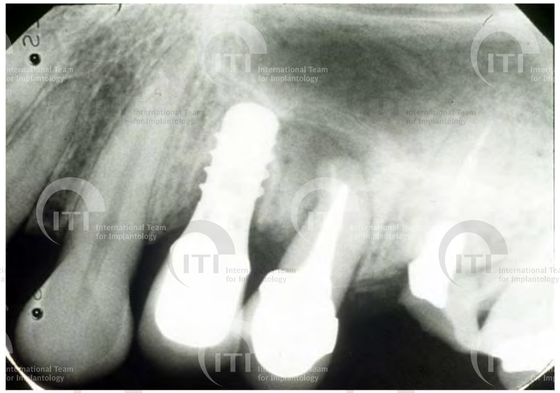
- **Information received prior to treatment was related to patient overall satisfaction**
  Levi A. et al. 2003
- **Communication between dentist and patients imperative for optimal results for both. Patient should be aware of the alternatives**

What is clinical success? *The patient's point of view.....*

Material: 195 cases of dental malpractice against 160 dentists

- One of the most common reasons involved **implant dentistry** & **most alleged negligence was failure of implant treatment planning and improper evaluation of the patient (Baxter 2003)**





Prosthetic treatment planning on the basis of scientific evidence

B. Pjeturrson & N.P.Lang J. Oral Rehab. 2008

Estimated Survival Rates	*Five Years*	*Ten Years*
Conventional Bridge	**94%**	**89%**
Resin Bonded Bridge	**88%**	**63%**
Single Tooth Implant	**95%**	**89%**
Implant Bridge	**95%**	**87%**
Tooth-Implant Bridge	**96%**	**78%**

- All patients periodontally healthy
- Final treatment option amount of hard and soft tissue to be considered together with functional & aesthetic demands

Treatment planning: evaluation of restorative, periodontal & implant related factors

Decision to extract the tooth with poor prognosis and replace it with a dental implant?

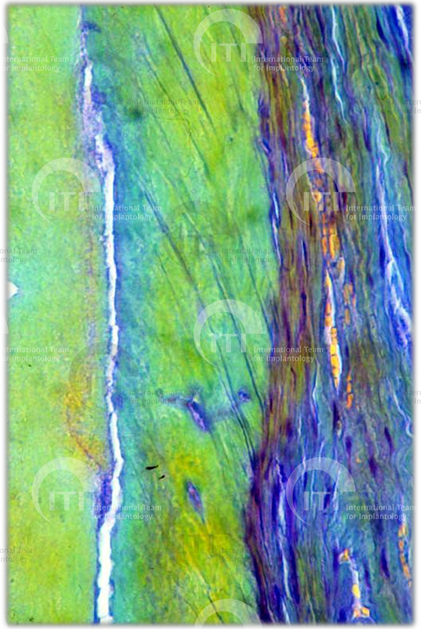
Prognosis is the prediction of the course of existing disease based on empirical data and should consider among other factors:

1. the severity of disease at treatment onset,
2. predictability of prescribed treatment,
3. clinician's skills &
4. patient's compliance

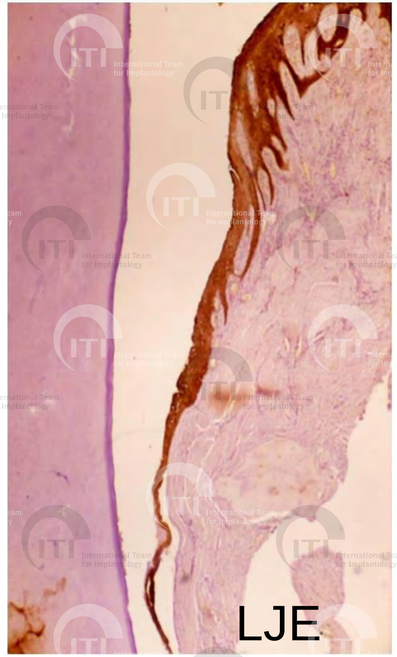
Can we change the prognosis and have predictable long-term results with periodontal regeneration procedures?

Final outcome? Tooth survival

(through successful periodontal treatment)



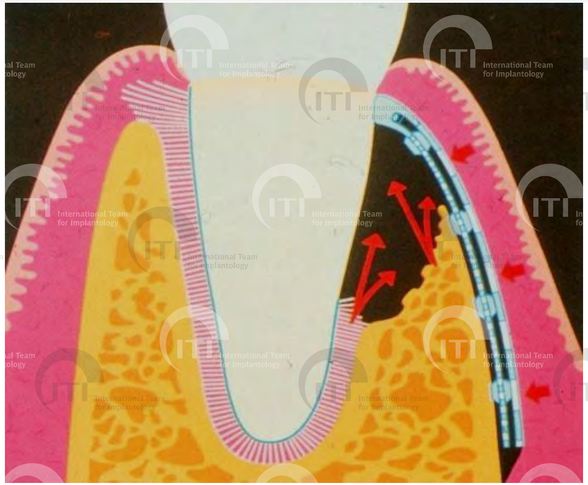
GTR biopsy

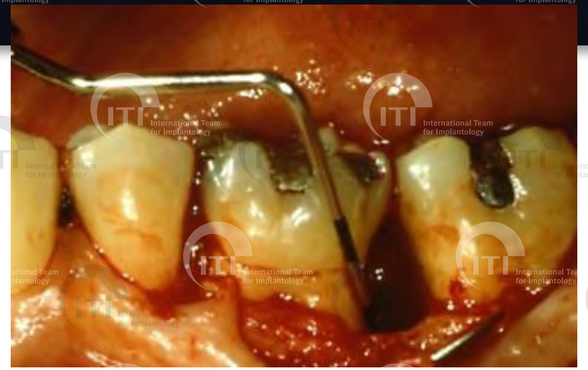


LJE

Regenerative procedures in periodontology

- Bone grafts/Bone substitutes
- Root conditioning
- Guided Tissue Regeneration
- Enamel Matrix Proteins/derivative
- Growth factors
- Combinations





Long-term tooth survival following regenerative treatment of intrabony defects

Cortellini & Tonetti *J Periodontol* 2004

Total 175 patients, severely compromised teeth (CAL loss 10.7± 2.4 mm, PPD 8.7± 2.3 mm, deep intrabony defects depth: 6.6 ± 2.1 mm.

Average follow–up: 8 ± 3.4 years

Definitions for survival analysis: tooth loss,

CAL loss of >2mm before GTR and

CAL loss > 2mm compared with the CAL at 1 year after GTR completion

12 months following GTR: CAL gain 4.6 ± 2 mm & residual PPD 2.8 ± 1 mm.

