



Review Article

Osseointegrated Implants and Osseoperception - A Review

Kumari Deepika^{1,*}, Atul Bhatnagar², Rekha Gupta³¹Senior Resident, Department of Prosthodontics, Maulana Azad Institute of Dental Sciences, New Delhi-110002, India²Professor and Head of Unit of Prosthodontics, Faculty of Dental Sciences, Institute of Medical Sciences, Banaras Hindu University, Varanasi, 221005, U.P., India³Professor and Head of Department of Prosthodontics, Maulana Azad Institute of Dental Sciences, New Delhi-110002, India

ARTICLE INFO

Article history:

Received 31.10.2021

Accepted 12.04.2022

Published 08.07.2022

* Corresponding author.

Kumari Deepika

deepika12031990@gmail.com

[https://doi.org/](https://doi.org/10.38138/JMDR/v8i1.21.17)

10.38138/JMDR/v8i1.21.17

ABSTRACT

There are many studies suggest that a peripheral feedback pathway can be restored with osseointegrated implants even after tooth loss. This implant mediated sensory-motor control, known as osseoperception may have important clinical implications in improving masticatory function with implant supported prosthesis. To understand this psychophysical integration of implants, available literature was evaluated using various online resources such as Pubmed, Google scholar, etc. using keywords like “osseoperception”, tactile sensibility, implant mediated sensory-motor control and mechanoreceptors. The long-term integration of an implant-bone restoration depends in part on optimal load distribution on the bearing tissue. Because natural teeth and implants vary in their anchorage mechanisms so there is a fundamental difference in the perception and control of the loading. The current review of literature deals with these issues and has been summarized under following heads:

- Mechanism of osseoperception
- Neurophysiological and psychophysical methods of assessing phenomenon of osseoperception
- Mechanoreceptors contributing to osseoperception
- Different concepts of osseoperception

Keywords: Osseointegration; osseoperception; active threshold; passive threshold; dental implant

1 INTRODUCTION

Today, dental implant is the most common treatment modality to replace missing teeth with a survival rate of 95% in most of the published long-term studies.⁽¹⁾ Treatment success of dental implants is generally defined by the stability of the implant. It is an indirect indication of osseointegration (a term originally proposed by Branemark et al. 1969). Albrektsson et al. (1981) defined osseointegration as “a direct functional and structural connection between living bone and the surface of a load carrying implant.”

When osseointegrated dental implants are mechanically loaded, a sensory action, often referred to as Osseoperception, is evoked. The term “Osseoperception” was coined by Prof. P-I Branemark and defined in various ways by many authors, one of which defined this phenomenon as a “conscious perception of external stimuli transmitted via a bone-anchored prosthesis by activation of neural endings

and/ or receptors in the peri-implant environment”.⁽²⁾ In the past, it has been studied that in a limb, part of which has been amputated, the number of sensory receptors gets reduced and thus impair the somatosensory feedback mechanisms. Many attempts have been made to provide sensation for amputees by sensory substitution (Kaczmarek et al., 1991). Sensory feedback systems used for limb prostheses may rely on pressure, electro tactile or vibrotactile skin stimulation (Kaczmarek et al, 1991; Patterson and Katz, 1992; Kyberd et al, 1993). The conventional socket prosthesis (soft tissue support) or a prosthesis anchored to the bone by means of a percutaneous osseointegrated implant (direct bone-implant contact) was used in the rehabilitation of patients with amputated limbs (Branemark et al, 1996). Conventional socket prosthesis does not carry enough sensory information to restore the necessary natural feedback pathways for motor function. It has been reported that patients with amputated limbs rehabilitated

with a bone-anchored prosthesis seem to have a subjectively improved ability to feel through their prosthesis & are able to differentiate between walking on different types of soils, from where the concept of 'osseoperception' emerged (Branemark, 1997; Rydevik, 1997).⁽³⁾

