

Jan. 29th, 2025

Proofreading in progress

To media representatives:

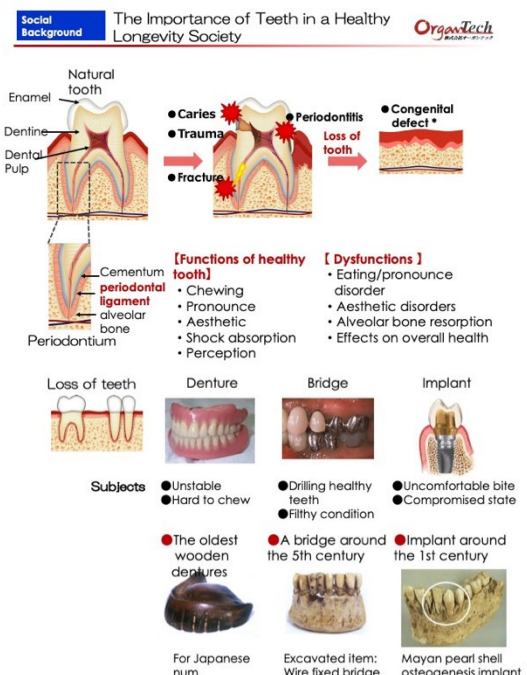
To whom it may concern:

General Incorporated Foundation
 Neurological Disease Research Institute, Southern Tohoku General Hospital
 Southern Tohoku Medical Clinic
 OrganTech Inc.

The First Clinical Research in the World, "Next-Generation Bio-Implants" with Periodontal Ligament Attachment

—Verifying the Safety and Effectiveness of "Organ Regeneration for Tooth Loss" for the First Time Globally—

Southern Tohoku General Hospital,
 Maxillofacial Implant Center (Center Director:
 Shohei Kasugai, Professor Emeritus, Tokyo
 University of Science, Former Professor,
 Department of Implant Oral Regenerative
 Medicine, Graduate School of Medical and Dental
 Sciences, Tokyo Medical and Dental University),
 Southern Tohoku Medical Clinic (Koriyama,
 Fukushima, Japan: Group President: Kazuo
 Watanabe, Chairman of the Board: Sadayoshi
 Watanabe, Hospital Director: Shinichi Konno, Clinic
 Director: Yasuo Fukaya), and OrganTech Inc.
 (Headquarters: Chuo-ku, Tokyo, Japan; CEO:
 Yoshio Shimo) will begin specified clinical research
 on next-generation bioimplants[*1] that will bond

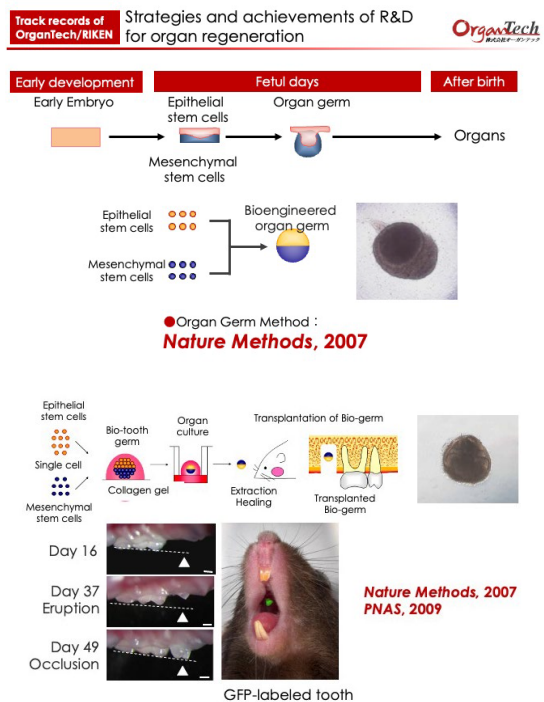


dental implants to the alveolar bone via the periodontal ligament in the same way as natural teeth, as "organ regenerative therapy for tooth loss." The technology for this specified clinical research was developed by research group led by Takashi Tsuji (Chairman and Founder of OrganTech Inc.) at the RIKEN, National Research and Development Agency, and will be the first in the world to verify its safety and effectiveness.

