



ORIGINAL ARTICLE

Periodontists and stem cell-based therapy for alveolar bone regeneration: A national survey

Darnell Kaigler^{1,2} | Jonathan Misch¹ | Abdusalam Alrmali^{1,3}  | Marita R. Inglehart^{1,4}

¹Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, Michigan, USA

²Department of Biomedical Engineering, College of Engineering, University of Michigan, Ann Arbor, Michigan, USA

³Department of Oral Medicine, Oral Pathology, Oral and Maxillofacial Surgery, University of Tripoli School of Dentistry, Tripoli, Libya

⁴Department of Psychology, College of Literature, Science and Arts (LS & A), University of Michigan, Ann Arbor, Michigan, USA

Correspondence

Darnell Kaigler, Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, MI 48109-1078, USA.
Email: dkaigler@umich.edu

Funding information

National Institute of Dental and Craniofacial Research, NIH, Grant/Award Number: R01DE028657; Major Ash Collegiate Professorship Fund

Abstract

Background: Stem cell-based therapy for bone regeneration has received attention in medical settings but has not yet been used in clinical practice for treating alveolar bone defects. The objectives of this study were to explore whether periodontists had heard about this approach, and if so how, how interested they were to learn about it, which attitudes and behavioral intentions they had related to using stem cell-based grafting, and what they would like to know before using this approach.

Methods: Anonymous survey data were collected from 481 members of the American Academy of Periodontology (response rate: 19.41%).

Results: Responses showed 35.3% had heard about stem cell-based therapy, mostly from publications (9.6%) and meetings (8.3%); 76.1% wanted to learn about it through in-person continuing education (CE) courses, 68.6% in online CE courses, and 57.1% from manuals; 73% considered this approach promising; and 54.9% preferred it to traditional approaches. It was important to them that it would result in more bone volume (93%), better bone quality (90.4%), and accelerated healing (83.2%). Also, 60.1% considered it likely/very likely that they would adopt this approach, 54% that patients would prefer it, and 62.1% that it would benefit their practice. When asked what they would like to know about this approach, information about short- and long-term outcomes, cost, and logistical considerations were most frequently named.

Conclusions: These findings provide the basis to develop educational interventions for periodontists about this novel approach and inform future research activities aimed to translate this approach to clinical practice.

KEYWORDS

alveolar bone grafting, bone regeneration, craniofacial bone regeneration, periodontists, stem cells, surveys and questionnaires

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2024 The Authors. *Journal of Periodontology* published by Wiley Periodicals LLC on behalf of American Academy of Periodontology.



1 | INTRODUCTION

In the rapidly evolving field of regenerative medicine, stem cell-based treatments have developed as strategies capable of transforming patient care. These innovative approaches place special emphasis on tissue regeneration and restoration, offering treatments for previously incurable diseases that were merely managed, rather than effectively treated.^{1,2} Employing appropriate cells for regenerating osseous defects in the periodontium and alveolus holds great promise as a potent strategy to foster alveolar tissue regeneration.³ Alveolar bone defects and deficiencies secondary to periodontal disease, tooth extraction, and trauma are very common and can be quite challenging to treat and manage.⁴ Improvements in dental bone materials and technologies have enabled the treatment of severe defects with progressively more predictable results.⁵ Dental implant therapy often requires bone-grafting with an estimated 50% of dental implant therapies requiring grafting before or at the time of implant placement, and approximately 2.2 million bone grafting procedures are being performed each year, with these numbers expected to rise.^{6,7} Further, a 2020 market report indicated that the dental bone graft market is expected to grow from \$450 million in 2020 to \$659 million by 2025.⁸ As more advanced cases are treated, this increase in cases will invariably be accompanied by an increased number of complications, especially for difficult augmentation cases.^{9,10}

Though reconstructive methods for alveolar bone regeneration have evolved over the past 25 years, these approaches still rely heavily upon the use of large autogenous grafts or large quantities of non-vital materials as part of guided bone regenerative procedures.¹¹ Despite being the “gold standard,” autogenous block grafting has been less utilized in recent years due to its invasiveness, technique sensitivity, and limited donor supply.¹² Alternative approaches using allografts (a tissue graft from a donor of the same species that is not genetically identical) and alloplasts (a synthetic material) have become therefore more widely used. Combination therapies such as using bone grafts (BGs) and biologics, or BGs and barrier membranes, have proven to be more effective compared to using single treatments alone.^{13,14} However, the limitation with the use of these grafts is that they are non-vital grafts and require long healing times (i.e., 6–9 months).¹² In addition, there is no consensus about what is the best material for an allograft or alloplast.¹⁵ In clinical settings, there is a need for more biologically based alternatives that yield faster and better clinical outcomes. Stem cell-based therapies could provide a solution to the current clinical limitations when treating large alveolar defects.^{1,16} While other health care disciplines such as orthopedics,¹⁷ plastic surgery,¹⁸

rheumatology,¹⁸ and cardiology¹⁸ have adopted stem-cell-based therapies in their scope of practice, no autologous stem-cell-based products are currently used in dentistry.¹⁹ As of now, over 6,000 clinical trials have been conducted utilizing stem cells. However, globally, only 44 registered clinical trials are focused on addressing oral diseases.¹⁹

