

Re-Inventing Japan Project
大学の世界展開力強化事業

Inter-university Exchange Program toward Medical and Dental Networking
in Southeast Asia

東南アジア医療・歯科医療ネットワークの構築を目指した大学間交流プログラム

Khon Kaen University

コンケン大学

Academic Exchange Seminar

学術交流セミナー



東京医科歯科大学
TOKYO MEDICAL AND DENTAL UNIVERSITY

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1.セミナー概要

日時：2014 年 3 月 21 日（金） 10：30～12：00

会場：コンケン大学

- a. 講師：東京医科歯科大学大学院医歯学総合研究科う蝕制御学分野
田上 順次教授

講義タイトル：Creating our future

- b. 講師：東京医科歯科大学大学院医歯学総合研究科歯周病学分野
和泉 雄一教授

講義タイトル：Periodontitis and Cardiovascular Diseases: The Link and Relevant Mechanisms

2.写真







Creating our furture

Junji TAGAMI


TMDU
 TOKYO MEDICAL AND DENTAL UNIVERSITY




Memorial Lecture on the occasion of MoU signing between KKU and TMDU
 March 21, 2014


Creating our future

Junji TAGAMI, DDS, PhD
 Professor and Dean
 Graduate School of Medical and Dental Sciences
 Tokyo Medical and Dental University
 Tokyo Japan







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Dental Education in Japan



Model Core Curriculum

Common Problems of the Past Curriculum


(Indicated by the 4th Report of the Discussion Group on 21st Century Medicine and Health Care)

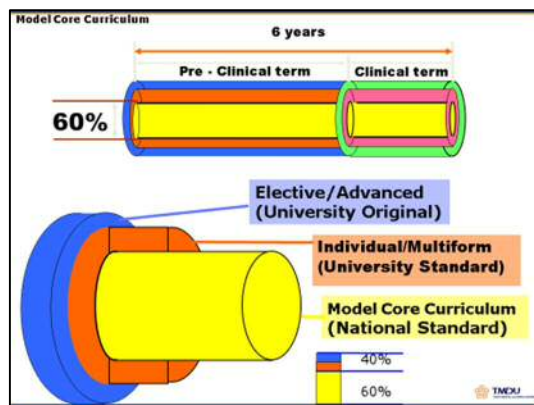
1. Overly-crowded curriculum
2. Unplanned increase of educational contents
3. Insufficient coordination between subjects
4. Diluted practical clinical training
5. Inadequate effort for teaching improvement

a nation-wide common guideline

Model Core Curriculum

March 27, 2001






Model Core Curriculum

Survey Research Collaborators Committee
on Improvement of Medical and Dental Education
March 27, 2001

Model Core Curriculum

Key concepts


1. Patient-oriented treatment
2. Integration between basic and clinical subjects
3. Learner-oriented curriculum
4. Quality improvement of clinical training
5. Proper assessment



Model Core Curriculum

Contents of Model Core Curriculum in Undergraduate Dental Education

- A. Principles of Medicine
- B. Essential Attitude as a Dentist
- C. Society and Dentistry
- D. Life Science
- E. Oral Biomaterials and Dental Materials Science
- F. Clinical Dentistry Education




Common Achievement Test

Common Achievement Test

This testing system comprises two kinds of examinations:

- Computer-Based Test (CBT)**
To evaluate students' knowledge
- Objective Structured Clinical Examination**
To assess their attitude and skills

The questions/task in the test are based on the contents of the Model Core Curriculum.



Vocational Training

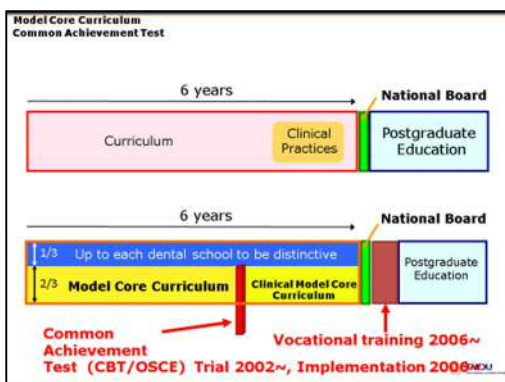
[1-year Compulsory] 2006~

~ 2005: Vocational Training

1-year or 2-year Vocational Training Course.

From 2006, Every dentist has to have Vocational Training in Accredited training institutions for 1-2 years after registration.





Cultivating Professionals with Knowledge and Humanity



Tokyo Medical and Dental University



TMDU Mission

Cultivating Professionals with Knowledge and Humanity

Three Educational Philosophies :

1. To provide students with a broad education and a rich sensibility
2. To educate creative people capable of diagnosing and solving problems independently
3. To train medical professionals with a rich international quality



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Dental Education at TMDU



Profile of Faculty of Dentistry, Tokyo Medical and Dental University

◆ Undergraduate schools

➤ Faculty

- ✧ Faculty of Medicine
 - School of Medicine
 - School of Health Care Sciences
- ✧ Faculty of Dentistry
 - School of Dentistry (Dentist)
 - School of Oral Health Care Sciences (Dental Hygienist & Dental Technician)



Education Philosophy

(TMDU Faculty of Dentistry)

Primarily to **foster dentists** who can promote and maintain health of the people by faithfully providing **comprehensive dental care** and can contribute to the **development dental medicine** and service from a **global perspective**.



Profile of Faculty of Dentistry, Tokyo Medical and Dental University

School of Dentistry: 6-year course

School of Oral Health Sciences: 4-year course

| 2010 | Male | Female | Total |
|--|------|--------|-------|
| School of Dentistry | 209 | 160 | 369 |
| School of OHS, Hygienist | 5 | 117 | 122 |
| School of OHS, Dental Technician (2011-) | 7 | 4 | 11 |