6 teeth lost (all patients smokers and 5 no SPT)

CAL was equal or coronal to pre-treatment in 92% of cases for 15 years after GTR

Loss of CAL compared to 1 year post GTR was observed in 37.8% of cases

Long-term tooth survival following regenerative treatment of intrabony defects
Cortellini & Tonetti *J Periodontol* 2004

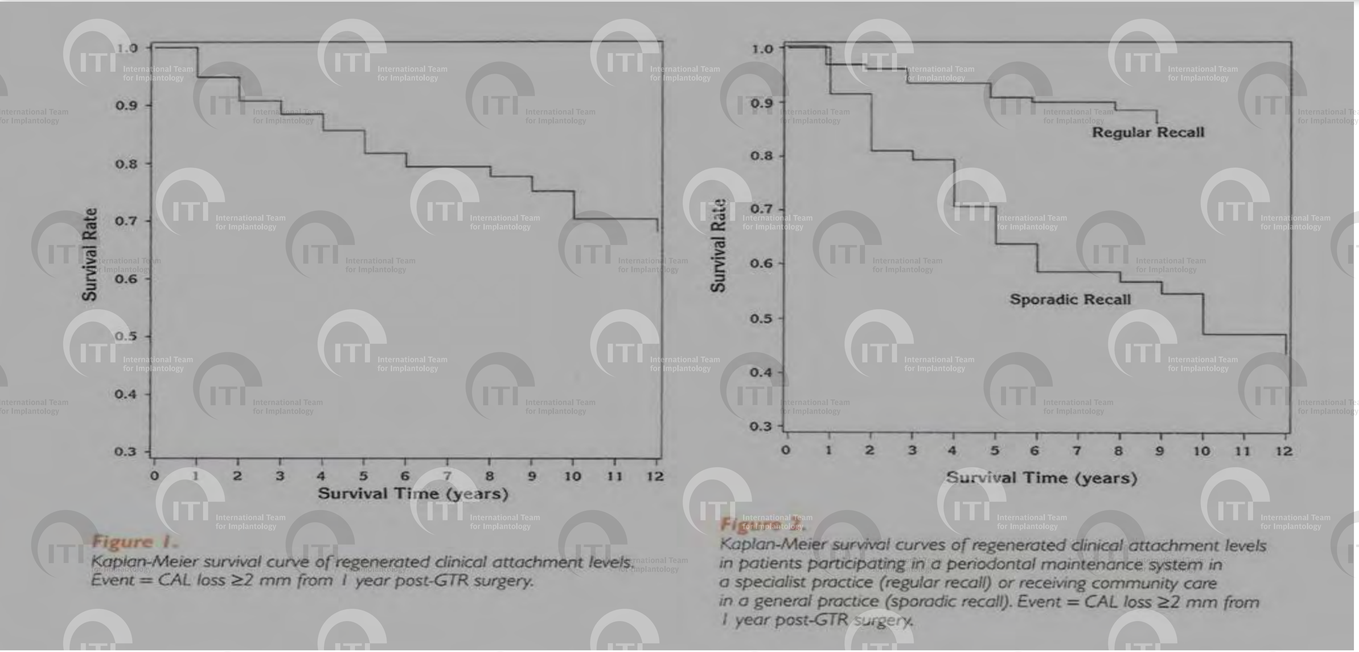


Figure 1.
Kaplan-Meier survival curve of regenerated clinical attachment levels. Event = CAL loss ≥2 mm from 1 year post-GTR surgery.

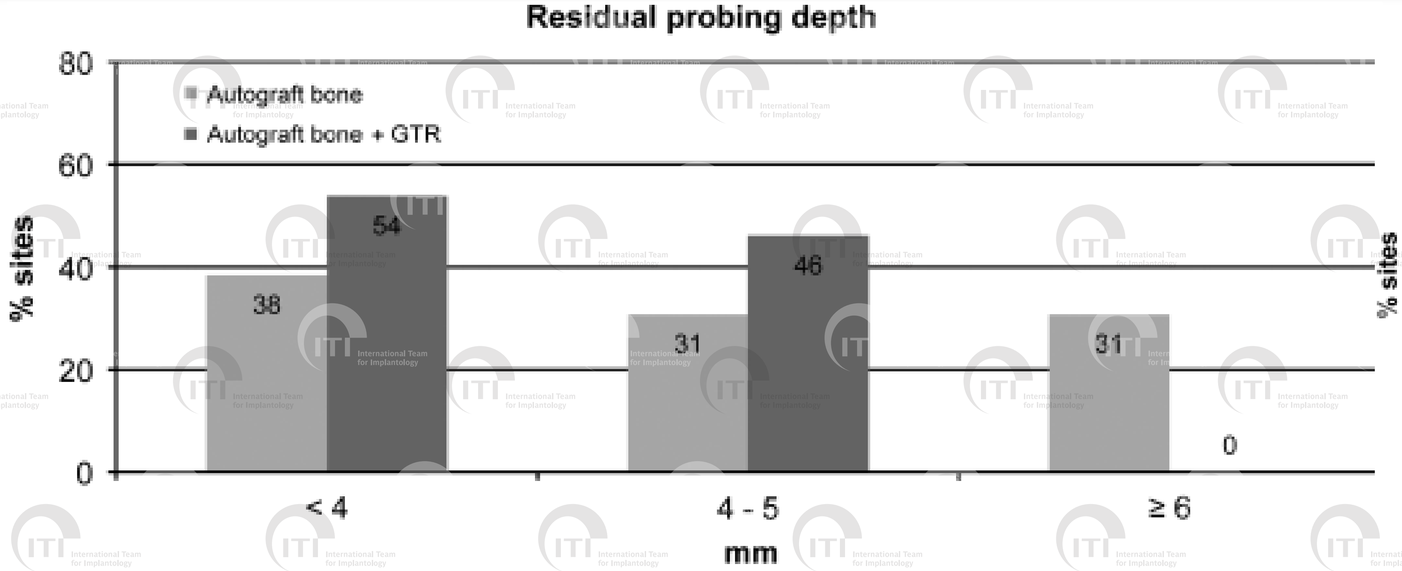
Figure 2.
Kaplan-Meier survival curves of regenerated clinical attachment levels in patients participating in a periodontal maintenance system in a specialist practice (regular recall) or receiving community care in a general practice (sporadic recall). Event = CAL loss ≥2 mm from 1 year post-GTR surgery.

Fig 1.: 66.2% did not present CAL loss >2 mm over the 6 year observation period

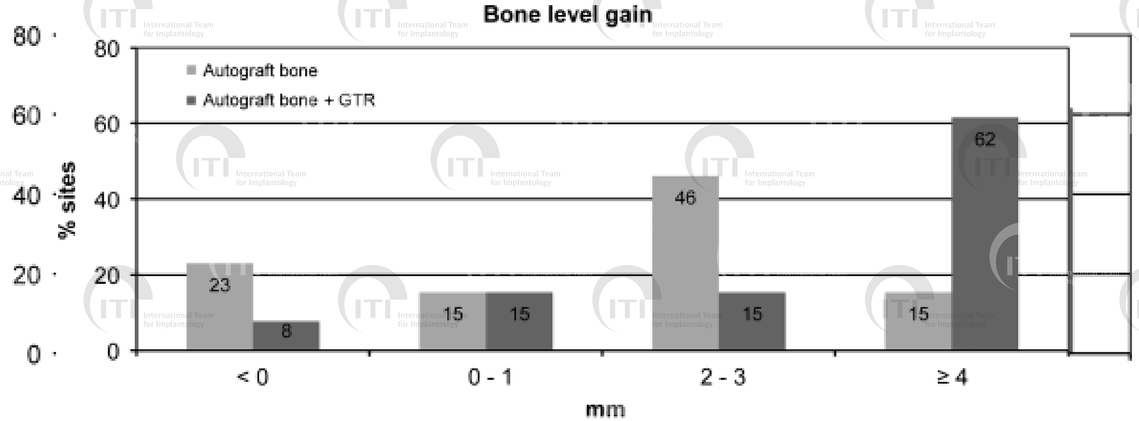
Fig. 2: regular SPT decreased risk of CAL loss

GTR and autogenous bone graft: a 10 year follow up.