Similar phenomenon can be seen after extraction of teeth. The periodontal ligament harbours very rich innervations, carrying refined mechanoreceptive properties by an intimate contact between collagen fibres and Ruffini-like endings that play an important role in peripheral feedback pathway. This peripheral pathway may be damaged after tooth extraction as periodontal ligament receptors are eliminated. Dentures can be compared with socket prosthesis and are not able to fully compensate for normal tooth loading and force transfer as the mucosal mechanoreceptor function is less efficient than the periodontal ligament function. Consequently, oral function remains impaired.⁽⁴⁾

The introduction of osseoperception unveiled the mechanisms responsible for sensory perceptions of external mechanical stimuli by oral implants, as sensory inputs also play a crucial role in function (Jacobs 1998; Van Steenberghe 2000). Because of rapid regeneration of nerves and consequent innervation in the vicinity of implants (Wang et al. 1998; Van Loven et al. 2000; Ysander et al. 2001), a substantial enhancement in the capacity to distinguish external mechanical stimuli has been reported by many patients rehabilitated with orthopedic and/or oral implants (Jacobs 1998; Van Loven et al. 2000). The osseoperception of implants results from neuropeptide and chatecholaminergic innervation of bone and periosteum (Bjurholm et al. 1988a, 1988b; Hill & Elde 1991), but the specific neurophysiological function of these structures in the vicinity of implants is still unknown (Herskovits et al. 1990).⁽⁵⁾

1.1 Mechanism of osseoperception

Sensory feedback pathway is different for implant than natural teeth. Oral kinesthetic and proprioceptive sensations involved in the detection of static jaw position and velocity of jaw movement and forces generated during contractions of the jaw muscles. While there has been extensive study of the neural basis of limb kinesthetic sensibility, we have much less understanding of the neural mechanisms of oral kinesthesia in dentate individuals and also in patients with implant-supported prostheses who lack periodontal mechanoreception. The CNS obtains information about the positions and movements of limbs and forces of limb muscle contraction, i.e., limb kinesthesia (Mc Closkey, 1978; Clark and Horch, 1986) by the following 2 mechanisms that also run for oral kinesthetic perception.

1. By monitoring a corollary discharge of the descending central command to muscles. This mechanism is thought to provide the sensation of muscular force which accompanies centrally generated voluntary motor commands (Mc Closkey, 1978, 1981; Bennett, 1997).

2. It is derived from mechanoreceptors activated during limb and jaw movements and at different limb and jaw positions (limb kinesthesia). In oral kinaesthesia (implant-supported prostheses) despite lacking periodontal mechanoreceptive input, this is derived from temporomandibular joint (TMJ), muscle, cutaneous, mucosal, and/or periosteal mechanoreceptors, and provides mechanosensory information in relation to jaw function and artificial tooth contacts. The relative contributions of these different mechanoreceptors to osseoperception in patients with implant-supported prostheses are unclear.⁽⁶⁾

1.2 Neurophysiological versus psychophysical methods

The oral tactile function has been examined by neurophysiological as well as psychophysical methods.

1.2.1. Neurophysiology

The human periodontal ligament contains various mechanoreceptor morphologies, which may all contribute to the exteroceptive function. Periodontal mechanoreceptors play the primary role in tactile function of teeth & are very sensitive to external forces applied to the teeth. The majority of the periodontal mechanoreceptor unit in man adapt slowly with low force threshold. This is in agreement with results from animal species. Periodontal mechanoreceptors also exhibit directional sensitivity which implies that they respond maximally to force applied in a particular direction. Furthermore, rate & magnitude of force applied to the tooth may modify the response characteristics of the mechanoreceptors.

Neurophysiological investigations on the sensory function of the trigeminal system in humans are scarce. Evidence can be found by non-invasive approaches for evaluation of oral tactile function. The first approach is the recording of the so-called trigeminal somato sensory evoked potentials (TSEP) after stimulation of receptors in the oral cavity.^(7,8) Another non-invasive method to assess sensory function is the visualization of brain activities by functional magnetic resonance imaging (fMRI).⁽⁹⁾

1.2.2. Psychophysics

Psychophysical studies on the oral sensory function are numerous and its major advantage is that these are simple non-invasive techniques that may be performed in a clinical environment. Psychophysics includes a series of well defined methodologies to help determining the threshold level of sensory receptors in man. Psychophysical methods allow connecting the psychological response of the patient to the physiological functions of the receptors involved. When performed meticulously and under standardized conditions, these studies may provide nearly as precise information as neurophysiological setups.

