

5th Anniversary

Nakao Foundation for Worldwide for Oral Health

Grant Research Results Handbook



Index

Thank you note from President Makiko Nakao	01
Nihon University	02
University of Adelaide	08
Queen's University Belfast	15
University of Bern	21
Charité Universitätsmedizin	27
University of Hong Kong	35
UZB Basel	42
Tohoku University	48



Thank you note

It is a great honor to announce about the 5th Anniversary of Foundation Nakao for Worldwide Oral Health which was established on September 18, 2018.

In 2018, Makoto Nakao, my husband who is GC's Chief Corporate Advisor established "Foundation Nakao for Worldwide Oral Health" in Switzerland by donating his own asset in order to make a further contribution to the global dentistry.

Based on the belief that improving QOL is essential for realizing a true healthy ageing society amid this era of 100-year life and further improving oral health is the mission for current and future dentistry, the foundation operates with the aim of promoting academic research and clinical research on new treatment as well as raising awareness about new facts, in view of challenges in our environment as below:

- Promoting Minimum Intervention (MI) Concept
- Shift to tooth functionality (focus on functionality)
- Further promoting the 8020 movement to increase the number of people with more than 20 own teeth at the age of 80
- Prevention of oral frailty
- Improvement of oral health among people across the world

In the past 5 years, Foundation Nakao has been successful in giving grants to 25 universities globally. This was only made possible because Foundation was managed by committed members of Foundation Board and Management Board of Foundation Nakao.

On this memorable 5th Anniversary, Foundation Nakao will be publishing Grant Research Results Handbook after the establishment of Foundation Nakao. This Handbook will report on 4 Grant Research which completed in under the critical situations of the Corona disaster.

We would like to thank all Board Members of Foundation and all the people who participated in promoting the Foundation Nakao Grant Initiative. We sincerely hope that this initiative could enhance activities of Global Oral health in the future.

Thank you again and we look forward to challenging for the 10th Anniversary of Foundation Nakao and hope to be seeing you then.



Makiko Nakao President of Foundation Nakao for Worldwide Oral Health



Nihon University



Granted Project

Name of the Institution	Nihon University School of Dentistry Department of Operative Dentistry
Grant Year	2020
Title	Prevention of tooth wear trough the inhibition of enamel micro-crack propagation
Duration	2020-2023
Theme	Oral health for aging population
Grant Amount	50'000 CHF

Team member



- Masashi Miyazaki, Chair and Professor of Department of Operative Dentistry Nihon University School of Dentistry, Tokyo, Japan
- Toshiki Takamizawa, Associate Professor of Department of Operative Dentistry Nihon University School of Dentistry, Tokyo, Japan
- Ryo Ishii, Assistant Professor of Department of Operative Dentistry Nihon University School of Dentistry, Tokyo, Japan
- Eizo Hirokane, Postdoctoral fellow, Department of Operative Dentistry Nihon University School of Dentistry, Tokyo, Japan
- Mark A Latta, Dean Emeritus, Professor of Department of General Dentistr Creighton University School of Dentistry, Omaha, NE, USA



Summary of the Research

Micro-cracks in enamel may be not only a starting point of tooth wear but also lead to tooth fracture, dentin hypersensitivity, and esthetic problems. The propagation of micro-cracks increases the risk of dental caries because they impair the continuity of the enamel surface. Bioactive materials have been developed for the purpose of strengthening tooth structure through the application of glass ionomer technologies. These materials can release not only fluoride but also several ions, leading to improve acid resistance and induce remineralization. Recently, a new type of glass ionomer cement (GIC) containing functional fillers of fluorozinc-silicate glass so called "BioUnion" has been developed. This GIC releases not only fluoride and calcium ions but also zinc ions. It is thought that the zinc-releasing GIC may strengthen enamel and dentin structure and inhibit the enamel micro-crack propagation and demineralization caused by daily mastication and acid attack. However, there is little information about the mechanical and structure aspects of enamel and dentin when using the zinc-releasing GIC. The purpose of this study was to understand the tooth wear mechanism through the enamel microcrack propagation and to grasp the effect of a GIC incorporating BioUnion filler on the inhibition of enamel microcrack propagation and dentin remineralization.

Fist, we conducted the experiment to reveal the mechanism of micro-crack propagation and tooth wear expansion based on impact-sliding wear testing that is duplicated occlusal conditions and the oral environment. Second, we investigated the ability of BioUnion GIC on dentin remineralization. Finally, the effect of the GIC incorporating on the inhibition of enamel crack propagation was also investigated.

The result of first experiment showed that the facet wear depth was significantly greater with the tapping pattern than with the grinding pattern. The patterns and number of cycles of mastication affected the wear progression of enamel. The second experiment showed that the BioUnon GIC might exhibit the potential to promote remineralization in the dentin. The result of third experiment indicated that the BioUnion GIC enhanced the hardness of the enamel surface and it is helpful to inhibit progression of enamel wear depth. In the EDX analysis, fluorine, zinc, aluminum, and silica were clearly detected when the enamel specimen was immersed in the deionized water with the BioUnion GIC for 32 days.



Major Publication Summary

The purpose of this study was to reveal the mechanism of micro-crack propagation and tooth wear expansion based on impact-sliding wear testing to duplicate occlusal conditions and the oral environment. Bovine teeth were used to determine enamel wear using a sliding impact wear testing machine. Zirconia balls were used as an antagonist. Wear simulation tests were performed to simulate the tapping and grinding patterns of bruxism. The antagonist first directly impacted the specimens from above with a mean force of 15 N at a rate of 0.5 Hz, and then slid horizontally against the slant with a speed of 3 mm/s. Each specimen was subjected to 5,000, 12,500, 25,000, and 50,000 cycles of sliding and impact motion. Two further modes were tested: 1) 5,000T: the antagonist impacted against the enamel surface five times before performing a sliding movement, and 2) 5,000G: the antagonist impacted against the enamel surface once before performing five sliding movements. Five thousand cycles of each cyclic motion were applied. After the wear simulation tests, the specimens were profiled using CLSM. The maximum depth (MD: µm) and mean volume loss (VL: mm3) were determined on 12 specimens for each group. The enamel facets after wear testing were observed using an SEM. The MD and VL values increased as the number of cycles increased. When MD values were compared after 5,000 cycles under the different cycle modes, a significant difference was detected between the 5,000 and 5000T modes, but no significant different with the 5,000G mode was detected. However, significant differences in VL values were detected between 5,000 and 5,000G. In terms of facet shape, the facets were round, with a greater amount of enamel loss, in the 5,000T group compared with the other groups, which had elliptical facet shapes. The results of this study, the facet wear depth was significantly greater with the tapping pattern than with the grinding pattern. The patterns and number of cycles of mastication affected the wear progression of enamel. (Eur J Oral Sci 130, e12831.)



Publication list

- 1. Namura Y, Uchida Y, Inaba M, Kaetsu R, Utsu A, Takamizawa T, Miyazaki M, Motoyoshi M (2022) Influence of masticating cycles and chewing patterns on inadvertent enamel wear caused by zirconia brackets. Eur J Oral Sci 130, e12831.
- 2. Shoji M, Kurokawa H, Takahashi N, Sugimura R, Takamizawa T, Iwase K, Katsuki S, Miyazaki M (2022) Evaluation of the effect of a glass ionomer cement containing fluoro-zinc-silicate glass on dentin remineralization using the ultrasonic pulse-echo method. Dent Mater J 41, 560-566.
- 3. Sagawa M, Namura Y, Uchida Y, Miyama W, Nishimura S, Yoneyama T, Takamizawa T, Motoyoshi M (2023) Enhancing enamel wear resistance around a glass ionomer cement containing BioUnion fillers. (Dent Mater J submitted)



Appreciation letter from the institution

First, we express deep gratitude for the Foundation Nakao to support our research. We are very honored to became one of the winners for the 1st Foundation Nakao Grant in 2020. Our department focuses on basic science for dental materials, transitional research, and clinical study to provide up-to-date information to dental students and dental professions. In addition, these research outcomes contribute to the dental field not only in our own country but also in all over the world.

We could conduct several investigations supported by the Foundation Nakao grant, and published some manuscripts to the international journals. However, we had to change original experimental protocol due to the recent pandemic. First, we were going to conduct a modified flexural fatigue test protocol at Creighton University in the USA as our first experimental protocol regarding the enamel microcrack study. However, we have not been allowed to go outside Japan due to our university regulations regarding Covid-19. Therefore, we had to change our experimental plan, and have omitted modified flexural fatigue test in the USA. We also thank Foundation Nakao for its generosity to change experimental protocol.

Although most grants in dental filed are domestic and have some limitations, the grant of Foundation Nakao is global and universities around the world have a chance to obtain its courtesy. The philosophy of Foundation Nakao is to contribute to the realization of a truly healthy long-living society and a high quality of life by supporting research and analysis to improve global oral health. The foundation's philosophy meets our university's mission and believe facing same directions. Therefore, this kind of grant is much valuable for university and research institution of the world. We would like to expand further researches based on achieved studies supported by Foundation Nakao grant. We sincerely thank Foundation Nakao.

