

# A survey of the opinions of Dentists regarding stem cells in Dentistry

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## ABSTRACT

Regenerative and stem cell therapy is a new field in dentistry. The opinions of dentists and their acceptance of the concepts are important in successful clinical implementation of these procedures.

**Objectives:** To determine the levels of awareness, attitudes and knowledge concerning the therapeutic potential of stem cells in regenerative dentistry among dentists and to determine whether a need exists for additional training in the field.

**Materials and Methods:** A questionnaire on regenerative dentistry was distributed to 140 dentists in the private sector in South Africa, consisting of three broad sections: Professional status; Opinions and Beliefs; and Clinical Practice. 130 copies were returned anonymously. A descriptive analysis of the frequencies was performed.

**Results:** The majority of the dentists (90%) had not received any training on stem cell therapies but many (73%) were interested in attending further training. Almost all participants (95%) would recommend regenerative therapies to their patients. The majority (80%) were willing to save teeth in cell banks for future therapeutic purposes.

**Conclusions:** Dentists are supportive of using stem cell and regenerative dental procedures and most are willing to undergo more training in regenerative dentistry. A majority felt that the topic should be included in the undergraduate course.

## INTRODUCTION

Research on adult stem cells is leading to new dental treatment protocols for caries, endodontics, periodontal and oral-maxillofacial procedures.<sup>1</sup> A characteristic of dental pulp stem cells, i.e. their plasticity, make them an important source of mesenchymal stem cells for regenerative therapies in dentistry and for tissue bioengineering in medicine.<sup>2</sup>

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## ACRONYMS

<b>AAE:</b>	American Association of Endodontics
<b>BMPs:</b>	bone morphogenetic proteins
<b>DPSCs:</b>	dental pulp stem cells
<b>iPS:</b>	cells pluripotent stem cells
<b>MSC:</b>	Mesenchymal stem cells

Regenerative dentistry potentially offers substantial benefits for dental patients.<sup>3</sup> Induced pluripotent stem cells (iPS cells) from dental pulp stem cells (DPSCs) may play an important role in tooth reconstruction.<sup>4</sup> The possibility of regeneration of dentine through the use of bone morphogenetic proteins (BMPs) has positive implications for the future of clinical dentistry, for example, in the development of improved pulp capping agents and alternatives to root canal therapy.<sup>3</sup>

A 2010 American Association of Endodontics (AAE) survey showed that nearly 75% of program directors were teaching regenerative endodontics in didactic and clinical settings.<sup>5</sup> According to the AAE position statement, Advanced Speciality Education Programmes were required, as from 2014, to provide in-depth instruction and clinical training in revascularization/regenerative endodontics.<sup>5</sup>

The value of pulpal regeneration is considered in two reviews<sup>6,7</sup> one of which, by Tatullo *et al* discusses the importance of stem cell research for neuronal regeneration.<sup>6</sup> Maeda and Akamine<sup>8</sup> examined the importance of stem cell research for tooth root and periodontal tissue regeneration for the avoidance of tooth loss in a world population with an increased longevity rate. Lin *et al.*<sup>9</sup> further discuss new approaches for periodontal reconstruction using regenerative procedures to help prevent tooth loss.

The use of adult stem cells for the regeneration of craniofacial structures holds potential in tissue engineering.<sup>10</sup> New non-invasive methods for obtaining autologous bone from stem cells derived from different tissues from the same patient are being researched.<sup>11</sup>

Besides the capacity of mesenchymal stem cells (MSCs) to differentiate, (which is important for tissue engineering), their immune-regulatory capacity and trophic activity are essential in the establishment of a regenerative micro-environment at sites of tissue injury. The bioactive factors secreted by MSCs inhibit scarring and apoptosis, while stimulating angiogenesis and mitosis of tissue-intrinsic progenitor or stem cells.<sup>12</sup>

Although scientifically promising, the development of stem cell research in dentistry may have been hampered by fears regarding potential abuse of the stem cell technology. While this research is a relatively new field in dentistry, it seems

to hold a great potential for treatment. However, very little information about its introduction to, and incorporation into, dentistry is available in the literature.