1. Background

Teeth are closely related to human life, such as eating and pronunciation, and their dysfunction is an important issue affected to quality of life (QOL). In particular, in Japan as an advanced aging country, the importance of medical care for oral organs such as teeth and salivary glands is increasing in order to realize a healthy and long-lived society. In dental treatment, functional replacement treatments using dentures, bridges, and implants are widely applied for tooth loss due to trauma, caries [*2], and periodontal disease. These previous dental treatments have been widely adopted due to their therapeutic efficacy in restoring chewing function and esthetics of patients. On the other hand, there has long been hoped to develop the technologies to restore the biological functions of natural teeth, such as perception of chewing comfort and infection prevention.

A major goal in dentistry is to realize "the tooth organ regenerative therapy" that will be restoring lost teeth. Organ regenerative therapy of teeth is expected to be a new treatment technique that will lead to fully aesthetical, physiological, and functional restoration. In 2007, we have successfully developed the "organ germ method [*4]," a three-dimensional cell manipulation technique for regenerating "organ germ [*3]," the seeds of organs, from the perspective of organ developmental biology. As a first in the world, we reported that transplantation of bioengineered tooth organ germ reconstructed by organ germ method resulted in regenerated teeth developing in the adult body, connecting with blood vessels and nerves, and this result attracted attention around the world (Nature Methods, 2007). Furthermore, in 2009, we clarified that transplantation of regenerated tooth germs into the site of tooth loss revealed that the regenerated teeth erupted [*5] from gingival surface, occluded, connected with bone via the periodontal ligament, and regenerated the nerve function that transmits external noxious stimuli to the central nervous system (PNAS, 2009).

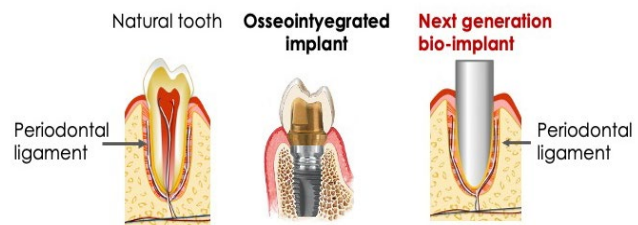




Although these studies played a major role as proof of concept in animal models of "tooth organ regeneration," the two types of stem cells required for regenerating tooth organ germ can only be extracted from fetuses and do not exist in adults. In addition, since it takes several years for permanent teeth to erupt in humans, it was thought that this would be difficult to achieve in the near future. While these results were highly praised academically around the world, dental researchers and dentists from around the world expressed their desire for the development of "tooth organ regeneration," as it is not necessary to regenerate all of the teeth exactly like natural teeth, and if periodontal ligament could be added to current osseointegrated implants, it would be possible to achieve "tooth organ regeneration" with almost all of the tooth functions.

Attempts to replace lost teeth with artificial materials have a long history, with iron implants discovered in the 2nd-3rd century AD ancient Roman period, and implants made from the shell of pearl oyster discovered in the 7th century AD Mayan civilization (owned by the Peabody Museum of Anthropology, Harvard University). The Mayan pearl oyster implants were already aesthetically equivalent to natural teeth, and subsequent research revealed that the pearl oysters were surprisingly bonded to the bone (Wikipedia, dental implants). After that, implants did not appear in dental clinical practice until the early 1900s, and although trial and error were carried out, they were not established. In the 1960s, Professor Brånemark and his colleagues from Sweden demonstrated that titanium could bond to bone, which developed into today's bone-bonded implants [*6], which have become the most effective treatment for tooth loss.

On the other hand, it is thought that there are some issues osseointegrated implants. The periodontal ligament plays an important role in the intrinsic functions of the tooth organ, such as shock absorption when biting, tooth sensation (chewing



comfort), infection prevention, and tooth movement concerned with aging and body growth. Current osseointegrated implants do not have the periodontal ligament, and in addition to lacking these functions, they are not suitable for young patients who are still growing, and from the perspective of oral hygiene in elderly care, teeth cannot be extracted when desired, which poses social issues.

Therefore, in 2009, we began to study the "next-generation bioimplants" that have periodontal ligament, based on "tooth organ regeneration" using bioengineered tooth germs.

