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Neuro-regenerative Dental Implants: From Osseointegration to Functional Sensory Integration- A Narrative Review

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Abstract
Despite all innovations, traditional endosseous dental implants became an important breakthrough in the field of oral rehabilitation their ability to form a reliable osseointegration. However, compared to natural teeth, implants do not have periodontal ligament (PDL) and mechanoreceptors. Therefore, there are some distinctions in masticatory forces perception and regulation. Osseoperception presupposes the possibility to perceive information through the tissues located around the implants, changes in peripheral nerves and brain mechanisms. Modern research provides the data about the possibility of spontaneous growth of nerves around the implants after the insertion. This process may depend on various conditions, including mechanical loading, implant design, and nerve growth stimulators. The main areas of current research include the ways to promote nerve regeneration around the implant using such approaches as nerve growth factors, neuropeptides, Schwann cells, dental stem cells, biomimetic implants, and responsive materials. Due to recent achievements in the field of mechanobiology, the effects of mechanical stimulation on nerve functions were explored. In particular, piezoelectric technologies may transform mechanical loading into electrical stimuli interacting with the sensory nervous system. The idea of neuro-osseointegration is suggested as a future concept that combines implant stability, nerve regeneration around the implant, mechanosensory function, and central sensory processing, neuroregenerative dental implants offer a promising new way to restore not just the structure and function of natural teeth but also their sensory abilities. The goal of the present narrative review is to examine the biological basis of tooth sensation, innervation around the implants, the mechanisms of osseoperception and the ways to promote nerve growth around the implants. It also explores how bioelectronic and mechanosensitive technologies can improve sensory integration.
Keywords: *Dental implants; osseointegration; osseoperception; peri-implant innervation; neural regeneration sensory integration.*

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I. INTRODUCTION

Modern dental implants are based upon the principle of osseointegration, by which the implant becomes directly anchored to the bone. This has led to the replacement of many teeth that were previously missing. However, a natural tooth is not directly anchored to the bone. Instead, the tooth is suspended within the alveolus by the periodontal ligament (PDL). The PDL contains various components such as fibroblasts, blood vessels, nerves and sensory elements that contribute to the overall health and functioning of the tooth [1-4]. Loss of the PDL after tooth extraction represents both a sensory and structural loss. Conventional implants restore the mechanical part of tooth replacement but do not recreate a true periodontal sensory system. Still, patients with osseointegrated implants can sense contact, pressure, and changes in biting force. This is often referred to as osseoperception [2,3,5,6]. Research in both experimental and human studies has shown peri-implant nerve fibers, neurophysiological responses, and changes in the brain after implant placement [4,6,7] Studies have also reported changes in neural activity and brain responses following implant placement [4,6,7], indicating that the nervous system can adapt to the presence of an implant. Neuroregenerative dental implants are being proposed with this goal, combining osseointegration with neural regeneration, mechanosensory function, and sensory feedback. Neuroregenerative implant implant is a next-generation dental implant designed not only to achieve osseointegration and mechanical stability, but also to promote or support regeneration, reconnection, and functional integration of nerves around the implant. Researches are being drawn on several disciplines, including implantology, periodontal biology, peripheral nerve repair, stem-cell research, biomaterials, mechanobiology, and bioelectronics under which experimental approaches have included Nerve growth factor (NGF) releasing implants , neuropeptide-based strategies, Schwann-cell applications, neural constructs derived from dental pulp stem cells, and biomimetic implant designs. More recently, investigators have examined surgical approaches for improving proprioceptive feedback, Piezo-dependent mechano-transduction, and piezoelectric devices capable of translating biting forces into electrical signals. This review brings the various areas of research such as peri-implant innervation and osseoperception, followed by biological and biomaterial-based approaches to neural regeneration, emerging mechanosensitive and bioelectronic technologies for functional neuro-osseointegration together within a common framework.

II. NEUROBIOLOGY OF THE NATURAL TOOTH

The periodontal ligament as a sensory organ

The PDL has a sensory role in addition to supporting the tooth. It forms a mechanosensory connection between the tooth and the surrounding alveolar bone. Its neural supply includes rapidly and slowly adapting afferent fibres associated with mechanosensory structures, together with free nerve endings involved in pain and other sensory functions. Human studies on neurophysiology show that periodontal afferents can detect tooth loading and provide information that helps control oral movements [1,3]. Periodontal mechanoreceptors respond to subtle tooth displacement as well as changes in biting force. Their signals contribute to the regulation of jaw-closing muscle activity and help the central nervous system determine where forces are applied and its magnitude. Post tooth extraction, the PDL and its special sensory function are lost. Inflammatory processes, vascular changes, osteogenesis and neural remodelling begins to occur. Thus, absence of periodontal mechanoreceptors affects the sensory information that reaches the trigeminal system. Traditional implants provide secure contact with the bone but they are unable to reproduce the precision of sensation offered by the natural periodontal apparatus. The above difference plays a vital role in the theory of neuro-regenerative implantology. Until now, the effectiveness of the implants was estimated in terms of survival, stability and functioning. However, in the future, the level of interaction between the implant and surrounding sensory structures might be evaluated.