The advancements in stem cell research and regenerative dentistry warrant serious consideration of the need to include this field of study in the education of dental students and in post graduate courses for qualified dentists.<sup>7,10,13,14</sup> An obligatory subject "Regenerative Medicine" for 5th year medical students was introduced at the Copernicus University, Bydgoszcz, Poland, after a brief survey completed by 1st year medical students, conducted by Bajek and Drewa.<sup>13</sup> Undergraduate students at Lahore Medical and Dental College, affiliated with the University of Health Sciences, Lahore, Pakistan, receive no clinical training in regenerative medicine but they do receive information in the form of lectures during the last two years of their training. They also observe regenerative procedures done by the faculty members, whilst postgraduate students do themselves perform guided tissue regenerative procedures. Undergraduate students at the Faculty of Dentistry, Griffiths University, Australia and the College of Dentistry, University of Dammam, Saudi Arabia, also receive no clinical training in regenerative dentistry. Whilst there is not much literature on the status, it appears that current undergraduate and postgraduate dental programmes do not equip the student with the in-depth knowledge and understanding required for the performance of stem cell-based procedures in dental treatments.

There is no evidence in the scientific literature on opinions, beliefs and attitudes of dentists regarding the potential of regenerative procedures in dentistry.<sup>15</sup> Recently a few surveys have examined perceptions of dentists regarding regenerative dental treatment options.<sup>15-19</sup> The status in medicine has been considered. In China, Deng *et al.*<sup>20</sup> conducted a survey on health care workers while a survey by Gucciardo *et al.*<sup>21</sup> focused on researchers and medical practitioners in Perinatology.

Currently, there is a lack of guidelines in the field of regenerative dentistry. The establishment of ethical guidelines will require a survey of practicing dentists to seek data about their attitudes towards regenerative dental procedures.<sup>15</sup> Considerable debate regarding the use of stem cell research exists in the scientific, ethical, and political fraternity.<sup>22</sup> The important questions deal with the impact upon national regulation and social behaviours as well as considering the advice of experts.<sup>22</sup>

The aims of this survey were to gain a current view of the opinions on the ethical aspects, to investigate the perceptions and awareness of dentists on stem cell procedures and to assess the potential for the acceptance of regenerative treatment as a routine amongst dentists in private practice.

## MATERIALS AND METHODS

### Questionnaire

Existing questionnaires on perceptions of the use of stem cells in dentistry and medicine<sup>15-19,22</sup> were examined and modified in compiling the questionnaire used in this study. The content validity was evaluated from an in-depth literature search on surveys conducted on regenerative dentistry. The questionnaire was further subjected to scrutiny after it was initially distributed to a smaller group of dentists as a pilot study to eliminate any discrepancies or duplication of questions.

This descriptive, cross sectional study was conducted among consenting dentists from private practice in both major and smaller cities in South Africa.

### Study sample

The survey was given as an anonymous questionnaire to practising dentists. A total of 140 copies of questionnaires were sent out. Ten were discarded as incomplete or no response.

The questionnaire consisted of three sections:  
Section A: Professional status  
Section B: Ethical opinions, beliefs and judgment  
Section C: Clinical practice

### Statistical analysis

The data was recorded in Excel ( $n = 130$ ) and the frequencies were analysed.

The data was examined in the three key areas, namely professional status, opinion and awareness and clinical practice. A descriptive analysis of the frequencies was performed.

## RESULTS

The overall response rate to the questionnaire was 93%. The questionnaire results are shown in Table 1.

### Professional status

Most of the participants were male (61.5%), the majority (70.8%) were less than 50 years old and about half the participants were below 40 years of age. A higher number of female dentists were found in the younger age groups with more males in the older, more clinically experienced group (43.8%). Most of the dentists (69.3%) practised in urban areas and 45% of the participants had been in private practice for 10 years or less. About half of the participants (45.4%) read scientific journals monthly or weekly with 10.8% doing so on a weekly basis. A minority of 10% of the participants had attended lectures on stem cells but a considerable majority (73%) were interested in attending more advanced training courses and lectures on the dental application of stem cells.

### Opinions and awareness

About half the participants (48.5%) were aware of the potential therapeutic applications of stem cells in dentistry, but 20% reported being unsure of these options. While two thirds (63.1%) of participants thought that dental stem cell banking will be useful for the regeneration of dental tissue, the majority (80%) were willing to save teeth for future regenerative dental procedures. About 28% of participants believed that within 10 years, some regenerative procedures will be used in clinical practice and 38% felt that it will take less than 20 years before dentists are able to implant teeth grown in the laboratory. About two thirds of participants (64.6%) felt that the regenerative dental treatment will be a better option than implant replacement while 29% of the participants were unsure. Most of the participants (83%) felt cost was the biggest obstacle to a patient accepting regenerative treatment and 48% of participants also felt that fear may be a limiting factor. A minority of the participants (37.7%) felt that there was a health hazard when regenerative dental procedures are used. Only 16.9% of the participants held ethical concerns regarding the use of stem cells in dentistry and indeed the majority (58.5%) had no ethical concerns whatever. While 60.8% of participants were not sure of the availability of stem cell banks for dental use, 58.5% would recommend a patient to store dental stem cells for future prospects. More than half the participants (78.4%) agreed that dental professional associations should regulate the use of stem cell and regenerative dentistry, while 33.6% advised that academic institutions should develop dental stem cell research.