Per Nygaard-Østby et al JCP 2010



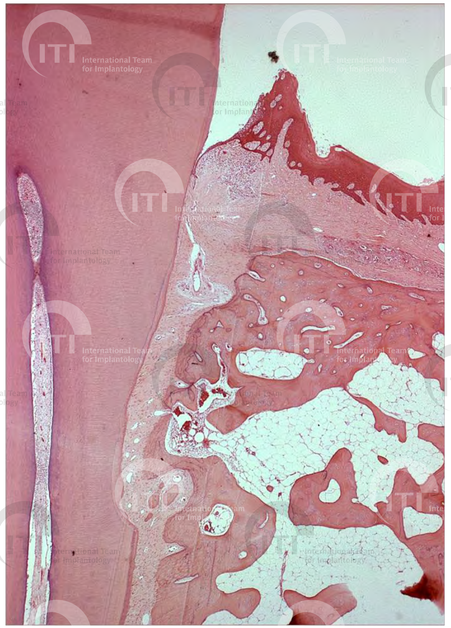
Fischer's exact test, p=0.15



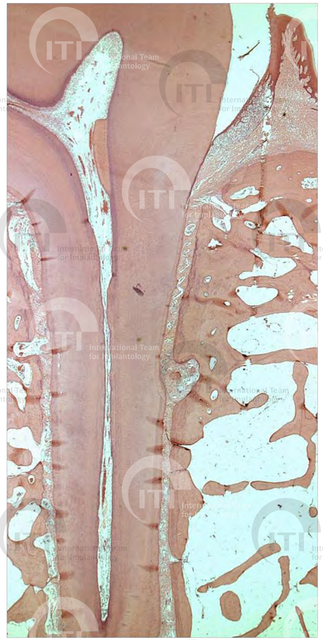
Fischer's exact test, p=0.11

Resolution of intrabony defercts can be maintained in the long-term under SPT

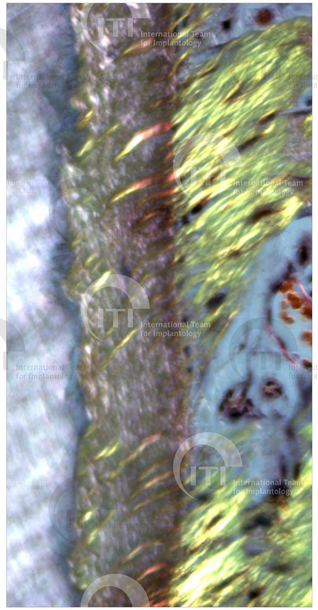
Structure of periodontal tissues formed following GTR treatment of intrabony defects. A histological study after 6 months and 2 years of healing. (Laurell L et al.)



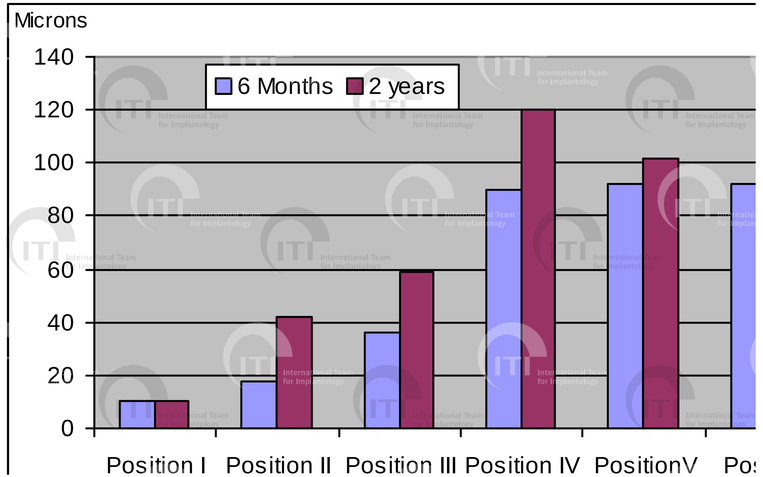
6 months



2 years

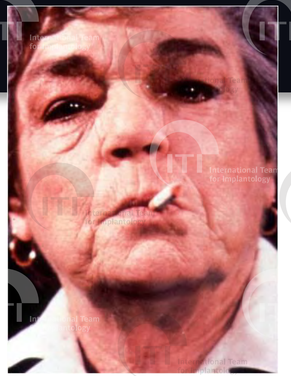


2 years

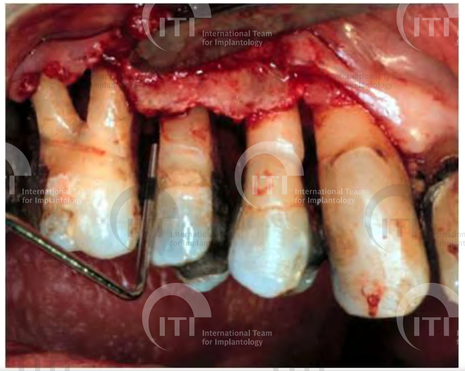


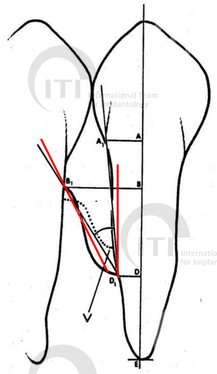
Prognostic Factors affecting outcome: Patient and defect

Patient:
Good oral hygiene, low levels of plaque score
Smoking affects negatively the outcome



Defect:
Morphology of defect
Radiographic defect angle: 25° (narrow defect) or 37° (wide defect)



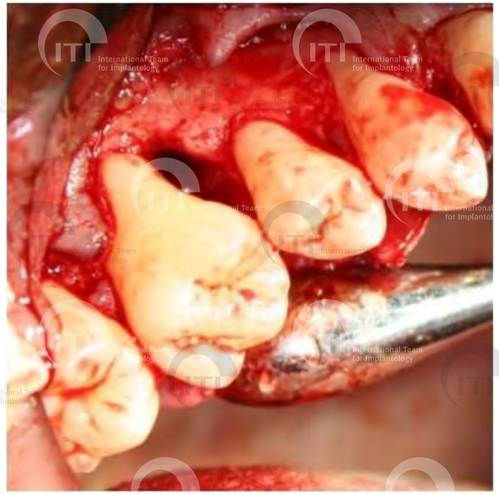


Prognostic Factors: Tooth

Endodontic condition
(properly perfomed)

Tooth mobility
Hypermobility was negatively and dose dependant associated with outcome

Membrane exposure: challenging technique-clinician's effect



3 days

7 days

14 days

Flap designs for papillae preservation: soft tissue management, maximal primary closure

Technique sensitive procedures: effect of flap design (SPPF vs. MWF)

Gingival blood flow changes evaluated by Laser Doppler Flowmetry following periodontal surgery (SPPF vs. MWF)

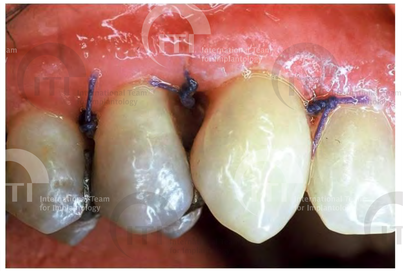
N. Donos, M. Retzepi, M. Tonetti J. Period. Res 2005
M. Retzepi, M. Tonetti, N. Donos J Clin Periodontology 2007a
M. Retzepi, M. Tonetti, N. Donos J. Clin Periodontology 2007b

LDF measurements before surgery, post anaesthesia, end of surgery, day 1, 2, 3, 4, 7, 15, 30, 60.