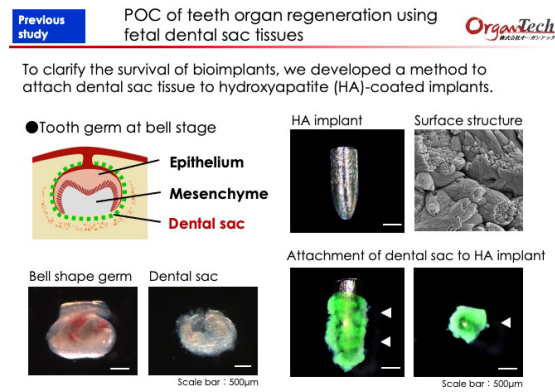
2. Overview of our technology

We have been promoting the development of "next-generation bioimplants via the

periodontal tissue integration" which are equivalent to natural teeth, based on a research strategy to regenerate periodontal tissues [*7] based on the tooth development program.

【Demonstration of the conceptual model using small animals】

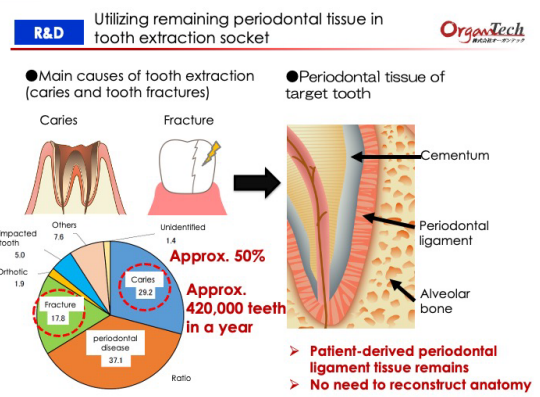
To demonstrate the conceptual model of our technology, dental sac tissue [*8] (immature tissue containing stem cells of all the components of periodontal tissue, including cementum, periodontal ligament, and alveolar bone) was extracted from fetal mice, wrapped around the implants coated with hydroxyapatite (HA), and transplanted into the site of tooth loss in adult mice. It



was observed that the periodontal tissue equivalent to that of natural teeth was newly formed around the implant and engrafted. The periodontal tissue of the bioimplant has physiological mobility through appropriate bone remodeling [*9] in response to orthodontic forces, and has even been shown to recover neural function capable of transmitting sensation and pain to the central nervous system. With this result, in 2014, we were the first in the world to demonstrate the concept of next-generation bioimplant treatment via periodontal tissue integration, which is structurally and physiologically capable of linking with the maxillofacial region [*10] (Oshima M. et al., Scientific Reports, 4: 6044, 2014).

【Verification of a practical model using large animals】

Since the bioimplant that proved the concept uses fetal dental sac tissues, the challenge for practical application was the need to use periodontal tissue derived from the patient (adult). We have data demonstrating the effectiveness of bioimplants using cultured adult periodontal ligament cells. However, it was expected that it would be difficult to widely disseminate this technology to general dental clinics, etc., because it is necessary to extract teeth to collect cells, and the cell culture process makes it a medical technology that falls under regenerative medicine (regenerative medicine product [*11]). Therefore, we



developed a treatment method that uses healthy periodontal tissue remaining in the alveolar bone wall of the tooth extraction socket [*13] as a practical cell material in cases where a tooth has been extracted due to secondary caries or fracture [*12]. This not only makes it possible to use patient-derived periodontal tissue in its anatomical structure, but also makes it possible to carry out the treatment within the scope of conventional dental treatment and implant treatment.

Next, we have been developing technology to stimulate the bonding and maturation of the periodontal tissue in the extraction sites and the surface of the implant. It has been revealed that mechanical stimuli affect the formation and maturation of periodontal tissues around

natural teeth, such as the maturation of periodontal ligament tissue and the optimization of fiber orientation [*14] through functional occlusion. We believe that the application of appropriate occlusal stimuli is important for the formation and maturation of periodontal tissues around implants, and have developed a transplant device to transmit occlusal stimuli non-invasively and indirectly to the implant. This is a transplant system created by dental technicians [*15] that positions and fixes the implant at an appropriate depth in the extraction socket so that it does not come into contact with the alveolar bone wall, and transmits the occlusal pressure applied to the adjacent teeth to the implant via the device.

R&D Development of bioimplant transplantation technology OrganTech

We have developed a bio-implant transplantation using the mechanism of induction of periodontal tissues caused by mechanical stress.