Masashi Miyazaki, DDS, PhD Professor and Chair of Operative Dentistry Nihon University School of Dentistry 1-8-13, Kanda-Surugadai Chiyoda-Ku Tokyo 101-8310 Japan



University of Adelaide



Granted Project

Name of the Institution	University of Adelaide in collaboration with University of Newcastle, University of Sydney, Australian Wine Research Institute, University of Minnesota and University of Michigan
Grant Year	2020 (extended till 2023)
Title	The relationship between oral health, multimorbidity, and polypharmacy in older adults living with dementia
Duration	4 years
Theme	Cariology, geriatric dentistry, preventive dentistry
Grant Amount	49,544.80 CHF

Research Team



Dr Sarbin Ranjitkar, Adelaide Dental School University of Adelaide



Dr Jenny Tan Adelaide Dental School University of Adelaide ALIS



Dr Mark Wotherspoon Private practice Wagga Wagga / AUS



Ms Claire Mills Private practice Adelaide / AUS



Dr Poornima Ramamurthy School of Health Sciences University of Newcastle New South Wales / AUS



Dr Natoiya Lloyd Australian Wine Research Institute Urrbrae / AUS



Dr Bing Li, Adelaide Dental School University of Adelaide AUS



Ms Tong Yu Goh Adelaide Dental School University of Adelaide AUS



Prof. Dileep Sharma School of Health Sciences University of Newcastle New South Wales / AUS



Dr Wei Zhang School of Computer Science University of Adelaide AUS



Assoc Prof Rahena Akhtar School of Dentistry University of Sydney New South Wales / AUS



Assoc Prof Boyen Huang School of Dentistry University of Minnesota



Prof Romesh Nalliah School of Dentistry University of Michigan



Introduction of the research team

Dr Sarbin Ranjitkar [BDS, BScDent(Hons), PhD, FPFA] is Senior Lecturer with a research focus on geriatric dentistry, craniofacial growth, 3D image analysis, and materials science. He has an H-Index of 19 (Scopus), having over 60 publications, and is a recipient of the IADR Oral Biology Award (2014). He is currently the Counsellor for the IADR, ANZ Division. He has held positions of the Honorary Treasurer for the IADR, APR (2020-2021) and Treasurer for the IADR, ANZ Division (Sep 2017 - Dec 2020).

Dr Jenny Tan [BDS, BScDent(Hons)] received a university medal for her honours degree in 2021. She is working as a general dentist in special needs clinics. She has experience in managing geriatric patients and those with dementia. Her research interests include craniofacial biology and oral health in individuals with special needs.

Dr Mark Wotherspoon [BDS] has had many years of experience in private practice as principal and practice owner as well as experience in the Public Service, Military Service and even Corrective services. He firmly believes in establishing best practice oral hygiene routines for his patients and educating other health professionals and the public of the close link between oral health and general health. He is an Adjunct Senior Lecturer and Clinical Team Leader CSU in Portable Dentistry and has successfully run his own private practice portable dental service -Dentist To Your Door since 2016.

Ms Claire Mills [BOH] is a dental therapist and hygienist. In 2018, Ms Mills founded Respect Dental, with the goal of bringing vital dental services to the ageing and anyone else that, for various reasons, find it hard to regularly visit a traditional dental practice.

Poornima Ramamurthy [MPH-MBA, BDS] is a Dentist with a public health expertise and currently works as an epidemiologist at the Eleanor Duncan Aboriginal Health Services in Central Coast (NSW). Her research focuses on the epidemiology, social determinants, and preventive aspects of dental caries, periodontal disease and oral cancer in culturally diverse population, including First Nations People. Poornima has published multiple research papers in dentistry and has won multiple research grants and awards in recognition of her extensive work in oral diseases.

Dr Natoiya Lloyd [BSc, PhD] is a Research Scientist at The Australian Wine Research Institute - Metabolomics Australia (Supported by NCRIS/BPA). For the past 8 years, Dr Natoiya Lloyd has been leading the Metabolomics Australia group and primarily drives collaborative initiatives and facilitating infrastructure access for researchers and industry across multiple sectors including biomedical, agriculture and food and beverage. She is experienced in project portfolio management, metabolomics, mass spectrometry and analytical chemistry.

Dr Bing Li [BDS, BScDent(Hons)] received a university medal for her honours degree in 2022. She is a general dentist working in private practice in New South Wales. She has research interest in microbiome analysis in oral health of children and the elderly.

Ms Tong Yu Goh is a Bachelor of Dentistry 3 student, who has keen in research on geriatric dentistry and the link between oral and general health.



Introduction of the research team

Professor Dileep Sharma [BDS, MDS, PhD, Grad Cert Acad Pract] is the Head of Discipline, Oral Health at School of Health Sciences, College of Health, Medicine & Wellbeing at the University of Newcastle. Previously, Dileep has been Councillor for Far North Queensland Section of the International Association for Dental Research, ANZ division (2018-2022). He has served as a peer-reviewer for various Q1 journals within dentistry and materials journals and a guest editor on multiple special issues focusing on contemporary topics such as dental implants and COVID-19. He sits on the reviewer panel for various funding bodies including National Health and Medical Research Council (NHMRC), Australian Dental Research Foundation and Tropical Australian Academic Health Centre.

Dr Wei Zhang [BE, ME, PhD] is Senior Lecturer at the School of Computer Science, The University of Adelaide, and Honorary Lecturer at Department of Computing, Macquarie University. Her research relates to three specific areas, including adversarial attacks on deep neural models for text, neural dialogue systems in smart space, and analysis of medical data.

Dr Rahena Akhter [PhD, BDS, FICD] is Discipline Head of Cariology at the Sydney Dental School, the University of Sydney. She specializes in Preventive Dentistry (PhD, Hokkaido University, Japan), is an expert in teaching caries management system (CMS) in the Doctor of Dental Medicine (DMD) and Bachelor of Oral Health Therapy (BOH) Program at SDS. Her broad experience in Japan, Bangladesh, and Australia includes working closely with high caries risk patients, and those with cerebral palsy and other developmental disability. Dr Akhter has presented at more than 80 national and international conferences, has won several international awards, and has secured multiple grants worth \$2.0M.

Associate Professor Boyen Huang is Assistant Dean for Faculty Development at the University of Minnesota School of Dentistry. Prior to this role, he has held executive, research and teaching posts at Charles Sturt University, James Cook University, Kyoto University, and University of Western Australia. He has also served as an executive and councilor at the Division and Regional levels of the International Association for Dental Research (IADR). His research has focused on biological and socio-behavioral risk factors for oral conditions such as dental and craniofacial anomalies, and traumatic dental injuries, with recent interest in telehealth and non-nutritive sucking behavior. In Minnesota, he is leading an international and interprofessional team on an mHealth research project to support the management of traumatic dental injuries.

Professor Romesh Nalliah [DDS, MHCM] is Clinical Professor and Associate Dean for Patient Services at the University of Michigan School of Dentistry. He has held many leadership roles in the Massachusetts Dental Society including Board Member, Delegate and Chair of Continuing Education. He has taught more than 100 continuing education programs for dentists, physicians and nurse practitioners and also served as Dental Director of Special Olympics for Massachusetts. For more than a decade, he has maintained a national and international reputation as an expert in health services research and public health. He has won several research awards and serves as Associate Editor for the Journal of Dental Education and as Editorial Board member of several journals. He brings expertise in data science into the clinical environment and has published studies related to efficiency and quality in hospitals, community health centers, and dental school clinics.



Summary of the Research

Background: Dementia is the most common neurocognitive disorder affecting the elderly. As the condition progresses, people lose independence and transit into residential aged care facilities (RACFs). Contemporary research in this field is limited, and studies from 15 years ago have reported high levels of dental caries and poor oral hygiene among RACFs living with dementia. Oral health outcomes in RACF residents living with and without dementia remain under-researched and under-funded, and lacks visibility and accountability, as concluded by the 2021 final report of the Royal Commission into Aged Care Quality and Safety (RCACQS) in Australia. The enquiry also identified oral care as a high priority area for those unable to self-care. In this context, there is a need to better understand the oral health status and disease risk in those residents.

The aims of the current study were (i) to assess the oral health status, multimorbidity, and polypharmacy status in people living with and without dementia in RACFs, and (ii) to assess the plaque microbiome and salivary metabolome associated with caries experience. The hypothesis was that residents living with dementia would have poorer oral health outcomes, multimorbidity, and polypharmacy status compared with those without.

Methods: The sample comprised 136 participants from two locations, including urban South Australia (24%) and regional New South Wales (76%). The majority of participants were females (61.0%) and aged between 85-95 years (41.9%). Data were collected for oral health using the Oral Health Assessment Tool (OHAT), multimorbidity from medical history, and polypharmacy from medication list. From a subset of South Australian participants (n = 23), additional data were collected for DMFT index, oral swabs (from carious lesions, cheeks, and dentures). Microbiome analysis was performed to identify the majority of bacterial species associated with carious lesions.

Results: The levels of oral problems, multimorbidity and polypharmacy were high, regardless of dementia status. The most common comorbidities were bone and joint conditions (71.1%) and cardiovascular conditions (70.1%). Participants with dementia were taking 6.0 ± 3.2 medications (mean \pm standard deviation) compared with 7.5 ± 4.0 without. Multivariate logistic regression showed malnutrition on the 'natural teeth' domain (p < 0.05), and xerostomic medications on the 'saliva' domain (p < 0.05). Additionally, microbiome and metabolome profiles were complex, with sound tooth surfaces being mainly colonised by oral commensal bacteria compared to pathogenic bacteria for carious lesions.

Conclusions and significance: RACF residents had high levels of poor oral health, multimorbidity, and polypharmacy regardless of dementia status. These data emphasise the need for all levels of government and community stakeholders to support the strained sector to improve the quality of life of vulnerable people. Additional resource allocation and appropriate policymaking is an increasingly pertinent issue for this sector on a global level.



Publication list

These are manuscripts under preparation and are expected to be published over the next 1-2 years:

Review articles

- 1. Oral health in dementia: implications for the dental and geriatric healthcare professional. (This narrative review article will be submitted to a dental clinical journal)
- 2. Oral health in dementia: critical appraisal of the evidence linking oral and systematic health. (This critical review article will be submitted to a journal with an aged care focus)
- 3. Dental caries status in people living with dementia in aged care facility versus community dwellings: a scoping review.
 - (This scoping review article will be submitted to a dental clinical journal)

Research report

- 4. Oral health status, multimorbidity, and polypharmacy in older Australians living with dementia in aged care facilities.
 - (This scientific article will be submitted either to a dental clinical journal or an aged care journal)
- 5. Combined microbiome and metabolome analyses associated with dental caries and dementia in older Australians.
 - (This scientific article will be submitted to an oral biology journal or a scientific journal specialising in multi-omics approach to diagnosis and management of diseases)



Appreciation letter from the institution



31 January 2024

Foundation Nakao for Worldwide Oral Health Fluhmattweg 13 6004 Luzern Switzerland

Dear Nakao Foundation Team,

Re: Letter of support for a research project on oral health in dementia

I am writing to express my gratitude for the Foundation's support for the project titled 'The relationship between oral health, multimorbidity, and polypharmacy in older adults living with dementia'.

