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Mitsuo Niinomi
Institute for Materials Research, Tohoku University

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Patrik Stenlund[a,b,c], Shingo Kurosu[d], Yuichiro Koizumi[d], Felicia Suska[a,b], Hiroaki Matsumoto[d], Akihiko Chiba[d], Anders Palmquist[a,b]
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T. Narushima
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Hidemi Kato[*1], Takeshi Wada[1], Sadeghilaridjani Maryam[2]
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Keiichi SASAKI

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Chuanbin Guo, Xingguang Duan*, Xiaojing Liu, Li Chen#, Guofang Shen$, Chengtao Wang$
*Department of Oral and Maxillofacial Surgery, Peking University School and Hospital of Stomatology, Beijing, China *Beijing Institute of Technology, #Tsinghua University, $Shanghai Jiao Tong University*

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Seoul National University School of Dentistry, Korea

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Chulalongkorn University Faculty of Dentistry, Thailand

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Department of Dental Education School of Dentistry Chonnam National University

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Lei Cheng, Yang Ge, Xinxuan Zhou, Xuedong Zhou

West China School of Stomatology, Sichuan University, Chengdu, China

State Key Laboratory of Oral Diseases, Sichuan University, Chengdu, China

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Roland Baron
Harvard Medical School and Harvard School of Dental Medicine, Boston, MA, USA

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Osamu SUZUKI[1*], Ph.D., Takahisa ANADA[1], Ph.D., Yukari SHIWAKU[1,2], DDS., Ph.D.
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Satoshi Fukumoto
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Hiroshi Egusa
Division of Molecular and Regenerative Prosthodontics Tohoku University Graduate School of Dentistry, Sendai, Japan

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Shinya Murakami
Department of Periodontology Osaka University Graduate School of Dentistry, Osaka, Japan

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Atsushi Ohazama
Division of Oral Anatomy, Department of Oral Biological Science, Niigata University Graduate School of Medical and Dental Sciences

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Department of BioMechanical Engineering, Delft University of Technology

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Medical Device Innovation Center and Department of Biomedical Engineering
National Cheng Kung University, Taiwan

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Yuji Matsuura
Graduate School of Dentistry, Tohoku University, Japan

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Tsunemoto KURIYAGAWA[1], Keiichi SASAKI[2], Chieko KUJI[3]
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Kouki Hatori
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Yuming Bai[1*], Xu Qin[2], Weikang Li[2], Jing Mao[2]
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Hao Yu*, Shao-long Cheng, Hui Cheng
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[1]Masahiko Ishida*, [1]Hideki Kitaura, [1]Keisuke Kimura, [1]Haruki Sugisawa, [1]Akiko Kishikawa, [2]Haruhiko Takada, [1]Teruko Takano-Yamamoto
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Effects of temperature-controllable atmospheric cold plasma jets on adhesive-dentin bonding

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Wnt5a attenuates Wnt3a-induced alkaline phosphatase expression in dental follicle cells

Yukihiko Sakisaka[1]*, Masahiro Tsuchiya[2,6], Takashi Nakamura[3], Masato Tamura[4], Hidetoshi Shimauchi[5], Eiji Nemoto[1]

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TLR3 activation in PDLSCs enhanced stem cell properties, immunomodulatory and osteogenic differentiation potential

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IL-12 induced immunomodulatory property in human periodontal ligament cells

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Rini Devijanti Ridwan*, Sidarningsih,Tuti Kusumaningsih

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Andra Rizqiawan *, Kei Tobiume ** and Nobuyuki Kamata**

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Wnt3a signaling induces murine dental follicle cells to differentiate into cementoblastic/osteoblastic cells via an osterix-dependent pathway

Eiji Nemoto[1]*, Yukihiko Sakisaka[1], Masahiro Tsuchiya[2,3], Masato Tamura[4], Takashi Nakamura[5], Sousuke Kanaya[1,6], Hidetoshi Shimauchi[7]

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Mizuki SUTO[1)]*、Sousuke KANAYA[1,2)]、Hidetoshi SHIMAUCHI[1)]、Eiji NEMOTO[1)]
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Kentaro Maruyama[1)], Akiko Henmi[2)], Hiroshi Okata[1)], Yasuyuki Sasano[2)]*
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Metabotropic glutamate receptor 1 promotes cell proliferation of cementoblasts via MAP kinase signaling pathways.

Sousuke Kanaya[1,2]*, Eiji Nemoto[1], Hidetoshi Shimauchi[3]
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Daisuke Seki *[1], Nobuo Takeshita [1], Toshihito Oyanagi [1], Ikuko Takano [1], Shutaro Sasaki [1], Masakazu Hasegawa [1], Teruko Takano-Yamamoto [1]
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Shuko Ikeno[1]*, Sousuke Kanaya[1], Eiji Nemoto[1], Mizuki Suto[1], Yukihiko Sakisaka[1], Hidetoshi Shimauchi[2]
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Nicotine exposure through the nicotinic acetylcholine receptors $\alpha 7$ induces the proliferation of oral cancer cell

Takashi Nishioka*[1,2], Hiroyuki Tada[3], Takashi Sasano[1]
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Yuri Takeda[1, 2]*, Naohiko Iguchi[1], Yoshiko Suto[1], Yoshihiro Yamaguchi[1, 2], Wataru Hashimoto[2], Tetsu Takahashi[2], Kouetsu Ogasawara[1]
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Inhibitory effects of 2-deoxy-D-glucose on the glucose metabolism of oral squamous cell carcinoma cells.

Jun Kitamura*[1,2], Jumpei Washio[2], Hiromitsu Morishima[1,2], Tamaki Ogawa[2], Tetsu Takahashi[1], Nobuhiro Takahashi[2].

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Hiromitsu Morishima*[1, 2], Jumpei Washio[2], Jun Kitamura[1, 2], Tamaki Ogawa[2], Tetsu Takahashi[1], Nobuhiro Takahashi[2].

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Takashi Yoshida[1], Kaori Takahashi[1], Minoru Wakamori[1]

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IWAMATSU-KOBAYASHI Yoko*, ORIMOTO Ai, VENKATAIAH Venkata Suresh, KANEHIRA Masafumi, HANDA Keisuke and SAITO Masahiro

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Ketut Suardita*, Ira Arundina, Maretaningtias Dwi Ariani

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Theresia Indah Budhy*; Ira Arundina

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Tadasu Sato*, Souichi Kokubun, Yoshinaka Shimizu, Hiroyuki Ichikawa

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VENKATAIAH Venkata Suresh*, ORIMOTO Ai, FYTAGI Masaharu, ZOU Wei, HANDA Keisuke and SAITO Masahiro
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PCR-dipstick DNA chromatography for multiplex and semi-quantitative analysis of plaque biofilm microbiota

Lingyang Tian[1]*, Takuichi Sato[1], Kousuke Niwa[2], Mitsuo Kawase[3], Gen Mayanagi[1], Yuki Abiko[1], Jumpei Washio[1], Nobuhiro Takahashi[1]
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A high sensitive fluorescence-mediated assessment of plaque metabolic activity

Jumpei Washio*, Kazuko Ishiguro, Daiki Irie, Airi Uchiyama, Nobuhiro Takahashi.
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Antimicrobial effects of *Hericium erinaceus* extracts. – In vitro and in human oral studies.

