

## Regeneration of Teeth in Operative Dentistry: A review

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### ABSTRACT

Operative dentistry has utilised regenerative methods to treat dental disease for many years. Clearly, the use of calcium hydroxide to encourage reparative or reactive dentin is one such treatment technique. The emergence of tissue engineering enables dentistry to advance its use of regeneration as a guiding principle for treating oral disease. Tissue engineering is a multidisciplinary field of study that combines biology, engineering, and clinical sciences to create new tissues and organs. It is founded on fundamental principles involving the identification of relevant cells, the building of conducive scaffolds, and an understanding of the morphogenic signals necessary to stimulate cells to rebuild missing tissues. This study focuses on the presentation and discussion of existing material on the engineering of enamel, dentin, and pulp, as well as complete teeth. Clearly, significant obstacles must be addressed before such tactics may be routinely employed in the clinic to treat patients. Existing research, however, indicates that the engineering of new dental structures to replace tissues lost as a result of caries or trauma will have a position in the future of operative dentistry.

### INTRODUCTION

In the late 1980s, a polymer chemist (Robert Langer) and an organ transplant surgeon (Joseph Vacanti) hypothesised that it would be possible to create a tissue or organ out of synthetic materials. By planting the cells that comprise this tissue onto a biodegradable scaffold, it is possible to regenerate an organ. This approach to regenerative medicine is known as tissue engineering, which is an interdisciplinary area that uses engineering and life science ideas to biological substitutes that restore, maintain, or improve tissue function.[2] In the early 1990s, a foundational book explaining the foundations of tissue engineering<sup>3</sup> and the successful engineering of cartilage in the shape of a human ear in the dorsum of mice<sup>4</sup> drew much attention and visibility to this new subject. Since then, medical practitioners have utilised tissue engineering more frequently to address a number of illnesses.

Humans have utilised tissue engineering-based procedures such as the production of new bone for patients with severe bone loss and the repair of severely burned skin on children.

In recent years, experts in the field of dentistry have begun to investigate the possibility of tissue engineering to restore missing tooth structures and, possibly, to replace an entire tooth. It is anticipated that in the next five to twenty years, tissue engineering, nanotechnology, and stem cells will play an increasingly important role in clinical dentistry.[7]

This article seeks to provide a comprehensive update on tissue engineering as it pertains to the regeneration of tooth structure. It is essential to note that the majority of these technologies are still under research and lack FDA approval for usage on humans. This paper explores the potential impact that tissue engineering may have on the future of clinical dentistry with an eye toward the future.

### **Lessons from molecular signaling events during odontogenesis**

The subject of tooth tissue engineering employs the following concepts: originate from early research into molecular signaling during odontogenesis and also based on research into mutations resulting in tooth-related traits

Morphogenic cues promoting differentiation and recognised functions of odontoblasts and ameloblasts be mediated by unique molecules. These molecular components

During the earliest stages, exchanges commence quite quickly. Tooth development and advancement till the tooth is fully formed.[8-10] Molecular signals move between tooth-forming cells are positioned by guiding their cells. Along mineralization fronts, differentiate and initiate differentiation. releasing fresh molecules (proteins). These proteins make up extracellular matrices, which will afterwards mineralized into dentin and enamel. Instances of

Signaling molecules are bone morphogenetic proteins (BMPs) and Amelogenin, which are covered in greater detail. A possible instance of such interplay between cells. Cell "A" secretes. Several proteins and one protein (represented by the symbol as a circle) for which cell "B" possesses a receptor.

Activation of this receptor by the released protein cell "A" induces intracellular signalling in cell "B" This leads to the production of an mRNA molecule, which will be secreted, will be translated into a new protein pertaining to the extracellular environment A similar occurrence seen during the development of teeth

Dentists are aware, despite this, that there is no substance on the market. All the physical, mechanical, and aesthetic features of enamel and dentin can now be replicated. In addition, there are circumstances in the clinic in which dentists do not have the optimal solution for their patients' demands.

A young patient (6-15 years old) with severe carious lesions in his or her permanent teeth is one example. At this age, the patient's occlusion is not mature and stable, hence one opts for

"temporary" restorations with a lengthy lifespan. In order to "buy time" until the patient is old enough to receive a ceramic inlay/onlay or a full crown, these restorations usually consist of massive resin composites, sometimes reconstructing entire cusps. Unfortunately, some patients return with failed restorations or fractured crowns, which may need tooth extraction.

If such a therapy technique were accessible, such patients could profit from dentin regeneration and tooth structural reinforcement. Numerous scientists have conducted extensive research on biological inducers of dentin mineralization; the following is a concise review of their findings.

Inducing reparative dentin to cure the loss of this tissue caused by the advancement of caries is not a novel concept. Urist 23 revealed for the first time that demineralized bone powder had inductive potential and resulted in ectopic bone production, which stimulated early research on the biological induction of dentin. Like bone, powdered demineralized dentin has the inherent capacity to stimulate mineralization.[24-26]

When applied directly to pulp-exposed areas, demineralized dentin stimulates the production of mineralized tissues locally.[17-18] In the early 1990s, it was revealed that some fractions of dentin, which probably include bone morphogenetic protein (BMP) activity, [29] stimulate reparative dentin production. This discovery led to an understanding of which components of the powdered dentin had the inductive power. [20-21] These observations correlated well with the work of developmental biologists who investigated the involvement of BMPs in the processes leading to the differentiation of odontoblasts and the creation of the dentin matrix<sup>10,32-35</sup> and recommended the possible use of BMPs for dentin regeneration.[19,16]

