Efficacy of Biologics for the Treatment of Periodontal Infrabony Defects: An American Academy of Periodontology Best Evidence Systematic review and Network Meta-Analysis

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Supplementary Appendix

Content of the Supplementary Appendix

Criteria for assessment of risk of bias for the included studies

The recommendation of the Cochrane collaboration group for randomized trials (Higgins et al., 2011) were utilized to assess the risk of bias of the included studies. This method includes the evaluation of the following 7 domains:

1. Random sequence generation. Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence).
2. Allocation concealment. Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.
3. Blinding of participants and personnel. Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
4. Blinding of outcome assessment. Detection bias due to knowledge of the allocated interventions by outcome assessors.
5. Incomplete outcome data addresses. Attrition bias due to amount, nature or handling of incomplete outcome data.
6. Selective reporting. Reporting bias due to selective outcome reporting.
7. Other bias. Bias due to problems not covered elsewhere in the table.

The risk of bias in each domain was be rated as low, unclear or high.

The overall risk of bias was categorized as follows:

- Low (plausible bias unlikely to seriously affect the results) if a study provided detailed information on the above parameters
- Unclear (plausible bias that raises some doubts about the results) if one or more domains were at unclear risk of bias
- High (plausible bias that seriously weakens confidence in the results) if one or more domains were at high risk of bias.

Supplementary Table 1. Levels of certainty in the body of evidence.

Level of Certainty in Effect Estimate	Description
High	**The body of evidence usually includes consistent results from well-designed, well-conducted studies in representative populations. This conclusion is unlikely to be strongly affected by the results of future studies**. *This statement is strongly supported by the best available evidence*.
Moderate	**As more information becomes available, the magnitude or direction of the observed effect could change, and this change could be large enough to alter the conclusion.** *This statement is based on preliminary determination from the current best available evidence, but confidence in the estimate is constrained by one or more factors, such as:* • The limited number or size of studies • Plausible bias that raises some doubt about the results • Inconsistency of findings across individual studies • Imprecision in the summary estimate • Limited applicability due to the populations of interest • Evidence of publication bias, or • Lack of coherence in the chain of evidence.
Low	**More information could allow a reliable estimation of effects on health outcomes.** *The available evidence is insufficient to support the statement, or the statement is based on extrapolation from the best available evidence. Evidence is insufficient or the reliability of estimated effects is limited by factors such as:* • The limited number or size of studies • Plausible bias that seriously weakens confidence in the results • Inconsistency of findings across individual studies • Imprecision in the summary estimate • Gaps in the chain of evidence • Findings not applicable to the populations of interest • Evidence of publication bias, or • A lack of information on important health outcomes.

Supplementary Table 2. Balancing level of certainty in the benefit estimate (i.e., test over control therapy) with potential for harm.

Level of Certainty	**Net benefit rating**		
	Clinical benefits outweigh potential harms	*Modest or uncertain additional clinical benefits outweigh potential harms or benefits balanced with potential harms*	*No clinical benefits or potential harms outweigh benefits*
High	Strong	In favor	Against
Moderate	In favor	Weak	Against
Low	*Expert opinion for/supports*	*Expert opinion for/supports or Expert opinion questions the use*	*Expert opinion against*

Supplementary Table 3. Definitions for the strength and direction of clinical recommendation.

Recommendation strength	Definition
Strong	Evidence strongly supports the recommendation of this intervention
In favor	Evidence favors the recommendation of this intervention
Weak	Evidence suggests recommending this intervention after other alternatives have been considered
Expert opinion for/supports	Evidence is lacking; the level of certainty is low. Expert opinion guides the recommendation of this intervention.
Expert opinion questions the use	Evidence is lacking; the level of certainty is low. Expert opinion questions the recommendation of this intervention.
Expert opinion against	Evidence is lacking; the level of certainty is low. Expert opinion suggests not recommending this intervention.
Against	Evidence suggests not recommending this intervention (ineffective or harmful).

Supplementary Table 4. Reference and the reason for the excluded articles.

Reason for exclusion	Reference
Study arm(s) with less than 10 patients (N=12)	(Bajaj et al., 2017; Howell et al., 1997; Ouyang & Qiao, 2006; Ridgway, Mellonig, & Cochran, 2008; Rodrigues, Acharya, & Thakur, 2011; Sculean, Donos, Windisch, et al., 1999; Sculean, Windisch, Keglevich, & Gera, 2005; Suchetha et al., 2015; Thakare & Deo, 2012; Vandana, Shah, & Prakash, 2004; Windisch et al., 2002; Yassibag-Berkman, Tuncer, Subasioglu, & Kantarci, 2007)
No biologics (N=4)	(Alzahrani, 2017; Dhote, Charde, Bhongade, & Rao, 2015; Gamal, Abdel-Ghaffar, & Iacono, 2016; Sculean, Schwarz, et al., 2007)
non-RCTs (N=3)	(Corbella, Alberti, Calciolari, Taschieri, & Francetti, 2019; Parashis, Andronikaki-Faldami, & Tsiklakis, 2004; Rosamma Joseph, Raghunath, & Sharma, 2012)
Biologics + GTR with non-absorbable barrier membranes (N=2)	(Döri et al., 2007b; Döri, Huszár, et al., 2008)
Suprabony defects (N=2)	(Iorio-Siciliano et al., 2021; Kizildağ, Çiçek, Arabaci, & Köse, 2018)
Outcomes of different approaches pooled together (N=2)	(Eickholz et al., 2014; Rollke et al., 2012)
Outcomes of interest not reported (N=1)	(Joshi, Padhye, & Gupta, 2019)
Unclear methodology and/or missing data (N=1)	(Yajamanya et al., 2017)
Endo-perio lesions (N=1)	(Ustaoğlu, Uğur Aydin, & Özelçi, 2020)
Animal study (N=1)	(Cochran et al., 2003)

Legend. GTR: guided tissue regeneration; RCT: randomized controlled trial.

Supplementary Table 5. Study characteristics.

Publication, reference	Centers	Setting	RCT design	Geographic location	Age	Inclusion of smokers	Patients (N)†, Females (%)	Funding
(Abu-Ta'a, 2016)	1	Univ.	Parallel-arm	Asia	60 (G1), 57 (G2)	No	20, 35	No
(Agarwal & Gupta, 2014)	1	Univ.	Split-mouth	Asia	NR	No	24, 41.7	No
(Agarwal, Gupta, & Jain, 2016)	1	Univ.	Parallel-arm	Asia	52	No	15, 33.3	No
(Agrali Ö, Kuru, Yarat, & Kuru, 2016)	1	Univ.	Parallel-arm	Asia	44.2	No	NR, 50	No
(Agrawal, Chandran, & Nadig, 2017)	1	Univ.	Parallel-arm	Asia	NR	No	14, NR (G1), 14, NR (G2), 12, NR (G3)	No
(Ahmad, Tewari, Narula, Sharma, & Tanwar, 2019)	1	Univ.	Parallel-arm	Asia	33.1 (G1), 37.8 (G2)	No	16, 56.3 (G1), 16, 62.5 (G2)	No
(Aimetti, Ferrarotti, Mariani, & Romano, 2017)	1	Univ.	Parallel-arm	Europe	42.2 (G1), 44.3 (G2)*	No	15, 53.3 (G1), 15, 66.7 (G2)*	No
(Ajwani et al., 2015)	1	Univ.	Split-mouth	Asia	30.5	No	20, 50	No
(Al Machot, Hoffmann, Lorenz, Khalili, & Noack, 2014)	1	Univ.	Parallel-arm	Europe	50.9 (G1), 51.8 (G2)	Yes	19, 36.8 (G1), 19, 57.9 (G2)	No
(Aslan, Buduneli, & Cortellini, 2020)	1	Priv. Practice	Parallel-arm	Asia	44.9 (G1), 43.9 (G2)	No	15, 66.7 (G1), 15, 53.3 (G2)	No
(Aspriello, Ferrante, Rubini, & Piemontese, 2011)	1	Univ.	Parallel-arm	Europe	56.6 (G1), 55.4 (G2)	No	28, 64.3 (G1), 28, 57.1 (G2)	No
(Atchuta et al., 2020)	1	Univ.	Parallel-arm	Asia	NR	No	13, NR	No
(Aydemir Turkal, Demirer, Dolgun, & Keceli, 2016)	1	Univ.	Split-mouth	Asia	38.5	No	25, 50	No
(Bahammam & Attia, 2021)	1	Univ.	Parallel-arm	Asia	NR	No	15, 45	No

(Bansal & Bharti, 2013)	1	Univ.	Split-mouth	Asia	NR	No	10, NR	No
(Bhutda & Deo, 2013)	1	Univ.	Split-mouth	Asia	40.7	No	15, NR	No
(Bodhare, Kolte, Kolte, & Shirke, 2019)	1	Univ.	Split-mouth	Asia	35.9	No	20, 45	No
(Bokan, Bill, & Schlagenhauf, 2006)	1	NR	Parallel-arm	Europe	56.6 (G1), 59.7 (G2), 55 (G3)	Yes	19, 52.6 (G1), 19, 57.9 (G2), 18, 50 (G3)	NR
(Bratthall et al., 2001)	6	Univ. and Priv. Practice	Split-mouth	Europe	50	Yes	88, 44.3	NR
(Camargo et al., 2001)	1	Univ.	Split-mouth	North America	42	Yes	24, NR	NR
(Camargo et al., 2005)	1	Univ.	Split-mouth	North America	41	Yes	28, 42.9	NR
(Chadwick, Mills, & Mealey, 2016)	1	Univ.	Parallel-arm	North America	54.9	Yes	17, NR (G1), 19, NR (G2)	No
(Chambrone et al., 2007)	1	Univ.	Split-mouth	South America	NR	Yes	13, 76.9	No
(Chambrone et al., 2010)	1	Univ.	Split-mouth	South America	38	Yes	10, 80	No
(Chandradas, Ravindra, Rangaraju, Jain, & Dasappa, 2016)	1	Univ.	Parallel-arm	Asia	42.5 (G1), 43.7 (G2), 47 (G3)	No	12, 50	No
(Chatterjee et al., 2017)	1	Univ.	Parallel-arm	Asia	NR	No	NR, NR	No
(Cortellini & Tonetti, 2011)	1	Priv. Practice	Parallel-arm	Europe	48.9 (G1), 47.2 (G2), 53.5 (G3)	Yes	15, 40 (G1), 15, 53.3 (G2), 15, 46.7 (G3)	No
(Crea, Dassatti, Hoffmann, Zafiropoulos, & Deli, 2008)	1	Univ.	Parallel-arm	Europe	46 (G1), 45.6 (G2)	No	19, 42.1 (G1), 20, 50 (G2)	No
(De Leonardis & Paolantonio, 2013)	1	Priv. Practice	Split-mouth	Europe	45.3	No	34, 71.4	No
(Demir, Sengün, & Berberoğlu, 2007)	1	Univ.	Parallel-arm	Asia	37.9 (G1), 34.1 (G2)	Yes	15, 53.3 (G1), 14, 57.1 (G2)	No

(Dilsiz, Canakci, & Aydin, 2010)	1	Univ.	Split-mouth	Asia	39.2	No	21, 57.1	No
(Döri, Arweiler, Gera, & Sculean, 2005)	1	Univ.	Parallel-arm	Europe	NR	Yes	12, 66.7	NR
(Döri et al., 2007a)	1	Univ.	Parallel-arm	Europe	NR	Yes	15, 53.3	No
(Döri, Nikolidakis, et al., 2008)	1	Univ.	Parallel-arm	Europe	NR	No	13, 53.8	No
(Döri et al., 2009)	1	Univ.	Parallel-arm	Europe	NR	No	15, 70	No
(Döri, Arweiler, Húszár, et al., 2013)	1	Univ.	Parallel-arm	Europe	NR	No	12, 54.2	No
(Döri, Arweiler, Szántó, et al., 2013)	1	Univ.	Parallel-arm	Europe	NR	Yes	11, 68.2	No
(Elbehwashy, Hosny, Elfana, Nawar, & Fawzy El-Sayed, 2021)	1	Univ.	Parallel-arm	Africa	32 (G1), 28.2 (G2)	No	10, 80 (G1), 10, 90 (G2)	No
(Elgendy & Abo Shady, 2015)	1	Univ.	Parallel-arm	Africa	44.3 (G1), 39.7 (G2)	Yes	20, NR	No
(Fickl, Thalmair, Kebschull, Böhm, & Wachtel, 2009)	1	Priv. Practice	Split-mouth	Europe	46.1	Yes	19, 68	No
(Fileto Mazzonetto et al., 2021)	2	Univ.	Parallel-arm	South America	32.3 (G1), 32 (G2), 51.8 (G3)	No	20, 85 (G1), 20, 75 (G2), 20, 45 (G3)	No
(Francetti, Del Fabbro, Basso, Testori, & Weinstein, 2004)	1	Univ.	Parallel-arm	Europe	46.5	Yes	12, 54.2	NR
(Francetti et al., 2005)	17	Univ. and Priv. Practice	Parallel-arm	Europe	59 (G1), 54.3 (G2)	No	64, 59 (G1), 46, 54.3 (G2)	Yes
(Froum, Weinberg, Rosenberg, & Tarnow, 2001)	1	Univ.	Split-mouth	North America	45.5	Yes	23, NR	NR
(Galav et al., 2016)	1	Univ.	Parallel-arm	Asia	NR	No	10, NR	No

(Gamal, Abdel Ghaffar, & Alghezwy, 2016)	1	Univ.	Parallel-arm	Africa	36.9	No	10, 30	No
(Ghezzi, Ferrantino, Bernardini, Lencioni, & Masiero, 2016)	1	Priv. Practice	Parallel-arm	Europe	56 (G1), 52.9 (G2)	Yes	10, 50 (G1), 10, 60 (G2)	No
(Grusovin & Esposito, 2009)	1	Priv. Practice	Parallel-arm	Europe	52.3 (G1), 51.5 (G2)	Yes	15, 46.7 (G1), 15, 60 (G2)	No
(Guida et al., 2007)	1	Univ.	Parallel-arm	Europe	44.1 (G1), 48.4 (G2)	Yes	14, 50 (G1), 13, 53.8 (G2)	No
(Gupta et al., 2014)	1	Univ.	Parallel-arm	Asia	NR	No	15, 50	NR
(Gurinsky, Mills, & Mellonig, 2004)	1	Univ.	Parallel-arm	North America	52 (G1), 47 (G2)	NR	20, 57.5	No
(Hanna, Trejo, & Weltman, 2004)	1	Univ.	Split-mouth	North America	NR	Yes	13, 61.5	NR
(Harnack et al., 2009)	1	Univ.	Split-mouth	Europe	NR	Yes	22, NR	Yes
(Hassan, Alagl, & Abdel-Hady, 2012)	1	Univ.	Split-mouth	Asia	41.4	No	12, 58.3	No
(Hazari et al., 2021)	1	Univ.	Parallel-arm	Asia	NR	No	10, NR	No
(Heijl, Heden, Svärdström, & Ostgren, 1997)	3	NR	Split-mouth	Europe	48	Yes	33, 78.8	Yes
(Hoffmann, Al-Machot, Meyle, Jervøe-Storm, & Jepsen, 2016)	5	Univ. and Priv. Practice	Parallel-arm	Europe	47.5 (G1), 47.2 (G2)	Yes	15, 53.3 (G1), 15, 60 (G2)	Yes
(Hoidal et al., 2008)	1	Univ.	Parallel-arm	North America	54 (G1), 49 (G2)	Yes	NR, 40.6 (G1), NR, 40.6 (G2)	Yes
(Ilgenli, Dundar, & Kal, 2007)	1	Univ.	Parallel-arm	Asia	NR	Yes	8, 62.5 (G1), 14, 57.1 (G2)	NR
(Iorio Siciliano et al., 2011)	1	Univ.	Parallel-arm	Europe	45.1 (G1), 44.4 (G2)	No	20, 45 (G1), 20, 60 (G2)	No
(Iorio-Siciliano et al., 2014)	1	Univ.	Parallel-arm	Europe	44.5 (G1), 44.3 (G2)	No	20, 45 (G1), 20, 65 (G2)	No
(Jalaluddin et al., 2017)	1	Univ.	Split-mouth	Asia	NR	No	10, 40	No

(Jalaluddin et al., 2018)	1	Univ.	Parallel-arm	Asia	35	NR	10, 40	NR
(Jayakumar et al., 2011)	3	Univ.	Parallel-arm	Asia	30.9 (G1), 32.6 (G2)	Yes	27, 55.6 (G1), 27, 51.9 (G2)	No
(Jepsen et al., 2008)	5	Univ. and Priv. Practice	Parallel-arm	Europe	46.2 (G1), 47.5 (G2)	Yes	35, 4 (G1), 38, 23.7 (G2)	Yes
(Kanoriya, Pradeep, Singhal, Garg, & Guruprasad, 2016)	1	Univ.	Parallel-arm	Asia	40.6 (G1), 39.6 (G2), 40.7 (G3)	No	30, 53.3 (G1), 30, 50 (G2), 30, 53.3 (G3)	No
(Kaushick, Jayakumar, Padmalatha, & Varghese, 2011)	1	Univ.	Split-mouth	Asia	NR	No	10, NR	No
(Kavyamala, G, Dwarakanath, & Anudeep, 2019)	1	Univ.	Split-mouth	Asia	35.5	No	12, 33.3	No
(Keles, Cetinkaya, Albayrak, Koprulu, & Acikgoz, 2006)	1	Univ.	Split-mouth	Asia	39.1	Yes	15, 46.7	NR
(Khosropanah, Shahidi, Basri, & Houshyar, 2015)	1	Univ.	Split-mouth	Asia	45	No	12, 58.3	No
(Kitamura et al., 2016) (Part A)	24	Univ.	Parallel-arm	Asia	53 (G1), 54.2 (G2)*	Yes	99, NR (G1), 205, NR (G2)*	Yes
(Kitamura et al., 2016) (Part B)	15	Univ.	Parallel-arm	Asia	55.2 (G1), 54.8 (G2), 56.3 (G3)*	Yes	43, NR (G1), 109, NR (G2), 108, NR (G3)*	Yes
(Kuru, Yilmaz, Argin, & Noyan, 2006)	1	Univ.	Parallel-arm	Asia	44.7	NR	10, NR (G1), 13, NR (G2)	NR
(J. Y. Lee et al., 2017)	1	Univ.	Parallel-arm	Asia	50.9 (G1), 43.6 (G2)	NR	16, 31.3 (G1), 16, 43.8 (G2)	No
(J. H. Lee, Kim, & Jeong, 2020)	1	Univ.	Parallel-arm	Asia	55.9 (G1), 53.4 (G2)	Yes	22, 45.5 (G1), 20, 53.4 (G2)	No
(Leknes, Andersen, Bøe, Skavland, & Albandar, 2009)	1	Univ.	Split-mouth	Europe	52.5	Yes	13, 61.5	No

(Lekovic et al., 2000)	1	NR	Split-mouth	NR	39	Yes	21, 61.9	No
(Lekovic et al., 2001)	1	NR	Split-mouth	NR	45	Yes	23, 43.5	NR
(Lekovic, Camargo, Weinlaender, Vasilic, & Kenney, 2002)	1	NR	Split-mouth	NR	40	Yes	21, 28.6	NR
(Lekovic et al., 2012)	1	Univ.	Split-mouth	Europe	44	No	17	No
(Liu, Huang, Chen, Han, & Ouyang, 2021)	1	Univ.	Split-mouth	Asia	36	No	14	No
(Losada, González, Garcia, Santos, & Nart, 2017)	1	Univ.	Parallel	Europe	50.2 (G1), 54.9 (G2)	Yes	25, 44 (G1), 21, 28.6 (G2)	NR
(Markou et al., 2009)	1	Univ.	Split-mouth	Europe	52.1	Yes	24	NR
(Maroo & Murthy, 2014)	1	Univ.	Split-mouth	Asia	38.4	No	15	Yes
(Martande et al., 2016)	1	Univ.	Parallel	Asia	37.6	No	90	Yes
(Mathur, Bains, Gupta, Jhingran, & Singh, 2015)	1	Univ.	Parallel	Asia	39.7	No	25	No
(Meyle et al., 2011)	5	Univ. and Priv. Practice	Parallel	Europe	46.9	No	38, NR (G1), 35, NR (G2)	Yes
(Minabe et al., 2002)	6	Priv. Practice	Parallel	Asia	51 (G1), 53 (G2), 48 (G3)	Yes	21, 57.1 (G1), 17, 58.8 (G2), 23, 47.8 (G3)	NR
(Mishra, Avula, Pathakota, & Avula, 2013)	1	Univ.	Parallel	Asia	NR	No	22, 50	No
(Moreno Rodriguez & Ortiz Ruiz, 2021)	1	Priv. Practice	Parallel	Europe	46.5 (G1), 50.3 (G2)	No	12, 50 (G1), 12, 25 (G2)	No
(Naqvi et al., 2017)	1	Univ.	Split-mouth	Asia	NR	No	10, 30	No
(Nevins et al., 2005)	11	Univ. and	Parallel	North America	49.4 (G1), 50.4 (G2),	Yes	177, 40	Yes

		Priv. Practice			52.8 (G3)			
(Nevins et al., 2013)	6	Univ. and Priv. Practice	Parallel	North America	49.4 (G1), 50.4 (G2), 52.8 (G3)	Yes	45, NR (G1), 43, NR (G2), 43, NR (G3)	Yes
(Ogihara & Tarnow, 2014)	1	Priv. Practice	Parallel	Asia	53 (G1), 56 (G2), 54 (G3)	No	21, 73.9 (G1), 23, 82.6 (G2), 23, 82.6 (G3)	No
(Ogihara & Wang, 2010)	1	Priv. Practice	Parallel	Asia	50.5 (G1), 55.6 (G2)	No	24, 83.3 (G1), 23, 82.6 (G2)	No
(Okuda et al., 2000)	1	Univ.	Split-mouth	Asia	56	No	16	No
(Okuda et al., 2005)	1	Univ.	Parallel	Asia	54.7 (G1), 56.4 (G2)	No	35, 80 (G1), 35, 60 (G2)	No
(Ozcelik, Cenk Haytac, & Seydaoglu, 2008)	1	Univ.	Split-mouth	Asia	NR	No	22, 45.5	No
(Ozdemir & Okte, 2012)	1	Univ.	Split-mouth	Asia	48.9	No	14, 64.3	No
(Panda et al., 2016)	1	Univ.	Split-mouth	Asia	39.2	No	16, 44.4	NR
(Paolantonio et al., 2020)	1	Univ.	Parallel	Europe	53	No	44, 31.8	No
(Patel, Gaekwad, Gujjari, & S, 2017)	1	Univ.	Split-mouth	Asia	44	No	13, 69.2	NR
(Pavani et al., 2021)	1	Univ.	Parallel	Asia	NR	Yes	30, NR	No
(Pham, 2021)	1	Univ.	Split-mouth	Asia	47.9	No	30, 26.7	No
(Piemontese, Aspriello, Rubini, Ferrante, & Procaccini, 2008)	1	Univ.	Parallel	Europe	NR	No	60, 48.3	No
(Pietruska et al., 2012)	1	Univ.	Parallel	Europe	NR	No	24, 66.7	No
(Pilloni et al., 2021)	1	Univ.	Parallel	Europe	41.8 (G1), 41.2 (G2)	No	16, 56.3 (G1), 16, 50 (G2)	No
(Pontoriero, Wennstrom, & Lindhe, 1999)	1	Univ.	Split-mouth	Europe	NR	NR	40, NR	NR

(Pradeep, Shetty, Garg, & Pai, 2009)	1	Univ.	Split-mouth	Asia	34.3	No	14, 42.9	No
(Pradeep et al., 2012)	1	Univ.	Parallel	Asia	36.8	No	50, 50	No
(Pradeep et al., 2015)	1	Univ.	Parallel	Asia	NR	No	120, 50	No
(Pradeep, Garg, Kanoriya, & Singhal, 2016)	1	Univ.	Parallel	Asia	NR	No	90, 50	No
(Pradeep, Bajaj, Rao, Agarwal, & Naik, 2017)	1	Univ.	Parallel	Asia	39.7	No	57, 45.2	No
(Ragghianti Zangrando et al., 2014)	1	Univ.	Split-mouth	South America	38.8	Yes	10, 80	No
(Ravi, Malaiappan, Varghese, Jayakumar, & Prakasam, 2017)	1	Univ.	Split-mouth	Asia	43.3	No	12, 64.3	No
(Ribeiro, Casarin, Júnior, Sallum, & Casati, 2011)	1	Univ.	Parallel	South America	48.1 (G1), 45.5 (G2)	No	14, 64.3 (G1), 15, 66.7 (G2)	No
(Rösing, Aass, Mavropoulos, & Gjermo, 2005)	1	Univ.	Split-mouth	Europe	NR	Yes	16, NR	NR
(Saini, Sikri, & Gupta, 2011)	1	Univ.	Split-mouth	Asia	40.3	No	20, 60	No
(Sanz et al., 2004)	7	Univ. and Priv. Practice	Parallel	Europe	50.9	Yes	35, 54.3 (G1), 32, 53.1 (G2)	Yes
(Scheyer, Velasquez-Plata, Brunsvold, Lasho, & Mellonig, 2002)	1	Priv. Practice	Split-mouth	North America	NR	Yes	17	No
(Schincaglia, Hebert, Farina, Simonelli, & Trombelli, 2015)	1	Univ.	Parallel	North America	50.1 (G1), 46.7 (G2)	Yes	15, 40 (G1), 13, 38.5 (G2)	Yes
(Schwarz, Sculean, Georg, & Becker, 2003)	1	Univ.	Parallel	Europe	NR	Yes	22, 45.5	NR
(Sculean, Donos, Blaes, et al., 1999)	1	Univ.	Split-mouth	Europe	NR	NR	16, 37.5	NR

(Sculean, Blaes, et al., 2001)	1	Univ.	Parallel	Europe	NR	Yes	34, 35.3	NR
(Sculean, Donos, Miliauskaite, Arweiler, & Brecx, 2001)	1	Univ.	Split-mouth	Europe	45	Yes	12, 50	NR
(Sculean, Windisch, et al., 2001)	1	Univ.	Parallel	Europe	36	Yes	56, 57.1	NR
(Sculean, Barbé, et al., 2002)	1	Univ.	Parallel	Europe	NR	Yes	28, 46.4	NR
(Sculean, Chiantella, Windisch, Gera, & Reich, 2002)	1	Univ.	Parallel	Europe	NR	Yes	24, 58.3	NR
(Sculean, Berakdar, Donos, Auschill, & Arweiler, 2003)	1	Univ.	Parallel	Europe	NR	Yes	22, 77.3	NR
(Sculean et al., 2004)	1	Univ.	Parallel	Europe	47	Yes	42, 57.1	NR
(Sculean, Pietruska, et al., 2005)	1	Univ.	Parallel	Europe	NR	No	30, 53.3	No
(Sculean, Berakdar, et al., 2006)	1	Univ.	Parallel	Europe	41	No	24, 58.3	NR
(Sculean, Schwarz, et al., 2006)	1	Univ.	Split-mouth	Europe	46	Yes	10, 60	NR
(Sculean, Pietruska, Arweiler, Auschill, & Nemcovsky, 2007)	1	Univ.	Parallel	Europe	NR	No	25, NR	No
(Sculean et al., 2008)	1	Univ.	Parallel	Europe	52	Yes	38, 57.1	No
(Sezgin, Uraz, Taner, & Çulhaoğlu, 2017)	1	Univ.	Split-mouth	Asia	NR	No	15, 46.7	No
(Shah, Patel, Dave, & Shah, 2015)	1	Univ.	Split-mouth	Asia	NR	No	20, NR	No
(Sharma & Pradeep, 2011)	1	Univ.	Parallel	Asia	35.3	No	35, 42.9	No

(Shukla, Chug, Mahesh, & Grover, 2016)	1	Univ.	Split-mouth	Asia	40	No	20, 65	NR
(Silvestri, Ricci, Rasperini, Sartori, & Cattaneo, 2000)	1	Univ.	Parallel	Europe	48.7 (G1), 43.4 (G2), 45.8 (G3)	No	10, 60 (G1), 10, 60 (G2), 10, 70 (G3)	NR
(Silvestri et al., 2003)	6	Univ. and Priv. Practice	Parallel	Europe	49.7 (G1), 47.8 (G2)	Yes	49, 51 (G1), 49, 57.1 (G2)	NR
(Sipos, Loos, Abbas, Timmerman, & van der Velden, 2005)	1	Univ.	Split-mouth	Europe	NR	Yes	11	Yes
(Thorat, Pradeep, & Pallavi, 2011)	1	Univ.	Parallel	Asia	30.3 (G1), 31.1 (G2)	No	16, 43.8 (G1), 16, 31.3 (G2)	No
(Thorat, Baghele, & S, 2017)	1	Univ.	Split-mouth	Asia	25	No	15	No
(Tonetti et al., 2002) and (Tonetti et al., 2004)	12	Univ. and Priv. Practice	Parallel	Europe and USA	48 (G1), 48 (G2)	Yes	83, 54.2 (G1), 83, 60.2 (G2)	Yes
(Velasquez-Plata, Scheyer, & Mellonig, 2002)	1	NR	Split-mouth	North America	NR	Yes	16	No
(Wachtel et al., 2003)	1	NR	Split-mouth	Europe	48	Yes	11	NR
(Windisch et al., 2021)	2	Univ.	Parallel	Europe	48.9 (G1), 47.8 (G2)	Yes	23, 60.9 (G1), 24, 58.3 (G2)	No
(Yamamiya et al., 2008)	1	Univ.	Parallel	Asia	55.8	No	30, 93.3	No
(Yilmaz, Cakar, Yildirim, & Sculean, 2010)	1	Univ.	Parallel	Asia	NR	No	20, 45 (G1), 20, 35 (G2)	No
(Zetterström et al., 1997)	10	Univ. and Priv. Practice	Parallel	Europe	51	Yes	104, 48.6 (G1), 33, 51.2 (G2)	Yes
(Zucchelli, Bernardi, Montebugnoli, & De, 2002)	1	Univ.	Parallel	Europe	50.2 (G1), 47.2 (G2), 48.8 (G3)	Yes	30, 60 (G1), 30, 50 (G2), 30, 43.3 (G3)	NR
(Zucchelli, Amore,	2	Univ. and	Parallel	Europe	47.2 (G1), 45.8 (G2)	Yes	30, 60 (G1), 30, 53.3 (G2)	NR

Montebugnoli, & De Sanctis, 2003)	Priv. Practice	

Legend. G1: treatment group 1; G2: treatment group 2; G3: treatment group 3; NR: not reported. Priv. Practice: private practice; Univ.: university; *: treatment arm not included in the quantitative analysis; †: number of patients included in the statistical analysis at the first follow-up time point (≥ 6 months).

