

Global Center of Excellence (GCOE) Program
International Research Center for Molecular Science in Tooth and Bone Diseases
The 4th International Symposium

Surface Modification and Design of Dental Implant

歯科インプラントの 表面改変とデザイン

February 11, 2010

Tokyo Medical and Dental University
Symposium Chair: Shohei KASUGAI

東京医科歯科大学 グローバル COE プログラム
歯と骨の分子疾患科学の国際教育研究拠点
第 4 回国際シンポジウム





P R O G R A M

9:30 – 9:45

Opening Remarks

Masaki NODA (Tokyo Medical and Dental University)

9:45 – 10:05

Clinical Impacts of Surface Modifications and Designs of Dental Implant

Shohei KASUGAI (Tokyo Medical and Dental University)

10:05 – 11:20

Osseointegration: Interfacial Cellular Behaviour and Fine Structure

Peter THOMSEN (University of Gothenburg, SWEDEN)

11:20 – 11:55

Photocatalytic Effects for the Functional Surface Modification to Dental Implants

Takashi SAWASE (Nagasaki University)

11:55 – 13:00

Lunch

13:00 – 13:35

Biofunctionalization of Titanium with Electrodeposition of Functional Molecules

Takao HANAWA (Tokyo Medical and Dental University)

13:35 – 14:10

Bio-functional Dental Implants with Pharmaceutical Surface Modification

Masao YOSHINARI (Tokyo Dental College)

14:10 – 14:45

Design and Surface Modification of Zirconia Implant

Seiji BAN (Kagoshima University)

14:45 – 15:00

Break

15:00 – 16:15

Different Implant and Abutment Surfaces and Designs: Evaluation of Early Wound Healing, Final Osseointegration and Soft tissue Integration

Peter SCHUPBACH

(Research Center for Implants and Biomaterials, SWITZERLAND)

16:20 – 17:10

Discussion

17:10

Closing Remarks

Shohei KASUGAI

18:00 –

Reception at “Tokyo Garden Palace”

Opening Remarks

Masaki NODA

Program Leader of Global Center of Excellence (GCOE) Program, “International Research Center for Molecular Science in Tooth and Bone Diseases”

Professor of Molecular Pharmacology, Medical Research Institute, Tokyo Medical and Dental University



It is our great pleasure to welcome all of the distinguished guest speakers and participants to the 4th International Symposium of Global Center of Excellence program of Tokyo Medical and Dental University. This program has been led by our President Takashi Ohyama and has been supported by the funding from Japanese government with the budget over 3 million dollars per year for five years. Our university is one of the top institutes in Japan and the world in terms of the research in the field of tooth and bone diseases.

We have been focusing on the researches in both clinical and basic area of tooth and bone diseases, especially to overcome obstacles in our field. We have many health issues on tooth and bone in the current era of Japan as we are facing with an ever experienced rapid increase of the aged population. Our symposium, regarding the surface modification of the implant, is really dealing with a timely issue. Advancement in this field of research is necessary to cure a number of patients who are suffering from the loss of mastication function. Needless to say, to regain and maintain mastication function is crucial for the maintenance of life. Thus, the research in this area is important for the establishment of high quality of active life in the aged population suffering from the loss of tooth.

I am very grateful to Professor Shohei Kasugai, who is the top leader of implantology in the world and Japan, to put together such a wonderful program. I hope that every participant in this symposium will enjoy the presentations and discussions and that we will have new ideas and collaboration based on this symposium.

Clinical Impact of Surface Modification and Design of Dental Implant

Shohei KASUGAI

Professor of Oral Implantology and Regenerative Dental Medicine, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, JAPAN



History of dental implant is extremely old; however, the finding of “osseointegration”, integration of pure titanium with bone, by Prof. Brånemark, in 1950s is a landmark of implant dentistry. Clinical trial of pure titanium screw type implants started in 1965 and its predictable outcome was reported in 1982. Then, the treatment with this type of implants spread all over the world. Up to now the advancement in every aspect of implant treatment, such as diagnostic tools, implants, surgery, prosthetic materials and manufacturing, is incredible. Currently, we can provide highly functional, esthetic and predictable outcomes to our patients. Among them, clinical impacts of surface modification and design of dental implant have been enormous. Surfaces of the most implants, which are available in the markets, are “modified”, such as acid-etched, blasted, anodic-oxidized and hydroxyapatite-coated, which promotes osseointegration resulting high implant survival rate even at the low bone quality site. Implant design obviously affects initial stability of the implant and stress distribution to the surrounding bone. Furthermore, the connecting structure and the micro gap between the abutment and the implant also affect the soft tissue and the marginal bone. Thus, deep understanding how surface modification and design of dental implant affect cellular and tissue responses will provide us new ideas to develop implants of next generation.