Healing following periodontal surgery (SPPF vs. MWF)

Non-smoker

Day 1

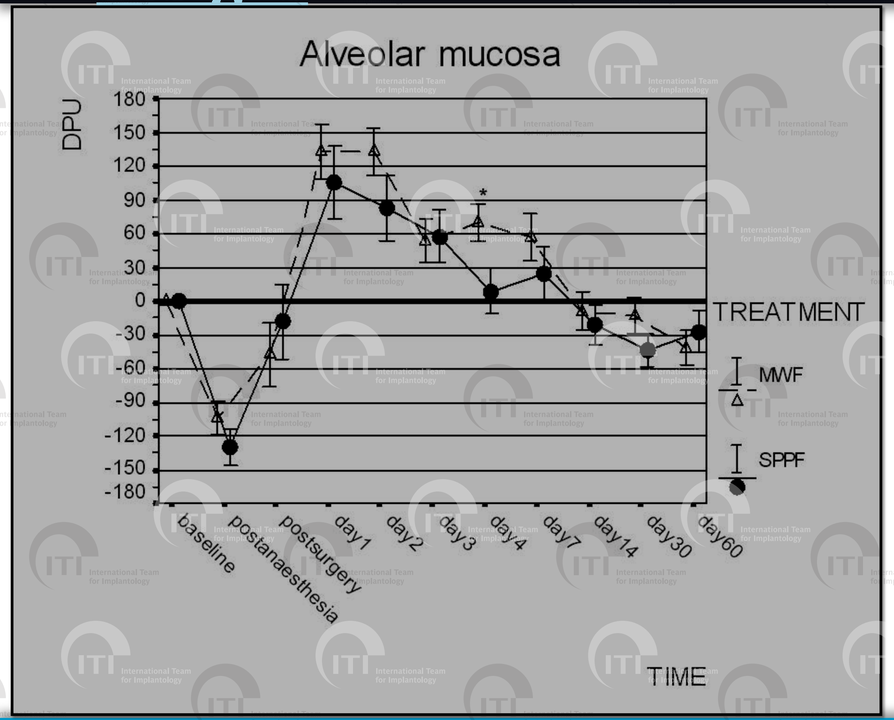


Day 3

Day 7

smoker

Gingival blood flow changes following different types of periodontal flap designs



Significant ischemia in both flaps following anaesthesia & immediately postoperatively

Hyperaemic response in both flaps on day 1, which tended to **resolve by day 4 at the SPPF**, but persisted until day 7 at the MWF

Improved clinical outcomes with Simplified Papillae Preservation flap could also be attributed to faster vascularization

Blood flow returned to baseline levels by day 14

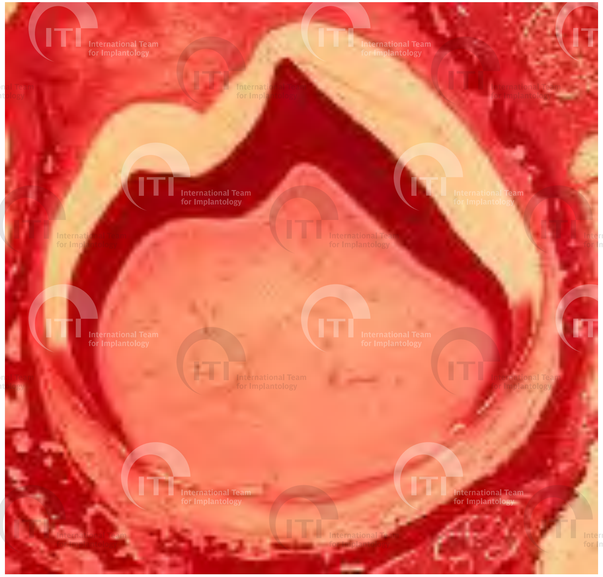
Enamel Matrix Derivative

Composition of the enamel matrix (Hammarström 1997):

90% amelogenin

10% proline containinig non amelogenins, tuftelin and other serum proteins

Sanz et al.: J Periodontol 2004
100% complication with GTR
6% complication with EMD



Five-year results following treatment of intrabony defects with enamel matrix proteins and guided tissue regeneration

A. Sculean, N. Donos, F. Schwarz, J. Becker, M. Brecx, N. Arweiler. 2004

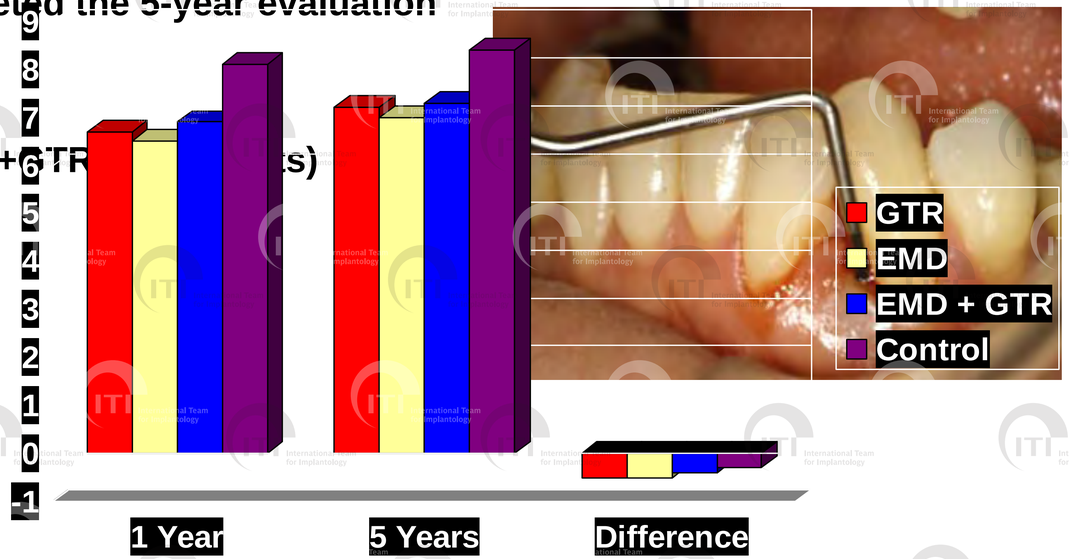
42 patients completed the 5-year evaluation

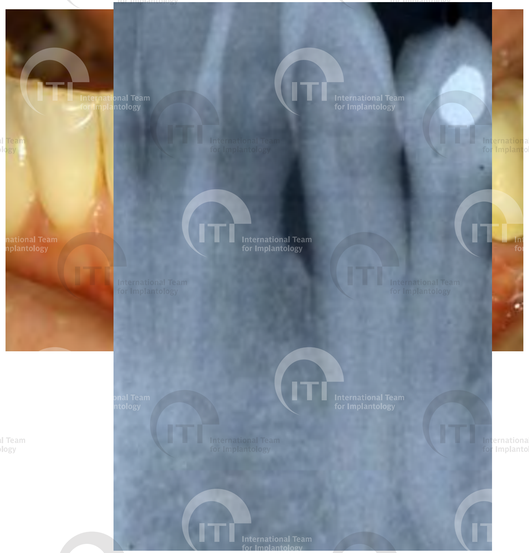
EMD (10 patients)

GTR (11 patients)

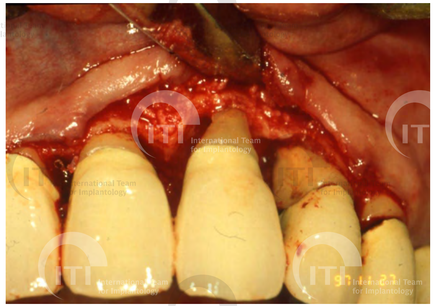
Combination EMD+GTR (ts)