In the psychophysical approach, a clear distinction should be made between the “passive” threshold or detection of the force applied to the teeth and the “active” one, where interocclusal detection of the small objects such as strips or foils of varying thickness is performed. The large discrepancies between active and passive thresholds can be explained by the fact that several receptor groups may respond to active testing (active threshold determination provide a means to observe a parameter of jaw motor control), this may involve the activation of mechanoreceptors, mainly originating from the peridontium but also from the muscles, inner ear, and TMJ. The periodontal mechanoreceptors involved in the passive threshold determination although not in a very physiological situation. It should, however, be realized that the foil materials used for active threshold detection may have different thermal and mechanical properties, resulting in conflicting results (Jacobs et al. 1992). Foil materials with high thermal conductivity (e.g. steel, aluminium) may lower the threshold level by activation of thermal receptors.⁽¹⁰⁾

The active detection task is further divided into a static and a functional threshold determination.⁽¹¹⁾ Absolute as well as differential threshold determination can be performed in both cases. The absolute threshold (RL, for the German Reiz Limen) is the stimulus amplitude at which a subject detects the stimulus, whereas the differential threshold (DL, for the German Differenz Limen) can be expressed as the smallest increment of the stimulus which is just detectable by the subject. The endosseous implants are less sensitive than natural teeth for the passive DL level of forces but seem equally sensitive at force levels in the order of chewing forces. Different stimulating devices are proposed for the passive detection of forces applied to a tooth. The active threshold is seven to eight times higher for dentures but only three to five times higher for implants when compared with tactile function of natural dentition. For the passive detection of forces applied to upper teeth, thresholds increased 75 times for dentures and 50 times for implants.

In psychophysical threshold determination, a threshold range rather than an absolute value exists. A subject uses his own criteria to discriminate between stimulus and noise. The reliability of the responses are affected by the subject's attention and psychological attitude. Unfortunately, tactile threshold determination is often performed without using an appropriate psychophysical methodology.⁽¹²⁾ Environmental factors should be well-controlled as background noise is distracting to patient and examiner. To minimize the effect of noise, testing should be done in a quiet room with stable background illumination.

1.3 Mechanoreceptors contributing to osseoperception

In oral motor function like biting, chewing, speech and oral manipulation, the brain relies on information from sense

organs in the orofacial structures to control motor function. Natural teeth are equipped with extremely sensitive tactile sensors – periodontal mechanoreceptors. These sensors provide information about tooth loads and are located in periodontal ligaments. Human teeth are sensitive to very small forces applied to the teeth. Pfaffmann⁽¹³⁾ noted that a 0.01-0.02 Newton force is sufficient to evoke a response from the majority of the mechanoreceptors of the cat's dental nerve. Removal of pulp did not change the response. Linden also found no significant difference between the threshold level of vital and non-vital teeth. It is evident that periodontal receptors responsible for the tactile function of teeth. In contrast, Loewenstein and Rathkamp⁽¹⁴⁾ reported an increased threshold for both pulpless and vital teeth covered with metal caps and suggested that both interdental and periodontal mechanoreceptors are concerned in tactile function. In edentulous jaws, the performance of detection or discrimination tasks is even worse. Although edentulous patients still keep mechanoreceptors in the gingiva and the periosteum of the jaw bone. These receptors only differ from periodontal ligament receptors in their receptive phase. Thus, “periodontal feedback” and its exteroceptive function not completely lost in edentulousness. When patients are rehabilitated with endosseous implants, the active absolute threshold level is increased when compare to the natural dentition but remains below the threshold noted in the denture wearers.^(15,16) The rapid elastic bone deformation during implant loading may trigger periosteal receptors which however remain less sensitive than the periodontal ligament receptors.

The role of mechanoreceptors in context to the implant-supported prostheses:

1.3.1. Joint Mechanoreceptors

Low-threshold mechanoreceptors are present in the TMJs and in other joints of the body. These receptors could potentially provide detailed information to jaw position and movement [described in the TMJs of rabbits; these have been classified as limited-range receptors (Lund and Matthews, 1981).

