## Outcomes of Regenerative Endodontic Treatment

Dr. Pedram Iranmanesh

DDS, MSc (Endodontics), PhD

Department of Endodontics, Isfahan University of Medical Sciences

### Failures

### Regenerative Endodontics: A Systematic Analysis of the Failed Cases

Waleed Almutairi, BDS, \*\* Ghaeth H. Yassen, BDS, MSD, PhD, \* Anita Aminoshariae, DDS, MS, \* Kristin A. Williams, DDS, MPH, \* and Andre Mickel, DDS, MSD\*

#### **Abstract**

Introduction: The aim of this systematic review was to analyze failed cases of regenerative endodontic treatment (RET) reported in the literature in terms of etiology, diagnosis, treatment protocols, signs of failure, and additional endodontic interventions. Methods: Electronic searches were performed in PubMed, Web of Science, and ProQuest Dissertations & Theses databases. All in vivo publications in humans that reported at least 1 failed case of RET were included in this systematic review. Failed RET cases were defined in the current study as any case that required an additional endodontic intervention or extraction after the completion of the initial RET. Results: A total of 28 studies that reported 67

Regenerative endodontics has been recommended as the treatment of choice in cases of immature teeth with necrotic pulps. The majority of clinical regenerative endodontic treatment

#### Significance

There is a need for a detailed description of the etiology, diagnosis, clinical protocols, and postoperative follow-up to provide a better understanding of the circumstances surrounding the failure or success of regenerative endodontic treatments.

(RET) cases reported in the literature have shown positive clinical outcomes (1, 2). The absence of clinical signs and symptoms and radiographic evidence of periapical healing have been recognized as the primary indications of a successful endodontic regeneration procedure (3). Additionally, increased thickness of the root walls and/ or increases in the length of the immature root as well as regaining the vitality of the

- 28 studies that reported 67 failed cases of RET were included
- Etiology in the initiation of RET;
  - 59% of these cases were caused by dental trauma,
  - and 30% were caused by dens evaginatus.
- 26 (39%) failed RET cases were detected at least 2 years
- 53 (79%) failed RET cases were presented with signs and/or symptoms of persistent infection.

Persistent infection was the main presentation in 79% of failed RET cases.

Furthermore, 39% of failed RET cases were identified after more than 2 years of follow-up.

Future studies should include a detailed description of the etiology, preoperative variables, intraoperative protocols, and postoperative follow-up

#### Journal Pre-proof

Does the Etiology of Pulp Necrosis affect Regenerative Endodontic Treatment Outcomes? A Systematic Review and Meta-Analyses

Simay Koc, Massimo Del Fabbro

PII: S1532-3382(20)30004-X

DOI: https://doi.org/10.1016/j.jebdp.2020.101400

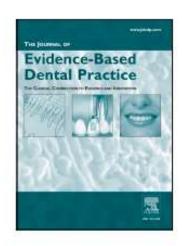
Reference: YMED 101400

To appear in: The Journal of Evidence-Based Dental Practice

Received Date: 25 August 2019

Revised Date: 1 December 2019

Accepted Date: 17 January 2020



	Traum	na	Carie	S		Risk Ratio		Risi	k Ratio		
Study or Subgroup	<b>Events</b>	Total	<b>Events</b>	Total	Weight	M-H, Fixed, 95% C	l	M-H, Fix	ced, 95%	CI	
Adel Alagl 2017	0	12	0	3		Not estimable					
Tuğba Bezgin 2015	1	8	0	2	36.0%	1.00 [0.05, 18.57]		-	•	F0.2	
Linsuwanont 2017	1	5	0	2	32.0%	1.50 [0.08, 26.86]		÷	-		6
Jidapa Silujjai 2017	1	5	0	2	32.0%	1.50 [0.08, 26.86]		0			ί.
Total (95% CI)		30		9	100.0%	1.32 [0.25, 6.98]					
Total events	3		0								
Heterogeneity: Chi <sup>2</sup> = 0	).05, df = 2	2 (P = (	0.98); l² =	0%			0.01	0.4	+	10	400
Test for overall effect: 2	Z = 0.33 (I	P = 0.7	4)				0.01	0.1 Favours Trauma	Favours	10 s Caries	100