Stem cell therapies have been an area of key interest in emerging technologies. We have recently reported the promising results of phase I/II clinical trials utilizing heterogeneous, bone marrow-derived mesenchymal stem cell populations (CD90+ and CD14+ enriched cell populations) for alveolar bone reconstruction. This approach utilizes autologous cell therapy and the results have demonstrated accelerated bone regeneration and better bone quality in the treatment of alveolar bone defects.^{20,21} In other periodontal contexts, the potential of autologous periodontal ligament stem cell transplantation in the repair and regeneration of periodontal intraosseous defects has been demonstrated.²² Additionally, several case reports have shown the potential use of dental pulp stem cells (DPSCs) for the treatment of intra-bony defects.^{23–25} In patients with bone defects resulting from periodontal disease, minimally invasive surgeries were performed and collagen sponges along with autologous or allogeneic DPSCs were applied. These treatments resulted in decreased probing depth, new fiber reinsertion, and new bone formation with minimal adverse effects, suggesting that DPSCs possess regenerative capabilities for periodontal tissues.^{23–25} Despite the promise of stem cell therapies, for clinical adoption of these therapies in dentistry, dental surgeons have to be open and willing to incorporate them within their respective scope of clinical practice.¹⁹ A clear understanding of the rationale and benefits for their use is therefore needed.

Periodontists need to have enough information about this new approach to develop an interest in using it. As this is a matter of crucial importance, the objectives of this study were to explore whether periodontists had heard about this approach, and if so, how they had heard, how interested they were to learn about it, which attitudes and behavioral intentions they had related to using stem cell-based grafting, and what they would like to know before using this approach in the future.

2 | MATERIALS AND METHODS

This study was determined to be exempt from Institutional Review Board (IRB) oversight by the Health Sciences and Behavioral Sciences IRB at the University of Michigan on October 31, 2019 (#HUM00160280) because the respondents answered the survey anonymously. It is survey research and has a cross-sectional study design.

Currently, when a patient has large horizontal and vertical alveolar bone defects, a dental surgeon might use any one of a variety of grafting techniques in efforts to regenerate the bone for dental implant reconstruction. Over the last decade, we have developed a stem cell therapy approach as an alternative to traditional approaches. This stem cell therapy is now being evaluated in clinical trials.

For this new stem cell therapy to regenerate a bone defect:

- You collect a small sample of bone from your patient by making a small incision in the gingiva or mucosa in an edentulous area of the jaw and using a bone scraper, collect a small sample of bone (0.2-0.3 cc) cells.
- This collected sample is sent to a facility that isolates the stem cells and grows them.
- After 2-3 weeks, you receive the stem cells back and place them on a biomaterial to be used as a bone graft to regenerate the bone defect.
- Previous clinical trials have shown accelerated healing and better bone quality using this approach.

FIGURE 1 Information provided at the beginning of the survey about stem cell-based bone grafting.

The respondents were 481 members of the American Academy of Periodontology (AAP) who responded anonymously to a mailed survey by returning it per postal mail to the research team.

The procedure consisted of mailing recruitment letters to 2500 postal addresses provided by the AAP of active members, explaining to these periodontists the purpose of the research and asking them to respond to an enclosed survey and return it to the research team in a provided stamped envelope. Twenty-two envelopes were undeliverable, and 481 responses were returned (response rate: 19.41%).

The survey materials were developed by the authors based on the objectives of the study. A draft was pilot tested with several periodontists and their feedback was considered to create the final version of the survey. The survey began with an explanation of stem cell-based bone grafting (see Figure 1). The first question asked whether the respondents had heard about stem cell bone grafting before. If they had heard about it before, an open-ended follow-up question inquired how they had heard about it. A set of four questions followed inquiring how interested the respondents were in learning more about this approach in continuing education courses, from manuals or in other ways. If they responded that they would like to learn in other ways, a follow-up question asked them to describe these “other ways of learning.” Next, a set of seven attitudinal questions and one behavioral intention question followed. Responses to these questions were made on a 5-point rating scale ranging from 1 = “not at all” to 5 = “very much.” The next question asked about the highest acceptable cost for the respondent when sending small bone

samples to a stem cell facility to grow the stem cells so that they could be used for grafting. After an open-ended question concerning what they would like to know about this new approach, some background questions inquired how long the respondents had practiced as periodontists and what percentage of their practice was dedicated to bone grafting.