OSSEOINTEGRATION, OSSEOPERCEPTION AND SENSORY INTEGRATION

Osseointegration and Osseo perception are two different terms pertaining to implant functions. Osseointegration is about the physical connection between the implant and bone, while Osseo perception pertains to sensory perception connected with Osseo-integrated implant without PDL. Furthermore, Jacobs and Van Steenberghe also proposed the idea that implant treatment could be involved in sensory-motor interactions and not just a replacement for missing tooth [2]. There was a systematic review conducted in 2016 where the results have proven Osseo perception, although there were notable differences in the studies conducted and uncertainty on the mechanisms of how it works. According to a systematic review by Song et al., there were 1,667 studies retrieved from the review and 22 were selected for inclusion in their study. It was shown that psychophysical studies have found that the tactile threshold of implant-supported prostheses is greater than that of natural teeth, while neurophysiological studies have shown cortical plasticity after implants[6]. Taken together, the available findings suggest that sensory recovery can occur around implants, but it does not reproduce the full sensory capacity of a natural tooth. Osseoperception should therefore not be interpreted as proof of complete restoration of the periodontal sensory system. It is more likely to represent the combined effect of several adaptations, including sensory receptors in peri-implant soft tissues, neural structures within bone, proprioceptive input from the masticatory muscles, and changes within the cortex.

EVIDENCE FOR PERI-IMPLANT NEURAL REGENERATION

Histological observations in humans provide important support for the possibility of neural involvement around osseointegrated implants. Corpas and colleagues examined retrieved implants and found myelinated and unmyelinated nerve fibres within Haversian canals of osteonal bone adjacent to the implant threads; myelinated fibres were also identified in woven bone [4]. No differentiated nerve endings were detected. Thus, although these findings confirm the presence of neural tissue, they do not establish that functional mechanoreceptors comparable to those of the PDL are present. In a rat model, Li and colleagues assessed mature and newly regenerated nerve fibres after implant placement using S100 and GAP-43 as markers, respectively [7]. The number of both fibre populations increased during the first 28 days. Reinnervation occurred earlier in the peri-implant soft tissues than in bone, while mature nerve fibres within bone gradually extended toward the implant surface [7]. These observations indicate that neural tissue can undergo an active healing and remodeling process after implant placement rather than remaining permanently absent. From a regenerative standpoint, the time-dependent nature of this process may provide a therapeutic window. If axonal sprouting and neural maturation occur after implantation, targeted delivery of neurotrophic signals, supportive neural cells, or bioinstructive materials could potentially influence the extent, organization, and functional outcome of peri-implant reinnervation.

III. STRATEGIES FOR NEURO-REGENERATION IN DENTAL IMPLANTS

Neurotrophic-factor delivery

Neurotrophic factors have considerable potential in peripheral nerve repair, with NGF being particularly relevant to the survival of sensory neurons and axonal extension. In a canine model of inferior alveolar nerve injury, Lee and colleagues evaluated an NGF-releasing implant. The treatment was associated with improvements in several measures of neural regeneration, including conduction velocity, peak voltage, axon number and density, and myelin thickness, while osseous attachment of the implant was maintained[8]. Another experimental strategy by Ye J et.al incorporated NGF into a chondroitin sulfate/hydroxyapatite coating, in Beagle dogs, this modified surface promoted early bone attachment and was associated with nerve regeneration around the implant[9]. Together, these findings suggest that osteogenic and neuroregenerative functions need not be addressed separately and could potentially be incorporated into a single implant system.

Neuropeptide-based approaches

Calcitonin Gene-Related Peptide (CGRP) has been suggested as another molecular therapy due to its role in neural function, vasculature, and bone. Ma et al. suggested that the local application of α-CGRP may aid in regenerating nerves during peri-implant healing through stimulating the growth of Schwann cells and influencing the behavior of the vasculature and bone[10]. This hypothesis rests on the connection between neural, vascular, and bone healing following injury to the tissues surrounding an implant.

Schwann-cell-based strategies

Schwann cells serve an important function in peripheral nerve regeneration. In response to nerve injury, they develop a reparative phenotype, produce neurotrophic and axon guidance factors, guide axonal growth, and aid in remyelination. The concept of Schwann cell transplants around a prosthetic device was hypothesized by Yuan. et al in order to enhance local neural support and thereby enhance the sensation [11]. Although Schwann cell transplantation for the purposes of enhancing neural support around dental implants is still a novel approach, its scientific feasibility is substantiated by known physiological functions of Schwann cells in peripheral nerve regeneration. In the future, implant surfaces may incorporate Schwann cells or other cell types that will provide neurotrophic support along with extracellular matrix alignment.