Supplementary Table 6. Morphology of the infrabony defects treated in the included trials

Defect morphology*	Publication, reference
1-wall defects only (or mainly 1-wall defect) (N=3)	(Iorio Siciliano et al., 2011; Iorio-Siciliano et al., 2014; J. H. Lee et al., 2020)
3-wall defects only (N=17)	(Ahmad et al., 2019; Chatterjee et al., 2017; Crea et al., 2008; Galav et al., 2016; Kanoriya et al., 2016; Martande et al., 2016; Mathur et al., 2015; Panda et al., 2016; Patel et al., 2017; Pavani et al., 2021; Pradeep et al., 2017; Pradeep et al., 2015; Pradeep et al., 2012; Sezgin et al., 2017; Sharma & Pradeep, 2011; Sipos et al., 2005; Windisch et al., 2021)
1-, 2-wall defects, combined 1-2 wall defects, or circumferential defects (N=9)	(Al Machot et al., 2014; Grusovin & Esposito, 2009; Hoffmann et al., 2016; Jepsen et al., 2008; Meyle et al., 2011; Moreno Rodriguez & Ortiz Ruiz, 2021; Nevins et al., 2005; Nevins et al., 2013; Paolantonio et al., 2020)
2- or 3-wall defects or combinations (N=38)	(Agarwal et al., 2016; Agrawal et al., 2017; Ajwani et al., 2015; Aslan et al., 2020; Aspriello et al., 2011; Atchuta et al., 2020; Bhutda & Deo, 2013; Bodhare et al., 2019; Camargo et al., 2005; Chadwick et al., 2016; Chambrone et al., 2010; Chambrone et al., 2007; Chandradas et al., 2016; Dilsiz et al., 2010; Elbehwashy et al., 2021; Gamal, Abdel Ghaffar, et al., 2016; Hanna et al., 2004; Kaushick et al., 2011; Kavyamala et al., 2019; Keles et al., 2006; Leknes et al., 2009; Lekovic et al., 2000; Lekovic et al., 2001; Lekovic et al., 2002; Lekovic et al., 2012; Mishra et al., 2013; Naqvi et al., 2017; Pham, 2021; Piemontese et al., 2008; Pradeep et al., 2016; Ragghianti Zangrando et al., 2014; Ravi et al., 2017; Scheyer et al., 2002; Shah et al., 2015; Thorat et al., 2017; Thorat et al., 2011; Velasquez-Plata et al., 2002; Yilmaz et al., 2010)
1- or 2-wall defects or combinations (N=14)	(Agarwal & Gupta, 2014; De Leonardis & Paolantonio, 2013; Döri et al., 2005; Döri, Arweiler, Húszár, et al., 2013; Döri, Arweiler, Szántó, et al., 2013; Döri et al., 2009; Döri, Nikolidakis, et al., 2008; Elgendy & Abo Shady, 2015; Guida et al., 2007; Harnack et al., 2009; Hassan et al., 2012; Hazari et al., 2021; Kuru et al., 2006; Losada et al., 2017)
1-, 2- or 3-wall defects or combinations (N=49)	(Agrali Ö et al., 2016; Aydemir Turkal et al., 2016; Bokan et al., 2006; Bratthall et al., 2001; Camargo et al., 2001; Cortellini & Tonetti, 2011; Demir et al., 2007; Döri et al., 2007a; Fickl et al., 2009; Fileto Mazzonetto et al., 2021; Francetti et al., 2004; Francetti et al., 2005; Ghezzi et al., 2016; Gurinsky et al., 2004; Heijl et al., 1997; Hoidal et al., 2008; Ilgenli et al., 2007; Jayakumar et al., 2011; Kitamura et al., 2016; Markou et al., 2009; Minabe et al., 2002; Ogihara & Tarnow, 2014; Ogihara & Wang, 2010; Okuda et al., 2000; Okuda et al., 2005; Ozcelik et al., 2008; Ozdemir & Okte, 2012; Pietruska et al., 2012; Sanz et al., 2004; Schincaglia et al., 2015; Schwarz et al., 2003; Sculean, Barbé, et al., 2002; Sculean et al., 2003; Sculean, Berakdar, et al., 2006; Sculean, Blaes, et al., 2001; Sculean, Chiantella, et al., 2002; Sculean, Donos, Blaes, et al., 1999; Sculean, Donos, et al., 2001; Sculean et al., 2004; Sculean et al., 2008; Sculean, Pietruska, et al., 2007; Sculean, Pietruska, et al., 2005; Sculean, Schwarz, et al., 2006; Sculean, Windisch, et al., 2001; Silvestri et al., 2003; Tonetti et al., 2004; Tonetti et al., 2002; Wachtel et al., 2003; Yamamiya et al., 2008)
Not reported (N=23)	(Abu-Ta'a, 2016; Aimetti et al., 2017; Bahammam & Attia, 2021; Bansal & Bharti, 2013; Froum et al., 2001; Gupta et al., 2014; Jalaluddin et al., 2018; Jalaluddin et al., 2017; Khosropanah et al., 2015; J. Y. Lee et al., 2017; Liu et al., 2021; Maroo & Murthy, 2014; Pilloni et al., 2021; Pontoriero et al., 1999; Pradeep et al., 2009; Ribeiro et al., 2011; Rösing et al., 2005; Saini et al., 2011; Shukla et al., 2016; Silvestri et al., 2000; Zetterström et al., 1997; Zucchelli et al., 2003; Zucchelli et al., 2002)

Legend. * Infrabony defect morphology classified as suggested by Nibali and coworkers (Nibali et al., 2021)

Supplementary Table 7. Weighted mean infrabony defect depth (IDD) at baseline among the different treatment arms

Treatment arm	Sites (N)	Weighted mean IDD (mm)
Autologous blood-derived products (ABPs)	488	4.87
Autologous blood-derived products + bone graft (ABPs + BG)	411	5.62
Bone graft alone (BG)	532	5.23
Enamel matrix derivative (EMD)	1431	5.27
Enamel matrix derivative + bone graft (EMD + BG)	593	5.50
Flap alone	973	4.89
Guided tissue regeneration (GTR)	215	4.76
Recombinant human platelet-derived growth factor + bone graft (rhPDGF + BG)	275	5.92
Overall	5051	5.21

Legend. * Infrabony defect morphology classified as suggested by Nibali and coworkers (Nibali et al., 2021)

Supplementary Table 8. Characteristics of the intervention.

Publication, reference	Intervention	Surgical technique	Sites (N) †	Mean IDD (mm)	Bone Graft/Carrier	Chemical Root conditioning	Follow-up visits (months)	Outcome measures of interest
(Abu-Ta'a, 2016)	EMD + BG	MPPT	20	NR	Allograft (DFDBA)	EDTA	12	Clinical outcomes
	EMD + BG	MPPT	20	NR	Allograft (DFDBA)	EDTA		
(Agarwal & Gupta, 2014)	ABP + BG	OFD	24	5.25 (Rx)	Allograft (DFDBA)	No	12	Clinical outcomes, 2D radiographic bone gain
	BG	OFD	24	5.12 (Rx)	Allograft (DFDBA)	No		
(Agarwal et al., 2016)	ABP + BG	OFD	30	5.32 (Rx)	Allograft (DFDBA)	No	12	Clinical outcomes, 2D radiographic bone gain
	BG	OFD	30	5.20 (Rx)	Allograft (DFDBA)	No		
(Agrali Ö et al., 2016)	EMD + BG	OFD	10	5.2 (DM)	Autogenous graft	EDTA	6	Clinical outcomes, 2D radiographic bone gain
	EMD	OFD	10	6.4 (DM)	No	EDTA		
	Flap	OFD	10	5.6 (DM)	No	No		
(Agrawal et al., 2017)	ABP	OFD	14	3 (Rx)	No	No	6	Clinical outcomes, 2D radiographic bone gain
	BG	OFD	12	3 (Rx)	Synthetic graft (CP)	No		
	ABP + BG	OFD	14	4 (Rx)	Synthetic graft (CP)	No		
(Ahmad et al., 2019)	ABP	M-MIST	16	2.99 (Rx)	No	No	6	Clinical outcomes, 2D radiographic bone fill and bone gain
	Flap	M-MIST	16	3.15 (Rx)	No	No		
(Aimetti et al., 2017)	EMD (flapless)*						12, 24	Clinical outcomes, 2D radiographic bone gain
	EMD	MIST	15	5.2 (Rx)	No	EDTA		

(Ajwani et al., 2015)	ABP	OFD	20	3.7 (Rx)	No	No	9	Clinical outcomes, 2D radiographic bone gain
	Flap	OFD	20	3.95 (Rx)	No	No		
(Al Machot et al., 2014)	EMD	MPPT	19	N/A	No	EDTA	6, 12	Clinical outcomes, 2D radiographic bone gain, wound healing outcomes, PROMs
	BG	MPPT	19	N/A	Synthetic graft (HA)	No		
(Aslan et al., 2020)	EMD + BG	EPPT	15	6.63	Xenograft (DBBM)	EDTA	12	Clinical outcomes
	Flap	EPPT	15	6.7	No	EDTA		
(Aspriello et al., 2011)	EMD + BG	OFD	28	5.5 (Rx)	Allograft (DFDBA)	EDTA	12	Clinical outcomes, 2D radiographic bone gain
	BG	OFD	28	5 (Rx)	Allograft (DFDBA)	EDTA		
(Atchuta et al., 2020)	Flap	OFD	13	N/A	No	No	6	Clinical outcomes, 2D radiographic bone gain
	BG	OFD	13	N/A	Allograft (DFDBA)	No		
	ABP + BG	OFD	13	N/A	Allograft (DFDBA)	No		
(Aydemir Turkal et al., 2016)	EMD + ABP*						6	Clinical outcomes, 2D radiographic bone fill and bone gain
	EMD	MPPT or SPPT	24	6.71 (DM) 6.35 (Rx)	No	EDTA		
(Bahammam & Attia, 2021)	ABP	OFD	15	4.6 (Rx)	No	No	6	Clinical outcomes, 2D radiographic bone gain
	BG	OFD	15	3.6 (Rx)	Synthetic graft (HA)	No		
	ABP + BG	OFD	15	4.4 (Rx)	Synthetic graft (HA)	No		
	Flap	OFD	15	3.9 (Rx)	No	No		
(Bansal & Bharti, 2013)	BG	OFD	10	NR	Allograft (DFDBA)	No	6	Clinical outcomes, 2D radiographic bone gain
	ABP + BG	OFD	10	NR	Allograft (DFDBA)	No		

(Bhutda & Deo, 2013)	EMD	OFD	15	4.8 (Rx)	No	EDTA	12, 60	Clinical outcomes, 2D radiographic bone fill and gain
	Flap	OFD	15	4.1 (Rx)	No	EDTA		
(Bodhare et al., 2019)	ABP + BG	OFD	20	5.85 (Rx)	Synthetic graft (Bioactive Glass)	No	6	Clinical outcomes, 3D radiographic outcomes (CBCT)
	BG	OFD	20	6.66 (Rx)	Synthetic graft (Bioactive Glass)	No		
(Bokan et al., 2006)	EMD	MPPT or SPPT	19	NR	No	EDTA	12	Clinical outcomes
	EMD + BG	MPPT or SPPT	19	NR	Synthetic graft (β-TCP)	EDTA		
	Flap	OFD	18	NR	No	No		
(Bratthall et al., 2001)	EMD	OFD	88	NR	No	Orto-phosphoric acid	8, 16	Clinical outcomes, 2D radiographic bone gain
	EMD	OFD	88	NR	No	Orto-phosphoric acid		
(Camargo et al., 2001)	EMD + BG	OFD	24	NR	Xenograft (DBBM)	EDTA	6	Clinical outcomes, bone outcomes (re-entry)
	Flap	OFD	24	NR	No	No		
(Camargo et al., 2005)	ABP + GTR	OFD	28	NR	Xenograft (DBBM)	No	6	Clinical outcomes, bone outcomes (re-entry)
	Flap	OFD	28	NR	No	No		
(Chadwick et al., 2016)	BG	OFD	19	4.82 (DM)	Allograft (DFDBA)	No	6	Clinical outcomes, 2D radiographic bone gain
	ABP	OFD	17	4.53 (DM)	No	No		
(Chambrone et al., 2010)	EMD	OFD	19	NR	No	EDTA	12, 24	Clinical outcomes
	Flap	OFD	19	NR	No	No		
(Chambrone et al., 2007)	EMD	OFD	13	NR	No	EDTA	6	Clinical outcomes
	Flap	OFD	13	NR	No	No		

(Chandradas et al., 2016)	ABP + BG	OFD	12	5.62 (Rx)	Xenograft (DBBM)	No	9	Clinical outcomes, 2D radiographic bone fill and bone gain
	ABP	OFD	12	5.27 (Rx)	No	No		
	Flap	OFD	12	5.13 (Rx)	No	No		
(Chatterjee et al., 2017)	Flap	OFD	28	NR	No	No	6, 9	Clinical outcomes, 2D radiographic bone fill
	ABP	OFD	28	NR	No	No		
	ABP	OFD	28	NR	No	No		
(Cortellini & Tonetti, 2011)	Flap	M-MIST	15	5.2 (DM)	No	No	12	Clinical outcomes, 2D radiographic bone fill and bone gain, surgical time, primary wound closure, wound healing outcomes, PROMs
	EMD	M-MIST	15	5.3 (DM)	No	EDTA		
	EMD + BG	M-MIST	15	5.2 (DM)	Xenograft (DBBM)	EDTA		
(Crea et al., 2008)	GTR (Non-Abs)*						12, 36	Clinical outcomes, 2D radiographic bone fill
	EMD	SPPT	19	4.7 (DM) 4.7 (Rx)	No	EDTA		
(De Leonardis & Paolantonio, 2013)	Flap	MPPT or SPPT	34	4.31 (Rx)	No	No	12, 24	Clinical outcomes, 2D radiographic bone gain
	EMD	MPPT or SPPT	34	4.55 (Rx)	No	EDTA		
	EMD + BG	MPPT or SPPT	34	4.49 (Rx)	Synthetic graft (β-TCP and HA)	EDTA		
(Demir et al., 2007)	ABP + BG	OFD	15	5.27 (DM)	Synthetic graft (Bioactive Glass)	No	9	Clinical outcomes, bone outcomes (re-entry)
	BG	OFD	14	6.14 (DM)	Synthetic graft (Bioactive Glass)	No		
(Dilsiz et al., 2010)	EMD + Nd:YAG Laser*						6, 12	Clinical outcomes
	EMD	OFD	21	4 (DM)	No	EDTA		

(Döri et al., 2005)	EMD + BG	OFD	12	4.1 (DM)	Xenograft (DBBM)	EDTA	12	Clinical outcomes
	EMD + BG	OFD	12	4 (DM)	Synthetic graft (β-TCP)	EDTA		
(Döri et al., 2007a)	ABP + GTR	OFD	15	5.2 (DM)	Xenograft (DBBM)	No	12	Clinical outcomes
	GTR	OFD	15	5.3 (DM)	Xenograft (DBBM)	No		
(Döri, Nikolidakis, et al., 2008)	EMD + ABP + BG*					No	12	Clinical outcomes
	EMD + BG	OFD	13	5.2 (DM)	Xenograft (DBBM)	EDTA		
(Döri et al., 2009)	ABP + BG	OFD	15	5.1 (DM)	Xenograft (DBBM)	No	12	Clinical outcomes
	BG	OFD	15	5 (DM)	Xenograft (DBBM)	No		
(Döri, Arweiler, Húszár, et al., 2013)	EMD + ABP + BG*					No	12, 60	Clinical outcomes
	EMD + BG	OFD	12	5 (DM)	Xenograft (DBBM)	EDTA		
(Döri, Arweiler, Szántó, et al., 2013)	EMD + BG	OFD	11	4.1 (DM)	Xenograft (DBBM)	EDTA	12, 120	Clinical outcomes
	EMD + BG	OFD	11	4 (DM)	Synthetic graft (β-TCP)	EDTA		
(Elbehwashy et al., 2021)	ABP	OFD	10	4.69 (Rx)	No	No	6	Clinical outcomes, 2D radiographic bone fill and bone gain
	ABP	OFD	10	3.98 (Rx)	No	No		
(Elgendy & Abo Shady, 2015)	BG	OFD	20	NR	Synthetic graft (HA)	No	6	Clinical outcomes
	ABP + BG	OFD	20	NR	Synthetic graft (HA)	No		
(Fickl et al., 2009)	EMD	MPPT	35	NR	No	EDTA	6, 12	Clinical outcomes, 2D radiographic bone gain, wound healing outcomes
	Flap	MPPT	35	NR	No	EDTA		
(Fileto Mazzonetto et al., 2021)	EMD	SPPT	20	4.31 (Rx)	No	No	6, 12	Clinical outcomes, 2D radiographic bone gain, PROMs
	Flap	SPPT	20	4.01 (Rx)	No	No		

	EMD	SPPT	20	4.35 (Rx)	No	No		
(Francetti et al., 2004)	Flap	SPPT	12	4.81 (Rx)	No	No	12, 24	Clinical outcomes, 2D radiographic bone fill and bone gain
	EMD	SPPT	12	5.93 (Rx)	No	EDTA		
(Francetti et al., 2005)	EMD	SPPT	82	5.76 (Rx)	No	EDTA	12, 24	Clinical outcomes, 2D radiographic bone fill and bone gain
	Flap	SPPT	55	5.25 (Rx)	No	No		
(Froum et al., 2001)	EMD	OFD	53	5.63 (DM)	No	Citric acid	12	Clinical outcomes, bone outcomes (re-entry)
	Flap	OFD	31	4.29 (DM)	No	Citric acid		
(Galav et al., 2016)	ABP	OFD	10	5.77 (Rx)	No	No	9	Clinical outcomes, 2D radiographic bone gain, bone outcomes (re-entry)
	BG	OFD	10	5.89 (Rx)	Autogenous graft	No		
(Gamal, Abdel Ghaffar, et al., 2016)	BG	MPPT or SPPT	9	3.7 (Rx)	Xenograft	No	6, 9	Clinical outcomes, 2D radiographic bone gain
	ABP + BG	MPPT or SPPT	10	4.2 (Rx)	Xenograft	No		
	ABP + BG	MPPT or SPPT	10	3.8 (Rx)	Xenograft	No		
(Ghezzi et al., 2016)	GTR	MIST	10	5.4 (DM)	Xenograft (DBBM)	No	12	Clinical outcomes
	EMD + BG	MIST	10	5.6 (DM)	Xenograft (DBBM)	EDTA		
(Grusovin & Esposito, 2009)	Flap	MPPT or SPPT	15	5.1 (DM)	No	EDTA	12	Clinical outcomes, 2D radiographic bone gain, healing outcomes, PROMs
	EMD	MPPT or SPPT	15	6.1 (DM)	No	EDTA		
(Guida et al., 2007)	EMD	MPPT or SPPT	14	6.5 (Rx)	No	EDTA	6, 12	Clinical outcomes, 2D radiographic bone gain
	EMD + BG	MPPT or SPPT	14	6.5 (Rx)	Autogenous graft	EDTA		
(Gupta et al., 2014)	EMD	OFD	22	4.73 (DM)	No	No	6	Clinical outcomes, 3D radiographic outcomes (CBCT)
	ABP	OFD	22	4.89 (DM)	No	No		

(Gurinsky et al., 2004)	EMD + BG	OFD	33	5.2 (DM)	Allograft (DFDBA)	No	6	Clinical outcomes, 2D radiographic bone fill and bone gain, bone outcomes (re-entry)
	EMD	OFD	34	4.9 (DM)	No	No		
(Hanna et al., 2004)	ABP + BG	OFD	13	6.53 (DM)	Xenograft (DBBM)	No	6	Clinical outcomes
	BG	OFD	13	6.07 (DM)	Xenograft (DBBM)	No		
(Harnack et al., 2009)	ABP + BG	MPPT	22	N/A	Synthetic graft (β-TCP)	No	6	Clinical outcomes, wound healing outcomes, bone outcomes (re-entry)
	BG	MPPT	22	N/A	Synthetic graft (β-TCP)	No		
(Hassan et al., 2012)	BG	OFD	12	NR	Autogenous graft	No	6, 12	Clinical outcomes
	ABP + BG	OFD	12	NR	Autogenous graft	No		
(Hazari et al., 2021)	ABP + BG	OFD	10	6.23 (Rx)	Synthetic graft	No	6	Clinical outcomes, 2D radiographic bone gain
	BG	OFD	10	6.1 (Rx)	Synthetic graft	No		
(Heijl et al., 1997)	EMD	MWF	34	4.8 (DM)	No	EDTA	8, 16, 36	Clinical outcomes, 2D radiographic bone fill and gain
	Flap	MWF	34	5 (DM)	No	EDTA		
(Hoffmann et al., 2016)	EMD	MPPT or SPPT	15	6.2 (DM)	No	EDTA	6, 12, 36	Clinical outcomes, bone outcomes (bone probing/sounding)
	EMD + BG	MPPT or SPPT	15	7.2 (DM)	Synthetic graft (β-TCP, CP and HA)	EDTA		
(Hoidal et al., 2008)	BG	OFD	20	4.83 (DM)	Allograft (DFDBA)	EDTA	6	Clinical outcomes, bone outcomes (re-entry)
	EMD + BG	OFD	17	4.5 (DM)	Allograft (DFDBA)	EDTA		
(Ilgenli et al., 2007)	ABP + BG	OFD	16	6 (Rx)	Allograft (DFDBA)	No	6	Clinical outcomes, 2D radiographic bone gain
	ABP	OFD	12	4.7 (Rx)	No	No		
	EMD	MPPT or SPPT	20	8.5 (DM)	No	EDTA	12	Clinical outcomes

(Iorio Siciliano et al., 2011)	GTR (Non-Abs)*							
(Iorio-Siciliano et al., 2014)	EMD + BG	MPPT or SPPT	20	6.1 (DM)	Xenograft (DBBM)	EDTA	12	Clinical outcomes
	GTR	MPPT or SPPT	20	6 (DM)	Xenograft (DBBM)	No		
(Jalaluddin et al., 2017)	Flap	OFD	10	3.1 (Rx)	No	No	6	Clinical outcomes, 2D radiographic bone fill and gain
	ABP	OFD	10	2.9 (Rx)	No	No		
(Jalaluddin et al., 2018)	ABP	OFD	10	2.9 (Rx)	No	No	6	Clinical outcomes, 2D radiographic bone fill and gain
	BG	OFD	10	4.1 (Rx)	Synthetic graft (β-TCP and HA)	No		
(Jayakumar et al., 2011)	BG	OFD	27	6.7 (DM)	Synthetic graft (β-TCP)	Tetracycline	6	Clinical outcomes, 2D radiographic bone fill and gain
	rhPDGF + BG	OFD	27	6.3 (DM)	Synthetic graft (β-TCP)	Tetracycline		
(Jepsen et al., 2008)	EMD	MPPT or SPPT	35	6.9 (DM)	No	EDTA	6	Clinical outcomes, bone outcomes (bone probing/sounding), wound healing outcomes, PROMs
	EMD + BG	MPPT or SPPT	38	6.7 (DM)	Synthetic graft (β-TCP, CP and HA)	EDTA		
(Kanoriya et al., 2016)	Flap	OFD	30	5.14 (Rx)	No	No	9	Clinical outcomes, 2D radiographic bone fill and bone gain
	ABP	OFD	30	5.25 (Rx)	No	No		
	ABP + Alendronate*							
(Kaushick et al., 2011)	ABP + BG	OFD	10	NR	Synthetic graft (β-TCP)	No	6	Clinical outcomes
	BG	OFD	10	NR	Synthetic graft (β-TCP)	No		
(Kavyamala et al., 2019)	rhPDGF + BG	OFD	12	NR	Synthetic graft (β-TCP)	No	6	Clinical outcomes, 2D radiographic bone fill and bone gain
	BG	OFD	12	NR	Synthetic graft (β-TCP)	No		