This funding has been instrumental in fostering interstate and international collaborations on oral frailty in older people living with dementia in residential aged care facilities. The foundation's support has enabled our research group to reach important milestones and to add knowledge to this field of global importance.

Several publications are under preparation from this project. The data will also provide a platform on which future studies will be developed to promote oral health and improve the quality of life of this group of vulnerable people.

Once again, I am very thankful to the Foundation's support. My team will keep you updated about future progress of this project. I look forward to potential future collaboration.

Your sincerely,

RICHARD LOGAN

Morhand Culy

PROF RICHARD M LOGAN, DEAN AND HEAD OF SCHOOL Adelaide Dental School/ Faculty of Health and Medical Sciences The University of Adelaide SA 5005 AUSTRALIA

Tel: +61 8 8303 5409 Email: dean.dentistry@adelaide.edu.au www.adelaide.edu.au

CRICOS provider number 00123M



Queen's University Belfast



Granted Project

Name of the Institution	Queen's University Belfast
Grant Year	2020
Title	Exploration of the relationship between poor oral health and cognitive decline in older adults living in nursing and residential homes
Duration	3 years
Theme	Healthy Ageing
Grant Amount	13'200 CHF

Team member



Dr Nicola Holland - A Specialist Trainee in Restorative Dentistry and is currently out of programme while working as a Dental Clinical Fellow in the Department of Health, NI. Nicola is also undertaking a MPhil research degree in the Centre for Public Health, QUB. Her research aims to investigate the oral health of care dependent older adults by utilising oral health assessment data, collected by the Community Dental Service (CDS) in Northern Ireland, to establish an epidemiological picture of the oral health of care home residents. Nicola has also contributed to the Enhancing Clinical Care Framework and Oral Cares Regional Dysphagia Guidelines. She is actively involved as a dental trainee representative for the BDA CCHDS executive committee, BMA NI Junior Doctors/Dentists committee and BDA NI Hospital Dentistry Forum.



Professor Gerry McKenna - Professor of Oral Health Services Research and Gerodontology / Consultant in Restorative Dentistry, Queen's University Belfast. Gerry is a specialist in Prosthodontics and Restorative Dentistry working as a Consultant in the Belfast NHS Health and Social Care Trust. His clinical duties are based in the Centre for Dentistry, Queens University Belfast where he also provides clinical supervision and teaching for dental undergraduates and postgraduates. Gerry holds a chair in Oral Health Services Research and Gerodontology within the Centre for Public Health where he leads Oral Health Research. His research is centred around optimising treatment options for older patients which positively impact their dental and overall health. Gerry is the current president of the British Dental Association Northern Ireland Branch and has previously been President of the British Society of Gerodontology, European College of Gerodontology and the Geriatric Oral Research Group within the International Association for Dental Research. He holds a King James IV Professorship from the Royal College of Surgeons Edinburgh, an adjunct Professorship in University College Cork and is a visiting Professor in both the Federal University of Goais, Brazil and Zurich University.



Summary of the Research

The oral health of care home residents is much worse than their community living peers and about half of all care home residents now retain some of their natural teeth. In addition, more than 50% of residents have some form dementia or cognitive impairment. A number of studies suggest an association between oral health and cognitive status but the quality of evidence is often poor. This project aimed to investigate the association using three high quality methods: a systematic review of existing evidence; and collecting data from residential care and nursing home patients.

Systematic review

This systematic review aimed to investigate the association between periodontitis and cognitive impairment amongst older, care dependent adults who reside in nursing and residential care homes. Systematic literature searches were performed to identify studies reporting on older adults, who were dependent on others for care and had been clinically diagnosed with periodontitis and cognitive impairment. Due to the diversity in presentation of the findings, results from the included studies are presented using a qualitative narration. A total of 698 studies were identified; and of those, 11 studies were included in the final full text review.

Nursing home residents who had been diagnosed with Alzheimer's disease showed evidence of poor oral health and oral health status showed deterioration as the severity of Alzheimer's disease increased. Periodontal indices were seen to be significantly higher in nursing home residents with Alzheimer's disease, compared to a similar cohort of older people living in the community. Several studies have found a potential relationship between increased probing pocket depth and cognitive impairment. Mean Community Periodontal Index of Treatment Need (CPITN) scores have been reported to be significantly higher in residents with dementia compared to those with no diagnosis of dementia. The findings from these studies suggest that a diagnosis of dementia is associated with severe periodontitis. However, conversely, a number of other studies included in the review were unable to find a statistically significant association between periodontitis and cognitive impairment or dementia. Oral health among nursing home residents was seen to be impaired and this finding was independent of the resident's dementia status. For interventional studies involving caregivers' education to improve the oral health of care-dependent nursing home residents, worse baseline conditions were an indicator for more substantial improvements in the periodontal indices for both dementia and non-dementia groups. Nursing home residents have varying care dependencies, can be medically compromised, and are often prescribed a variety of medications. Longitudinal studies using carefully designed study methodology would be required to assess the association between periodontitis and cognitive impairment in this complex cohort. It was not possible to determine the direction of association from the studies examined, however, it is hypothesised that the relationship between periodontitis and cognitive impairment may be bi-directional and multifactorial. There is no definitive consensus on the association between periodontitis and cognitive impairment among care dependent older adults. Further research is required in this field if any relationship is to be determined between periodontitis and cognitive impairment, with robust methodology applied.



Summary of the Research

Epidemiological Study of Care Home Residents

In Northern Ireland the CDS provides periodic extraoral and intraoral examination of older adults living in nursing homes as part of an oral health screening programme. This allows the dental staff to identify oral health problems in order to plan patients' ongoing care. This screening data is stored by the Health and Social Care Board and is the basis for our data collection. Oral health screening data which was collected between 31st Jan 2019 and 31st Jan 2023 was entered, curated and analysed. Oral health screening data has been collected for 1116 residents (76% of all residents) in 43 nursing and residential care homes (Table 1). Reasons listed for residents not undergoing an oral health screening included; "sleeping", "in hospital" and "poor cooperation". 68% of residents were female. The majority of residents were dentate (n=753, 67.5%) with 40 residents experiencing dental pain at the time of screening (5.6%). The total number of teeth present ranged from 1-31 (mean=10). A large proportion of residents had retained roots in situ (n=396; 52.6%; range: 1-24) (Table 2). A total of 197 residents had caries charted on coronal or root surfaces (26.2%). 473 (46.8%) care home residents wore dentures, with the majority constructed from acrylic resin (95.6%). A large proportion of residents had active caries (17.2%) and large numbers of retained roots (37.4%). These results should be interpreted with caution as the challenges encountered in data collection within the care home setting may mean that clinical examinations have reduced accuracy. This project is the first to provide an epidemiological picture of the oral health status of care home residents in Northern Ireland. The study illustrates the high levels of oral health need amongst care home residents with 69.5% dentate but with high levels of retained roots and active caries present on coronal and root surfaces.



Publication list

- 1. The Association between Periodontitis and Cognitive Impairment in Care Dependent Older Adults: A Systematic Review. Holland N, Nic Iomhair A, Kelly N, Cullen L, McEvoy C, Lappin C, Srinivasan M, McKenna G. Journal of Dentistry 2024; under review.
- 2. Oral health of nursing and residential home residents in Northern Ireland: an epidemiological study. Holland N, Cullen L, McEvoy C, Lappin C, McKenna G. Paper in preparation; abstract accepted for IADR General Session, 2024.



Appreciation letter from the institution



Dear Mrs Nakao and the Nakao Foundation Board,

Re: Exploration of the relationship between poor oral health and cognitive decline in older adults living in nursing and residential homes

I am writing to express my gratitude, on behalf of Queen's University Belfast, for the funding to support this important work. This funding has enabled Professor McKenna and Dr Holland to carry out research on oral health in older adults, including a systematic review and a large scale epidemiological study of over 1000 patients. I am very confident that once these outputs have been published that these will be highly cited and well received by the oral health research community. I hope that Queen's University Belfast can be successful in winning future funding from the Nakao Foundation to support our ongoing program in oral health services research focused on older adults: https://www.qub.ac.uk/research-

centres/CentreforPublicHealth/Research/HealthServicesGlobalHealth/OralHealthCare/

Kind regards,

Professor Jayne Woodside,

Director, Centre for Public Health

Myn Woodule

Queen's University Belfast



University of Bern



Granted Project

Name of the Institution	University of Bern, School of Dental Medicine Department of Restorative, Preventive and Pediatric Dentistry
Grant Year	2020
Title	Oral health, oral related quality of life and nutritional aspects in retired-age population in the Canton of Bern
Duration	3 years
Theme	Oral health and quality of life in the elderly population
Grant Amount	46`550.45 CHF

Team member

Project leaders / Researchers



PD Dr. C. Tennert



Prof. Dr. M. Schimmel



Prof. Dr. G. Campus



Dr. R. Borg Bartolo

Examiners



PD Dr. C. Tennert - Lindsay Duay - Laura Kohli - Celine Gübelin - Sarah Dellenbach - James Imhof - Valerie Gasser - Patric Maibach - Maurus Jäggi - Maria Prasinou



Summary of the Research

The objectives of the study are to evaluate the prevalence of oral treatment needs and the quality life related to oral status in the elderly population living in the Canton of Bern and to analyze the association between the oral data collected with demographic, socioeconomic factors, systemic health, Body Mass Index and Mini Nutritional Assessment measurements. Oral examination revealed clinical parameters, e.g. caries scores, gingiva index, plaque index, periodontal status, presence of prosthetic rehabilitation, number of occlusal functional units and masticatory performance. A total of 237 participants were examined. The majority of the examined sample lived in rural areas (53%), were married (67%) and retired (66%). No statistically significant differences among groups were detected with respect to the area of living, civil status, and education level. Regarding the medical conditions, 37% of the individuals reported high blood pressure values, while 68.80% of the group ≥75 reported to be affected by cardiovascular disease. Most of the patients were non-smokers.