Study or Subgroup	Carie Events		DE Events		Weight	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Fig. 100 - Philipping - Philipping	LVCIILO	Total	LVCIIIS	Total		76 90 000000 10 1000	
Jidapa Silujjai 2017	0	2	3	10	46.2%	0.52 [0.04, 7.59]	
Linsuwanont 2017	0	2	3	8	53.8%	0.43 [0.03, 6.12]	
Total (95% CI)		4		18	100.0%	0.47 [0.07, 3.11]	
Total events	0		6				
Heterogeneity: Chi <sup>2</sup> = 0.01, df = 1 (P = 0.92); $I^2 = 0\%$							
Test for overall effect: Z = 0.78 (P = 0.44)							0.001

comparing teeth with caries vs. dens evaginatus, and trauma vs. caries confirmed that

there was no evidence for difference in outcomes

### Discoloration

# Alternative to Avoid Tooth Discoloration after Regenerative Endodontic Procedure: A Systematic Review

Luciane Geanini Pena dos Santos<sup>1</sup>, Luiz Alexandre Chisini<sup>1</sup>, Camila Guerner Springmann<sup>2</sup>, Beatriz Dulcineia Mendes de Souza<sup>2</sup>, Fernanda Geraldo Pappen<sup>1</sup>, Flávio Fernando Demarco<sup>1</sup>, Mara Cristina Santos Felippe<sup>2</sup>, Wilson Tadeu Felippe<sup>2</sup>

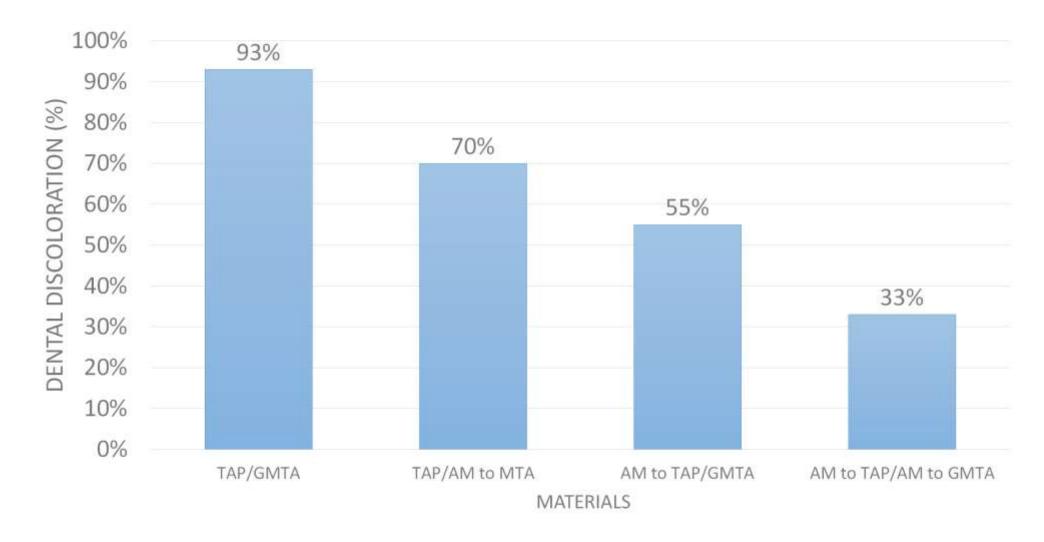
This systematic review aimed to evaluate whether alternative materials to conventional triple antibiotic paste (TAP - metronidazole, ciprofloxacin, and minocycline) and grey mineral trioxide aggregate (GMTA) could avoid tooth discoloration in teeth submitted to Regenerative Endodontic Procedure (REP). It was also investigated if dental bleaching is able to reverse the color of darkened teeth due to REP. The search was conducted in four databases (Medline via PubMed, Scopus, ISI Web of Science and BVS - Virtual health library), following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. The retrieved papers were uploaded in the software EndNote™ and two reviewers independently selected the studies and extracted the data. Only studies in

#### ISSN 0103-6440



<sup>1</sup>Graduate Program in Dentistry, UFPel - Universidade Federal de Pelotas, Pelotas, RS, Brazil <sup>2</sup>Department of Dentistry, UFSC - Universidade Federal de Santa Catarina, Florianópolis, SC, Brazil

Correspondence: Flávio Fernando Demarco, Rua Gonçalves Chaves, 457, 5º andar, CEP 96015-560 Pelotas, RS, Brazil. Tel.: +55-53-3222-6690. e-mail: ffdemarco@gmail.com



Alternative materials to GMTA: WMTA, Biodentine, and CEM
Alternatives to minocycline are cefaclor, amoxicillin or clindamicine. Double antibiotic paste)

Alternatives to Triple Antibiotic Pastes and Gray MTA avoid tooth discoloration

Dental bleaching is able to reverse partially the color of discolored

Minocycline seems to be the main responsible for discoloration induced by TAP.