(Keles et al., 2006)	ABP + GTR	OFD	15	N/A	Synthetic graft (Bioactive glass)	No	6	Clinical outcomes, 2D radiographic bone gain and bone fill
	GTR	OFD	15	N/A	Synthetic graft (Bioactive glass)	No		
(Khosropanah et al., 2015)	BG	OFD	12	N/A	Allograft (DFDBA)	No	6	Clinical outcomes, 3D radiographic outcomes (CBCT)
	ABP + BG	OFD	12	N/A	Allograft (DFDBA)	No		
(Kitamura et al., 2016) (part A of the study)	Flap	MWF	107	4.88 (Rx)	No	No	12, 24, 36	Clinical outcomes, 2D radiographic bone gain and bone fill
	FGF-2*							
(Kitamura et al., 2016) (part B of the study)	Flap	MWF	43	5.75 (Rx)	No	No	12, 24, 36	Clinical outcomes, 2D radiographic bone fill and bone gain
	EMD	MWF	43	5.58 (Rx)	No	No		
	FGF-2*							
(Kuru et al., 2006)	EMD	OFD	10	5.68 (DM)	No	No	8	Clinical outcomes, 2D radiographic bone gain
	EMD + BG	OFD	13	5.48 (DM)	Synthetic graft (Bioactive glass)	No		
(J. H. Lee et al., 2020)	BG	OFD	23	4.3 (Rx)	Xenograft (DPBM)	No	6, 12, 24	Clinical outcomes, 2D radiographic bone gain, wound healing outcomes, PROMs
	EMD + BG	OFD	23	4.6 (Rx)	Xenograft (DPBM)	No		
(J. Y. Lee et al., 2017)	rhPDGF + BG	OFD	16	N/A	Xenograft (EDBM)	No	6	Clinical outcomes, 2D radiographic bone gain
	rhPDGF + BG	OFD	16	N/A	Synthetic graft (β-TCP)	No		
(Leknes et al., 2009)	EMD	OFD	13	NR	No	EDTA	6, 12	Clinical outcomes
	BG	OFD	13	NR	Synthetic graft (Bioactive glass)	EDTA		
(Lekovic et al., 2000)	EMD	OFD	21	NR	No	No	6	Clinical outcomes, bone outcomes (re-entry)
	EMD + BG	OFD	21	NR	Xenograft (DBBM)	No		

(Lekovic et al., 2001)	EMD + BG	OFD	23	NR	Xenograft (DBBM)	No	6	Clinical outcomes, bone outcomes (re-entry)
	BG	OFD	23	NR	Xenograft (DBBM)	No		
(Lekovic et al., 2002)	ABP + GTR	OFD	21	NR	Xenograft (DBBM)	No	6	Clinical outcomes, bone outcomes (re-entry)
	ABP + BG	OFD	21	NR	Xenograft (DBBM)	No		
(Lekovic et al., 2012)	ABP	OFD	17	NR	No	No	6	Clinical outcomes, 2D radiographic bone gain, wound healing outcomes, bone outcomes (re-entry)
	ABP + BG	OFD	17	NR	Xenograft (DBBM)	No		
(Liu et al., 2021)	ABP + GTR	OFD	14	4.8 (Rx)	Xenograft	No	6, 12, 24	Clinical outcomes
	GTR	OFD	14	4.4 (Rx)	Xenograft	No		
(Losada et al., 2017)	EMD	OFD	25	5.24 (Rx)	No	EDTA	6, 12	Clinical outcomes, 2D radiographic bone gain
	EMD + BG	OFD	21	4.66 (Rx)	Synthetic graft (CP)	EDTA		
(Markou et al., 2009)	ABP	OFD	24	6.09 (Rx)	No	No	6	Clinical outcomes, 2D radiographic bone fill
	ABP + BG	OFD	24	5.58 (Rx)	Allograft (FDBA)	No		
(Maroo & Murthy, 2014)	rhPDGF + BG	OFD	15	NR	Synthetic graft (β-TCP)	No	6, 9	Clinical outcomes, 2D radiographic bone fill and bone gain
	BG	OFD	15	NR	Synthetic graft (β-TCP)	No		
(Martande et al., 2016)	ABP + Atorvastatin*						9	Clinical outcomes, 2D radiographic bone fill and bone gain
	ABP	OFD	30	5.13 (Rx)	No	No		
	Flap	OFD	30	4.97 (Rx)	No	No		
(Mathur et al., 2015)	ABP	OFD	19	N/A	No	No	6	Clinical outcomes, 2D radiographic bone gain
	BG	OFD	19	N/A	Autogenous graft	No		

(Meyle et al., 2011)	EMD + BG	OFD	38	5.9 (Rx)	Synthetic graft (HA and β-TCP)	EDTA	12	Clinical outcomes, 2D radiographic bone gain, bone outcomes (bone probing/sounding)
	EMD	OFD	35	5.6 (Rx)	No	EDTA		
(Minabe et al., 2002)	EMD + GTR	OFD	24	5.7 (DM)	No	EDTA	6, 12	Clinical outcomes
	EMD	OFD	22	5.4 (DM)	No	EDTA		
	GTR	OFD	23	5.8 (DM)	No	No		
(Mishra et al., 2013)	rhPDGF	M-MIST	11	4.04 (Rx)	No	No	6	Clinical outcomes, 2D radiographic bone fill and bone gain
	Flap	M-MIST	11	3.64 (Rx)	No	No		
(Moreno Rodriguez & Ortiz Ruiz, 2021)	EMD	NIPSA	12	5.92 (DM)	No	EDTA	12	Clinical outcomes
	EMD + BG	NIPSA	12	6.08 (DM)	Xenograft	EDTA		
(Naqvi et al., 2017)	ABP + BG	OFD	10	NR	Synthetic graft (Bioactive Glass)	No	6, 9	Clinical outcomes
	BG	OFD	10	NR	Synthetic graft (Bioactive Glass)	No		
(Nevins et al., 2005)	rhPDGF + BG	OFD	60	6 (DM)	Synthetic graft (β-TCP)	Tetracycline	6	Clinical outcomes, 2D radiographic bone fill and bone gain
	rhPDGF + BG	OFD	61	5.7 (DM)	Synthetic graft (β-TCP)	Tetracycline		
	BG	OFD	59	5.7 (DM)	Synthetic graft (β-TCP)	Tetracycline		
(Nevins et al., 2013)	rhPDGF + BG	OFD	45	NR	Synthetic graft (β-TCP)	Tetracycline	12, 24, 36	Clinical outcomes, 2D radiographic bone fill and bone gain
	rhPDGF + BG	OFD	43	NR	Synthetic graft (β-TCP)	Tetracycline		
	BG	OFD	43	NR	Synthetic graft (β-TCP)	Tetracycline		
(Ogihara & Tarnow, 2014)	EMD + BG	OFD	21	NR	Allograft (FDBA)	EDTA	12, 36	Clinical outcomes, OPAL gain (re-entry), radiographic bone gain,
	EMD + BG	OFD	23	NR	Allograft (DFDBA)	EDTA		

	EMD	OFD	23	NR	No	EDTA		
(Ogihara & Wang, 2010)	Orthodontic treatment and EMD + BG*						12	Clinical outcomes, OPAL gain (re-entry)
	EMD + BG	OFD	23	NR	Allograft (DFDBA)	EDTA		
(Okuda et al., 2000)	EMD	OFD	18	4.5 (DM)	No	EDTA	12	Clinical outcomes
	Flap	OFD	18	4.28 (DM)	No	EDTA		
(Okuda et al., 2005)	ABP + BG	OFD	35	4.9 (DM)	Synthetic graft (HA)	No	12	Clinical outcomes, 2D radiographic bone gain
	BG	OFD	35	4.4 (DM)	Synthetic graft (HA)	No		
(Ozcelik et al., 2008)	EMD	OFD	22	NR	No	EDTA	6, 12	Clinical outcomes, wound healing outcomes, PROMs
	EMD + LLLT*							
(Ozdemir & Okte, 2012)	BG	OFD	14	N/A	Synthetic graft (β-TCP)	No	6	Clinical outcomes, 2D radiographic bone fill and bone gain
	ABP + BG	OFD	14	N/A	Synthetic graft (β-TCP)	No		
(Panda et al., 2016)	ABP + GTR	OFD	16	3.5 (Rx)	No	No	9	Clinical outcomes, 2D radiographic bone gain
	GTR	OFD	16	3.29 (Rx)	No	No		
(Paolantonio et al., 2020)	ABP + BG	OFD	22	9.61 (Rx)	Autogenous graft	No	12	Clinical outcomes, 2D radiographic bone gain
	EMD + BG	OFD	22	9.61 (Rx)	Autogenous graft	EDTA		
(Patel et al., 2017)	ABP	OFD	13	NR	No	No	6, 9, 12	Clinical outcomes, 2D radiographic bone fill
	Flap	OFD	13	NR	No	No		
(Pavani et al., 2021)	Flap	OFD	10	NR	No	No	6	Clinical outcomes, 3D radiographic outcomes (CBCT)
	ABP + BG	OFD	10	NR	Synthetic graft (β-TCP)	No		
	BG	OFD	10	NR	Synthetic graft (β-TCP)	No		

(Pham, 2021)	ABP	OFD	30	NR	No	No	6, 12	Clinical outcomes, 2D radiographic bone fill and bone gain
	GTR	OFD	30	NR	No	No		
	Flap	OFD	30	NR	No	No		
(Piemontese et al., 2008)	ABP + BG	OFD	30	5.3 (Rx)	Allograft (DFDBA)	No	12	Clinical outcomes, 2D radiographic bone gain
	BG	OFD	30	5.1 (Rx)	Allograft (DFDBA)	No		
(Pietruska et al., 2012)	EMD + BG	OFD	12	5.6 (DM)	Synthetic graft (CP)	EDTA	12, 48	Clinical outcomes
	EMD	OFD	12	5.7 (DM)	No	EDTA		
(Pilloni et al., 2021)	EMD	SFA	16	NR	No	EDTA	12, 18, 24	Clinical outcomes
	Hyaluronic acid*							
(Pontoriero et al., 1999)	GTR (Non-Abs)*						12	Clinical outcomes
	GTR	OFD	20	4.2 (G1) and 4.4 (G2)(DM)	No	No		
	EMD	OFD	10	4.2 (DM)	No	EDTA		
	Flap	OFD	40	3.98 (DM)	No	No		
(Pradeep et al., 2009)	ABP	OFD	14	4.6 (Rx)	No	No	9	Clinical outcomes, 2D radiographic bone fill and bone gain, 3D radiographic outcomes (CT)
	ABP + BG	OFD	14	4.99 (Rx)	Xenograft	No		
(Pradeep et al., 2012)	ABP	OFD	30	5.06 (Rx)	No	No	9	Clinical outcomes, 2D radiographic bone fill and bone gain
	ABP	OFD	30	4.90 (Rx)	No	No		
	Flap	OFD	30	4.83 (Rx)	No	No		
(Pradeep et al., 2015)	Flap	OFD	30	5.26 (Rx)	No	No	9	Clinical outcomes, 2D radiographic bone fill and bone gain
	ABP	OFD	30	5.25 (Rx)	No	No		

	Flap + metformin* ABP + metformin*							
(Pradeep et al., 2016)	Flap ABP ABP + Rosuvastatin*	OFD OFD	30 30	5.87 (Rx) 5.97 (Rx)	No No	No No	9	Clinical outcomes, 2D radiographic bone gain
(Pradeep et al., 2017)	ABP ABP + BG Flap	OFD OFD OFD	29 32 29	5.63 (Rx) 6.03 (Rx) 5.80 (Rx)	No Synthetic graft (HA) No	No No No	9	Clinical outcomes, 2D radiographic bone fill and bone gain
(Ragghianti Zangrando et al., 2014)	EMD Flap	OFD OFD	25 18	N/A N/A	No No	EDTA No	24	2D radiographic bone gain
(Ravi et al., 2017)	ABP + GTR GTR	OFD OFD	19 19	N/A N/A	No No	No No	6	Clinical outcomes, 2D radiographic bone gain
(Ribeiro et al., 2011)	EMD Flap	MIST MIST	14 15	5.24 (Rx) 5.61 (Rx)	No No	No No	6	Clinical outcomes, 2D radiographic bone gain
(Rösing et al., 2005)	EMD Flap	OFD OFD	16 16	3.57 (Rx) 3.67 (Rx)	No No	EDTA EDTA	6, 12	Clinical outcomes, 2D radiographic bone gain
(Saini et al., 2011)	ABP + BG BG	OFD OFD	20 20	4.9 (Rx) 4.65 (Rx)	Synthetic graft (β-TCP) Synthetic graft (β-TCP)	No No	6, 9	Clinical outcomes, 2D radiographic bone gain
(Sanz et al., 2004)	EMD GTR	OFD OFD	35 32	6.2 (DM) 5.9 (DM)	No No	Y No	12	Clinical outcomes

(Scheyer et al., 2002)	EMD + BG	OFD	17	5 (DM)	Xenograft (DBBM)	EDTA	6	Clinical outcomes, bone outcomes (re-entry)
	BG	OFD	17	4.4 (DM)	Xenograft (DBBM)	EDTA		
(Schincaglia et al., 2015)	rhPDGF + BG	SFA	15	7.7 (DM)	Synthetic graft (β-TCP)	No	6	Clinical outcomes, 2D radiographic bone gain, wound healing outcomes, PROMs
	rhPDGF + BG	DFA (MPPT or SPPT)	13	5.8 (DM)	Synthetic graft (β-TCP)	No		
(Schwarz et al., 2003)	EMD	OFD	11	3.8 (DM)	No	EDTA	6	Clinical outcomes
	EMD + Er:YAG laser*							
(Sculean, Donos, Blaes, et al., 1999)	EMD	OFD	16	NR	No	EDTA	8	Clinical outcomes
	GTR	OFD	16	NR	No	No		
(Sculean, Blaes, et al., 2001)	EMD	OFD	17	3.8 (DM)	No	EDTA	12	Clinical outcomes
	EMD	OFD	17	3.5 (DM)	No	EDTA		
(Sculean, Donos, et al., 2001)	EMD	OFD	16	4.1 (DM)	No	EDTA	12, 48	Clinical outcomes
	GTR	OFD	16	4.2 (DM)	No	No		
(Sculean, Windisch, et al., 2001)	EMD	OFD	14	3.8 (DM)	No	EDTA	12	Clinical outcomes
	GTR	OFD	14	3.7 (DM)	No	No		
	EMD + GTR	OFD	14	4 (DM)	No	EDTA		
	Flap	OFD	14	3.9 (DM)	No	No		
(Sculean, Barbé, et al., 2002)	EMD + BG	OFD	14	3.9 (DM)	Synthetic graft (Bioactive glass)	EDTA	12	Clinical outcomes
	BG	OFD	14	3.7 (DM)	Synthetic graft (Bioactive glass)	EDTA		
	EMD + BG	OFD	12	NR	Xenograft (DBBM)	EDTA	12	Clinical outcomes

(Sculean, Chiantella, et al., 2002)	BG	OFD	12	NR	Xenograft (DBBM)	EDTA		
(Sculean et al., 2003)	EMD	OFD	11	3.3 (DM)	No	EDTA	6	Clinical outcomes
	EMD + Cox2 inhibitor*							
(Sculean et al., 2004)	EMD	OFD	11	3.9 (DM)	No	EDTA	12, 60	Clinical outcomes
	GTR	OFD	11	3.8 (DM)	No	No		
	EMD + GTR	OFD	10	3.7 (DM)	No	EDTA		
	Flap	OFD	10	3.8 (DM)	No	No		
(Sculean, Pietruska, et al., 2005)	EMD + BG	OFD	16	4.3 (DM)	Synthetic graft (Bioactive glass)	EDTA	12	Clinical outcomes, bone outcomes (re-entry)
	EMD	OFD	16	4.1 (DM)	No	EDTA		
(Sculean, Berakdar, et al., 2006)	EMD	OFD	12	4.2 (DM)	No	EDTA	12	Clinical outcomes
	EMD	OFD	12	4.1 (DM)	No	No		
(Sculean, Schwarz, et al., 2006)	EMD	OFD	10	4 (DM)	No	EDTA	12, 96	Clinical outcomes
	GTR	OFD	10	4.1(DM)	No	No		
(Sculean, Pietruska, et al., 2007)	EMD + BG	OFD	12	4.4 (DM)	Synthetic graft (Bioactive glass)	EDTA	12, 48	Clinical outcomes
	EMD	OFD	13	4.5 (DM)	No	EDTA		
(Sculean et al., 2008)	EMD	OFD	11	4.2 (DM)	No	EDTA	12, 120	Clinical outcomes
	GTR	OFD	11	4.1 (DM)	No	No		
	EMD + GTR	OFD	10	4 (DM)	No	EDTA		
	Flap	OFD	10	3.9 (DM)	No	No		

(Sezgin et al., 2017)	ABP + BG	OFD	15	8.44 (Rx)	Xenograft	No	6	Clinical outcomes, 2D radiographic bone gain
	BG	OFD	15	8 (Rx)	Xenograft	No		
(Shah et al., 2015)	ABP	OFD	20	NR	No	No	6	Clinical outcomes
	BG	OFD	20	NR	Allograft (DFDBA)	No		
(Sharma & Pradeep, 2011)	ABP	OFD	28	5.18 (Rx)	No	No	9	Clinical outcomes, 2D radiographic bone fill and bone gain
	Flap	OFD	28	4.99 (Rx)	No	No		
(Shukla et al., 2016)	BG	OFD	20	NR	Synthetic graft (CP)	No	9	Clinical outcomes
	ABP + BG	OFD	20	NR	Synthetic graft (CP)	No		
(Silvestri et al., 2000)	Flap	MWF	10	5.2 (DM)	No	No	12	Clinical outcomes
	GTR (Non-Abs*)							
	EMD	NR	10	5.9 (DM)	No	EDTA		
(Silvestri et al., 2003)	GTR (Non-Abs*)						12	Clinical outcomes
	EMD	PPT or MPPT	49	6.4 (DM)	No	EDTA		
(Sipos et al., 2005)	EMD	MPPT or SPPT	12	4.8 (DM)	No	EDTA	6, 12	Clinical outcomes
	EMD + GTR (Non-Abs*)							
(Thorat et al., 2011)	Flap	OFD	16	4.41 (Rx)	No	No	9	Clinical outcomes, 2D radiographic bone fill and bone gain
	ABP	OFD	16	4.52 (Rx)	No	No		
(Thorat et al., 2017)	Flap	OFD	15	NR	No	No	12	Clinical outcomes, 2D radiographic bone fill and bone gain
	ABP	OFD	15	NR	No	No		

(Tonetti et al., 2002) and (Tonetti et al., 2004)	EMD	MPPT or SPPT	83	5.8 (DM)	No	EDTA	12	Clinical outcomes, wound healing outcomes, complications, PROMs
	Flap	MPPT or SPPT	83	5.4 (DM)	No	EDTA		
(Velasquez-Plata et al., 2002)	EMD	OFD	16	4.9 (DM)	No	EDTA	7	Clinical outcomes, bone outcomes (re-entry)
	EMD + BG	OFD	16	5.3 (DM)	Xenograft (DBBM)	EDTA		
(Wachtel et al., 2003)	EMD	MPPT	11	4.8 (DM)	No	EDTA	6, 12	Clinical outcomes, wound healing outcomes
	Flap	MPPT	11	4.4 (DM)	No	No		
(Windisch et al., 2021)	EMD	MIST or M-MIST	23	4.39 (DM)	No	EDTA	12	Clinical outcomes, wound healing outcomes
	EMD	MPPT or SPPT	24	4.63 (DM)	No	EDTA		
(Yamamiya et al., 2008)	ABP + BG	OFD	15	4.9 (DM)	Synthetic graft (HA)	No	12	Clinical outcomes, 2D radiographic bone gain
	ABP + Human cultured periosteum sheets*							
(Yilmaz et al., 2010)	EMD + BG	OFD	20	5.4 (DM)	Autogenous graft	EDTA	12	Clinical outcomes
	EMD	OFD	20	5.2 (DM)	No	EDTA		
(Zetterström et al., 1997)	EMD	OFD	208	NR	No	Phosphoric Acid	8, 36	Clinical outcomes, 2D radiographic bone fill and bone gain
	Flap	OFD	33	NR	No	Phosphoric Acid		
(Zucchelli et al., 2002)	EMD	SPPT	30	6.1 (DM)	No	EDTA	12	Clinical outcomes, wound healing outcomes, complications, PROMs
	GTR (Non-Abs)*							
	Flap	SPPT	30	6.2 (DM)	No	EDTA		
(Zucchelli et al., 2003)	EMD + BG	SPPT	30	6.7 (DM) 6.1 (Rx)	Xenograft (DBBM)	EDTA	12	Clinical outcomes, 2D radiographic bone gain
	EMD	SPPT	30	6.8 (DM) 6.1 (Rx)	No	EDTA		

Legend. 2D: two dimensional; ABP: autologous blood-derived products; β-TCP: beta-tricalcium phosphate; BG: bone graft; Cox2: cyclo-oxygenase-2; CP: calcium phosphosilicate; DBBM: demineralized bovine bone mineral; DFA: double flap approach; DFDBA: demineralized freeze-dried bone allograft; DPBM: demineralized porcine bone matrix; EDTA: ethylenediaminetetraacetic acid; EMD: enamel matrix derivative; EPPT: entire papilla preservation technique; FDBA: freeze-dried bone allograft; FGF-2: fibroblast growth factor-2; G1: group 1; G2: group 2; GTR: guided tissue regeneration; HA: hydroxyapatite; IDD: infrabony defect depth, measured as the vertical distance from the alveolar crest to the deepest location of the osseous defect, either intrasurgically through direct measurement (DM) or radiographically (Rx). LLLT: low-level laser therapy; M-MIST: modified-minimally invasive surgical technique; MIST: minimally invasive surgical technique; MPPT: modified papilla preservation technique; MWF: modified Widman flap; N/A: not available (defect depth evaluated using other references or fix points); NR: not reported; Non-Abs: non-absorbable membrane used; OFD: open flap debridement; OPAL: open probing attachment level; PPT: papilla preservation technique; PROMs: patient-reported outcome measures; rhPDGF: recombinant human platelet-derived growth factor-BB; SFA: single flap approach; SPPT: simplified papilla preservation technique; *: treatment arm not included in the quantitative analysis. †: number of sites included in the statistical analysis at the fist follow-up time point (≥ 6 months).

Supplementary Table 9. Risk of bias assessment

Publication, reference	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Domain 6	Domain 7	Overall Risk of Bias
(Abu-Ta'a, 2016)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Agarwal & Gupta, 2014)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Agarwal et al., 2016)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Agrali Ö et al., 2016)	Low	Low	Low	Unclear	Low	Low	Low	Low
(Agrawal et al., 2017)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Ahmad et al., 2019)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Aimetti et al., 2017)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Ajwani et al., 2015)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Al Machot et al., 2014)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Aslan et al., 2020)	Low	Low	Low	Low	Low	Low	Low	Low
(Aspriello et al., 2011)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Atchuta et al., 2020)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Aydemir Turkal et al., 2016)	Low	Low	Low	Low	Low	Low	Low	Low
(Bahammam & Attia, 2021)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Bansal & Bharti, 2013)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Bhutda & Deo, 2013)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Bodhare et al., 2019)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Bokan et al., 2006)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear

(Bratthall et al., 2001)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Camargo et al., 2001)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Camargo et al., 2005)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Chadwick et al., 2016)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Chambrone et al., 2007)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Chambrone et al., 2010)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Chandradas et al., 2016)	Low	Low	Low	Low	Low	Low	Low	Low
(Chatterjee et al., 2017)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Cortellini & Tonetti, 2011)	Low	Low	Low	Low	Low	Low	Low	Low
(Crea et al., 2008)	Low	Low	Low	Low	Low	Low	High	High
(De Leonardis & Paolantonio, 2013)	Low	Low	Low	Low	Low	Low	Low	Low
(Demir et al., 2007)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Dilsiz et al., 2010)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Döri et al., 2005)	Low	Unclear	Low	Low	Unclear	Low	Unclear	Unclear
(Döri et al., 2007a)	Low	Unclear	Low	Low	Unclear	Unclear	Unclear	Unclear
(Döri, Nikolidakis, et al., 2008)	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
(Döri et al., 2009)	Low	Unclear	Low	Low	Low	Low	High	High
(Döri, Arweiler, Húszár, et al., 2013)	Low	Unclear	Low	Unclear	Low	Low	High	High
(Döri, Arweiler, Szántó, et al., 2013)	Low	Unclear	Low	Unclear	Low	Low	High	High

(Elbehwashy et al., 2021)	Low	Low	Low	Low	Low	Low	Low	Low
(Elgendy & Abo Shady, 2015)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Fickl et al., 2009)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Fileto Mazzonetto et al., 2021)	Low	Low	Low	Low	Low	Low	Low	Low
(Francetti et al., 2004)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Francetti et al., 2005)	Low	Unclear	Low	Low	High	Low	Low	High
(Froum et al., 2001)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Galav et al., 2016)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Gamal, Abdel Ghaffar, et al., 2016)	Low	Unclear	Low	Low	Low	High	High	High
(Ghezzi et al., 2016)	Low	Low	Low	Low	Low	Low	Low	Low
(Grusovin & Esposito, 2009)	Low	Unclear	Low	High	Unclear	Unclear	Low	High
(Guida et al., 2007)	Unclear	Unclear	Low	High	Low	Low	Low	High
(Gupta et al., 2014)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Gurinsky et al., 2004)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Hanna et al., 2004)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Harnack et al., 2009)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Hassan et al., 2012)	Low	Unclear	Unclear	Unclear	Low	High	High	High
(Hazari et al., 2021)	Low	Unclear	Unclear	Unclear	Low	Unclear	Low	Unclear
(Heijl et al., 1997)	Unclear	Low	Low	Low	Unclear	Low	Low	Unclear
(Hoffmann et al., 2016)	Low	Low	Low	Low	Low	Low	Low	Low

(Hoidal et al., 2008)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Ilgenli et al., 2007)	Low	Unclear	Unclear	Unclear	Low	High	High	High
(Iorio Siciliano et al., 2011)	Low	Low	Low	Low	Low	Low	Low	Low
(Iorio-Siciliano et al., 2014)	Low	Low	Low	High	Low	Low	Low	High
(Jalaluddin et al., 2017)	Low	Low	Low	Low	High	Low	High	High
(Jalaluddin et al., 2018)	Low	Low	Low	Low	High	Low	High	High
(Jayakumar et al., 2011)	Low	Low	Low	Low	Low	Low	Low	Low
(Jepsen et al., 2008)	Low	Low	Low	Low	Low	Low	Low	Low
(Kanoriya et al., 2016)	Low	Low	Low	Low	Low	Low	Low	Low
(Kaushick et al., 2011)	Low	Low	Low	Low	High	Low	High	High
(Kavyamala et al., 2019)	Low	Low	Low	Low	Low	Low	Low	Low
(Keles et al., 2006)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Khosropanah et al., 2015)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Kitamura et al., 2016) (Part A)	Low	Low	Low	Low	Low	Low	Low	Low
(Kitamura et al., 2016) (Part B)	Low	Low	Low	Low	Low	Low	Low	Low
(Kuru et al., 2006)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(J. Y. Lee et al., 2017)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(J. H. Lee et al., 2020)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Leknes et al., 2009)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Lekovic et al., 2000)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear

(Lekovic et al., 2001)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Lekovic et al., 2002)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Lekovic et al., 2012)	High	Low	Low	Low	Low	Low	Low	High
(Liu et al., 2021)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Losada et al., 2017)	Low	Low	Low	Low	Unclear	Low	Low	Unclear
(Markou et al., 2009)	Low	Low	Low	Low	Low	Low	Low	Low
(Maroo & Murthy, 2014)	Low	Low	Low	Low	Low	Low	Low	Low
(Martande et al., 2016)	Low	Low	High	High	Low	Low	Low	High
(Mathur et al., 2015)	Low	Low	Unclear	Unclear	Unclear	Low	Low	Unclear
(Meyle et al., 2011)	Low	Low	Low	Low	Low	Low	Low	Low
(Minabe et al., 2002)	Low	Low	Unclear	Unclear	Low	Low	Low	Low
(Mishra et al., 2013)	Low	Low	Low	Low	Low	Low	Low	Low
(Moreno Rodriguez & Ortiz Ruiz, 2021)	Low	Low	Low	Low	Low	Low	Low	Low
(Naqvi et al., 2017)	Unclear	Unclear	High	Unclear	Low	Low	Unclear	High
(Nevins et al., 2005)	Low	Low	Low	Low	Low	Low	Low	Low
(Nevins et al., 2013)	Low	Low	Low	Low	Low	Low	Low	Low
(Ogihara & Tarnow, 2014)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Ogihara & Wang, 2010)	Low	Unclear	High	Low	Low	Low	Low	Unclear
(Okuda et al., 2000)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Okuda et al., 2005)	Low	Low	Low	Low	Low	Low	Low	Low