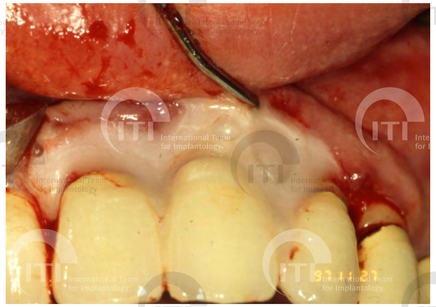
OFD: 10 patients

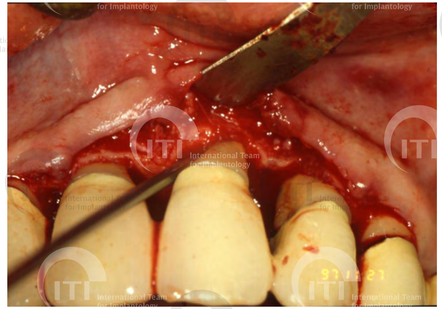


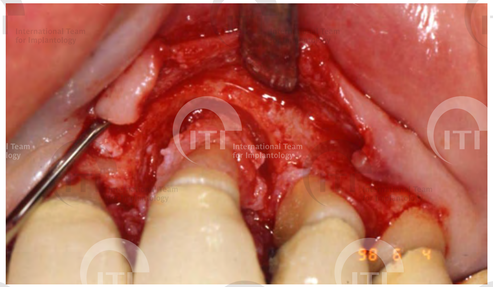


Healing of human intrabony defects following treatment with enamel matrix proteins or guided tissue regeneration. Sculean, Donos et al. 1999