● **Technical concept of bio-implant transplantation**

Simulation of implantation
 BIOING® (Wada Precision Casting Laboratory)

External stimuli
 Occlusal pressure

External stimuli
 Occlusal pressure

External stimuli

Mechanical stress

Fixture

Fixture

Occlusal pressure

- Implant size selection using CT data
- Determination of implant position in extraction pit & manufacturing of device

Fixes the implant in place without contacting the socket wall

Non-invasive and indirect transmission of mechanical stimuli promotes periodontal tissue attachment

R&D Large animal model of bio-implant OrganTech

To verify the bioimplant established in the mouse model, we have been examining the bone survival in the jaw bone using dogs.

Day 0 9 weeks 18 weeks Engrafting bio-implant

Scale bar: 1cm

H&E staining High magnified image Periotest at 18weeks after engraftment

Imp

Periodontal ligament

Alveolar bone

Natural tooth
 Approx. 2.2

Bio-implant
 2.9 ± 1.1

In fact, when we conducted testing on large animals using an implant device capable of transmitting mechanical stimuli and utilizing an extraction socket, dental X-rays showed that the surrounding alveolar bone had moved closer together 9 weeks after implantation, and the alveolar dura line [*17] became clearly visible around the entire implant, with a single layer of periodontal ligament space [*16] between them.

The bioimplant, which had taken root in the oral cavity 18 weeks after implantation, was shown to function within the dentition without any abnormal findings such as loss, and to have the same level of physiological mobility as natural teeth. Histological analysis revealed a periodontal ligament region similar to that of natural teeth around the entire circumference

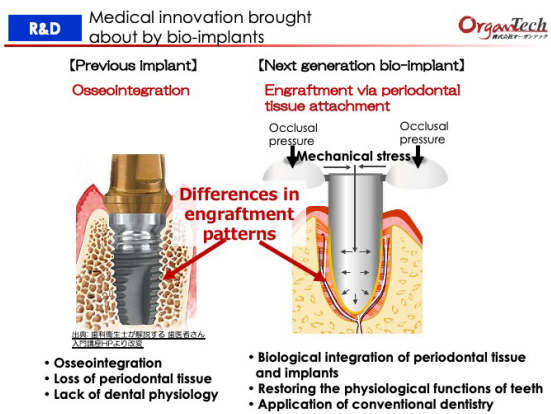
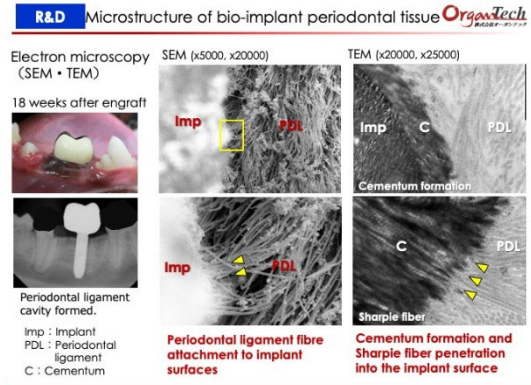
of the implant, and the course of the periodontal ligament connecting the implant to the alveolar bone was confirmed.

Furthermore, when the microstructure of the periodontal tissue around the bioimplant was analyzed using a scanning electron microscope [*18], dense periodontal ligament fibers were confirmed on the implant surface, and periodontal ligament fibers were shown to be attached to the implant surface. In addition, a transmission electron microscope [*19] confirmed the formation

of cementum on the HA coating on the implant surface, and also revealed the presence of Sharpie fibers [*20] penetrating into the cementum. These results demonstrated the survival of the bioimplant through the attachment of periodontal tissue in a large animal model.

【Medical innovation and social contributions brought about by the results of this research】

The bioimplant technology using tooth extraction sockets is based on conventional implant treatment, but is highly original because the transplantation technique and engraftment method are essentially different. It restores the physiological function of lost teeth, and also enables the expansion of application to younger patients, who have been contraindicated until now, and treatment to connect with natural teeth. Furthermore, since it is embedded in the tooth extraction socket, no drilling operation is required, which reduces the invasiveness to the patient. Another advantage is that difficult dental problems in removing implants from elderly patients who have become dependent on care can be dealt with in the same way as tooth extraction procedures at the care site. This technology is considered to be a technological development that can bring innovation to future dental care and contribute to an aging society.





