



## Ligaplant: Engineering nature's precision in dental implant - A review of literature

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### Abstract

Dental implants have revolutionized tooth replacement, with osseointegrated implants standing out due to their high long-term success rates. However, a critical limitation of these implants is the absence of the periodontal ligament (pdl), which naturally exists in teeth. The lack of pdl results in ankylosed implants that lack the physiological mobility, proprioception, and shock-absorbing capacities seen in natural dentition. Moreover, implants without pdl are more susceptible to peri-implant inflammation, potentially leading to greater bone loss compared to natural teeth.

This review addresses the shortcomings of current implant designs and explores the concept of ligaplant—a tissue-engineered solution aimed at regenerating an artificial pdl around dental implants. Leveraging advancements in bioengineering, ligaplant represents a next-generation implant system capable of mimicking the functional dynamics of natural teeth by offering proprioception and shock absorption. This innovation holds the potential to bridge the gap between conventional osseointegrated implants and nature's design, paving the way for improved implant longevity and patient outcomes.

This paper provides a comprehensive analysis of the clinical importance of ligaplant in implant dentistry, its potential benefits, and the future possibilities of tissue engineering in periodontal regeneration.

**Keywords:** Dental implant surgery, ligaplant, osseointegration, periodontal ligament stem cells (pdlscs), tissue engineering & regenerative medicine

### Introduction

In contemporary dental practice, implants have emerged as a prevalent alternative to removable methods of tooth replacement. To date, Osseo integrated implants have been widely regarded as the most desirable option due to their impressive long-term clinical survival rate<sup>[1]</sup>.

Osseointegration was originally defined as a direct structural and functional connection between ordered living bone and the surface of load carrying implant<sup>[1]</sup>.

The main shortcoming of these implants is that these lack the periodontal ligaments as present in the natural dentition. The Osseo integrated implants are ankylosed and lack physiological mobility as the natural teeth and also lack the shock absorbing capacity as compared to the natural teeth<sup>[1, 2]</sup>.

Periodontal ligaments consist of various types of cells like fibroblasts, osteoblasts, cementoblasts, cementoclasts, osteoclasts and undifferentiated mesenchymal stem cells responsible for the productive relationship among the bone and the tooth. These cells are all important in the dynamic relationship between the tooth and the bone. Periodontal ligaments, present in between the alveolar bone and cementum of the teeth, have a crucial role in the regulation of the bone as well as tooth support in the alveolus<sup>[2]</sup>.

PDL performs the various functions, as Different types of progenitor cells are seen in these tissues, crucial for maintaining the homeostasis of the periodontium<sup>[2]</sup>.

The PDL also has an important interaction with the adjacent bone, playing the role of the periosteum, at the bone side facing the root. It also provides proprioception and acts as a shock absorber by providing cushioning effect<sup>[2, 3]</sup>.

Due to lack of periodontal ligament inflammation around implant may cause serious bone loss then does the inflammation around the natural tooth with PDL<sup>[3]</sup>.

These problems could be resolve only if implant with PDL could be develop.

Efforts have been made for years to compensate for this obvious difference by “shock-absorbing systems” built into the implant or its superstructure.

As a critical solution, bioengineering advancements need to be assembled to regenerate an artificial periodontium surrounding the implant. This can be achieved by new generation periodontio integrated tissue engineered Ligaplant<sup>[2]</sup>.

These innovative dental implants go beyond tooth replacement and they mimic natural tooth function by providing shock absorption and proprioception.

This paper delves into the intricacies of Ligaplant its clinical importance in implant dentistry and the promising future it holds within tissue engineering technology for periodontal regeneration.

### Review

#### Search methodology

We searched the literature on the topic of Ligaplant with the keywords Ligaplant, tissue engineered ligament, osseointegration, tissue engineering, periodontio integrated implant, from 2008 to 2024 in various databases and libraries.

This Prisma flow diagram represents the various steps of the systemic review of the Literature for this article. We have compiled articles containing methodology, studies and case reports on the concept of Ligaplant, its success, advantages and disadvantages, characteristics and clinical aspects.