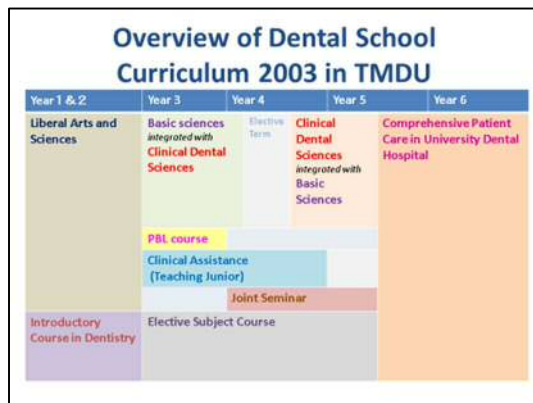


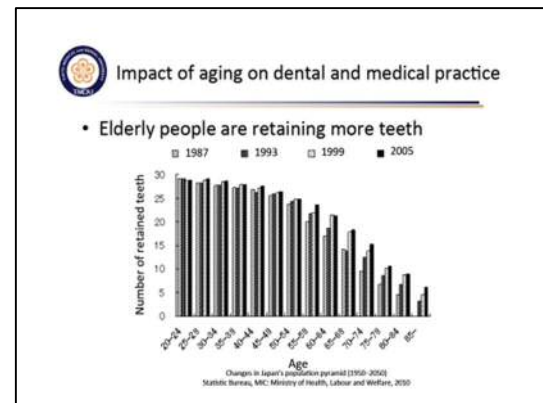
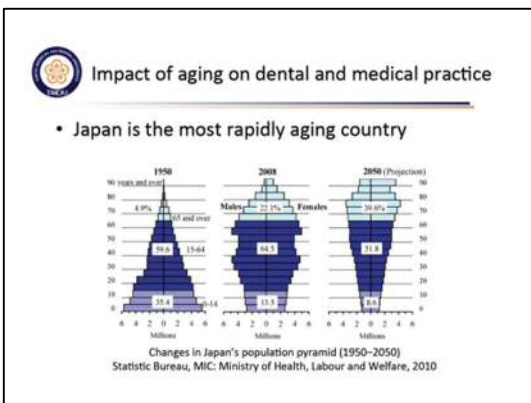
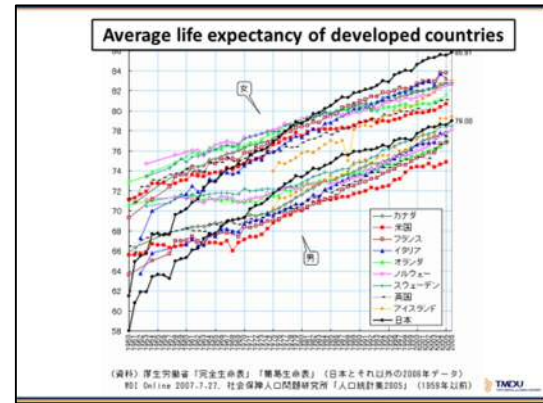
TMDU Dental School Curriculum 2005 (2005~)

Characteristic points

- 2-semester system
- Module system
- Integrated courses
- Clear objectives and syllabus
- 60 min. class
- Teaching juniors (Junior-Senior relation)
- PBL course (year 3)
- Students Research Term for 7 weeks up to 14 weeks (year 4)



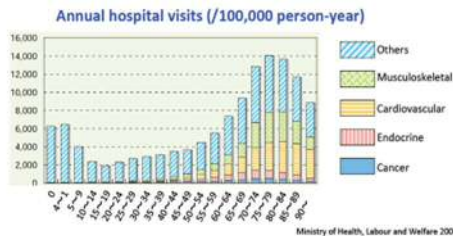






Impact of aging on dental and medical practice

- The older, the more comorbidity



Impact of aging on dental and medical practice

- Japan is the most rapidly aging country
- Elderly people are retaining more teeth
- The older, the more comorbidity
- Many issues making elderly's care complicated



CHANGE



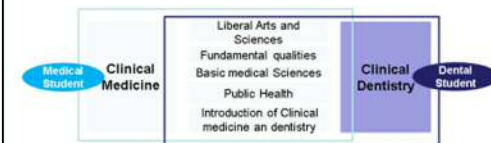
Impact of aging on dental and medical practice

- Many issues to make elderly care complicated
 - ① Physiological changes
 - ② Pathological changes (common geriatric conditions)
 - ③ High impact of pharmacotherapy
 - ④ Blurred boundary between dental and medical care

Curriculum Reform 2011

Medical sciences and Medical subjects which closely related to dental treatment were taught in traditional curriculum before.

For new curriculum, we implemented the concept of "Interprofessional Education (IPE)" in addition to traditional concept.



TMDU Dental School Curriculum 2011 Integrating Medical and Dental education

Anticipated changes and future needs of the society
Coordinated/integrated/comprehensive
patient-centered care
"between Medicine and Dentistry"

Based on the 2010 census (2011.06.29), by Japanese government, 128 million people live in Japan. The percentage of people 65 and older is 23.1%, which is the highest in the world, followed by Italy and Germany (20.4%). Consequently, dentists need to treat a larger number of patients with systemic co-morbidities, and the provision of best available care requires more interaction and cooperation with physicians and other medical and dental professions than before.



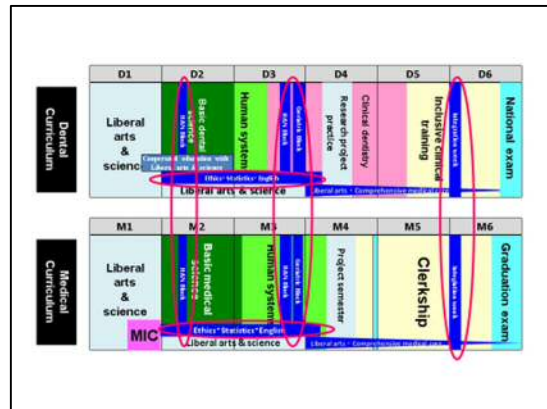
Curriculum reform (in 2011) aims to enhance competencies of our dental students at the time of graduation

Competencies are:

1. Scientifically and practically well trained
2. Comprehensive patient care with understanding of the general conditions of the patients
3. Life-long learning skills
4. Problem-solving skills
5. Interpersonal and communication skills
6. Understanding of public health
7. Professionalism

Curriculum 2011

- Extended periods of conventional units
- More clinical dental modules should be performed by PBL tutorial.
- Hybrid programs of basic and clinical sciences.
- Integrated MedDent education program
- Integrated MedDent education program launched in 2011 (of the 1st-year students).



“Fundamentals Unit”

Dental and medical students learn together English, bioethics, and biostatistics in the “Fundamentals Unit”.

- For 3 years, from 2nd year to 4th year
- Every Thursday morning
- Some topics will be in English.



“Head and Neck Units”

Basic and clinical aspects of the head and neck region in the corresponding “Head and Neck Units”.

- Staff of Anatomy, Histology, Embryology, Physiology teach integrated classes in basic courses.
- Medical and Dental students participate in joint session of Dissection.
- Staff of Ophthalmology, Otorhinolaryngology, Head and Neck Surgery, Oral Surgery teach integrated classes in clinical course. (Cases-based, Patient oriented etc..)