(Ozcelik et al., 2008)	Low	Low	High	High	Low	Low	Low	High
(Ozdemir & Okte, 2012)	Low	Low	Unclear	Unclear	Low	Low	Low	Unclear
(Panda et al., 2016)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Paolantonio et al., 2020)	Low	Low	Low	Low	Low	Low	Low	Low
(Patel et al., 2017)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Pavani et al., 2021)	Unclear	High	High	High	High	Unclear	High	High
(Pham, 2021)	Low	Low	Unclear	Low	Low	Low	Low	Low
(Piemontese et al., 2008)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Pietruska et al., 2012)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Pilloni et al., 2021)	Low	Low	Low	Low	Low	Low	Low	Low
(Pontoriero et al., 1999)	Low	Low	Low	Low	Unclear	Low	Low	Low
(Pradeep et al., 2009)	Low	High	Unclear	High	Low	Low	Low	High
(Pradeep et al., 2012)	Low	Low	Low	Low	Low	Low	Low	Low
(Pradeep et al., 2015)	Low	Low	Low	Low	Low	Low	Low	Low
(Pradeep et al., 2016)	Low	Unclear	Unclear	Unclear	Low	Low	Unclear	Unclear
(Pradeep et al., 2017)	Low	Low	Low	Low	Low	Low	Low	Low
(Ragghianti Zangrando et al., 2014)	Low	Low	Low	Unclear	High	High	Unclear	High
(Ravi et al., 2017)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Ribeiro et al., 2011)	Low	Low	Low	Low	Low	Low	Low	Low
(Rösing et al., 2005)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear

(Saini et al., 2011)	Low	Unclear	Unclear	Unclear	Low	Low	Unclear	Unclear
(Sanz et al., 2004)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Scheyer et al., 2002)	Low	Low	Low	Low	Low	Low	Low	Low
(Schincaglia et al., 2015)	Low	Low	Low	Low	Low	Low	Low	Low
(Schwarz et al., 2003)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Sculean, Donos, Blaes, et al., 1999)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Sculean, Blaes, et al., 2001)	Low	Low	High	Low	Low	Low	Low	High
(Sculean, Donos, et al., 2001)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Sculean, Windisch, et al., 2001)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Sculean, Barbé, et al., 2002)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Sculean, Chiantella, et al., 2002)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Sculean et al., 2003)	Low	Unclear	Unclear	Unclear	Low	Low	Low	Unclear
(Sculean et al., 2004)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Sculean, Pietruska, et al., 2005)	Low	Low	Unclear	Unclear	Low	Low	Low	Unclear
(Sculean, Berakdar, et al., 2006)	Low	Low	Low	Low	Low	Low	Low	Low
(Sculean, Schwarz, et al., 2006)	Low	Low	Low	Low	Low	Low	Low	Low
(Sculean, Pietruska, et al., 2007)	Low	Low	Unclear	Unclear	Low	Low	Low	Low
(Sculean et al., 2008)	Low	Low	Low	Low	Low	Low	Low	Low

(Sezgin et al., 2017)	Low	Low	Low	Low	Low	Unclear	Low	Low
(Shah et al., 2015)	Low	Low	Low	Low	Low	Low	Low	Low
(Sharma & Pradeep, 2011)	Low	Low	Low	Low	Low	Low	Low	Low
(Shukla et al., 2016)	Low	Unclear	Unclear	Low	Unclear	Low	Low	Unclear
(Silvestri et al., 2000)	Unclear	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Silvestri et al., 2003)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Sipos et al., 2005)	Low	Low	Low	Low	Low	Low	Low	Low
(Thorat et al., 2011)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Thorat et al., 2017)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Tonetti et al., 2002) and (Tonetti et al., 2004)	Low	Low	Low	Low	Low	Low	Low	Low
(Velasquez-Plata et al., 2002)	Low	Low	Low	Low	Low	Low	Low	Low
(Wachtel et al., 2003)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Windisch et al., 2021)	Low	Low	Low	Low	Low	Low	Low	Low
(Yamamiya et al., 2008)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear
(Yilmaz et al., 2010)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Zetterström et al., 1997)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Zucchelli et al., 2002)	Low	Unclear	Low	Low	Low	Low	Low	Unclear
(Zucchelli et al., 2003)	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear

Legend. Domain 1: risk of selection bias – random sequence generation; Domain 2: risk of selection bias – allocation concealment; Domain 3: risk of performance bias – blinding of participants and personnel; Domain 4: risk of detection bias – blinding of outcome assessment; Domain 5: risk of attrition bias – incomplete outcome data; Domain 6: risk of reporting bias – selective reporting; Domain 7: other risk of bias.

Supplementary Table 10. Clinical outcomes of infrabony defects treated with autologous blood-derived products (ABPs).

Publication, reference	Treatment	Bone graft	Baseline			Time (months)	Follow-up		
			Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)
(Agarwal & Gupta, 2014)	ABP† + BG	AllG	7.23	8.42	1.19	12	3.58	5.27	1.73
(Agarwal et al., 2016)	ABP* + BG	AllG	7.13	8.18	1.05	12	2.98	4.45	1.52
(Agrawal et al., 2017)	ABP*	No	NR	NR	NR	6	(Only median reported)	(Only median reported)	(Only median reported)
	ABP* + BG	SG	NR	NR	NR	6	(Only median reported)	(Only median reported)	(Only median reported)
(Ahmad et al., 2019)	ABP*	No	7.5	6.87	-0.62	6	3.38	2.81	-0.56
(Ajwani et al., 2015)	ABP*	No	5.9	9.5	3.6	9	4	7.7	3.9
(Atchuta et al., 2020)	ABP*+ BG	AllG	6.25	6.21	-0.04	6	2.65	2.81	0.16
(Bahammam & Attia, 2021)	ABP*	No	7.3	NR	NR	6	4.6	NR	NR
	ABP* + BG	SG	6.7	NR	NR	6	3.7	NR	NR
(Bansal & Bharti, 2013)	ABP* + BG	AllG	NR	NR	NR	6	NR	NR	NR
(Bodhare et al., 2019)	ABP* + BG	SG	8.75	9.25	0.45	6	3	4.2	1.2
(Chadwick et al., 2016)	ABP*	No	6.91	6.32	-0.56	6	4.79	5.29	0.5
(Chandradas et al., 2016)	ABP*	No	8.27	9	0.73	9	4.45	5.36	0.91
	ABP* + BG	XG	8.67	9.25	0.58	9	4.42	5.17	0.75
(Chatterjee et al., 2017)	ABP*	No	NR	NR	NR	9	NR	NR	NR
	ABP*	No	NR	NR	NR	9	NR	NR	NR
(Demir et al., 2007)	ABP† + BG	SG	7.8	8.53	0.73	9	4.2	5.4	1.2

(Döri et al., 2009)	ABP† + BG	XG	8.6	9.9	1.3	12	3.4	5.3	1.9
(Elbehwashy et al., 2021)	ABP*	No	6.8	8.25	1.45	6	3.35	4	0.65
	ABP*	No	6.9	7.45	0.55	6	2.8	3.55	0.75
(Elgendy & Abo Shady, 2015)	ABP* + BG	SG	7.12	7.4	0.28	6	3.82	3.9	0.08
(Galav et al., 2016)	ABP*	No	7.3	NR	NR	9	3.2	NR	NR
(Gamal, Abdel Ghaffar, et al., 2016)	ABP‡ + BG	XG	6.8	4.6	NR	6	2.8	3.1	NR
	ABP* + BG	XG	6.1	3.8	NR	6	3.2	2.3	NR
	ABP‡ + BG	XG	6.8	4.6	NR	9	2.5	2.6	NR
	ABP* + BG	XG	6.1	3.8	NR	9	2.5	2.6	NR
(Gupta et al., 2014)	ABP*	No	6.2	6.8	0.6	6	4.4	4.93	0.53
(Hanna et al., 2004)	ABP† + BG	XG	6.92	6.92	0	6	3.38	3.69	0.3
(Harnack et al., 2009)	ABP† + BG	SG	(Only median reported)	(Only median reported)	(Only median reported)	6	(Only median reported)	(Only median reported)	(Only median reported)
(Hassan et al., 2012)	ABP† + BG	AutG	7.28	NR	NR	6	2.52	NR	NR
						12	2.31	NR	NR
(Hazari et al., 2021)	ABP* + BG	SG	7.6	NR	NR	6	5	NR	NR
(Ilgenli et al., 2007)	ABP†	No	7.5	8.4	0.9	6	5.4	6.9	1.5
	ABP† + BG	AllG	8.3	9.06	0.76	6	3.7	4.3	0.6
(Jalaluddin et al., 2017)	ABP†	No	8	12.7	4.7	6	3.7	9	5.3
(Jalaluddin et al., 2018)	ABP†	No	8	12.7	4.7	6	3.7	9	5.3
(Kanoriya et al., 2016)	ABP*	No	7.96	7.6	1.69	9	4.26	3.4	1.45
(Kaushick et al., 2011)	ABP† + BG	SG	7.3	NR	NR	6	3	NR	NR

(Khosropanah et al., 2015)	ABP† + BG	AllG	8.6	8.7	1.1	6	4	5	1.5
(Lekovic et al., 2002)	ABP† + BG	XG	7.96	NR	NR	6	3.98	NR	NR
(Lekovic et al., 2012)	ABP*	No	7.82	NR	NR	6	4.47	NR	NR
	ABP* + BG	XG	7.94	NR	NR	6	3.47	NR	NR
(Markou et al., 2009)	ABP†	No	7.17	8.08	0.91	6	3.33	3.83	0.5
	ABP + BG	AllG	7.08	8.58	1.5	6	3.58	4.92	1.34
(Martande et al., 2016)	ABP*	No	8.23	9.88	1.65	9	4.46	5.89	1.43
(Mathur et al., 2015)	ABP*	No	7.67	6.87	NR	6	5	4.33	NR
(Naqvi et al., 2017)	ABP* + BG	SG	6	NR	NR	6	2.15	NR	NR
	ABP* + BG	SG	6	NR	NR	9	2.4	NR	NR
(Okuda et al., 2005)	ABP† + BG	SG	7.7	8.4	0.7	12	3	5	1.9
(Ozdemir & Okte, 2012)	ABP† + BG	SG	7	7.5	0.6	6	4	5	1
(Paolantonio et al., 2020)	ABP* + BG	AutG	7.43	8.25	0.96	12	3.21	4.82	1.61
(Patel et al., 2017)	ABP*	No	8.3	7.1	NR	6	5.3	3.9	NR
	ABP*	No	8.3	7.1	NR	9	4.5	3.5	NR
	ABP*	No	8.3	7.1	NR	12	4.1	3.4	NR
(Pavani et al., 2021)	ABP* + BG	SG	6.1	NR	NR	6	1.8	NR	NR
(Pham, 2021)	ABP*	No	7.57	8.23	0.66	6	4.27	4.9	0.63
	ABP*	No	7.57	8.23	0.66	12	2.77	3.23	0.46
(Piemontese et al., 2008)	ABP† + BG	AllG	7.8	8.4	0.6	12	3.5	4.8	1.3
(Pradeep et al., 2009)	ABP†	No	7.71	NR	NR	9	4.21	NR	NR
	ABP† + BG	XG	8.14	NR	NR	9	3.64	NR	NR
	ABP*	No	7.83	6.2	NR	9	4.06	3.03	NR

(Pradeep et al., 2012)	ABP†	No	7.9	6.16	NR	9	4.13	3.23	NR
(Pradeep et al., 2015)	ABP*	No	8.6	10.24	1.64	9	4.6	5.96	1.36
(Pradeep et al., 2016)	ABP*	No	7.83	5.7	NR	9	3.8	2.4	NR
(Pradeep et al., 2017)	ABP*	No	8.17	6.4	NR	9	4.27	3.37	NR
	ABP* + BG	SG	8.37	6.63	NR	9	4.1	2.97	NR
(Saini et al., 2011)	ABP† + BG	SG	6.3	5.1	NR	6	3	2.75	NR
	ABP† + BG	SG	6.3	5.1	NR	9	3.5	3.3	NR
(Sezgin et al., 2017)	ABP* + BG	XG	7.46	8.33	0.87	6	2.53	3.86	1.33
(Shah et al., 2015)	ABP*	No	7.07	NR	NR	6	3.27	NR	NR
(Sharma & Pradeep, 2011)	ABP*	No	8.56	6.87	0.88	9	4.02	3.56	0.79
(Shukla et al., 2016)	ABP† + BG	SG	7.05	8.25	NR	9	3.35	2.63	NR
(Thorat et al., 2011)	ABP*	No	7.88	8.38	0.5	9	3.19	4	0.81
(Thorat et al., 2017)	ABP*	No	8.17	8.33	0.51	12	4.17	4.33	0.33
(Yamamiya et al., 2008)	ABP† + BG	SG	7.6	8	0.4	12	3.3	5.3	2.1

Legend. ABP: autologous blood-derived products; AllG: allograft; AutG: autogenous graft; BG: bone graft; CAL: clinical attachment level; NR: Not reported; PD: pocket depth; REC: recession depth; SG: synthetic graft; XG: xenograft; *: Platelet-rich fibrin (PRF) was used as ABP; †: Platelet-rich plasma (PRP) was used as ABP; ‡: Platelet rich growth factor (PRGF) was used as ABP

Supplementary Table 11. Clinical outcomes of infrabony defects treated with enamel matrix derivative (EMD).

Publication, reference	Treatment	Bone graft	Baseline			Time (months)	Follow-up		
			Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)
(Abu-Ta'a, 2016)	EMD + BG	AllG	NR	NR	NR	12	NR	NR	NR
	EMD + BG	AllG	NR	NR	NR	12	NR	NR	NR
(Agrali Ö et al., 2016)	EMD	No	8.3	13.7	5.4	6	3.3	9.2	5.9
	EMD + BG	AutG	7.93	13.05	5.12	6	3.22	9.51	6.28
(Aimetti et al., 2017)	EMD	No	7.3	9	1.7	12	3.7	5.5	1.8
						24	3.6	5.4	1.8
(Al Machot et al., 2014)	EMD	No	6.6	9.8	3.3	6	3.4	7.8	4.4
	EMD	No	6.6	9.8	3.3	12	3.4	7.7	4.3
(Aslan et al., 2020)	EMD + BG	XG	9.33	11.66	2.33	12	2.83	5.36	2.53
(Aspriello et al., 2011)	EMD + BG	AllG	(Only median reported)	(Only median reported)	(Only median reported)	12	(Only median reported)	(Only median reported)	(Only median reported)
(Aydemir Turkal et al., 2016)	EMD	No	6.58	8.13	1.54	6	2.71	4.83	2.13
(Bhutda & Deo, 2013)	EMD	No	7.24	8.08	0.84	12	3.12	4.12	1
						60	3.4	4.9	1.5
(Bokan et al., 2006)	EMD	No	8.6	10.3	2.4	12	4.7	6.5	3.1
	EMD + BG	SG	8.6	9.8	1.3	12	4.5	5.8	1.9
(Bratthall et al., 2001)	EMD	No	7.8	NR	NR	8	4.4	NR	NR
	EMD	No	7.8	NR	NR	8	4.5	NR	NR
	EMD	No	7.8	NR	NR	16	4.1	NR	NR
	EMD	No	7.8	NR	NR	16	4.2	NR	NR

Camargo et al., 2001)	EMD + BG	XG	7.33	NR	NR	6	3.54	NR	NR
(Chambrone et al., 2007)	EMD	No	6.42	7.5	1.08	6	2.67	5	2.33
(Chambrone et al., 2010)	EMD	No	6.3	7.97	1.67	12	2.3	5.01	2.71
						24	2.09	4.78	2.69
(Cortellini & Tonetti, 2011)	EMD	No	7.8	9.9	2.1	12	3.4	5.7	2.3
	EMD + BG	XG	7.3	10.1	2.9	12	3.3	6.4	3.1
(Crea et al., 2008)	EMD	No	6.6	7.5	0.9	12	3.2	4.7	1.5
						36	3.5	5	1.5
(De Leonardis & Paolantonio, 2013)	EMD	No	8.73	9.25	0.51	12	5.22	6.51	1.29
						24	4.97	6.29	1.32
	EMD + BG	SG	8.79	9.36	0.57	12	4.79	5.89	1.1
						24	4.54	5.73	1.19
(Dilsiz et al., 2010)	EMD	No	7.3	9.3	2	6	3.1	6.1	3
	EMD	No	7.3	9.3	2	12	3	6.4	3.4
(Döri et al., 2005)	EMD + BG	XG	7.9	8.8	0.9	12	3.2	4.5	1.3
	EMD + BG	SG	7.8	8.8	1	12	3.2	4.7	1.5
(Döri, Nikolidakis, et al., 2008)	EMD + BG	XG	8.8	10.5	1.8	12	2.8	5.5	2.7
(Döri, Arweiler, Húszár, et al., 2013)	EMD + BG	XG	8.8	10.6	1.8	12	3.3	6.1	2.8
						60	3.8	6.3	2.5
(Döri, Arweiler, Szántó, et al., 2013)	EMD + BG	XG	8	8.9	0.9	12	3.5	5.3	1.8
	EMD + BG	SG	8.1	9.1	1	12	3.3	5.4	2.1
	EMD + BG	XG	8	8.9	0.9	120	4.1	5.8	1.7
	EMD + BG	SG	8.1	9.1	1	120	4.1	6.1	2

(Fickl et al., 2009)	EMD	No	NR	NR	NR	6	NR	NR	NR
						12	NR	NR	NR
(Fileto Mazzonetto et al., 2021)	EMD	No	6.7	7.4	0.7	6	4.7	5.8	1.1
	EMD	No	6.6	7.9	1.3	6	4.4	6	1.6
	EMD	No	6.7	7.4	0.7	12	4.3	5	0.7
	EMD	No	6.6	7.9	1.3	12	4.2	5.9	1.7
(Francetti et al., 2004)	EMD	No	7.86	9.43	1.57	12	3.14	5.29	2.15
						24	3	5.14	2.14
(Francetti et al., 2005)	EMD	No	8.06	8.91	0.85	12	4.06	5.5	1.44
						24	4.04	5.4	1.36
(Froum et al., 2001)	EMD	No	7.99	NR	NR	12	3.05	NR	NR
(Ghezzi et al., 2016)	EMD + BG	XG	8.2	9.2	1	12	3.3	4.8	1.5
(Grusovin & Esposito, 2009)	EMD	No	7.8	8.7	0.8	12	3.6	5.3	1.7
(Guida et al., 2007)	EMD	No	9.6	10.6	1.1	6	4.5	6.2	1.7
	EMD	No	9.6	10.6	1.1	12	3.9	6.1	2.1
	EMD + BG	AutG	9.1	10.3	1.1	6	4.5	5.9	1.4
	EMD + BG	AutG	9.1	10.3	1.1	12	4	5.4	1.4
(Gupta et al., 2014)	EMD	No	6.87	7	0.13	6	5.07	5	-0.07
(Gurinsky et al., 2004)	EMD	No	7.5	8.1	0.6	6	3.6	4.9	1.3
	EMD + BG	AllG	7.5	8.2	0.7	6	4	5.2	1.2
(Heijl et al., 1997)	EMD	No	7.8	9.4	1.6	8	4.4	7.1	2.7
						16	4.5	7	2.5
						36	4.6	7.1	2.5
	EMD	No	7.2	10	2.8	6	3.5	7.8	4.3

(Hoffmann et al., 2016)						12	3.7	8	4.4
						36	3.3	6.2	2.9
						6	4.4	8	3.7
	EMD + BG	SG	7.2	9.8	2.6	12	3.8	7.8	4.1
						36	3.3	5.8	2.4
(Hoidal et al., 2008)	EMD + BG	AllG	7.24	7.74	0.5	6	4.68	6.26	1.59
(Iorio Siciliano et al., 2011)	EMD	No	9.4	10.5	1.2	12	6.5	8.1	1.9
(Iorio-Siciliano et al., 2014)	EMD + BG	XG	8.2	9.3	1.2	12	3.6	5.5	1.8
(Jepsen et al., 2008)	EMD	No	7.1	10.1	3	6	4.5	8.3	3.8
	EMD + BG	SG	6.9	9.3	2.4	6	5	8	3
(Kitamura et al., 2016)	EMD	No	NR	NR	NR	24	NR	NR	NR
	EMD	No	NR	NR	NR	36	NR	NR	NR
(Kuru et al., 2006)	EMD	No	9.47	NR	NR	8	4.44	NR	NR
	EMD + BG	SG	9.77	NR	NR	8	4.04	NR	NR
(J. H. Lee et al., 2020)	EMD + BG	XG	7.8	8.5	0.7	6	5.7	7	1.3
	EMD + BG	XG	7.8	8.5	0.7	12	5.4	7	1.6
	EMD + BG	XG	7.8	8.5	0.7	24	5.4	6.9	1.5
(Leknes et al., 2009)	EMD	No	6.5	10.7	4.2	6	4	9.7	5.7
	EMD	No	6.5	10.7	4.2	12	4	10.5	6.5
(Lekovic et al., 2000)	EMD	No	7.33	NR	NR	6	5.41	NR	NR
	EMD + BG	XG	7.74	NR	NR	6	3.71	NR	NR
(Lekovic et al., 2001)	EMD + BG	XG	6.36	NR	NR	6	3.41	NR	NR
(Losada et al., 2017)	EMD	No	7.88	8.96	1.2	6	4.16	5.96	1.76
	EMD	No	7.88	8.96	1.2	12	4.04	5.72	1.68

	EMD + BG	SG	7.95	9.57	1.61	6	4.71	7.28	2.66
	EMD + BG	SG	7.95	9.57	1.61	12	4.8	7.19	2.47
(Meyle et al., 2011)	EMD	No	7.1	10.1	3	12	4.2	8.2	4
	EMD + BG	SG	6.9	9.3	2.4	12	4.1	7.6	3.5
(Minabe et al., 2002)	EMD	No	6	8.2	2.2	6	2.4	5.5	3.1
	EMD	No	6	8.2	2.2	12	2.4	5.6	3.2
(Moreno Rodriguez & Ortiz Ruiz, 2021)	EMD	No	10.75	11.33	0.58	12	2.5	3	0.83
	EMD + BG	XG	9,5	10.42	0.83	12	2.67	3.33	1
(Ogihara & Tarnow, 2014)	EMD	No	6.56	7.13	0.57	12	3.43	4.09	0.66
	EMD	No	6.56	7.13	0.57	36	3.61	4.13	0.52
	EMD + BG	AllG	6.57	7.3	0.73	12	2.19	3.14	0.95
	EMD + BG	AllG	6.57	7.3	0.73	36	2.14	3.1	0.96
	EMD + BG	AllG	6.43	7.26	0.83	12	2.74	3.74	1
	EMD + BG	AllG	6.43	7.26	0.83	36	2.7	3.65	0.95
Ogihara and Wang, 2010)	EMD + BG	AllG	7	7.57	0.57	12	2.29	3.29	1
(Okuda et al., 2000)	EMD	No	6.33	6.72	0.39	12	3.39	4.94	1.61
(Paolantonio et al., 2020)	EMD + BG	AutG	7.64	8.46	0.82	12	3.68	5.18	1.5
(Pietruska et al., 2012)	EMD	No	8.8	10.4	1.6	12	4.1	6.9	2.9
	EMD	No	8.8	10.4	1.6	48	4.4	7.2	2.8
	EMD + BG	SG	8.8	10.6	2.1	12	4.3	7.4	3.2
	EMD + BG	SG	8.8	10.6	2.1	48	4.7	7.6	3
(Pilloni et al., 2021)	EMD	No	7.25	7.37	0.12	12	3	4.25	1.25
	EMD	No	7.25	7.37	0.12	18	2.87	4.31	1.44
	EMD	No	7.25	7.37	0.12	24	2.75	4.44	1.69

(Pontoriero et al., 1999)	EMD	No	8	9.1	0.8	12	3.6	6.2	1.7
(Ribeiro et al., 2011)	EMD	No	7.09	NR	NR	6	3.53	NR	NR
(Rösing et al., 2005)	EMD	No	7.57	NR	NR	6	3.85	NR	NR
	EMD	No	7.57	NR	NR	12	3.4	NR	NR
(Sanz et al., 2004)	EMD	No	7.9	9.5	1.6	12	4.1	6.4	2.3
(Scheyer et al., 2002)	EMD + BG	XG	7.5	7.9	0.4	6	3.2	4.1	0.9
(Schwarz et al., 2003)	EMD	No	8.6	10.7	2.1	6	4.6	7.5	2.9
(Sculean, Donos, Blaes, et al., 1999)	EMD	No	8.1	10.3	2.1	8	4.3	7.2	2.9
(Sculean, Blaes, et al., 2001)	EMD	No	9.1	11	1.9	12	4.5	7.5	3.2
	EMD	No	9	10.6	1.6	12	4.3	7.3	2.9
(Sculean, Donos, et al., 2001)	EMD	No	8.1	9.8	1.7	12	3.8	6.4	2.6
	EMD	No	8.1	9.8	1.7	48	4.7	6.8	2.1
(Sculean, Windisch, et al., 2001)	EMD	No	8.4	10.6	2.2	12	4.3	7.2	2.9
(Sculean, Barbé, et al., 2002)	EMD + BG	SG	8.07	9.64	1.5	12	3.92	6.42	2.5
(Sculean, Chiantella, et al., 2002)	EMD + BG	XG	10	10.9	0.9	12	4.3	6.2	1.7
(Sculean et al., 2003)	EMD	No	8.6	9.5	0.9	6	4.7	6.5	1.8
(Sculean et al., 2004)	EMD	No	8.2	9.9	1.7	60	3.9	7	3
(Sculean, Pietruska, et al., 2005)	EMD	No	8.5	10.2	1.5	12	4	6.3	2.4
	EMD + BG	SG	8.5	10.4	1.9	12	4.4	7.1	2.8
(Sculean, Berakdar, et al., 2006)	EMD	No	9.3	10.8	1.5	12	4	7.1	3
	EMD	No	9.3	11	1.8	12	4.2	7.3	3.2

(Sculean, Schwarz, et al., 2006)	EMD	No	8.1	9.5	1.4	12	4	6.3	2.3
	EMD	No	8.1	9.5	1.4	96	4.7	6.7	2
(Sculean, Pietruska, et al., 2007)	EMD	No	8.6	10.4	1.8	48	4.4	7	2.7
	EMD + BG	SG	8.6	10.3	1.7	48	4.5	6.9	2.4
(Sculean et al., 2008)	EMD	No	8.4	10.4	2	120	4.8	7.5	2.7
(Silvestri et al., 2000)	EMD	No	7.7	9.1	1.3	12	2.9	4.6	1.7
(Silvestri et al., 2003)	EMD	No	8.5	9.9	1.8	12	3.2	5.8	2.6
(Sipos et al., 2005)	EMD	No	6.95	10.94	3.99	6	4.69	10	5.31
	EMD	No	6.95	10.94	3.99	12	4.09	9.66	5.55
(Tonetti et al., 2002) and (Tonetti et al., 2004)	EMD	No	8	9.4	1.4	12	4.1	6.3	2.2
(Velasquez-Plata et al., 2002)	EMD	No	6.6	NR	NR	7	2.8	NR	NR
	EMD + BG	XG	6.9	NR	NR	7	2.9	NR	NR
(Wachtel et al., 2003)	EMD	No	7	7.7	0.8	6	3.7	4.9	1.2
	EMD	No	7	7.7	0.8	12	3.1	4.1	1
(Windisch et al., 2021)	EMD	No	7.22	8.82	1.65	12	2.78	4.78	2
	EMD	No	7.25	8.71	1.46	12	3.21	4.92	1.71
(Yilmaz et al., 2010)	EMD	No	8.2	11.3	3.1	12	3.5	7.8	4.3
	EMD + BG	AutG	8.4	11.7	3.3	12	2.8	7.5	4.7
(Zetterström et al., 1997)	EMD	No	7.4	8.7	1.3	8	3.1	5.6	2.5
	EMD	No	7.5	8.8	1.3	36	3.7	5.9	2.2
(Zucchelli et al., 2002)	EMD	No	9.2	9.9	0.8	12	4	5.8	1.7
	EMD	No	9.2	10.1	0.9	12	3.4	5.2	1.8

(Zucchelli et al., 2003)	EMD + BG	XG	9.4	10.3	0.9	12	3.2	4.5	1.3

Legend. AllG: allograft; AutG: autogenous graft; BG: bone graft; CAL: clinical attachment level; EMD: enamel matrix derivative; NR: Not reported; PD: pocket depth; REC: recession depth; SG: synthetic graft; XG: xenograft.

