



REVIEW ARTICLE

LIGAPLANT- A REVOLUTIONARY CONCEPT OF PERIODONTIO-INTEGRATED IMPLANTS

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ABSTRACT

Missing tooth replacement is a patient's demand dentists have to meet without fail. Replacement by implants has gained a lot of popularity among patients nowadays. Oseo-integrated implants present a challenge of excessive stress accumulating at the crestal region of the implants leads to bone loss whereas, periodontal-integrated implants i.e.,- leadplants have the potential of PDL regeneration thus mimicking the natural tooth in distributing the forces throughout the length of the root. The regenerated periodontal ligament dissipates these forces through the compression and redistribution of its fluid elements, as well as through its fiber system and hence provides shock absorption and cushioning effect to the implant in response to these forces. Although it is a technique sensitive procedure, leadplants can alleviate problems which implant usually faces such as infrasonic defects, gingival recession of the missing tooth site. Thus, it can be understood that generating a periodontal-like tissue around implants is possible and might be the future in the field of implantology. An online search was done on Google Scholar search platform, on the topic of leadplant. Relevant articles have been referred to throw some light on this concept. This review article includes references of publications from 1982-2020, which is related to promising outcomes of use of periodontio-integrated implants over the conventional oseo-integrated ones.

KEYWORDS- Dental implants, Periodontal Ligament, Ligaplant, Periodontio-integrated implant.

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INTRODUCTION-

The periodontal ligament is composed of connective tissue which is highly cellular and vascular, that surrounds the tooth root and connects it to the inner lining of the alveolar bone¹. Apart from its physical, formative and remodelling, nutritional, and sensory functions, the periodontal ligament also provides progenitor cells which make formation and remodelling of alveolar bone possible which then plays the role of periodontium in the alveolar socket that holds and contains the root of the tooth^{2, 3, 4, 5}.

The periodontal ligament attaches to cementum and the alveolar bone and primarily consisting of collagen fibres, fibroblast, cement oblasts, osteoblasts, osteoclasts and their progenitors. The ends of PDL fibres are embedded in cementum and the alveolar bone called as the Sharpey's fibres and they are directed perpendicular to the tooth surface. This type of arrangement maintains the structural integrity of the PDL and also enables the distribution of masticatory forces onto the alveolar bone⁶.

Regeneration of lost periodontium can be done by the periodontal therapy especially in cases of severe destruction where attachment to tooth has been lost. Regeneration of periodontal ligament fibres and insertion of same into the root surface leads to formation of new attachment. The same concept of PDL regeneration has been carried out for replacement of lost tooth on the surface of dental implants.

Periodontal ligament having regenerative capacity and thus this concept is used to formulate tissue engineered periodontal ligament cells on the implant surface thus mimicking the natural tooth. This forms the new emerging era in the field of dentistry with implant and periodontal ligament together known as ligaplant^{7, 8}.

HISTORICAL BACKGROUND

For the development of possible periodontal ligament around an implant, several experiments have been carried out and a lot of research was put to work i.e., for the creation of a bio-root, which would provide ideal conditions for the implant-supported treatments in future^{9, 10}.

Nyman et al.¹¹ in 1982 explained that the periodontal ligament and its cells have the capability to restore the connective tissue attachment. Nunez et al.¹² (2012) have further confirmed the regenerative potential of periodontal ligament-derived cells in his principle study.

A study was conducted by Buser et al in 1990, in which he found that the periodontal ligament cells could be a source of regeneration as they have the ability to cover the surface of dental implants during healing period.

Several in vivo experiments have demonstrated the formation of cementum-like tissue with an intervening periodontal ligament, when the dental implants were placed in proximity to tooth roots by Buser et al.(1900), Caiazza et al. (1991), Warrier et al (1993). The possible explanation of this event appeared to be due to the migration of cementoblast and periodontal ligament fibroblast precursor cells towards dental implants due to contact or proximity of these cells to those of implants¹³.

This potential of customized periodontal biomimetic hybrid scaffolds for engineering human tooth-ligament interfaces to be applied clinically has been demonstrated by Park et al¹⁴. There is indeed a growing body of evidence validating the significant potential of the in vivo formation of ligamentous attachments to the biomaterials.

Piatelli et al. 1994 evaluated the potential of different cells of the forming tooth bud to induce formation of dental hard tissues and PDL around titanium implants and showed it is positive result.

