Acellular dermal matrix and subepithelial connective tissue grafts for root coverage: A systematic review

Sarah Ivy Gallagher, Debora Candace Matthews

INTRODUCTION

Gingival recession is the apical migration of the gingival margin, exposing the root surface. It may affect more than half of adults. It is prevalent in a wide range of the population, from those with periodontal disease to those with high standards of oral hygiene. It is associated with increasing age. Several different periodontal plastic surgery procedures were developed to obtain root coverage, with varying degrees of success; these include the free gingival graft, lateral pedicle flap, coronally positioned flap, and guided tissue regeneration. The primary goal of these procedures is esthetic. Secondary goals include decreasing sensitivity, restoring root caries, and facilitating oral hygiene.

In 1985, Langer and Langer introduced the subepithelial connective tissue graft (SCTG) to improve the predictability of root coverage for teeth with gingival recession. The dual blood supply from the graft and the overlying flap is crucial to this goal. SCTG is the gold standard for localized recession defects due to its predictability in increasing the width of keratinized gingiva and in obtaining root coverage.

However, the need for a donor site restricts the applications of SCTG. The size and number of sites that can be treated during one procedure are limited. Tissue thickness in the palate and anatomical limitations, including the size and depth of the palate, affect the amount of donor tissue that can be harvested. Although Langer and Langer argue that the SCTG donor site is closed, and therefore, less uncomfortable than that of a free gingival graft, the donor site still increases morbidity. There is the potential for necrosis, increased postoperative pain, and hemorrhage.

The shortcomings of SCTG have driven the search for allograft alternatives. Some of the allograft substitutes utilized in mucogingival surgery have included sclera, dura mater, and freeze-dried skin grafts. However, the use of these materials did not result in tissue that is identical to that of host tissue.

This review found that an ADMG would be a suitable root coverage substitute for an SCTG when avoidance of the second surgical site is preferred.

Key words: Acellular dermis, connective tissue, gingival recession, meta-analysis, systematic review

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Life Cell, Inc. developed the first acellular dermal matrix material (ADM). ADM was first used in 1992 in the treatment of burns and subsequently in a wide variety of plastic surgeries. The first reported use of ADM in gingival grafting for the purpose of root coverage was in 1994 (Silverstein et al., 1996 cited in [9]). Since then, it has been used in many types of periodontal plastic surgery, including the treatment of alveolar ridge deficiencies, guided tissue regeneration, and the alteration of gingival pigmentation.[10] There are now five main products on the market from different companies.[11] Comparisons between products have been very limited. There are no significant differences in root coverage or other clinical parameters between the most commonly used products, AlloDerm® (BioHorizons, Birmingham, AL) and Puros® Dermis (Zimmer Dental, Carlsbad, CA).[12,13]

In the formation of ADM, a proprietary process strips the epidermis and cells from donated human skin and freeze-dries the remaining basement membrane and extracellular matrix. With the elimination of the cells, any potential source of infection or immunological reaction has also been eliminated, rendering ADM biocompatible.[14] ADM serves as an architectural scaffold to facilitate the migration of and repopulation by the host’s fibroblasts, blood vessels, and epithelial cells.[15] It is subsequently replaced by and fully integrated into the host tissues.[16]

ADM has two different sides. The basal lamina side is compatible with repopulation by epithelial cells. The connective tissue side allows for the migration of fibroblasts and blood vessels.[17] Some authors argue that the orientation of the ADM affects the outcome of periodontal plastic procedures.[7] However, in a randomized controlled trial (RCT) of a root coverage procedure, there were no differences in clinical outcomes when comparing the basal lamina side against the tooth and the connective tissue side against the tooth.[18]

SCTG and ADM graft (ADMG) differ in their healing processes. As SCTG is an autograft, it survives through anastomoses between the graft’s vessels and those of the recipient site.[19] Hence, the flap does not need to completely cover the connective tissue graft. In contrast, the nonvital ADMG relies entirely on the migration of host cells and vessels for nutrition and repair. It depends on direct contact between the graft and the flap, and thus, it requires complete coverage with a tensionless flap. Exposure of ADMG may result in partial failure of the graft.[20] Due to these differences, some authors recommend different surgical techniques for ADMG than those Langer and Langer had proposed for SCTG, including broader flaps, with or without vertical releasing incisions, to allow for a greater blood supply, and thus, greater access to nutrition and cells.[19,21,22]