Dr. Shohei Kasugai received his DDS and Ph.D. degrees from Tokyo Medical and Dental University (TMDU). He was a post-doctoral fellow at University of Toronto from 1989 to 1991. He worked as an educator and a researcher in Department of Pharmacology in TMDU for 20 years, focusing on therapeutic drug development for osteoporosis and bone response to dental implant materials. In 2000, he became a professor of Department of Oral Implantology and Regenerative Dental Medicine and a director of Dental Implant Clinic in TMDU. His research is focused on developing biocompatible implant and bone regeneration. He received awards from International Association for Dental Research, Pharmaco-Kinetics Society, Japanese Association for Oral Biology and Academy of Osseointegration. He is a board member of Japanese Academy of Maxillofacial Implant and a committee member of Japanese Society of Oral Implantology and an active member of AO and EAO.

Osseointegration: interfacial cellular behaviour and fine structure

Peter THOMSEN

Professor of Biomaterials, Institute of Clinical Sciences, Sahlgrenska Academy
at University of Gothenburg, Sweden



Oral rehabilitation using osseointegrated titanium implants is a prime example of treatment concepts which have revolutionized modern health care. Increasing interest has been put on the surface properties of implanted materials, being the part of the implant which interacts with biological processes on different time and scale lengths. A major question is how material surface chemical and topographical properties are translated and conveyed to the biological system *in vivo*? Such knowledge would permit an intentional modulation of specific biological events.

The host response to implanted materials follows a dynamic course which involves sequential steps of bleeding, inflammation, bone formation and remodeling. Our research group has concentrated upon developing and applying techniques for sampling and preserving cells and extracellular matrix components at the immediate interface. Recent successful efforts to resolve the fine structure of intact implant-bone interfaces are described. Further, gene expression patterns of implant adherent cells during the early stages after implantation in bone will be demonstrated. The biological effects of machined, anodically oxidized and laser-treated titanium surface modifications will be used as examples. Data suggests that modification of surface properties has an important effect on the ultrastructure, down to the atomic level, of bone-implant interfaces *in vivo*. Further, the extent of involvement of inflammation, bone formation and bone resorption *in vivo* is strongly influenced by implant surface modifications during the early stage of regeneration. The potential importance of these experimental observations will be discussed in relation to clinical treatment using osseointegrated oral implants and bone-anchored limb amputation prostheses.

Professor Peter Thomsen received his training in experimental cell biology with Professor P-I Brånemark and Professor Lars E Ericson at the Department of Anatomy, University of Gothenburg, Sweden.

Following a 4-year fellowship with the Swedish Medical Research Council, he succeeded Professor Brånemark and received the Professorship and Chair of Biomaterials in the Faculty of Medicine, in 1994. He was Visiting Professor at the Interdisciplinary Research Center in Biomedical Materials, University College London, 1999-2000. He was awarded International Fellow of Biomaterials Science and Engineering in 2000. In 2003, he received the George Winter Award for excellence in biomaterials research. Dr Thomsen was a co-founder and Director of the first Interdisciplinary Swedish National Graduate School in Biomaterials 1998-2005. He became the Scientific Leader for the Institute for Biomaterials and Cell Therapy (IBCT) in 2005. In 2007, he was appointed Director of BIOMATCELL VINN Excellence Center of Biomaterials and Cell Therapy, a 10-year governmental research program on implant material properties, stem cells and regeneration of the musculoskeletal system.

Dr Thomsen's research is focussed on the processes that occur in the interface between implant and tissue. His research group is devoted to the connections between material surface properties and *in vivo* inflammation and regeneration. The group has a track-record in the development and application of novel techniques to resolve the fine structure and cell behaviour of such interfaces. Current research projects include mechanisms of osseointegration, strategies to improve the potential for bone regeneration and the translation of this knowledge to orthopaedics and dentistry.