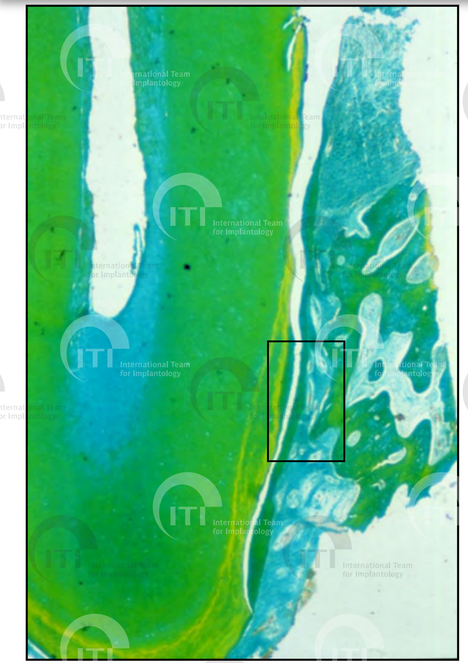




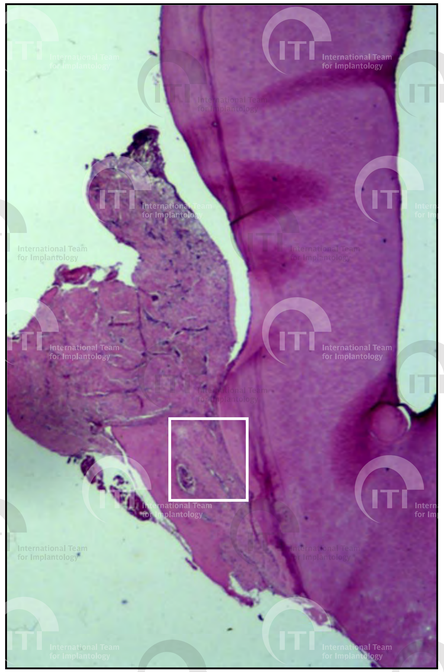




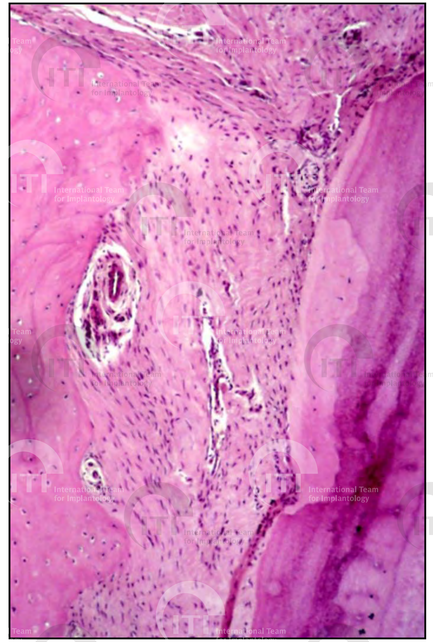
Human biopsy GTR vs. EMD



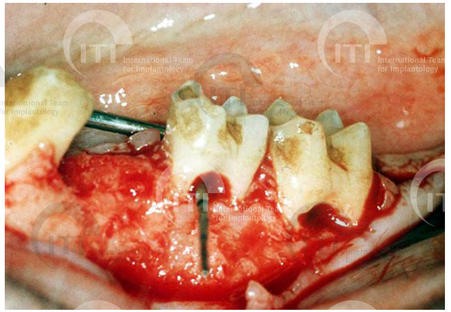
GTR



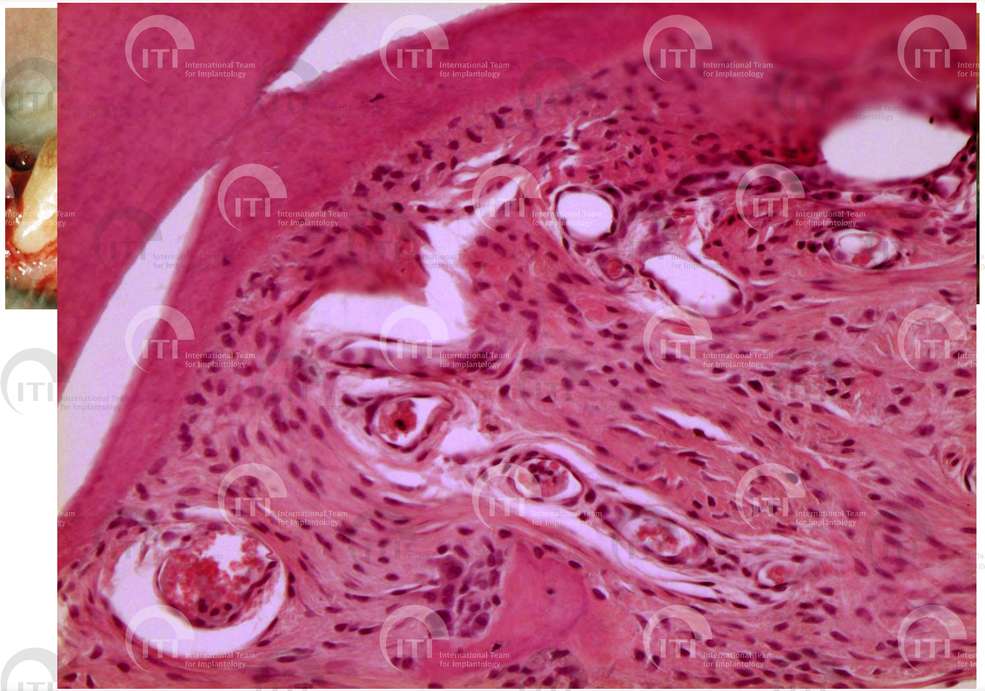
EMD

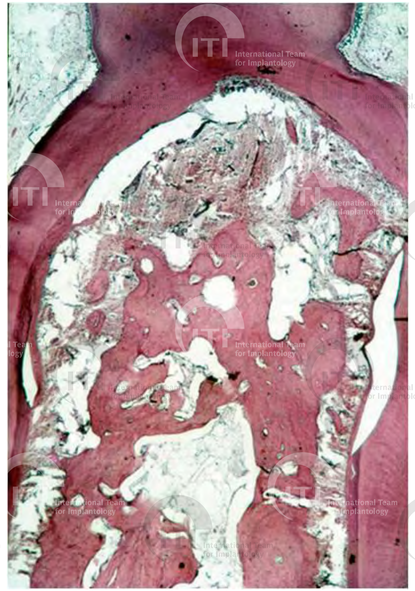


Treatment of Class III furcation involvements with GTR/+EMD Donos et al. 2003



Clinical challenge



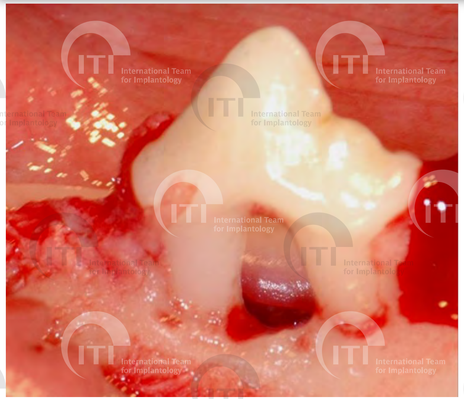


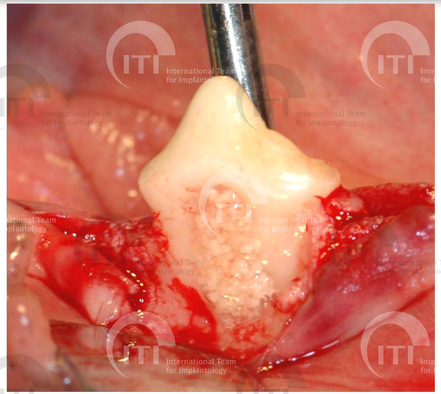
EMD

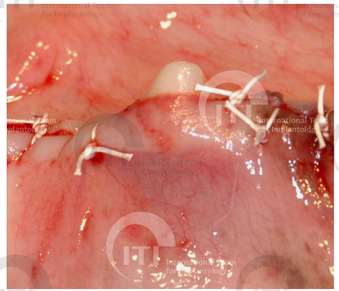
EMD + GTR

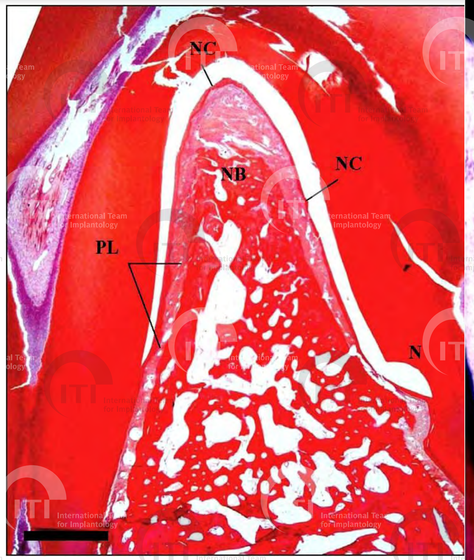
Treatment of Class III furcation (acute) defects. Importance of animal model in regeneration.

Mardas et al. In manuscript









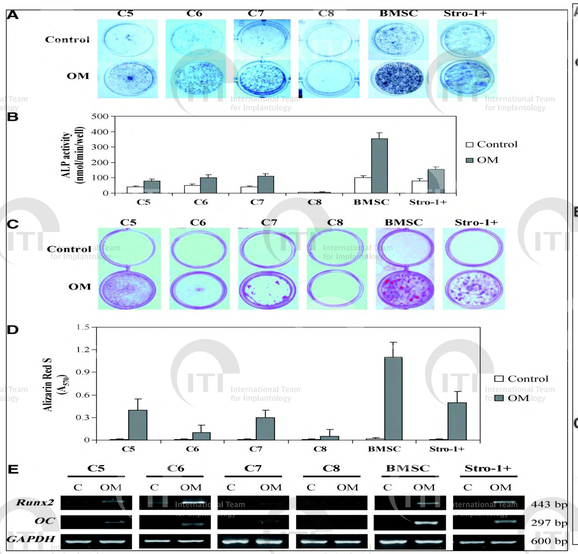
30 days

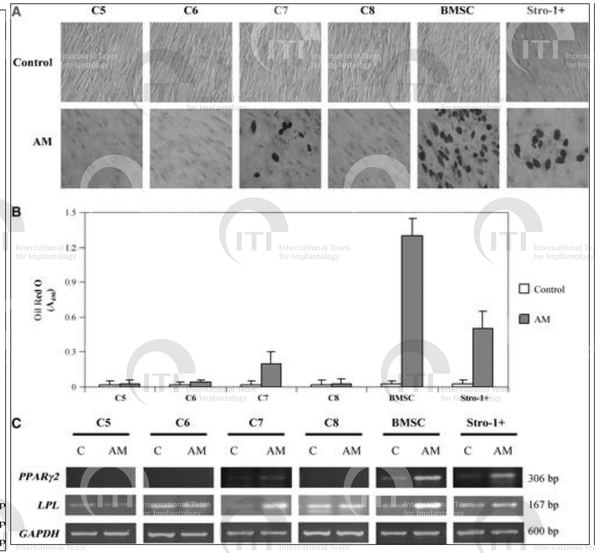
5 months control

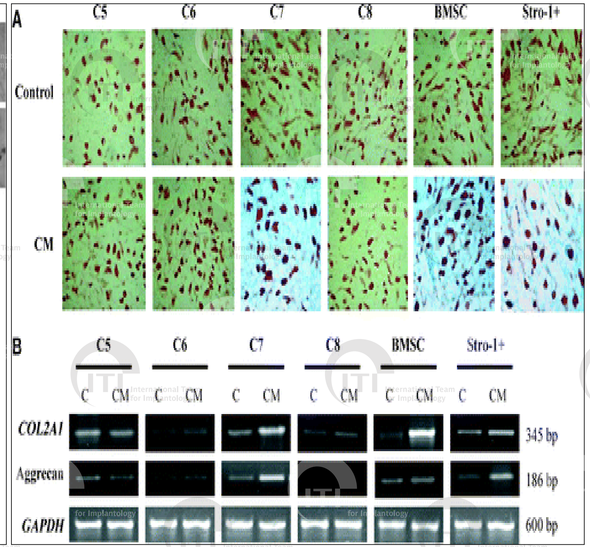
5 months

Isolation & characterization of stem cell clones from adult human ligament

W. Singnatanadgit, N. Donos, I. Olsen Tissue Enginneering Part A, 2009







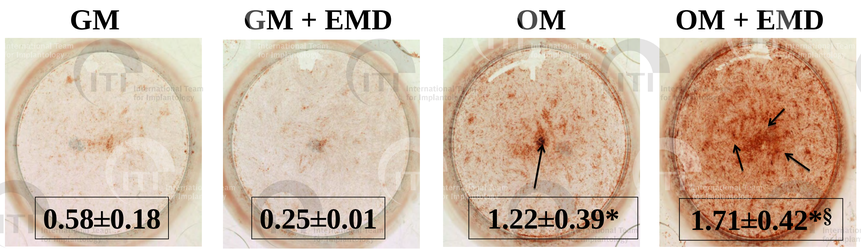
Periodontal ligament contains clonal population of cell(s) capable of ***osteogenic, adipogenic & chondrogenic*** differentiation *in vitro*