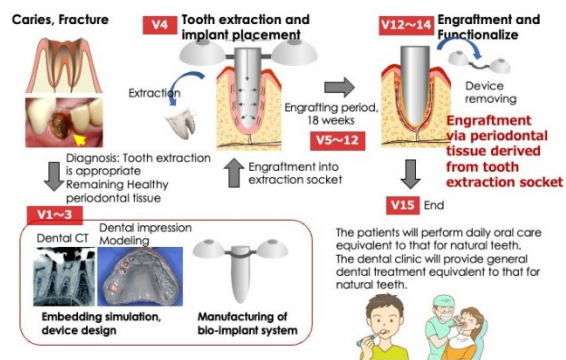
3. Overview of the specified clinical research

This specified clinical research will be implemented at the Minami Tohoku Medical Clinic in Koriyama City, Fukushima Prefecture. The research overview is as follows.

Research Name	A study to evaluate the efficacy and safety of periodontal ligament-bound implants using the periodontal ligament tissue remaining in the tooth extraction sites
Target patients	Patients who require tooth extraction due to root fracture, crown fracture, caries, avulsed teeth, etc.
Criteria of Patient	<p>Patients who meet all of the following criteria:</p> <ol style="list-style-type: none"> 1) Single-rooted teeth from the upper and lower jaw anterior teeth to premolars that require extraction due to caries or tooth fractures. However, healthy periodontal tissue remains around the root of the tooth to be extracted. 2) The teeth on either side of the tooth to be extracted are natural teeth with healthy periodontal tissue. In addition, appropriate occlusion can be obtained with the opposing teeth. 3) Age 18 or older at the time of obtaining consent. 4) Written consent is obtained from the patient regarding participation in this clinical research.
Research Director	Shohei Kasugai, DDS, PhD
Period	Feb. 1st, 2025 – Jan. 31st, 2027 (planned) *From first consultation to completion: Approximately 15 months
Medical institution	General Incorporated Association, Institute of Neurological Diseases, Southern Tohoku General Hospital, Southern Tohoku Medical Clinic
Number of cases	6 cases

【Treatment procedure】

The treatment will take 15 months from the first consultation to completion. During that time, you will visit the hospital 15 times at set times. During the first three visits, we will determine whether this treatment is appropriate, select the implant that is best suited to the tooth to be extracted, and create a device to fix the implant and adjacent teeth. During the fourth visit, the target tooth will be extracted and the implant will be inserted at the same time. For up to 18 weeks after transplantation, we will observe the progress and check the implant's survival and the formation of the periodontal ligament. During this time, you will be asked to avoid biting hard objects or rubbing the implanted area with a toothbrush. Between 18 and 36 weeks, the device that fixed the implant and the adjacent teeth will be removed, and treatment will end 48 weeks after transplantation. After that, you will be able to chew as you would with your natural teeth and brush your teeth as usual.



【Predicted risks and responses】

This clinical study is the world's first implant treatment that allows for implantation through periodontal tissue bonding, and is a first-in-human trial using an unapproved product. Therefore, the safety of the patients participating in the study will be given top priority and treatment will be performed with great care, but there is a possibility of infection at the implant site and bone resorption around the implant. Please note that treatment such as implant removal may be performed while monitoring the progress of treatment. If the implant is removed, appropriate dental treatment will be performed, including regular implant treatment.

4. Significance of this clinical study and future research and development

Implant treatment is developing as a treatment for tooth loss. The global implant market was US\$4.436 billion in 2021, but is expected to grow to US\$8.037 billion in 2030 (1.2 trillion yen at 150 yen per dollar; Market Report "Global Dental Implant Market 2023-2030" by DataM Intelligence). Furthermore, the Japanese Dental Association's "Dental Innovation Roadmap to 2040 <Extending Healthy Lifespan>, II. New Materials and Equipment" predicts that in the first period (2019-2025), "next-generation bioimplants with functions similar to natural teeth will be developed," and in the third period (2033-2039), "next-generation



bioimplant treatments with functions similar to natural teeth will become common" (Journal of the Japanese Dental Association: 39, 5-30, 2020). Next-generation bioimplants are a new dental treatment with functions similar to natural teeth, which is a departure from the concept of bonded implants, and are significant in terms of their development in oral medicine and health and longevity.

In OrganTech's research and development pipeline for next-generation bioimplants, this specific clinical study is positioned as a treatment for single-rooted teeth with a first-generation bioimplant that uses the periodontal ligament of the extraction socket. On the other hand, molars have multiple roots, so OrganTech plans to continue research and development in the future as the next research and development pipeline. Furthermore, for cases where the periodontal ligament cannot be used due to periodontal disease or other reasons, or for treatment of teeth that have been lost for a long time, we plan to develop new treatment techniques, including the regeneration of the periodontal ligament and alveolar bone, as second-generation bioimplants.