1.3.2. Muscle Mechanoreceptors

i. **Golgi tendon organs:** are found at the musculo-tendinous junction in series, with a small number of extrafusal muscle fibers, activated by the pull of the muscle fibers and with muscle contraction. Golgi tendon organs are the most appropriate mechanoreceptors for signalling during voluntary contractions such as biting.

ii. **Muscle spindles:** are the most complex somatosensory receptor in the body with sophisticated physiological properties and they provide detailed information on muscle length and rate of length change. These receptors help in the assessment of jaw position and movement.

1.3.3. Cutaneous Mechanoreceptors

Cutaneous mechanoreceptors in the facial skin are activated by skin stretching or contraction of facial muscles and may operate as proprioceptors involved in facial kinaesthesia and motor control.

1.3.4. Mucosal Mechanoreceptors

When natural teeth are present, periodontal mechanoreceptors are important for refined interdental discriminative function. Whereas after tooth loss, in implant-supported prostheses opposing complete dentures, this oral kinesthetic perception could come from the activation of mucosal receptors beneath the complete denture and possibly periosteal and/or mucosal mechanoreceptors in the vicinity of the implant fixture (Jacobs and Van Steenberghe, 1991).

1.3.5. Periosteal Mechanoreceptors

The periosteum contains free nerve endings, complex unencapsulated and encapsulated endings. By pressure or stretching of the periosteum through the action of masticatory muscles and the skin, free nerve endings gets activated. When applying forces to osseointegrated implants in the jaw bone, it might be assumed that the pressure build-up in the bone is sometimes large enough to allow deformation of the bone and its surrounding periosteum (Sakada, 1983; Capra and Dessem, 1992).⁽⁶⁾

After activation of peripheral receptors or mechanoreceptors, nerve impulse generate action potential and motor response is triggered (Figure-1).⁽¹⁷⁾

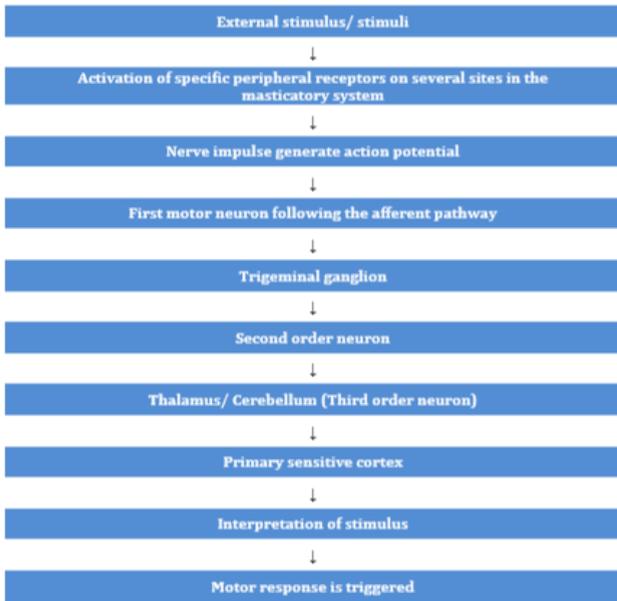


Fig. 1: Motor response after mechano receptor activation (Ramfjord & Ash 1972; Sakada 1974; Van Loven et al. 2000)

1.4 Different concepts of osseoperception

1.4.1. Partial generation of Peridontal Ligament

Buser et al (1990)⁽¹⁸⁾ in their study placed titanium implants in the mandible of monkeys where apical root portions were retained. The histological examination revealed that a cementum layer with inserting collagen fibers was achieved around implants. These results concluded that dental implants with a true PDL can be accomplished.

Takata et al (1993)⁽¹⁹⁾ studied that a new connective tissue attachment can occur on a hydroxyapatite surface(HA) when PDL-derived cells with the ability to form new connective tissue attachment are allowed to populate the surface of HA in an experiment.

Warrer et al (1993)⁽²⁰⁾ also found that a PDL can form on titanium dental implants in areas where a void is present between the surrounding bone and the implant at the time of insertion.