MATSUSHITA KENJI*, TOKUDA MASAYUKI, KAWAI JUNYA, SAKUTA TETSUYA,OYAMA TORU, MIYASHITA KEIKO, EMOTO MAKIKO, MORIMOTO YOKO, TOKUDA MASAYUKI
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Interaction of MapZ and FtsZ determine the cell shape of *Streptococcus mutans*

Yongliang Li[1], Shicheng Wei[1]*, Yujie Sun[2]*

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Porphyromonas gingivalis-induced production of IL-31 by human mast cells resulting in dysfunction of gingival epithelial barrier

Hiroyuki Tada*[1], Aya Takase[1], Takashi Nishioka[2], Kenji Matsushita[3], Haruhiko Takada[1]

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Inhibitory effects of fluoride on the carbohydrate metabolism of oral Bifidobacterium

Ayumi Manome*[1, 2,] Yuki Abiko[2, 3,] Junko Kawashima[4], Satoshi Fukumoto[1], Nobuhiro Takahashi[2]

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Endodontic Pathogens Related with Osteomylitis Avoid Innate Immune Control by Disabling Neutrophils

Aritsune Matsui[1,2] , Tetsu Takahashi[1], Susan R Rittling[2]

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Fluoride-coated tooth surface inhibits bacteria-induced pH fall at the biofilm/tooth interface

Tomoko Ishiguro[1,2*], Gen Mayanagi[3], Azusa Fukushima[2], Keiichi Sasaki[2] and Nobuhiro Takahashi[1]

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Balancing the mechanical properties of high-pressure torsion processed Co-Cr-Mo alloys by short-time solution treatment

[1]Murat Isik*, [2]Mitsuo Niinomi, [2]Huihong Liu, [2]Masaaki Nakai, [3]Ken Cho, [4]Zenji Horita, [5]Takayuki Narushima
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Autogenous teeth used as bone graft material for dental implant

Dong Wu[*], Jiang Chen, Wenxiu Huang, GengsenZou, Dongdong You
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Modification of Titanium Substrates with Chimeric Peptides Comprised of Antimicrobial and Titanium-binding Motifs Connected by Linkers to Inhibit Biofilm Formation

Zihao Liu[*], Xu Zhang[†], Ping Gao[†]
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Development and performance of a Ti-based beta-type alloy for biomedical applications using Mn and Mo additions

Pedro Fernandes Santos[*,1], Mitsuo Niinomi[1], Huihong Liu[1], Masaaki Nakai[1], Ken Cho[2], Takayuki Narushima[1]

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Abnormal deformation behavior of Ti-29Nb-13Ta-4.6Zr-O alloys for biomedical applications

Huihong Liu *, Mitsuo Niinomi, Masaaki Nakai, Cong Xin
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Yuemin Chen[*1, 2], Yumin Wang[1, 2], Lishan Lei[1, 2], Ronghui_Zhou[1, 2], Xiaojing Huang[#1, 2]
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Biofunctionalization of microgroove titanium surfaces with an antimicrobial peptide to enhance their bactericidal activity and cytocompatibility.

Lin Zhou*,Yingzhen Lai,Wenxiu Huang, Dong Wu,Jiang Chen
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Titanium Surface modification with single polydopamine enhances bone mesenchymal stem cells response *in vitro* and osseointegration *in vivo*

Ting Ma[a,*], Xiyuan Ge[b,+], Xi Jiang[a] , Biru Zhang[a], Shengnan Jia[a], Yu Zhang[a,+] , Ye Lin[a,+]
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Evaluation in Hydroxyapatite Film Containing TiO2 Particles fabricated by Powder Jet Deposition

Kuniyuki Izumita*[1)], Ryo Akatsuka[1)], Akihiko Tomie[2)], Chieko Kuji[2)], Tsunemoto Kuriyagawa[2)], Keiichi Sasaki[1)]
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Effects of Octa-arginine in Transfection Efficiency of Calcium Phosphate Nanoparticles.

Juan Vanegas Sáenz[1*], Taichi Tenkumo[2], Yuya Kamano[3], Egusa Hiroshi[3], Keiichi Sasaki[1].
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Reconstruction of a dog mandibular segmental defect by octacalcium phosphate collagen composite

Tadashi Kawai*[1], Keiko Matsui[1], Yushi Ezoe[1], Yuji Tanuma[1], Hidenori Tanaka[2], Fumihiko Kajii[2, 3], Atsushi Iwai[2], Tetsu Takahashi[1], Osamu Suzuki[4], Shinji Kamakura[3]
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Regulation of degradation rate and pattern of dental collagen membrane *in vivo*

Jian-min HAN*, Hong LIN
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Stimulation of pomegranate fruit extract on post tooth extraction wound of cavia cobaya on the expression of FGF-2

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Masatoshi Takahashi[1*], Takumu Ikeda[2], Takaki Nakatogawa[2], Shogo Horii[2], Naoto Yamamoto[2], Hanako Sakatsume[1], Mary Kanyi[1], Kanako Kuroda[1], Yukyo Takada[1]
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Can *in vivo* efficacy of dentin desensitizers be predicted by *in vitro* dentin permeability measurements?

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Division of Operative Dentistry, Department of Restorative Dentistry[1], Division of Periodontology and Endodontology[2], Liaison Center for Innovative Dentistry4, Tohoku University Graduate School of Dentistry, Vokkaligara Sangha Dental School and Hospital, Bangalore/India[3],

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Nanotopography of mineralized collagen determines nanostructure of regenerated bone

Shuai Liu*, Yu Fu, Yue Sun, Da-Tong Chang, Yan Liu, Yan-Heng Zhou
Department of Orthodontics, Peking University School of Stomatology

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Xinxuan Zhou[1, *], Xuedong Zhou[1, 2], Keke Zhang[1], Mingyun Li[1], Biao Ren[1], Lei Cheng[1,2]
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Reconstruction Genes Encoding Secretory Leukocyte Protease Inhibitors To Improve Inhibition Ability as A Candidate of Material Wound Healing

Elly Munadziroh* ; Abdul Rahman
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Effect of anti-caries dental adhesive on multi-species biofilms

Yang Ge[1,2, *], Suping Wang[1,2], Xuedong Zhou[1,2], Hockin H. K. Xu[3], Michael D. Weir[3], Biao Ren[1], Mingyun Li[1], Lei Cheng[1,2]
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Histopathological and histomorphometrical characteristics of *in vivo* behavior of concentrated growth factor in rabbits

***Tone Takeshi, Shimizu Yoshinaka, Saito Haruka, Sato Takumi, Ito Hidetoshi, Oikawa Mariko, Takahashi Tetsu, Kumamoto Hiroyuki**

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Crosstalk between osteoclasts and osteoblasts on biphasic calcium phosphates with different chemical composition and structure

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P3-22

Wound healing by synthetic octacalcium phosphate in rat tibial bone defect

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P3-23

Incorporation of calcium phosphate microparticles into cellular aggregates using an oxygen-permeable spheroid culture device.

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Session IV: Biomechanical Interface

P4-1

Osteogenetic effect of low-magnitude high-frequency loading and parathyroid hormone on implant interface in ovariectomized rats

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P4-2

The influence of superstructure design on implant-supported FPDs.

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Session V: Social Interface

P5-1

Influence of dento-maxillary prosthesis adjustment on salivary cortisol

Moe Kosaka*, Yuka I Sumita, Toshihiko Suzuki, Hisashi Taniguchi, Keiichi Sasaki
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P5-2

A Study of needs for empowerment of dental education of University of Health Sciences of Lao

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ABSTRACTS of SYMPOSIA

Symposium I: Biomaterials in interface science

S1-1
Low-modulus titanium alloys suitable for rods in spinal fixation devices

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Spinal fixation using pedicle screws and implant rods has recently begun to be applied to rigid connections in the vertebrae of the spine. The implant rod is essential to connect adjacent vertebrae and correct the position of the degenerated spine. However, doctors have reported a number of problems with implant rods. First, the pedicle screw and implant rod system carries the risk of adjacent segmental degeneration due to the stress concentration that arises from the difference in stiffness between the system and the spine. Therefore, an implant rod with a low Young's modulus is necessary to prevent adjacent segmental degeneration. Second, the implant rod must be bent along the position of the personalized spinal curve in situ. Some doctors have pointed out that it is difficult to bend the implant rod along the spinal curve because it springs back toward its initial position when bent. This phenomenon is referred to as ''spring-back''. Thus, it is essential to improve the ease with which the rod can be bent into its intended shape; that is, the spring-back must be lowered.