When analyzing dental caries prevalence, 15% of the subjects have been diagnosed with active caries. These are to the best of our knowledge the first data collected within Switzerland and therefore virtually impossible to compare with previous publication: nevertheless, when comparing this prevalence with the one gathered from adjacent countries such as Germany and France, these data are slightly lower with those reported.

Overall, the individuals from the analyzed cohort showed good oral health: the majority of subjects had more than 20 teeth (86 %) and did not wear any removable prosthesis (91%).

Based on the obtained results, the majority of the in interviewed subjects displayed good to optimal chewing abilities and their ability was correlated to the number of present teeth and the presence of a removable prostheses. The masticatory performance was positively associated to working status and the number of present restorations. Gender and educational level didn't show a statistically significant association with chewing performance.

The results of the present cross-sectional, monocentric study show that despite the high awareness of the importance of home care plaque control, the frequent visit to a dentist, dental caries and periodontitis are still present in adults and elderly Swiss subjects, but are lower compared to other neighboring countries. These findings indicate, that there is a high level of attention concerning oral health in that Swiss population. However, the oral health related quality of life (GOHAI) was perceived lower compared to neighboring countries.



Major Publication Summary

Roccuzzo A, Borg-Bartolo R, Schimmel M, Tennert C, Manton DJ, Campus G. Evaluation of the Oral Health Conditions and Oral Health-Related Quality of Life in a Community-Dwellers Population Aged ≥ 45 Years in the Canton of Bern: A Preliminary Pilot Study. Int J Environ Res Public Health. 2023 Mar 4;20(5):4557. doi: 10.3390/ijerph20054557. PMID: 36901566; PMCID: PMC10001686.

The objective of this study was to evaluate the oral health conditions and oral health related quality of life in community-dwellers aged \geq 45 years in the Canton of Bern, Switzerland.

One hundred subjects (63% males; mean age: 73 years) were randomly selected using a cluster procedure within the Canton of Bern, underwent a clinical examination after filling questionnaires on the socioeconomical level, medical history, oral health behavior and Geriatric Oral Health Assessment Index (GOHAI). Descriptive analysis and multinomial regression models were applied to investigate the association between oral health diseases (i.e. dental caries and periodontitis) and specific patients' characteristics.

The mean number of decayed, missing and filled teeth was 0.30, 4.20, 8.75, respectively. Mean DMFT score was 13.35. Dental caries prevalence was 15.00%, periodontitis prevalence 46.00%. Logistic regression models revealed that living in an urban area was associated with lower odds (OR 0.03, CI 0.00 - 0.36) of having periodontal disease. Male gender was associated with lower odds for dental caries (OR 0.31, CI 0.09 - 1.01), total lack of professional tooth cleaning was associated with higher odds for dental caries (OR 41.99, CI 0.01 - 0.38). Ordinal logistic regression revealed that both the presence of dental caries (RR 12.80, CI 1.47 - 111.20) and periodontal (RR 6.91, CI 1.16 - 84.00) disease were statistically significantly associated with rheumatoid arthritis.

Within the limitations of this study, the findings indicate that untreated dental caries and periodontal disease are quite prevalent within the Swiss population, despite the high level of self-performed oral hygiene and access to the dental care system.



Publication list

- 1. Roccuzzo A, Borg-Bartolo R, Schimmel M, Tennert C, Manton DJ, Campus G. Evaluation of the Oral Health Conditions and Oral Health-Related Quality of Life in a Community-Dwellers Population Aged ≥ 45 Years in the Canton of Bern: A Preliminary Pilot Study. Int J Environ Res Public Health. 2023 Mar 4;20(5):4557. doi: 10.3390/ijerph20054557. PMID: 36901566; PMCID: PMC10001686.
- 2. Tennert C, Borg-Bartolo R, Schimmel M, Rocuzzo A, Campus G. Evaluation of the chewing function in a community-dwellers population aged ≥ 45 years: a cross-sectional study. Journal of Oral Rehabilitation, submitted 06/2023.



Appreciation letter from the institution

Dear Mister or Madam, dear Mr. Mita

Our research group is honored to receive the grant from the Nakao Foundation for Worldwide Oral Health for our study. The objectives of the study were to evaluate the prevalence of oral treatment needs and the quality of life related to the oral status in the elderly population living in the Canton of Bern and to analyze the association between the oral data collected with demographic, socioeconomic factors, systemic health, Body Mass Index and Mini Nutritional Assessment measurements.

With your grant, we were able to hire a dentist and researcher, Dr. Roberta Borg-Bartolo, who was hired part-time to assist in receiving the contact information of the elderly citizens of the Canton of Bern and to organize and perform the oral examinations, data collection and analysis of the collected data. Besides Dr. Borg-Bartolo, seven dental students in their fourth and fifth year of dental studies and postgraduate students of the University of Bern assisted in visiting the participants and performing the oral examinations for this study as part of their Master thesis.

Your grant also enabled us to cover the costs of all materials needed for the examinations (head lamps, printed documents, instruments), travel expenses for all examiners visiting the participants, postage costs to invite possible participants for study participation. The grant also made it possible to purchase informatics, including lap tops, software (partly rented, partly purchased) for collecting and analyzing the data.

We are fortunate to have the support of the Foundation Nakao to enable such a large and important epidemiological research project.

Thank you very much for your support.

PD Dr. med. dent. Christian Tennert

C. Y



Charité Universitätsmedizin



Granted Project

Name of the Institution	Charité Universitätsmedizin
Grant Year	2020-2022
Title	Applying Machine Learning through Video-recognition to expand the use of Minimal Intervention Dentistry in Low-and Middle-Income Countries
Duration	2 years
Theme	MI Dentistry
Grant Amount	98'000 CHF

Team member

Jesus Gomez Rossi

Dentist and health economist.

Falk Schwendicke

Professor and Head of Department, Oral Diagnostics, Digital Health and Health Services Research.

Joachim Krois

Senior data scientist in the department ODDH2, Charité - Universitätsmedizin Berlin.

Csaba Rohrer

Data scientist

Ben Feldberg

Dentist and data researcher at the Charité



Introduction of the research team

Jesus Gomez Rossi: Dentist and health economist. His research is focussed on the understanding and development of digital health solutions such as social media strategies and Al applied to healthcare, hardware and integration of biosensors for real-time biomarker measurement and new forms of health service provision for high need populations in different income settings. Jesus leads the efforts of our multi-disciplinary team to analyse and solve problems such as poor oral health outcomes in nursing homes or technical limitations in implantable devices from an economic and technical perspective. All his projects demand forward-thinking strategies that push for greater digitalisation, with the final aim of increasing access for everyone to higher quality healthcare.

Falk Schwendicke: Professor and Head of Department, Oral Diagnostics, Digital Health and Health Services Research. Demonstrable track record of clinical and scientific excellence in the field of diagnostics, operative, preventive and data-driven dentistry. Falk's research is aimed at answering questions of high clinical relevance. His research focus is on cariology and restorative dentistry, preventive and public health dentistry, dental diagnostics and Al as well as health economics and health services research. He has authored over 300 articles, edited various books and provided over 20 book chapters on a range of issues, from caries management to health economics. Falk was awarded a range of prestigious awards, among them the Basil Bibby and Lion Award of the IADR, numerous awards of the German Society of Conservative Dentistry as well as the David Sackett Award of the German Network for Evidence-based Medicine. He reviews for over 40 peer-reviewed journals, among them the Lancet, as well as various national funding agencies. He serves as Associate Editor of the Journal of Dental Research and has been on the editorial board of various dental journal before. His work on Al for dental imagery analysis led to the first dental Charité spin-off, dentalXrai GmbH.

Joachim Krois: Senior data scientist in the department ODDH2, Charité - Universitätsmedizin Berlin. He works primarily in the areas of statistics, predictive modeling, machine learning, computer vision, epidemiology, and health services research. One focus of his work is the development of concrete solutions to improve dental diagnostics by applying machine learning techniques. Joachim Krois is an advocate of the data dentistry paradigm. Here, the complexity of decision making in the medical field is addressed by critically evaluating the costs, benefits, and trustworthiness of prognostic systems. He is part of the ITU/WHO Focus Group Artificial Intelligence for Health (AI4H), where he works collaboratively and interdisciplinarily on benchmarking for AI algorithms in the topic group "Dental diagnostics and digital dentistry". The aim is to improve the generalizability and trustworthiness of AI systems.

Csaba Rohrer: Data scientist with a strong focus on computer vision and deep learning. Csaba is a recent graduate of a double-degree program offered by the EIT Digital Master School. Apart from data science his curriculum included a minor in innovation and entrepreneurship as well. His diverse skillset made him attracted to the interdisciplinary field of digital dentistry. He is intrigued by the challenge of bringing artificial intelligence and clinical experience together. Csaba applies state-of-the-art data analysis and machine learning techniques to improve dental diagnostics and to further the research at Charité.

Ben Feldberg: Is a dentist and data researcher at the Charité which a track on participating at different projects focused on AI and dental public health. Ben has a global oral health focus to help disfavored populations.