Furthermore, since the next-generation implant directly bonds the periodontal ligament, a ligament, to metal and functions, it is possible that it could be applied to future "cyborg" technology. In that sense, the next-generation implant can be called a "dental cyborg," the first step toward cyborgs. In the future, it is thought that applying this technology will enable people to create arms and legs made of metal, which can be moved at will by connecting them to the ends of their own muscles using ligaments and tendons, and that perception can be achieved by applying the already developed method of sending and receiving electrical signals, thereby opening up the world of cyborgs.

5. Research Support

Non-clinical studies on periodontal ligament-attached implants were supported by:

- Research funds from the Organ Induction Research Team, RIKEN, Japan (2014–2024).
- Joint research funding from RIKEN, Tokushima University, and Organ Technologies Inc.
- Japan Society for the Promotion of Science (JSPS), Grant-in-Aid for Scientific Research (A), Principal Investigator: Takashi Tsuji (2008–2010),
"Development of Fundamental Technologies for Tooth Regenerative Medicine Systems," 48,620,000 yen.
- JSPS, Grant-in-Aid for Scientific Research (A), Principal Investigator: Takashi Tsuji (2013–2015),
"Development of Fundamental Technologies for Next-Generation Organ Regenerative Medicine," 47,190,000 yen.
- JSPS, Grant-in-Aid for Scientific Research (A), Principal Investigator: Takashi Tsuji (2019–



2021),

"Development of Fundamental Technologies for Innovative Organ Induction through Organ Formation Fate Conversion," 39,120,000 yen.

- Japan Agency for Medical Research and Development (AMED), 2018, Research and Development Projects for Medical Devices and Systems for Realizing Future Medicine, Support Program for Innovative Medical Devices [Medical Device Development Research], Principal Investigator: Masamitsu Oshima, Project Number: 18he1902004h0001, *"Development of Next-Generation Bioimplant Systems for Comprehensive Regeneration of Periodontal Tissue Structure and Function."*
- JSPS, Grant-in-Aid for Scientific Research (C), Principal Investigator: Masamitsu Oshima (2019–2021), Project Number: 19K10208, *"Development of Bioartificial Tooth Roots Based on the Formation and Maturation Mechanisms of Periodontal Tissues under Occlusal Mechanical Stress."*
- The Terumo Life Science Foundation, Development Grant II (Medical Device Development) (2019–2022), Principal Investigator: Masamitsu Oshima, *"Development of Dental Bioimplants with Functional Periodontal Tissue Structures."*
- Development support from the Drug Discovery and Medical Technology Platform Program of RIKEN's Science and Technology Hub Promotion Headquarters.
- Contributions from RIKEN for *"Basic and Applied Research for Next-Generation Organ Regenerative Medicine."*

6. Speaker Profiles at this Press Conference

■ Takashi Tsuji, PhD.

Chairman and Founder, Organ Technologies Inc.

Visiting Professor, Tokyo Dental College Oral Science Research Center, Kitasato University Graduate School of Medical Sciences

【Career Summary】

1989: Researcher, Central Research Institute, Yamanouchi Pharmaceutical (now Astellas Pharma)

1992: Completed doctoral coursework without a degree, Department of Biology, Graduate School of Science, Kyushu University

1994: Senior Researcher, Pharmaceutical Research Institute, Japan Tobacco Inc.

2001: Associate Professor, Department of Biotechnology, Faculty of Industrial Science and



- Technology, Tokyo University of Science
- 2007: Professor, Department of Biotechnology, Faculty of Industrial Science and Technology, Tokyo University of Science
- 2009: Professor, Research Organization for Science & Technology, Tokyo University of Science (also served as Professor at the Graduate School of Industrial Science and Technology)
- 2010: Professor, Intellectual Property Strategy Program, Graduate School of Innovation Studies, Tokyo University of Science
- 2014: Group Director, Organ Induction Research Group, RIKEN Center for Developmental Biology
- 2015: Team Leader, Organ Induction Research Team, RIKEN Center for Multicellular System Formation (reorganized)
- 2017: Project Leader, Drug Discovery and Medical Technology Platform Program, Science and Technology Hub Promotion Headquarters, RIKEN (until March 2024)
- 2019: Team Leader, Organ Induction Research Team, RIKEN Center for Biosystems Dynamics Research (reorganized)
- 2024: Chairman and Founder, Organ Technologies Inc.