### Mature Teeth

#### **REVIEW ARTICLE**

Regenerative Endodontic
Procedures for the Treatment
of Necrotic Mature Teeth with
Apical Periodontitis: A
Systematic Review and
Meta-analysis of Randomized
Controlled Trials



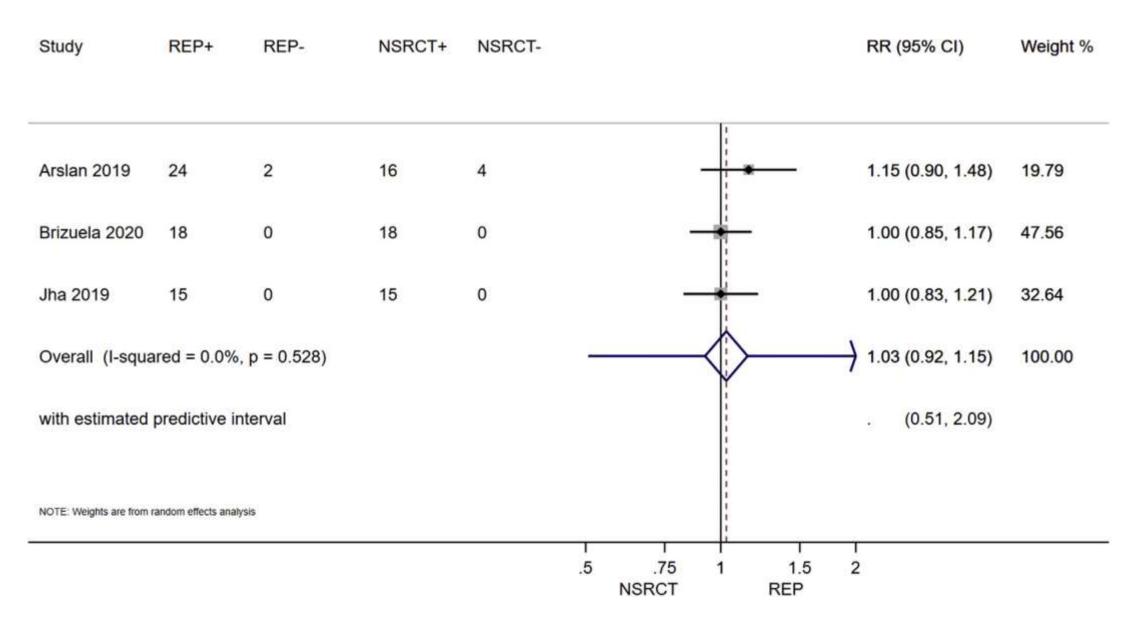
Antonios Glynis, DMD, MSc,\*
Federico Foschi, BDS, MSc,
PhD, FDS RCS, FHEA,†
Ismini Kefalou, DDS,\*
Despina Koletsi, DDS, MSc,
DMD, MSc, DLSHTM,
PGCHEd,§ and
Giorgos N. Tzanetakis, DDS,
MSc, MSc, PhD||

#### **ABSTRACT**

Introduction: Regenerative endodontic procedures (REPs) are intended to repair and regenerate part of the pulp-dentin complex. The aim of this study was to systematically appraise the existing evidence on the effectiveness of REPs on mature teeth with pulp necrosis and apical periodontitis. Methods: Electronic database and hand searches were performed on 8 databases of published and unpublished literature from inception to January 3, 2021, for the identification of randomized controlled trials (RCTs) or prospective clinical

#### SIGNIFICANCE

The results of the present systematic review highlight the potential of regenerative endodontic procedures to be considered as viable



A forest plot of subgroup analysis of survival rates.