Summary of the Research

Our research project focused on leveraging artificial intelligence (AI) to improve dental care accessibility and affordability, particularly in Low- and Middle-Income Countries (LMIC). We developed an ML-based video classifier capable of detecting oral pathologies and suggesting MI interventions to deliver highly cost-effective interventions. We recognized that evidence-based approaches like Minimally Intervention Dentistry (MID) and Atraumatic Restorative Treatment have made high-quality dentistry more accessible in low-technological contexts. However, the crucial initial step of diagnosis and treatment planning still requires dental expertise, limiting the involvement of non-dental professionals. We first aimed to develop an AI solution recommending MI interventions that could be delivered by a broader spectrum of medical practitioners such as nurses or dental assistants worldwide.

Our algorithm focused on recommending treatments that do not involve permanently removing tooth substance using rotary dental equipment, making it a potentially more cost-effective alternative. To assess its cost-effectiveness, we developed a Markov model that compared the Al approach to different standards of oral care. The model considered various strategies and therapeutic alternatives in dentistry to address oral diseases.

As a control, we used standard German dental care and adjusted its costs and effects to Germany. In the scenario where patients received no dental healthcare, costs were incurred only in the case of dental emergencies. We calculated the net benefit of each strategy combination based on willingness-to-pay thresholds and changes in Quality-Adjusted Life Years (QALYs) or tooth retention years.

Our findings revealed that AI, coupled with Minimally Invasive (MI) dentistry, led to increased tooth retention for populations currently without access to dental care delivered by professionals and was less costly than the standard of care delivered by dental practices. However, for high-income countries, AI was up to 12 years less effective than the control group. When considering the cost-effectiveness of interventions, AI using MI dentistry appeared to be the most likely option within a willingness to pay (WTP) in the price range of 0 to 10 Euros. Beyond 20 Euros, the marginal benefit of paying additional costs for preserving each tooth favored control strategies. This indicates that in settings with a lower WTP for dental care such as in lower- and middle-income settings our approach could favor the strategy we developed, thereby improving access to dental care. Our cost-effectiveness analysis demonstrated the synergy between AI and MI dentistry in addressing tooth decay and extending tooth retention. Although the research is still in early stages, AI seems to be capable of achieving diagnostic accuracy to a degree that justifies its use-case and implementation by improving outcomes at a moderate increase in cost compared to standard care.

Despite its limitations, AI tools facilitating caries screening under MI principles can be tremendously beneficial in treating dental caries, particularly in resource-limited settings. Our research underscores the transformative impact AI can have in tackling the global burden of oral diseases.

Overall, we are confident that our study provides valuable insights into the potential of AI and MI dentistry as a cost-effective approach to improve oral healthcare accessibility and outcomes.



We are in the finishing stages of the following two publications:

Research Summary - Article 1

Applying Machine Learning to treatment recommendation of MI interventions

Our study aimed to demonstrate that a machine learning model can achieve comparable accuracy to trained dental professionals in detecting and classifying clinically detectable caries lesions. Caries, the most prevalent non-communicable disease worldwide, disproportionately affects individuals in Low- and Middle-Income countries (LMIC), where access to dental care is limited and costs of dental technology are high.

To address this challenge, we proposed the application of Artificial Intelligence (AI) in dental diagnosis and treatment planning to provide high-quality care at lower costs. Our team utilized AI/ML techniques to analyze photographies and videos of the oral cavity and recommend interventions aimed to slow down, arresting or treating caries.

We had to create and integrate multiple datasets to significant improvements in our results compared to the previous version. The inclusion of diverse data, improved annotation quality, and data-science factors contributed to these advancements. Using a ResNet-18 classification model trained on clinical images of teeth, we achieved an overall accuracy of 76.72% across all four classes, with sensitivity and precision values of 82.78% and 75.25%, respectively.

We employed the stochastic gradient descent optimizer with learning rate decay and early stopping, while the best performing model had a batch size of 80 and learning rate adjusted from 0.01 to 0.001 after 15 iterations.

Our algorithm demonstrated strong sensitivity (over .82) in correctly classifying healthy teeth. The inclusion of orthodontic database data significantly improved precision, F1 scores, and specificity by up to .15. The updated model exhibited sensitivity over .785, enhanced F1 and precision values, and increased negative predictive values (NPV) by more than 6%.

Although the algorithm encountered challenges in differentiating between early stage and deep caries, leveraging additional information from X-rays could potentially enhance its performance. The algorithm's ability to recommend atraumatic restorative techniques for advanced caries showed comparatively lower performance. However, the precision and F1 scores for the category suggesting direct referral to the dentist experienced modest but significant improvements.

In some cases, the algorithm's recommendations differed from the initial annotations made by human experts, with reviewers finding the algorithm's suggestions more likely to be correct. Notably, the algorithm performed well even in challenging scenarios, such as patients with severe oral health issues.

In conclusion, our research showcases the potential of machine learning in achieving accurate caries detection and classification. The application of AI in dental care has promising implications for improving access to high-quality oral healthcare, particularly in LMICs where resources are scarce. Further advancements, such as incorporating additional data sources and refining the algorithms performance, could amplify its clinical utility and benefit a larger population.



**Image taken from the final report submitted to the Nakao Foundation

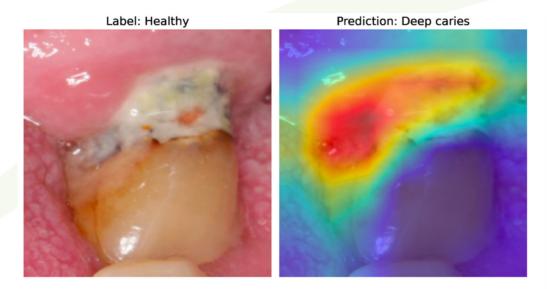


Image 8. This tooth was recommended to be assessed by a dentist by the <u>algorithm, yet</u> marked as healthy by the original annotation standards due to the coverage of its surface with dental calculus. Upon revision, although it is technically true that the tooth is covered by calculus, the reviewers considered that in this case, the algorithm is more likely to be right. It is likely that the algorithm has outperformed our own expectations and a more elaborate assessment of data for training as well as methods for evaluation would be necessary to improve its performance.

Research Summary - Article 2

Cost-effectiveness analysis applying Machine Learning to treatment recommendation of MI interventiosn in dentistry

A cost-effectiveness model was developed using Markov modeling on an annual interval at the tooth level to compare the cost-effectiveness of artificial intelligence (AI) with different standards of oral care. The model considered four different strategies that utilized various therapeutic alternatives in dentistry to tackle oral diseases. The strategies included AI-assisted Minimally Invasive Dentistry (MI), standard German dental care as the control, and other dental care approaches.

To assess the cost-effectiveness, the model incorporated factors such as costs, Quality-Adjusted Life Years (QALYs), and tooth retention-years. The net benefit of each strategy combination was calculated based on the ceiling threshold of willingness to pay (WTP) and the change in QALYs or tooth retention-years. Al, in combination with MI dentistry, demonstrated increased tooth retention and cost-effectiveness compared to standard dentists.



In high-income countries, AI was found to be slightly less effective than the control group, resulting in up to 12 years less effectiveness. However, it still provided notable benefits in terms of improved tooth retention and cost reduction. The cost-effectiveness of the different strategies varied depending on the WTP. At lower WTP levels (0 to 10 Euros), no intervention was preferred, and AI with MI dentistry emerged as the most likely cost-effective option. As the WTP increased (above 20 Euros), the marginal benefit of paying additionally to preserve each tooth favored the control strategies.

The study's results and discussions underscored the significant potential of AI in enhancing MI dentistry and addressing the burden of oral diseases, particularly in low- and middle-income settings. The combination of AI and MI dentistry was found to have a highly synergetic approach for tackling tooth decay, leading to an extension in tooth retention. These findings provide valuable insights into the technical and cost-related aspects of implementing AI in dental care, highlighting its promising role in improving oral health outcomes.

**Image taken from the final report submitted to the Nakao Foundation

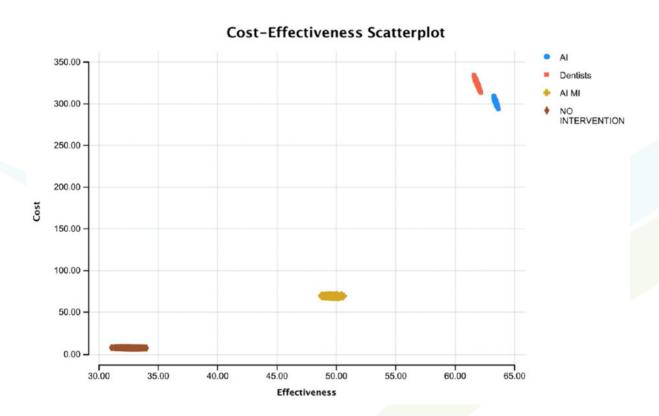


Image 9. Cost effectiveness results of 1000 simulations per intervention strategy. AI: Modern dentistry using AI assessment on x-rays. Dentists: Standard modern dentistry. AI-MI: Our new algorithm recommending preventive strategies for caries arresting in a setting of low-and middle-income countries. NO INTERVENTION: Base-case analysis in dentistry where patientsonly attended a dental practice in cases of emergency and for extractions.



Appreciation letter from the institution

Jesus Gomez Rossi Aßmannhauserstrasse 4-6 Berlin, 14197

15.07.2023

To the GC Nakao Foundation for World Oral Health Subject: Letter of Appreciation for Funding Research in MI Dentistry

Dear GC Nakao Foundation for World Oral Health,

I hope this letter finds you in good health and high spirits. I am writing to express my deepest gratitude and appreciation for the generous support and funding provided by the GC Nakao Foundation for World Oral Health for my research in the field of MI Dentistry.