Low Young's modulus β-type titanium alloys have been developed and studied intensively in recent years for biomaterial applications. Ti–29Nb–13Ta–4.6Zr alloy (TNTZ) is a β-type titanium alloy that was developed by the authors. It is composed solely of nontoxic and non-allergenic elements, and its Young's modulus is lower than that of conventional biomaterials such as commercially pure titanium (CP-Ti), Ti–6Al–4V ELI (Ti-64), and SUS316L stainless steel (SUS316L). The bio-compatibility of TNTZ with living tissue has been proved in animal tests using rabbits. The effectiveness of a low Young's modulus to prevent bone resorption and contribute to good bone remodeling has also been proved by implanting intramedullary rods and bone plates made of TNTZ, Ti-64, and SUS 316 stainless steel into fracture models made in the tibiae of rabbits. Mechanical biocompatibilities such as tensile strength and ductility, and fatigue strength, including the Young's modulus, of TNT can be widely controlled by subjecting it to thermo-mechanical treatments, making it a promising material for spinal implant rods.

However, β-type Ti-Cr and Ti-Cr-O system alloys were developed after TNTZ to better prevent spring-back in implant rods. Spring-back was remarkably suppressed in Ti-Cr and Ti-Cr-O system alloys because the deformation-induced ω phase transformation, which increased the Young's modulus only in the deformed part, because a high Young's modulus lowers the spring-back. In Ti-Cr-O system alloys, mechanical biocompatibility such as the balance of strength and ductility was significantly improved by deformation-induced twinning, including the deformation-induced ω phase transformation. Ti-Cr-O system alloys are also expected to be used for implant rods. Cr is said to be a high-risk element from the view point of allergy reactions, but Ti-Cr and Ti-Cr-O system alloys have exhibited good compatibility with living cells.

Therefore, the suitability of the mechanical biocompatibilities, such as the Young's modulus, tensile properties, and fatigue strength, and the biocompatibility of TNTZ and Ti-Cr-O system alloys for the rods of spinal fixation devices will be discussed.

S1-2

Mechanical and biological response of biomedical Co-Cr-Mo alloy produced by additive manufacturing using electron beam melting (EBM)

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Osseous healing and the establishment of a direct contact (i.e.osseointegration) between bone and the material components intotal hip arthroplasties is a requirement for the long-term clinicalsuccess of uncemented prostheses. The osseointegration allowsan effective load transfer via the prosthetic component to thesurrounding bone. Metal components, such as Co-Cr-Moalloys (denoted CCM), are frequently used due to their excel-lent mechanical stability and corrosion resistance, but they have nevertheless been regarded as inferior to Ti6Al4V in terms of osseointegration and bone anchorage. Less bone wasobserved around CoCr-based implants compared with Ti6Al4Vimplants in a canine model, but it was suggested that this differ-ence could be due to the difference in the stiffness of the materialsrather than the difference in surface chemistry. The stiffnessof a material could be tailored by the design, where the intro-duction of an open cellular structure by additive manufacturing(AM) will reduce the stiffness in order to match the mechani-cal properties of the surrounding bone. Another importantmaterial requirement for hip replacements is the wear resistance,where significantly less wear have been found for CoCr basedalloys, especially CoCr F75, in comparison with titanium basedalloys.

Electron beam melting (EBM) is an AM method for pro-duction of metal implants, where complex geometries withinterconnected porosities can be built. The biocompatibility of as-built material has been evaluated for commercially pureTi and Ti6Al4V implants in vitro and for Ti6Al4V in vivousing a rabbit model and a sheep model, with excellentresults. The methodology uses the local melting of metal pow-der to build a 3D structure layer by layer from a computer-aideddesign (CAD) drawing. This means that the local diffusion ofelements could occur during manufacture.

The aim of the present study was to evaluate the bone for-mation and bone anchorage around EBM-produced implantsof CCM alloy and the effect of an addition of 0.04% Zr tothe starting powder metal. An established experimental modelin rabbit was used, enabling the analysis of both the trabec-ular and cortical bone responses after eight weeks of healing.

The microstructures and mechanical properties of Co-29Cr-6Mo alloy with C and N additions, produced by additive manufacturing using electron beam melting (EBM) method, were studied using X-ray diffraction, electron back scatter diffraction, transmission electron microscope, Vickers hardness tests, and tensile tests, focusing on the influences on the build direction and the various heat treatments after build. It is found that the microstructures for the as built specimens were changed from columnar to equiaxed grain structure with average grain size of approximately 10-20μm due to the heat treatment employing the reverse transformation from a lamellar (hcp + Cr_2N) phase to an fcc. Our results will contribute to the development of biomedical Ni-free Co–Cr–Mo–N-C alloys, produced by EBM method, with refined grain size and good mechanical properties, without requiring any hot workings.

The bone response to Co-Cr-Mo is regarded as inferior to that of titanium and are usually cemented in THR. A low amount of Zr in the Co-Cr-Mo alloy would improve the bone response and biomechanical anchorage. The results showed significantly higher implant stability for the Co-Cr-Mo alloy with an addition of 0.04% Zr after eight weeks of healing in rabbits, while no major differences were observed in the amount of bone formed around the implants.

Finally, a comparison with electron beam melting and laser beam melting methods are discussed in terms of melting and solidification behavior.

S1-3

Fatigue properties of NiTi wires used in biomedical applications

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NiTi alloys are commonly used to fabricate biomedical stents because of the superelasticity, shape memory, and high corrosion resistance of such alloys. Materials used for stents must have a high fatigue resistance to withstand the cycles of pulsation-induced expansion and contraction. Practical NiTi-based stents are fabricated via vacuum induction melting (VIM), hot forging, repeated cold-working and annealing, a shape-memory treatment, laser cutting, and finally, surface polishing. During VIM, the alloy is unavoidably contaminated by light elements, such as O, C, and N, which remain in the final product. When NiTi is used for medical devices, the C and O+N contents are limited to a maximum of 0.05 mass% by ASTM standard F2063. The presence of these elements changes not only the mechanical properties and transformation temperatures of the alloy, but also the formation behavior of non-metallic inclusions, even when the composition is standard-compliant. Non-metallic inclusions have been reported to reduce the fatigue strength of NiTi because they can act as crack-initiation sites [1]. $Ti_4Ni_2O_x$-type oxides ($x \le 1$) and $Ti(C,N,O)_x$-type carbides are the main non-metallic inclusions in NiTi, which form depending upon the O and C contents of the alloy [2]. However, no studies have reported the relationship between the fatigue properties of fine NiTi wires and the phases of the non-metallic inclusions.

In this study, 160-μm-diameter NiTi wires with O and C contents of 0.01−0.04 mass% and 0.003−0.04 mass%, respectively, were fabricated. The diameter of the wires was chosen to approximate the size of the struts in medical stents. The surface of the wires was pickled to remove any oxide layers that had formed during the heat treatment. The phases of the non-metallic inclusions in the wires were determined to be a $Ti_4Ni_2O_x$-type oxide, a $Ti(C,N,O)_x$-type carbide, or a mixture of both. The fatigue properties of the wires were evaluated by rotating-bending fatigue tests in 35 mL of Hanks' solution at 310 K; detailed descriptions of the procedures performed have been reported elsewhere [3].

The fatigue strength of the NiTi wires ranged from 300 to 500 MPa depending upon the O and C contents. The fracture surface of the wires after the fatigue tests consisted of a crack-initiation site, fatigue crack-propagation region, and final overload region. Scanning electron microscopy (SEM) images of the fracture surface of the wires revealed that $Ti_4Ni_2O_x$-type non-metallic inclusions were present at the crack-initiation sites of the wires containing such inclusions. The cracks were initiated at the interface between a $Ti_4Ni_2O_x$-type inclusion and a void in a surface particle-void assembly (PVA). On the other hand, surface grooves, which were formed during the cold-drawing and/or pickling processes, appeared to be the crack-initiation sites for the wires containing $Ti(C,N,O)_x$-type carbides as the main non-metallic inclusions. This suggests that $Ti_4Ni_2O_x$-type inclusions and/or surface defects, such as PVAs related to $Ti_4Ni_2O_x$-type inclusions, cause cracks and reduce the fatigue strength of NiTi wires containing such inclusions.