The resulting mucosa is histologically similar in SCTG and ADMG.[7,14] There is complete incorporation of the graft without any gross inflammatory reaction. Hence, the ADMG does not initiate a foreign body reaction.[15,16] Root resorption and ankylosis do not occur.[19] In both SCTG and ADMG, the interface consists of a long junctional epithelium coronally and connective tissue attachment apically. Núñez et al. found regeneration with newly formed cementum and alveolar bone in both graft types in an experiment on mini-pigs.[15] The abundance of elastin in ADM, which is retained after incorporation of the graft, allows for its histological differentiation from the surrounding tissues because elastin is not a primary component of human gingiva.[7,14]

Although systematic reviews that evaluate the use of ADMG exist, they are wide in scope and include all major root coverage procedures together. The most recent review included literature up to 2013 and included systematic reviews, randomized clinical trials, controlled clinical trials, case series, and case reports.[23] The only meta-analysis that limited itself to ADMG in mucogingival surgery is from 2005.[24] A focused comparison of ADMG to SCTG has not been done to date.

The purpose of this systematic review is to evaluate whether patients with gingival recession will benefit from an ADMG in ways that are comparable to the gold standard of the SCTG.

**MATERIALS AND METHODS**

**Objective**

The following is the systematic review’s focused question in a PICO format:[25] Population (P): Adults with gingival recession on natural dentition; intervention (I): ADMG; comparison (C): SCTG; outcome (O): Primary-root coverage; secondary-attachment level change, keratinized tissue (KT) change, change in esthetics, patient preference for type of procedure, and adverse effects; study type (S): Controlled clinical trials with follow-ups of 6 months or longer. For the primary outcome, root coverage, recession reduction, and change in the recession were considered synonyms.

**Search strategy**

The review was conducted according to PRISMA guidelines.[26] Comprehensive search strategies were developed for PubMed, Excerpta Medica Database (EMBASE), and Cochrane Central Register of Controlled Trials (CENTRAL). The searches were performed for articles published up to and including March 31, 2016, without language restrictions [Table 1]. For PubMed, combinations of Medical Subject Headings (MeSH) terms, key words, and free terms were utilized. The search strategies were as follows:

**Table 1: Search strategy for the Cochrane Central Register of Controlled Trials**

| # | Search term                                      |
|---|-------------------------------------------------|
| #1 | 'gingiva recession':ab, ti                      |
| #2 | 'gingival recession':ab, ti                      |
| #3 | #1 or #4                                        |
| #4 | (acellular near/2 (dermal or dermis)):ti, ab    |
| #5 | allopatch                                       |
| #6 | enduragen                                       |
| #7 | primatrix                                       |
| #8 | surederm                                        |
| #9 | surgimen                                        |
| #10| alloderm                                        |
| #11| perioderm                                       |
| #12| puro dermis                                     |
| #13| oracell                                         |
| #14| #4 or #9 or #12                                 |
| #15| #14 and #5                                      |
PubMed
((((acellular allograft*[tw]) OR acellular dermal matrix[tw]) OR aloderm[tw]) OR puros dermis[tw]) OR perioderm*[tw]) OR oracell[tw]) OR surederm[tw]) OR acellular dermis[tw]) AND (((“gingival recession”[MeSH Terms] OR “gingival recession”[All Fields]) OR gingiva atroph*[tiab]) OR gingival atroph*[tiab]).

EMBASE
‘gingival recession’/exp OR ‘gingiva recession’.ab, ti OR ‘gingival recession’.ab, ti AND (‘acellular dermal matrix’/exp OR ‘allopatch’ OR ‘enduragen’ OR ‘primatrix’ OR ‘surederm’ OR ‘surgimend’ OR ‘acellular dermal matrix’ OR ‘acellular dermis’ OR ‘acellular human dermis’ OR ‘alloderm’/exp OR alloderm: ab, ti OR perioderm: ab, ti OR ‘puros dermis’:ab, ti OR oracell: ab, ti OR surederm: ab, ti).

In addition, the references of any potential clinical trials and prior systematic reviews were examined to identify any relevant studies not found through the database search. The grey literature search was conducted through http://www.opengrey.eu/, http://www.clinicaltrials.gov, and http://webofknowledge.com/.

Screening process
Two reviewers independently screened and selected the included studies. The initial screening involved the analysis of titles and abstracts. The authors then read the full text of all articles that appeared to fit the inclusion criteria or were unclear. Any disagreements were settled through discussion. In the case where the same data were reported in two articles, the study with the longer follow-up was used.