I am truly honored to have been selected as a recipient of your funding, and I am incredibly grateful for the opportunity it has provided me to delve into the exciting realm of AI applied to dentistry. I would like to kindly thank you for your support during these years in which I could dedicate myself with important questions aimed at improving oral healthcare with a global health perspective, and I am proud to be associated with your foundation.

Throughout my research journey, I have felt accompanied by the professionalism and friendliness exhibited by the members of the GC Nakao Foundation. From the initial application process to the subsequent interactions and collaborations, your team has demonstrated unwavering support and guidance.

The financial assistance provided by your foundation has not only allowed me to explore the use of new Al models for various use-cases within dentistry but has also played a crucial role in advancing scientific progress in this domain. Your support has facilitated the development and implementation of innovative techniques and methodologies on the field, studied also under the perspective of an economic evaluation. We are currently working on several scientific publications, made possible by your funding, which will add valuable insights to the field of MI Dentistry.

Moreover, I am grateful to share that this research project has been transformative in my career trajectory. The knowledge and expertise gained through this endeavor have ignited a passion within me to translate these results into real-world applications. As a result, I have decided to establish my own company in the private sector, dedicated to implementing the advancements in Al-driven dentistry that I have learned during this research project. This decision was largely influenced by the support and confidence instilled in me by the GC Nakao Foundation. I am eager to contribute to the improvement of oral healthcare in practical and tangible ways, and I am confident that my company will be able to make a positive impact.

The impact of your foundation's support extends far beyond my personal research endeavors. By investing in the future of dentistry and oral healthcare, you are empowering professionals like myself to make tangible improvements in the lives of individuals in underserved communities. Your commitment to bridging the healthcare gap and addressing the needs of low- and middle-income countries through technological advancements is exemplary.

Once again, I would like to express my heartfelt appreciation to the GC Nakao Foundation for World Oral Health for believing in my research and providing me with this invaluable opportunity. I am humbled and honored to be a part of your efforts to revolutionize oral healthcare through Al-driven solutions. I am confident that our collective work will bring about positive changes and improve the quality of life for countless individuals around the world.

Thank you once again for your unwavering support, professionalism, and commitment. I look forward to sharing the outcomes of my research with you and contributing further to the mission of the GC Nakao Foundation for World Oral Health.

With sincere appreciation and warm regards,

Jesus Gomez Rossi



University of Hong Kong



Granted Project

Name of the Institution The University of Hong Kong Faculty of Dentistry			
Grant Year	2021		
Title	Age-tech for Oral Frailty in Hong Kong		
Duration	June 2022-July 2023		
Theme Artificial intelligence for oral muscle functions improvements			
Grant Amount	49'700 CHF		

Team member







Introduction of the research team

Our research team is directed by an Associate Professor Dr. James Tsoi (PI), a Research Assistant Professor in the Department of Chinese and Bilingual Studies Dr. Winsy Wong (CO-I) and a Clinical Assistant Professor Dr. Walter Lam (CO-I). It was performed by 3 PhD students from the Faculty of Dentistry and 3 registered speech therapists in Hong Kong.

Dr James Tsoi is an Associate Professor in Dental Materials Science and Assistant Dean (Innovation) at HKU Faculty of Dentistry. He received BSc in Applied and Analytical Chemistry and PhD in Dental Materials Science, all at the University of Hong Kong. He also holds the Memberships of Royal Society of Chemistry (MRSC) and British Computer Society (MBCS), and Fellow in Advanced HE (FHEA). Dr. Tsoi is actively engaged in a number of research areas including Dental materials science (particularly test method development, mechanical behaviours, bonding and ceramics), biomaterials (scaffold), digital dentistry (CAD/CAM and AI) and dental education (basic science and e-learning). He has authored more than 115 peer-reviewed journal articles, graduated 34 MSc and 11 PhDs, and has been awarded 8 times with his students in various international conferences since he joined as an HKU Dentistry member in 2012. He is currently serving on the editorial boards of several SCI journals (including Dental Materials), being Member-at-large in the Academy of Dental Materials (ADM) and Hong Kong head-of-delegate in ISO/TC 106 (Dentistry). He was recently elected and will serve as Vice President in IADR-DMG after the IADR Bogota meeting in Jun 2023.

Dr Winsy Wong (BSc, MPhil, PhD) is a Research Assistant Professor of the Department of Chinese and Bilingual Studies, Faculty of Humanities of The Hong Kong Polytechnic University. She obtained her qualifications in speech therapy and her PhD from The University of Hong Kong. She has been a researcher, lecturer, clinical educator and clinician who specializes in neurogenic communication disorders, she supervises students in speech therapy clinic. Her research interests include cognitive communication disorders and aphasiology, exploration on approaches to rehabilitation, as well as factors associated with treatment outcomes.

Dr Walter Lam (BDS, MDS (Pros), AdvDipProsthodont (HKU), FHKAM (Dental Surgery), FCDSHK (Pros), MFDS RCSEd, MPros RCSEd, FDS RCSEd, MFDS RCPSG, FDS RCPSG, FRACDS) is a specialist in prosthodontics in Hong Kong. Currently, he is the Clinical Assistant Professor in Prosthodontics at HKU Faculty of Dentistry, supervising undergraduates and master students for their clinics and research activities. Dr Lam has published more than 30 papers with research interests include digital dentistry, CAD/CAM, robotic dentistry, dental implant, quality of life and geriatrics.



Summary of the Research

We held 12 meetings (12 x 3 hrs) during the project execution for interim work reporting, refining the sampling method, literature reviewing, and data analysis. All instruments were used properly with no damage or failure; all consumables were used as planned and sufficient supplies were available at the end of the project.

We carried out 10 lectures on oral muscles in the activity centers in the different regions to publicize the importance of oral muscle exercises and introduce instruments for testing oral muscles. In total, we recruited 113 participants from six regions across Hong Kong and collected more than 452 times of data. Based on 70 participants who completed the whole study by July 2023, it is revealed that the occlusal force increased from 648.30±391.48 N to 870.88±603.98 N (p<0.001), and reached 842.79±506.04 N (p<0.001) in the maintenance phase, while chewing ability raised dramatically from 215.87±75.72 mg/dL to 238.87±74.84 mg/dL (p=0.002), and after 8-week of oral exercise training, the average value is 252.66±78.74 mg/dL (p<0.001). Moreover, maximum tongue pressure (28.25±6.66 KPa) and tongue endurance (7.02±5.73 s) significantly improved to 31.73±6.64 KPa (p<0.001), and 8.48±4.96 s (p=0.004) for post training, and the maintenance phase saw a constant rise to 33.3±6.43 KPa (p<0.001) and 8.74±5.16 s (p<0.001) compared to the averaged baseline, respectively. The preliminary results suggested that oral exercises delivered by the HOE app may be easy and effective strategy in strengthening the oral muscles and improving oral biomechanics of the elderly. This study has been presented at the 2023 IADR/LAR General Session for WCPD-Interactive Talk at Bogotá, Colombia and finalist for the Neal Garrett Award.



Global population aging is one of the most critical demographics and medical problems in the world. Age-related changes in the oral environment pose risks for older adults, e.g., oral frailty. Exploring and understanding oral muscle function is of great significance to society. Maintenance of oral muscle functions is important to the elderly; utilizing Artificial intelligence (AI) as self-health-management support has shown promise, yet no study has explored the efficacy of AI-based self-administered smartphone apps for oral muscle training. This project aims to develop a smartphone APP with real-time feedback features to improve oral biomechanical functions of healthy adults.



A total of 113 neurologically healthy Hong Kong citizens over 50 years old were recruited in this study from June to October 2022. A set of 12 oral exercises of the tongue, lips, and jaw were conducted with guidance provided in the e-Oral app, in which visual-audio demonstrations and immediate feedback on facial movements by Ensemble of Regression Tree (ERT) face landmark detector was given to the users. Baseline assessments were conducted 4- and 1-week before training began. Assessments after 1-week and 4-week post-training were conducted to reflect the performance on immediate post-training and at maintenance phase. Primary outcomes were measured on oral functions, including occlusal force, masticatory efficiency, tongue strength, along with dry mouth condition, and oral health-related quality of life, while secondary outcomes were comprised of oral diadochokinesis and swallowing ability. The usability of the APP was evaluated by a self-written questionnaire. Generalized Estimating Equations (GEE) models were used to compare the pre/post performance on various oral functions analyzed with SPSS Statistics (v28) at =0.05. Seventy out of 113 participants completed all four inspections to be included in our analytical sample. GEE model reported significant improvements in occlusal force, masticatory efficiency, tongue strength and endurance, and DDK after eight weeks of oral exercise. The trial was reported following the SPIRIT-Al extension guideline.

We systematically collected oral muscles information from Hong Kong citizens for the first time. Additionally, this is the first Al-assisted self-administered exercise app developed for oral muscle training. The positive outcomes in oral functions obtained from our study provides initial evidence on the application of Al technology in smartphone gadgets, which provides a cost-effective, convenient, and reliable means for oral motor training for the elderly.



Publication list

- 1. Rosalind Sin Man Chan#, Winsy Wing Sze Wong#, Tian Yu Zhou, Kira Ying Liu, Hiu Tung Tsang, Chun Lam Luk, Tsz Hei Chan, Walter Yu Hang Lam, James Kit Hon Tsoi*. Cascade Regression Algorithm-Based Mobile APP Improves Oral Muscle Functions for Healthy Adults: A Multi-center, Self-controlled Clinical Tria, submitted to journal.
- 2. Winsy Wing Sze Wong#, Rosalind Sin Man Chan#, Tian Yu Zhou, Kira Ying Liu, Hiu Tung Tsang, Chun Lam Luk, Tsz Hei Chan, Walter Yu Hang Lam, James Kit Hon Tsoi*. Evaluation of Oral Muscle Functions among Healthy Adults in Hong Kong, in progress.