“Geriatrics Unit”

Physiology, pathology, and social aspects of geriatric population in the “Geriatrics Unit”

- For 2 weeks, the end of 3rd year
- Interprofessional education for comprehensive understandings of Geriatric Medicine and Dentistry.



“Comprehensive Care Unit”

Final-year students from all schools come together and engage in Interprofessional group work to learn comprehensive care delivery in the “Comprehensive Care Unit”

- Interprofessional Education to learn the way of collaboration among medical and dental professions.



- Medical and Dental module
- Revision of current modules
- Revision of management system
- Establishing “ Center for Interprofessional Education”

International projects

[illegible]

コンテストの受賞者

Dental Externship

- **Recognition of Credit Provision by the TMDU Faculty of Dentistry**

- (1) English ability
 - (2) Completion of an English course to prepare for overseas programs (Dental English)
 - (3) Completion of the Dental Health Education Preparation course
 - (4) Completion of a crisis management course
 - (5) Submission of a course report (portfolio) in English and Japanese
 - (6) Evaluation from overseas supervisors
 - (7) Presentation at a feedback session
- (The requirement above is an example and the requirements vary depends on the program.)

Harmonization in Dental Education Asia

— ASEAN-Japan Information Sharing —

1. Information Sharing for the Harmonization and Further Development of Dental Education in Southeast Asia.
2. Lifelong Training Course Planning and Establishment for the Provision of Continuing Education Opportunities for Dental Health Professionals in Southeast Asia.
3. Supplying Information on Research and Education at TMDU and Studying in Japan for Prospective Students from Southeast Asia.
4. Establishment of a Medical and Dental Care Network for Japanese Nationals in Southeast Asia.

International Projects



Tokyo Medical and Dental University
Global Center of Excellence (GCOE) Program



**International Research Center for
Molecular Sciences in Tooth and Bone Diseases**

-Dental Clinical Research-

Clinical Dentistry

Yuichi Izumi, D.D.S., Ph.D.
Department of Periodontology

Shohei Kasugai, D.D.S., Ph.D.
Department of Oral Implantology & Regenerative Dental Medicine

Ken Omura, D.D.S., Ph.D.
Department of Oral and Maxillofacial Surgery

Hideaki Suda, D.D.S., Ph.D.
Department of Pulp Biology and Endodontics

Keiji Moriyama, D.D.S., Ph.D.
Department of Maxillofacial Orthognathics

Junji Tagami, D.D.S., Ph.D.
Department of Cariology and Operative Dentistry



Department of Oral and Maxillofacial Surgery

Prof. Ken Omura



Contents lists available at SciVerse ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Development of oral cancer screening test by detection of squamous cell carcinoma among exfoliated oral mucosal cells

Takuma Kugimoto^a, Kei-ichi Morita^{b,*}, Ken Omura^{c,d,e}

^aOral and Maxillofacial Surgery, Department of Oral Restoration, Division of Oral Health Sciences, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan

^bDepartment of Advanced Molecular Diagnosis and Maxillofacial Surgery, Head Neck Cancer Research Center, Tokyo Medical and Dental University, Tokyo, Japan

^cGlobal Center of Excellence (GCE) Program, International Research Center for Molecular Science in Teeth and Bone Diseases, Tokyo Medical and Dental University, Tokyo, Japan

Table 1
Primers for the genes used in real-time polymerase chain reaction.

| Gene symbol | Accession number | Product size (bp) | Sense primer | Antisense primer |
|-------------|------------------|-------------------|-----------------------------|---------------------------|
| β-actin | NM_001101.3 | 175 | 5'-TGCCATCATGAGGAGTGGG-3' | 5'-GCTTATGATGAGGAGGATG-3' |
| SCC1 | NM_008789.2 | 179 | 5'-CTGCTGGCTGAAAGGAGG-3' | 5'-CTGTGCTGCTGCTGCTG-3' |
| IL13 | NM_005814.4 | 103 | 5'-AGAAACATCATCTGCTGAGAG-3' | 5'-GTGAGGAGGAGGAGGAGG-3' |
| TGFα | NM_005912.2 | 105 | 5'-AGAGCTCTCTCTCTCTCTCT-3' | 5'-TGGGAGGAGGAGGAGG-3' |
| HM-19NA | BC022011.1 | 170 | 5'-GGATGAGGAGGAGGAGG-3' | 5'-AGCTTGTCTCTCTCTCTCT-3' |

Oral Oncology 48 (2012) 794–798

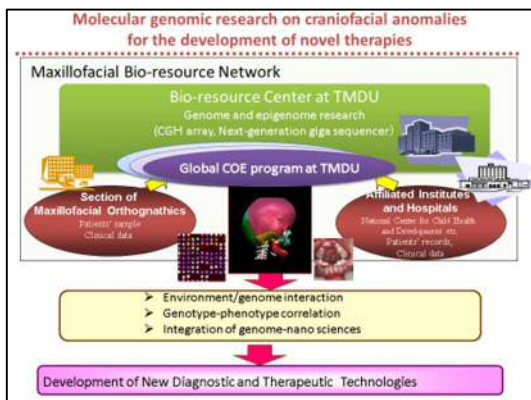
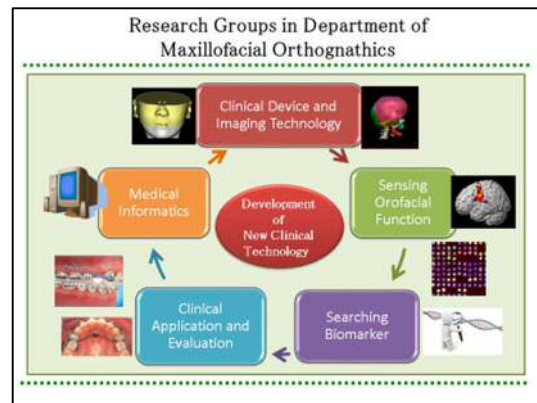
Development of oral cancer screening test by detection of squamous cell carcinoma among exfoliated oral mucosal cells

| Biomarkers | |
|---------------------------|---------------|
| SCCA1 | |
| Sensitivities | |
| OSCC and oral leukoplakia | 72.0 (77/107) |
| OSCC | 74.2 (66/89) |
| Oral leukoplakia | 61.1 (11/18) |
| Tumor size | |
| Tumor ≤ 2 cm | 86.7 (26/30) |
| 2 cm < Tumor ≤ 4 cm | 71.8 (28/39) |
| 4 cm < Tumor | 60.0 (12/20) |
| Tumor growth types | |
| Endophytic type | 65.5 (36/55) |
| Exophytic type | 91.7 (11/12) |
| Superficial type | 90.5 (19/21) |
| Specificities | 73.1 (57/78) |