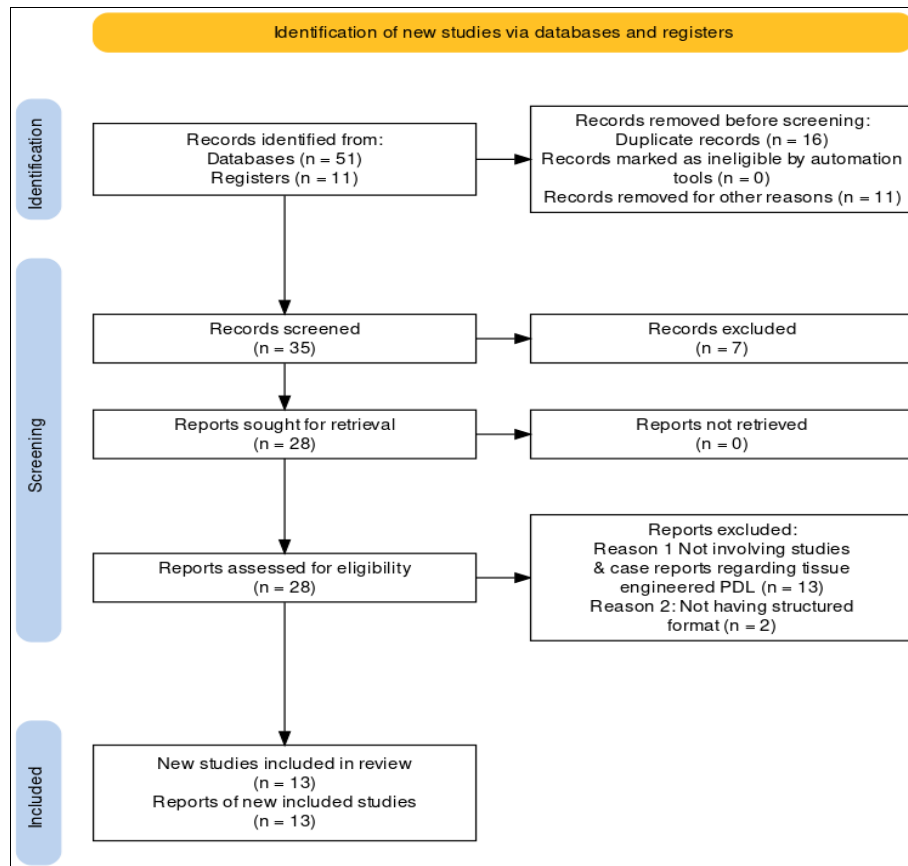


Fig 1: PRISMA flow diagram for literature search

**What Is Ligaplant?**

The combination of PDL cells with implant biomaterial is called Ligaplants (Figure.2) [3].

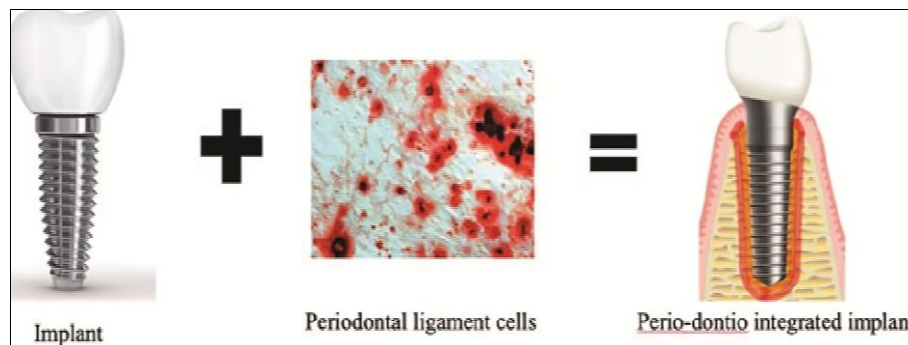


Fig 2: Ligaplant

By combining periodontal ligament cells with implant biomaterial, the ligaplant creates periodontal ligaments that improve the quality of force distribution between the prosthesis and teeth abutments supported by the implants by enabling micro-movements and shock absorption [3, 4]. These implants can be used to improve physiological outcomes and overcome the limitations of traditional implants and potentially extend the life of the prosthesis. They resemble the appearance and function of natural teeth. This new dimension in the field of implantology is known as Ligaplants [4].

**Concept to Obtain Ligaplant?  
Tissue Engineering**

The Ligaplant Foundation's core idea is to use biodegradable polymers to create scaffolds that promote cell growth and tissue formation alongside growth

factors. With its proven ability to regenerate biomechanical tissue and restore innervation, the Foundation is at the forefront of tissue engineering technology. By harnessing advancements in various fields, tissue engineering has become a popular approach to repairing damaged tissues [4]. The goal is to gather specific cells, arrange them on a scaffold, and stimulate their growth with growth factors to promote tissue regrowth, ultimately advancing the field of stomatology [3, 4, 5]. The tissue engineering concept is understood as a triangle that proposes that combining these three primary constituents will promote regeneration. The crucial components are cells, signalling molecules, and scaffolds, also known as the matrix (Figure.3 & 4) [3, 5]. Scaffold is a three-dimensional structure that helps cells migrate and proliferate, forms a matrix, and aids in the development of tissue [3, 5].