For the statistical analysis, the paper-pencil survey responses were entered into an SPSS (IBM SPSS Statistics for Windows, Version 28; IBM Corp., Armonk, NY, USA) data file. Descriptive statistics such as frequency distributions, percentages, and means were computed to provide an overview of the responses to the closed-ended questions. Inferential statistics were used to determine if there were significant relationships between the respondents’ years of practice and percentage of bone grafting in their professional lives and the attitudinal and behavioral responses and their interest in additional information about this approach. Pearson correlation coefficients were computed to explore the relationships between these answers. The significance level was set at $p < 0.001$.

3 | RESULTS

A total of 481 surveys of the 2478 successfully mailed surveys were returned (response rate: 19.41%). Table 1 provides an overview of the respondents’ background and practice characteristics. The number of years practiced as a periodontist ranged from 1 to 46 years (Mean = 17.60 years) and the percentage of their professional activities consisting of bone grafting large horizontal/vertical bone defects ranged



TABLE 1 Overview of periodontists' background characteristics.

Background characteristics	Mean <i>N</i> = 481	SD/Range
Number of years practiced in specialty	Mean = 17.60	SD = 10.343 Range: 1 - 46
Practice characteristics	Frequencies <i>N</i> = 481	Percentages
Practice/employment situation:		
- Solo practice	272	57.3%
- Group practice	162	34.1%
- Academic appointment	24	5.1%
- Military/VA	6	1.3%
- Other	11	2.3%
Location of work place:		
- Rural (<5000 people)	4	0.8%
- Small town/city (5000–24,999)	37	7.8%
- Moderate-sized city (25,000–250,000)	171	36.2%
- Suburb of a large city	94	19.9%
- Large city (>250,000)	167	35.3%
% of practice consisting of bone grafting large horizontal/vertical bone defects	Mean = 23.82%	SD = 19.329 Range: 0%–85%

TABLE 2 Frequencies/percentages of responses concerning previously received information about stem cell-based bone grafting.

Information about stem cell-based bone grafting	Frequencies <i>N</i> = 481	Percentages
Have you heard about this stem cell therapy approach before?	Yes: 170 No: 299	Yes: 35.3% No: 62.2%
How did you hear about this approach? I learned from:	Frequencies <i>N</i> = 481	Percentages
Education at conferences/meetings:		
- AAP/AAOMS meeting	27	5.6%
- At meeting/seminar/conference	23	4.8%
- Continuing education/study club	6	1.3%
<i>Total</i>	56	11.6%
Research:		
- Journal	28	5.8%
- Literature/research/publications	25	5.2%
<i>Total</i>	53	11.0%
Learned in educational setting:		
- Lectures	12	2.5%
- During periodontics residency	13	2.7%
<i>Total</i>	25	5.2%
Heard from others	18	3.7%
Heard about stem cell therapy outside of dentistry	16	3.3%
TOTAL	168	34.9%

Abbreviations: AAOMS, American Association of Oral and Maxillofacial Surgeons; AAP, American Academy of Periodontology.

from 0% to 85% (Mean = 23.82%). Most respondents practiced in a solo practice (57.3%), with about a third (34.1%) practicing in a group practice. The locations of the practice ranged widely from rural areas (0.8%) to moderate sized (36.2%) and large cities (35.3%).

Slightly more than a third of the respondents had heard about stem cell-based bone grafting before (35.3%) (see Table 2). About one in 10 respondents had heard about it at conferences or meetings (11.6%) and through research-related publications (11.0%). When asked how interested


TABLE 3 Responses related to interest in learning about stem cell-based bone grafting.

How interested are you to learn about stem cell-based bone grafting:	1^a	2	3	4	5	Mean SD	Years in practice/ % bone grafting r²
- in an in-person CE course?	2.8%	6.4%	14.7%	28.2%	47.9%	4.12 1.059	0.12 $p < 0.01$ / 0.18 $p < 0.001$
- in an online CE course?	6.5%	5.7%	19.1%	27.9%	40.8%	3.91 1.186	0.03/0.10 $p < 0.05$
- with the help of a manual?	7.4%	12.1%	23.4%	31.0%	26.1%	3.56 1.209	0.07/0.04
- in other ways?	34.0%	7.7%	30.9%	14.9	12.8%	2.64 1.403	0.03/0.12 $p < 0.05$
Open ended answers concerning “Other ways of learning”						Frequency N = 81 of 481	Percentage 16.84%
In person:							
- IP hands on practice/mentoring						15	3.1%
- IP representative						9	1.8%
- IP CE/lectures/seminar/lunch & learn/study club						11	2.3%
- in person							
- IP in office demonstration						1	0.2%
- IP mini residency						4	0.8%
Subtotal:						2	0.4%
Online learning:							
- YouTube/video/DVD						9	1.8%
- webinar/online tutorial/forum						9	1.8%
Subtotal:						18	3.7%
Publications:							
- clinical research-based publication						8	1.7%
- literature based publication						4	0.8%
- peer-reviewed publications						2	0.4%
Subtotal:						14	2.9%
Conference based:							
- AAP annual meeting						5	1.0%
- CE/lecture						2	0.4%
Subtotal:						7	1.5%
Total						81	16.8%