Study	REP+	REP-	NSRCT+	NSRCT-				RR (95% CI)	Weight %
Arslan 2019	13	13	1	19		-		<b>—</b> 10.00 (1.42, 70.19)	30.04
Brizuela 2020	9	9	3	15			<b>-</b> 87	3.00 (0.97, 9.30)	69.96
Overall (I-square	ed = 19.5%, p	= 0.265)					>	4.31 (1.36, 13.62)	100.00
NOTE: Weights are from	random effects anal	ysis							
57					.2 .5 NSRCT		10 EP		

The random effects meta-analysis for a positive response to electric stimuli comparing REPs and conventional NSRCT

TABLE 4 - The Summary of Findings Table for the Quality of the Evidence according to Grading of Recommendations Assessment, Development and Evaluation (GRADE)

#### REPs vs NSRCTs for successful treatment and positive stimuli response

Patient or population: patients with necrotic mature teeth with periapical lesions

Settings: university Intervention: REPs Comparison: NSRCTs

Outcomes	Illustrative compa	arative risks* (95% CI)		No. of	Quality of the	Comments
	Assumed risk	Corresponding risk	Relative effect (95% CI)	participants (studies)	evidence (GRADE)	
Success of treatment	Study population 906/1000	933/1000 (833–1000)	RR = 1.03 (0.92-1.15)	112 (3 studies)	⊕ ⊕ ⊕ ⊖ moderate <sup>†</sup>	None
Positive response to electric stimuli	Study population 105/1000	454/1000 (143–1000)	RR = 4.31 (1.36–13.62)	82 (2 studies)	⊕ ⊕ ⊕ ⊖ moderate <sup>‡</sup>	None

The result highlight the potential of regenerative endodontic procedures to be considered as viable alternative treatment modalities

with high success rates

in cases of mature teeth presenting with pulp necrosis and apical periodontitis.



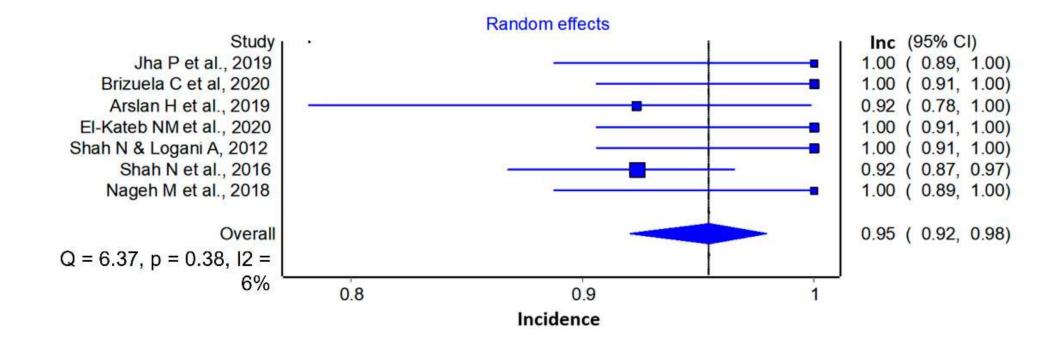


Article

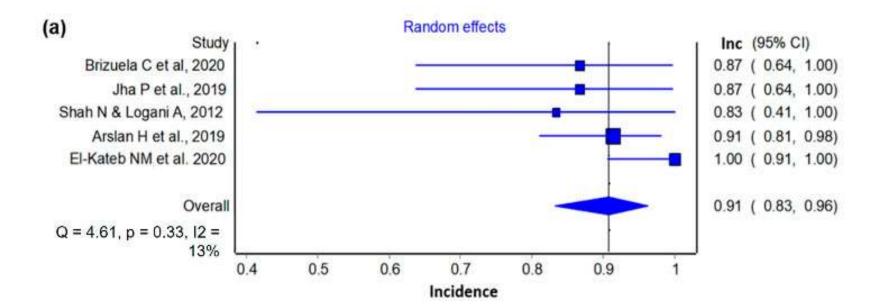
#### Prognosis of Regenerative Endodontic Procedures in Mature Teeth: A Systematic Review and Meta-Analysis of Clinical and Radiographic Parameters