He has also served as a visiting professor at institutions such as Louis Pasteur University in France (2008), Keio University, Kitasato University, Tokyo University of Science, Kwansai Gakuin University Graduate School, and Kobe University Graduate School of Medicine (until 2024). Currently, he is a visiting professor at Kitasato University Graduate School of Medical Sciences and Tokyo Dental College.

■ Masamitsu Oshima, DDS, PhD

Associate Professor, Department of Oral Function and Occlusal Reconstruction, Graduate School of Biomedical Sciences, Tokushima University

【Career Summary】

- 2009: Ph.D. (Dentistry), Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University
- 2009: Postdoctoral Researcher, Graduate School of Industrial Science and Technology, Tokyo University of Science
- 2011: Assistant Professor, Research Organization for Science & Technology, Tokyo University of Science
- 2013: Assistant Professor, Graduate School of Medicine, Dentistry and Pharmaceutical



Sciences, Okayama University

2017: Associate Professor, Department of Oral Function and Occlusal Reconstruction,
Graduate School of Biomedical Sciences, Tokushima University

2017: Project Manager, Drug Discovery and Medical Technology Platform Program,
Science and Technology Hub Promotion Headquarters, RIKEN (part-time, until
March 2024)

■ Shohei Kasugai, DDS, PhD.

Director, Maxillofacial Implant Center, General South-Tohoku Medical Clinic, Brain
Research Institute;

Professor Emeritus, Tokyo Medical and Dental University

【Career Summary】

1979: Graduated from Tokyo Medical and Dental University Faculty of Dentistry

1983: Ph.D. (Dentistry), Graduate School of Dentistry, Tokyo Medical and Dental
University

1983: Assistant, Department of Dental Pharmacology, Faculty of Dentistry, Tokyo Medical
and Dental University

1989: Postdoctoral Researcher, Faculty of Dentistry, University of Toronto

1991: Lecturer, Department of Dental Pharmacology, Faculty of Dentistry, Tokyo Medical
and Dental University

1995: Associate Professor, Department of Dental Pharmacology, Faculty of Dentistry,
Tokyo Medical and Dental University

2000: Professor, Department of Oral Functional Anatomy, Graduate School of Medical and
Dental Sciences, Tokyo Medical and Dental University

2001: Director, Implant Clinic, Dental Hospital, Tokyo Medical and Dental University

2004: Professor, Department of Implant Dentistry and Oral Regenerative Medicine,
Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental
University

2020: Professor Emeritus, Tokyo Medical and Dental University

2020: Director, Maxillofacial Implant Center, General South-Tohoku Medical Clinic, Brain
Research Institute

【Current Roles and Positions】

Specialist, Japanese Society of Oral Implantology

Instructor, Japanese Society of Oral Implantology



Instructor, Japanese Society of Maxillofacial Implantology

President, Society for BioIntegration

Executive Director, Japanese Society of Maxillofacial Implantology

Executive Director, Japanese Division of the International Congress of Oral Implantologists (ICOI)

7. Terminology Explanation

*1. Bio-implant

An implant in which a metal implant is combined with periodontal ligament cells.

*2. Dental caries

Commonly referred to as cavities, a condition where tooth structure (enamel and dentin) is dissolved by acids produced by bacteria in the mouth.

*3. Organ germ

Refers to the “seed” of an organ formed during organ development. Most organs are formed from two types of cells: epithelial cells and mesenchymal cells.

*4. Organ germ method

A method for artificially creating organ primordia, developed in 2007 by Tsuji's research team. It has demonstrated the functional regeneration of various organs such as teeth, hair, and glands.

*5. Eruption

The process in which a tooth emerges by breaking through the gum tissue.

*6. Osseointegrated implant

A composite tissue consisting of cementum, periodontal ligament, and alveolar bone, covering the tooth root surface. It is also a general term that includes the gingiva. Cementum is a hard tissue that covers the root surface, alveolar bone supports the teeth, and the periodontal ligament is fibrous connective tissue that connects the cementum to the alveolar bone. Periodontal tissue supports the teeth and acts as a cushion for occlusal forces.

*7. Periodontal tissue

A composite tissue consisting of cementum, periodontal ligament, and alveolar bone, covering the tooth root surface. It is also a general term that includes the gingiva. Cementum is a hard tissue that covers the root surface, alveolar bone supports the teeth, and the periodontal ligament is fibrous connective tissue that connects the cementum to the alveolar bone. Periodontal tissue supports the teeth and acts as a cushion for occlusal forces.