Oral Oncology 48 (2012) 794–798

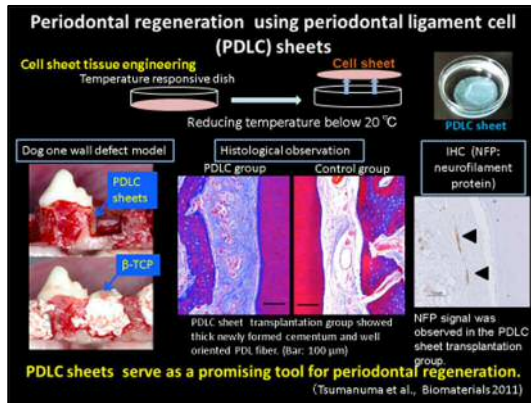
Department of Maxillofacial Orthognathics


Prof. Keiji Moriyama



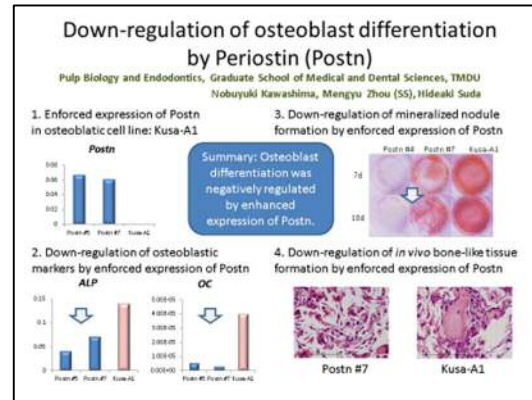
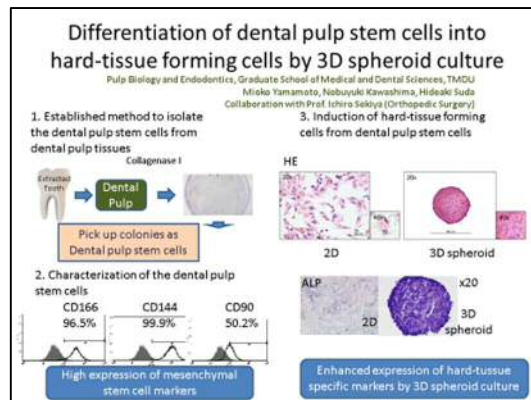
Department of Periodontology


Prof. Yuichi Izumi



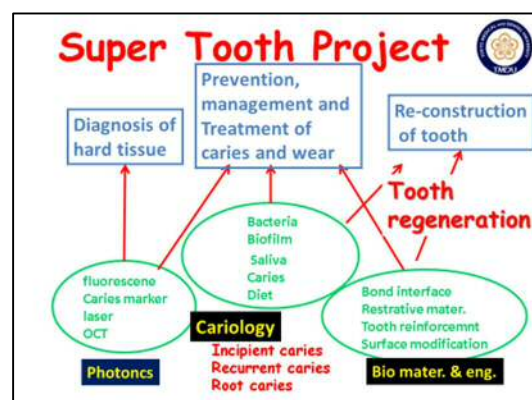


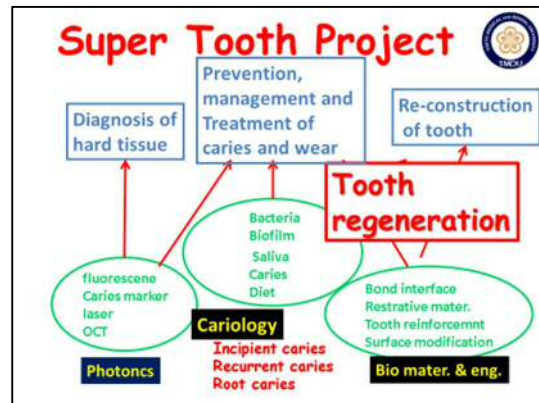
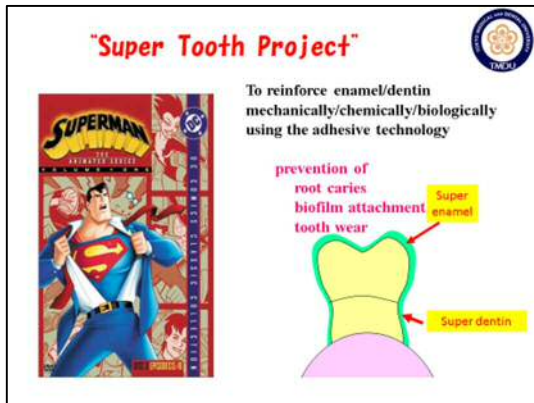
**Department of
Pulp Biology and Endodontics
Prof. Hideaki Suda**





**Department of
Cariology and Operative Dentistry
Prof. Junji Tagami**





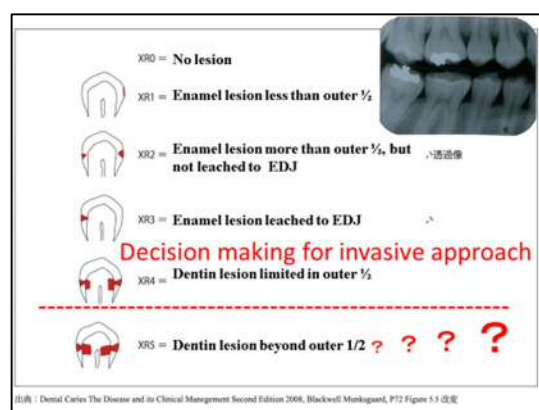
OCT

The 1st International Symposium and Mini-Exhibition

Optical Coherence Tomography in Dentistry

Date: June 20-21, 2013

Place: TMDU Faculty of Dentistry Auditorium



WILEY ONLINE LIBRARY

Early View publication on
www.wileyonlinelibrary.com
(Issue and page numbers not yet assigned;
citable using Digital Object Identifier - DOI)