Choi (2000)⁽²¹⁾ in study on dog mandible found that cultured PDL cells can form tissue resembling a true PDL around implants.

Jahangiri et al (2005)⁽²²⁾ in animal study (beagle dog) succeeded to partially regenerate the periodontal ligament on an implant surface. In this study, orthodontic tooth movement was initiated following implant placement to tip the first pre-molar roots into contact with the implant; an animal model was established in which the proximity of tooth-to-implant contact lead to partial generation of PDL on a bioactive implant surface

1.4.2. Mechanoreceptors in the Periosteum

It has been studied that existing mechanoreceptors in the periosteum may also play a role in tactile function upon implant stimulation in a study by Jacobs and van Steenberghe (1991).⁽⁶⁾

1.4.3. Reinnervation (Free- nerve endings)

Histologically, it has been seen that there may be some reinnervation around osseointegrated implants.

Tanaka et al (1996)⁽²³⁾ in immunocytochemical study of nerve fibres containing substance P in the junctional epithelium of rats found that substance P & free nerve endings respond to pain, touch and pressure.

Lambrichts (1998)⁽²⁴⁾ in animal study reported the presence of neural fibres in the immediate vicinity of implants in the cat's jaw. Whereas Wang et al (1998)⁽²⁵⁾ reported that nerve fibres increase their density over time at the implant/ bone interface. In a study by Ysander et al (2001)⁽²⁶⁾, the nerve fibres were detected in the remodelled bone adjacent to the implants.

1.4.4. Muscle spindle and joint receptors

According to Klineberg & Murray (1999)⁽⁶⁾, sensory response comes from the muscle spindle and joint receptors

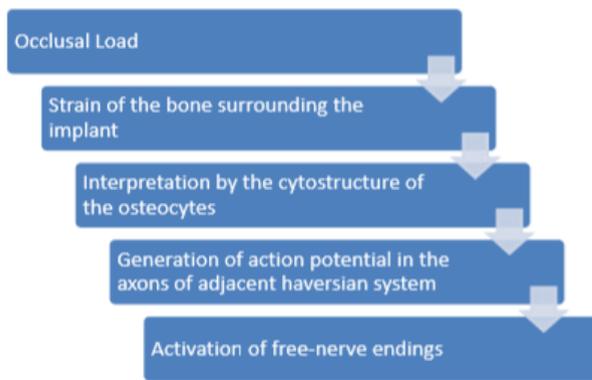


Fig. 2: Activation of nerve endings after implant loading

that substitute for the PDL of natural teeth.

1.4.5. Nerve regeneration in response to Implant Loading

Bonte et al (1993)⁽²⁷⁾ in animal study on cat jaw muscle observed that when forces are applied to a tooth, periodontal mechanoreceptors, which evoke reflex inhibitions to motor units in the jaw-closing muscles, are stimulated; however, there is evidence that mechanoreceptors situated distant to the periodontium can also evoke such reflexes.

It has been documented that reinnervation in association with controlled forces directed to implants results in proprioception. This is due to the regeneration of new nerve fibers around the implant with physiologic loading when osseointegration is near to woven bone.

Wada et al (2001)⁽²⁸⁾ observed the effects of occlusal forces on the distribution of neurofilament protein (NFP) positive nerve fibres around peri-implant bone in animal study. Indeed, it has been shown that there is degeneration of envioning neural fibres by surgical trauma during endosseous implant placement but soon after there is sprouting of new fibres gradually during the first week of healing.

1.4.6. Peri-implant Bone deformation responsible for tactile sensibility

In an animal study by Saul Weiner et al (2004)⁽²⁹⁾, it was found that loading of implants elicit a sensory response in the inferior alveolar nerve observed in neurophysiologic recordings. In an animal study by Fujii et al (2003)⁽³⁰⁾, they found that the peri-implant epithelium shows the same innervations as that in normal junctional epithelium. Similar results were seen by Suzuki et al (2005)⁽³¹⁾.