The concentration of metallic ions eluted by the Hanks' solution baths during the fatigue tests was measured with inductively coupled plasma-mass spectrometry (ICP-MS). The concentrations of Ti and Ni ions were less than 10 mass ppb, regardless of the wire composition. This is evidence of the high corrosion resistance of NiTi wires.

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S1-4

Dealloying Toxic Ni from SUS316L Surface

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SUS316L (18%Cr-12%Ni-2.5%Mo-<0.03%C) is one the most popular metallic materials for the biomedical usages such as implants, operation tools and so on because of its lower cost, good corrosion resistance, and excellent workability with compared to other types of biomedical metallic materials. Although Ni stabilizes austenitic FCC structure giving the excellent workability, elution of the toxic Ni ion into the human body sometimes cases various health problems. In SUS316L, elution of Ni ion is suppressed by the stable passive thin film caused by the Cr element. However, there still remains some risk of Ni elution. In this paper, we remove Ni element from the SUS316L surface by our original dealloying technique with metallic melt, then we evaluate its effect on the corrosion resistance and Ni ion elution in a simulated human body fluid.

By dealloying treatment at 700℃ for 30 mins, Ni concentration was successfully reduced from 12% to 2.2% in 30~40 μm depth. However, not only Ni, but also the other elements in SUS316L were removed by dealloying treatment at 900℃ for 30 mins, resulting in decreasing thickness of the sample without apparent composition change. By removing Ni, corrosion potential of SUS316L decreased from -240 mV to -400 mV (vs. Ag/AgCl), however, passive region is observed up to ~100 mV, which is almost the same potential with that of the original SUS316L. Results on the Ni-ion elution will be presented at the conference.

S1-5
Bio-ceramic Coating by Laser Chemical Vapor Deposition

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Titanium (Ti) and its alloys are reliable for use as biomaterials due to their strength, ductility and durability in the human body; however, the tissue compatibility of metallic biomaterials is insufficient for biomedical applications and they require a few months for bone-regeneration. Although the microstructure and phase of metallic materials are generally well-controlled by thermomechanical treatment in order to satisfy the mechanical properties required for biomedical applications, tissue compatibility should be improved while maintaining the microstructure and mechanical properties of these materials. The surface modification, in particular bio-ceramic coating by chemical vapor deposition (CVD), is a promising way to improve the tissue compatibility of biomaterials, and CVD can construct functionally graded structure by changing deposition conditions, which could be the ideal structure between ceramic coating and tissue of the human body.

CVD has advantages of good conformal coverage and morphology control. Common CVD (thermal CVD) needs high-temperature to implement coating, while the degradation of metal substrate should be minimized. Laser CVD (LCVD) has been used to prepare whiskers, nano-dots and thin film semiconductors, and LCVD has never employed for wide-area thick and high-speed coating. We have been developing LCVD to optimizing microstructure of bio-ceramic coating enabling low-temperature and high-speed deposition. Since human bone is similar in makeup calcium hydroxyapatite (HAp, $Ca_{10}(PO_4)_6(OH)_2$) ceramics, materials of the Ca–P–O system are commonly used as bio-ceramic coatings on metallic bio-materials to accelerate the bone regeneration. We have used LCVD to prepare HAp, α-tricalcium phosphate (α-TCP, α-$Ca_3(PO_4)_2$), β-tricalcium phosphate (β-TCP, β-$Ca_3(PO_4)_2$) and tetracalcium phosphate (TTCP, $Ca_4P_2O_9$) films with a variety of morphology and oriented textures by controlling CVD conditions. The deposition rate of HAp depended on deposition conditions showing as high as 100 $\mu m\ h^{-1}$, about 100 times grater than that of common sputtering.

Although Ca-P-O system films have been commonly investigated for the bio-ceramic coating, we have been seaching alternate candidateds such as Ca-based compounds by LCVD. We have found that ruddlesden-popper $Ca_4Ti_3O_{10}$ films are promising bio-active ceramic coatings among the Ca–Ti–O compounds. By LCVD, the $Ca_4Ti_3O_{10}$ film was formed with cauliflower-like morphology beneficial for the bone regeneration. The deposition rates were 100–230 $\mu m\ h^{-1}$. By immersion in the Hanks' solution, HAp formed significantly on the $Ca_4Ti_3O_{10}$ film, compared to conventional $CaTiO_3$ films. Besides, the $Ca_4Ti_3O_{10}$ film coating is promising to form the functionally garded structure from $Ca_4Ti_3O_{10}$ to HAp, realizing strong bonding to Ti implants by $Ca_4Ti_3O_{10}$ and good biocompatibility by HAp formed on the $Ca_4Ti_3O_{10}$ film.

Since alumina (A_2O_3) is one of the most common ceramic materials with good mechanical properties, Ca–Al–O system compounds are promising for bio-ceramic coating. To date, $CaAl_2O_4$ was reported as a dental material that had necessary bioactivity and mechanical properties. Recently, we have prepared $Ca_3Al_2O_6$, $Ca_{12}Al_{14}O_{33}$, $CaAl_2O_4$, $CaAl_4O_7$ and $CaAl_{12}O_{19}$ films by LCVD, and found that the magetoplumbite $CaAl_{12}O_{19}$ film showed the oriented growth forming faceted feather-like columnar nanometer-sized grains and exhibited supeior HAp formation ability by immersion in the Hanks' solution.

Symposium II: Innovation for oral science and application

S2-1
Where is the fairway of our voyage?

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Circumstances surrounding the universities have been changing dizzyingly and dramatically in Japan according to the situations of universities in US and Western Europe. The universities, especially national universities are facing the urgent self-reformation to establish their for self-sustainability including the financial aspect and to advance their international competitiveness. These trends can be the same in other east Asian countries and Australia.

Dental schools are tossed about into such heavy waves. Our vessels are petty with a small number of passengers, a limited number of crew members and limited financial resources in comparison with the other faculties of big universities. Where is our fairway to avoid the drafting? Where is our destination port? Can we find our North Star or Southern Cross navigating our voyage? This symposium can provide the dental schools on similar voyages with an opportunity to discover the navigation marks and lighthouses for their own seaways.

Mission of the dental school is originally and generally to advance health through innovative high-level education, scientific discovery, and the highest-quality care for all communities. However, for our survival in the universities and societies under the current tough and competitive situation, and for advancing dentistry in position among various disciplines, it is obviously required to accomplish influential and visible outcomes. We should make out much effective and practical strategies for education, researches and contributions to human society and life.

To make it a reality, re-acknowledging the nature and position of dentistry; dental science may be important. Dentistry/dental science is, needless to say, an applied science contributing human health and QOL, based on the various fields of sciences, including biology, health science, engineering, machining. material science and so on. To advance our dentistry further, interdisciplinary collaborative research and education should be conducted. The outcomes of collaborative projects should be translated into reality in our real fields, which can contribute to our collaborators of different disciplines. Recently, oral health and dental management are becoming to attract the attention of the society in conjunction with health promotion. Most of our seeds are relatively close to the social implementation. We should not miss the opportunity, where our interdisciplinary researches and educations can be models of good practices for the industrial-academic cooperation and industrial-academic-government cooperation.

The estimate of the situation mentioned above is one of the channel marks to depict the fairway of our voyage. There can be various kinds of channel marks from different perspectives, which should be shared among leading dental schools through the discussion in the symposium.

S2-2

Development of Robot-assisted Surgery (RAS) System for CMF

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Medical robots have been developed rapidly in recent years. Clinical application of Da Vinci system showed its advantages. Currently, there is no specialized robot system for cranio-maxillofacial surgery. We developed a cranio-maxillofacial surgical robot system focusing on the reconstruction of mandibular defects.