Pantaleo Scelza <sup>1</sup>, Fabiano Gonçalves <sup>2</sup>, Isleine Caldas <sup>1</sup>, Fernanda Nunes <sup>1</sup>, Emanuelle Stellet Lourenço <sup>2</sup>, Sandro Tavares <sup>2</sup>, Marcela Magno <sup>3</sup>, Andrea Pintor <sup>3</sup>, Pietro Montemezzi <sup>4</sup>, Emanuele Di Edoardo <sup>5</sup>, Carlos Fernando de Almeida Barros Mourão <sup>6</sup>, <sup>8</sup>, Gutemberg Alves <sup>6</sup> and Miriam Zaccaro Scelza <sup>7</sup>, <sup>8</sup>

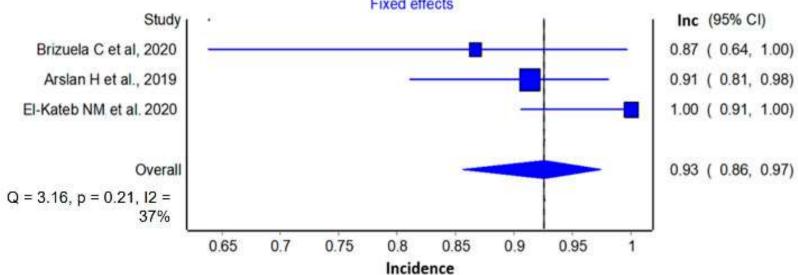
- Geriatric Dentistry Department, Universidade Federal Fluminense, Niterói 24020-140, RJ, Brazil; pantaleoscelza@terra.com.br (P.S.); isleinecaldas@hotmail.com (I.C.); nandasouzanunes@gmail.com (F.N.)
- Post-Graduate Program in Dentistry, Universidade Federal Fluminense, Niterói 24020-140, RJ, Brazil; fabianopalmeira@hotmail.com (F.G.); emanuelle\_stellet@yahoo.com.br (E.S.L.); sandro.tavares04@gmail.com (S.T.)
- Department of Pediatric Dentistry and Orthodontics, Universidade Federal do Rio de Janeiro, Rio de Janeiro 21941-902, RJ, Brazil; marcela.magno@hotmail.com (M.M.); andrea\_pintor@hotmail.com (A.P.)
- Independent Researcher, 24128 Bergamo, Italy; m.montemezzi@libero.it
- Independent Researcher, 20100 Milan, Italy; emanueledr.diedoardo@libero.it



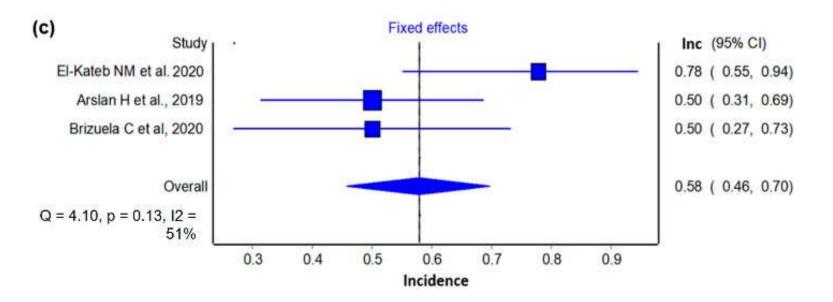
Success rate



(b) Fixed effects

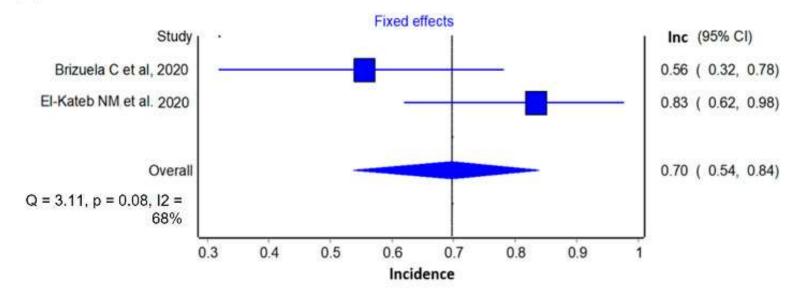


incidence of periapical lesion reduction



incidence of positive electrical test response

(d)



incidence of positive cold test response

high incidence of success of REP on the healing of mature teeth with a necrotic pulp

reduction on the periapical lesion and positive responses to sensitivity tests

However, the low certainty of the available evidence indicates the need for more clinical studies for paradigm shift

