Scaffolds Use In Regenerative Endodontics: an Analysis of *In-Vivo* Studies

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Objectives

To determine if regenerative endodontic procedures completed in immature necrotic permanent teeth [population] with the addition of a scaffold material [intervention] have better outcomes than those completed with a patient's on blood clot [control].

To propel future endodontic research at Boston Children's Hospital specifically pertaining to alternatives to the traditional blood clot used as a biological scaffold in regenerative endodontics.

Background

Pulpal necrosis is a serious, irreversible condition describing the death of vital tissue inside a tooth due to causes such as trauma, caries, and developmental abnormalities; this condition can represent especially devastating consequences for pediatric patients with immature permanent dentition. [1, 2, 3]

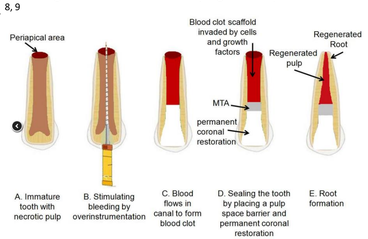
Regenerative endodontics is a treatment which provides several benefits including its ability to restore pulpal components and functions including continued root development and apical closure for necrotic immature teeth. [4]

Recent advancements in tissue engineering have identified three critical components - stem cells, growth factors, and scaffolds - and their spatial and temporal assembly as the foundation of pulpal tissue regeneration. [5,6]

The use of the blood clot as a scaffold is consistent with its use in the majority of published regenerative endodontic procedures. [2]

Dental providers at Boston Children's Hospital have encountered some difficulty in achieving the formation of a blood clot as a scaffold. In addition to this challenge, blood clots also lack certain properties of an ideal scaffold such as the incorporation of growth factors and appropriate mechanical properties. [7]

There are various alternatives to blood clots as a scaffold including platelet rich plasma (PRP), platelet rich fibrin (PRF), and hydrogels which may be able to bypass several of the aforementioned challenges associated with relying on the patient's own ability to generate a scaffold. [8, 9]



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10. Photo credit:: https://dentagama.com/img/21121501492?EndodonticRevascularization.png

Methods

A literature review was conducted on the basis of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRIMSA-ScR) Checklist. A search of the existing literature was conducted on Pubmed, Web of science, Embase and Cochrane using the following search keywords: "regenerative endodontic procedures," "immature permanent teeth," and "scaffolds." A total of 341 articles were reviewed; of these, 12 met our inclusive criteria.

Inclusive Criteria:

- *In-vivo* clinical studies
- Human subjects
- Prospective, retrospective studies and review articles
- Primary endodontic treatment
- Necrotic and immature teeth
- Follow up >6 months
- Articles specific to evaluation of scaffold materials
- Clinical technique for regenerative endodontic procedures as described by the American Association of Endodontics.

Conclusions

Current literature demonstrates that platelet rich (PRP, PRF) biological scaffolds have numerous in-vivo studies that demonstrate adequate comparable success rates to the traditional blood clot (BC) scaffold.

Clinical *in-vivo* studies show that platelet based scaffolds (PRP, PRF) offer comparable effectiveness when compared to traditional blood clot scaffold.

Regenerative procedures completed with PRP/PRF/BC scaffolds show similar clinical (asymptomatic, absence of infection) and radiographic (apical closure, continued root formation, increased dentinal wall thickness) success rates.

Regained pulp vitality is difficult to achieve and predict even after regenerative procedures, regardless of scaffold material utilized.

Similarities in success rates leave the impression that success is more dependent on clinical technique (standardized AAE protocol by a highly trained clinician) and case selection rather than scaffold material selection.

A disadvantage with PRP/PRF based scaffolds is the extra necessary step of drawing blood and centrifuging for extraction of the material.

PRP/PRF based biological scaffolds can prove useful when the availability of bleeding is absent during a regenerative procedure.

Current literature lacks well designed *in-vivo* studies involving scaffolds that are synthetic or derived from other biological sources.