Dental pulp stem cells

Dental stem cells have been considered valuable owing to their accessibility in the oral cavity and having the potential of being both neural and neurotrophic. Martens et al. found that human dental pulp stem cells could exhibit Schwann cell properties, produce neurotrophic factors, facilitate neurite outgrowth, and be involved in neurite myelination in an aligned collagen matrix [12]. This is potentially the first step towards bridging the field of dental regeneration with neuroregeneration via the use of an implant. An artificial implant surface or scaffold might theoretically include Schwann-like cells that were derived from dental stem cells in an aligned matrix that facilitates directional growth of axons. However, for a potential clinical application, this technique requires further investigation with respect to cell viability, neural connectivity, and improved sensory function.

Biomimetic implant architectures

Implants fail to have the viscoelastic and mechanoreceptive attributes of the PDL in order to counteract this weakness, a bionic implant containing nano-springs inside to buffer the stress and facilitate neuronal regeneration through NGF was suggested[13]. This design aims to modify the distribution of the masticatory load while enabling osseointegration and osseoperception.Significance of this approach lies in the fact that it tries to compensate for the deficiencies of a biological and mechanical nature simultaneously. Rather than using the surface of the implant as an agent for carrying a regenerative molecule, the structure of the implant is used as well. The implant functions as a biomimetic system that actively modifies force transmission. Although the design remains conceptual and has not been clinically validated, it illustrates a broader direction for implant development: future devices may need to reproduce selected functions of the PDL rather than simply occupy the anatomical space previously occupied by it.

Mechanotransduction and the Piezo Family

Mechanical loading is an inherent part of implant function. Cells within bone and dental tissues sense mechanical forces through mechanotransduction pathways, among which the Piezo family of mechanosensitive ion channels has attracted considerable interest. Piezo1 is widely expressed in non-neural cells, including cells associated with bone, while Piezo 2 is strongly linked to sensory neurons, proprioception, and mechanosensation [15]. The possible role of Piezo signalling in neuroregenerative implants remains largely conceptual, but it may be important. An implant–bone–nerve interface will ultimately need to convert mechanical loading into appropriate biological responses. Calcium entry through Piezo channels could provide a molecular link between mechanical strain, cellular adaptation, bone remodelling, and sensory signalling. Dong and colleagues, in their 2025 review, summarized emerging evidence for Piezo involvement in mechanosensitive processes in bone and dental tissues and discussed its potential relevance to regenerative applications [15]. Piezo biology should nevertheless be interpreted cautiously. Current evidence does not demonstrate that dental implants already produce Piezo-mediated proprioception. Instead, Piezo signalling provides a mechanistic hypothesis that can be tested in peri-implant neural and osteogenic tissues. Future experiments could investigate whether implant geometry, surface nanotopography, loading conditions, or locally delivered biomolecules modify Piezo1 and Piezo2 activity around implants.

Surgical and Biological Strategies

Recent research has begun to move beyond the question of whether osseoperception occurs and toward the possibility of deliberately enhancing proprioceptive feedback, Das and colleagues discussed surgical considerations relevant to this goal, emphasizing the mechanosensory contribution of the PDL and the potential for tissue interfaces to provide sensory input that more closely resembles natural tooth function [14]. This represents a broader change in the way implant design may be approached. Future sensory-oriented implants may depend on more than the choice of titanium or ceramic. Implant positioning, peri-implant tissue architecture, loading conditions, surface chemistry, and regenerative interventions may need to be considered together as components of a single sensory-rehabilitation strategy.

Biological Neuroregeneration to Bioelectronic Sensory Implants

Biological nerve regeneration is only one possible route toward restoring sensory feedback. Developments in smart materials have raised another possibility: converting mechanical loading into electrical signals. Rather than recreating the natural PDL, this strategy creates an artificial mechanosensory interface intended to interact with neural pathways that are already present. Cao and colleagues reported a 3D-printed piezoelectric implanted tooth consisting of a zirconia outer sheath and a lead-free barium calcium zirconate titanate piezoelectric core [16]. The device was designed to translate occlusal loading into electrical signals. In mice, real-time neurological measurements showed brain responses to simulated occlusal stimulation, while the authors reported subjective recovery of masticatory perception in more than 90% of the clinical cases included in their study. This work is notable because it broadens the concept of what a sensory implant could be. A neuroregenerative device would seek to restore sensation through newly regenerated biological neural tissue, whereas a bioelectronic device could generate sensory feedback through an engineered sensing mechanism. At present, the piezoelectric approach should be interpreted cautiously. The clinical findings reported by Cao and colleagues represent an early technology-development study, and independent validation, standardized psychophysical testing, long-term safety evaluation, and controlled clinical trials are required. Nevertheless, the study demonstrates that functional sensory integration is becoming an engineering target rather than merely an observational phenomenon.