# As a final point





Systematic Review

#### Regenerative Endodontic Procedures: An Umbrella Review

Luísa Bandeira Lopes <sup>1,2,\*</sup>, João Albernaz Neves <sup>2,3</sup>, João Botelho <sup>2,4</sup>, Vanessa Machado <sup>2,4</sup> and José João Mendes <sup>2,4</sup>

- Dental Pediatrics Department, Egas Moniz—Cooperativa de Ensino Superior, 2829-511 Almada, Portugal
- <sup>2</sup> Clinical Research Unit (CRU), Centro de Investigação Interdisciplinar Egas Moniz (CiiEM), Egas Moniz—Cooperativa de Ensino Superior, 2829-511 Almada, Portugal; jalbernazneves@gmail.com (J.A.N.); jbotelho@egasmoniz.edu.pt (J.B.); vmachado@egasmoniz.edu.pt (V.M.); jmendes@egasmoniz.edu.pt (J.J.M.)
- Endodontics Department, Egas Moniz—Cooperativa de Ensino Superior, 2829-511 Almada, Portugal
- Evidenced-Based Hub, CiiEM, Egas Moniz—Cooperativa de Ensino Superior, 2829-511 Almada, Portugal
- \* Correspondence: luisabpmlopes@gmail.com

Abstract: The Regenerative Endodontic Procedure (REP) is a biologically based method in which a damaged pulp-dentin complex is replaced by a new vital tissue. This umbrella review aimed to critically assess the available systematic reviews (SRs) on REP. An electronic database search was conducted (PubMed-Medline, CENTRAL, Scielo, Web of Science, and LILACS) until December

29 Systematic Reviews (SRs)

The quality of evidence produced by the available SRs was not favorable.

Future high standard SRs and well-designed clinical trials are warranted

### Conclusion

• بر اساس هرم شواهد

اکثر مطالعات در حیطه رژنراسیون اندودانتیکس در پایین ترین سطح قرار داشتند سطح ۵ شامل: گزارش مورد، نظرات شخصی

• نتایج مطالعات در حیطه رژنراسیون اندودانتیکس شامل ارزیابی های زیر بود:

۱. بالینی

۲. رادیوگرافیک

۳. هیستولوژیک

• در مقایسه درمان رژنراسیون اندودانتیکس و پلاگ MTA: موفقت و بقا بدون تقاوت بود (مطالعه ترابی نژاد).

• در مقایسه درمان رژنراسیون اندودانتیکس و اپیکسیفکاسیون: برتری دیده نشد ( مطالعه متاآنالیز) افزایش طول ریشه (مطالعه کارآزمایی بالینی)

#### • در دندان های نابالغ

نتایج مربوط به نرخ موفقت، رفع پاتوز پری اپیکال عالی بود نتایج مربوط به پارامترهای رادیولوژیک متفاوت بود

• دردندان های بالغ (در مقایسه با درمان های مرسوم) پاسخ به EPT به صورت چشمگیری برتر بود

#### • در ارزیابی هیستولوژیک

- ۱. بافت تشکل شده ناشی از ترمیم و باسازی می باشد.
  - ۲. باقی مانده پالپ به بازسازی کمک می کند.
  - ۳. بافت پری اپیکال سالم به بازسازی کمک می کند.

- نمود اصلی شکست رژنراسیون اندودانتیکس عفونت پایدار
- برخی از مراحل رژنراسیون اندودانتیکس بر نتایج آن تاثیرگذار بود. خمیر آنتی بوتیک: ضخامت ریشه هیدورکسید کلسیم: بسته شدن اپیکال
  - اتیولوژی بر نتایج رژنراسیون اندودانتیکس بی تاثیر بود.

• عامل اصلی تغییر رنگ رژنراسیون اندودانتیکس جز مینوسیکلین در خمیر آنتی بیوتیک سه گانه

• مروی جامع (Umbrella review) بر روی مطالعات مروری منظم مربوط به نتایج رژنراسیون اندودانتیکس

نیاز به کارآزمایی های بالینی برای حصول به نتایج قطعی

# Thank you