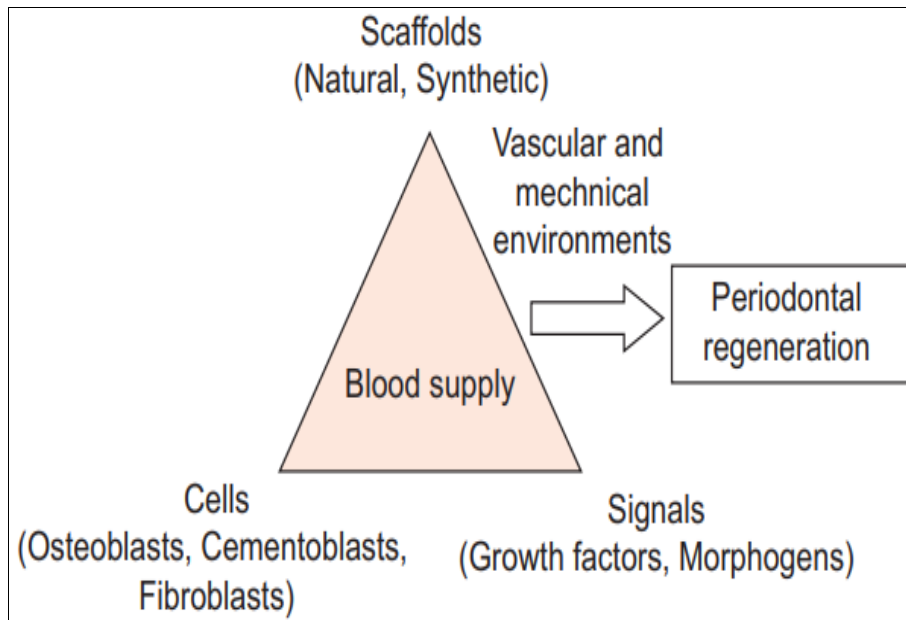


Fig 3: Concept of tissue engineering

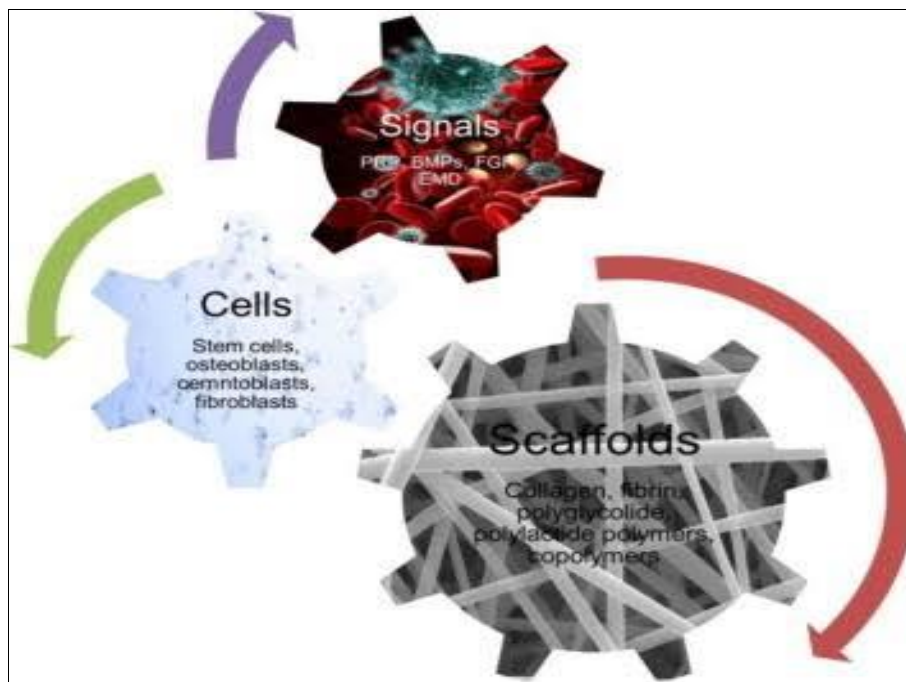


Fig 4: Primary constituents of Tissue engineering

The cells are cultured using signalling molecules over a biodegradable matrix and scaffolds before being transplanted into the body. This method is referred to as the *in vitro* method<sup>[3]</sup>.

Conversely, the grown essential components are implanted in the tissue lesions, and the body's natural healing process ensues, resulting in regeneration. This method, known as the "*in vivo* technique," uses these three tissue defect site components to induce intrinsic healing activity<sup>[3]</sup>.

**Procedure for Obtaining Ligaplant**

**In-vivo Method**

After the donor tooth has been extracted, it is immediately replanted into its natural socket 14 days before transplantation. Due to the activation of the healing process in the periodontal ligament caused by the intentional trauma, cell proliferation and differentiation occurs. The tooth can

be transplanted after fourteen days when the cell culture is at its peak and various cells are attached to the root surface by freshly formed Sharpey Fibers<sup>[3, 4]</sup>.