Takata et al.,¹⁵ in 1994 in an animal study examined whether connective tissue attachment could occur on implant materials by repopulating periodontal ligament derived cells and found that while new connective tissue attachment was seen on bioactive materials such as bioglass and hydroxyapatite, little or no cementum deposition was seen on bioinert materials such as titanium alloy and partially stabilized zirconium, i.e., the formation of new connective tissue attachment was due to the bioactivity of the materials. Choi,(2000)¹⁶ placed implants with the cultured autologous periodontal ligament cells in the mandibles of the dogs and histologically revealed that after 3 months of healing, a layer of cementum-like tissue with inserting collagen fibers had been achieved on some implant surfaces, demonstrating that cultured periodontal ligament cells can form tissue resembling a true periodontal ligament around implants¹⁰.

OSSEOINTEGRATED IMPLANTS VERSUS PERIODONTIO-INTEGRATED IMPLANTS

Eliminating localized bone loss around osseointegrated implants is a clinical challenge yet to be overcome¹⁷. Excessive stress accumulating at the crestal

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region of the implants leads to bone loss at this region¹⁸. This concentration of stresses at the crestal region is mainly because of the lack of the periodontal ligament in that area, which is essential for distribution of the forces throughout the length of the root. Periodontal ligament has it as one of its functions to dissipate these forces through the compression and redistribution of its fluid elements, as well as through its fiber system and hence providing shock absorption and cushioning effect to the teeth in response to these forces¹⁹. Furthermore, the periodontal ligament has a sensitive proprioceptive mechanism and is therefore it is capable of detecting and reacting to various range of forces applied to the teeth. When these forces are transmitted through the periodontal ligament, they result in the remodelling of the alveolar bone to allow tooth movements (as seen in orthodontics) or in the widening of the periodontal ligament space leading to an increase in tooth mobility in response to excessive forces (e.g., occlusal trauma)²⁰. The osseointegrated dental implants on the other hand, physiologically differ from natural teeth as they lack periodontal ligament support and hence when loaded mechanically, evoke a peculiar sensation, which has been termed as osseoperception^{10, 21}.

Patients with osseo-integrated implants will be feeling tangible sensation only when a force greater than that required to evoke sensation in natural teeth is applied. Thus, the ability of dental implants to adapt to occlusal trauma is reduced due to this lack of periodontal proprioceptive mechanism, resulting in micro fractures of the crestal bone which would eventually cause bone loss.

Moreover, osseointegrated implants with teeth presents a biomechanical challenge due to the differential support and mobility provided by the implant and the tooth, consequently showing a higher rate of failures and complications²². However, when tooth-implant supported restorations would be fabricated using support from periodontio-integrated implants higher success rates can be expected due to similar resilience of tissues supporting teeth and implants.

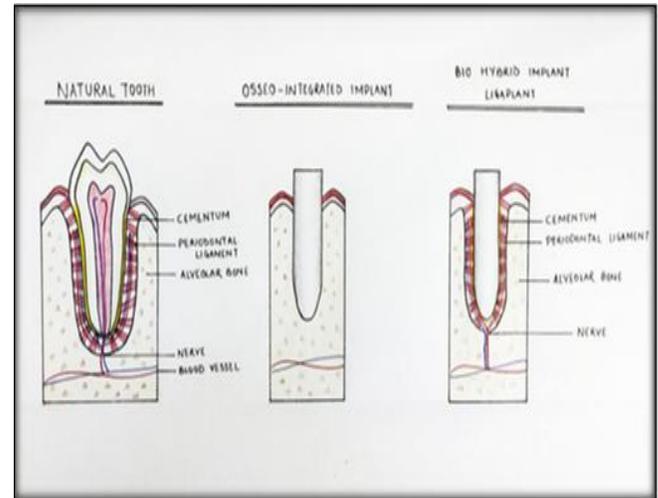


Figure 1: Diagram showing difference between natural tooth, osseo-integrated implant and ligaplant.

PROCEDURE TO OBTAIN THE LIGAPLANT

Temperature-responsive culture dishes preparation:

Polystyrene culture dishes were spread with N-isopropylacrylamide monomer in 2-propanol solution. Then these dishes were then subjected to electron beam irradiation with an Area Beam Electron Processing System. These temperature-responsive polymer-grafted (poly N-isopropylacrylamide) dishes were subjected to cold water and rinsed to remove ungrafted monomer and sterilized with ethylene oxide².