Photocatalytic Effects for the Functional Surface Modification to Dental Implants

Takashi SAWASE

Professor of Applied Prosthodontics, Graduate School of Biomedical Sciences,
Nagasaki University, JAPAN



The implant finish, that is, the surface property, has been recognized as an important factor for successful osseointegration. Ever since this factor was proposed, surface topography has focused on promoting early and secure bone formation around dental implants. These topographical modifications have boosted the success rate of the implant therapy, especially in patients with poor bone quality sites and have significantly reduced the healing period. Today, state of the art studies focus on further chemical and/or nano level modifications with taking into account the affinities of cells, proteins, and ions to make the surface “bioactive”.

It is well known that the thin titanium oxide layer on the pure titanium is the source of the biocompatibility. In addition, titanium oxide shows several interesting functions under UV light illumination, for example, anti bacterial property, hydrophilicity, dirtiness prevention, NOx decomposition, and deodorization, so called photocatalytic activities.

For the past decade, our group has applied the photocatalytic activities on the implant surface. Drastic anti-bacterial property was proven since the viabilities of various periodontal pathogens were suppressed to less than 1% after UV illumination. Furthermore, super-hydrophilicity with the water contact angle of less than 1° resulted in promptly trapping proteins on the surface, and subsequently enhancing cell adhesion, spreading, and proliferation. The following in vivo rabbit or dog studies presented significantly enhanced the time of bone apposition. In my presentation, our research activity details will be briefly disclosed and future strategies of the implant with photocatalytic properties will be discussed.

Dr. Takashi Sawase graduated from the Nagasaki University School of Dentistry in 1989, and obtained his doctorate in dental science in 1993. He is currently professor and chairman of the Department of Applied Prosthodontics at the Graduate School of Biomedical Sciences, Nagasaki University and also appointed director of Oral and Maxillofacial Implant Center at the Nagasaki University Hospital. His research has been thoroughly focused on surface analysis and modification of biomaterials. From 1996 to 1998, Dr. Sawase was invited as a visiting scientist at the Department of Biomaterials/Handicap Research, Gothenburg University. During these two years, extensive research on the surface oxide layer properties of titanium implants, and their bone responses were conducted. His current research interests include photocatalytic effects of titanium dioxide and their application to implant materials. His latest research focuses on the novel functional analysis of bone around loaded implants by the preferential alignment of hydroxyapatite crystals, which may contribute to the determination of ideal implant designs. Dr. Sawase is an editorial board member of the Clinical Implant Dentistry and Related Research, and is a reviewer for numerous international and domestic journals. He also dedicates his time to dental practice, and is a specialist in Prosthodontics and Implant Dentistry.

Biofunctionalization of Titanium with Electrodeposition of Functional Molecules

Takao HANAWA

Professor, Denpartment of Metals, Institute of Biomaterials and Bioengineering,
Tokyo Medical and Dental University, JAPAN



Surface modification is an important and predominant technique for obtaining biofunction in metals for biomedical use including dentistry. Dental implants are requires Biofunctional molecules, poly(ethylene glycol)(PEG) was immobilized to titanium surface to control the adsorption of proteins and adhesion of cells, platelets, and bacteria. To bifunctionalize the surface of metals, PEG molecules are immobilized to titanium, cobalt-chromium-molybdenum alloy and 316L type stainless steel with electrodeposition. PEG molecules strongly and efficiently immobilized to titanium surface with electrodeposition, compared than that with immersion. In addition, concentration of active hydroxyl groups on surface oxides on metals influences the immobilization amounts of PEG. PEG-immobilized surface inhibited the adsorption of protein, adhesion of cells, adhesion of platelet, and adhesion of bacteria on titanium. This technique is directly applied to the immobilization of biomolecules such as collagen. On the other hand, to immobilize peptide containing Arg-Gly-Asp (RGD) to the electrodeposited PEG on Ti, PEG with an $-NH_2$ group and a $-COOH$ group (NH_2 -PEG-COOH) must be employed. One terminal group, $-NH_2$, is required to bind stably with a surface oxide on a metal. The other terminal group, $-COOH$, is useful to bond biofunctional molecules such as RGD. NH_2 -PEG-COOH works as a binder of RGD to metals surface and molecular structure except terminals is hydrophobic and inhibit the adsorption of proteins; RGD part probably works as a bone formation site. This RGD/PEG/Ti surface accelerated calcification by MC3T3-E1 cell. This electrodeposition technique is applied to most of metal substrates and molecules having electric charges.