Abbreviations: AAP, American Academy of Periodontology; CE, continuing education; IP, in person.

^aThe answers ranged from 1 = “not at all,” 2 = “a little,” 3 = “somewhat,” 4 = “interested,” to 5 = “very interested.”

they were to learn more about this approach, 76.1% were much/very much interested in learning through an in-person continuing education (CE) course, 68.7% through an online CE course, 57.1% through manuals, and 27.7% were interested to learn in other ways (see Table 3). A total of 8.7% were interested in receiving education by others and 3.7% in web-based learning.

The more years of practice the respondents had, the more they were interested in learning about this topic through in-person CE courses ($r = 0.12$; $p < 0.01$). The higher the percentage of bone grafting procedures they performed in their professional lives, the more they wanted

to learn about stem cell-based bone grafting through in-person CE courses ($r = 0.18$; $p < 0.001$), in online CE courses ($r = 0.10$; $p < 0.05$), and in other ways ($r = 0.12$; $p < 0.05$).

Table 4 provides an overview of the responses concerning the respondents' attitudes towards the use of stem cell-based bone grafting. The majority were positive in their responses concerning how important is it that this approach results in more bone volume (93.1%), in better bone quality (90.3%), and in accelerated healing (83.3%). In addition, 73.1% considered the approach as promising, 62.3% believed that it would be beneficial for their practice


TABLE 4 Responses related to attitudes and behavioral intentions concerning stem cell-based bone grafting.

Attitudes: How important is it that this approach results:	Percentage of responses					Mean SD	Pearson correlations	
	1 ¹	2	3	4	5		Years of practice	% bone grafting
- in more bone volume?	0.6%	1.3%	5.0%	19.3%	73.8%	4.64 0.694	0.01	-0.08
- in better bone quality?	0.8%	1.0%	7.8%	24.5%	65.8%	4.53 0.754	0.07	-0.06
- in accelerated healing?	0.4%	3.6%	12.8	31.2%	52.1%	4.31 0.857	0.11 <i>p</i> < 0.05	0.14 <i>p</i> < 0.01
How promising is this approach?	0.4%	1.5%	25.1%	37.1%	36.0%	4.07 0.839	0.23 <i>p</i> < 0.001	0.09 <i>p</i> < 0.05
How much benefit would it be for your practice to offer this approach?	3.6%	4.6%	29.5%	35.7	26.6%	3.77 1.009	0.18 <i>p</i> < 0.001	0.09
How much would you prefer this approach to the traditional approach?	2.5%	6.1%	36.3%	33.8%	21.3%	3.65 0.964	0.23 <i>p</i> < 0.001	0.13 <i>p</i> < 0.01
How much do you think your patients would prefer this approach?	2.5%	10.7%	32.6%	30.5%	23.6%	3.62 1.037	0.18 <i>p</i> < 0.001	0.06
Behavioral intention	1 ¹	2	3	4	5	Mean SD	<i>r</i> (Years)	<i>r</i> (%)
How likely are you to adopt this approach in the future?	2.7%	5.3%	33.5%	35.9%	22.6%	3.70 0.966	0.22 <i>p</i> < 0.001	0.19 <i>p</i> < 0.001

Note: The answers ranged from 1 = "not at all," 2 = "a little," 3 = "somewhat," 4 = "much," to 5 = "very much."

to offer this approach, and 54.1% that their patients would prefer this approach. The majority (56.5%) responded that they would adopt this approach in the future.

The longer the respondents had practiced as periodontists, the more promising they considered the approach ($r = 0.23$; $p < 0.001$), the more they preferred it to the traditional approach ($r = 0.23$; $p < 0.001$), and the more likely they thought it would be that they would adopt it in the future ($r = 0.22$; $p < 0.001$). The higher the percentage of bone grafting in their professional activities, the more likely they thought it would be to adopt stem cell bone grafting in the future ($r = 0.19$; $p < 0.001$).

In response to the question concerning the highest acceptable cost to for sending small bone samples to a stem cell facility to grow the stem cells for grafting, the answers ranged widely from \$50 to \$5000 (Mean = \$572.22). Fifteen respondents provided responses between \$2000 and \$5000.