Cells isolation and cell culture:

An extracted tooth is taken as the source of human periodontal cells and is isolate from the same. Periodontal tissue is scraped from the middle third of the root after extraction, with a scalpel blade. The harvested tissue is placed into culture dishes containing = Dulbecco's modified Eagle's minimal essential medium, supplemented with 10% fetal bovine serum and 100units/mL of penicillin streptomycin. These outgrowth cells are then cultured in a humidified atmosphere of 5% CO₂ at 37°C for 48 hours which will allow attachment of the cells to the dishes. The dishes are washed to eliminate debris and the medium is changed at intervals of three times a week. For the harvestation of the cell sheet, human periodontal ligament cells are plated on temperature- responsive culture dishes(35 mm in diameter) at a cell density of 1x10⁵ and cultured at 37°C supplemented with 50mg/mL ascorbic acid 2-phosphate, 10nM dexamethasone and 10nM β-glycerophosphate that function as an osteo-differentiation medium^{2, 23}.

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C. Culture of PDL cells in a Bioreactor:

Hydroxyapatite (HAP) coated titanium pin was placed in a hollow plastic cylinder leaving a gap of 3mm around the pin. Culture medium was continuously pumped through the gap. Single cells suspension (periodontal ligament cell suspension), obtained from human, and are seeded first into plastic vessels under a flow of growth medium for duration of 18 days^{2, 23}.

PRECAUTIONS WHILE PREPARING**LIGAPLANT**

- 1) Proper sterilization protocols must be maintained throughout the procedure^{7, 24}.
- 2) Proper culturing and cell growth is necessary; otherwise it may lead to the formation of non-periodontal ligament cell types.
- 3) PDL formation is favoured by a cushion of appropriate thickness, but on the other hand, the prolonged cell culturing may favour the appearance of non-PDL type of cells. The bioreactor has been constructed with the aim to resemble the PDL situation during cell growth in order to preserve the cell differentiation state and to obtain adequate cell stimulation²⁵.
- 4) Micromechanical movements of the growth medium is necessary for firm attachment of the cells to the implant⁷.
- 5) Cells are placed and positioned into a narrow space between the ligaplant and surrounding hollow cylinder. It is thereby expected that the phenotype of PDL is favoured by a tight attachment of cells to the implant. Thus, minute mechanical movements of the medium flow should be present in the preparation of ligaplants and space present in between the implants and the culture should be optimal²⁵.
- 6) Adequate duration of surface treatment must be maintained for the success of the ligaplant which will bring big improvements to the implant system².

ADVANTAGES

- 1) Ligaplants have the advantage of mimicking the anatomy of natural teeth which has periodontal ligament around it along with the alveolar process²⁶.
- 2) Ligaplants become firmly integrated without interlocking and without direct bone contacts, despite the initial fitting being loose in order to spare the PDL cell cushion. Formation of bone began and movements of ligaplants inside the bone suggested of an intact tissue communication occurring between bone and the implant surface^{2, 25}.

- 3) Ligaplants can alleviate problems with implant usually faces such as infrabony defects, gingival recession of the missing tooth site. Thus it is possible to be applicable in periodontal bony defects, where conventional implants could not be installed.
- 4) In cases leading to peri-implantitis, amount of bone loss is reduced.

DISADVANTAGES

- 1) It's a technique sensitive procedure. Hence, proper care must be taken.
- 2) High cost. It is known to be costly procedure because of limited facilities and members to perform this research²⁵.
- 3) Host acceptance of the implant or PDL growth in the socket cannot be predicted. It may also lead to failure of implant by the host²⁷.
- 4) One should be cautious while culturing the ligaplants about the proper maintenance of temperature, duration of culture etc. All of these make it a cumbersome procedure²⁶.

RECENT STUDIES ON LIGAPLANTS

In 2005, researchers such as Akira et al. Parlar et al., Jahangir et al. also explored the effect of remaining PDL and the feasibility of the the PDL around a dental implant^{28,29,30}.

The phenomenon of a tooth getting replaced by a dental implant relies on the mechanical and biological capability of the anatomical substitute and its ability to restore the lost physiological functions. L Carvalho et al. [2006] determined the PDL effects on the dynamic load transfer mechanism, from the tooth to the alveolar bone, evaluating the equivalent dynamic stiffness of the ligament structure. In this study, a porcine fresh mandible with a tooth was used, experimental procedure was carried out to identify the dynamic transmissibility of the entire system. The transmissibility function provided information about the stiffness and damping of the PDL, information that can assist the design of an improved dental implant system³¹.