Effects of EMD on osteogenic genes in PDL cells *in vitro*. *H. Amin, I. Olsen, N. Donos.*

Relative gene expression			
Expression time	**Gene**	**Osteogenic medium (OM)[1]**	**OM + EMD[2]**
Early	ALP	1.35 ± 0.03	**4.27 ± 0.32[§]**
	OP	1.30 ± 0.60	**4.10 ± 0.62[§]**
Late	OC	2.51 ± 0.87*	**3.93 ± 0.98[§]**
	BSP	1.87 ± 0.58	**5.42 ± 1.12[§]**

[1] compared with growth medium (GM) alone, defined as 1.0
[2] compared with OM alone, defined as 1.0
[*] p<0.05 compared with GM alone [§]p<0.05 compared with OM alone

Effects of EMD on terminal osteogenic differentiation- alizarin red staining



The arrows show the alizarin red positive bone-like nodules, and numbers are the alizarin red staining intensities

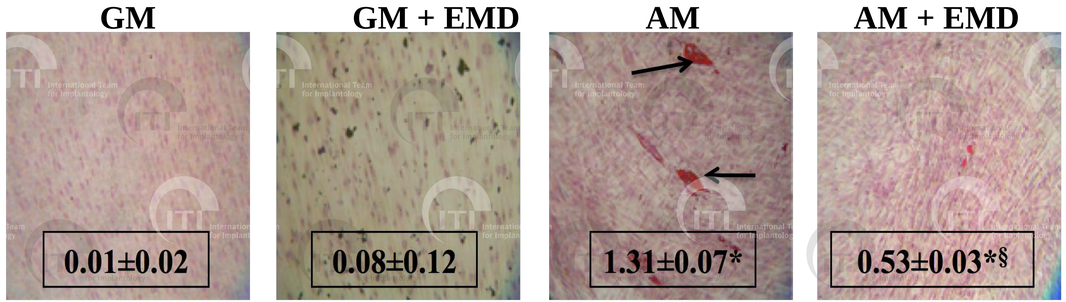
EMD stimulated early and late osteogenic marker genes and markedly up-regulated terminal osteogenesis

Effects of EMD on adipogenic genes

Relative gene expression			
Expression time	**Gene**	**Adipogenic medium (AM)[1]**	**AM + EMD[2]**
Early	PPARγ2	4.63 ± 0.52*	**0.42 ± 0.71[§]**
Late	LPL	611.80 ± 18.56*	**0.05 ± 0.47[§]**

[1] compared with GM alone, defined as 1.0
[2] compared with AM alone, defined as 1.0
[*] p<0.05 compared with GM alone [§]p<0.05 compared with AM alone

Effects of EMD on terminal adipogenic differentiation- oil red O staining



The arrows show the oil red O positive lipid-like droplets, and numbers are the oil red O staining intensities

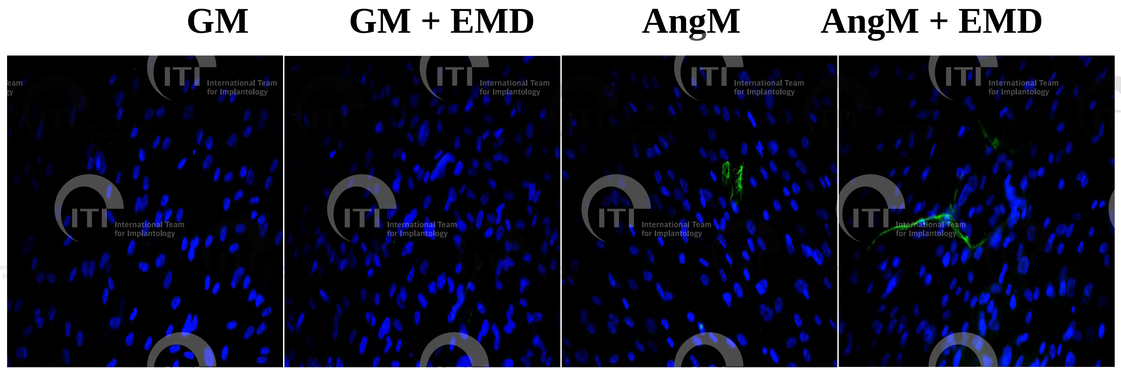
EMD strongly down-regulated early and late adipogenic marker genes and strongly inhibited terminal adipogenesis

Effects of EMD on angiogenic genes *in vitro*

Relative gene expression			
Expression time	**Gene**	**AngM[1]**	**AngM + EMD[2]**
Early	Ang-1	1.69 ± 0.38*	**2.51 ± 0.66[§]**
Late	vWF	2.54 ± 0.65*	**4.02 ± 0.94[§]**

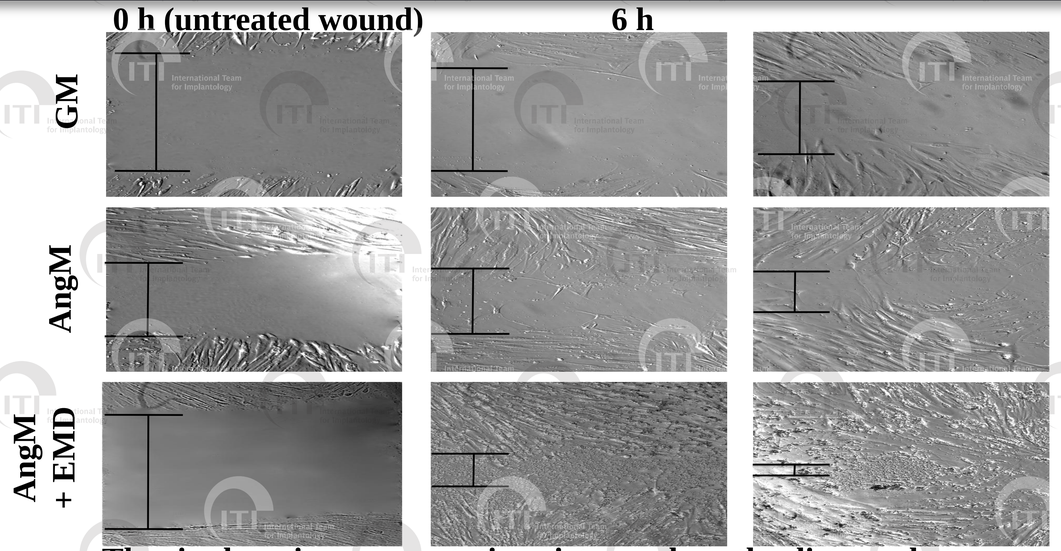
[1] compared with GM alone, defined as 1.0
[2] compared with AngM alone, defined as 1.0
* $p<0.05$ compared with GM alone [§]$p<0.05$ compared with AngM alone