Table 5 provides an overview of the open-ended responses to the question of what the respondents would like to know before adopting stem cell-based bone grafting. The most frequently provided answers were outcome-related questions (32%) such as the general success rate (8.2%), the amount of volume (6.7%), and the comparison between the outcomes of this new approach and the traditional approach (5.9%). Clinical considerations

(16.1%) centered around questions concerning complications (5.2%), logistics/techniques (4.4%), and patient-related answers (15.2%). The most common patient-related answers focused on the cost for the patient (14.2%). Research-related responses (14.7%) stressed the need for high-quality research. More than one in 10 respondents raised questions concerning how well it would work (11.5%) and had practice management-related questions (10.8%).

4 | DISCUSSION

The purpose of this research was to explore what periodontists already know or want to know about the potential of a new stem cell-based bone grafting technique and how willing they are to adopt this new approach in the future. One indicator for their level of interest was that nearly one of five recipients of this survey responded. This response rate was more positive than expected based on survey response-related research.^{26,27} A second indicator of interest in this topic was the fact that more than one open-ended response was received from each respondent and that these open-ended responses showed a genuine curiosity concerning this topic. It is also worthwhile to consider that the respondents ranged widely in the years



TABLE 5 Frequencies/percentages of responses concerning what the respondents would like to know before adopting this new approach.

Outcome-related answers	Frequency N = 660	Percentage
General success rate	54	8.2%
Amount of volume	44	6.7%
Compare success to current approach	39	5.9%
Long term stability	26	3.9%
Bone quality of the graft	19	2.9%
Increased bone height	13	2.0%
Outcomes	12	1.8%
Difference in bone quality	4	0.6%
Subtotal	211	32.0%
Clinical considerations		
Complications	34	5.2%
Logistics/techniques	29	4.4%
Safety	14	2.1%
Feasibility	13	2.0%
Clinical considerations	6	0.9%
Post op pain	6	0.9%
Indications/contradictions	2	0.3%
Compatibility with other bone grafts/membranes	1	0.2%
Can a less invasive approach be used?	1	0.2%
Subtotal	106	16.1%
Patient-related concerns		
Cost for patient	94	14.2%
Patient	5	0.8%
Systemic status of patient affect success?	1	0.2%
Subtotal	100	15.2%
Research-related responses		
Research results needed	37	5.6%
Randomized/clinical trials needed	31	4.7%
Case studies/longitudinal studies	15	2.3%
Research	13	2.0%
Sub total	96	14.7%
How well it works		
Healing time	22	3.3%
How well it works	16	2.4%
Predictability	15	2.3%
Side effects	11	1.7%
Challenges/barriers to technology	6	0.9%
Negative outcomes/cancer	4	0.6%
Validity	2	0.3%
Subtotal	76	11.5%
Practice management concerns		
Time involved	28	4.2%
Cost to practice	25	3.8%
Insurance coverage	9	1.4%
Practice management concerns	5	0.8%
Prep time	2	0.3%
Best company/lab to use	2	0.3%
Subtotal	71	10.8%
Total	660	100%



they had practiced as periodontists. This fact is interesting because research on the diffusion of innovation showed that the age of health care professionals can affect the degree of acceptance of technological innovations in the health care field.²⁸ The wide age range of respondents to our study is therefore promising because it could potentially indicate a widespread interest among periodontists. This consideration was also supported by the fact that not only periodontists with a high percentage of their professional activities dedicated to bone grafting responded, but that periodontists with no bone grafting or very low percentages of bone grafting activities participated in this survey.

Given that stem cell-based therapies have been successfully adopted by other health care providers such as orthopedic surgeons and endocrinologists,^{29,30} it was surprising that only about a third of periodontists had heard about this approach before. However, the fact that the absolute majority were interested in learning more about it through in-person and online CE courses as well as with the help of manuals was encouraging. The high interest for in-person education could stem from using advanced grafting techniques and thus looking for hands-on and in-person training that would support the use of this approach in their professional lives.

Even more interesting is the finding that the longer periodontists had practiced, the more they wanted to attend in-person CE courses. Stem cell-based bone grafting was clearly not just of interest to more previously graduated periodontists but was of interest to periodontists across the life/career span. Not surprising was the finding that periodontists with higher percentages of bone grafting procedures in their practices were more interested in learning about this topic.