3 Biophotonics 1-8 (2013) / DOI 10.1002/bph.201200210

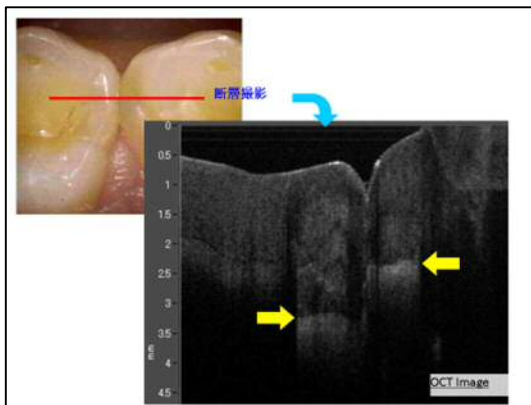
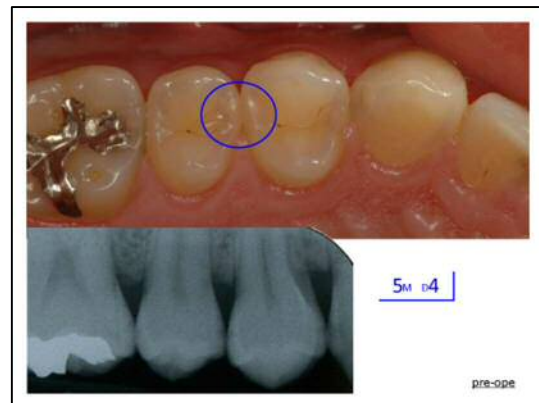
Journal of BIOPHOTONICS

FULL ARTICLE

Noninvasive cross-sectional imaging of proximal caries using swept-source optical coherence tomography (SS-OCT) *in vivo*

Yasushi Shimada^{1,3}, Hisaichi Nakagawa¹, Alireza Sadr², Ikumi Wada¹, Masatoshi Nakajima¹, Tomi Nikaido¹, Masayuki Otsubo¹, Junji Tagami^{1,2}, and Yasunori Sano¹





Estimation of Enamel and Dentin Mineral Content from Refractive Index

I. Harini^{1,2}, A. Sadr², Y. Shimada³, S. Nakashima¹, Y. Sumi³, J. Tagami^{1,2}

¹Cariology and Operative Dentistry, Department of Restorative Sciences, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan
²Global Center of Excellence (GCOE) Program, International Research Center for Molecular Science in Tooth and Bone Diseases, at TMDU, Tokyo, Japan
³Department for Advanced Dental Research Center of Advanced Medicine for Dental and Oral Diseases, National Center for Geriatrics and Gerontology

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47 | 1 | 13

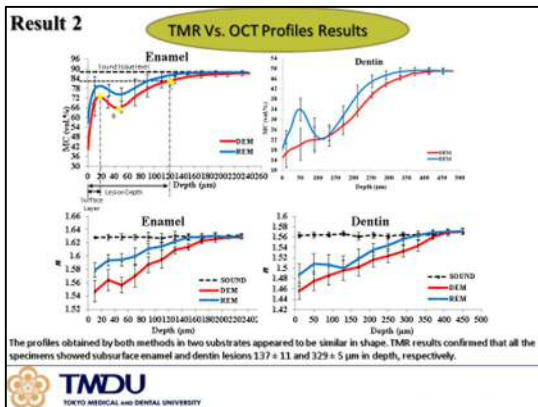
Journal of the European Organization for Caries Research (EORC)

Caries Research

Volume 47, Number 1, February 2013

ISSN 1023-6165

KARGER

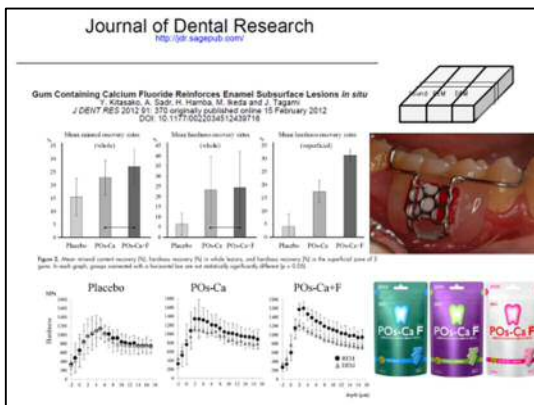
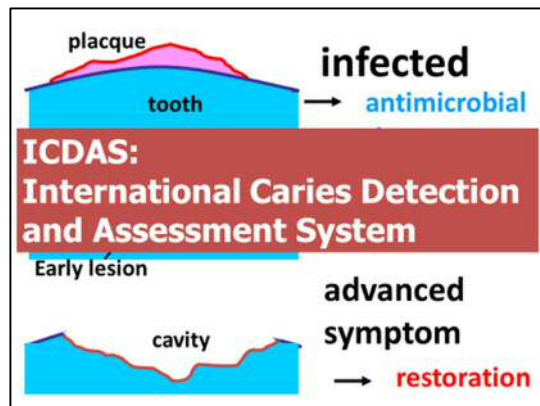
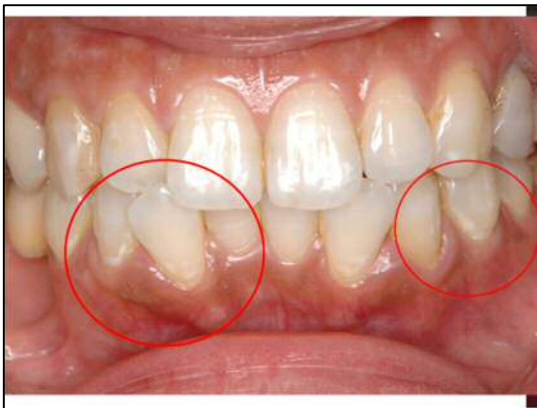


Conclusion :

No more TMR

MC and structure of lesion could be determined with a good accuracy from local n (**Refractive Index**). Compositional changes of enamel crystals through remineralization also affect n . Measurement of n has important clinical implications, n may serve as an indicator for caries diagnosis and monitoring.

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Thank you for your attention.



4. 聴講者による評価(フォーム)

LECTURE EVALUATION FORM

Professor Junji TAGAMI

On March 21, 2014 : 15.15-16.00 P.M.

Lecture on "Creation Our Future"

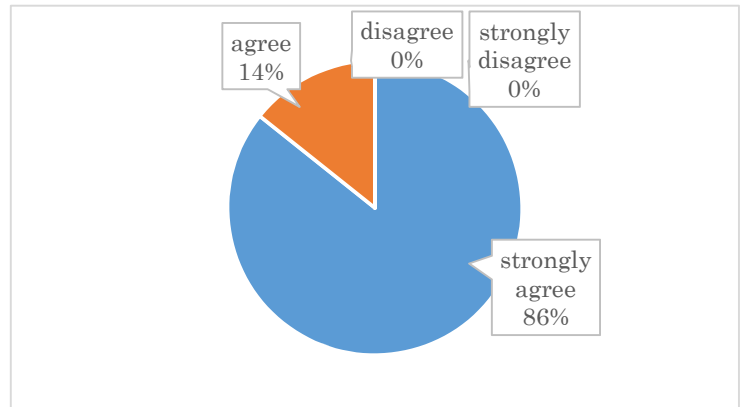
At the Faculty of Dentistry, Khon Kaen University, Thailand