Quality assessment
Both authors independently evaluated the methodological quality of the included studies, following the Cochrane Collaboration’s criteria for assessing the risk of bias.[27] The authors classified each of the studies as low risk of bias, high risk of bias, or unclear in the categories of sequence generation, allocation concealment, binding of participants and personnel, binding of outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias. In terms of binding of participants or personnel, the authors followed the Cochrane Collaboration’s guidelines that a study is at low risk of bias when a lack of binding was unlikely to affect its findings.

Data extraction
For each of the included studies, both authors independently extracted and recorded the data regarding the setting, population, intervention, comparison, outcomes, and study design. In one case of missing data, the author of the included study was contacted through e-mail for clarification.

Statistical analysis
Continuous and dichotomous variables that were reported in more than one study were analyzed using Review Manager (RevMan) software (RevMan [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). The mean differences with 95% confidence intervals were calculated for continuous variables. The level of statistical significance was set at \( P < 0.05 \). The random-effects model for heterogeneity was used. Heterogeneity was evaluated using the \( I^2 \) statistical tests. Publication bias was assessed through graphical analysis of the symmetry of a funnel plot.

RESULTS

Literature search
The search of PubMed, EMBASE, and the CENTRAL generated 158 titles after the elimination of duplicates. Duplicates were eliminated automatically using Covidence software (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org). The search of the grey literature and reading of references did not yield any additional articles. After the initial screening of titles and abstracts, both authors read the full texts of 31 articles. At that point, 14 records were excluded for not meeting the inclusion criteria [Supplementary Table 1]. The remaining 17 studies were included in the meta-analysis [Figure 1].

![Flow diagram of the screening and selection process. n – number of papers](image-url)
Study characteristics
The characteristics of the included studies are presented in Table 2. They were all university-based, randomized controlled trials with sample sizes of 5 to 30. The duration ranged from 6 months to 5 years. Ten studies employed split-mouth designs and six used parallel designs. One used a combination of split-mouth and parallel design.[47] All but one study[49] excluded smokers.

Inclusion criteria for 16 studies were limited to patients with Miller Class I or II gingival recession defects. An additional study was restricted to Miller Class II defects.[43] The ADM

| Study                  | Methods           | Study length | Participants | Surgical methods | Postoperative | Outcome | Notes                        |
|------------------------|------------------|--------------|--------------|------------------|---------------|---------|-----------------------------|
| Aichelmann et al., 2001[41] | RCT, split-mouth design | 6 months    | 22 participants; Miller Class I or II recessions of at least 2 mm | SCTG ADMG (CT side toward tooth); releasing incisions; no root conditioning | NSAID and amoxicillin (dose and duration not provided); dressing; suture removal at 10 days; no CHX | ΔMRC | Supported in part by LifeCell Corporation |
| Barros et al., 2015[39]   | RCT, split-mouth design | 12 months   | 15 participants; Miller Class I or II recessions of at least 3 mm | SCTG ADMG (CT side toward tooth); releasing incisions and extended flap technique; root conditioning with EDTA | NSAID and amoxicillin (500 mg tid for 7 days); no dressing; suture removal at 15 days; 0.12% CHX | ΔMRC | In some cases, more than one tooth was treated in a procedure |
| de Souza et al., 2008[46] | RCT, split-mouth design | 12 months   | 7 participants; Miller Class I or II recessions | SCTG ADMG (CT side toward flap); releasing incisions; root conditioning with tetracycline | Amoxicillin (500 mg tid for 7 days); dressing; suture removal at 15 days; 0.12% CHX | ΔMRC | |
| Gholami et al., 2013[41]  | RCT, split-mouth design | 6 months    | 16 participants; Miller Class I or II recessions | SCTG ADMG (CT side toward flap); double papillary flap; root conditioning with tetracycline | Acetaminophen and amoxicillin (500 mg tid for 7 days); dressing; suture removal at 10 days; 0.12% CHX | ΔMRC | |
| Goyal et al., 2013[42]    | RCT, parallel design | 6 months    | 30 participants; Miller Class II recessions of at least 4 mm | SCTG ADMG (orientation not provided); releasing incisions; no root conditioning | NSAID and doxycycline hyclate (200 mg on 1st day and 100 mg/day for 7 days); dressing; suture removal at 10 days; 0.2% CHX | ΔMRC | |
| Joly et al., 2007[43]     | RCT, split-mouth design | 6 months    | 10 participants; Miller Class I or II recessions of at least 3 mm | SCTG ADMG (orientation not provided); no releasing incisions; conditioned with tetracycline | NSAID and acetaminophen; no dressing; suture removal at 14 days; 0.12% CHX | ΔMRC | |
| Koudale et al., 2012[44]  | RCT, parallel design | 6 months    | 10 participants; Miller Class I or II recessions of at least 2 mm | SCTG ADMG (CT side toward flap); releasing incisions; no root conditioning | NSAID, acetaminophen, and amoxicillin (500 mg tid for 7 days); dressing; suture removal at 14 days; 0.12% CHX | ΔMRC | |
| Moslemi et al., 2011[46]  | RCT, split-mouth design | 5 years     | 15 participants; Miller Class I or II recessions of at least 2 mm | SCTG ADMG (CT side toward tooth); releasing incisions; no root conditioning | NSAID; dressing; suture removal at 10 days; 0.2% CHX | ΔMRC | Follow-up to Haghighati et al., 2009[38] |