IV. FUNCTIONAL NEURO-OSSEOINTEGRATION

The term functional neuro-osseointegration is proposed as a conceptual framework rather than an established clinical diagnosis or treatment. Functional neuro osseointegration would involve the coordinated integration of an implant with bone, peri-implant soft tissues, neural pathways, and mechanical signaling systems to provide both stable anchorage and meaningful sensory feedback. A future neuroregenerative implant could incorporate several components: an osteoconductive and mechanically optimized core; a bioactive surface capable of supporting osteoblast and Schwann-cell interactions; localized release of neurotrophic factors; aligned extracellular-matrix or nanofibrous structures to guide axons; dental stem-cell-derived neural support cells; vascular-promoting signals; and mechanosensitive or piezoelectric elements. A future system could also incorporate mechanosensitive or piezoelectric components. The ultimate goal should not be a higher density of nerve fibres alone; rather, success should be demonstrated by functional sensory outcomes, such as improved tactile thresholds, discrimination of bite force, masticatory control, neurophysiological responses, and potentially measurable changes in cortical representation.

Evidence Landscape and Translational Readiness

Strategy	Primary target	Evidence base	Translational status	Key supporting reference(s)
Osseoperception	Sensory adaptation and mechanosensory feedback	Human + animal studies	Clinically observed; mechanism incompletely defined	Song et al. [1]
Peri-implant reinnervation	Peri-implant nerve fibres and neural integration	Human + animal studies	Biologically demonstrated; functional significance	Huang et al. [2]; Corpas et al. [3]; Song et al. [4]

			requires further clarification	
NGF delivery	Axonal regeneration with concurrent osseointegration	Animal/preclinical studies	Promising but experimental; controlled delivery remains a challenge	Lee et al. [5]; Ye et al. [6]
CGRP/neuropeptide signalling	Neural–vascular–bone signalling and osseoperception	Hypothesis/conceptual evidence	Hypothesis-generating; direct implant-based validation is needed	Ma et al. [7]
Schwann cells	Axonal support, remyelination and neurotrophic signalling	Conceptual + in vitro/preclinical implant literature	Preclinical/conceptual; clinical implant evidence is lacking	Yuan et al. [8,9]
Dental pulp stem cells	Schwann-like differentiation and neurite guidance	In vitro studies	Preclinical; requires validation in peri-implant models	Martens et al. [10]
Bionic implant architecture	Stress cushioning, load transfer and potential sensory integration	Conceptual/hypothesis study	Experimental concept; requires animal and clinical validation	He et al. [11]
Piezoelectric implanted tooth	Conversion of occlusal force into electrical signals for sensory feedback	Animal + early clinical testing	Early translational stage; clinical evidence remains limited	Cao et al. [12]

Table 1 summarizes the principal approaches being investigated for neuroregenerative and sensory-integrated dental implants. The level of supporting evidence varies considerably across these strategies, and direct clinical evidence demonstrating intentional neural regeneration around dental implants is still limited

V. FUTURE RESEARCH DIRECTIONS

Develop standardized definitions to make clear distinctions between peri-implant nerve supply, osseoperception, neural integration, and measurable proprioception. Conduct long-term human studies incorporating histological surrogates, quantitative sensory assessment, bite-force discrimination, electromyography, and neuroimaging. Develop implant coatings with controlled-release systems capable of delivering NGF and other neurotrophic factors to defined peri-implant sites. Evaluate Schwann-cell- and dental-stem-cell-derived neural structures in appropriate peri-implant experimental models. Develop aligned nanofibrous or hydrogel interfaces that can provide directional guidance for axonal growth without compromising bone formation or integration.

VI. CONCLUSION

Neuro-regenerative dental implants, which aim to expand the existing implantation therapy beyond the classical osseointegration by providing biological and functional sensory integration. However, this field is still in its early stages. Most nerve regeneration strategies are still in preclinical phases. The connection between peri-implant nerve fibers and real mechanoreception is not fully known, and there is a lack of standardized sensory measures in humans. Future research needs to be centered on well-conducted investigations that correlate nerve regeneration at the tissue level with sensory effects. Successful implementation would result in transforming the dental implant into the biologically integrated and functionally active device. Neuro-osseointegration can become a promising future concept for the dental implants, but more translational research is needed for applying it to the routine practice.

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