According to Skada S (1974)⁽³²⁾, it is evident that oral implants offer another type of loading and force transfer than teeth, considering an intimate bone-to-implant contact with elastic bone properties different from viscoelasticity of the periodontal ligament in natural dentition. Thus, forces

applied to osseointegrated implants are directly transferred to the bone and bone deformation may lead to receptor activation in the peri-implant bone and the neighbouring periosteum.

Yamashiro T et al (2001)⁽³³⁾, studied that bone strain, either compression or elongation, may serve to activate free nerve endings that project through the inferior alveolar nerve (IAN) to regions of the trigeminal system in the pons where jaw motor activity is mediated (Figure-2.). Schulte (1995)⁽³⁴⁾ studied tactile sensibility of implants versus natural teeth. Passive tactile sensibility seems to be less clearly localized in the case of implants when compared to natural teeth. He had found that the deformation of the peri-implant bone, which might cause stretching of the periosteum was responsible for tactile sensibility.

1.5 Residual Nerve Fibres

Heasman PA (1984)⁽³⁵⁾ found that after extraction of teeth, the myelinated fibre content of the inferior alveolar nerve is reduced by 20%. This finding indicates that fibres originally innervating the tooth and periodontal ligament are still present in the inferior alveolar nerve. Linden and Scott (1989)⁽³⁶⁾ succeeded to stimulate nerves of periodontal origin in healed extractions sockets, which implies that some nerve endings remain functional. Nevertheless, most of the surviving mechanoreceptive neurons represented in the mesencephalic nucleus may lose some functionality.⁽³⁷⁾

Recently, it has been also seen that immediately placed implants followed by immediate loading indicate better tactile function due to better peri-implant innervation recovery in comparison to delayed implant placement and delayed loading. This mechanism is still unclear it can be assumed that immediate implant placement after extraction leaves the nerves in place with activation that prevents degeneration. Upon implant loading, sufficient stimulation of dedifferentiated Schwann cells and/or activation of peri-implant nerve signals might occur to promote peri-implant nerve regeneration.⁽³⁸⁾

2 CONCLUSION

The ankylosed implants have better tactile sensibility even after lacking PDL, implying that there is partial substitution of sensory feedback in the presence of implants. This implant-mediated sensory-motor control may have important clinical implications, because it improves the masticatory efficiency and inhibitory reflex response in the masticatory muscles that prevents traumatic occlusion. It also helps in assessing sensory discriminative potentials and thus decreasing the risk of overloading. Further researches and long-term studies are required to understand this physiological & psychophysical integration of the implant for improving masticatory function and implant success.