Supplementary Table 12. Clinical outcomes of infrabony defects treated with recombinant human platelet-derived growth factor (rhPDGF).

Publication, reference	Bone graft	Baseline			Time (months)	Follow-up		
		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)
(Jayakumar et al., 2011)	SG	8.7	8.4	0.4	6	4.4	4.7	0.3
(Kavyamala et al., 2019)	SG	7.33	8	0.66	6	2.66	3.66	0.91
(J. Y. Lee et al., 2017)	XG	8.25	10.81	2.56	6	3.25	5.31	2.06
	SG	8.31	9.63	1.32	6	3.56	5.53	1.97
(Maroo & Murthy, 2014)	SG	8.33	8.53	0.2	6	3.6	3.87	0.27
	SG	8.33	8.53	0.2	9	2.87	3.2	0.27
(Mishra et al., 2013)	No	7.73	7.91	0.18	6	3.55	4.55	1
(Nevins et al., 2005)	SG	8.6	9.1	0.5	6	NR	5.3	NR
	SG	8.2	8.8	0.6	6	NR	NR	NR
(Schincaglia et al., 2015)	SG	8.7	9.7	1.1	6	4.5	5.7	1.2
(Schincaglia et al., 2015)	SG	7.7	8.5	0.8	6	4.1	5.2	1.2

Legend. CAL: clinical attachment level; NR: Not reported; PD: pocket depth; REC: recession depth; SG: synthetic graft; XG: xenograft.

Supplementary Table 13. Clinical outcomes of infrabony defects treated with Guided Tissue Regeneration procedures (GTR).

Publication, reference	Bone graft	Membrane	Baseline			Time (months)	Follow-up		
			Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)
Döri et al., 2007a)	XG	CM (R)	8.9	11.1	1.9	12	3.4	6.5	3.2
(Ghezzi et al., 2016)	XG	CM (R)	7.8	8.5	0.7	12	3.1	4.5	1.4
(Iorio-Siciliano et al., 2014)	XG	CM (R)	8.1	9.3	1.1	12	3.7	5.6	1.8
(Keles et al., 2006)	SG	PLA (R)	NR	8.3	NR	6	NR	4.3	NR
(Liu et al., 2021)	XG	CM (R)	4.8	4.8	0	6	2.4	2	-0.4
						12	2.4	2.1	-0.3
						24	2.4	2.1	-0.3
(Minabe et al., 2002)	No	CM (R)	6.5	7.4	0.9	6	2.7	4.4	1.7
						12	2.4	4.7	2.3
(Panda et al., 2016)	No	CM (R)	7	7.63	0.63	9	3.81	4.25	0.44
(Pham, 2021)	No	CM (R)	7.6	8.17	0.57	6	4.37	4.97	0.6
						12	2.97	3.63	0.66
(Pontoriero et al., 1999)	No	PLA (R)	7.9	8.9	1	12	3.1	5.5	1.4
	No	Polymers (R)	7.9	8.5	0.6	12	3.8	5.5	1.1
(Ravi et al., 2017)	No	CM (R)	6.11	5.97	NR	6	2.74	0.55	NR
(Sanz et al., 2004)	No	PLA (R)	8	9.7	1.7	12	4.7	7.2	2.5
(Sculean, Donos, Blaes, et al., 1999)	No	Polymers (R)	8.3	10.1	1.8	8	4.3	7.1	2.9

(Sculean, Donos, et al., 2001)	No	Polymers (R)	8.1	9.8	1.7	12	3.6	6.6	3
						48	4.7	6.9	2.2
(Sculean, Windisch, et al., 2001)	No	Polymers (R)	8.4	10.3	1.9	12	4.2	7.2	3
(Sculean et al., 2004)	No	Polymers (R)	8.3	9.9	1.6	60	4.4	7.2	2.8
(Sculean, Schwarz, et al., 2006)	No	Polymers (R)	8.2	9.7	1.5	12	3.6	6.7	3.1
						96	4.5	6.8	2.3
(Sculean et al., 2008)	No	Polymers (R)	8.4	10.3	1.9	120	5	7.5	2.5

Legend. CAL: clinical attachment level; CM: collagen membrane; ePTFE: expanded polytetrafluoroethylene; NR: not reported; PD: pocket depth; PLA: polylactic acid; R: resorbable membrane; REC: recession depth; SG: synthetic graft; XG: xenograft.

Supplementary Table 14. Clinical outcomes of infrabony defects treated with biologics and guided tissue regeneration.

Publication, reference	Bone graft, membrane	Baseline			Time (months)	Follow-up		
		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)
Autologous blood-derived products + Guided tissue regeneration (ABP + GTR)								
(Camargo et al., 2005)	XG, CM	8.12	NR	NR	6	3.06	NR	NR
(Döri et al., 2007a)	XG, CM	8.9	10.9	1.9	12	3.4	6.4	3
(Keles et al., 2006)	SG, PLA	NR	7.9	NR	6	NR	3.9	NR
(Lekovic et al., 2002)	XG, CM	7.81	NR	NR	6	3.62	NR	NR
(Liu et al., 2021)	XG, CM	4.6	4.9	0.3	6	1.9	2.9	1
					12	1.9	3.2	1.3
					24	1.9	3.1	1.2
(Panda et al., 2016)	No, CM	6.81	7.56	0.75	9	2.94	3.13	0.19
(Ravi et al., 2017)	No, CM	6.92	6.82	NR	6	2.79	0.82	NR
Enamel matrix derivative + Guided tissue regeneration (EMD + GTR)								
(Minabe et al., 2002)	No, CM	7	8.2	1.2	6	2.8	5.3	2.5
					12	2.9	5.3	2.4
(Sculean, Windisch, et al., 2001)	No, Polymers	8.6	10	1.1	12	4.3	6.6	2.2
(Sculean et al., 2004)	No, Polymers	8.4	9.8	1.4	60	4.4	7.2	2.9
(Sculean et al., 2008)	Polymers	8.6	10.2	1.6	120	5.1	7.3	2.2

Legend. ABP: autogenous blood-derived products; CAL: clinical attachment level; CM: collagen membrane; NR: not reported; PD: pocket depth; REC: recession depth; SG: synthetic graft; XG: xenograft.

Supplementary Table 15. Clinical outcomes of infrabony defects treated with bone graft alone.

Publication, reference	Bone graft	Baseline			Time (months)	Follow-up		
		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)
(Agarwal & Gupta, 2014)	AllG	7.25	8.44	1.19	12	3.6	6.04	2.42
(Agarwal et al., 2016)	AllG	7.12	8.18	1.07	12	3.52	5.57	2.07
(Al Machot et al., 2014)	SG	6.6	9.6	2.9	6	3.9	8	4.1
	SG	6.6	9.6	2.9	12	4.1	8.1	4.1
(Atchuta et al., 2020)	AllG	6.63	6.63	0	6	3.08	3.13	0.05
(Bahammam & Attia, 2021)	SG	7.6	NR	NR	6	5.2	NR	NR
(Bodhare et al., 2019)	SG	9.05	9.95	0.9	6	3.4	5.75	2.35
(Chadwick et al., 2016)	AllG	6.82	7.05	0.24	6	4.82	5.89	1.08
(Demir et al., 2007)	SG	8.36	9.7	0.72	9	5.07	6.21	1.14
(Döri et al., 2009)	XG	8.5	9.6	1.1	12	3.2	4.9	1.7
(Elgendy & Abo Shady, 2015)	SG	6.75	7.1	0.35	6	3.42	3.55	0.13
(Galav et al., 2016)	AutG	7.4	NR	NR	9	2.6	NR	MR
(Gamal, Abdel Ghaffar, et al., 2016)	XG	6.1	4.2	NR	6	3.4	2.5	NR
	XG	6.1	4.2	NR	9	2.3	2.4	NR
(Hanna et al., 2004)	XG	6.08	6.38	0.3	6	4.15	4.31	0.15
(Hassan et al., 2012)	AutG	7.19	NR	NR	6	3.14	NR	NR
	AutG	7.19	NR	NR	12	2.81	NR	NR
(Hazari et al., 2021)	SG	6.9	NR	NR	6	5.4	NR	NR

(Hoidal et al., 2008)	AllG	6.53	7	0.48	6	4.08	5.38	1.3
(Jalaluddin et al., 2018)	SG	8.2	13.1	4.9	6	4	9.1	5.1
(Jayakumar et al., 2011)	SG	7.7	7.8	0.1	6	4.5	5	0.5
(Kaushick et al., 2011)	SG	7.3	NR	NR	6	4	NR	NR
(Kavyamala et al., 2019)	SG	7.5	7.75	0.16	6	3.75	4.66	1
(Khosropanah et al., 2015)	AllG	7.8	7.9	0.3	6	3.6	4.4	1.2
(J. H. Lee et al., 2020)	XG	7.3	7.8	0.5	6	5.8	7	1.2
	XG	7.3	7.8	0.5	12	5.5	6.8	1.3
	XG	7.3	7.8	0.5	24	5.4	6.7	1.3
(Leknes et al., 2009)	SG	6.9	12.4	5.5	6	4.5	11	6.5
(Leknes et al., 2009)	SG	6.9	12.4	5.5	12	4.3	10.5	6.2
(Lekovic et al., 2001)	XG	6.01	NR	NR	6	3.3	NR	NR
(Maroo & Murthy, 2014)	SG	7.93	8.2	0.27	6	4.53	5.27	0.73
	SG	7.93	8.2	0.27	9	3.8	4.53	0.8
(Mathur et al., 2015)	AutG	7.93	7.87	NR	6	5.53	5.2	NR
(Naqvi et al., 2017)	SG	5.9	NR	NR	6	2.9	NR	NR
	SG	5.9	NR	NR	9	3	NR	NR
(Nevins et al., 2005)	SG	8.3	8.8	0.5	6	NR	5.3	NR
(Okuda et al., 2005)	SG	7.9	8.8	0.8	12	4.2	6.8	2.6
(Ozdemir & Okte, 2012)	SG	7	7	0	6	4	6	2
(Pavani et al., 2021)	SG	5.6	NR	NR	6	2.15	NR	NR

(Piemontese et al., 2008)	AllG	7.4	8.1	0.8	12	4.7	5.9	1.2
(Saini et al., 2011)	SG	6.35	4.5	NR	6	3.3	2.8	NR
	SG	6.35	4.5	NR	9	4.15	3.4	NR
(Scheyer et al., 2002)	XG	7.1	7.5	0.4	6	3.2	3.8	0.6
(Sculean, Barbé, et al., 2002)	SG	8.07	9.78	1.64	12	3.85	6.71	2.92
(Sculean, Chiantella, et al., 2002)	XG	9.7	10.1	0.5	12	3.2	5.2	2
(Sezgin et al., 2017)	XG	7.07	7.73	0.66	6	2.86	4.46	1.6
(Shah et al., 2015)	AllG	6.97	NR	NR	6	3.4	NR	NR
(Shukla et al., 2016)	SG	6.95	7.4	NR	9	2.9	2.4	NR

Legend. AllG: allograft; AutG: autogenous graft; CAL: clinical attachment level; NR: Not reported; PD: pocket depth; REC: recession depth; SG: synthetic graft; XG: xenograft.

Supplementary Table 16. Clinical outcomes of infrabony defects treated with papilla preservation techniques alone.

Publication, reference	PPT	Baseline			Time (months)	Follow-up		
		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)
(Ahmad et al., 2019)	M-MIST	7.06	6.81	-0.25	6	2.88	2.81	-0.19
(Aslan et al., 2020)	EPPT	9.26	11.4	2.13	12	3.06	5.56	2.5
(Cortellini & Tonetti, 2011)	M-MIST	7.5	9.6	2.1	12	3.1	5.5	2.4
(De Leonardis & Paolantonio, 2013)	MPPT or SPPT	8.7	9.3	0.6	12	6.11	7.76	1.64
	MPPT or SPPT	8.7	9.3	0.6	24	6.33	7.94	1.61
(Fileto Mazzonetto et al., 2021)	SPPT	6.7	7.5	0.8	6	4.9	6.5	1.6
	SPPT	6.7	7.5	0.8	12	4.8	5.9	1.1
(Francetti et al., 2004)	SPPT	6.71	8.29	1.58	12	4.14	6	1.86
	SPPT	6.71	8.29	1.58	24	3.71	5.57	1.86
(Francetti et al., 2005)	SPPT	7.11	7.98	0.87	12	4.11	6.02	1.91
	SPPT	7.11	7.98	0.87	24	3.6	5.47	1.87
(Grusovin & Esposito, 2009)	MPPT or SPPT	7.2	8.5	1.3	12	3.3	5.2	1.9
(Mishra et al., 2013)	M-MIST	7.64	7.64	0	6	3.82	4.37	0.55
(Ribeiro et al., 2011)	MIST	7.12	NR	NR	6	3.57	NR	NR
(Tonetti et al., 2002) and (Tonetti et al., 2004)	MPPT or SPPT	7.7	9.1	1.4	12	4.4	6.6	2.2
(Wachtel et al., 2003)	MPPT	6.5	7.2	0.7	6	4.3	5.1	0.9
	MPPT	6.5	7.2	0.7	12	4.4	5.5	1

(Zucchelli et al., 2002)	SPPT	8.9	10	1.1	12	4.4	7.4	3.1

Legend. CAL: clinical attachment level; EPPT: entire papilla preservation technique; M-MIST: modified-minimally invasive surgical technique; MIST: minimally invasive surgical technique; MPPT: modified papilla preservation technique; NR: Not reported; PD: pocket depth; PPT: papilla preservation technique; REC: recession depth; SPPT: simplified papilla preservation technique.

Supplementary Table 17. Clinical outcomes of infrabony defects treated with access flap surgery alone.

Publication, reference	Flap approach	Baseline			Time (months)	Follow-up		
		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)		Mean PD (mm)	Mean CAL (mm)	Mean REC (mm)
(Agrali Ö et al., 2016)	OFD	7.6	12.1	4.7	6	3.2	10.5	7.3
(Ajwani et al., 2015)	OFD	6.2	9.2	3.4	9	4.6	7.9	3.7
(Atchuta et al., 2020)	OFD	5.21	5.81	0.6	6	2.85	3.19	0.34
(Bahammam & Attia, 2021)	OFD	6.6	NR	NR	6	5.7	NR	NR
(Bhutda & Deo, 2013)	OFD	6.82	7.32	0.5	12	4.6	5.27	0.67
	OFD	6.82	7.32	0.5	60	4.9	5.72	0.82
(Bokan et al., 2006)	OFD	9.8	10.2	1.1	12	6	8.1	2.6
(Camargo et al., 2001)	OFD	7.16	NR	NR	6	5.52	NR	NR
(Camargo et al., 2005)	OFD	5.12	NR	NR	6	7.96	NR	NR
(Chambrone et al., 2007)	OFD	6.08	6.74	0.66	6	2	3.16	1.16
(Chambrone et al., 2010)	OFD	6.13	7.76	1.63	12	2.64	4.88	2.24
	OFD	6.13	7.76	1.63	24	2.85	5.17	2.32
(Chandradas et al., 2016)	OFD	8.33	8.83	0.5	9	5.33	7.16	1.83
(Froum et al., 2001)	OFD	7.32	NR	NR	12	5.08	NR	NR
(Heijl et al., 1997)	MWF	7.8	9.3	1.5	8	5.1	7.6	2.5
	MWF	7.8	9.3	1.5	16	5.1	7.5	2.4
	MWF	7.8	9.3	1.5	36	5.2	7.1	1.9
(Jalaluddin et al., 2017)	OFD	7.3	11.7	4.4	6	3.4	8.2	4.8

(Kanoriya et al., 2016)	OFD	8.03	7.56	1.6	9	5.16	4.53	1.66
(Kitamura et al., 2016)	MWF	6.2	NR	NR	24	3.5	4.4	0.9
	MWF	6.2	NR	NR	36	3.4	4.2	0.8
(Martande et al., 2016)	OFD	7.9	9.6	1.7	9	5.13	6.9	1.77
(Okuda et al., 2000)	OFD	6.22	6.83	0.61	12	4	6	1.83
(Patel et al., 2017)	OFD	7.9	6.8	NR	6	6.8	5.9	NR
	OFD	7.9	6.8	NR	9	6	5.3	NR
	OFD	7.9	6.8	NR	12	5.5	4.7	NR
(Pavani et al., 2021)	OFD	5.6	NR	NR	6	2.3	NR	NR
(Pham, 2021)	OFD	7.4	8.1	0.7	6	4.83	5.87	1.04
	OFD	7.4	8.1	0.7	12	4.03	4.73	0.7
(Pontoriero et al., 1999)	OFD	7.5	8.5	1	12	3.8	6.7	1.9
	OFD	7.5	8.4	0.8	12	4.3	6.8	1.7
	OFD	7.2	8.2	1	12	3.9	6.4	1.5
	OFD	7.9	8.6	0.7	12	4.4	6.8	1.7
(Pradeep et al., 2012)	OFD	7.76	6.26	NR	9	4.8	3.43	NR
(Pradeep et al., 2015)	OFD	8.77	10.4	1.63	9	5.76	7.46	1.7
(Pradeep et al., 2016)	OFD	7.87	5.63	NR	9	4.77	3.17	NR
(Pradeep et al., 2017)	OFD	8.03	6.57	NR	9	5.07	3.9	NR
(Ragghianti Zangrando et al., 2014)	OFD	NR	NR	NR	24	NR	NR	NR
(Rösing et al., 2005)	OFD	7.38	NR	NR	6	3.36	NR	NR
	OFD	7.38	NR	NR	12	2.99	NR	NR

(Sculean, Windisch, et al., 2001)	OFD	8.6	10.1	1.8	12	4.9	8.4	3.5
(Sculean et al., 2004)	OFD	8.2	9.7	1.5	60	5.5	8.4	3.2
(Sculean et al., 2008)	OFD	8.6	10.4	1.8	120	5.1	8.6	3.5
(Sharma & Pradeep, 2011)	OFD	8.08	6.23	0.92	9	4.87	3.46	1.56
(Silvestri et al., 2000)	MWF	7.7	8.7	1	12	6.3	7.5	1.2
(Thorat et al., 2011)	OFD	6.75	6.94	0.19	9	3.19	4.69	1.5
(Thorat et al., 2017)	OFD	7.83	7.17	0.47	12	6.33	6.83	0.67
(Zetterström et al., 1997)	OFD	7.4	8.7	1.3	8	3.7	6.1	2.4
	OFD	7.5	9	1.5	36	4.3	6.8	2.5

Legend. CAL: clinical attachment level; MWF: modified Widman flap; NR: Not reported; OFD: open flap debridement; PD: pocket depth; REC: recession depth.

Supplementary Table 18. Two-dimensional radiographic outcomes of infrabony defects treated with autologous blood-derived products (ABPs).

Publication, reference	Treatment	Carrier	Time (months)	Mean Rx bone fill (%)	Mean linear Rx bone gain (mm)
(Agarwal & Gupta, 2014)	ABP + BG	AllG	12	NR	3.02
(Agarwal et al., 2016)	ABP + BG	AllG	12	NR	3.5
(Agrawal et al., 2017)	ABP	No	6	NR	NR
	ABP + BG	SG	6	NR	NR
(Ahmad et al., 2019)	ABP	No	6	37.4	1.1
(Ajwani et al., 2015)	ABP	No	9	NR	2.6
(Atchuta et al., 2020)	ABP + BG	AllG	6	NR	5.35
(Bahammam & Attia, 2021)	ABP	No	6	NR	2.2
	ABP + BG	SG	6	NR	2.31
(Bansal & Bharti, 2013)	ABP + BG	AllG	6	NR	2.13
(Chadwick et al., 2016)	ABP	No	6	NR	1.1
(Chandradas et al., 2016)	ABP	No	9	49.6	2.55
	ABP + BG	XG	9	61.53	3.47
(Chatterjee et al., 2017)	ABP	No	9	73.09	NR
	ABP	No	9	76.45	NR
(Elbehwashy et al., 2021)	ABP	No	6	48.3	2.29
	ABP	No	6	40.62	1.63
(Galav et al., 2016)	ABP	No	9	NR	1.16
(Gamal, Abdel Ghaffar, et al., 2016)	ABP + BG	XG	6	NR	1.5
	ABP + BG	XG	6	NR	1.5

	ABP + BG	XG	9	NR	2.1
	ABP + BG	XG	9	NR	1.7
(Hazari et al., 2021)	ABP + BG	XG	6	NR	2.05
(Ilgenli et al., 2007)	ABP	No	6	NR	0.6
	ABP + BG	AllG	6	NR	3.8
(Jalaluddin et al., 2017)	ABP	No	6	38.4	0.8
(Jalaluddin et al., 2018)	ABP	No	6	41.7	0.8
(Kanoriya et al., 2016)	ABP	No	9	46	2.42
(Lekovic et al., 2012)	ABP	No	6	NR	2.21
	ABP + BG	XG	6	NR	4.06
(Markou et al., 2009)	ABP	No	6	41.29	NR
	ABP + BG	AllG	6	45.42	NR
(Martande et al., 2016)	ABP	No	9	47.91	2.46
(Mathur et al., 2015)	ABP	No	6	NR	2.93
Okuda et al., 2005)	ABP + BG	SG	12	NR	3.5
(Ozdemir & Okte, 2012)	ABP + BG	SG	6	28.6	0.8
(Paolantonio et al., 2020)	ABP + BG	AutG	12	NR	2.93
(Patel et al., 2017)	ABP	No	6	32.9	NR
	ABP	No	9	42	NR
	ABP	No	12	45.2	NR
(Pham, 2021)	ABP	No	6	26.45	2.37
	ABP	No	12	45.25	4.13
(Piemontese et al., 2008)	ABP + BG	AllG	12	NR	3.3

(Pradeep et al., 2009)	ABP	No	9	43.81	1.96
	ABP + BG	XG	9	58.14	2.89
(Pradeep et al., 2012)	ABP	No	9	55.41	2.8
	ABP	No	9	56.85	2.7
(Pradeep et al., 2015)	ABP	No	9	48	2.53
(Pradeep et al., 2016)	ABP	No	9	NR	3.17
(Pradeep et al., 2017)	ABP	No	9	56.46	3.2
	ABP + BG	SG	9	63.39	3.87
(Saini et al., 2011)	ABP + BG	SG	6	NR	2.4
	ABP + BG	SG	9	NR	3.2
(Sezgin et al., 2017)	ABP + BG	XG	6	NR	2.55
(Sharma & Pradeep, 2011)	ABP	No	9	48.26	2.5
(Thorat et al., 2011)	ABP	No	9	46.92	2.12
(Thorat et al., 2017)	ABP	No	12	46.13	3.09
(Yamamiya et al., 2008)	ABP + BG	SG	12	NR	3.2

Legend. ABP: autologous blood-derived products; AllG: allograft; AutG: autogenous graft; BG: bone graft; NR: not reported; SG: synthetic graft; XG: xenograft.

Supplementary Table 19. Two-dimensional radiographic outcomes of infrabony defects treated with enamel matrix derivative (EMD).

Publication, reference	Treatment	Carrier	Time (months)	Mean Rx bone fill (%)	Mean linear Rx bone gain (mm)
(Agrali Ö et al., 2016)	EMD	No	6	65.98	NR
	EMD + BG	AutG	6	64.56	NR
(Aimetti et al., 2017)	EMD	No	12	NR	3.4
	EMD	No	24	NR	3.8
(Al Machot et al., 2014)	EMD	No	6	NR	1.8
	EMD	No	12	NR	1.6
(Aspriello et al., 2011)	EMD + BG	AllG	12	(Only median reported)	(Only median reported)
(Aydemir Turkal et al., 2016)	EMD	No	6	17.31	1.21
(Bhutda & Deo, 2013)	EMD	No	60	66.66	3.2
(Bratthall et al., 2001)	EMD	No	8	NR	0.8
	EMD	No	8	NR	0.7
	EMD	No	16	NR	1
	EMD	No	16	NR	1
(Cortellini & Tonetti, 2011)	EMD	No	12	71	3.3
	EMD + BG	XG	12	78	3.3
(Crea et al., 2008)	EMD	No	12	49.1	NR
	EMD	No	36	56.9	NR
(De Leonardis & Paolantonio, 2013)	EMD	No	12	NR	2.32
	EMD	No	24	NR	2.61
	EMD + BG	SG	12	NR	3.17
	EMD + BG	SG	24	NR	3.35

(Fickl et al., 2009)	EMD	No	6	NR	1.4
	EMD	No	12	NR	2.5
(Fileto Mazzonetto et al., 2021)	EMD	No	12	NR	1.24
	EMD	No	12	NR	0.84
(Francetti et al., 2004)	EMD	No	12	49.16	2.96
	EMD	No	24	57.44	3.44
(Francetti et al., 2005)	EMD	No	12	53.7	3.09
	EMD	No	24	55.2	3.18
(Grusovin & Esposito, 2009)	EMD	No	12	NR	2.5
(Guida et al., 2007)	EMD	No	12	NR	2.3
	EMD + BG	AutG	12	NR	2.2
(Gurinsky et al., 2004)	EMD	No	6	55.3	2.6
	EMD + BG	AllG	6	74.9	3.7
(Heijl et al., 1997)	EMD	No	8	13	0.9
	EMD	No	16	31	2.2
	EMD	No	36	36	2.6
(Kitamura et al., 2016)	EMD	No	24	16.15	0.96
	EMD	No	36	23.29	1.34
(Kuru et al., 2006)	EMD	No	8	NR	2.15
	EMD + BG	SG	8	NR	2.76
(J. H. Lee et al., 2020)	EMD + BG	XG	6	NR	2
	EMD + BG	XG	12	NR	2.3
	EMD + BG	XG	24	NR	2.5
	EMD	No	6	NR	2.44

(Losada et al., 2017)	EMD	No	12	NR	2.6
	EMD + BG	SG	6	NR	2.33
	EMD + BG	SG	12	NR	2.71
(Meyle et al., 2011)	EMD	No	12	NR	1.49
	EMD + BG	SG	12	NR	2.19
(Ogihara & Tarnow, 2014)	EMD	No	12	NR	3.3
	EMD	No	36	NR	3.26
	EMD + BG	AllG	12	NR	4.23
	EMD + BG	AllG	36	NR	4.19
	EMD + BG	AllG	12	NR	4.26
	EMD + BG	AllG	36	NR	4.29
(Paolantonio et al., 2020)	EMD + BG	AutG	12	NR	2.68
(Ragghianti Zangrando et al., 2014)	EMD	No	24	NR	-0.04
(Ribeiro et al., 2011)	EMD	No	6	NR	1.52
(Rösing et al., 2005)	EMD	No	6	NR	0.33
	EMD	No	12	NR	1.55
(Zetterström et al., 1997)	EMD	No	8	15	1.2
	EMD	No	36	31	2.4
(Zucchelli et al., 2003)	EMD	No	12	NR	4.3
	EMD + BG	XG	12	NR	5.3

Legend. AllG: allograft; AutG: autogenous graft; BG: bone graft; EMD: enamel matrix derivative; NR: not reported; SG: synthetic graft; XG: xenograft.