The ability of pulp cells from (erupted) permanent teeth to respond to inductive cues mediated by BMPs is contingent on the existence of their particular receptors. In fact, BMP receptors (BMPR-IA, -IB, and II) were detected in pulp cells extracted from adult human teeth. [17] Early attempts to promote dentin regeneration using recombinant human proteins utilised BMP-7,38-40 BMP-2, and BMP-4. [21-22] Using collagen-based matrices, the administration of these recombinant proteins induced reparative dentin within two to four months at pulp-exposed areas. The general mechanism behind this reaction is the replacement of stimulating substances in direct contact with the dental pulp by reparative dentin. <sup>36</sup> This feature is seen , where the reparative dentin generated by BMP-7 extends laterally to the floor of the cavity preparation and is not restricted to the pulp-exposed region. The discovery that the area of reparative dentin generated by BMP-7 is exactly related to the amount of BMP-7 applied strengthens this hypothesis. <sup>38</sup> These studies imply that it may be possible to generate a predetermined amount of dentin. In such a circumstance, the physician would be able to reinforce the coronal structure of teeth with significant caries. Notably, after mineralization of the reparative dentin (6 months after treatment), the pulp-lining cells appear non-polarized and flat .

BMP-2, -4, and -7 are not the only molecules capable of inducing dentin formation. When administered to dentin, Growth/differentiation factor 11 (Gdf11) is capable of causing reparative dentin.

#### **Pulp cells by means of a gene transfer technique**

45 Recent research has shown that bone sialoprotein (BSP) induces the differentiation of dental pulp cells into cells that generate an extracellular matrix that is ultimately calcified into reparative dentin at the site of pulp exposure. 46-47 Intriguingly, the scientists discovered distinct morphological differences between the reparative dentin caused by BSP or two types of Amelogenin and that induced by BMP-7. [18-19] These findings reveal the exciting prospect that, in the future, the doctor may be able to select the optimal biological inducer of reparative dentin based on the patient's needs.

Complex is the study of biological inducers of reparative dentin. Undoubtedly, overcoming the inherent problems of treating a tooth with an inflammatory pulp will be one of the most challenging challenges in the future. In addition to stimulating mineralization, these teeth may require a therapeutic drug that controls the inflammatory response and inhibits its progression. Further development of acceptable carriers for the biological inducer of mineralization to be used at the pulp exposure location and possibly in a portion of the cavity preparation is an additional significant issue.

These carriers must be biocompatible and possess physical and mechanical qualities suitable for use in restorative dentistry. In order to prevent microleakage and consequent contamination of the pulp exposure site prior to mineralization of the reparative dentin, a well-sealed restoration will be crucial. The US Food and Drug Administration has not granted approval for the use of a biological inducer for the regeneration of dentin as of yet (FDA, Rockville, MD, USA). However, the FDA has authorised the use of recombinant human BMPs for medicinal applications, such as the acceleration of bone fusion in the treatment of slow-healing bone fractures. Such approval suggests that biological inducers of reparative dentin may find their way into dental clinics once their efficacy and safety have been evaluated in preclinical models and carefully conducted clinical trials.

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### **Regenerative Dentistry: Making the Entire Tooth**

In theory, the optimal method for replacing a tooth lost due to caries or trauma is to produce a new tooth using the patient's own cells. This therapeutic approach was inconceivable till a couple decades ago. Recent advancements in tissue engineering, developmental biology, and stem cell biology have made tooth regeneration increasingly feasible. Clearly, there are numerous barriers to overcome before a patient's full tooth can be engineered. However, the following body of study provides evidence that the way one thinks about restorative dentistry in the future may differ significantly from the way one thinks about it today.

Using cells from the dental pulps of unerupted molars and a scaffold, the Yelick research group at the Forsyth Institute revealed in 2002 for the first time that enamel, dentin, pulp, and a structure resembling a growing root may be produced.<sup>14</sup> In a second article from the same group, the development of the original method for tooth engineering was demonstrated by collecting donor cells, expanding them in culture for a number of days, and then seeding them onto scaffolds.<sup>15</sup> This significant discovery raised the potential that the cells necessary for the bioengineering of teeth could be produced from tiny biopsies taken from the same patient. The sequence of events leading to the creation of artificial teeth resembles the natural odontogenesis process, which is intriguing.<sup>[16]</sup>

Until this method can be used in the clinic, there are unquestionably other obstacles that must be overcome in the field of tooth engineering. A) The scaffold layout will require extensive work before it can fulfil its duty of providing a favourable environment for tooth growth; B) It will be crucial for the clinician to have control over the size and shape of the tooth to be formed and for the procedure's results to be predictable. By altering the quantity of mesenchymal cells connected with epithelial cells in the implants, it is possible to control the shape of the crown and manufacture teeth with predetermined morphologies, according to a recent publication.<sup>80</sup> And

C) the technique for tooth engineering should be reasonably straightforward, regulated, and clinically practical.

## CONCLUSIONS

Dr. Buonocore observed, "Narrow, stereotypical thinking that fails to rationally appraise and utilise the potential of new ideas is unlikely to lead to significant advancement. therapeutic approaches. Fortunately, such attitude has never hindered the dental profession. [21] Dr. Buonocore disrupted traditional paradigms and was met with criticism, as seen by his statement that "the introduction of the successful use of adhesives was naturally accompanied by questions and debates. However, Dr. Buonocore was definitely ahead of his time, and his contributions to dentistry are being felt by dental practitioners and patients all over the world today. In the subject of dental tissue engineering, there are probably more questions than answers.

### Regenerating tooth structures is a difficult task

Dentists attempt to replicate odontogenic processes that nature has already perfected. Conceptually, there is little dispute that tooth structure is the best material for replacing tooth structure. The question facing the field is: Can it be done in a predictable, therapeutically feasible, and practical manner?

The ultimate goal of this field is to regenerate either individual tooth structures or the complete tooth in order to address the repercussions of tooth-related disorders.

### Acknowledgements

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