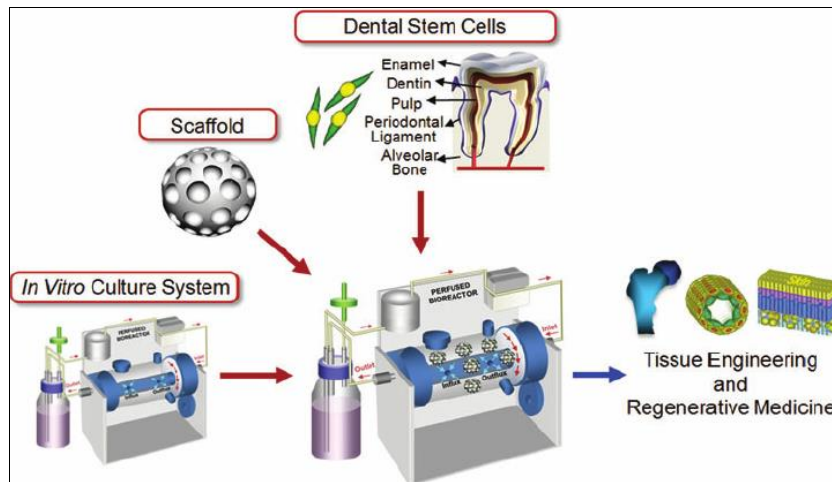
**Ex-Vivo Method**

An identical *ex vivo* cell culture using tissue engineering around an artificial root is a new concept for producing Ligaplant.

The following are essential components for regeneration and reconstruction:

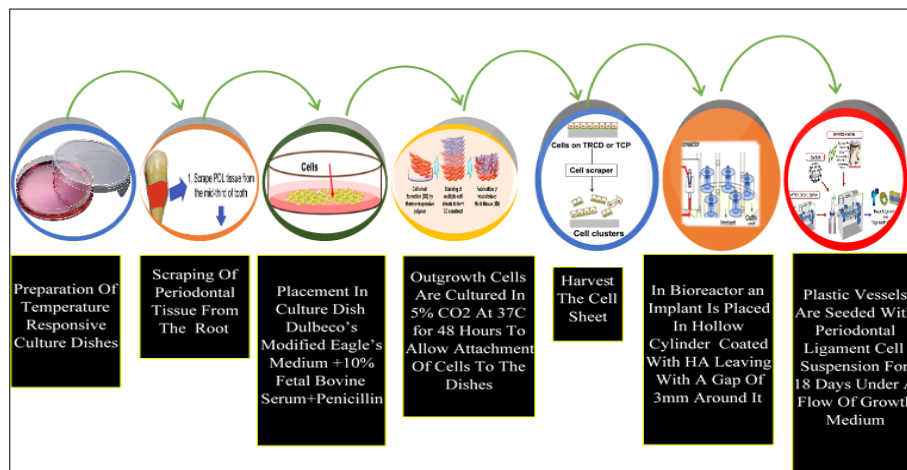
- Scaffolds;
- Signals;
- Cells

PDL cells are grown on biodegradable scaffolds or matrix with the aid of signalling molecules (Figure.5)<sup>[6]</sup>.



**Fig 5:** Dental stem cell-based tissue engineering. *In vitro* 3D tissue-engineered construct can be developed by combining dental stem cells with proper 3D cell carrier and bioreactor culture system, and can be applied to tissue engineering and regenerative medicine

**Steps in Preparation of Ligaplant**



**Step 1: Preparation of Temperature-Responsive Culture Dishes**

The Area Beam Electron Processing System (ABEPS) is used to process polystyrene culture dishes that contain N-isopropyl acrylamide monomer and 2, propanolol fluid. High-energy electrons are irradiated onto a material using the ABEPS system, which produces the desired reaction. Polystyrene culture dishes are sterilised with ethylene oxide after the remaining monomer has been eliminated by rinsing them with cold water [2, 7].