*8. Dental sac tissue



Undifferentiated connective tissue surrounding the tooth germ, the primordial form of teeth during the embryonic stage. Cementum, periodontal ligament, and alveolar bone, all components of periodontal tissue, develop from the dental sac tissue. As the tooth germ grows, periodontal tissue is formed around the root.

*9. Bone remodeling

Also known as bone metabolism, it is a process where osteoblasts (bone-forming cells) and osteoclasts (bone-resorbing cells) work together to replace old bone with new bone. Bone remodeling occurs continuously in all bones and is essential for orthodontic treatment, where teeth need to move.

*10. Maxillofacial region

Refers to the entire jaw, including the upper and lower dental arches, palate, tongue, and soft tissues within the oral cavity, as well as the face, including the eyes, nose, cheeks, and lips. The maxillofacial region is closely related to the oral cavity and plays a vital role in essential functions such as eating, swallowing, speech, and breathing, as well as in human communication.

*11. Regenerative medical products

Products manufactured by culturing live cells or tissues from humans or animals for purposes such as reconstructing or repairing body structures and functions, treating or preventing diseases, or for genetic therapy. Before use in medical treatments, regenerative medical products undergo nonclinical studies (such as animal testing), clinical research, and trials to verify their safety and efficacy. Approval from the Ministry of Health, Labour and Welfare is required before they can be used in human treatment.

*12. Fracture

Refers to a break in a tooth. When the crown breaks, it is called a crown fracture; when the root breaks, it is called a root fracture.

*13. Extraction site

A cavity in the alveolar bone that remains after a tooth is extracted. After extraction, the cavity is filled with blood and covered by a scab called a blood clot, which facilitates the healing of the alveolar bone and gingiva. In this study, the aim is to promote fixation using the healthy periodontal tissue that remains on the alveolar bone wall after tooth extraction.

*14. Fiber alignment

A cavity in the alveolar bone that remains after a tooth is extracted. After extraction, the cavity is filled with blood and covered by a scab called a blood clot, which facilitates the healing of the alveolar bone and gingiva. In this study, the aim is to promote fixation using the healthy periodontal tissue that remains on the alveolar bone wall after tooth



extraction.

*15. Dental technology

A medical skill involving the fabrication and repair of dental prostheses, such as fillings, crowns, dentures, and orthodontic devices, under the direction of a dentist. Dental technicians create customized devices tailored to each patient.

*16. Periodontal ligament space

A gap (periodontal ligament region) located between the tooth root and alveolar bone, observed in dental X-rays. The periodontal ligament is a soft tissue and appears as a space (periodontal ligament space) in X-ray images. It is seen in healthy natural teeth but is not observed in conventional implants, which are directly integrated with the alveolar bone.

*17. Lamina dura

A thin layer forming the inner wall of the alveolar bone surrounding the root, observed as a white line on dental X-rays in healthy teeth. When the connection between the root and alveolar bone is disrupted due to periodontitis or trauma, changes such as widening of the periodontal ligament space and discontinuity of the lamina dura may occur.

*18. Scanning electron microscope

A device used to observe a sample's surface by irradiating it with electron beams and detecting the emitted electron signals. The brightness of each point reflects the signal strength, creating an image of the sample's surface structure. SEM has higher resolution than optical microscopes and is widely used in fields such as materials science, semiconductor devices, medicine, and biology.

*19. Transmission electron microscope

A device that uses a high-voltage electron beam to achieve magnifications of several million times, allowing detailed analysis of the internal structures of samples, such as arrangement, structure, and crystal defects. TEM provides much higher resolution than optical microscopes and is used extensively in biological fields for observing cells and proteins.

*20. Sharpie fibers

Collagen fibers found in connective tissues and soft tissues such as the periodontal ligament and periosteum. In dental anatomy, Sharpie fibers are the main component of the periodontal ligament fibers, connecting the cementum to the alveolar bone. Anatomically, two types of Sharpie fibers connect the respective tissues: (a) alveolar bone and principal periodontal ligament fibers, and (b) principal periodontal ligament fibers and cementum. These fibers form a continuous structure, the cementum–periodontal ligament–alveolar bone complex.



8. Contact Information

●Inquiries about Clinical Research

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