Appreciation letter from the institution



To the Nakao Foundation

Letter of Appreciation

On behalf of our Home Oral Exercise research group, I would like to express my sincere gratitude towards the Nakao Foundation. We are extremely thankful for your support which is helpful in the evaluation of oral muscle functions and Al-assisted self-administered exercise APP.

With the support of your foundation, we were able to systematically collect data on the oral muscle function of Hong Kong citizens for the first time, filling this gap and enabling us to better understand the relationship between Hong Kong citizens' age, gender, and occupation with regards to occlusal force, tongue muscle strength, and masticatory efficiency. In addition, we seminally developed a smartphone APP using ensemble of regression trees (ERT) for oral muscle exercises, it is the first time that apply the ERT on a mobile device with real-time feedback features which allows people easy-equipped and ready-to-oral exercises anytime they want. The results validated that the participants' oral muscles had been properly trained and their oral muscles' strength had been improved, from our hypotheses to real-world conditions.

We believe the findings are appropriate and relevant to your foundation in light of our study focusing on aging, oral frailty prevention, and aiming to create a digital health application that improves the quality of life. Moreover, it has intensified multidisciplinary research in the fields of dentistry and speech and hearing studies.

Yours sincerely,

Dr James Tsoi BSc PhD MRSC MBCS FHEA

Assistant Dean (Innovation)

Taught Postgraduate Program Director and Associate Prof. in Dental Materials Science Leader, Clinical Artificial Intelligence Research Theme

Applied Oral Sciences and Community Dental Care

Faculty of Dentistry, HKU



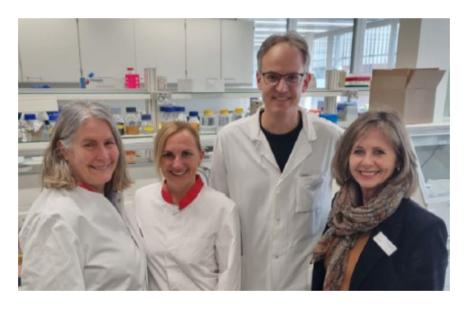
University Center for Dental Medicine, UZB, Basel



Granted Project

Name of the Institution	University Center for Dental Medicine, U/B, Basel			
Grant Year	2021			
Title	Antimicrobial effects of oral probiotic strains			
Duration	2021-2023			
Theme	Oral Health for Ageing Population			
Grant Amount	50'000 CHF			

Team member



Dr. Eva M. Kulik - Laboratory Manager, Department Research

Dr. Elisabeth Caroline Reichardt - Assistant Professor, Department of Pediatric Dentistry and Orthodontics

Prof. Dr. Michael M. Bornstein - Head of Department of Oral Health and Medicine

Christl Hoesch - Assistant of Prof. Michael Bornstein

Prof. Dr. Carlalberta Verna - Head of Department of Pediatric Dentistry and Orthodontics (not on the photo)



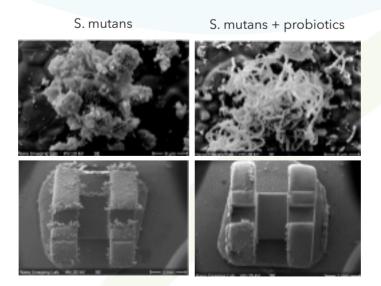
Antimicrobial effects of oral probiotic strains

Aim: The presented experimental in-vitro study was performed to evaluate the potential antimicrobial effects of two Streptococcus salivarius strains applied as probiotics under conditions of orthodontic application. Both strains are established producers of bacteriocin-like inhibitory substances (BLIS) which was supposed to act against caries-associated clinical isolates of S. mutans.

Material and Methods: The potential activity of S. salivarius strain M18 resp. K12 against S. mutans was determined after 48 hours of co-cultivation in a flow chamber setting to simulate as close as possible the in vivo human oral conditions. Hydroxyapatite (HA) discs bonded with orthodontic appliances (brackets) were placed in these flow chambers containing artificial saliva as liquid (GC Fuji Ortho LC). After co-incubation of S. mutans with S. salivarius M18 resp. K12, samples were taken from the HA discs. The colony forming units were determined using selective blood agar plates to investigate quantitatively growth of the bacterial species. Furthermore, the bacteria were analyzed microscopically by live/dead staining and scanning electron microscopy (SEM) to evaluate formation and potential inhibition of biofilm on the HA discs. All experiments were repeated three times, B. fragilis was used as negative control.

Results: In our experiments we could show that the co-cultivation of S. mutans and S. salivarius M18 resp. K12 led to a complete inhibition of S. mutans colonies at the HA discs after 48 hours in the flow chamber (p < 0.5). Furthermore, SEM analysis revealed that biofilm formation was also inhibited under co-cultivation with both strains of S. salivarius.

Conclusion: S. salivarius probiotics are suited and can be recommended for approaches to inhibit cariogen-associated S. mutans under conditions of orthodontic application in vitro. Additionally, also biofilm formation could be prevented. The in vitro system of the flow chamber used in our experiments allows a simulation of the human oral condition and thus evaluation of both, anti-cariogenic activity of probiotic strains and prevention biofilm formation by S. mutans.





Publication list

- Reichardt E., Geraci J., Sachse S., Rödel J., Pfister W., Löffler B., Wagner Y., Eigenthaler M., Wolf M. (2019) Qualitative and quantitative changes in the oral bacterial flora occur shortly after implementation of fixed orthodontic appliances. Am J Orthod Dentofacial Orthop. 156:735-44.
- 2. Hirschfeld J., Reichardt E., Sharma P., Hilber A., Meyer-Marcotty P., Stellzig-Eisenhauer A., Schlagenhauf U., Sickel F. (2019) Interest in orthodontic tooth alignment in adult patients affected by periodontitis: a questionnaire-based cross-sectional pilot study. J Periodontol. 90,957-65.
- 3. Reichardt E., Krug R., Bornstein M. M., Tomasch, J., Verna C., Krastl, G. (2021) Orthodontic Forced Eruption of Permanent Anterior Teeth with Subgingival Fractures: A Systematic Review. Int J Environ Res Public Health, 18:23,12580.
- 4. Reichardt E., Decker S., Dalstra M., Nalabothu P., Steineck M., Fernandez L., Verna C. (2022) The Effect of Ligature Type on Lateral Tooth Movement during Orthodontic Treatment with Lingual Appliances-An In Vitro Study. Materials (Basel, Switzerland), 15:3365.
- 5. Reichardt E., Shyp V., Alig, L., Verna C., Kulik E., Bornstein M. (2024) Antimicrobial effect of probiotic bacteriocins on Streptococcus mutans biofilm in a dynamic oral flow chamber model an in vitro study, J Oral Mircobiol, 16: 2304971.

Peer-reviewed full-length articles

- Reichardt E., Geraci J., Sachse S., Rödel J., Pfister W., Löffler B., Wagner Y., Eigenthaler M., Wolf M. (2019) Qualitative and quantitative changes in the oral bacterial flora occur shortly after implementation of fixed orthodontic appliances. Am J Orthod Dentofacial Orthop. 156:735-44.
- 2. Hirschfeld J., Reichardt E., Sharma P., Hilber A., Meyer-Marcotty P., Stellzig-Eisenhauer A., Schlagenhauf U., Sickel F. (2019) Interest in orthodontic tooth alignment in adult patients affected by periodontitis: a questionnaire-based cross-sectional pilot study. J Periodontol. 90,957-65.
- 3. Bartzela T., Theuerkauf B., Reichardt E., Spielmann M., Opitz C. (2021) Clinical characterization of 266 patients and family members with cleft lip and/or palate with associated malformations and syndromes. Clin Oral Investig. 25:5531-5540.
- 4. Grimm S., Mundethu A., Symmank J., Hennig C., Walter C., Reichardt E., Wehrbein H., Jacobs C. (2021) Compressive force strengthened the pro-inflammatory effect of zoledronic acid on il-1ß stimulated human periodontal fibroblasts. Clin Oral Investig. 25:3453-3461.



Publication list

- 5. Reichardt E., Krug R., Bornstein M. M., Tomasch, J., Verna C., Krastl, G. (2021) Orthodontic Forced Eruption of Permanent Anterior Teeth with Subgingival Fractures: A Systematic Review. Int J Environ Res Public Health, 18:23,12580.
- 6. Reichardt E., Decker S., Dalstra M., Nalabothu P., Steineck M., Fernandez L., Verna C. (2022) The Effect of Ligature Type on Lateral Tooth Movement during Orthodontic Treatment with Lingual Appliances-An In Vitro Study. Materials (Basel, Switzerland), 15:3365.
- 7. Berli C.*, Reichardt E.*, Filippi A. (2022) Survey on the prevalence of occupational injuries to the head and teeth in automotive repair and maintenance in Switzerland. Swiss Dent J. 16;132:334-341. (*shared first authorship)
- 8. Fuhrer Y., Eggmann F., Reichardt E., Filippi A. (2022) Head and dental injuries among farriers and hoof care practitioners: A nationwide survey in Switzerland. Dent Traumatol. e: 10.1111/edt.12794.
- 9. Reichardt E., Shyp V., Alig, L., Verna C., Kulik E., Bornstein M. (2024) Antimicrobial effect of probiotic bacteriocins on Streptococcus mutans biofilm in a dynamic oral flow chamber model an in vitro study, J Oral Mircobiol, 16: 2304971.
- 10. Conference Paper Plaschke B., Reichardt E., Mellmann A., Petzl W., Zerbe H., Dobrindt U. (2010) Comparative analysis of Escherichia coli bovine mastitis isolates. Reprod Domest Anim. 45:40.
- 11. Book chapters Elisabeth Reichardt (2022) The orthodontic emergency (ch. 35). In Fit for the dental emergency service, 1st ed.; Filippi A., Fabio Saccardin F., Kühl S., Eds.; Quintessence, Berlin; Germany.
- 12. Elisabeth Reichardt (2023) The orthodontic treatment (chapter). The dental treatment of people with special needs, 1st ed.; Filippi A., Filippi C., Neuhaus K., Eds.; Quintessence, Berlin; Germany.