**Table 1: Survey results**

Question	%	n	
<b>A. Professional status</b>			
1. In which field/s of dentistry do you mostly practise?			
a. General Practitioner	95.4	124	
b. Endodontics	1.5	2	
c. Orthodontics	1.5	2	
d. Periodontics	0.8	1	
e. Prosthodontics	0.8	1	
2. How many years have you been in practice?			
a. 0 – 10 years	45.4		
b. 11-20 years	23.8		
c. >20 years	30.8		
3. Where is your primary place of practice located? (name of city/town)			
a. Cape Town	23.1	30	
b. Johannesburg	20	26	
c. Durban	20	26	
d. Nelspruit	10.7	14	
e. Tzaneen	10.0	13	
f. Rustenburg	10.0	13	
g. Port Elizabeth	4.6	6	
h. Harare	0.8	1	
i. Windhoek	0.8	1	
4. What is your gender?			
a. Male	61.5	80	
b. Female	38.5	50	
5. What is your age?			
a. 20-30 years	22.3	29	
b. 31 - 40 years	28.5	37	
c. 41 - 50 years	20.0	26	
d. 51 - 60 years	20.0	26	
e. 60+ years	9.2	12	
6. How frequently do you read scientific dental journals?			
a. Weekly	10.8	14	
b. Monthly	34.6	45	
c. Once in a while	53.1	69	
d. Never	1.5	2	
7. Have you attended a training course/program/lecture on dental application of stem cells			
a. Yes	10	13	
b. No	90	117	
8. Would you be interested in attending more advanced training courses regarding dental application of stem cells?			
a. Very interested	73.1	85	
b. Neutral	10	13	
c. Not interested	16.9	22	
<b>B. Opinions and awareness</b>			
9. Are you aware of the potential therapeutic applications of stem cells in dentistry?			
a. Yes	48.5	63	
b. Not sure	20	26	
c. No	31.5	41	
10. Do you think that dental stem cell banking will be useful for regeneration of dental tissues?			
a. Agree	63.1	82	
b. Neutral	32.3	42	
c. Disagree	4.6	6	
<b>Question</b>			
11. Should regenerative therapy be incorporated into the dentistry undergraduate course?			
a. Agree	73.9	96	
b. Neutral	20	26	
c. Disagree	6.2	8	
12. How many years do you think it will take for some regenerative stem cell therapies to be used in dentistry?			
a. 0 - 10 years	28.5	37	
b. 11 - 20 years	27.7	36	
c. > 20 years	11.5	15	
d. Unsure	32.3	42	
13. How many years do you think it will take before dentists are able to implant new teeth grown in a laboratory?			
a. 0 - 10 years	15.4	20	
b. 11 - 20 years	23.1	30	
c. > 20 years	22.3	29	
d. Unsure	38.5	50	
e. Never	0.8	1	
14. In your opinion what do you think would be the biggest obstacle to a patient accepting regenerative dental treatment?			
a. Cost	Yes	83.8	109
	Not sure	10.1	13
	No	5.3	7
b. Fear	Yes	48.9	64
	Not sure	22.5	29
	No	28.6	37
c. Other		0	0
15. Would you be willing to save teeth and dental tissue for future regenerative dental treatment?			
a. Yes	80	104	
b. Not sure	13.8	18	
c. No	6.2	8	
16. Do you think that regenerative dental treatment will be a better treatment option than tooth implant placement?			
a. Yes	64.6	84	
b. Not sure	29.2	38	
c. No	6.2	8	
17. Are you concerned about any potential health hazards regarding the use of stem cells as part of regenerative dentistry?			
a. Yes	37.7	49	
b. Not sure	29.2	38	
c. No	33.1	43	
18. Do you believe that stem cell clinics will deliver future dental treatments?			
a. Yes	58.5	76	
b. Not sure	33.8	44	
c. No	7.7	10	
19. Do you believe that dental professional associations should regulate the use of stem cell and regenerative dentistry?			
a. Yes	78.4	102	
b. Not sure	16.2	21	
c. No	5.4	7	
20. Do you have any ethical concerns regarding use of stem cells in dentistry?			
a. Yes	16.9	22	
b. Not sure	24.6	32	
c. No	58.5	76	
21. Are there any dental stem cell banks in South Africa?			
a. Yes	14.6	19	
b. Not sure	60.8	79	
c. No	24.6	32	