Contd...
Table 2: Contd...

| Study                     | Methods | Study length | Participants | Surgical methods                  | Postoperative | Outcome | Notes |
|---------------------------|---------|--------------|--------------|-----------------------------------|---------------|---------|-------|
| Novaes et al., 2001<sup>[46]</sup> | RCT, split-mouth design | 6 months   | 9 participants; Miller Class I or II | SCTG ADMG (CT side toward flap); releasing incisions; root conditioning with tetracycline | Amoxicillin (500 mg tid for 7 days); dressing; suture removal at 15 days; 0.12% CHX | ΔMRC |          |
| Paolantino et al., 2002<sup>[47]</sup> | RCT, parallel design | 12 months  | 30 participants; Miller Class I or II recessions of at least 3 mm | SCTG ADMG (CT side toward tooth); releasing incisions when needed; no root conditioning | Analgesics; no dressing; suture removal at 15 days; 0.12% CHX | ΔMRC | Recession sites on the same side as the participant's dominant hand were chosen for the experimental group. If there was more than one recession, only the worst site was included in study |
| Rahmani and Lades, 2006<sup>[48]</sup> | RCT, split-mouth/parallel design | 6 months   | 14 participants; Miller Class I or II recessions | SCTG ADMG (CT side toward tooth); releasing incisions; no root conditioning | No prescriptions mentioned; dressing; suture removal not specified; 0.2% CHX (starting 2 days prior; the duration of use not specified) | ΔMRC | 6 participants were split-mouth; 8 participants were randomized to SCTG or ADMG groups |
| Mansouri et al., 2010<sup>[49]</sup> | RCT, split-mouth design | 6 months   | 5 participants; Miller Class I or II recessions of at least 2 mm | SCTG ADMG (CT side toward flap); releasing incisions; no root conditioning | NSAID and amoxicillin; dressing; suture removal at 15 days; 0.2% CHX | ΔMRC |          |
| Shori et al., 2013<sup>[50]</sup> | RCT, parallel design | 6 months   | 20 participants; Miller Class I or II recessions of at least 3 mm | SCTG ADMG (CT side toward tooth); releasing incisions; no root conditioning | NSAID, acetaminophen, and amoxicillin (500 mg tid for 7 days); dressing; suture removal not specified; 0.2% CHX | ΔMRC |          |
| Taiyeb Ali et al., 2015<sup>[51]</sup> | RCT, parallel design | 6 months   | 6 participants; Miller Class I or II recessions of at least 3 mm* | SCTG ADMG (CT side toward tooth); releasing incisions; no root conditioning | 0.12% CHX | ΔMRC | No other postoperative details |
| Tal et al., 2002<sup>[52]</sup> | RCT, split-mouth design | 12 months  | 7 participants; Miller Class I or II recessions of at least 4 mm | SCTG ADMG (CT side toward flap); releasing incisions; root conditioning with tetracycline | NSAID and amoxicillin (500 mg tid for 10 days); dressing; suture removal at 10-14 days; 0.2% CHX | ΔMRC |          |
| Thakare et al., 2015<sup>[53]</sup> | RCT, parallel design | 6 months   | 30 participants; Miller Class I or II recessions of at least 2 mm | SCTG ADMG (CT side toward flap); releasing incisions; no root conditioning | NSAID and acetaminophen; dressing; suture removal at 14 days; 0.2% CHX | ΔPRC |          |
| Thomas et al., 2013<sup>[54]</sup> | RCT, split-mouth design | 6 months   | 10 participants; Miller Class I or II recessions | SCTG ADMG (CT side toward tooth); releasing incisions; no root conditioning | NSAID and amoxicillin (500 mg tid for 5 days); dressing; suture removal at 14 days; 0.2% CHX | ΔMRC |          |
product used was AlloDerm®, except in one study where the product was not specified. Of the studies that provided the ADM orientation, the number of studies (eight) where the connective tissue side was placed toward the tooth treated was nearly equal to the number (seven) that placed the basement membrane side toward the tooth. In ten studies, amoxicillin was prescribed, and in one, doxycycline hyclate was prescribed postoperatively. All but one prescribed chlorhexidine rinses post-operatively for varying lengths or time. Six studies used tetracycline as part of the surgical protocol; one used ethylenediaminetetraacetic acid.