Dr. Takao Hanawa is professor, Denpartment of Metals, Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, since July 1, 2004. Dr. Hanawa graduated Hokkaido University, Department of Metallurgical Engineering at 1981, and is given D.D.Sc form Hokkaido University at 1989 and Ph.D. form Tohoku University at 1998. He has experiences as Assistant Professor at Hokkaido University School of Dentistry, Associate Professor in Tokushima University School of Dentistry, and Dupty-Director-General, Biomaterials Research Centerm, National Institute for Materials Science. He also occupies a position of Professor, Graduate School of Engineering, The University of Tokyo since April, 2009. Main academic awards are as follows: 1995 The Award for Young Investigator of Japanese Society for Biomaterials, 1999 Minister Award of Science and Technology Agency, Japan, 2001 Award for Distinguished Service, Japan Institute of Metals, 2004 Award for Developmental Engineering, Japan Institute of Metals, 2005 JSAO- Grant-Award, Japanese Society for Artificial Organs, 2009 The Award of Japanese Society for Biomaterials. Number of refereed original articles is 175, that of reviews is 70, and that of book chapters and edited books is 37. The research interest is metallic biomaterials, dental materials, biofunctionalization of metals, and metal-tissue interactions.

Bio-functional Dental Implants with Pharmaceutical Surface Modification

Masao YOSHINARI

Professor of Oral Implants Research

Oral Health Science Center, Tokyo Dental College, JAPAN



Since biomaterials contact many different tissues, those materials must have optimum surface compatibility with the host bone tissue and soft tissue, as well as anti-microbial properties on exposed region of the mucosa. Such materials can be created under well-controlled conditions by modifying the surfaces of materials that contact those tissues. This paper is focused on the surface modification of biomaterials for developing “Bio-functional dental implants”, which are compatible with all host tissues, using a cold-plasma technique and a material-binding artificial peptide.

At the bone tissue/implant interface, a thin calcium phosphate coating with rapid heating was effective in controlling the dissolution without cracking the coating. These thin calcium phosphate coatings may directly promote osteogenesis, but also enable immobilization and subsequent DDS. Simvastatin is effective candidate that is reported to increase the expression of BMP-2. Thin-film coating of hexamethyldisiloxane was activated by O₂-plasma treatment. QCM-D analysis demonstrated that simvastatin was immobilized on the plasma-treated surfaces due to introduction of O₂-functional groups. At the soft tissue/implant interface, multi-grooved surface topographies and utilizing the adhesive proteins such as fibronectin or laminin-5 may help in providing a biological seal around the implant. At the oral fluid/implant interface, F⁺-implantation and immobilization of anti-microbial peptides conjugated with titanium binding peptides were responsible for inhibiting the biofilm accumulation.

Prof. Masao Yoshinari received a B.E. in Electronics from the Ibaraki University in 1972. In 1974, he joined the Department of Dental Materials Science, Tokyo Dental College as a Research Assistant. He became Assistant Professor in 1980, and earned a Ph.D. in Dental Materials Science in 1986 from Tokyo Dental College. He then became Associate Professor in 1998, and Chief Professor in 2008, Division of Oral Implants Research, Oral Health Science Center, Tokyo Dental College. Prof. Yoshinari is a member of Editor of Journal of the Japanese Society for Oral Implantology, and a member of ISO Standards Development and Technical Committee ISO/TC 106/SC8 (Dental Implantology). He also serves as a Director of Basic Science of Dental Implantology, Japanese Society for Oral Implantology, and a leader of Research Group in the Oral Health Science Center, Tokyo Dental College. His current research interests include: 1) surface modifications of implant materials, 2) drug delivery systems for tissue engineering.