Please take a minute or two to complete this questionnaire by ticking your response to the statements.

| | Strongly Agree | Agree | Disagree | Strongly Disagree |
|--|----------------|-------|----------|-------------------|
| 1. The choice of topic was relevant me. | | | | |
| 2. The Lecturer had a) good knowledge of subject | | | | |
| b)Presented it well | | | | |
| 3. There was sufficient opportunity for open discussion/questions. | | | | |
| 4. Did the Lecturer meet your expectations? | | | | |
| 5. Overall, I would rate this session as being | Excellent | Good | Average | Poor |
| | | | | |
| 6. Do you wish the Lecturer to be invited here again? | Yes | | No | |
| | | | | |
| 7. Any comments? | | | | |

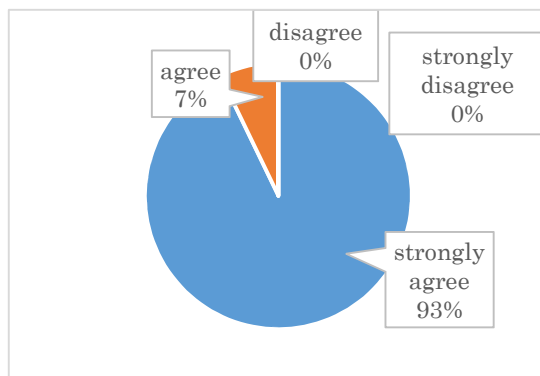
聴講者による評価結果（グラフ）

1. The choice of topic was relevant me.

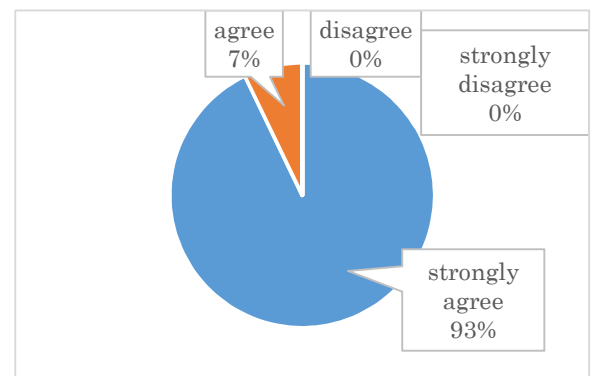


2. The Lecturer had

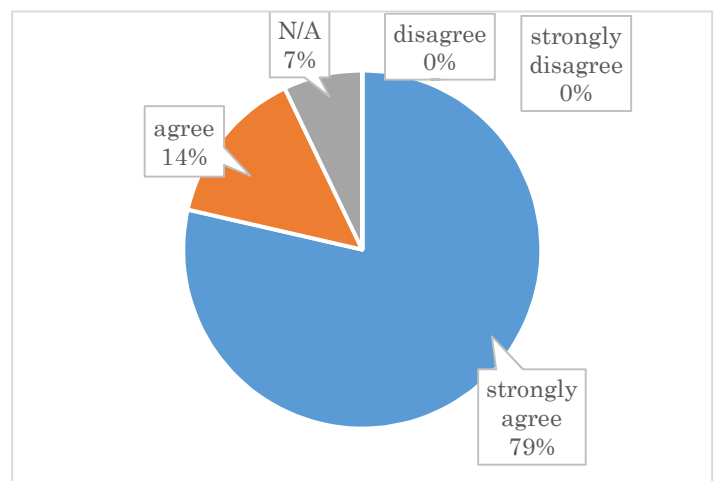
a) good knowledge of subject



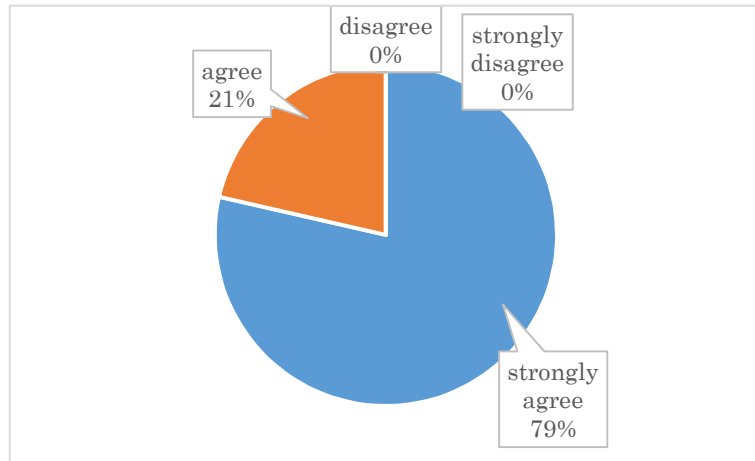
b) Presented it well



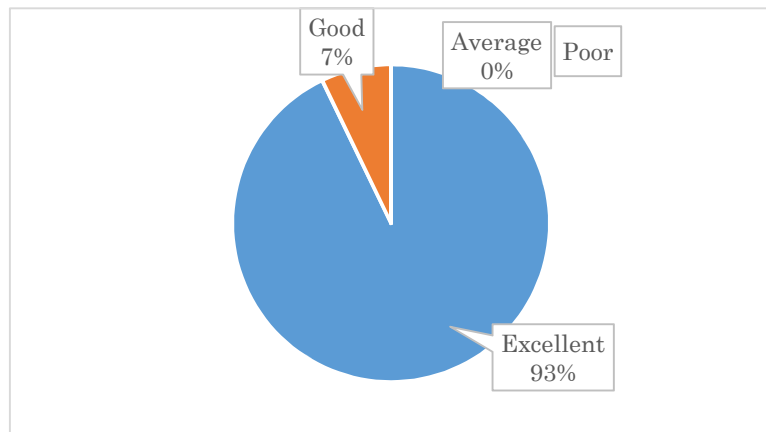
3. There was sufficient opportunity for open discussion/questions.



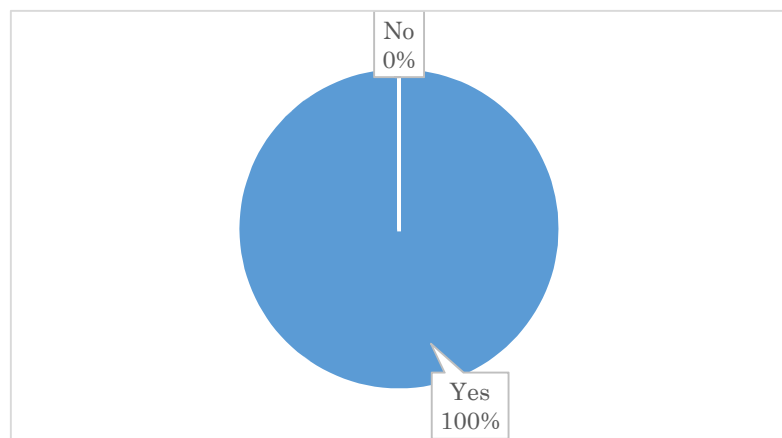
4. Did the Lecturer meet your expectations?