With the funding of the 863 project of science and technology ministry (China), we developed a virtual operation planning system for four typical operations: reconstruction of mandibular defects, orbit reconstruction, skull base tumor resection and orthognathic surgery, a navigation system and a robot with three arms for mandibular reconstruction. In the virtual surgical plan system, the operation pattern was designed based on surgeons' habits and experiences. The software system was easy to be used with many functions for designing different surgical procedures. In surgical navigation system for guiding the robot, the hardware of the navigation system was assembled, and the software system of real-time registration was realized. The robot was designed and assembled. It had three arms and was able to finish the bone graft placement precisely and automatically under the navigation guidance according to the preoperative design. The whole system was assessed by model and animal experiment with good results.

S2-3

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S2-4

How to facilitate the movement of qualified dental professionals to provide dental services across ASEAN member states?

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The Association of Southeast Asian Nations (ASEAN) was formed on 8 August 1967 by Indonesia, Malaysia, the Philippines, Singapore and Thailand. Since then, membership has expanded to include Brunei, Cambodia, Laos, Myanmar and Vietnam. This political and economic organization has emphasized regional cooperation and formed ASEAN community in 2003 in three aspects; economic, security and sociocultural. Most progressingly, the regional alliance has established an ASEAN Economic Community which aims to make ASEAN to be more dynamic and to become competitive economic community by making it a single market within 2015. The single market comprises of five core elements; free flow of goods, services, investment, capital and skilled labor. Those include free flow of qualified dental professionals and services. This presentation will review the works that have been done by the ASEAN Joint Coordinating Committee for Dental Practitioners in order to facilitate the movement of qualified dental professionals. The preparation plan for the free flow of dental professionals will also be proposed and one of the key processes is to set up common competencies ASEAN dentists followed by curriculum reform of all dental schools in the region.

S2-5

Exemplifying Applied Innovation in Oral Science: Can tongue progenitors repair broken heart? – Kinship between oral and cardiac development and stem cell biology

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Background: Oral health care is typically viewed as separate from the general health system. Linking oral and systemic health through research provides opportunities to understand causal links between oral and systemic diseases, to use the oral environment as a model for systemic illnesses, to advance education, training and clinical care for patient benefit and to emphasise the importance of oral health to the community and government. This research is interdisciplinary through teams of clinicians and researchers with the goal to make profound changes to health care delivery and policy. Some examples of our research into oral-systemic links include the influence of changing agricultural practice on the oral microbiome; the role of *P. gingivalis* on Rheumatoid Arthritis; teeth as biomarkers for systemic disease; oral osseointegration as a model for general orthopaedic management and the influence of orofacial pain on psychological well-being. An exciting recent example links orofacial and cardiac researchers with the goal to regenerate damaged cardiac tissue.
Orofacial (masticatory, tongue and facial expression) muscles are currently classified as skeletal muscles. However, increasing evidence suggests that, during embryogenesis, the orofacial muscles share a common origin of a pharyngeal mesoderm myogenic progenitor cell pool with the cardiomyocytes, and that therefore they have more similarity with the heart than skeletal muscles of the limb and trunk. Furthermore, there are additional similarities in these muscles including fatigue resistance and cardiac gap-junction protein. These properties are not shared with skeletal myocytes. In this study, we aim to identify the regulatory mechanisms that govern the fate and phenotypes of the orofacial muscle to explore the potential use of the orofacial progenitors for cardiac repair. **Methods:** Mouse embryonic (days 9 to 16) and adult tongue and masticatory muscles were collected and probed for cardiac and skeletal muscle transcription factors (TF) using immunohistochemistry, transgenic lineage tracking and PCR. **Results:** The data have shown that a significant portion of mouse orofacial muscles were derived from the progenitors bearing the key cardiac TF Nkx2-5. The Nkx2-5 gene and protein, as well as other cardinal cardiac TFs such as GATA4, Mf2C and Tbx1 were continuously expressed in the tongues of the embryonic mouse and persisted in adults. In the adults, the Nkx2-5 protein expressions were found in orofacial muscle satellite cells, indicating the existence of undifferentiated cell-pool that has cardiomyocyte potentials. Orofacial muscles also possess skeletal myocyte markers such as Pax3/7 and MyoD, suggesting they are unique “hybrid” muscle types. **Conclusion:** Orofacial muscles possess a range of cardiac transcription factors during the development and in their satellite progenitors which may be differentiated into cardiomyocytes. Understanding the mechanism of the orofacial muscle differentiation will significantly contribute to the knowledge of orofacial development and may also help to find additional cell source for cardiac repair.

S2-6
Pursuing Excellence and Humanism

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At the beginning of the 21st century, Chonnam National University School of Dentistry set a goal to make the school one of the premier dental schools in the world, and developed strategic plans to attain the goal by the year 2020, termed Vision 2020. Since then, the school has added another crucial goal; educating dental students and professionals with philosophy in humanism for the next generation. Three major areas of our strategic plans are: Advanced Education, Globalization, and Specialization. The specific goals include: 1) Produce internationally recognized dental professionals; 2) Assure global competition in dental research activities; 3) Establish national and international volunteer system; 4) Provide an environment conductive to high-tech education and research activities. To name a few of the changes during the past ten years, the education system has changed from College of Dentistry to Graduate Professional School of Dentistry (2005); the new dental school building and hospital have been established (2007); both BK21 research initiative (2003-2013), and MRC research project (2011-2017) have been funded by the Korean government. Other accomplishments, current progress, and future plans toward achieving the specific goals are briefly discussed in this presentation.

S2-7

Biomaterials in caries prevention and treatment

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Dental caries is the most widespread disease and an economic burden. Novel biomaterials are developed to inhibit caries by controlling biofilm plaques and enhancing remineralization. Releasing and non-releasing nanoparticles were added into dental materials to promote their anti-caries capabilities. Our previous studies have been struggling to develop novel anti-caries materials which might have triple benefits: good mechanical properties, antibacterial effects and remineralization potentials. Nanoparticles of amorphous calcium phosphate (NACP) released calcium/phosphate ions, remineralized tooth-lesions and neutralized acids. Different kinds of Quaternary ammonium monomers (QAMs) have been proven to be effective in inhibiting the growth and metabolism of biofilms. Dental materials containing QAMs also changed the proportion of bacteria in biofilms and made it from caries propensity to healthy tendency. In conclusion, novel biomaterials had remarkable anti-caries properties to serve as "bioactive" materials and revealed its potential value for anti-caries clinical applications.

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Special Lecture:

Cross-talk between Bone Cells and the Regulation of Bone Remodeling

Roland Baron

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Local and systemic bone loss, as in periodontal disease or osteoporosis for instance, is the result of a dysregulation of the bone remodeling process. An imbalance between bone resorption and bone formation, leads to loss of bone mass and microstructure and ultimately to loss of tooth support and/or fragility fractures. Bone remodeling is initiated by the recruitment of osteoclast precursors which form mature osteoclasts that resorb bone locally. These cells also recruit locally osteoblasts at the end of the resorptive period, though a process called "coupling", and these cells form a new packet of bone at the same site, maintaining bone structure. Recent studies indicate that the ability of osteoclasts to induce coupling is in part dependent on the material properties of the substrate they attach to. In contrast bone modeling activity consists of continuous bone resorption or formation leading to changes in bone shape, in particular during skeletal growth. In recent years the role of the third cell type in bone, the osteocyte, has been further elucidated and indicated that osteocytes sense mechanical and metabolic cues and translate these cues into the appropriate regulation of remodeling at the bone surface. The development of novel therapeutic approaches in the last few years has not only provided a diversity of treatment modalities but also shed new light on the complex mechanisms by which skeletal homeostasis, including trabecular and cortical bone, is regulated. Treatment with anti-resorptives is associated with a decrease in remodeling activity, including bone formation, due to disrupted coupling. In contrast, inhibition of cathepsin K decreases bone resorption while maintaining bone formation, maintaining the appropriate cross-talk between bone cells. Bone mass can also be efficiently increased by treatment with bone anabolics. Daily injections of PTH increase bone formation but also bone resorption, effectively increasing bone turnover with a positive balance. The secondary increase in bone resorption may affect intracortical remodeling. Weekly administration of PTH, the use of PTHrP or combination with denosumab may avoid in part the increase in resorption, illustrating again the importance of cross-talk between bone cells. Wnt signaling plays a critical role in the cross-talk process and novel anabolics are targeting sclerostin in order to enhance locally, at the level of osteoblasts and osteocytes, the activity of Wnt signaling. These compounds have a dual anabolic-anti-resorptive effect that, albeit limited in time, increases efficiently bone density at trabecular and cortical sites. Taken together, all these new therapeutic developments appear to not only provide promising prospects for the treatment of osteoporosis but are also providing novel insights on the mechanisms by which skeletal homeostasis is regulated. In particular they all point towards a crucial role of the cross-talk between the three cell types in bone, osteoclasts, osteoblasts and osteocytes.