Appreciation letter from the institution

University Center for Dental Medicine Basel UZB Mattenstrasse 40 4058 Basel Switzerland www.uzb.ch



Foundation Nakao for Worldwide Oral Health Fluhmattweg 13 6004 Luzern Switzerland

Basel, December 2023

Nakao Research Grant 2021

Dear Sir or Madam of the Foundation Nakao

Our research team from the University Center for Dental Medicine UZB in Basel would like to thank for the grateful support of the Nakao Research Grant from 2021. Thanks to the financial support of the Nakao Foundation, it was possible to initiate our research on the antimicrobial effect of oral probiotics.

The results of this research are an important step towards preventing caries and demineralization in the oral cavity.

We would like to thank the Nakao Foundation once again for this great support.

Kind regards

Dr. med. dent. Elisabeth Reichardt

lichardt

Assistant Professor

Department of Pediatric Dentistry and Orthodontics



Tohoku University

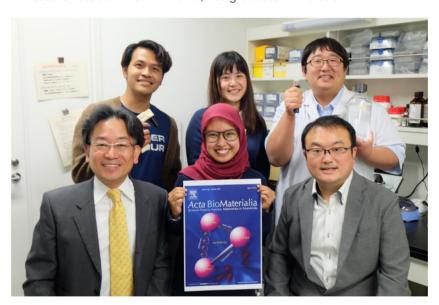


Granted Project

Name of the	Tohoku University Graduate School of Dentistry Division of Molecular and Regenerative Prosthodontics			
Grant Year	2021-2022			
Title	Biomimetic titanium surface modification for in situ periodontal tissue regeneration around dental implants			
Duration	1. April 2021-31. August 2023			
Theme	Health science			
Grant Amount	48'900 CHF			

Team member

- KEY CONTACT PERSON: Hiroshi Egusa, Professor and Chair
- Lead member: Masahiro Yamada, Associate professor
- Collaborative researcher: Jun Watanabe, Assistant professor
- Research assistant #1: Nadia Kartikasari, Postgraduate PhD student
- Research assistant #2: Watcharaphol Tiskratok, Postgraduate PhD student
- Research assistant #3: Xindie He, Postgraduate PhD student

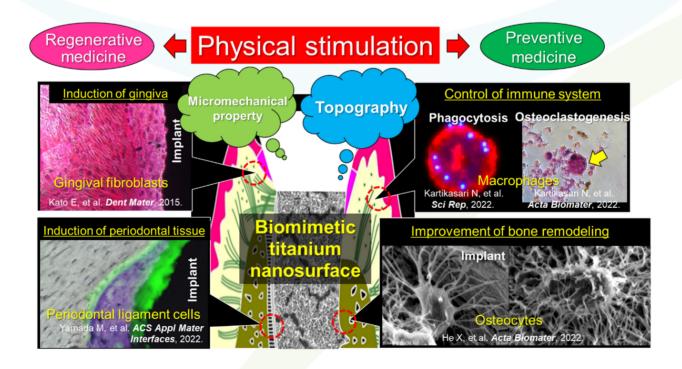


Watcharaphol Tiskratok - Xindie He - Jun Watanabe Hiroshi Egusa - Nadia Kartikasari - Masahiro Yamada



Summary of the Research

Osseointegrated dental implants exhibit several clinical issues related to the lack of periodontal tissue comprising bone tissue, periodontal ligament (PDL), and tooth root cementum (TRC). Since the titanium surface cannot differentiate heterogeneous periodontal ligament cells (PDLCs) into cementoblasts, periodontal tissue does not regenerate around dental implants even if the PDLCs come into contact with the surface. Various types of immue cells are also involved in periodontal regeneration. Biomimetics attracts attention as a tissue engineering technology to induce stem-cell differentiation by artificially mimicking the characteristics of living tissue. We created a novel, smart titanium nanosurface almost completely mimicking the nanotopography and micromechanical properties of the TRC surface. Titanium implants with a TRC-mimetic nanosurface induced periodontal-like gingiva by regulating gingival fibroblasts (Kato E, et al. Dent Mater, 2015). The TRC-mimetic titanium implant supports the in vivo induction of PDL together with a decellularized matrix in presence of mesenchymal stem cells with characteristics similar to the PDLCs. In addition, functions of immune cells involved in tissue regeneration around biomaterials might be modulated by physical microenvironment of local tissue. Therefore, we hypothesized that the TRCmimetic titanium implant induces functional periodontal tissue in alveolar bone by regulating endogenous PDLCs and immuno cells without exogenous biological resources, such as stem cells or growth factors. The present study aimed to determine whether a TRC-mimetic titanium implant induces functional periodontal tissue formation in the tooth extraction sockets by regulating endogenous cells such as PDLCs, osteocytes or immune cells. In conclusion, titanium nanosurface mimicking physical microenvironment of TRC in nanotopography and micromechanical properties induces periodontal tissue with physiological function and immunological systems around titanium implant, by regulating stem or immune cells responsible for the roles with physical stimuli from the surface.





The periodontium supports the teeth by dentoalveolar fibrous joints which serves the unique oral functions. Endogenous regeneration of the periodontium around artificial teeth (dental implants) provides a cost-effective solution for extension of healthy life expectancy but remains a challenge in regenerative medicine. Biomimetics can create smart biomaterials that tune endogenous cells at a tissue-material interface. Here, we created a smart titanium nanosurface mimicking the surface nanotopography and micromechanical properties of the tooth root cementum (TRC), which is essential for the induction of dentoalveolar fibrous joints to regenerate the periodontium. After transplantation into the rat renal capsule, only the titanium artificial tooth with the TRC-mimetic nanosurface formed a complex dentoalveolar fibrous joint structure, with bone tissue, periodontal ligament (PDL), and TRC, in the decellularized jawbone matrix. TRC-mimetic titanium implants induce the formation of functional periodontium, even in a jawbone implantation model, which generally causes osseointegration (ankyloses). In human PDL cells, TRC analogousness in the surface mechanical microenvironment regulates matrix mineralization through bone sialoprotein expression and phosphorous metabolism, which are critical for cementogenesis. Therefore, the titanium nanosurfaces with nanotopographical and mechanical microenvironments mimicking the TRC surface induces dentoalveolar fibrous joints for periodontal regeneration by interfacial tuning of endogenous cells.

Yamada M, Kimura T, Nakamura N, Watanabe J, Kartikasari N, He X, Tiskratok W, Yoshioka H, Shinno H, Egusa H. Titanium Nanosurface with a Biomimetic Physical Microenvironment to Induce Endogenous Regeneration of the Periodontium. ACS Appl Mater Interfaces. 14(24):27703-27719, 2022. doi: 10.1021/acsami.2c06679.

^{*}Descriptions and figures are cited without modification from the following paper.



Publication list

- 1. Tiskratok, W., Yamada, M.*, Watanabe, J., Pengyu, Q., Kimura, T. and Egusa, H.*: Mechanoregulation of osteoclastogenesis-inducing potentials of fibrosarcoma cell line by substrate stiffness. Int J Mol Sci 24: 8959, 2023.
- 2. Tiskratok, W., Yamada, M.*, Watanabe, J., Kartikasari, N., Kimura, T. and Egusa, H.*: Substrate stiffness controls proinflammatory responses in human gingival fibroblasts. Sci Rep 13: 1358, 2023.
- 3. Kartikasari, N., Yamada, M.*, Watanabe, J., Tiskratok, W., He, X. and Egusa H.*: Titania nanospikes activate macrophage phagocytosis by ligand-independent contact stimulation. Sci Rep 12, 12250, 2022.
- 4. He, X., Yamada, M.*, Watanabe, J., Tiskratok, W., Ishibashi, M., Kitaura, H., Mizoguchi, I. and Egusa, H.*: Titanium nanotopography induces osteocyte lacunar-canalicular networks to strengthen osseointegration. Acta Biomater 151: 613-627, 2022.
- 5. Yamada, M.*, Kimura, T., Nakamura, N., Watanabe, J., Kartikasari, N., He, X., Tiskratok, W., Yoshioka, H., Shinno, H. and Egusa, H.*: Titanium nanosurface with a biomimetic physical microenvironment to induce endogenous regeneration of the periodontium. ACS Appl Mater Interfaces 14: 27703-27719, 2022.
- Kartikasari, N., Yamada, M.*, Watanabe, J., Tiskratok, W., He, X., Kamano, Y. and Egusa, H.*:
 Titanium surface with nanospikes tunes macrophage polarization to produce inhibitory factors for osteoclastogenesis through nanotopographic cues. Acta Biomater 137: 316-330, 2022.



Appreciation letter from the institution

Prof. Hiroshi Egusa, DDS, PhD Division of Molecular and Regenerative Prosthodontics Tohoku University Graduate School of Dentistry 4-1 Seiryouchou, Aoba-ku, Sendai, Japan, 980-8575

19 March 2023

Dear Mrs. Makiko Nakao

On behalf of Tohoku University and the research team I would like to take this opportunity to thank you for your generous grant to our research project, "Biomimetic titanium surface modification for in situ periodontal tissue regeneration around dental implants."

By receiving this grant, our university was able to determine whether a TRC-mimetic titanium implant induces functional periodontal tissue formation in the tooth extraction sockets in which some PDLCs remained on the socket bone wall.

We appreciate your willingness to support the Worldwide Oral Health by giving grants to global dental community and we also would like to support this important initiative by our research in the future.

Respectfully,

Hiroshi Egusa Division of Molecular and Regenerative Prosthodontics Tohoku University Graduate School of Dentistry



Foundation Nakao for Worldwide Oral Health
Fluhmattweg 13
6004 Luzern
Switzerland

TEL: 0041 41 203 27 25

info@foundation-nakao.com