5. Overall, I would rate this session as being



6. Do you wish the Lecturer to be invited here again?



Periodontitis and Cardiovascular Diseases: The Link and Relevant Mechanisms

Yuichi IZUMI

Periodontitis and cardiovascular diseases: the link and relevant mechanisms

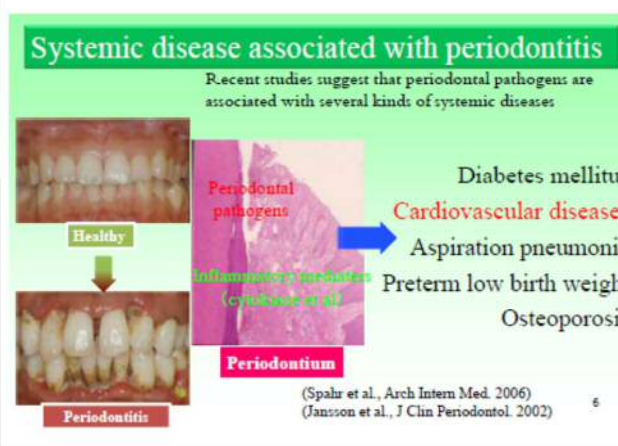
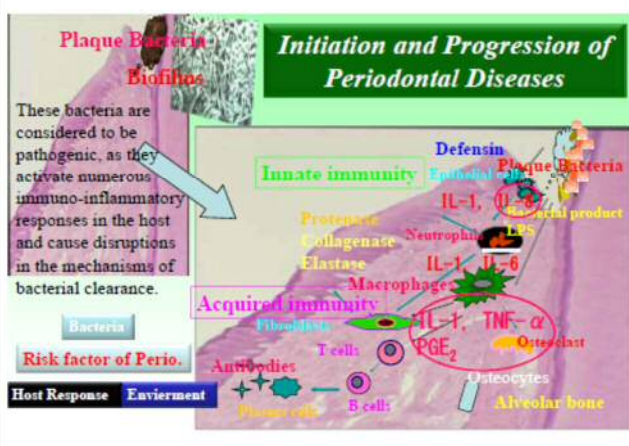
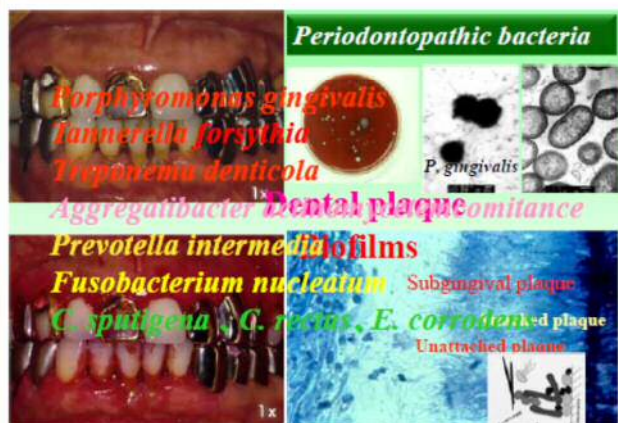
Yuichi Izumi
Department of Periodontology, TMDU

1

Topics of the presentation

- Periodontal diseases
- Impacts of periodontitis on cardiovascular diseases
 - ✓ Coronary heart disease
 - ✓ Myocardial infarction
 - ✓ Myocarditis
 - ✓ Cardiac hypertrophy
 - ✓ Peripheral vascular disease
 - ✓ Abdominal aortic aneurysm
 - ✓ Buerger's disease
- Potential mechanism of the association between periodontitis and cardiovascular diseases
- Effects of periodontal treatment on cardiovascular diseases
- Conclusion

2



(Spahr et al., Arch Intern Med. 2006)
(Jansson et al., J Clin Periodontol. 2002)

6



The estimated area of pocket epithelium in contact with biofilms in a patient with moderate to severe periodontitis. If one assumes 28 teeth each represented by a circle with an average diameter of 10 mm with pocket of 7 mm, the total area of pocket epithelium in contact with biofilm would be about 55~72 cm².

Periodontitis and Cardiovascular diseases



Periodontitis and Coronary heart disease

Patients

Coronary heart disease: 28 patients

Acute coronary syndrome: 15 patients

Chronic CHD: 13 patients

Samples

Subgingival plaque, Saliva, Blood

Sakurai et al. recently revealed that there is an association between periodontitis and acute coronary syndrome. A total of 28 CHD patients participated in the study. Coronary angiography, periodontal examination and dental radiography were performed in all patients.

Sakurai K et.al. *Int Heart J*, 2007 9

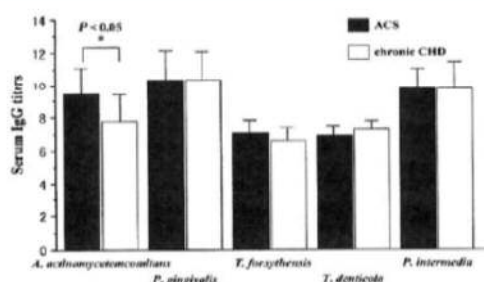
Prevalence of Periodontopathic bacteria in Oral and/or Blood Samples (PCR)

| | Oral Sample(%) | | Blood Sample(%) | |
|---------------------------------|----------------|-------------|-----------------|-------------|
| | ACS | Chronic CHD | ACS | Chronic CHD |
| <i>P. gingivalis</i> | 14 (93) | 10 (77) | 0 | 0 |
| <i>T. forsythia</i> | 15 (100) | 12 (92) | 0 | 0 |
| <i>T. denticola</i> | 12 (80) | 11 (85) | 4 (27) | 2 (15) |
| <i>A. actinomycetemcomitans</i> | 5 (33)* | 0 | 1 (7) | 0 |
| <i>P. intermedia</i> | 10 (67) | 7 (54) | 0 | 0 |

33% of the ACS patients harbored A.a in oral samples, whereas no A.a was found in the patients with chronic CHD. *; p<0.05

10

Serum IgG antibody to Periodontopathic bacteria



ACS showed significantly higher serum IgG titers to A.a compared with chronic CHD. We concluded that a specific periodontal pathogens may play a crucial role in the development of ACS.