Design and Surface Modification of Zirconia Implant

Seiji BAN

Professor of Biomaterials Science, Graduate School of Medical and Dental Sciences

Kagoshima University, JAPAN



Zirconia ceramics have been increasingly applied to dental crowns and bridges, in combination with the development of computer-aided design and computer-aided machining (CAD/CAM). Furthermore, zirconia ceramics have been expanded to the various clinical applications in dentistry such as implant and post. From more than 20 years ago, biocompatibility of zirconia has been investigated as dental implant material in vitro and in vivo. It is conceived that zirconia is bioinert. We also reported that biocompatibility of two kinds of zirconia, Y-TZP and NANOZR, was similar to commercially pure titanium. Our results demonstrated that MC3T3-E1 on all the plates appeared to be attached and proliferated well. And, there were no significant differences in the proliferation between them. It implies that both zirconia are chemically stable to be inert on the cell proliferation such as titanium. Therefore, to apply zirconia as an implant, the surface of zirconia should be modified to act as bioactive. There are generally two approaches: The zirconia surface is made a porous quality and is chemically modified. Recently, a few dental implant made of zirconia was introduced in Europe. For example, “Z-Look₃”, Z-Systems Co., and “White Sky Implant”, bredent medical Co., were marketed with sandblasting. “ZIRALDENT”, Metoxit Co., has the porous ZrO₂ surface, so called “ZIRCAPORE”. The surface of “CeraRoot”, Oral iceberg S.L., is acid etched, so called “Ice Surface”. These surfaces are roughened and/or porous surfaces, but not chemically modified. And, the common design of these zirconia implants is one-piece type.

I was born on July 10th, 1951, in Osaka. In April 1970, I entered Nagoya Institute of Technology (NIT). In March 1974, after finishing the four-year undergraduate course, I became a student in master course of the inorganic materials science of NIT. In March 1976, after finishing the two-year master course, I obtained the master degree of engineering from NIT. In April 1976, I was employed as a research staff at Tokai Rika Denki Co. Ltd. In March 1982, I was employed as an assistant professor at School of Dentistry, Aichi-Gakuin University. In October 1987, I received the doctor degree of dentistry from Aichi-Gakuin University. From August 1988 to August 1989, I studied in leave at College of Dentistry, University of Florida. In March 1995, I received the doctor degree of engineering from NIT. In April 2001, I was employed as a professor at Faculty of Dentistry, Kagoshima University. In April 2003, the affiliation changed from Faculty of Dentistry to Graduate School of Medical and Dental Sciences due to the reorganization. In April 2003, I received the best paper award from the Japanese Society for Dental Materials and Devices. From April 2008 to the present, I have served as an Editor-in-Chief of Dental Materials Journal and as a member of Board of Director of the Japanese Society for Dental Materials and Devices. For the past several years, I have been doing research work in the field of dental application of high strength ceramics such as zirconia.

Different implant and abutment surfaces and designs: Evaluation of early wound healing, final osseointegration and soft tissue integration"

Peter SCHUPBACH

Director of Research Center for Implants and Biomaterials, Switzerland



The osseointegration rate of titanium dental implants is related to their composition and surface texture. The impact of various commercially as well as experimental surfaces on early wound healing, osseointegration, maintenance on primary and long term stability will be shown and the clinical implications elucidated. In a second part, a review of the multiple factors influencing the outcome of the periimplant soft tissue integration will be given. Detailed research data of the junctional epithelium adherence and resulting sealing towards the oral cavity, as well as the connective tissue interface to implants, will be compared for machined, acid etched, oxidized and microstructured implant collars. Also, detailed histological research data of the soft tissue adaptation to machined versus zirconium dioxide abutments will be demonstrated. The second part will be closed by an evaluation of the risks having rough surfaces exposed to the periimplant soft tissues and eventually to the oral cavity. A third part finally will deal with the influence of various implant as well as abutment designs on the osseointegration as well as on the soft tissue integration. Basic research data as well as clinical data will be presented.

Peter Schupbach studied natural sciences at the Federal Technical High School of Switzerland and did in 1979 his degree as Doctor of Science. He spent over 20 years at the Dental Institute of the University of Zurich as a head of a histological group. He has a PhD in biology and was lecturer at the Faculty of Medicine of the University Zurich for "Oral Biology and Pathophysiology". He is member of several international organizations and author or co-author of over 70 peer-reviewed publications in the fields of implantology, bone augmentation, tissue regeneration, oral microbiology and oral pathophysiology. He is an international lecturer in implantology. Today he runs a Research Center for Implants and Biomaterials in Switzerland. He is Adjunct Professor at the School of Dentistry, Medical College of Georgia, Augusta and since 2008 he is Associate Professor of Periodontics at the School of Medicine, Robert Schattner Center, University of Pennsylvania, USA. He also is a consultant for the "The International Journal of Periodontics and Restorative Dentistry" and faculty member of the "Global Institute for Dental Education" (gIDE, Los Angeles, US).

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