Quality assessment
There were methodological flaws in the majority of the included trials; only one study was judged to be at low risk of bias in all seven categories [Table 3]. Many of the RCTs did not adequately blind the outcome assessors. Some trials did not provide the method of randomization. In Paolantonio et al.’s 2002 trial, the recession on the same side as the subject’s dominant hand was chosen as the experimental site. If there was more than one recession, the worst site was chosen. This presents selection bias, preventing the study from being truly randomized.

Mean root coverage
Eleven studies reported the mean root coverage in mm. The mean difference was -0.03 mm (95% confidence interval [CI]: -0.26, 0.21; P = 0.83) in Taijeb’s study, with a 3-month follow-up. The mean difference was 1 mm (95% CI: 0.20, 1.80; P = 0.01) in De Souza’s study reported a 12-month follow-up with a mean difference of -0.15 mm (95% CI: -0.81, 0.5; P = 0.66). For the studies with the 6-month follow-up, the mean difference was -0.11 mm (95% CI: -0.33, 0.11; P = 0.31). The data overall exhibited moderate heterogeneity with an I² value of 40% [Supplementary Figure 1].

Percent root coverage
Eight studies reported the root coverage in terms of percentage. The mean difference was -0.80% (95% CI: -5.98, 4.37; P = 0.76). The data exhibited low heterogeneity with an I² of 30% [Figure 2].

Gain in clinical attachment
Twelve studies reported the gain in clinical attachment in mm. The mean difference was -0.13 mm (95% CI: -0.40, 0.14; P = 0.35). The data exhibited low to moderate heterogeneity with an I² of 34% [Figure 3].

Gain in width of keratinized tissue
Thirteen studies reported the gain in width of KT in mm. The mean difference was -0.43 mm (95% CI: -0.72, -0.15; P = 0.003), in favor of ADMG. However, there was substantial heterogeneity with an I² of 57% [Figure 4].

Other data
Patient-related outcomes, postoperative complications, and adverse events could not be included in the meta-analysis as only one study reported on patient-related outcomes.

Publication bias
The funnel plot for the outcome of root coverage was relatively symmetrical, indicating that there was no evidence of publication bias [Supplementary Figure 2].

DISCUSSION
The results of this systematic review and meta-analysis found that ADMG had a small but statistically significant advantage in terms of KT. At <1 mm, this difference is not clinically significant. There was no statistically significant difference between the treatment modalities in terms of mean root coverage, percent root coverage, and mean gain in clinical attachment. Hence, patients with gingival recession will benefit from an ADMG in ways that are comparable to the gold standard of SCTG.

In contrast to this review’s findings, Chambrone et al.’s 2008 systematic review found SCTG to be superior in reducing gingival recession. Although their later 2010 systematic review