REFERENCES

- 1) Fugazzotto PA. Success and failure rates of osseointegrated implants in function in regenerated bone for 72 to 133 months. *Int J Oral Maxillofac Implants*. 2005;20:77–83. Available from: <https://pubmed.ncbi.nlm.nih.gov/9048450/>.
- 2) Abarca M, Steenberghe D, Malevez C, Jacobs R. The neurophysiology of osseointegrated oral implants. A clinically underestimated aspect. *Journal of Oral Rehabilitation*. 2006;33(3):161–169. Available from: <https://doi.org/10.1111/j.1365-2842.2005.01556.x>.
- 3) Jacobs R, Brånemark R, Olmarker K, Rydevik B, Van Steenberghe D, Brånemark P. Evaluation of the psychophysical detection threshold level for vibrotactile and pressure stimulation of prosthetic limbs using bone anchorage or soft tissue support. *Prosthetics & Orthotics International*. 2000;24(2):133–142. Available from: <https://doi.org/10.1080/03093640008726536>.
- 4) Jacobs R, Steenberghe DV. From osseoperception to implant-mediated sensory-motor interactions and related clinical implications*. *Journal of Oral Rehabilitation*. 2006;33(4):282–292.
- 5) Onur MA, Sezgin A, Gurdinar A, Sommer A, Akca K, Cehreli MC. Neural response to sandblasted/acid-etched, TiO₂-blasted, polished, and mechanochemically polished/nanostructured titanium implant surfaces. *Clinical Oral Implants Research*. 2006;17(5):541–547. Available from: <https://doi.org/10.1111/j.1600-0501.2006.01255.x>.
- 6) Klineberg I, Murray G. Osseoperception: Sensory Function and Proprioception. *Advances in Dental Research*. 1999;13(1):120–129. Available from: <https://doi.org/10.1177/08959374990130010101>.
- 7) Van Loven K, Jacobs R, Van Hees J, Van Huffel S, Van Steenberghe D. Trigeminal somatosensory evoked potentials in humans. *Electromyogr Clin Neurophysiol*. 2001;41:357–375.
- 8) Swinnen A, Van Huffel S, Van Loven K, Jacobs R. Detection and multichannel SVD-based filtering of trigeminal somatosensory evoked potentials. *Medical and Biological Engineering and Computing*. 2000;38(3):297–305.
- 9) Spiegel J, Tintera J, Gawehn J, Stoeter P, Treede RDD. Functional MRI of human primary somatosensory and motor cortex during median nerve stimulation. *Clinical Neurophysiology*. 1999;110(1):47–52. Available from: [https://doi.org/10.1016/s0168-5597\(98\)00043-4](https://doi.org/10.1016/s0168-5597(98)00043-4).
- 10) Lindhe J, Lang NP, Karring T. *Clinical Periodontology and Implant Dentistry*. 5th ed. 2008.
- 11) Owall B. Interocclusal perception during mastication: a review of literature. *Swed Dent J*. 1976;69:7–13.
- 12) Jacobs R, Steenberghe D. Role of periodontal ligament receptors in the tactile function of teeth: a review. *Journal of Periodontal Research*. 1994;29(3):153–167. Available from: <https://doi.org/10.1111/j.1600-0765.1994.tb01208.x>.
- 13) Pfaffmann C. Afferent impulses from the teeth due to pressure and noxious stimulation. *The Journal of Physiology*. 1939;97(2):207–219. Available from: <https://doi.org/10.1113/jphysiol.1939.sp003800>.
- 14) Loewenstein WR, Rathkamp R. A Study on the Pressureceptive Sensibility of the Tooth. *Journal of Dental Research*. 1955;34(2):287–294. Available from: <https://doi.org/10.1177/00220345550340021701>.
- 15) Lundqvist S, Haraldson T. Occlusal perception of thickness in patients with bridges on osseointegrated oral implants. *European Journal of Oral Sciences*. 1984;92(1):88–92.
- 16) Jacobs R, Steenberghe DV. Comparative evaluation of the oral tactile function by means of teeth or implant-supported prostheses. *Clinical Oral Implants Research*. 1991;2(2):75–80.
- 17) Batista M, Bonachela W, Soares J. Progressive recovery of osseoperception as a function of the combination of implant-supported prostheses. *Clinical Oral Implants Research*. 2008;19(6):565–569.
- 18) Buser D, Warrer K, Karring T. Titanium implants with a true periodontal ligament: an alternative to osseointegrated implants? *Int J Oral Maxillofac Implants*. 1990;5:113–116. Available from: <https://pubmed.ncbi.nlm.nih.gov/2133335/>.
- 19) Takata T, Katauchi K, Akagawa Y, Nikai H. New periodontal ligament formation on a synthetic hydroxyapatite surface. *Clinical Oral Implants Research*. 1993;4(3):130–136. Available from: <https://doi.org/10.1034/j.1600-0501.1993.040303.x>.