Symposium III: Regenerative oral science

S3-1
Efficacy of calcium phosphate-based scaffold materials on mineralized and non-mineralized tissue regeneration

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It has become recognized that biomaterials used for cellular scaffolds provide not only the site to proliferate but also activate their functions. Amorphous calcium phosphate (ACP) has been shown to enhance formation of a three dimensional tissue construct from dental pulp cells by augmenting the intercellular adhesion[1]. We have reported that formation of reparative dentine was enhanced if dental pulp is exposed directly to octacalcium phosphate (OCP)[2]. The stimulatory capacity of OCP on the cellular activity we found in vitro studies include 1) osteoblastic differentiation from bone marrow stromal cells[3,4]; 2) osteoclast formation from bone marrow cells in the presence of osteoblasts[5]; 3) odontoblastic differentiation from rat dental pulp cells[2]. On the contrary, chondrogenic differentiation was inhibited by OCP if the cells were contacted by the surface of this materials[6]. In an in vivo study, we observed that mesenchymal stem cells promote new bone formation in the presence of OCP within reconstituted atelo-collagen matrix[7]. Mechanical mixture of OCP with ACP enhanced bone regeneration of critical-sized rat calvaria defect more than that by the single use of each material[8]. It is likely that the stimulatory capacity of OCP is stemmed from the physicochemical property induced by the intrinsic material characteristics of OCP associated with the advancement of hydrolysis irreversibly to hydroxyapatite (HA)[3]. OCP adsorbed some of growth factors for osteoblasts and osteoclasts from serum constituents[9], which could be induced upon the change of the adsorption affinity during the hydrolysis into HA[10, 11]. One of OCP-based materials is capable of healing not only the calcified tissues but also a non-calcified tissue tendon insertion[12]. The perspective on the possible role of biomaterials, including calcium phosphate materials, will be discussed.

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S3-2

Gap junctional communication regulates salivary gland branching morphogenesis

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Cell-cell interaction via the gap junction regulates cell growth and differentiation, leading to formation of organs of appropriate size and quality. Gap junctions are specialized membrane channels that allow for transfer of small molecules, ions, metabolites and secondary messengers between the cytoplasm of connected cells. Gap junctions are produced as the result of oligomerization of 6 different connexin (Cx) proteins, which form a connexon that is delivered to the plasma membrane. A connexon exists either as a single unit within the plasma membrane, known as a hemichannel, or is associated with a connexon from an opposing cell to form a gap junction channel.

A mutation in the gene encoding the nearly ubiquitously expressed connexin43 (Cx43) results in development of oculodentodigital dysplasia (ODDD), a predominantly autosomal dominant disease that is characterized by several common clinical phenotypes such as syndactyly of the digits, microdontia, enamel hypoplasia, ophthalmic defects and craniofacial abnormalities. Cx43 plays an important role in skeletal development, as well as survival of osteoblasts and osteocytes. However, the role of Cx43 on salivary gland morphogenesis has never clearly understood.

To determine the role of connexin43 in salivary gland development, we analyzed its expression in developing submandibular glands (SMGs). Conenxin43 (Cx43) was found to be expressed in salivary gland epithelium, especially in terminal buds, but not in ducts. In ex vivo organ cultures of SMGs, addition of the gap junctional inhibitor 18α-glycyrrhetinic acid (18α-GA) and oleamide inhibited SMG branching morphogenesis, suggesting that gap junctional communication contributes to salivary gland development. In Cx43-/- salivary glands, submandibular and sublingual gland size was reduced as compared with those from heterozygotes. In the initial stage of salivary gland development, the branching structure is known to be facilitated by growth factors including fibroblast growth factor (FGF). Another report found that in the early stage of branch initiation, clefts are formed in acini, with fibronectin, an extracellular matrix, involved in that formation. Platelet-derived growth factor (PDGF) produced by salivary epithelial cells induces FGF expression in mesenchymal tissue of salivary glands. We found evidence of epithelial-mesenchymal interaction, which induced FGF activity in salivary gland epithelium. The expression of *Pdgfa*, *Pdgfb*, *Fgf7*, and Fgf10, which induced branching of SMGs in Cx43-/- samples, were not changed as compared with those from heterozygotes. Furthermore, the blocking peptide for Cx43 showed inhibition of terminal bud branching. FGF10 induced branching morphogenesis, while it did not rescue the Cx43-/- phonotype, thus that Cx43 may regulate FGF10 signaling during salivary gland development. FGF10 is expressed in salivary gland mesenchyme and regulates epithelial proliferation. FGF10 was shown to induce ERK1/2 phosphorylation in salivary epithelial cells, while that in HSY cells was dramatically inhibited by 18α-GA. On the other hand, PDGF-AA and PDGF-BB separately induced ERK1/2 phosphorylation in primary cultured salivary mesenchymal cells regardless of the presence of 18α-GA. Together, our results suggest that Cx43 regulates FGF10-induced ERK1/2 phosphorylation in salivary epithelium, but not in mesenchyme, during the process of SMG branching morphogenesis.

S3-3

iPS Cell-Based Strategies in Bone Tissue Engineering

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Tissue engineering is a new frontier in dentistry with the aim of achieving the regeneration of missing oral tissues, and engineering applications using stem cells in the field of dentistry await the establishment of a stem cell source that allows for easy collection by dentists. Induced pluripotent stem (iPS) cells can be generated through the reprogramming of somatic cells from different tissues by forced expression of defined exogenous factors. These iPS cells efficiently generated from accessible tissues have the potential to be used for various clinical applications. The oral gingiva is an easily obtainable tissue for dentists, and cells can be isolated from patients with minimal discomfort. We successfully generated iPS cells from adult mouse or human gingival fibroblasts via transduction of the Yamanaka factors without c-Myc oncogene. Gingival fibroblasts demonstrate a higher reprogramming efficiency than the skin fibroblasts which have been conventionally used for the generation of iPS cells. These iPS cells were capable of osteogenic differentiation, which could form new bone in the animal models. The generation of iPS cells from the gingiva is expected to provide a breakthrough, especially in the dental sciences, because it offers a promising method for the facile production of pluripotent stem cells by dental researchers. In this presentation, generation and basic aspects of osteogenic capacity of the gingiva-derived iPS cells will be discussed, with an emphasis on potential applications of the iPS cell technologies in the future of dentistry.

S3-4

Emerging Regenerative Approaches for Periodontal Regeneration
- the future perspective of cytokine therapy and stem cell therapy -

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It has been demonstrated that it has already been confirmed mesenchymal stem cells and progenitor cells of osteoblasts or cementoblasts can be identified within periodontal ligament (PDL). Thus, improving and/or enhancing the biological potential of these cells and stimulating the periodontal regeneration are recognized as being clinically possible. One of the most physiologically efficient methods to stimulate these cells is the use of human recombinant cytokines.

Basic Fibroblast Growth Factor (FGF-2) is known to be deeply involved in the proliferation, migration and differentiation of a variety of cells and to strongly induce angiogenesis. Utilizing beagle dogs and non-human primates, we revealed that topical application of recombinant FGF-2 to the experimentally-prepared intraosseous bone defects induced statistically significant periodontal tissue regeneration in the defects.