Supplementary Table 20 Two-dimensional radiographic outcomes of infrabony defects treated with recombinant human platelet-derived growth factor (rhPDGF).

Publication, reference	Bone graft	Time (months)	Mean Rx bone fill (%)	Mean linear Rx bone gain (mm)
(Jayakumar et al., 2011)	SG	6	65.6	3.7
(Kavyamala et al., 2019)	SG	6	73.59	3.28
(J. Y. Lee et al., 2017)	XG	6	NR	5.91
	SG	6	NR	4.16
(Maroo & Murthy, 2014)	SG	6	80.12	3.35
	SG	9	94.3	4.05
(Mishra et al., 2013)	No	6	36.2	1.89
(Nevins et al., 2005)	SG	6	57	2.6
	SG	6	34	1.5
(Nevins et al., 2013)	SG	12	60.5	2.88
	SG	24	68.3	3.32
	SG	12	53.7	2.25
	SG	24	57.3	NR
(Schincaglia et al., 2015)	SG	6	NR	2
(Schincaglia et al., 2015)	SG	6	NR	2.1

Legend. NR: Not reported; SG: synthetic graft; XG: xenograft.

Supplementary Table 21. Two-dimensional radiographic outcomes of infrabony defects treated with bone graft alone or guided tissue regeneration

Publication, reference	Bone graft or Barrier Membrane	Time (months)	Mean Rx bone fill (%)	Mean linear Rx bone gain (mm)
(Agarwal & Gupta, 2014)	AllG	12	NR	2.37
(Agarwal et al., 2016)	AllG	12	NR	2.49
(Al Machot et al., 2014)	SG	6	NR	1.7
	SG	12	NR	1.6
(Atchuta et al., 2020)	AllG	6	NR	5.39
(Bahammam & Attia, 2021)	SG	6	NR	1.49
(Bansal & Bharti, 2013)	AllG	6	NR	1.93
(Chadwick et al., 2016)	AllG	6	NR	1.14
(Galav et al., 2016)	AutG	9	NR	1.79
(Gamal, Abdel Ghaffar, et al., 2016)	XG	6	NR	1.5
	XG	9	NR	1.6
(Hazari et al., 2021)	SG	6	NR	1.95
(Jalaluddin et al., 2018)	SG	6	50	1.9
(Jayakumar et al., 2011)	SG	6	47.5	2.8
(Kavyamala et al., 2019)	SG	6	45.74	2.75
(J. H. Lee et al., 2020)	XG	6	NR	1.5
	XG	12	NR	1.8
	XG	24	NR	2
	SG	6	57.54	2.14

(Maroo & Murthy, 2014)	SG	9	67.99	2.5
(Mathur et al., 2015)	AutG	6	NR	1.76
(Nevins et al., 2005)	SG	6	18	0.9
(Nevins et al., 2013)	SG	12	32.6	1.42
	SG	24	41.5	1.81
(Okuda et al., 2005)	SG	12	NR	2.7
(Ozdemir & Okte, 2012)	SG	6	37	1.1
(Pham, 2021)	CM	6	22.2	2
	CM	12	42.15	3.97
(Piemontese et al., 2008)	AllG	12	NR	2.7
(Saini et al., 2011)	SG	6	NR	2.05
	SG	9	NR	2.5
(Sezgin et al., 2017)	XG	6	NR	1.98

Legend. AllG: allograft; AutG: autogenous graft; CM: collagen (barrier) membrane; NR: not reported; SG: synthetic graft; XG: xenograft.

Supplementary Table 22. Two-dimensional radiographic outcomes of infrabony defects treated with flap surgery alone.

Publication, reference	Flap approach	Time (months)	Mean Rx bone fill (%)	Mean linear Rx bone gain (mm)
Flap surgery with papilla preservation				
(Ahmad et al., 2019)	M-MIST	6	33.89	1.07
(Cortellini & Tonetti, 2011)	M-MIST	12	77	3.5
(De Leonardis & Paolantonio, 2013)	MPPT or SPPT	12	NR	0.13
	MPPT or SPPT	24	NR	0.23
(Fickl et al., 2009)	MPPT	6	NR	0.7
	MPPT	12	NR	1.1
(Fileto Mazzonetto et al., 2021)	SPPT	12	NR	0.92
(Francetti et al., 2004)	SPPT	12	30.14	1.44
	SPPT	24	38.49	1.84
(Francetti et al., 2005)	SPPT	12	35.4	1.86
	SPPT	24	45.7	2.4
(Grusovin & Esposito, 2009)	MPPT or SPPT	12	NR	2.5
(Mishra et al., 2013)	M-MIST	6	35.02	1.85
(Ribeiro et al., 2011)	MIST	6	NR	0.95
Flap surgery without papilla preservation				
(Agrali Ö et al., 2016)	OFD	6	35.31	NR
(Ajwani et al., 2015)	OFD	9	NR	1.3
(Atchuta et al., 2020)	OFD	6	NR	2.58
(Bahammam & Attia, 2021)	OFD	6	NR	1.1

(Bhutda & Deo, 2013)	OFD	60	31.71	1.3
(Chandradas et al., 2016)	OFD	9	24.69	1.21
(Chatterjee et al., 2017)	OFD	9	54.22	NR
(Heijl et al., 1997)	MWF	8	-2	-0.1
	MWF	16	-4	-0.2
	MWF	36	0	0
(Jalaluddin et al., 2017)	OFD	6	27.3	0.8
(Kanoriya et al., 2016)	OFD	9	7.33	0.38
(Kitamura et al., 2016) (part A of the study)	MWF	24	14.26	NR
	MWF	36	21.58	NR
(Kitamura et al., 2016) (part B of the study)	MWF	24	11.7	0.63
	MWF	36	13.3	0.68
(Martande et al., 2016)	OFD	9	5.54	0.27
(Patel et al., 2017)	OFD	6	7.3	NR
	OFD	9	16.4	NR
	OFD	12	21.6	NR
(Pham, 2021)	OFD	6	10.21	1
	OFD	12	23.13	2.23
(Pradeep et al., 2012)	OFD	9	1.56	0.13
(Pradeep et al., 2015)	OFD	9	9.14	0.49
(Pradeep et al., 2016)	OFD	9	NR	1.43
(Pradeep et al., 2017)	OFD	9	15.96	0.93
(Ragghianti Zangrando et al., 2014)	OFD	24	NR	0.7

(Rösing et al., 2005)	OFD	6	NR	1.2
	OFD	12	NR	1.39
(Sharma & Pradeep, 2011)	OFD	9	1.8	0.09
(Thorat et al., 2011)	OFD	9	28.66	1.24
(Thorat et al., 2017)	OFD	12	10.48	1.67
(Zetterström et al., 1997)	OFD	8	4	0.3
	OFD	36	0	0

Legend. M-MIST: modified-minimally invasive surgical technique; MIST: minimally invasive surgical technique; MPPT: modified papilla preservation technique; MWF: modified Widman flap; NR: Not reported; OFD: open flap debridement; SPPT: simplified papilla preservation technique.

Supplementary Table 23. Early wound healing outcomes following treatment of infrabony defects.

Publication, reference	Comparison	Flap approach	Wound healing index	Time (days)	Mean Scores (points)	Conclusions, main remarks
(Al Machot et al., 2014)	EMD vs BG	MPPT	EHI as proposed by Wachtel et al. 2003	7 14	EMD: 1.67 BG: 1.9 EMD: 1.64 BG: 1.68	NSSD between EMD and BG for EHI at 7 and 14 days. After 2 weeks, 63% of the subjects in both groups showed complete flap closure (without a fibrin line in the interproximal area)
(Cortellini & Tonetti, 2011)	EMD + BG vs EMD vs Flap	M-MIST	Evaluation of primary closure	7 14 42	Complete closure 97.8% sites Complete closure 100% sites Complete closure 100% sites	Complete closure in all the sites except one, regardless of the use of EMD or EMD + BG
(Fickl et al., 2009)	EMD vs Flap	MPPT	EHI as proposed by Wachtel et al. 2003	7 14	EMD: 1.77 Flap: 1.77 EMD: 1.37 Flap: 1.17	NSSD between EMD and Flap alone. Complete closure observed in 97% of the Flap alone-treated sites and in 91% of the EMD-treated sites
(Grusovin & Esposito, 2009)	EMD vs Flap	MPPT or SPPT	EHI as proposed by Wachtel et al. 2003	7		NSSD between EMD and Flap alone. Complete closure without fibrin line (EHI 1) in 73.3% of EMD-treated sites and in 86.7% of Flap alone-treated sites
(Harnack et al., 2009)	ABP + BG vs BG	MPPT	EHI as proposed by Wachtel et al. 2003	3 7 14 28	ABP + BG: 3 BG: 3 ABP + BG: 2.75 BG: 2.75 ABP + BG: 2.25 BG: 2.25 ABP + BG: 1 BG: 1	NSSD between ABP + BG and BG
(Jepsen et al., 2008)	EMD + BG vs EMD	MPPT or SPPT	EHI as proposed by Wachtel et al. 2003	7 14	EMD + BG: 2.13 EMD: 1.97 EMD + BG: 1.63 EMD: 1.31	NSSD between EMD + BG and EMD. There was a tendency for less bone fill in defects exhibiting EHI of 3, as opposed to defects with EHI 1 or 2

(J. H. Lee et al., 2020)	EMD + BG vs BG	OFD	Presence of dehiscence, fenestration, swelling, spontaneous bleeding, ulceration	14		NSSD between the two groups. EMD + BG had less cases with dehiscence, fenestration, swelling and spontaneous bleeding, but more cases with ulcerations than EMD alone
(Ozcelik et al., 2008)	EMD + LLLT* vs EMD	OFD	Degrees of swelling and color/redness	7, 30, 60		SSD lower swelling at sites treated with LLLT after 1 week. NSSD for swelling at the other time points and for color
(Schincaglia et al., 2015)	Two different techniques in combination with rhPDGF + BG	SFA vs DFA (MPPT or SPPT)	EHI as proposed by Wachtel et al. 2003	14	SFA: 1.13 DFA (MPPT or SPPT): 3	SSD higher EHI for SFA over DFA. 80% of the sites treated with SFA showed complete flap closure vs 46% for DFA-treated sites
(Tonetti et al., 2004)	EMD vs Flap	MPPT or SPPT	Composite index of healing complication (including lack of primary closure, wound dehiscence, granulation tissue at the wound margin or suppuration)			Complicated healing in 19.2% of control subjects and 21.7% of test subjects. Complicated healing did not affect CAL gain at 1 year.
(Wachtel et al., 2003)	EMD vs Flap	MPPT	EHI as proposed by the Authors	7 14	EMD: 1.85 Flap: 1.65 EMD: 1.39 Flap: 1.19	NSSD between EMD and Flap alone. Complete closure at the 2-week post-op observed in 96% of the Flap alone-treated sites and in 89% of the EMD-treated sites
(Windisch et al., 2021)	Two different techniques in combination with EMD	MIST or M-MIST vs MPPT or SPPT	EHI as proposed by Wachtel et al. 2003	7	MIST or M-MIST: 1.48 MPPT or SPPT: 1.83	SSD favoring MIST or M-MIST over MPPT or SPPT.
(Zucchelli et al., 2002)	EMD vs GTR* vs Flap	SPPT				No wound edge necrosis or flap dehiscence in the EMD and Flap groups.

Legend. ABPs: Autologous-derived blood products; BG: bone graft; CAL: clinical attachment level; DFA: double flap approach; EHI: Early wound-healing index (Wachtel et al., 2003); EMD: enamel matrix derivative; LLLT: low-level laser therapy; M-MIST: modified-minimally invasive surgical technique; MIST: minimally invasive surgical technique; MPPT: modified papilla preservation technique; MWF: modified Widman flap; NSSD: not statistically significant; OFD: open flap debridement; rhPDGF: recombinant human platelet-derived growth factor; SFA: single flap approach; SPPT: simplified papilla preservation technique; SSD: statistically significant; *treatment arm not included in the analysis.

Supplementary Table 24. Bone healing outcomes following periodontal regeneration of infrabony defects assessed with surgical re-entry.

Publication, reference	Intervention	Time of the re-entry (months)	Mean Defect fill (mm)	Mean alveolar crest resorption (mm)
Autologous-derived blood products (ABPs)				
(Camargo et al., 2005)	PRP + GTR	6	5.12*	0.72
	Flap		1.66	1.16
(Demir et al., 2007)	PRP + BG	9	3	0.33
	BG		3.14	0.21
(Galav et al., 2016)	PRF	9	2.4	NR
	BG		3.2	NR
(Harnack et al., 2009)	PRP + BG	6	1.7	NR
	BG		1.68	NR
(Lekovic et al., 2002)	PRP + BG	6	4.82	0.92
	PRP + GTR		4.96	1.23
(Lekovic et al., 2012)	PRF + BG	6	4.06*	0.94
	PRF		2.21	1.06
Enamel matrix derivative (EMD)				
(Camargo et al., 2001)	EMD + BG	6	3.93*	0.38
	Flap		1.08	0.41
(Froum et al., 2001)	EMD	12	3.83*	0.46
	Flap		1.47	1.29*
(Gurinsky et al., 2004)	EMD + BG	6	3.7*	0.1
	EMD		2.6	0.9*
(Hoidal et al., 2008)	EMD + BG	6	1.91	-0.24

	BG		2.33	0.05
(Lekovic et al., 2000)	EMD + BG	6	3.82*	0.42
	EMD		1.33	0.53
(Lekovic et al., 2001)	EMD + BG	6	2.88	0.53
	BG		2.84	0.42
(Scheyer et al., 2002)	EMD + BG	6	3.2	0.6
	BG		3	0.7
(Sculean, Pietruska, et al., 2005)	EMD + BG	NR	NR	NR
	BG		NR	NR
(Velasquez-Plata et al., 2002)	EMD + BG	6 - 8	4*	0.4
	EMD		3.1	0.6

Legend. ABP: autologous blood-derived product; BG: bone graft; EMD: enamel matrix derivative; NR: not reported; PRP: platelet-rich plasma; PRF: platelet-rich fibrin; * statistically significantly higher than the other treatment arm/group.

Supplementary Table 25. Weighted mean defect fill and mean alveolar crest resorption following regeneration of infrabony defects with different techniques evaluated with surgical re-entry.

Intervention	Treatment arms (N)	Sits (N)	Weighted Mean Defect fill (mm)	Weighted Mean alveolar crest resorption (mm)
ABP	2	27	2.28	1.06
ABP + BG	4	75	3.37	0.76
ABP + GTR	2	49	5.05	0.94
EMD	4	124	2.98	0.61
EMD + BG	7	154	3.37	0.29
BG	6	103	2.61	0.36
Flap	3	83	1.42	0.97

Legend. ABP: autologous blood-derived product; BG: bone graft; EMD: enamel matrix derivative. GTR: guided tissue regeneration.

Supplementary Table 26. Patient-reported outcome measures (PROMs) following treatment of infrabony defects

Publication, reference	Comparison	Flap approach	Time (days)	Mean Intensity of Pain (VAS)	Painkiller prescription and Mean Painkillers tablet intake (N)	Other PROMs
(Al Machot et al., 2014)	EMD vs BG	MPPT	14	NR	No medications prescribed	Patients' self - reported postoperative healing events (pain, bleeding, swelling) assessed as "No", "Mild", "Moderate" or "Severe". SSD less bleeding with EMD over BG. NSSD for pain and swelling
(Cortellini & Tonetti, 2011)	EMD + BG vs EMD vs Flap	M-MIST	7	EMD + BG: 1.2 EMD: 1.2 Flap: 1.1 (NSSD)	Ibuprofen 600 mg EMD + BG: 0.5 EMD: 0.3 Flap: 0.4 (NSSD)	None of the subjects reported intra-operative pain.
(Fileto Mazzonetto et al., 2021)	EMD (G1) vs EMD (G2) vs Flap (G3)	SPPT	15	EMD (G1): 1.8 EMD (G2): 0.9 Flap (G3): 1.1 (NSSD)	Painkiller type NR EMD (G1): 1.5 EMD (G2): 1.3 Flap (G3): 0.6 (NSSD)	SSD higher pain during the procedure for flap alone vs EMD SSD higher root hypersensitivity for EMD (G1) and Flap over EMD (G2) NSSD for Edema, hematoma or fever. SSD higher interference with daily activities for flap over EMD
			180	NR	NR	SSD improvement in OHIP-14 for all the groups
(Grusovin & Esposito, 2009)	EMD vs Flap	MPPT or SPPT	360	NR	Nimesulide 100 mg	Satisfaction: 93.3% of subjects in each group was pleased or very pleased with the results. Esthetics: 86.7% of subjects in the Flap group and 73.3% group was pleased or very pleased with the results. 100% of subjects in each group was willing to undergo surgery again (if necessary)
(Jepsen et al., 2008)	EMD + BG vs EMD	MPPT or SPPT	7	NR	NR	Patients' self - reported postoperative healing events (pain, bleeding, swelling) assessed as "No", "Mild", "Moderate" or "Severe". NSSD between the two groups
(J. H. Lee et al., 2020)	EMD + BG vs BG	OFD	14	EMD + BG: 2.9 BG: 4.1 (SSD)	Ibuprofen 200 mg tid	Swelling (VAS): 2.5 for EMD + BG and 3.2 for BG (NSSD). Swelling duration (VAS): 2.4 for EMD + BG and 3.3 for BG (SSD). Pain duration (VAS): 2.6 for EMD + BG and 3.4 for BG (SSD)
(Ozcelik et al., 2008)	EMD + LLLT* vs EMD	OFD	7	SSD less pain in the LLLT group for day 1 and day 2	NR	NR

(Schincaglia et al., 2015)	Two different techniques in combination with rhPDGF + BG	SFA vs DFA (MPPT or SPPT)	14 days	SSD lower for SFA at day 1, 2 and 6	Ibuprofen 600 mg SFA: 2.73 DFA: 8.69 (SSD)	SSD greater dose of painkiller intake in the DFA vs SFA group at day 1 (3.2 vs 1.1) NSSD dose of painkiller intake in the other days
(Tonetti et al., 2004)	EMD vs Flap	MPPT or SPPT	7	EMD: 2.8 Flap: 3.1 (NSSD)	Ibuprofen 600 mg or Acetaminophen 500 mg EMD: 4.3 Flap: 5.3 (NSSD)	Intrasurgical pain (VAS): 2.1 for EMD and 1.8 for Flap (NSSD). Hardship of the surgery (VAS): 2.8 for EMD and 2.3 for Flap (NSSD). Duration of pain (hours): 3.1 for EMD and 2.7 for Flap (NSSD). Interference with daily activities (VAS): 3.6 for EMD and 3.2 for Flap (NSSD).
(Zucchelli et al., 2002)	EMD vs GTR* vs Flap	SPPT	NR	NR	NR	Lower morbidity in the EMD group over the GTR group†

Legend. BG: bone graft; DFA: double flap approach; EMD: enamel matrix derivative; G1: group 1; G2: group 2; G3: group 3; GTR: guided tissue regeneration; M-MIST: modified minimally invasive surgical technique; LLLT: low-level laser therapy; MPPT: modified papilla preservation technique; NR: not reported; NSSD: not statistically significant; rhPDGF: recombinant human platelet-derived growth factor; SFA: single flap approach; SD: statistically significant; SPPT: simplified papilla preservation technique; VAS: visual analogue scale (0-10); *treatment arm not included in the analysis. † Method utilized for the PROM assessment not specified.

REFERENCES

Abu-Ta'a, M. (2016). Adjunctive Systemic Antimicrobial Therapy vs Asepsis in Conjunction with Guided Tissue Regeneration: a Randomized, Controlled Clinical Trial. *Journal of contemporary dental practice, 17*(1), 3-6. doi:10.5005/jp-journals-10024-1794

Agarwal, A., & Gupta, N. D. (2014). Platelet-rich plasma combined with decalcified freeze-dried bone allograft for the treatment of noncontained human intrabony periodontal defects: a randomized controlled split-mouth study. *International journal of periodontics & restorative dentistry, 34*(5), 705-711. doi:10.11607/prd.1766

Agarwal, A., Gupta, N. D., & Jain, A. (2016). Platelet rich fibrin combined with decalcified freeze-dried bone allograft for the treatment of human intrabony periodontal defects: a randomized split mouth clinical trail. *Acta odontologica Scandinavica, 74*(1), 36-43. doi:10.3109/00016357.2015.1035672

Agrali Ö, B., Kuru, B. E., Yarat, A., & Kuru, L. (2016). Evaluation of gingival crevicular fluid transforming growth factor-β1 level after treatment of intrabony periodontal defects with enamel matrix derivatives and autogenous bone graft: A randomized controlled clinical trial. *Niger J Clin Pract, 19*(4), 535-543. doi:10.4103/1119-3077.183306

Agrawal, I., Chandran, S., & Nadig, P. (2017). Comparative Evaluation of the Efficacy of Platelet-rich Fibrin and Calcium Phosphosilicate Putty alone and in Combination in the Treatment of Intrabony Defects: A Randomized Clinical and Radiographic Study. *Contemp Clin Dent, 8*(2), 205-210. doi:10.4103/ccd.ccd_1147_16

Ahmad, N., Tewari, S., Narula, S. C., Sharma, R. K., & Tanwar, N. (2019). Platelet-rich fibrin along with a modified minimally invasive surgical technique for the treatment of intrabony defects: a randomized clinical trial. *J Periodontal Implant Sci, 49*(6), 355-365. doi:10.5051/jpis.2019.49.6.355

Aimetti, M., Ferrarotti, F., Mariani, G. M., & Romano, F. (2017). A novel flapless approach versus minimally invasive surgery in periodontal regeneration with enamel matrix derivative proteins: a 24-month randomized controlled clinical trial. *Clin Oral Investig, 21*(1), 327-337. doi:10.1007/s00784-016-1795-2

Ajwani, H., Shetty, S., Gopalakrishnan, D., Kathariya, R., Kulloli, A., Dolas, R. S., & Pradeep, A. R. (2015). Comparative evaluation of platelet-rich fibrin biomaterial and open flap debridement in the treatment of two and three wall intrabony defects. *J Int Oral Health, 7*(4), 32-37.

Al Machot, E., Hoffmann, T., Lorenz, K., Khalili, I., & Noack, B. (2014). Clinical outcomes after treatment of periodontal intrabony defects with nanocrystalline hydroxyapatite (Ostim) or enamel matrix derivatives (Emdogain): a randomized controlled clinical trial. *Biomed Res Int, 2014*, 786353. doi:10.1155/2014/786353

Alzahrani, A. S. (2017). Gingival Crevicular Fluid Release Profile of Vascular Endothelial Cell Growth Factor and Platelet-Derived Growth Factors-BB Following Minimally Invasive Flap Reflection during Treatment of Intrabony Defects: A Randomized Clinical Trial. *J Int Acad Periodontol, 20*(1), 3-11.

Aslan, S., Buduneli, N., & Cortellini, P. (2020). Clinical outcomes of the entire papilla preservation technique with and without biomaterials in the treatment of isolated intrabony defects: A randomized controlled clinical trial. *J Clin Periodontol, 47*(4), 470-478. doi:10.1111/jcpe.13255

Aspriello, S. D., Ferrante, L., Rubini, C., & Piemontese, M. (2011). Comparative study of DFDBA in combination with enamel matrix derivative versus DFDBA alone for treatment of periodontal intrabony defects at 12 months post-surgery. *Clin Oral Investig, 15*(2), 225-232. doi:10.1007/s00784-009-0369-y

Atchuta, A., Gooty, J., Guntakandla, V., Palakuru, S., Durvasula, S., & Palaparthy, R. (2020). Clinical and radiographic evaluation of platelet-rich fibrin as an adjunct to bone grafting demineralized freeze-dried bone allograft in intrabony defects. *Journal of Indian Society of Periodontology, 24*(1), 60-66. doi:10.4103/jisp.jisp_99_19

Aydemir Turkal, H., Demirer, S., Dolgun, A., & Keceli, H. G. (2016). Evaluation of the adjunctive effect of platelet-rich fibrin to enamel matrix derivative in the treatment of intrabony defects. Six-month results of a randomized, split-mouth, controlled clinical study. *J Clin Periodontol, 43*(11), 955-964. doi:10.1111/jcpe.12598

Bahammam, M. A., & Attia, M. S. (2021). Expression of Vascular Endothelial Growth Factor Using Platelet Rich Fibrin (PRF) and Nanohydroxyapatite (nano-HA) in Treatment of Periodontal Intra-Bony Defects - A Randomized Controlled Trial. *Saudi J Biol Sci, 28*(1), 870-878. doi:10.1016/j.sjbs.2020.11.027

Bajaj, P., Agarwal, E., Rao, N. S., Naik, S. B., Pradeep, A. R., Kalra, N., . . . Kumari, M. (2017). Autologous Platelet-Rich Fibrin in the Treatment of 3-Wall Intrabony Defects in Aggressive Periodontitis: A Randomized Controlled Clinical Trial. *J Periodontol, 88*(11), 1186-1191. doi:10.1902/jop.2017.120661

Bansal, C., & Bharti, V. (2013). Evaluation of efficacy of autologous platelet-rich fibrin with demineralized-freeze dried bone allograft in the treatment of periodontal intrabony defects. *J Indian Soc Periodontol, 17*(3), 361-366. doi:10.4103/0972-124X.115663

Bhutda, G., & Deo, V. (2013). Five years clinical results following treatment of human intra-bony defects with an enamel matrix derivative: a randomized controlled trial. *Acta odontologica Scandinavica, 71*(3-4), 764-770. doi:10.3109/00016357.2012.728245

Bodhare, G. H., Kolte, A. P., Kolte, R. A., & Shirke, P. Y. (2019). Clinical and radiographic evaluation and comparison of bioactive bone alloplast morsels when used alone and in combination with platelet-rich fibrin in the treatment of periodontal intrabony defects-A randomized controlled trial. *J Periodontol, 90*(6), 584-594. doi:10.1002/jper.18-0416

Bokan, I., Bill, J. S., & Schlagenhauf, U. (2006). Primary flap closure combined with Emdogain alone or Emdogain and Cerasorb in the treatment of intra-bony defects. *Journal of clinical periodontology, 33*(12), 885-893. doi:10.1111/j.1600-051X.2006.01010.x

Bratthall, G., Lindberg, P., Havemose-Poulsen, A., Holmstrup, P., Bay, L., Soderholm, G., . . . Skold Bell, H. (2001). Comparison of ready-to-use EMDOGAIN-gel and EMDOGAIN in patients with chronic adult periodontitis. *J Clin Periodontol, 28*(10), 923-929. doi:10.1034/j.1600-051x.2001.028010923.x

Camargo, P. M., Lekovic, V., Weinlaender, M., Vasilic, N., Kenney, E. B., & Madzarevic, M. (2001). The effectiveness of enamel matrix proteins used in combination with bovine porous bone mineral in the treatment of intrabony defects in humans. *Journal of clinical periodontology, 28*(11), 1016-1022. doi:10.1034/j.1600-051x.2001.281105.x

Camargo, P. M., Lekovic, V., Weinlaender, M., Vasilic, N., Madzarevic, M., & Kenney, E. B. (2005). A reentry study on the use of bovine porous bone mineral, GTR, and platelet-rich plasma in the regenerative treatment of intrabony defects in humans. *Int J Periodontics Restorative Dent, 25*(1), 49-59.