Question	%	n
22. In a clinical practice, will you recommend a patient to store dental stem cells and explain its future prospects?		
a. Yes	58.5	76
b. Not sure	28.5	37
c. No	13.1	17
<b>C. Clinical practice:</b>		
23. Which of the following are sources of dental stem cells?		
a. Dental pulp, Apical papilla, Gingiva	64.6	84
b. Enamel	0	0
c. Do not know	35.4	46
24. Can stem cell tissue regenerative technology be applicable to dentistry?		
a. Yes	68.4	89
b. Not sure	30	39
c. No	1.5	2
25. Can dental stem cells be used to develop non-dental tissues/organs?		
a. Yes	28.4	37
b. Not sure	65.4	85
c. No	6.2	8
26. Which of the following procedures can benefit by the application of dental stem cells?		
a. Continued root formation	56.2	73
b. Regeneration of enamel	56.2	73
c. Pulp/dentin tissue engineering and regeneration	56.2	73
d. Do not know	43.8	57
27. Which of the following would most help newly qualified dental professionals to be better able to gain knowledge about stem cells?		
a. More hands-on training and short courses to improve knowledge about stem cells in practice	96.2	125
b. Topics related to stem cells to be included in the undergraduate curriculum	96.2	125
c. Do not know	3.8	5
28. In your opinion how should dental stem cell research be developed in future?		
a. Under Public Sector initiatives	8.5	11
b. Under Private Sector initiatives	16.2	21
c. Under Public-Private Partnership	40.8	53
d. Academic institutions	33.1	43
e. Other Specify:	0	0
29. Do you use any type of regenerative procedures in your practice, such as membranes, scaffolds or bioactive materials?		
a. Regularly	9.2	12
b. Once in a while	28.4	37
c. Do not use	62.4	81
30. Which of the following regenerative treatments are the most valuable?		
a. Healing of peri-radicular bone, continued root development in immature teeth and pulp tissue revitalization within a root canal.	62	81
b. Tooth re-implantation	28	36
c. None of the above	10	13
31. What percentage of cases in your practice involve necrotic immature teeth monthly?		
a. 0	21.5	28
b. 1%	43.8	57
c. 2%	15.4	20
d. 2% or more	19.3	25

### Clinical practice and knowledge

Most of the respondents (64.6%) knew the origin of dental stem cells. Continued root formation with stem cells and the regeneration of pulp/dentine complex was regarded as the most beneficial application of dental stem cells by the participants (56.2%). Most of the participants (78.5%) delivered treatment involving necrotic immature teeth every month while the remaining participants (21.5%) reported that in their clinic such treatment was not routine. More than half the participants considered tribiotic paste and pulpal regeneration to be the optimal treatment for necrotic pulp in immature teeth; 17.7% felt that MTA apical plug and back fill with obturation material is the optimal treatment, while 25.8% used calcium hydroxide either alone or with MTA. A minority of the participants (37.6%) were already using some form of regenerative therapy in their practice such as membranes, scaffolds or bioactive materials. The remaining participants (62.8%) did not use any form of regenerative therapy in their practices. In a theoretical case where participants could not provide regenerative treatment, almost all participants (84.6%) were willing to refer the patient to a practitioner who did provide that option. Almost all the participants (96.9%) would most likely recommend stem cell and regenerative treatment to their patients if it is the most effective treatment option. Almost all the participants (96.2%) felt that for practising dentists, short courses to improve knowledge about stem cells in practice and more hands-on training would be advantageous, The introduction to the undergraduate programme of topics related to stem cells would benefit the incipient qualified dental professionals.

### DISCUSSION

The discovery of stem cells in the pulps of permanent and deciduous teeth<sup>1</sup> and the possibility of using dental pulp stem cells for tissue engineering has prompted much research in this field. Stem cell research is a fast growing field in medicine with about 20,000 publications for tissue engineering or regenerative medicine in 2015 and 1,300 publications in dentistry in 2015 (Pubmed search). There is therefore, enthusiasm for the incorporation of regenerative procedures into dental practices, and a growing demand for more lectures, together with incorporation into undergraduate teaching programmes.