In a yet another study done by Marei (2009), implantation of titanium fixture with porous hollow root-form poly (DL-Lactide-co-Glycolide) scaffold seeded with autogenous bone marrow-derived mesenchymal stem cells in goats showed periodontium-like tissue with newly formed bone both at 10 days and after 1 month, substantiating that undifferentiated mesenchymal stem cells were capable of differentiating to provide the three critical

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tissues required for periodontal tissue regeneration: Cementum, bone and periodontal ligament around the titanium implants³².

Gault et al. 2 in 2010 did a scientific breakthrough by demonstrating for the first time the tissue engineering of the periodontal ligament and cementum-like structures on oral implants in humans, to encourage the forming of implant-ligament biological interfaces or ligaplants which are capable of true and functional loading. In the research-work carried out by Gault, it was found that the periodontal ligament fibroblasts could be harvested from hopeless teeth of mature individuals and could be cultured in bioreactors to preserve their state of differentiation. In total eight implants were inserted and out of them, one was still in place and functioning even after 5 years and even showed substantial bone regeneration in the adjacent bone defect 2 years post implantation. Thus it can be implied that in future, the clinical use of ligaplants might also be able to help avoid bone grafting, or its expense, inconvenience and discomfort to the patient.

Rinaldi and Arana Chavez in 2010 showed results by doing an animal study that that thin cementum like layer formed at longer times after implantation at the areas in which the PDL was in contact with the implant.

The clonogenic potential of human dental and periodontal tissues such as the dental pulp and the PDL and their potential for tooth and periodontal repair and/or regeneration was discussed by Javier Caton et al. (2011). They also proposed novel therapeutic approaches using stem cells or progenitor cells, which are targeted to regenerate the lost dental or periodontal tissue³³

Lately, Kano et al.(2012) suggested that implants surrounded by periodontal ligament-like tissue could be developed, when immediately after the extraction, tooth-shaped hydroxyl-apatite coated titanium implants were placed into the tooth socket where some periodontal ligament still remained; maintenance of original periodontal tissue domains most likely being the cause of prevention of osseointegration of the implants³⁴

Kiong and Arjunker in 2014 stated that ligaplants as tooth replacement have decisive advantages as compared with osseointegration devices, due to their periodontal tissue regeneration²⁵

It was confirmed by Kaoro washio et al. (2018) that PDL-derived cells cultured with osteoinductive medium had

the ability to induce cementum formation. Structure similar to periodontium was formed around a titanium implant, an environment similar to one existing around a natural tooth. Dental implants combined with a cell sheet technique when clinically applied, might come out to be feasible as an alternative implant therapy. Moreover, application of this technique may act as an innovative role in not only just periodontal, but also other fields of dentistry such as prosthetic and orthodontic etc^{35, 36}.

The phenomenon of regenerating the lost periodontal tissues has been one of the most important subjects in the research area. Since it's discovery, Kengo Iwasaki et al. [2019] used periodontal ligament stem cells (PDLSCs), and transplanted into periodontal bony defects to examine their regenerative potential. Periodontal defects were successfully regenerated using periodontal ligament stem cell sheets, fabricated by cell sheet engineering in animal models, and for which clinical human trials are underway^{36, 37}.

CONCLUSION

Since the ligaplant is not tightly fitted to its site, the ligaplant surgery is relatively easy. Ligaplant is advantageous compared to osseointegration devices, due to their periodontal tissue regeneration capability. Patients however also have the advantage of not going through the inconvenience and discomfort of bone grafting, instead they can go for ligalants for a better outcome.

A major concern remains in the form of rational application of stem cell based tissue-engineering technology to be practiced in clinics. Apart from being a technique sensitive procedure, tissue engineering applications requires a considerable amount of cost and time. Although, a predictable and feasible method for producing dental implants with periodontal-like ligament has not been innovated, it has now been understood that generating a periodontal-like tissue around implants is possible and is the coming future in the field of implant logy. This revolutionary approach to develop periodontal-integrated implants; however, opens up exciting possibilities for both periodontologists and oral implantologists and offers many interesting possibilities of utilizing ready-made, off-the-shelf biological tooth replacements that could be delivered to serve as hybrid-material-living oral implants to patients.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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