Based on the results of a series of *in vitro* analyses, we have suggested the following mode of action of FGF-2 to induce periodontal regeneration. During the early stages of periodontal tissue regeneration, FGF-2 stimulates the proliferation and migration of PDL cells while maintaining their multipotent nature, inducing differentiation into hard tissue-forming cells such as osteoblasts and cementoblasts. Furthermore, FGF-2 induces angiogenesis and increases extracellular-matrix production such as osteopontin, hyaluronan from PDL cells, thus leading to a local environment suitable for the periodontal regeneration. These result in the enhanced periodontal tissue regeneration at the FGF-2-applied site.

Completing the above-mentioned preclinical studies, we conducted human clinical trials using human recombinant FGF-2 in Japan. These were randomized controlled double-blinded clinical trials of dose responses including placebo comparison. As a result, a significant difference in % increase in alveolar bone height at 2- or 3-walled intrabony defects of the patients was demonstrated by standardized radiographs between Placebo Group and 0.3%-FGF-2 Group at 9 months after the treatment. This suggests that topical application of FGF-2 can be efficacious in regeneration of periodontal tissue of periodontitis patients.

For ideal periodontal regeneration, it is crucial to fully introduce the concept of “tissue engineering”. If we need to treat severe bony defects or horizontal bone destruction with FGF-2, it is essential to introduce the concept of a “scaffold” into the carrier of FGF-2 drug. An FGF-2 carrier that could provide a formable and osteoconductive scaffold for undifferentiated progenitor cells within PDL would dramatically increase both the dental and craniofacial application of FGF-2 drug. Developing the intelligent scaffold for FGF-2 drug is now under investigation.

It has been demonstrated that the number of mesenchymal stem cells or progenitor cells of osteoblasts or cementoblasts in PDL is decreased with age. Thus, it may be a reasonable idea to transplant mesenchymal stem cells into periodontal tissue defects to stimulate periodontal regeneration at the site. Researchers, including our group, have found that mesenchymal stem cells can be obtained from various tissues such as bone marrow and adipose tissues. We revealed that adipose-tissue derived stem cells (ADSC) can differentiate into hard-tissue forming cells and PDL cells and that the transplantation of ADSC enhances periodontal regeneration at the applied sites by using beagle dog models.

The combined effectiveness of ‘cytokine therapy’ and ‘stem cell therapy’ need to be assessed in the future, to allow the establishment of ‘periodontal tissue engineering’.

S3-5
Molecular mechanisms regulating tooth number

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Teeth develop via a dynamic and complex reciprocal interaction between dental epithelium and cranial neural crest-derived mesenchyme. These interactions contain a series of inductive and permissive processes that lead to the determination, differentiation, and organization of odontogenic cells. Tooth number, shape and position are consistent in mammals and are subject to strict genetic control. Multiple signaling pathways including Sonic hedgehog (Shh), Transforming growth factor (Tgf), Bone morphogenetic protein (Bmp), Wnt, Fibroblast growth factors (Fgf), Notch and Nuclear factor kappa B (NF-kB) are known to play critical roles in regulating tooth development. Recent studies show that these signaling pathways interact through positive and negative feedback loops to regulate tooth number, shape, and spatial pattern. It has also been shown that transcription factors are involved in epithelial-mesenchymal interactions through the signaling loops between tissue layers by responding to inductive signals and regulating the expression of other signaling molecules. It is believed that dozens of different molecules together form complex molecular networks that regulate tooth development. Although substantial research efforts over the last decade have elucidated many aspects of the molecular mechanisms that control tooth development, the mechanisms regulating this process still remain unclear.

Teeth are found in most vertebrates, and have played a central role in their evolution. During tooth evolution, the total number of teeth per dentition has generally decreased, whereas tooth morphological complexity has increased. Tooth development also shares morphological and molecular similarities with other skin appendages such as hairs, glands and even feathers. Findings in tooth evolution are therefore a key feature to understanding the molecular mechanisms of tooth development.

Determining the molecular basis of tooth development will provide invaluable knowledge for tooth regeneration. I will present recent findings on the molecular mechanisms of tooth development, especially those regulating tooth number.

Symposium IV: Medical device innovation for diagnosis and treatment of biosis-abiosis interface

S4-1
Smart Instrument Design for Challenging Minimally Invasive Applications

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Imagine that it would be possible to treat any patient in an early phase of a disease at any location in the body using tiny instruments that cause no trauma to healthy tissue. Our challenge is to develop a new generation of devices with highly advanced functionality at the tip for instantaneous diagnosis and targeted treatment, allowing diagnosis and therapy in one single procedure. Examples are thin steerable needles, catheters with multifunctional tip than can be manoeuvred in branching blood vessel system, water jet cutting to treat cartilage in narrow joints. Tailored, slender and multi-steerable instruments, having optical fibers inside, can be used to transmit diagnostic information and to perform local treatment during currently challenging oncological and cardiovascular procedures.

There are many advantages for the patient, however the minimally invasive approach is more challenging for the surgeon and interventionist. When slender instruments are inserted through tiny incisions in the skin or through tiny openings, the degrees of freedom are reduced, depth perception is limited due to the 2D view on a monitor, and haptic feedback is inhibiting by friction in instruments. Therefore training is required. To support training, we develop training system to enable residents to learn outside patients. These training systems are based on fundamental research into the field of eye-hand coordination, haptic feedback and objective assessment methods for psychomotor skills.

With the introduction of new technology in the operating room (OR), the environment has become technologically complex and prone to errors. The complexity of the perioperative process, with its involvement of many people from different disciplines, makes structured and meaningful extraction of information about the workflow highly challenging. Therefore, improving the safety and efficiency of the perioperative process requires reliable and objective systems to monitor the workflow throughout all phases of the care pathway. To improve monitor the work flow in the OR, we started the DORA Digital Operating Room Assistant, project. In this project we aim to automatic monitor activities such as instrument and equipment give feedback when hazards occur related to instrument and equipment use. Furthermore, we aim to automatic determine the work flow in the OR for better OR planning and to determine when processes deviate from standard.

MISIT group: Within the Minimally Invasive Surgery and Interventional Technology group (MISIT) we work in a multidisciplinary team to improve minimally invasive techniques (www.misit.nl). The group consists of mechanical, biomedical, and electrical engineers, industrial designers, and clinicians. The MISIT group works on the development of novel instruments, performs research on the interaction between instrument and tissue and finally, develop methods to improve the interaction between instruments and the users in the operating room environment.

S4-2

Open Technologies and Workflows in Digital Dentistry

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The Medical Devices Innovation Center (MDIC), National Cheng Kung University has built up the most complete and professional digital dentistry design workflow with cutting edge equipment integrated with software design research from our development team. MDIC, ISO13485 certified, can provide the best digital dentistry total solutions. MDIC is establishing the Intelligent Manufacturing system Laboratory for dentists and dental technicians towards digital dentistry training and restoration design services. The digital dental laboratory is able to control the entire digital process from digital impressions to the CAD/CAM creation of the restoration and model milling. The intraoral scanner is used to make digital impressions from chair-side or from traditional impressions. For the design to CNC process, we employ three different software packages for the design portion with third-party systems. After importing the digital impression, one or more of these packages is used to design the restoration. The design is then sent to one of our three 5-axis milling machines for production. The CNC machines are chosen for machining or milling of the prosthetics from wax, PMMA, zirconia, chromium cobalt, resin nano-ceramic, glass ceramics, lithium disilicate, silicate ceramics or titanium. As a remote solution, these design packages can reside geographically distant from the CNC machines. Our R&D team has designed a cloud solution based on a single network appliance that can be deployed to each pertinent location. Data from the design package is stored on the local network appliance which is then automatically synced to the remote network appliance. These remote work orders are then milled by the remote technician. We can design and produce common digital dentistry products in-house, including crowns and bridges, veneers, inlays and onlays, temporary crowns and virtual diagnostic wax-ups. Our laboratory is also equipped to handle advanced clinical cases such as implant planning, digital smile design analysis and customized surgical guides, custom abutment, implant bridge and bar design, and orthodontics. Our research laboratory has produced digital animation for patient education and communication, and designed a cloud management solution for digital design database. For academics and training, we have developed a full range of digital technology training programs to help design and operate clinics including total digital solutions for operating partners interested in denture design or digital manufacturing and management.