Effects of EMD on terminal angiogenic differentiation-VE-cadherin staining

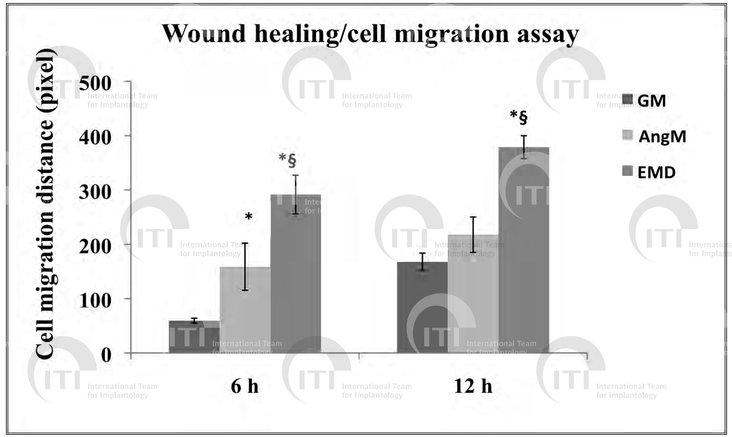


EMD stimulated early and late angiogenic marker genes and terminal angiogenic differentiation (VE-cadherin positive cells)

Effects of EMD on primary PDL wound healing *in vitro*



The size bars in representative pictures show the distance between wounds



* p<0.05 compared with GM alone

§ p<0.05 compared with AngM alone

EMD stimulated *in vitro* healing of the PDL cell wound & appeared to heal the wound completely by 12 h

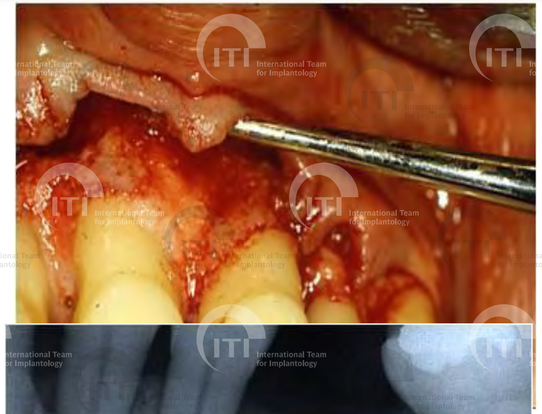
Clinical outcomes with bioactive agents alone or in combination with grafting or guided tissue regeneration

Leonardo Trombelli and Roberto Farina

Research Centre for the Study of Periodontal Diseases, University of Ferrara, Ferrara, Italy

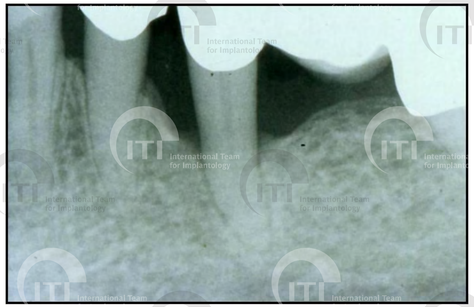
EMD alone or in combination with grafts can be effectively used to treat intra-osseous defects and the clinical results appear to be stable for a long-term

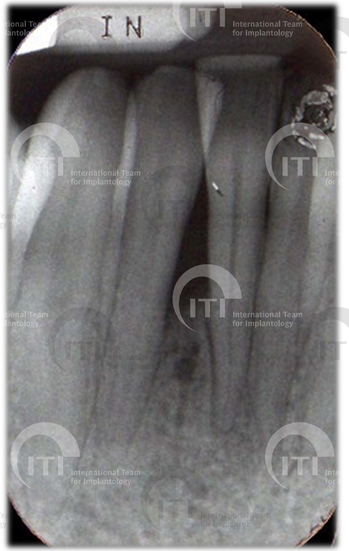
Periodontal regeneration: change of prognosis at the appropriate defect & patient



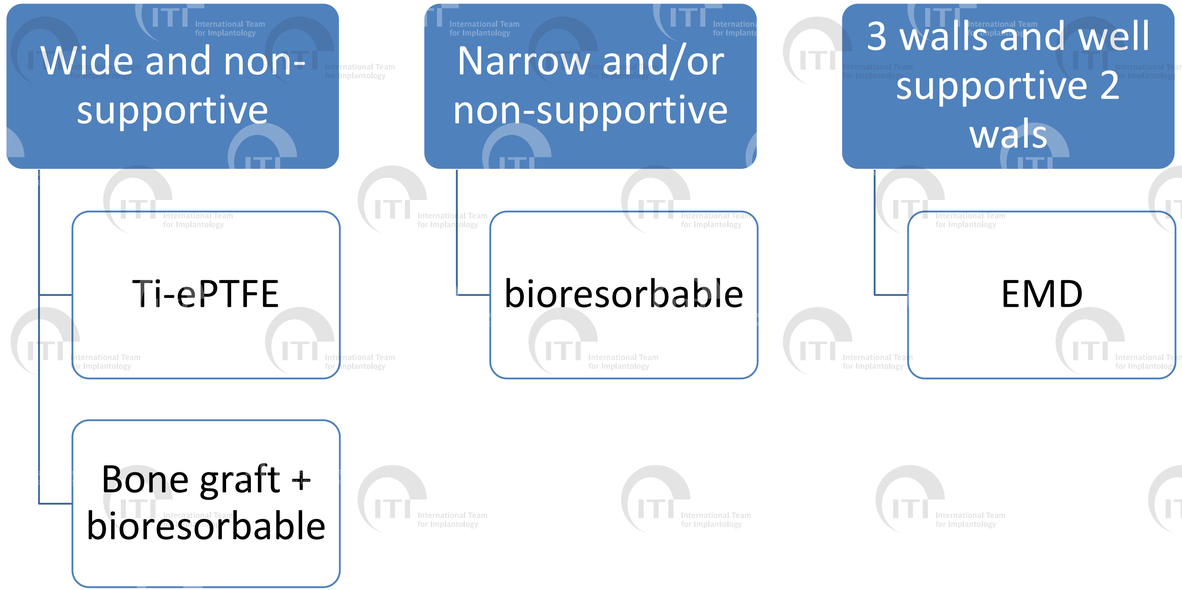
Courtesy Prof. Sculean

Change of tooth prognosis (“strategic” position & financial consideration)



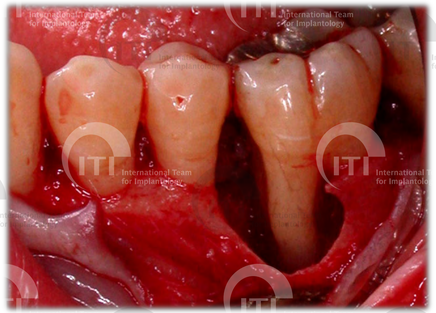


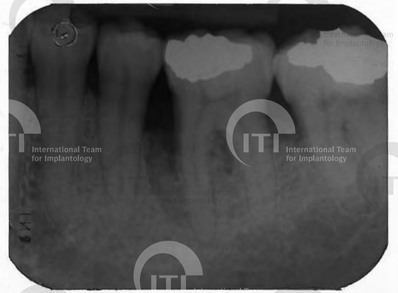
Selection of regenerative material- deep intrabony component (Cortellini & Tonetti)



What are the longevities of teeth and implants? Holm-Pedersen et al. 2007

- Teeth with healthy periodontal tissues have a high longevity (up to 99.5% over 50 years)
- Periodontally compromised teeth, but treated and under SPT, 92-93% survival of the teeth
- Survival of dental implants up to 94% after 10 years
- Multiple restorative aspects lead to critical appraisal of the value of a tooth
- **However, dental implants do not surpass the longevity of successfully treated natural teeth**





12 months after GTR

Thanks for Your attention!