**Step 2: Cells and Cell Culture**

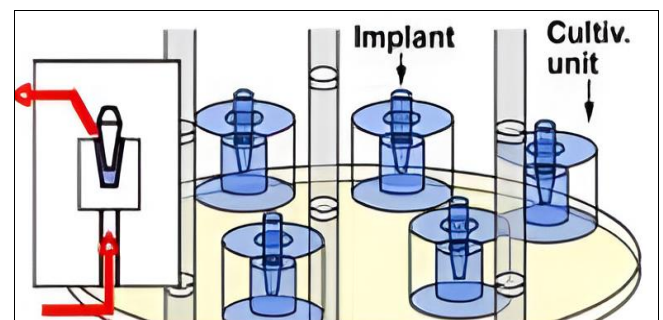
Next, using a scalpel blade to scrape the middle third of the root periodontal tissues from an extracted tooth, human periodontal ligament cells are obtained. The tissues are then placed in culture dishes that have been modified Eagle's minimal essential medium by Dulbecco and supplemented with 10% fetal bovine serum and 100 units/ml of penicillin-streptomycin. These out-of-growth cells are then cultured for 48 hours at 37 degrees in a humidified atmosphere with 5% carbon dioxide to help the cells adhere to the dishes. Washing these dishes removes the debris, and the medium needs to be changed at least three times a week. The human periodontal ligament cells are cultured on 35mm diameter temperature-responsive culture dishes at 37oC with the following conditions: 50 mg/mL of ascorbic acid 2-phosphate, 10nM

glycerophosphate, 10nM dexamethasone, and a cell density of  $1 \times 10^5$ . It facilitates Osseo differentiation, which is necessary to obtain the cell sheets [7, 8].

**Step 3: Culture of PDL Cells in a Bioreactor**

After that, an implant coated with hydroxyapatite is inserted into a hollow plastic cylinder, leaving a 3 mm space surrounding it. The periodontal ligament cell suspension is then seeded into these plastic cylinders, and they are left in a stream of growth medium for eighteen days to allow the PDL cells surrounding the implant to regenerate (Figure. 6) [2, 7, 8].

Figure 7 depict procedure of peri implant periodontium formation.



**Fig 6:** Bioreactor

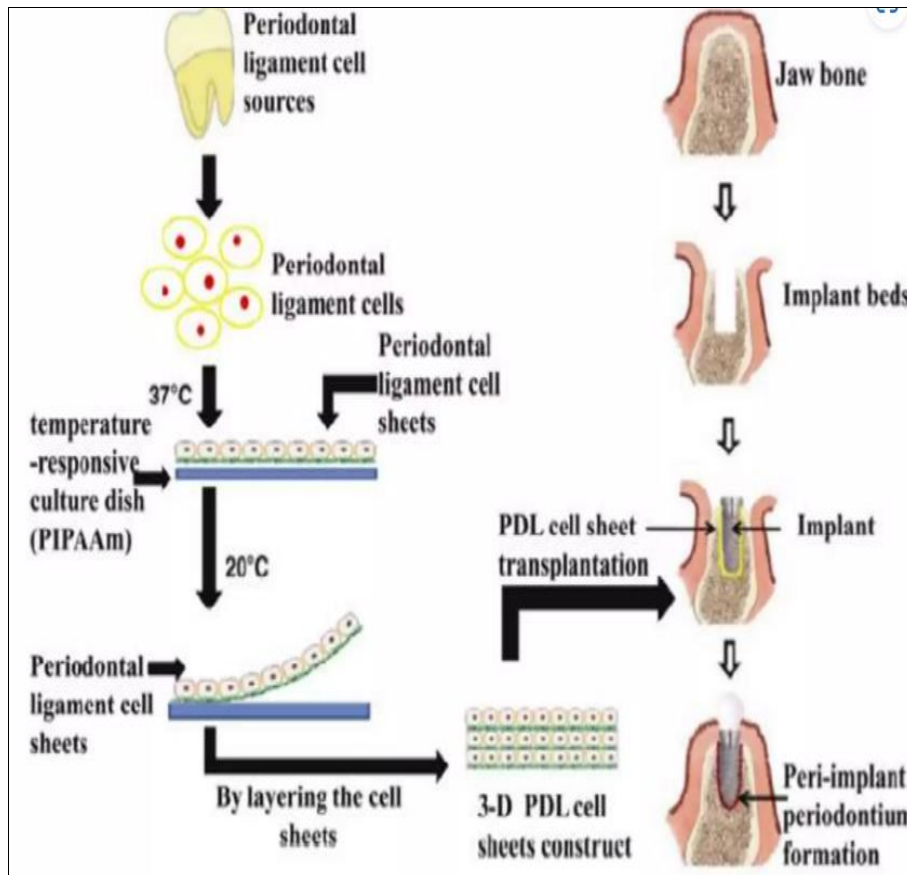


Fig 7: Peri implant periodontium formation

**Precautions during preparation**

1. During the ligaplant preparation process, there should be small mechanical movements in the medium flow [6].
2. The ideal space between the implant and the culture should be there [8].
3. To get a quality Ligaplant the surface treatment time should be optimal [9].
4. Additionally, adequate sterilization is required.
5. To stop the growth of cells other than periodontal ligament cells, the cell culture should be optimal [8].