Chadwick, J. K., Mills, M. P., & Mealey, B. L. (2016). Clinical and Radiographic Evaluation of Demineralized Freeze-Dried Bone Allograft Versus Platelet-Rich Fibrin for the Treatment of Periodontal Intrabony Defects in Humans. *Journal of Periodontology, 87*(11), 1253-1260. doi:10.1902/jop.2016.160309

Chambrone, D., Pasin, I. M., Chambrone, L., Pannuti, C. M., Conde, M. C., & Lima, L. A. (2010). Treatment of infrabony defects with or without enamel matrix proteins: a 24-month follow-up randomized pilot study. *Quintessence international (Berlin, Germany : 1985), 41*(2), 125-134.

Chambrone, D., Pasin, I. M., Conde, M. C., Panutti, C., Carneiro, S., & Lima, L. A. (2007). Effect of enamel matrix proteins on the treatment of intrabony defects: a split-mouth randomized controlled trial study. *Brazilian oral research, 21*(3), 241-246. doi:10.1590/s1806-83242007000300009

Chandradas, N. D., Ravindra, S., Rangaraju, V. M., Jain, S., & Dasappa, S. (2016). Efficacy of platelet rich fibrin in the treatment of human intrabony defects with or without bone graft: A randomized

controlled trial. *J Int Soc Prev Community Dent, 6*(Suppl 2), S153-159. doi:10.4103/2231-0762.189753

Chatterjee, A., Pradeep, A. R., Garg, V., Yajamanya, S., Ali, M. M., & Priya, V. S. (2017). Treatment of periodontal intrabony defects using autologous platelet-rich fibrin and titanium platelet-rich fibrin: a randomized, clinical, comparative study. *J Investig Clin Dent, 8*(3). doi:10.1111/jicd.12231

Cochran, D. L., Jones, A., Heijl, L., Mellonig, J. T., Schoolfield, J., & King, G. N. (2003). Periodontal regeneration with a combination of enamel matrix proteins and autogenous bone grafting. *J Periodontol, 74*(9), 1269-1281. doi:10.1902/jop.2003.74.9.1269

Corbella, S., Alberti, A., Calciolari, E., Taschieri, S., & Francetti, L. (2019). Enamel matrix derivative for the treatment of partially contained intrabony defects: 12-month results. *Aust Dent J, 64*(1), 27-34. doi:10.1111/adj.12654

Cortellini, P., & Tonetti, M. S. (2011). Clinical and radiographic outcomes of the modified minimally invasive surgical technique with and without regenerative materials: a randomized-controlled trial in intra-bony defects. *Journal of clinical periodontology, 38*(4), 365-373. doi:10.1111/j.1600-051X.2011.01705.x

Crea, A., Dassatti, L., Hoffmann, O., Zafiropoulos, G. G., & Deli, G. (2008). Treatment of intrabony defects using guided tissue regeneration or enamel matrix derivative: a 3-year prospective randomized clinical study. *J Periodontol, 79*(12), 2281-2289. doi:10.1902/jop.2008.080135

De Leonardis, D., & Paolantonio, M. (2013). Enamel matrix derivative, alone or associated with a synthetic bone substitute, in the treatment of 1- to 2-wall periodontal defects. *J Periodontol, 84*(4), 444-455. doi:10.1902/jop.2012.110656

Demir, B., Sengün, D., & Berberoğlu, A. (2007). Clinical evaluation of platelet-rich plasma and bioactive glass in the treatment of intra-bony defects. *Journal of clinical periodontology, 34*(8), 709-715. doi:10.1111/j.1600-051X.2007.01108.x

Dhote, R., Charde, P., Bhongade, M., & Rao, J. (2015). Stem Cells Cultured on Beta Tricalcium Phosphate (β-TCP) in Combination with Recombinant Human Platelet-Derived Growth Factor - BB (rh-PDGF-BB) for the Treatment of Human Infrabony Defects. *Journal of stem cells, 10*(4), 243-254.

Dilsiz, A., Canakci, V., & Aydin, T. (2010). The combined use of Nd: YAG laser and enamel matrix proteins in the treatment of periodontal infrabony defects. *Journal of Periodontology, 81*(10), 1411-1418. doi:10.1902/jop.2010.100031

Döri, F., Arweiler, N., Gera, I., & Sculean, A. (2005). Clinical evaluation of an enamel matrix protein derivative combined with either a natural bone mineral or beta-tricalcium phosphate. *J Periodontol, 76*(12), 2236-2243. doi:10.1902/jop.2005.76.12.2236

Döri, F., Arweiler, N., Húszár, T., Gera, I., Miron, R. J., & Sculean, A. (2013). Five-year results evaluating the effects of platelet-rich plasma on the healing of intrabony defects treated with enamel matrix derivative and natural bone mineral. *J Periodontol, 84*(11), 1546-1555. doi:10.1902/jop.2013.120501

Döri, F., Arweiler, N. B., Szántó, E., Agics, A., Gera, I., & Sculean, A. (2013). Ten-year results following treatment of intrabony defects with an enamel matrix protein derivative combined with either a natural bone mineral or a β-tricalcium phosphate. *J Periodontol, 84*(6), 749-757. doi:10.1902/jop.2012.120238

Döri, F., Huszár, T., Nikolidakis, D., Arweiler, N. B., Gera, I., & Sculean, A. (2007a). Effect of platelet-rich plasma on the healing of intra-bony defects treated with a natural bone mineral and a collagen membrane. *J Clin Periodontol, 34*(3), 254-261. doi:10.1111/j.1600-051X.2006.01044.x

Döri, F., Huszár, T., Nikolidakis, D., Arweiler, N. B., Gera, I., & Sculean, A. (2007b). Effect of platelet-rich plasma on the healing of intrabony defects treated with an anorganic bovine bone mineral and expanded polytetrafluoroethylene membranes. *J Periodontol, 78*(6), 983-990. doi:10.1902/jop.2007.060349

Döri, F., Huszár, T., Nikolidakis, D., Tihanyi, D., Horváth, A., Arweiler, N. B., . . . Sculean, A. (2008). Effect of platelet-rich plasma on the healing of intrabony defects treated with Beta tricalcium phosphate and expanded polytetrafluoroethylene membranes. *J Periodontol, 79*(4), 660-669. doi:10.1902/jop.2008.070473

Döri, F., Kovács, V., Arweiler, N. B., Huszár, T., Gera, I., Nikolidakis, D., & Sculean, A. (2009). Effect of platelet-rich plasma on the healing of intrabony defects treated with an anorganic bovine bone mineral: a pilot study. *J Periodontol, 80*(10), 1599-1605. doi:10.1902/jop.2009.090058

Döri, F., Nikolidakis, D., Húszár, T., Arweiler, N. B., Gera, I., & Sculean, A. (2008). Effect of platelet-rich plasma on the healing of intrabony defects treated with an enamel matrix protein derivative and a natural bone mineral. *J Clin Periodontol, 35*(1), 44-50. doi:10.1111/j.1600-051X.2007.01161.x

Eickholz, P., Rollke, L., Schacher, B., Wohlfeil, M., Dannewitz, B., Kaltschmitt, J., . . . Kim, T. S. (2014). Enamel matrix derivative in propylene glycol alginate for treatment of infrabony defects with or without systemic doxycycline: 12- and 24-month results. *J Periodontol, 85*(5), 669-675. doi:10.1902/jop.2013.130290

Elbehwashy, M. T., Hosny, M. M., Elfana, A., Nawar, A., & Fawzy El-Sayed, K. (2021). Clinical and radiographic effects of ascorbic acid-augmented platelet-rich fibrin versus platelet-rich fibrin alone in intra-osseous defects of stage-III periodontitis patients: a randomized controlled clinical trial. *Clinical oral investigations*. doi:10.1007/s00784-021-03929-1

Elgendy, E. A., & Abo Shady, T. E. (2015). Clinical and radiographic evaluation of nanocrystalline hydroxyapatite with or without platelet-rich fibrin membrane in the treatment of periodontal intrabony defects. *Journal of Indian Society of Periodontology, 19*(1), 61-65.

Fickl, S., Thalmair, T., Kebschull, M., Böhm, S., & Wachtel, H. (2009). Microsurgical access flap in conjunction with enamel matrix derivative for the treatment of intra-bony defects: a controlled clinical trial. *Journal of clinical periodontology, 36*(9), 784-790. doi:10.1111/j.1600-051X.2009.01451.x

Fileto Mazzonetto, A. L., Casarin, R. C. V., Santamaria, M. P., Andere, N., Araújo, C. F., Videira Clima da Silva, R., . . . Sallum, A. W. (2021). Clinical, radiographic, and patient-centered outcomes after use of enamel matrix proteins for the treatment of intrabony defects in patients with aggressive periodontitis: A 12-month multicenter clinical trial. *J Periodontol, 92*(7), 995-1006. doi:10.1002/jper.20-0493

Francetti, L., Del Fabbro, M., Basso, M., Testori, T., & Weinstein, R. (2004). Enamel matrix proteins in the treatment of intra-bony defects. A prospective 24-month clinical trial. *J Clin Periodontol, 31*(1), 52-59. doi:10.1111/j.0303-6979.2004.00437.x

Francetti, L., Trombelli, L., Lombardo, G., Guida, L., Cafiero, C., Roccuzzo, M., . . . Del Fabbro, M. (2005). Evaluation of efficacy of enamel matrix derivative in the treatment of intrabony defects: a 24-month multicenter study. *Int J Periodontics Restorative Dent, 25*(5), 461-473.

Froum, S. J., Weinberg, M. A., Rosenberg, E., & Tarnow, D. (2001). A comparative study utilizing open flap debridement with and without enamel matrix derivative in the treatment of periodontal intrabony defects: a 12-month re-entry study. *Journal of Periodontology, 72*(1), 25-34. doi:10.1902/jop.2001.72.1.25

Galav, S., Chandrashekar, K. T., Mishra, R., Tripathi, V., Agarwal, R., & Galav, A. (2016). Comparative evaluation of platelet-rich fibrin and autogenous bone graft for the treatment of infrabony defects in chronic periodontitis: Clinical, radiological, and surgical reentry. *Indian J Dent Res, 27*(5), 502-507. doi:10.4103/0970-9290.195634

Gamal, A. Y., Abdel Ghaffar, K. A., & Alghezwy, O. A. (2016). Crevicular Fluid Growth Factors Release Profile Following the Use of Platelet-Rich Fibrin and Plasma Rich Growth Factors in Treating Periodontal Intrabony Defects: A Randomized Clinical Trial. *J Periodontol, 87*(6), 654-662. doi:10.1902/jop.2016.150314

Gamal, A. Y., Abdel-Ghaffar, K. A., & Iacono, V. J. (2016). Gingival crevicular fluid vascular endothelial cell growth factor and platelet-derived growth factor-BB release profile following the

use of perforated barrier membranes during treatment of intrabony defects: a randomized clinical trial. *J Periodontal Res, 51*(3), 407-416. doi:10.1111/jre.12321

Ghezzi, C., Ferrantino, L., Bernardini, L., Lencioni, M., & Masiero, S. (2016). Minimally Invasive Surgical Technique in Periodontal Regeneration: a Randomized Controlled Clinical Trial Pilot Study. *International journal of periodontics & restorative dentistry, 36*(4), 475-482. doi:10.11607/prd.2550

Grusovin, M. G., & Esposito, M. (2009). The efficacy of enamel matrix derivative (Emdogain) for the treatment of deep infrabony periodontal defects: a placebo-controlled randomised clinical trial. *European journal of oral implantology, 2*(1), 43-54.

Guida, L., Annunziata, M., Belardo, S., Farina, R., Scabbia, A., & Trombelli, L. (2007). Effect of autogenous cortical bone particulate in conjunction with enamel matrix derivative in the treatment of periodontal intraosseous defects. *Journal of Periodontology, 78*(2), 231-238. doi:10.1902/jop.2007.060142

Gupta, S. J., Jhingran, R., Gupta, V., Bains, V. K., Madan, R., & Rizvi, I. (2014). Efficacy of platelet-rich fibrin vs. enamel matrix derivative in the treatment of periodontal intrabony defects: a clinical and cone beam computed tomography study. *J Int Acad Periodontol, 16*(3), 86-96.

Gurinsky, B. S., Mills, M. P., & Mellonig, J. T. (2004). Clinical evaluation of demineralized freeze-dried bone allograft and enamel matrix derivative versus enamel matrix derivative alone for the treatment of periodontal osseous defects in humans. *Journal of Periodontology, 75*(10), 1309-1318. doi:10.1902/jop.2004.75.10.1309

Hanna, R., Trejo, P. M., & Weltman, R. L. (2004). Treatment of intrabony defects with bovine-derived xenograft alone and in combination with platelet-rich plasma: a randomized clinical trial. *Journal of Periodontology, 75*(12), 1668-1677. doi:10.1902/jop.2004.75.12.1668

Harnack, L., Boedeker, R. H., Kurtulus, I., Boehm, S., Gonzales, J., & Meyle, J. (2009). Use of platelet-rich plasma in periodontal surgery--a prospective randomised double blind clinical trial. *Clin Oral Investig, 13*(2), 179-187. doi:10.1007/s00784-008-0223-7

Hassan, K. S., Alagl, A. S., & Abdel-Hady, A. (2012). Torus mandibularis bone chips combined with platelet rich plasma gel for treatment of intrabony osseous defects: clinical and radiographic evaluation. *Int J Oral Maxillofac Surg, 41*(12), 1519-1526. doi:10.1016/j.ijom.2012.02.009

Hazari, V., Choudhary, A., Mishra, R., Chandrashekar, K. T., Trivedi, A., & Pathak, P. K. (2021). Clinical and Radiographic Analysis of Novabone Putty with Platelet-Rich Fibrin in the Treatment of Periodontal Intrabony Defects: A Randomized Control Trial. *Contemp Clin Dent, 12*(2), 150-156. doi:10.4103/ccd.ccd_101_20

Heijl, L., Heden, G., Svärdström, G., & Ostgren, A. (1997). Enamel matrix derivative (EMDOGAIN) in the treatment of intrabony periodontal defects. *Journal of clinical periodontology, 24*(9 Pt 2), 705-714. doi:10.1111/j.1600-051x.1997.tb00253.x

Higgins, J. P., Altman, D. G., Gotzsche, P. C., Juni, P., Moher, D., Oxman, A. D., . . . Cochrane Statistical Methods, G. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ, 343*, d5928. doi:10.1136/bmj.d5928

Hoffmann, T., Al-Machot, E., Meyle, J., Jervøe-Storm, P. M., & Jepsen, S. (2016). Three-year results following regenerative periodontal surgery of advanced intrabony defects with enamel matrix derivative alone or combined with a synthetic bone graft. *Clin Oral Investig, 20*(2), 357-364. doi:10.1007/s00784-015-1522-4

Hoidal, M. J., Grimard, B. A., Mills, M. P., Schoolfield, J. D., Mellonig, J. T., & Mealey, B. L. (2008). Clinical evaluation of demineralized freeze-dried bone allograft with and without enamel matrix derivative for the treatment of periodontal osseous defects in humans. *J Periodontol, 79*(12), 2273-2280. doi:10.1902/jop.2008.080259

Howell, T. H., Fiorellini, J. P., Paquette, D. W., Offenbacher, S., Giannobile, W. V., & Lynch, S. E. (1997). A phase I/II clinical trial to evaluate a combination of recombinant human platelet-derived growth factor-BB and recombinant human insulin-like growth factor-I in patients with periodontal disease. *J Periodontol, 68*(12), 1186-1193. doi:10.1902/jop.1997.68.12.1186

Ilgenli, T., Dundar, N., & Kal, B. I. (2007). Demineralized freeze-dried bone allograft and platelet-rich plasma vs platelet-rich plasma alone in infrabony defects: a clinical and radiographic evaluation. *Clin Oral Investig, 11*(1), 51-59. doi:10.1007/s00784-006-0083-y

Iorio Siciliano, V., Andreuccetti, G., Siciliano, A. I., Blasi, A., Sculean, A., & Salvi, G. E. (2011). Clinical outcomes after treatment of non-contained intrabony defects with enamel matrix derivative or guided tissue regeneration: a 12-month randomized controlled clinical trial. *J Periodontol, 82*(1), 62-71. doi:10.1902/jop.2010.100144

Iorio-Siciliano, V., Andreuccetti, G., Blasi, A., Matarasso, M., Sculean, A., & Salvi, G. E. (2014). Clinical outcomes following regenerative therapy of non-contained intrabony defects using a deproteinized bovine bone mineral combined with either enamel matrix derivative or collagen membrane. *J Periodontol, 85*(10), 1342-1350. doi:10.1902/jop.2014.130420

Iorio-Siciliano, V., Blasi, A., Stratul, S. I., Ramaglia, L., Octavia, V., Salvi, G. E., & Sculean, A. (2021). Healing of periodontal suprabony defects following treatment with open flap debridement with or without an enamel matrix derivative: a randomized controlled clinical study. *Clinical oral investigations, 25*(3), 1019-1027. doi:10.1007/s00784-020-03392-4

Jalaluddin, M., Mahesh, J., Mahesh, R., Jayanti, I., Faizuddin, M., Kripal, K., & Nazeer, N. (2018). Effectiveness of Platelet Rich Plasma and Bone Graft in the Treatment of Intrabony Defects: A Clinico-radiographic Study. *Open Dent J, 12*, 133-154. doi:10.2174/1874210601812010133

Jalaluddin, M., Singh, D. K., Jayanti, I., Kulkarni, P., Faizuddin, M., & Tarannum, F. (2017). Use of Platelet Rich Plasma in the Management of Periodontal Intra-Osseous Defects: A Clinical Study. *J Int Soc Prev Community Dent, 7*(2), 105-115. doi:10.4103/jispcd.JISPCD_28_17

Jayakumar, A., Rajababu, P., Rohini, S., Butchibabu, K., Naveen, A., Reddy, P. K., . . . Pavan Kumar, S. (2011). Multi-centre, randomized clinical trial on the efficacy and safety of recombinant human platelet-derived growth factor with β-tricalcium phosphate in human intra-osseous periodontal defects. *Journal of clinical periodontology, 38*(2), 163-172. doi:10.1111/j.1600-051X.2010.01639.x

Jepsen, S., Topoll, H., Rengers, H., Heinz, B., Teich, M., Hoffmann, T., . . . Jervøe-Storm, P. M. (2008). Clinical outcomes after treatment of intra-bony defects with an EMD/synthetic bone graft or EMD alone: a multicentre randomized-controlled clinical trial. *J Clin Periodontol, 35*(5), 420-428. doi:10.1111/j.1600-051X.2008.01217.x

Joshi, A. A., Padhye, A. M., & Gupta, H. S. (2019). Platelet derived growth factor-BB levels in gingival crevicular fluid of localized intrabony defect sites treated with platelet rich fibrin membrane or collagen membrane containing recombinant human platelet derived growth factor-BB: A randomized clinical and biochemical study. *J Periodontol, 90*(7), 701-708. doi:10.1002/jper.18-0496

Kanoriya, D., Pradeep, A. R., Singhal, S., Garg, V., & Guruprasad, C. N. (2016). Synergistic Approach Using Platelet-Rich Fibrin and 1% Alendronate for Intrabony Defect Treatment in Chronic Periodontitis: a Randomized Clinical Trial. *Journal of Periodontology, 87*(12), 1427-1435. doi:10.1902/jop.2016.150698

Kaushick, B. T., Jayakumar, N. D., Padmalatha, O., & Varghese, S. (2011). Treatment of human periodontal infrabony defects with hydroxyapatite + β tricalcium phosphate bone graft alone and in combination with platelet rich plasma: a randomized clinical trial. *Indian J Dent Res, 22*(4), 505-510. doi:10.4103/0970-9290.90278

Kavyamala, D., G, N. V. S., Dwarakanath, C. D., & Anudeep, M. (2019). Evaluation of the Efficacy of a 1:1 Mixture of beta-TCP and rhPDGF-BB in the Surgical Management of Two- and Three-Wall Intraosseous Defects: A Prospective Clinical Trial. *Int J Periodontics Restorative Dent, 39*(1), 107-113. doi:10.11607/prd.3829

Keles, G. C., Cetinkaya, B. O., Albayrak, D., Koprulu, H., & Acikgoz, G. (2006). Comparison of platelet pellet and bioactive glass in periodontal regenerative therapy. *Acta Odontol Scand, 64*(6), 327-333. doi:10.1080/00016350600758651

Khosropanah, H., Shahidi, S., Basri, A., & Houshyar, M. (2015). Treatment of Intrabony Defects by DFDBA Alone or in Combination with PRP: A Split-Mouth Randomized Clinical and Three-Dimensional Radiographic Trial. *J Dent (Tehran), 12*(10), 764-773.

Kitamura, M., Akamatsu, M., Kawanami, M., Furuichi, Y., Fujii, T., Mori, M., . . . Murakami, S. (2016). Randomized Placebo-Controlled and Controlled Non-Inferiority Phase III Trials Comparing Trafermin, a Recombinant Human Fibroblast Growth Factor 2, and Enamel Matrix Derivative in Periodontal Regeneration in Intrabony Defects. *J Bone Miner Res, 31*(4), 806-814. doi:10.1002/jbmr.2738

Kizildağ, A., Çiçek, Y., Arabaci, T., & Köse, O. (2018). The effect of leukocyte-platelet-rich fibrin on bone morphogenetic protein-2 and insulin-like growth factor-1 levels in patients with chronic periodontitis: a randomized split mouth clinical trail. *Growth factors (Chur, Switzerland), 36*(5-6), 239-245. doi:10.1080/08977194.2018.1551217

Kuru, B., Yilmaz, S., Argin, K., & Noyan, U. (2006). Enamel matrix derivative alone or in combination with a bioactive glass in wide intrabony defects. *Clinical oral investigations, 10*(3), 227-234. doi:10.1007/s00784-006-0052-5

Lee, J. H., Kim, D. H., & Jeong, S. N. (2020). Adjunctive use of enamel matrix derivatives to porcine-derived xenograft for the treatment of one-wall intrabony defects: Two-year longitudinal results of a randomized controlled clinical trial. *J Periodontol, 91*(7), 880-889. doi:10.1002/jper.19-0432

Lee, J. Y., Na, H. J., Kim, H. M., Lee, S. C., Lee, J. Y., Chung, C. P., . . . Park, Y. J. (2017). Comparative Study of rhPDGF-BB Plus Equine-Derived Bone Matrix Versus rhPDGF-BB Plus β-TCP in the Treatment of Periodontal Defects. *International journal of periodontics & restorative dentistry, 37*(6), 825-832. doi:10.11607/prd.3401

Leknes, K. N., Andersen, K. M., Bøe, O. E., Skavland, R. J., & Albandar, J. M. (2009). Enamel matrix derivative versus bioactive ceramic filler in the treatment of intrabony defects: 12-month results. *J Periodontol, 80*(2), 219-227. doi:10.1902/jop.2009.080236

Lekovic, V., Camargo, P. M., Weinlaender, M., Nedic, M., Aleksic, Z., & Kenney, E. B. (2000). A comparison between enamel matrix proteins used alone or in combination with bovine porous bone mineral in the treatment of intrabony periodontal defects in humans. *J Periodontol, 71*(7), 1110-1116. doi:10.1902/jop.2000.71.7.1110

Lekovic, V., Camargo, P. M., Weinlaender, M., Vasilic, N., Djordjevic, M., & Kenney, E. B. (2001). The use of bovine porous bone mineral in combination with enamel matrix proteins or with an autologous fibrinogen/fibronectin system in the treatment of intrabony periodontal defects in humans. *Journal of Periodontology, 72*(9), 1157-1163. doi:10.1902/jop.2000.72.9.1157

Lekovic, V., Camargo, P. M., Weinlaender, M., Vasilic, N., & Kenney, E. B. (2002). Comparison of platelet-rich plasma, bovine porous bone mineral, and guided tissue regeneration versus platelet-rich plasma and bovine porous bone mineral in the treatment of intrabony defects: a reentry study. *J Periodontol, 73*(2), 198-205. doi:10.1902/jop.2002.73.2.198

Lekovic, V., Milinkovic, I., Aleksic, Z., Jankovic, S., Stankovic, P., Kenney, E. B., & Camargo, P. M. (2012). Platelet-rich fibrin and bovine porous bone mineral vs. platelet-rich fibrin in the treatment of intrabony periodontal defects. *J Periodontal Res, 47*(4), 409-417. doi:10.1111/j.1600-0765.2011.01446.x

Liu, K., Huang, Z., Chen, Z., Han, B., & Ouyang, X. (2021). Treatment of periodontal intrabony defects using bovine porous bone mineral and guided tissue regeneration with/without platelet-rich fibrin: a randomized controlled clinical trial. *J Periodontol*. doi:10.1002/jper.20-0860

Losada, M., González, R., Garcia, À., Santos, A., & Nart, J. (2017). Treatment of Non-Contained Infrabony Defects With Enamel Matrix Derivative Alone or in Combination With Biphasic Calcium Phosphate Bone Graft: a 12-Month Randomized Controlled Clinical Trial. *Journal of Periodontology, 88*(5), 426-435. doi:10.1902/jop.2016.160459

Markou, N., Pepelassi, E., Vavouraki, H., Stamatakis, H. C., Nikolopoulos, G., Vrotsos, I., & Tsiklakis, K. (2009). Treatment of periodontal endosseous defects with platelet-rich plasma alone or in

combination with demineralized freeze-dried bone allograft: a comparative clinical trial. *J Periodontol, 80*(12), 1911-1919. doi:10.1902/jop.2009.090216

Maroo, S., & Murthy, K. R. (2014). Treatment of periodontal intrabony defects using β-TCP alone or in combination with rhPDGF-BB: a randomized controlled clinical and radiographic study. *Int J Periodontics Restorative Dent, 34*(6), 841-847. doi:10.11607/prd.2030

Martande, S. S., Kumari, M., Pradeep, A. R., Singh, S. P., Suke, D. K., & Guruprasad, C. N. (2016). Platelet-Rich Fibrin Combined With 1.2% Atorvastatin for Treatment of Intrabony Defects in Chronic Periodontitis: A Randomized Controlled Clinical Trial. *J Periodontol, 87*(9), 1039-1046. doi:10.1902/jop.2016.150306

Mathur, A., Bains, V. K., Gupta, V., Jhingran, R., & Singh, G. P. (2015). Evaluation of intrabony defects treated with platelet-rich fibrin or autogenous bone graft: A comparative analysis. *Eur J Dent, 9*(1), 100-108. doi:10.4103/1305-7456.149653

Meyle, J., Hoffmann, T., Topoll, H., Heinz, B., Al-Machot, E., Jervøe-Storm, P. M., . . . Jepsen, S. (2011). A multi-centre randomized controlled clinical trial on the treatment of intra-bony defects with enamel matrix derivatives/synthetic bone graft or enamel matrix derivatives alone: results after 12 months. *J Clin Periodontol, 38*(7), 652-660. doi:10.1111/j.1600-051X.2011.01726.x

Minabe, M., Kodama, T., Kogou, T., Takeuchi, K., Fushimi, H., Sugiyama, T., & Mitarai, E. (2002). A comparative study of combined treatment with a collagen membrane and enamel matrix proteins for the regeneration of intraosseous defects. *Int J Periodontics Restorative Dent, 22*(6), 595-605.