S4-3

Detection of early caries by laser-induced breakdown spectroscopy

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Dentists usually diagnose dental caries by appearances of the teeth and touching them using a dental probe. However, these methods sometimes cause errors and severe pain. In particular, it is difficult to found early caries that shows only slight change in the color. Recently, some groups have reported that they used, for detection of dental caries, laser-induced breakdown spectroscopy (LIBS). LIBS is a method for elemental analysis which is based on spectral analysis of plasma emission generated by irradiation of high-powered laser pulses. In these previous studies, detections of caries were performed by analyzing main atomic lines of Ca, Mg and Sr in the visible wavelength. However, the sensitivity and the accuracy were not sufficient for detection of early caries. In this paper, we expand the spectral region under analysis to ultraviolet light to improve the sensitivity of caries detection.

In our experimental setup, a Q-switched Nd:YAG laser with an operating wavelength of 1064 nm was used as the light source for plasma generation. The laser light was delivered by a hollow optical fiber to the sample surface and the plasma emission from tooth samples was detected by a quartz optical-glass fiber. The emission spectra were obtained by using a fiber-optic spectrometer with spectral resolution of 0.1 nm in the range of 200–340 nm. In addition, argon gas that increases plasma production efficiently was introduced on to the sample to detect elements that shows emission peaks with low levels.

To measure LIBS spectrum of healthy tooth, emissions by 50 laser shots were averaged and the integration time of each emissions were 100 ms. In measured LIBS spectrum, there were emission peaks of various inorganic components in the tooth and they are stronger in the long wavelengths. As tooth decay progresses, inorganic elements precipitated when crystalls of hydroxyapatite are demineralize. However, in our preliminary tests, we found that the changes in the peak heights of these elements showing strong emission peaks in long wavelengths are too small between caries and healthy part to detect early caries.

Then we newly focus on emission in ultraviolet wavelengths. In LIBS spectra of healthy and caries-affected parts measured in ultraviolet wavelengths of 200-220 nm, obvious differences are seen in the spectra and the density of Zn is higher in caries part than the healthy part. In contrast, the density of Ca decreases in caries part. It is known that zinc exists at high concentration in the outer layer of enamel, and therefore, we assume that zinc was strongly detected in early state of dental decay that stays only at the very surface of tooth. Based on the above result, we calculated intensity ratios between the peak of Zn at the wavelength of 202.5 nm and that of Ca at 317.9 nm. By using the ratio between the components that act inversely to the dental decay, we can improve the sensitivity while suppressing the effects of power fluctuation in the laser and emitted plasma. The averages of intensity ratios were 0.0044 for the sound tooth, 0.013 for the initial caries, and 0.017 for dentin caries. This result demonstrates that there is a significant difference in the averaged ratio between healthy and caries-affected parts. In addition, even early caries can be distinguished from healthy part by setting a boundary between 0.008 and 0.009 in the ratios between Zn at 202.5 nm and Ca at 317.9 nm.

S4-4

New Technology for Bio-Medical Interface Creation utilizing Powder Jet Deposition

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The machining phenomena of powder jet machining transit from removal process to deposition process depending on kinetic energy of impacting particles. The deposition mechanism of powder jet machining was studied with smoothed particle hydrodynamics (SPH) and molecule dynamics (MD) simulations. The deformation of a particle and a substrate by impact was successfully simulated. From the result, a thick film is generated due to the repetition of the deposition of the stagnation areas. The blasting experiments were also conducted to study the machining mechanism at transition condition. The machining surface was analyzed with SEM and TEM. It was that found from these results, the removal process of the substrate material and deposition process of particles onto the substrate occur concurrently under the transition conditions. A hydroxyapatite film has been successfully deposited on a human tooth with powder jet machining.

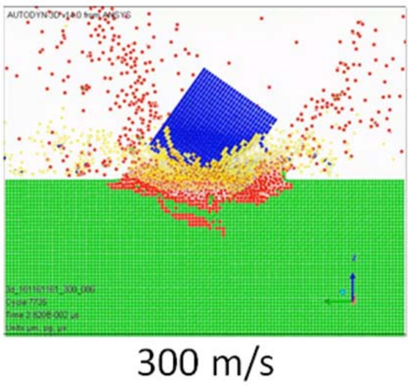

Fig. 1 Substrate fracture of SPH simulation

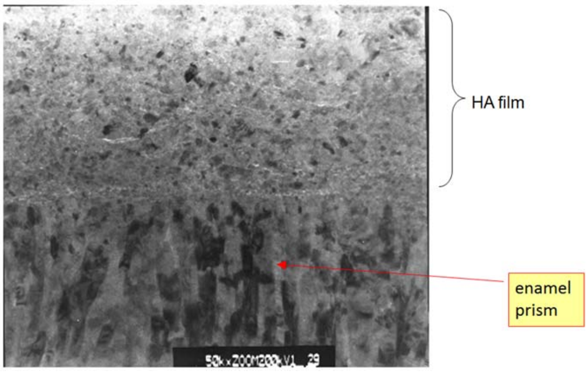

Fig. 2 TEM photograph of HA film on the enamel

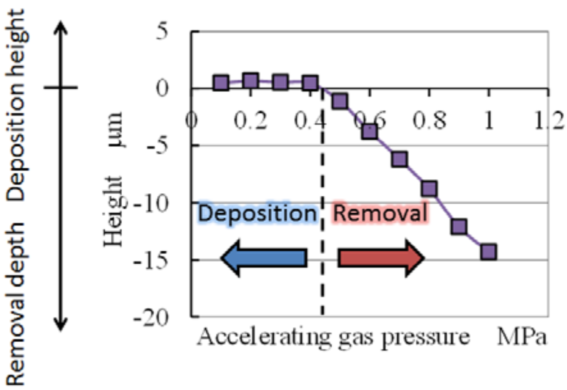

Fig. 3 Transition phenomenon in the powder jet process

S4-5

Acoustic diagnosis device for dentistry

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"Atherosclerosis[1),]joint contracture[2)], prostatic cancer[3)] and dental caries", what is a common point among them? It is the change of tissue elasticity. Atherosclerosis, joint contracture and prostatic cancer show higher elastic property than physiological state of each tissue. However, dental caries (dentin caries) shows lower elastic property than sound dentin. Thus there are a lot of diseases which show the abnormal elastic property. Although many medical doctors and dentists have noticed the change of tissue elasticity due to the pathological state, the diagnostic device to examine the tissue elastic property objectively has not well developed yet. In general, the tissue elastic modulus correlates with the acoustic property. In other words, the mechanical property of tissue is in proportion to the acoustic property. Therefore, the change of the acoustic property indicates the change of the elastic property.

At Tohoku University acoustic microscopy (AM) for medicine and biology has been developed and applied for more than twenty years. Application of AM in medicine and biology has three major features and objectives. First, specific staining is not required for characterization or observation. Second, it provides the elastic property and information of the subject, because acoustic properties have close correlation with the mechanical property of the subject. Third, it makes the observation easy and rapid, one scanning takes less than one minutes. Based on these advantages, AM is able to give us rapid examination and quick diagnosis.

The acoustic microscopy (AMS-50SI, HONDA ELECTRONICS CO., LTD, Toyohashi, Japan) clearly visualizes the color distribution of the acoustic properties of the subject. The acoustic properties include the sound speed propagating in the sample and the acoustic impedance of the sample. In this presentation, I would like to show the change of the sound speed propagating in the rat periodontal ligament and the change of the acoustic impedance of human carious dentin. Moreover, recently portable caries detector has been developed by Saijo Laboratory of Tohoku University Graduate School of Biomedical Engineering. Measuring the acoustic impedance of the surface of the tooth, this device could detect the carious lesion (soft lesion).

The acoustic examination device may be a powerful apparatus not only to visualize the morphological appearance but also to diagnose the pathological or functional state.

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