Question	%	n
32. What do you consider to be the optimal treatment for necrotic pulp in immature teeth?		
a. Calcium hydroxide apexification	11.3	14
b. Calcium hydroxide application followed by MTA apical plug and backfilling with obturation material	14.5	18
c. MTA apical plug and back-fill with obturation material	17.7	22
d. Tribiotic paste and pulpal regeneration	56.5	76
33. In a case where you can't provide regenerative treatment, would you be willing to refer your patient to a practitioner who does provide regenerative treatment?		
a. Yes	84.6	110
b. Not sure	10.8	14
c. No	3.8	6
34. What would make you most likely to recommend stem cell and regenerative treatments to your patients?		
a. If it is the most effective treatment option	95.3	122
b. If it is safe and reliable	3.1	4
c. If it is the most cost-effective option	1.5	2
d. I would not recommend it	1.5	2

In this study the dentists demonstrated a willingness to attend further training on stem cells which may be indicative of the acceptance of the newer treatment modality of regenerative dentistry. This was further emphasised by the fact that most of the dentists were willing to save teeth for future use with stem cell banking, recognizing the potential of these regenerative procedures. Participants who believed that stem cell banking would be useful for regeneration of dental tissue were also willing to refer patients to a practitioner who could provide the treatment in cases where they were unable to do so themselves. Although most of the dentists believed that stem cell tissue regeneration will be applicable to dental therapies, most were unsure whether these dental stem cells could be used to develop non-dental tissue or organs.

Most of the dentists who participated in this survey read scientific dental journals on a weekly or monthly basis indicating that they are keeping abreast with latest dental advancements and research. This may be the source of the majority having current knowledge on the origin of stem cells. A minority of the dentists in our study (10 % of participants) had received some measure of continued education on regenerative dentistry in the form of lectures, symposiums or seminars, compared with data reported from other studies which ranged attendance from 16% to 50%.<sup>16,18</sup> In a similar study amongst endodontists, Epelman *et al.*, (2009) found that 56% (n=53) of the respondents had received continued education on stem cells/regenerative dental treatments. It should be noted however, that the above studies were conducted on registrars specializing and endodontists compared with the current study in which general dentists were surveyed. There was a positive interest (73%) shown amongst the present sample to attend additional training course and lecture programmes on stem cells as well as supporting the concept of the incorporation of regenerative therapy into the undergraduate programme (73,9%). Utneja *et al* showed that 86.6% of participants in their study advised the incorporation of regenerative therapy into the undergraduate dentistry programme.<sup>19</sup> A similar study, conducted amongst medical doctors, found that the majority of the physicians interviewed did not have specific knowledge on stem cells (59%), most (65%) of those involved did not attend additional training courses regarding stem cells, but most were interested in stem cells (70%), suggesting that they believe in the potential benefits of developing stem cells therapies.<sup>22</sup>

Most dentists felt that regenerative dentistry is a better option than implant dentistry and that it will take less than 20 years before teeth can be replaced using regenerative procedures. Most participants felt that stem cell therapy did not pose a health hazard and only 5% had ethical concerns with the use of stem cells in dentistry.

Most respondents would recommend stem cell regenerative procedures if it is the most effective treatment. This reflects on the attitude of the dentists to provide the best and most effective care to their patients. Cost did not seem to be the main priority in offering this treatment modality.

Subjects who believed that stem cell banking would be useful for regeneration of dental tissue were also willing to refer patients to a practitioner who could provide regenerative treatment in cases where they were unable to do so themselves. Currently, 23% of dentists use some type of regenerative procedures in their practice, such as membranes, scaffolds and bioactive materials.

Most dentists felt that a joint Public-Private partnership would be most appropriate to develop the future of dental stem cell treatment and considered that the Dental Association should be involved in this process.

## CONCLUSION

The data from this survey revealed that dentists showed high levels of awareness regarding the use of stem cells in dentistry. Respondents were willing to save teeth in stem cell banks for future use. Dentists showed interest in incorporating regenerative procedures into their practices, were willing to undergo further training and were eager to attend more lectures on stem cells and regenerative procedures. Dentists also felt that dental regenerative procedures should be introduced in the undergraduate dental curriculum.

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