Despite the finding that only about a third of the respondents had heard about stem cell-based bone grafting before, the attitudes toward this new approach were quite positive and provided clear guidance for future research needed to satisfy the great interest in this area. The majority of periodontists considered it important to have empirical evidence that this approach results in accelerated wound healing, better bone quality, and in more bone volume compared to the traditional approach. These attitudes underscore the importance of conducting clinical research that evaluates efficacy in the context of periodontal and bone tissue regeneration. As an example, there is recent evidence of engineered periodontal scaffolds offering the capacity to position amorphous cell sheets precisely within the periodontal ligament space. These scaffolds utilize porous structures to support and secure the material next to the root surface, effectively filling the periodontal defect. This is an innovative stem cell-based approach that

holds great promise for the regeneration of periodontal tissues in periodontal defects.^{31–34}

It is also important to note that the absolute majority of the respondents indicated that they considered this new approach as promising and that they would prefer this new approach to the traditional approach. This finding is consistent with research concerning the potential of using stem cells both in plastic surgery as well as in orthopedic surgery.^{35–37}

The majority also responded that using this approach would benefit their practice and that patients would prefer this approach to the traditional approach. Overall, periodontists' attitudes towards stem cell-based therapy were quite positive. These positive attitudes might explain why the majority responded that they were likely/very likely to adopt this approach in the future.

The responses to the open-ended question concerning what the respondents would like to know about this new approach are noteworthy because they show a combination of interest in empirical evidence for the superiority of this approach, in information about the clinical procedures and logistics, as well as about practice-related considerations. They wanted to know about the results of well-designed clinical trials and studies that demonstrate the effectiveness and benefits of this approach compared to traditional methods. This interest in solid empirical evidence was also found in studies with physicians.³⁸

Additionally, periodontists also indicated that they considered practice-related considerations when contemplating stem cell-based therapy.^{39–42} For example, the cost of the procedure was referenced as being an important consideration for adoption of stem cell-assisted bone grafting. This fact might be related to a lack of information concerning the cost of the procedure. This consideration was supported by the very wide range of answers to the questions concerning the highest acceptable cost for procuring stem cells, which ranged from \$50 to \$5000. While this large range of responses might be due to misunderstanding the question, it can also be considered as a sign that information concerning the cost of the procedure needs to be provided. In this context, it might be helpful to consider that the cost of stem cell therapy in medical settings ranges widely to over \$100,000.⁴³ This cost would be exorbitant for stem cell therapies for alveolar bone regeneration but based upon our past clinical trials,^{20,21} cost estimates for such treatment in dental applications are between \$5000 and \$10,000. Further strategies to make the procedure more cost effective will be important for ultimate clinical adoption.

Overall, the results of this survey were promising for the future adoption of stem cell-supported bone grafting in periodontal offices. It showed that there is a need for



future research and especially for educational interventions aimed at not only educating future periodontists in residency programs but also practicing periodontists in continuing education courses about this new approach.

This study had two limitations. The first limitation was that additional provider background characteristics such as sex, or practice characteristics such as patients' socioeconomic backgrounds, should have been included in this survey. However, given that this survey was the first questionnaire of its kind exploring the topic, it was important to be succinct to improve the response rate. A second limitation was that at the time this survey was developed, there was a lack of research concerning which information periodontists would want or need. This lack of prior research resulted in adding open-ended questions. Based on the answers to these open-ended questions, future research can now more precisely ask targeted closed-ended questions that will increase understanding of how to assure optimal translation of the empirical evidence into clinical practice.

5 | CONCLUSIONS

Based on these findings, it can be concluded that the majority of periodontists are not familiar with the potential of stem cell-supported bone grafting for their own clinical practice. However, once introduced to the topic, they are motivated to gain access to more education and information about this content area and have exceptionally positive attitudes towards potentially adopting this new approach. The majority are likely/very likely to adopt this approach in the future. They would like to know more about (1) the empirical evidence showing that this new approach is superior to the traditional approaches, (2) the clinical and logistic considerations when implementing this technique, and (3) the practice characteristics-related considerations including the costs for patients and benefits for their practice.

AUTHOR CONTRIBUTIONS

Darnell Kaigler, Jonathan Misch, and Marita R. Inglehart conceived and designed the study. Jonathan Misch and Marita R. Inglehart collected the data. Marita R. Inglehart analyzed the data, and all authors worked on drafting the manuscript and gave final approval of the submitted version.

ACKNOWLEDGMENTS


This research was made possible by funds from the National Institute of Dental and Craniofacial Research, NIH (R01DE028657) and the Major Ash Collegiate Professorship Fund, located at the University of Michigan School

of Dentistry. We want to thank the American Academy of Periodontology for providing the addresses of its members to mail the surveys.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest with this study. The authors do not have any financial interests, either directly or indirectly, in the products or information listed in the paper.