- 20) Warrer K, Karring T, Gotfredsen K. Periodontal Ligament Formation Around Different Types of Dental Titanium Implants. I. The Self-Tapping Screw Type Implant System. *Journal of Periodontology*. 1993;64(1):29–34. Available from: <https://doi.org/10.1902/jop.1993.64.1.29>.
- 21) Choi BH. Periodontal ligament formation around titanium implants using cultured periodontal ligament cells: a pilot study. *Int J Oral Maxillofac Implants*. 2000;15:193–196.
- 22) Jahangiri L, Hessamfar R, Ricci JL. Partial generation of periodontal ligament on endosseous dental implants in dogs. *Clinical Oral Implants Research*. 2005;16(4):396–401. Available from: <https://doi.org/10.1111/j.1600-0501.2005.01152.x>.
- 23) Tanaka T, Kido MA, Ibuki T, Yamaza T, Kondo T, Nagata E. Immunocytochemical study of nerve fibers containing substance P in the junctional epithelium of rats. *Journal of Periodontal Research*. 1996;31(3):187–194.
- 24) Lambrichts I. Histological and ultrastructural aspects of bone innervation. Jacobs R, editor;Leuven, Belgium. Osseoperception. 1998.
- 25) Wang YH, Kojo T, Ando H. Nerve regeneration after implantation in peri-implant area. A histological study on different implant materials in dogs. Jacobs R, editor;Leuven, Belgium. Osseoperception. 1998.
- 26) Ysander M, Branemark R, Olmarker K. Intramedullary osseointegration: development of a rodent model and study of histology and neuropeptide changes around titanium implants. *J Rehabil Res Dev*. 2001;38:183–190. Available from: <https://pubmed.ncbi.nlm.nih.gov/11392651/>.
- 27) Bonte B, Linden RW, Scott BJ, Steenberghe DV. Role of periodontal mechanoreceptors in evoking reflexes in the jaw-closing muscles of the cat. *The Journal of Physiology*. 1993;465(1):581–594.
- 28) Wada S, Kojo T, Wang YHH, Ando H, Uchida Y, Nakanishi E, et al. Effect of loading on the development of nerve fibers around oral implants in the dog mandible. *Clinical Oral Implants Research*. 2001;12(3):219–224.
- 29) Weiner S, Sirois D, Ehrenberg D, Lehrmann N, Simon B, Zohn H. Sensory responses from loading of implants: A pilot study. *The International Journal of Oral & Maxillofacial Implants*. 2004;19(1). Available from: <https://pubmed.ncbi.nlm.nih.gov/14982354/>.
- 30) Fujii N, Ohnishi H, Shirakura M, Nomura S, Ohshima H, Maeda T. Regeneration of nerve fibres in the peri-implant epithelium incident to implantation in the rat maxilla as demonstrated by immunocytochemistry for protein gene product 9.5 (PGP9.5) and calcitonin gene-related peptide (CGRP). *Clinical Oral Implants Research*. 2003;14(2):240–247. Available from: <https://doi.org/10.1034/j.1600-0501.2003.140216.x>.
- 31) Suzuki Y, Matsuzaka K, Ishizaki K, Tazaki M, Sato T, Inoue T. Characterization of the peri-implant epithelium in hamster palatine mucosa: Behavior of Merkel cells and nerve endings. *Biomedical Research*. 2005;26(6):257–269.
- 32) Sakada S. Mechanoreceptors in fascia, periosteum and periodontal ligament. *Bull Tokyo Med Dent Univ*. 1974;21:11–13.
- 33) Yamashiro T, Fukunaga T, Kobashi N, Kamioka H, Nakanishi T, Takigawa M, et al. Mechanical Stimulation Induces CTGF Expression in Rat Osteocytes. *Journal of Dental Research*. 2001;80(2):461–465. Available from: <https://doi.org/10.1177/00220345010800021201>.
- 34) Schulte W. Implants and the periodontium. *Int Dent J*. 1995;45:16–26.
- 35) Heasman PA. The myelinated fibre content of human inferior alveolar nerves from dentate and edentulous subjects. *Journal of Dentistry*. 1984;12(4):283–286.
- 36) Linden RWA, Scott BJJ. The effect of tooth extraction on periodontal ligament mechanoreceptors represented in the mesencephalic nucleus of the cat. *Archives of Oral Biology*. 1989;34(12):937–941. Available from: [https://doi.org/10.1016/0003-9969\(89\)90049-6](https://doi.org/10.1016/0003-9969(89)90049-6).
- 37) Mishra SK, Chowdhary R, Chrcanovic BR, Brånemark PI. Osseoperception in Dental Implants: A Systematic Review. *Journal of Prosthodontics*. 2016;25(3):185–195.
- 38) Huang Y, Dessel JV, Martens W, Lambrichts I, Zhong WJJ, Ma GWW, et al. Sensory innervation around immediately vs. delayed loaded implants: a pilot study. *International Journal of Oral Science*. 2015;7(1):49–55.