### Table 3: Risk of bias of included studies

| Sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessors | Incomplete outcome data | Selective outcome reporting | Other sources of bias |
|---------------------|------------------------|---------------------------------------|------------------------------|-------------------------|----------------------------|----------------------|
| Aichelmann-Reidy et al., 2001 | L | L | L | L | U | L | U |
| Barros et al., 2015 | L | L | L | L | L | U | L |
| De Souza et al., 2008 | L | L | L | L | H | L | U |
| Gholami et al., 2013 | U | U | U | H | L | L | L |
| Goyal et al., 2014 | H | H | H | H | L | L | L |
| Joly et al., 2007 | L | L | L | H | L | L | U |
| Koudale et al., 2012 | L | L | L | L | H | L | U |
| Moslemi et al., 2011 | L | U | L | L | U | L | L |
| Novaes et al., 2001 | U | U | H | L | L | L | U |
| Paolantonio et al., 2002 | H | H | L | H | U | L | H |
| Rahmani and Lades 2006 | L | L | L | L | H | L | U |
| Sadat Mansouri et al., 2010 | L | L | L | H | L | U | L |
| Shori et al., 2013 | L | L | L | H | L | L | U |
| Taijeb Ali et al., 2015 | L | L | L | H | U | L | L |
| Tal et al., 2002 | U | L | L | L | L | L | U |
| Thakare et al., 2015 | L | L | L | H | L | L | L |
| Thomas et al., 2013 | L | L | L | H | U | L | L |

L – Low risk of bias; H – High risk of bias; U – Unclear risk of bias
did not find a statistically significant difference between SCTG and ADMG, they emphasized that this finding was based on a small number of RCTs. Neither review found statistically significant differences in gain in clinical attachment between the treatment modalities. They did not discuss how the two treatment modalities related in terms of KT gains, except to say that they both significantly increased KT. Chambrone et al.’s 2015 systematic review also found similar gains overall for ADMG and SCTG; however that review continued to argue for the superiority of SCTG. Capski et al.’s 2005 meta-analysis did not find differences between the treatment modalities in terms of gingival recession coverage and KT gains; they could not analyze clinical attachment gain. No previous systematic review could make strong comparisons between the SCTG and the ADMG.

Interestingly, our meta-analysis found in favor of ADMG in terms of KT gains. This goes against the findings of five included studies, which found that SCTG had an advantage with this parameter. The remainder of the studies did not find statistically significant differences between the treatment modalities. The finding of this meta-analysis should be tempered by the substantial heterogeneity of the studies. The mechanism by which ADMG could increase KT has not been identified. The keratinizing influence could be primarily from the dermal source of the graft or, more likely, from the migration by host cells with the potential to induce keratinization of the overlying epithelium. Some authors report the keratinization of ADMG takes longer than SCTG. However, this could not be evaluated in this meta-analysis.

There are distinct limitations to the evidence. Each included study was university-based and thus, was conducted under ideal conditions. Only one study had a long-term follow-up. Hence, the applicability to clinical situations is limited. Many of the studies had significant sources of bias; for example, the description of the method of randomization was inadequate in some cases.

Further research of better methodological quality and larger sample sizes would provide better confidence in the results of this review. As there is only one RCT that evaluated relapse of root coverage (and found it to be significant for both treatment modalities), the stability of ADMG needs to be measured with longer-term follow-ups. Additional research particularly into patient-based outcomes, including post-operative discomfort, would also be beneficial as this information should be a major consideration, after efficacy, in the decision-making process. Future studies should more fully report complications, such as ADMG exposure. An area of clinical interest that has not been evaluated is whether ADMG should be avoided with thin gingival tissues to prevent dehiscence.

Based on weak-to-moderate evidence from a systematic review conducted according to PRISMA principles, there appears to be no clinical difference between the two treatment modalities. In conclusion, for patients with gingival recession, for whom the additional cost is not a barrier and who would prefer not to have a second surgical site, an ADMG appears to be comparable to the gold standard of the SCTG.

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**Conflicts of interest**

There are no conflicts of interest.

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### Supplementary Figure 1: Forest plot for mean root coverage (mm)

### Supplementary Table 1: Characteristics of excluded studies

| Study  | Reason for study exclusion |
|--------|----------------------------|
| Chambrone et al., 2008[3] | Review |
| Chambrone et al., 2010[28] | Review |
| Chambrone and Tatakis, 2015[23] | Review |
| Gapski et al., 2005[24] | Wrong outcomes |
| Griffin et al., 2006[39] | Same data as study with a longer follow-up |
| Haghighat et al., 2009[36] | Wrong outcomes |
| Harris, 2000[31] | Wrong outcomes |
| Harris, 2001[32] | Wrong outcomes |
| Harris, 2004[33] | Wrong study design |
| Hirsch et al., 2005[34] | Wrong study design |
| Hofmänner et al., 2012[35] | Wrong study design |
| Mahajan et al., 2007[39] | Wrong study design |
| Novaes and de Barros, 2008[36] | Review |
| Pini-Prato et al., 2014[37] | Review |
| Tatakis et al., 2015[38] | Review |