ORCID

Abdusalam Alrmali  <https://orcid.org/0000-0001-7437-6279>

REFERENCES

1. Hoang DM, Pham PT, Bach TQ, et al. Stem cell-based therapy for human diseases. *Signal Transduct Target Ther*. 2022;7:272. doi:10.1038/s41392-022-01134-4
2. Zakrzewski W, Dobrzyński M, Szymonowicz M, Rybak Z. Stem cells: past, present, and future. *Stem Cell Res Ther*. 2019;10:68. doi:10.1186/s13287-019-1165-5
3. Kawaguchi H, Hirachi A, Hasegawa N, et al. Enhancement of periodontal tissue regeneration by transplantation of bone marrow mesenchymal stem cells. *J Periodontol*. 2004;75:1281-1287.
4. Tsuchida S, Nakayama T. Recent clinical treatment and basic research on the alveolar bone. *Biomedicines*. 2023;11:843. doi:10.3390/biomedicines11030843
5. Titsinides S, Agrogiannis G, Karatzas T. Bone grafting materials in dentoalveolar reconstruction: a comprehensive review. *Jpn Dent Sci Rev*. 2019;55:26-32.
6. Cha HS, Kim JW, Hwang JH, Ahn KM. Frequency of bone graft in implant surgery. *Maxillofac Plast Reconstr Surg*. 2016;38:19. doi:10.1186/s40902-016-0064-2
7. Zhao R, Yang R, Cooper PR, et al. Bone grafts and substitutes in dentistry: a review of current trends and developments. *Molecules*. 2021;26:3007. doi:10.3390/molecules26103007
8. Latimer JM, Maekawa S, Yao Y, et al. Regenerative medicine technologies to treat dental, oral, and craniofacial defects. *Front Bioeng Biotechnol*. 2021;9:704048. doi:10.3389/fbioe.2021.704048
9. Esposito M, Grusovin MG, Felice P, et al. The efficacy of horizontal and vertical bone augmentation procedures for dental implants—a Cochrane systematic review. *Eur J Oral Implantol*. 2009;2:167-184.
10. Jepsen S, Schwarz F, Cordaro L, et al. Regeneration of alveolar ridge defects. Consensus report of group 4 of the 15th European Workshop on Periodontology on Bone Regeneration. *J Clin Periodontol*. 2019;46(21):277-286.
11. Sheikh Z, Sima C, Glogauer M. Bone replacement materials and techniques used for achieving vertical alveolar bone augmentation. *Materials*. 2015;8:2953-2993.
12. Urban I, Montero E, Sanz-Sánchez I, et al. Minimal invasiveness in vertical ridge augmentation. *Periodontol 2000*. 2023;91:126-144.
13. Tavelli L, Chen CYJ, Barootchi S, Kim DM. Efficacy of biologics for the treatment of periodontal infrabony defects: an American Academy of Periodontology best evidence systematic review and network meta-analysis. *J Periodontol*. 2022;93:1803-1826.