**Characteristics of ligaplant [2]**

1. Ligaplants induces proprioception i.e. it enhances the sense of movement and position or sensory perception.
2. It facilitates the distribution of masticatory and occlusal forces.
3. Unlike traditional implants, they have the ability to absorb shock.
4. Different kinds of undifferentiated cells give the implant its osteoconductive qualities.
5. It offers anchoring that is similar to natural dentition, permitting tooth movement throughout orthodontic treatment.
6. Ligaplant provides enough anchoring to sustain the development of alveolar bone housing.

**Advantages of Ligaplant over Traditional Implant**

**Enhanced Biological Integration [8, 10]**

- Mimics natural tooth insertion, promoting a more natural integration with the alveolar process.
- Facilitates the formation of cementum and periodontal attachment, crucial for bone remodeling and mobility.

**Improved Functional Dynamics [8, 9, 10]**

- Provides proprioception, restoring the natural sense of tooth movement and position.
- Acts as a shock absorber during masticatory function, distributing forces to the alveolar process and reducing the risk of bone defects.

**Disadvantages**

1. The process is very technique sensitive. It is important to use caution when cultivating ligaplants. For the process to be successful, the temperature must be right. A precise and close monitoring of a few other variables is also necessary, including the cells used for culturing and the length of the culture. Errors in the process could result in the development of specific non-periodontal ligament cells, which would be fatal for the ligaplant [9, 10].
2. The cost of creating Ligaplants can be high due to limited facilities.
3. Inadequate host acceptance of the implant or an inability of the PDL cells to proliferate could also lead to failure [8, 10].
4. Sometimes, extended cell culture results in the appearance of non-PDL cell types [9].

**Studies Based Evidence**

Buser D *et al* concluded in their study that titanium implants placed after extraction of retained root tips showed that implants had PDL formation on their surface along with a cementum layer [11].

Choi *et al* in 2000 placed implants containing cultured autologous PDL cells into the dogs' mandibles. Three months later, histological analysis showed that some implant surfaces had developed a layer of cementum-like

tissue with collagen fibers inserted, proving that PDL cells in culture can form tissue that resembles a real PDL surrounding implants [12].

In a 2009 study by Marei, he populated porous scaffolds with mesenchymal stem cells and placed titanium implants in goats. Ten days later and one month later, new bone formation was observed along with periodontium-like tissue. This suggests that cementum, bone and periodontal ligament-like tissue can be differentiated by mesenchymal stem cells into vital periodontal tissue around titanium implants [13].

Gault *et al* used Ligaplast cells in 2010, i.e. PDL cells, with implant biomaterial for dentures. In addition to clinical research on humans, the study also included animal experiments on mice. The surface of the Ligaplast showed signs of PDL formation in the human trial, as well as the formation of a new tissue layer that resembled a repair cement and a structure similar to the lamina dura that surrounds a natural tooth [7].

It was reported by Kano *et al* in 2012 that implants surrounded by PDL-like tissue could be developed. This could be achieved by leaving some PDL in place after extraction and quickly placing titanium implants in the form of a hydroxyapatite coated tooth [14].

Nunez *et al* 2012 confirmed that PDL-derived cells have great potential for regeneration [15].

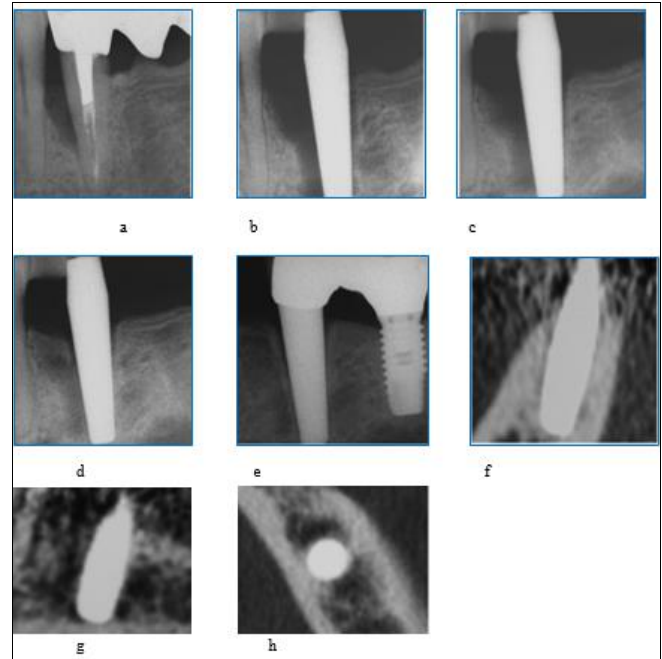
According to Kiong and Arjunker in 2014, ligaplast as tooth replacements have a number of advantages over osseointegration devices. This is primarily due to their ability to regenerate periodontal tissue. Because the implant does not need to be firmly in place, the ligament transplant process is quite simple [8].