Additional research is necessary in order to identify novel scaffolds and to further improve overall success rates for regenerative treatment for the immature necrotic permanent tooth.

Results

Article	Type of Study	Number of Teeth	Scaffold Material	Control Y or N	Periapical Healing/No new PARL	Asymptomatic/No Clinical Infection	Pulp Vitality Tests	Apical closure	Dentinal wall thickening	Root Lengthening
(Zeid, 2021)	Prospective	23	BC	N/A	BC: 100% (23/23)	100% (23/23)	Mixed results	Significant (P = 0.0003)	Significant (0.0006)	Insignificant (p=0.164)
(Alagl, 2017)	RCT	30	PRP	BC	PRP: 100% (15/15) BC: 100% (15/15)	PRP: 100% BC: 100%	Mixed results	PRP: 93% (14/15) BC: 53% (8/15)	N/A	PRP: 93% (14/15) BC: 53% (8/15)
(Bezgin, 2015)	RCT	20	PRP	BC	PRP: 100% (10/10) BC: 90% (9/10)	PRP: 100% (10/10) BC: 100% (10/10)	Mixed results	PRP: 70% (7/10) BC: 60% (6/10)	N/A	N/A
(Cehreli, 2022)	Case Series	5	BC	N/A	100% (5/5)	100% (5/5)	BC: 20% (1/5)	100% (5/5)	100% (5/5)	N/A
(Chan, 2017)	Prospective	28	BC	N/A	86% (24/28)	93% (26/28)	BC: 0% (28/28)	85% (22/26)	81% (8/22)	92% (22/24)
(Chrepa, 2020)	Care Series	51	BC	N/A	92% (47/51)	92% (47/51)	BC: 54% (26/48)	92% (43/47)	92% (43/47)	92% (43/47)
(ElSheshtawy, 2020)	RCT	22	PRP	BC	Changes significant in both groups	PRP: 86% (12/14) BC: 88% (15/17)	PRP: 7% (1/14) BC: 0% 0 (17)	Changes significant in both groups	Changes significant in both groups	Changes significant in both groups
(Kritika, 2021)	Prospective	23	PRF	N/A	100% (23/23)	100% (23/23)	N/A	Significant (P < 0.001)	Mixed results	Significant (P < 0.001)
(Lv, 2018)	Retrospective	10	PRF	BC	PRF: 100% (5/5) BC: 100% (5/5)	PRF: 100% (5/5) BC: 100% (5/5)	N/A	PRF: 80% (4/5) BC: 80% (4/5)	PRF: 80% (4/5) BC: 80% (4/5)	PRF: 80% (4/5) BC: 80% (4/5)
(Nawal, 2020)	Case Series	6	PRF	N/A	PRF: 100%	PRF: 100%	PRF: 0% (0/6)	Mean 30% closure	Significant increase	Significant increase
(Shivashankar, 2017)	RCT	60	PRF, PRP	BC	PRF: 88% (16/18) BC: 100% (15/15) PRP: 100 (19/19)	PRF: 100% (18/18) BC: 100% (15/15) PRP: 100 (19/19)	N/A	PRF: 88% (16/18) BC: 100% (15/15) PRP: 100 (19/19)	PRF: 88% (16/18) BC: 100% (15/15) PRP: 100 (19/19)	PRF: 88% (16/18) BC: 100% (15/15) PRP: 100 (19/19)
(Ulusoy, 2019)	RCT	73	PP, PRP, PRF	BC	PRF: 94% (16/17) PRP: 100% (18/18) PP: 100% (17/17) BC: 95% (20/21)	PRF: 94% (16/17) PRP: 100% (18/18) PP: 100% (17/17) BC: 95% (20/21):	86% (63/73) of total treatment tested positive	PRF: 94% (16/17) PRP: 100% (18/18) PP: 100% (17/17) BC: 95% (20/21)	PRF: 94% (16/17) PRP: 100% (18/18) PP: 100% (17/17) BC: 95% (20/21)	PRF: 94% (16/17) PRP: 100% (18/18) PP: 100% (17/17) BC: 95% (20/21)