14. Avila-Ortiz G, Ambruster J, Barootchi S, et al. American Academy of Periodontology best evidence consensus statement on the use of biologics in clinical practice. *J Periodontol.* 2022;93:1763-1770.
15. Ferraz MP. Bone grafts in dental medicine: an overview of autografts, allografts and synthetic materials. *Materials.* 2023;16:4117. doi:10.3390/ma16114117
16. Larsson L, Decker AM, Nibali L, et al. Regenerative medicine for periodontal and peri-implant diseases. *J Dent Res.* 2016;95:255-266.
17. Maniar HH, Tawari AA, Suk M, Horwitz DS. The current role of stem cells in orthopaedic surgery. *Malays Orthop J.* 2015;9:1-7.
18. Hoang DM, Pham PT, Bach TQ, et al. Stem cell-based therapy for human diseases. *Signal Transduct Target Ther.* 2022;7:272. doi:10.1038/s41392-022-01134-4
19. Aly RM. Current state of stem cell-based therapies: an overview. *Stem Cell Investig.* 2020;15(7):8. doi:10.21037/sci-2020-001
20. Kaigler D, Pagni G, Park CH, et al. Stem cell therapy for craniofacial bone regeneration: a randomized, controlled feasibility trial. *Cell Transplant.* 2013;22:767-777.
21. Kaigler D, Avila-Ortiz G, Travan S, et al. Bone engineering of maxillary sinus bone deficiencies using enriched CD90+ stem cell therapy: a randomized clinical trial. *J Bone Miner Res.* 2015;30:1206-1216.
22. Chen Y, Wang X, Wu Z, et al. Epigenetic regulation of dental-derived stem cells and their application in pulp and periodontal regeneration. *PeerJ.* 2023;3(11):e14550. doi:10.7717/peerj.14550
23. Aimetti M, Ferrarotti F, Gamba MN, et al. Regenerative treatment of periodontal intrabony defects using autologous dental pulp stem cells: a 1-year follow-up case series. *Int J Periodontics Restorative Dent.* 2018;38:51-58.
24. Costa LA, Eiro N, Vaca A, Vizoso FJ. Towards a new concept of regenerative endodontics based on mesenchymal stem cell-derived secretomes products. *Bioengineering.* 2022;10:1-18. doi:10.3390/bioengineering10010004
25. Srithanyarat SS, Choosiri M, Sa-Ard-Iam N, Petcharat P, Osathanon T. Characteristics of mesenchymal stem cells from supracrestal gingival connective tissue. *J Periodontol.* 2023;94:439-450.
26. Hardigan PC, Succar CT, Fleisher JM. An analysis of response rate and economic costs between mail and web-based surveys among practicing dentists: a randomized trial. *J Community Health.* 2012;37:383-394.
27. McKernan SC, Reynolds JC, McInroy B, Damiano PC. Randomized experiment on the effect of incentives and mailing strategy on response rates in a mail survey of dentists. *J Public Health Dent.* 2022;82:484-490.
28. Barchielli C, Marullo C, Bonciani M, et al. Nurses and the acceptance of innovations in technology-intensive contexts: the need for tailored management strategies. *BMC Health Serv Res.* 2021;21:639. doi:10.1186/s12913-021-06628-5
29. Lee DH, Kim SA, Song JS, et al. Cartilage regeneration using human umbilical cord blood derived mesenchymal stem cells: a systematic review and meta-analysis. *Medicina.* 2022;58:1801. doi:10.3390/medicina58121801
30. Pires IGS, Silva E Souza JA, de Melo Bisneto AV, et al. Clinical efficacy of stem-cell therapy on diabetes mellitus: a systematic review and meta-analysis. *Transpl Immunol.* 2022;75:101740. doi:10.1016/j.trim.2022.101740
31. Mosaddad SA, Rasoolzade B, Namanloo RA, Azarpira N, Dortaj H. Stem cells and common biomaterials in dentistry: a review study. *J Mater Sci Mater Med.* 2022;18:33-55.
32. Fraser D, Caton J, Benoit DSW. Periodontal wound healing and regeneration: insights for engineering new therapeutic approaches. *Front Dent Med.* 2022;3:815810. doi:10.3389/fdmed.2022.815810
33. Sallum EA, Ribeiro FV, Ruiz KS, Sallum AW. Experimental and clinical studies on regenerative periodontal therapy. *Periodontol 2000.* 2019;79:22-55.
34. Moreno Sancho F, Leira Y, Orlandi M, et al. Cell-based therapies for alveolar bone and periodontal regeneration: concise review. *Stem Cells Transl Med.* 2019;8:1286-1295.
35. Saliban AA, Widgerow ASD, Abrouk M, Evans GRD. Stem cells in plastic surgery: a review of current clinical and translational applications. *Arch Plast Surg.* 2013;40:666-675.
36. Houdek MT, Wyles CC, Collins MS, et al. Stem cells combined with platelet-rich plasma effectively treat corticosteroid-induced osteonecrosis of the hip: a prospective study. *Clin Orthop Relat Res.* 2018;476:388.
37. Shapiro SA, Arthurs JR, Heckman MG, et al. Quantitative T2 MRI mapping and 12-month follow-up in a randomized, blinded, placebo-controlled trial of bone marrow aspiration and concentration for osteoarthritis of the knees. *Cartilage.* 2019;10:432.
38. Smith C, Crowley A, Munsie M, et al. Academic physician specialists' views toward the unproven stem cell intervention industry: areas of common ground and divergence. *Cytotherapy.* 2021;23:348-356.
39. Deng Y, Liang Y, Liu X. Biomaterials for periodontal regeneration. *Dent Clin North Am.* 2022;66:659-672.
40. Bassir SH, Wisitrasameewong W, Raanan J, et al. Potential for stem cell-based periodontal therapy. *J Cell Physiol.* 2016;231:50-61.
41. Genco RJ. Commentary: the evolution of periodontology: science always wins. *J Periodontol.* 2014;85:1308-1312.
42. Huang L, Salmon B, Yin X, Helms JA. From restoration to regeneration: periodontal aging and opportunities for therapeutic intervention. *Periodontol 2000.* 2016;72:19-29.
43. Knoepfler P. Stem cell therapy cost in 2023. The Niche. Trusted stem cell blog. Comments /June 15, 2023. <https://ipscell.com/2023/06/stem-cell-therapy-cost-in-2023-new-data/>

How to cite this article: Kaigler D, Misch J, Alrmali A, Inglehart MR. Periodontists and stem cell-based therapy for alveolar bone regeneration: A national survey. *J Periodontol.* 2024;1-10. <https://doi.org/10.1002/JPER.23-0506>