Kaoro Washio *et al* in 2018 confirmed that PDL-derived cells cultured with osse-induction medium had the ability to induce cementum formation. A periodontal-like structure had been formed around a titanium implant, an environment similar to that around a natural tooth [16].

Kengo Iwasaki *et al* in 2019 used periodontal ligament stem cells (PDLSCs) and transplanted them into periodontal bone defects to access their regenerative capacity. By using cell sheet technology, they were able to successfully regenerate periodontal defects in animal models using periodontal stem cell sheets. Clinical trials with these cell layers in humans are currently underway [17].

### Human Clinical Investigation of Ligaplasts

In 2010, Gault *et al* achieved a significant scientific breakthrough by demonstrating, for the first time in humans, the application of tissue engineering principles for the regeneration of periodontal ligament and cementum-like structures around oral implants, leading to the development of "ligaplasts" capable of sustaining genuine functional loading. Notably, their research revealed that periodontal ligament fibroblasts could be sourced from compromised teeth of mature individuals and cultured in bioreactors, preserving their differentiated state. This innovative approach opens avenues for regenerative therapies in implant dentistry, offering promising prospects for enhancing the longevity and performance of dental implants. Here is one of the case reports by Gault *et al* of human trial and loading (Figure 8 a-h) [7].



Ligaplast, radiography. (a) Before surgery, root fracture in tooth #34 plus bone defect mesially (left) to the fractured root. (b) Same location immediately after ligaplast implantation. (c) Partial bone regeneration after 24 weeks. (d) After 24 months, note the almost complete replenishment of the major defect. (e) Forty-two months; the periodontium has partially restructured with a fairly regular desmodontal space and reinforced bony demarcation around this space. (f-h) Tomography analysis after 24 months; frontal view (f), side view (g), top view (h). The ligaplast is surrounded by bone trabeculae. Ligaplast dimensions: 15 mm in length, 5–7 mm in width.

### Discussion

The re-establishment of the periodontal ligament (PDL) around the implant has not been adequately addressed.

Unlike natural teeth, osseointegrated implants directly attached to the adjacent alveolar bone lack the presence of natural periodontal tissue.

Hence, it is imperative to design dental implants in conjunction with tissue-engineered PDL to establish a biological connection capable of performing specific physiological functions. According to research conducted by Nyman *et al.* in 1982, periodontal ligament cells can regenerate connective tissue attachment on tooth surfaces [18].

Additionally, findings from Buser *et al.* in 1990 concluded that titanium implants utilized to replace retained root tips exhibited the development of a cementum layer and PDL on their surfaces [11].

Numerous *in vitro* studies show that when dental implants are positioned near the radicular portion of the tooth, cementum-like tissue with an intervening PDL forms [2, 4, 6, 8].

Recent advances and research have enhanced the utilization of cell sheet engineering for replacing cementum around dental implants by incorporating periodontal ligament stem cells. Hence, the combination of bioengineering technique improved with adult stem cells emerges as a promising strategy for regenerative therapies and consumption with contemporary implant designs [19].

The future scope potential clinical application includes restoring sensation, periodontal tissue regenerations and a decrease in a need for bone grafting.

Continued research is imperative to ascertain the most effective treatment options tailored to individual patient needs. The emerging concept of ligaplasts is currently undergoing investigation, necessitating exploration into several key facets, including:

**Clinical Efficacy:** Evaluation of the clinical success rate of ligaplasts in promoting periodontal ligament and cementum-like structures around oral implants<sup>[2, 19, 20]</sup>.

**Integration Mechanisms:** Understanding the nature of integration between ligaplasts and the surrounding bone tissue to ensure functional stability and longevity<sup>[7, 13, 20]</sup>.

**Practical Implementation:** Assessing the feasibility of adopting ligaplast technology in clinics or institutions lacking an integrated laboratory setup<sup>[18, 19, 20]</sup>.

**Cost Considerations:** Determining the economic viability of incorporating ligaplast into dental implant procedures, including initial investment and long-term maintenance costs.

**Protocol Development:** Investigating whether the placement of Ligaplasts requires a distinct protocol or can be seamlessly integrated into existing implant placement procedures<sup>[19]</sup>.

Comprehensive exploration of these pivotal dimensions through methodologically robust research endeavours is paramount for advancing the understanding and clinical translation of ligaplast technology, ultimately enhancing the efficacy and quality of care in implant dentistry<sup>[2, 7]</sup>.