Mishra, A., Avula, H., Pathakota, K. R., & Avula, J. (2013). Efficacy of modified minimally invasive surgical technique in the treatment of human intrabony defects with or without use of rhPDGF-BB gel: a randomized controlled trial. *Journal of clinical periodontology, 40*(2), 172-179. doi:10.1111/jcpe.12030

Moreno Rodriguez, J. A., & Ortiz Ruiz, A. J. (2021). Apical approach in periodontal reconstructive surgery with enamel matrix derivate and enamel matrix derivate plus bone substitutes: a randomized, controlled clinical trial. *Clin Oral Investig*. doi:10.1007/s00784-021-04256-1

Naqvi, A., Gopalakrishnan, D., Bhasin, M. T., Sharma, N., Haider, K., & Martande, S. (2017). Comparative Evaluation of Bioactive Glass Putty and Platelet Rich Fibrin in the Treatment of Human Periodontal Intrabony Defects: A Randomized Control Trial. *J Clin Diagn Res, 11*(7), Zc09-zc13. doi:10.7860/jcdr/2017/23831.10149

Nevins, M., Giannobile, W. V., McGuire, M. K., Kao, R. T., Mellonig, J. T., Hinrichs, J. E., . . . Lynch, S. E. (2005). Platelet-derived growth factor stimulates bone fill and rate of attachment level gain: results of a large multicenter randomized controlled trial. *J Periodontol, 76*(12), 2205-2215. doi:10.1902/jop.2005.76.12.2205

Nevins, M., Kao, R. T., McGuire, M. K., McClain, P. K., Hinrichs, J. E., McAllister, B. S., . . . et al. (2013). Platelet-derived growth factor promotes periodontal regeneration in localized osseous defects: 36-month extension results from a randomized, controlled, double-masked clinical trial. *Journal of Periodontology, 84*(4), 456-464. doi:10.1902/jop.2012.120141

Nibali, L., Sultan, D., Arena, C., Pelekos, G., Lin, G. H., & Tonetti, M. (2021). Periodontal infrabony defects: Systematic review of healing by defect morphology following regenerative surgery. *J Clin Periodontol, 48*(1), 100-113. doi:10.1111/jcpe.13381

Ogihara, S., & Tarnow, D. P. (2014). Efficacy of enamel matrix derivative with freeze-dried bone allograft or demineralized freeze-dried bone allograft in intrabony defects: a randomized trial. *J Periodontol, 85*(10), 1351-1360. doi:10.1902/jop.2014.130520

Ogihara, S., & Wang, H. L. (2010). Periodontal regeneration with or without limited orthodontics for the treatment of 2- or 3-wall infrabony defects. *Journal of Periodontology, 81*(12), 1734-1742. doi:10.1902/jop.2010.100127

Okuda, K., Momose, M., Miyazaki, A., Murata, M., Yokoyama, S., Yonezawa, Y., . . . Yoshie, H. (2000). Enamel matrix derivative in the treatment of human intrabony osseous defects. *J Periodontol, 71*(12), 1821-1828. doi:10.1902/jop.2000.71.12.1821

Okuda, K., Tai, H., Tanabe, K., Suzuki, H., Sato, T., Kawase, T., . . . Yoshiex, H. (2005). Platelet-rich plasma combined with a porous hydroxyapatite graft for the treatment of intrabony periodontal defects in humans: a comparative controlled clinical study. *J Periodontol, 76*(6), 890-898. doi:10.1902/jop.2005.76.6.890

Ouyang, X. Y., & Qiao, J. (2006). Effect of platelet-rich plasma in the treatment of periodontal intrabony defects in humans. *Chin Med J (Engl), 119*(18), 1511-1521.

Ozcelik, O., Cenk Haytac, M., & Seydaoglu, G. (2008). Enamel matrix derivative and low-level laser therapy in the treatment of intra-bony defects: a randomized placebo-controlled clinical trial. *J Clin Periodontol, 35*(2), 147-156. doi:10.1111/j.1600-051X.2007.01176.x

Ozdemir, B., & Okte, E. (2012). Treatment of intrabony defects with beta-tricalciumphosphate alone and in combination with platelet-rich plasma. *J Biomed Mater Res B Appl Biomater, 100*(4), 976-983. doi:10.1002/jbm.b.32660

Panda, S., Sankari, M., Satpathy, A., Jayakumar, D., Mozzati, M., Mortellaro, C., . . . Del Fabbro, M. (2016). Adjunctive Effect of Autologus Platelet-Rich Fibrin to Barrier Membrane in the Treatment of Periodontal Intrabony Defects. *J Craniofac Surg, 27*(3), 691-696. doi:10.1097/scs.0000000000002524

Paolantonio, M., Di Tullio, M., Giraudi, M., Romano, L., Secondi, L., Paolantonio, G., . . . Femminella, B. (2020). Periodontal regeneration by leukocyte and platelet-rich fibrin with autogenous bone graft versus enamel matrix derivative with autogenous bone graft in the treatment of periodontal intrabony defects: A randomized non-inferiority trial. *J Periodontol, 91*(12), 1595-1608. doi:10.1002/jper.19-0533

Parashis, A., Andronikaki-Faldami, A., & Tsiklakis, K. (2004). Clinical and radiographic comparison of three regenerative procedures in the treatment of intrabony defects. *International journal of periodontics & restorative dentistry, 24*(1), 81-90.

Patel, G. K., Gaekwad, S. S., Gujjari, S. K., & S, C. V. (2017). Platelet-Rich Fibrin in Regeneration of Intrabony Defects: A Randomized Controlled Trial. *J Periodontol, 88*(11), 1192-1199. doi:10.1902/jop.2017.130710

Pavani, M. P., Reddy, K., Reddy, B. H., Biraggari, S. K., Babu, C. H. C., & Chavan, V. (2021). Evaluation of platelet-rich fibrin and tricalcium phosphate bone graft in bone fill of intrabony defects using cone-beam computed tomography: A randomized clinical trial. *J Indian Soc Periodontol, 25*(2), 138-143. doi:10.4103/jisp.jisp_621_19

Pham, T. A. V. (2021). INTRABONY DEFECT TREATMENT WITH PLATELET-RICH FIBRIN, GUIDED TISSUE REGENERATION AND OPEN-FLAP DEBRIDEMENT: A RANDOMIZED CONTROLLED TRIAL. *J Evid Based Dent Pract, 21*(3), 101545. doi:10.1016/j.jebdp.2021.101545

Piemontese, M., Aspriello, S. D., Rubini, C., Ferrante, L., & Procaccini, M. (2008). Treatment of periodontal intrabony defects with demineralized freeze-dried bone allograft in combination with platelet-rich plasma: a comparative clinical trial. *J Periodontol, 79*(5), 802-810. doi:10.1902/jop.2008.070436

Pietruska, M., Pietruski, J., Nagy, K., Brecx, M., Arweiler, N. B., & Sculean, A. (2012). Four-year results following treatment of intrabony periodontal defects with an enamel matrix derivative alone or combined with a biphasic calcium phosphate. *Clin Oral Investig, 16*(4), 1191-1197. doi:10.1007/s00784-011-0611-2

Pilloni, A., Rojas, M. A., Marini, L., Russo, P., Shirakata, Y., Sculean, A., & Iacono, R. (2021). Healing of intrabony defects following regenerative surgery by means of single-flap approach in conjunction with either hyaluronic acid or an enamel matrix derivative: a 24-month randomized controlled clinical trial. *Clin Oral Investig, 25*(8), 5095-5107. doi:10.1007/s00784-021-03822-x

Pontoriero, R., Wennstrom, J., & Lindhe, J. (1999). The use of barrier membranes and enamel matrix proteins in the treatment of angular bone defects. A prospective controlled clinical study. *J Clin Periodontol, 26*(12), 833-840. doi:10.1034/j.1600-051x.1997.00833.x

Pradeep, A. R., Bajaj, P., Rao, N. S., Agarwal, E., & Naik, S. B. (2017). Platelet-Rich Fibrin Combined With a Porous Hydroxyapatite Graft for the Treatment of 3-Wall Intrabony Defects in Chronic Periodontitis: A Randomized Controlled Clinical Trial. *J Periodontol, 88*(12), 1288-1296. doi:10.1902/jop.2012.110722

Pradeep, A. R., Garg, V., Kanoriya, D., & Singhal, S. (2016). Platelet-Rich Fibrin With 1.2% Rosuvastatin for Treatment of Intrabony Defects in Chronic Periodontitis: A Randomized Controlled Clinical Trial. *J Periodontol, 87*(12), 1468-1473. doi:10.1902/jop.2016.160015

Pradeep, A. R., Nagpal, K., Karvekar, S., Patnaik, K., Naik, S. B., & Guruprasad, C. N. (2015). Platelet-rich fibrin with 1% metformin for the treatment of intrabony defects in chronic periodontitis: a randomized controlled clinical trial. *J Periodontol, 86*(6), 729-737. doi:10.1902/jop.2015.140646

Pradeep, A. R., Rao, N. S., Agarwal, E., Bajaj, P., Kumari, M., & Naik, S. B. (2012). Comparative evaluation of autologous platelet-rich fibrin and platelet-rich plasma in the treatment of 3-wall intrabony defects in chronic periodontitis: a randomized controlled clinical trial. *J Periodontol, 83*(12), 1499-1507. doi:10.1902/jop.2012.110705

Pradeep, A. R., Shetty, S. K., Garg, G., & Pai, S. (2009). Clinical effectiveness of autologous platelet-rich plasma and Peptide-enhanced bone graft in the treatment of intrabony defects. *J Periodontol, 80*(1), 62-71. doi:10.1902/jop.2009.080214

Ragghianti Zangrando, M. S., Chambrone, D., Pasin, I. M., Conde, M. C., Pannuti, C. M., & de Lima, L. A. (2014). Two-year randomized clinical trial of enamel matrix derivative treated infrabony defects: radiographic analysis. *BMC Oral Health, 14*, 149. doi:10.1186/1472-6831-14-149

Ravi, S., Malaiappan, S., Varghese, S., Jayakumar, N. D., & Prakasam, G. (2017). Additive Effect of Plasma Rich in Growth Factors With Guided Tissue Regeneration in Treatment of Intrabony Defects in Patients With Chronic Periodontitis: A Split-Mouth Randomized Controlled Clinical Trial. *J Periodontol, 88*(9), 839-845. doi:10.1902/jop.2017.160824

Ribeiro, F. V., Casarin, R. C., Júnior, F. H., Sallum, E. A., & Casati, M. Z. (2011). The role of enamel matrix derivative protein in minimally invasive surgery in treating intrabony defects in single-rooted teeth: a randomized clinical trial. *J Periodontol, 82*(4), 522-532. doi:10.1902/jop.2010.100454

Ridgway, H. K., Mellonig, J. T., & Cochran, D. L. (2008). Human histologic and clinical evaluation of recombinant human platelet-derived growth factor and beta-tricalcium phosphate for the treatment of periodontal intraosseous defects. *Int J Periodontics Restorative Dent, 28*(2), 171-179.

Rodrigues, S. V., Acharya, A. B., & Thakur, S. L. (2011). An evaluation of platelet-rich plasma without thrombin activation with or without anorganic bone mineral in the treatment of human periodontal intrabony defects. *Platelets, 22*(5), 353-360. doi:10.3109/09537104.2011.552135

Rollke, L., Schacher, B., Wohlfeil, M., Kim, T. S., Kaltschmitt, J., Krieger, J., . . . Eickholz, P. (2012). Regenerative therapy of infrabony defects with or without systemic doxycycline. A randomized placebo-controlled trial. *J Clin Periodontol, 39*(5), 448-456. doi:10.1111/j.1600-051X.2012.01861.x

Rosamma Joseph, V., Raghunath, A., & Sharma, N. (2012). Clinical effectiveness of autologous platelet rich fibrin in the management of infrabony periodontal defects. *Singapore Dent J, 33*(1), 5-12. doi:10.1016/j.sdj.2012.10.003

Rösing, C. K., Aass, A. M., Mavropoulos, A., & Gjermo, P. (2005). Clinical and radiographic effects of enamel matrix derivative in the treatment of intrabony periodontal defects: a 12-month longitudinal placebo-controlled clinical trial in adult periodontitis patients. *Journal of Periodontology, 76*(1), 129-133. doi:10.1902/jop.2005.76.1.129

Saini, N., Sikri, P., & Gupta, H. (2011). Evaluation of the relative efficacy of autologous platelet-rich plasma in combination with β-tricalcium phosphate alloplast versus an alloplast alone in the treatment of human periodontal infrabony defects: a clinical and radiological study. *Indian journal of dental research, 22*(1), 107-115. doi:10.4103/0970-9290.80008

Sanz, M., Tonetti, M. S., Zabalegui, I., Sicilia, A., Blanco, J., Rebelo, H., . . . Suvan, J. E. (2004). Treatment of intrabony defects with enamel matrix proteins or barrier membranes: results from a multicenter practice-based clinical trial. *J Periodontol, 75*(5), 726-733. doi:10.1902/jop.2004.75.5.726

Scheyer, E. T., Velasquez-Plata, D., Brunsvold, M. A., Lasho, D. J., & Mellonig, J. T. (2002). A clinical comparison of a bovine-derived xenograft used alone and in combination with enamel matrix derivative for the treatment of periodontal osseous defects in humans. *J Periodontol, 73*(4), 423-432. doi:10.1902/jop.2002.73.4.423

Schincaglia, G. P., Hebert, E., Farina, R., Simonelli, A., & Trombelli, L. (2015). Single versus double flap approach in periodontal regenerative treatment. *J Clin Periodontol, 42*(6), 557-566. doi:10.1111/jcpe.12409

Schwarz, F., Sculean, A., Georg, T., & Becker, J. (2003). Clinical evaluation of the Er: YAG laser in combination with an enamel matrix protein derivative for the treatment of intrabony periodontal defects: a pilot study. *Journal of clinical periodontology, 30*(11), 975-981. doi:10.1034/j.1600-051x.2003.00412.x

Sculean, A., Barbé, G., Chiantella, G. C., Arweiler, N. B., Berakdar, M., & Brecx, M. (2002). Clinical evaluation of an enamel matrix protein derivative combined with a bioactive glass for the treatment of intrabony periodontal defects in humans. *J Periodontol, 73*(4), 401-408. doi:10.1902/jop.2002.73.4.401

Sculean, A., Berakdar, M., Donos, N., Auschill, T. M., & Arweiler, N. B. (2003). The effect of postsurgical administration of a selective cyclo-oxygenase-2 inhibitor on the healing of intrabony defects following treatment with enamel matrix proteins. *Clin Oral Investig, 7*(2), 108-112. doi:10.1007/s00784-003-0200-0

Sculean, A., Berakdar, M., Willershausen, B., Arweiler, N. B., Becker, J., & Schwarz, F. (2006). Effect of EDTA root conditioning on the healing of intrabony defects treated with an enamel matrix protein derivative. *J Periodontol, 77*(7), 1167-1172. doi:10.1902/jop.2006.050300

Sculean, A., Blaes, A., Arweiler, N., Reich, E., Donos, N., & Brecx, M. (2001). The effect of postsurgical antibiotics on the healing of intrabony defects following treatment with enamel matrix proteins. *J Periodontol, 72*(2), 190-195. doi:10.1902/jop.2001.72.2.190

Sculean, A., Chiantella, G. C., Windisch, P., Gera, I., & Reich, E. (2002). Clinical evaluation of an enamel matrix protein derivative (Emdogain) combined with a bovine-derived xenograft (Bio-Oss) for the treatment of intrabony periodontal defects in humans. *Int J Periodontics Restorative Dent, 22*(3), 259-267.

Sculean, A., Donos, N., Blaes, A., Lauermann, M., Reich, E., & Brecx, M. (1999). Comparison of enamel matrix proteins and bioabsorbable membranes in the treatment of intrabony periodontal defects. A split-mouth study. *Journal of Periodontology, 70*(3), 255-262. doi:10.1902/jop.1999.70.3.255

Sculean, A., Donos, N., Miliauskaite, A., Arweiler, N., & Brecx, M. (2001). Treatment of intrabony defects with enamel matrix proteins or bioabsorbable membranes. A 4-year follow-up split-mouth study. *J Periodontol, 72*(12), 1695-1701. doi:10.1902/jop.2001.72.12.1695

Sculean, A., Donos, N., Schwarz, F., Becker, J., Brecx, M., & Arweiler, N. B. (2004). Five-year results following treatment of intrabony defects with enamel matrix proteins and guided tissue regeneration. *J Clin Periodontol, 31*(7), 545-549. doi:10.1111/j.1600-051X.2004.00518.x

Sculean, A., Donos, N., Windisch, P., Brecx, M., Gera, I., Reich, E., & Karring, T. (1999). Healing of human intrabony defects following treatment with enamel matrix proteins or guided tissue regeneration. *J Periodontal Res, 34*(6), 310-322. doi:10.1111/j.1600-0765.1999.tb02259.x

Sculean, A., Kiss, A., Miliauskaite, A., Schwarz, F., Arweiler, N. B., & Hannig, M. (2008). Ten-year results following treatment of intra-bony defects with enamel matrix proteins and guided tissue regeneration. *Journal of clinical periodontology, 35*(9), 817-824.

Sculean, A., Pietruska, M., Arweiler, N. B., Auschill, T. M., & Nemcovsky, C. (2007). Four-year results of a prospective-controlled clinical study evaluating healing of intra-bony defects following

treatment with an enamel matrix protein derivative alone or combined with a bioactive glass. *J Clin Periodontol, 34*(6), 507-513. doi:10.1111/j.1600-051X.2007.01084.x

Sculean, A., Pietruska, M., Schwarz, F., Willershausen, B., Arweiler, N. B., & Auschill, T. M. (2005). Healing of human intrabony defects following regenerative periodontal therapy with an enamel matrix protein derivative alone or combined with a bioactive glass. A controlled clinical study. *J Clin Periodontol, 32*(1), 111-117. doi:10.1111/j.1600-051X.2004.00635.x

Sculean, A., Schwarz, F., Chiantella, G. C., Donos, N., Arweiler, N. B., Brecx, M., & Becker, J. (2007). Five-year results of a prospective, randomized, controlled study evaluating treatment of intra-bony defects with a natural bone mineral and GTR. *J Clin Periodontol, 34*(1), 72-77. doi:10.1111/j.1600-051X.2006.01007.x

Sculean, A., Schwarz, F., Miliauskaite, A., Kiss, A., Arweiler, N., Becker, J., & Brecx, M. (2006). Treatment of intrabony defects with an enamel matrix protein derivative or bioabsorbable membrane: an 8-year follow-up split-mouth study. *J Periodontol, 77*(11), 1879-1886. doi:10.1902/jop.2006.060002

Sculean, A., Windisch, P., Chiantella, G. C., Donos, N., Brecx, M., & Reich, E. (2001). Treatment of intrabony defects with enamel matrix proteins and guided tissue regeneration. A prospective controlled clinical study. *J Clin Periodontol, 28*(5), 397-403. doi:10.1034/j.1600-051x.2001.028005397.x

Sculean, A., Windisch, P., Keglevich, T., & Gera, I. (2005). 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, 25*(2), 139-147.

Sezgin, Y., Uraz, A., Taner, I. L., & Çulhaoğlu, R. (2017). Effects of platelet-rich fibrin on healing of intra-bony defects treated with anorganic bovine bone mineral. *Braz Oral Res, 31*, e15. doi:10.1590/1807-3107BOR-2017.vol31.0015

Shah, M., Patel, J., Dave, D., & Shah, S. (2015). Comparative evaluation of platelet-rich fibrin with demineralized freeze-dried bone allograft in periodontal infrabony defects: A randomized controlled clinical study. *J Indian Soc Periodontol, 19*(1), 56-60. doi:10.4103/0972-124x.145803

Sharma, A., & Pradeep, A. R. (2011). Treatment of 3-wall intrabony defects in patients with chronic periodontitis with autologous platelet-rich fibrin: a randomized controlled clinical trial. *J Periodontol, 82*(12), 1705-1712. doi:10.1902/jop.2011.110075

Shukla, S., Chug, A., Mahesh, L., & Grover, H. S. (2016). Effect of Addition of Platelet-rich Plasma to Calcium Phosphosilicate Putty on Healing at 9 Months in Periodontal Intrabony Defects. *J Contemp Dent Pract, 17*(3), 230-234. doi:10.5005/jp-journals-10024-1832

Silvestri, M., Ricci, G., Rasperini, G., Sartori, S., & Cattaneo, V. (2000). Comparison of treatments of infrabony defects with enamel matrix derivative, guided tissue regeneration with a nonresorbable membrane and Widman modified flap. A pilot study. *Journal of clinical periodontology, 27*(8), 603-610. doi:10.1034/j.1600-051x.2000.027008603.x

Silvestri, M., Sartori, S., Rasperini, G., Ricci, G., Rota, C., & Cattaneo, V. (2003). Comparison of infrabony defects treated with enamel matrix derivative versus guided tissue regeneration with a nonresorbable membrane. *Journal of clinical periodontology, 30*(5), 386-393. doi:10.1034/j.1600-051x.2003.10146.x

Sipos, P. M., Loos, B. G., Abbas, F., Timmerman, M. F., & van der Velden, U. (2005). The combined use of enamel matrix proteins and a tetracycline-coated expanded polytetrafluoroethylene barrier membrane in the treatment of intra-osseous defects. *Journal of clinical periodontology, 32*(7), 765-772. doi:10.1111/j.1600-051X.2005.00754.x

Suchetha, A., Lakshmi, P., Bhat, D., Mundinamane, D. B., Soorya, K. V., & Bharwani, G. A. (2015). Platelet concentration in platelet concentrates and periodontal regeneration-unscrambling the ambiguity. *Contemp Clin Dent, 6*(4), 510-516. doi:10.4103/0976-237X.169850

Thakare, K., & Deo, V. (2012). Randomized controlled clinical study of rhPDGF-BB + β-TCP versus HA + β-TCP for the treatment of infrabony periodontal defects: clinical and radiographic results. *International journal of periodontics & restorative dentistry, 32*(6), 689-696.

Thorat, M., Baghele, O. N., & S, R. P. (2017). Adjunctive Effect of Autologous Platelet-Rich Fibrin in the Treatment of Intrabony Defects in Localized Aggressive Periodontitis Patients: a Randomized Controlled Split-Mouth Clinical Trial. *International journal of periodontics & restorative dentistry, 37*(6), e302. doi:10.11607/prd.2972

Thorat, M., Pradeep, A. R., & Pallavi, B. (2011). Clinical effect of autologous platelet-rich fibrin in the treatment of intra-bony defects: a controlled clinical trial. *J Clin Periodontol, 38*(10), 925-932. doi:10.1111/j.1600-051X.2011.01760.x

Tonetti, M. S., Fourmousis, I., Suvan, J., Cortellini, P., Brägger, U., & Lang, N. P. (2004). Healing, post-operative morbidity and patient perception of outcomes following regenerative therapy of deep intrabony defects. *J Clin Periodontol, 31*(12), 1092-1098. doi:10.1111/j.1600-051X.2004.00615.x

Tonetti, M. S., Lang, N. P., Cortellini, P., Suvan, J. E., Adriaens, P., Dubravec, D., . . . Wallkamm, B. (2002). Enamel matrix proteins in the regenerative therapy of deep intrabony defects. *J Clin Periodontol, 29*(4), 317-325. doi:10.1034/j.1600-051x.2002.290407.x

Ustaoğlu, G., Uğur Aydin, Z., & Özelçi, F. (2020). Comparison of GTR, T-PRF and open-flap debridement in the treatment of intrabony defects with endo-perio lesions: a randomized controlled trial. *Med Oral Patol Oral Cir Bucal, 25*(1), e117-e123. doi:10.4317/medoral.23231

Vandana, K. L., Shah, K., & Prakash, S. (2004). Clinical and radiographic evaluation of Emdogain as a regenerative material in the treatment of interproximal vertical defects in chronic and aggressive periodontitis patients. *International journal of periodontics & restorative dentistry, 24*(2), 185-191.

Velasquez-Plata, D., Scheyer, E. T., & Mellonig, J. T. (2002). Clinical comparison of an enamel matrix derivative used alone or in combination with a bovine-derived xenograft for the treatment of periodontal osseous defects in humans. *J Periodontol, 73*(4), 433-440. doi:10.1902/jop.2002.73.4.433

Wachtel, H., Schenk, G., Böhm, S., Weng, D., Zuhr, O., & Hürzeler, M. B. (2003). Microsurgical access flap and enamel matrix derivative for the treatment of periodontal intrabony defects: a controlled clinical study. *J Clin Periodontol, 30*(6), 496-504. doi:10.1034/j.1600-051x.2003.00013.x

Windisch, P., Iorio-Siciliano, V., Palkovics, D., Ramaglia, L., Blasi, A., & Sculean, A. (2021). The role of surgical flap design (minimally invasive flap vs. extended flap with papilla preservation) on the healing of intrabony defects treated with an enamel matrix derivative: a 12-month two-center randomized controlled clinical trial. *Clinical oral investigations*. doi:10.1007/s00784-021-04155-5

Windisch, P., Sculean, A., Klein, F., Tóth, V., Gera, I., Reich, E., & Eickholz, P. (2002). Comparison of clinical, radiographic, and histometric measurements following treatment with guided tissue regeneration or enamel matrix proteins in human periodontal defects. *J Periodontol, 73*(4), 409-417. doi:10.1902/jop.2002.73.4.409

Yajamanya, S. R., Chatterjee, A., Hussain, A., Coutinho, A., Das, S., & Subbaiah, S. (2017). Bioactive glass versus autologous platelet-rich fibrin for treating periodontal intrabony defects: A comparative clinical study. *J Indian Soc Periodontol, 21*(1), 32-36. doi:10.4103/0972-124X.201628

Yamamiya, K., Okuda, K., Kawase, T., Hata, K., Wolff, L. F., & Yoshie, H. (2008). Tissue-engineered cultured periosteum used with platelet-rich plasma and hydroxyapatite in treating human osseous defects. *Journal of Periodontology, 79*(5), 811-818. doi:10.1902/jop.2008.070518

Yassibag-Berkman, Z., Tuncer, O., Subasioglu, T., & Kantarci, A. (2007). Combined use of platelet-rich plasma and bone grafting with or without guided tissue regeneration in the treatment of anterior interproximal defects. *J Periodontol, 78*(5), 801-809. doi:10.1902/jop.2007.060318

Yilmaz, S., Cakar, G., Yildirim, B., & Sculean, A. (2010). Healing of two and three wall intrabony periodontal defects following treatment with an enamel matrix derivative combined with autogenous bone. *J Clin Periodontol, 37*(6), 544-550. doi:10.1111/j.1600-051X.2010.01567.x

Zetterström, O., Andersson, C., Eriksson, L., Fredriksson, A., Friskopp, J., Heden, G., . . . et al. (1997). Clinical safety of enamel matrix derivative (EMDOGAIN) in the treatment of periodontal defects. *Journal of clinical periodontology, 24*(9 Pt 2), 697-704. doi:10.1111/j.1600-051x.1997.tb00252.x

Zucchelli, G., Amore, C., Montebugnoli, L., & De Sanctis, M. (2003). Enamel matrix proteins and bovine porous bone mineral in the treatment of intrabony defects: a comparative controlled clinical trial. *Journal of Periodontology, 74*(12), 1725-1735. doi:10.1902/jop.2003.74.12.1725

Zucchelli, G., Bernardi, F., Montebugnoli, L., & De, S. M. (2002). Enamel matrix proteins and guided tissue regeneration with titanium-reinforced expanded polytetrafluoroethylene membranes in the treatment of infrabony defects: a comparative controlled clinical trial. *Journal of Periodontology, 73*(1), 3-12. doi:10.1902/jop.2002.73.1.3