## Conclusion

The advent of periodontal tissue engineering has ushered in a transformative era in implant dentistry, marked by the introduction of ligaplasts as an innovative modality aimed at addressing the limitations of conventional implants. While preclinical studies on animals have demonstrated promising outcomes, there remains a pressing need for the development of more feasible and practical methodologies for obtaining periodontal ligament attached implants. Additionally, further human studies are warranted to thoroughly evaluate the efficacy and success of this novel strategy. With its inherent advantages over traditional implants, including enhanced stability and promotion of optimal dental performance with minimal patient discomfort, ligaplasts represent a groundbreaking addition to the field of implant dentistry. Through ongoing research and clinical exploration, ligaplasts hold the potential to emerge as a revolutionary advancement, offering unparalleled benefits through the regeneration of periodontal tissues and paving the way for improved patient outcomes in dental implant procedures.

## References

- Gulati M, Anand V, Govila V, Jain N, Rastogi P, Bahuguna R, *et al.* Periodontio-integrated implants: A revolutionary concept. *Dental Research Journal*,2014;11(2):154
- Bajaj P, Shirbhate U, Dare S. Ligaplasts: Uprising regimen in the glebe of implant dentistry. *Cureus*, 2023, 15(9).
- Aeran H, Tuli AS, Anamika. Ligaplasts: Recreation of a natural link in implant dentistry: A review. *International Journal of Oral Health Dentistry*,2021;15:3–7.
- Saleem M, Kaushik M, Ghai A, Tomar N, Singh S. Ligaplasts: A revolutionary concept in implant

- dentistry. *Annals of Maxillofacial Surgery*,2020;10(1):195–7.
- Pandit N, Malik R, Philips D. Tissue engineering: A new vista in periodontal regeneration. *Journal of Indian Society of Periodontology*,2011;15(4):328–37.
- Sanketh AK, Kalavathy N, Shetty MM, Kumar PR, Anuradha V, Mundhra H, *et al.* Ligaplasts: The next generation implants. *RGUHS Journal of Dental Sciences*, 2022, 14(1).
- Gault P, Black A, Romette JL, Fuente F, Schroeder K, Thillou F, *et al.* Tissue-engineered ligament: Implant constructs for tooth replacement. *Journal of Clinical Periodontology*,2010;37(8):750–8.
- Kiong AL, Arjunker R. Tissue-engineered ligament: Implant constructs for tooth replacement (ligaplasts). *Journal of Pharmaceutical Sciences and Research*,2014;6(3):158.
- Singh R, Raj S, Singh GB, Nikunj AM, Chaurasia S. Ligaplasts: Periodontio-integrated implants. *Journal of Dental and Medical Sciences*,2019;18(7):61–4.
- Garg H, Deepa D. Bioengineered periodontal ligament: Ligaplasts, a new dimension in the field of implant dentistry – Mini review. *Journal of Oral Research and Review*,2018;10(2):92.
- Buser D, Warrer K, Karring T. Formation of a periodontal ligament around titanium implants. *Journal of Periodontology*,1990;61(9):597–601.
- Choi BH. Periodontal ligament formation around titanium implants using cultured periodontal ligament cells: A pilot study. *International Journal of Oral and Maxillofacial Implants*,2000;15(2).
- Marei MK, Saad MM, El-Ashwah AM, El-Backly RM, Al-Khodary MA. Experimental formation of periodontal structure around titanium implants utilizing bone marrow mesenchymal stem cells: A pilot study. *Journal of Oral Implantology*,2009;35(3):106–129.
- Kano T, Yamamoto R, Miyashita A, Komatsu K, Hayakawa T, Sato M. *et al.* Regeneration of periodontal ligament for apatite-coated tooth-shaped titanium implants with and without occlusion using rat molar model. *Journal of Hard Tissue Biology*,2012;21(2):189–202.
- Nunez J, Sanz-Blasco S, Vignoletti F, Muñoz F, Arzate H, Villalobos C. *et al.* Periodontal regeneration following implantation of cementum and periodontal ligament-derived cells. *Journal of Periodontal Research*,2012;47(1):33–44.
- Washio K, Tsutsumi Y, Tsumanuma Y, Yano K, Srithanyarat SS, Takagi R. *et al.* *In vivo* periodontium formation around titanium implants using periodontal ligament cell sheet. *Tissue Engineering Part A*,2018;24(15–16):1273.
- Iwasaki K, Akazawa K, Nagata M, Komaki M, Honda I, Morioka C. *et al.* The fate of transplanted periodontal ligament stem cells in surgically created periodontal defects in rats. *International Journal of Molecular Sciences*,2019;20(1):192.
- Nyman S, Gottlow J, Karring T, Lindhe J. The regenerative potential of the periodontal ligament: An experimental study in the monkey. *Journal of Clinical Periodontology*,1982;9(3):257–65.
- Jibi J, Rao BL, Sruthi YS, Pratyusha T, Chitra C. A novel approach in implant dentistry-ligaplasts. *International Journal of Scientific Research*,2019;8(3):43–5.
- Katari RS, Peloso A, Orlando G. Tissue engineering. *Advances in Surgery*,2014;48(1):137–54.