Periodontal status and *Prevotella intermedia* antibody in acute coronary syndrome[☆]

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^b Health Care Center, Kumamoto University, Kumamoto, Japan

^c Department of Oral and Maxillofacial Surgery, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

^d Taisan CO., LTD., Takahashi, Japan

^e Periodontology Department of Hard Tissue Engineering, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan

Soejima H, et al, *Int J Cardiol*, 2009. 12

Table 2

Patient Characteristics in the acute coronary syndrome and stable angina groups

| Characteristics | Acute coronary syndrome (n=21) | Stable angina (n=39) | P value |
|---|--------------------------------|----------------------|---------|
| Age (yr) | | | |
| Mean | 68±11 | 67±5 | 0.975 |
| Range | 50-92 | 49-89 | |
| Men/women | 17/4 | 46/34 | 0.005 |
| Hypertension number (%) | 19 (48) | 19 (79) | 0.057 |
| Smoking number (%) | 19 (48) | 34 (89) | 0.002 |
| Diabetes mellitus number (%) | 19 (48) | 24 (60) | 0.207 |
| Obesity number (%) | 4 (19) | 11 (30) | 0.152 |
| Total cholesterol (mg/dl) | 176±31 | 178±35 | 0.812 |
| HDL cholesterol (mg/dl) | 46±11 | 54±20 | 0.017 |
| Triglyceride (mg/dl) | 180±26 | 111±61 | 0.006 |
| Number of coronary arteries narrowed >50% | | | 0.972 |
| 1-vessel | 11 | 49 | |
| 2-vessel | 8 | 24 | |
| 3-vessel | 4 | 16 | |
| Stenting on packing | | | 0.003 |
| Packing length (cm) | 5.0, 1.5-9.0 | 2.0, 0.0-4.0 | |
| Packing length (cm) | 4.0, 0.0-5.5 | 4.0, 0.0-1.0 | 0.104 |
| Packing length (cm) | 1.0, 0.0-5.0 | 3.0, 1.0-5.0 | 0.016 |
| Packing length (cm) | 2.0, 0.0-5.0 | 1.0, 0.0-3.5 | 0.130 |
| Packing length (cm) | 4.0, 0.0-5.0 | 8.0, 0.0-5.0 | 0.117 |
| Packing length (cm) | 13.0, 5.0-17.5 | 8.0, 5.0-15.0 | 0.004 |
| Packing length (cm) | 20.0, 14.0-27.0 | 17.0, 11.0-26.0 | 0.003 |

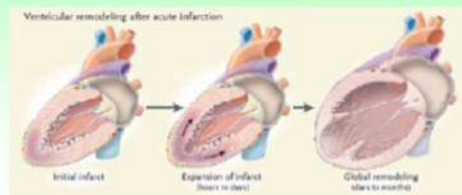
HDL=high density lipoprotein (median, 25-75th).

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Background

Myocardial infarction

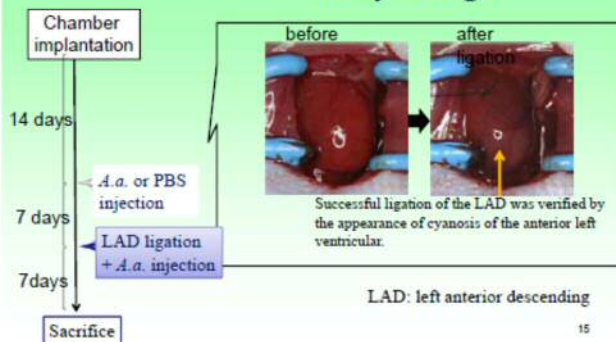
- ◆ Myocardial infarction and the following ventricular remodeling are the most common cause of chronic heart failure.



Mariell et al., N Engl J Med. 2003

Material and Methods

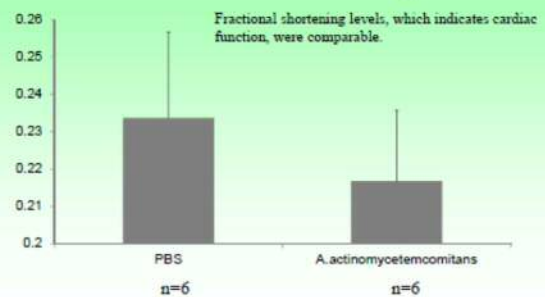
Study Design



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Results

Fractional Shortening



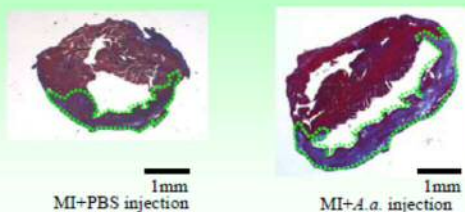
Hanatani et al., Int Heart J. 2012 16

Results

Histopathological Image

Mallory Staining

The infarction area increased in A.a.-injected group.

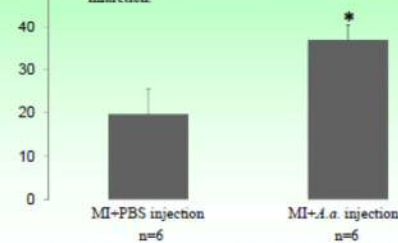


Hanatani et al., Int Heart J. 2012 17

Results

Infarction Area/Ischemic Myocardium Ratio

A.a injection increased the infarction area /ischemic myocardium ratio. From the present data, A.a accelerated the progression of myocardial infarction.



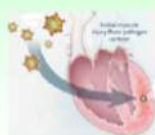
* p < 0.05

Hanatani et al., Int Heart J. 2012 18

Background

Myocarditis

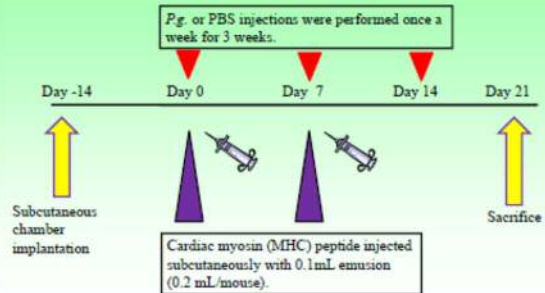
- ◆ Myocarditis is an inflammatory heart disease which leads to sudden death.
- ◆ However, no effective treatment has been elucidated. (Suzuki et al., Expert Opin Ther Targets. 2011)
- ◆ It is said that viral and bacterial infections and autoimmune diseases may be the cause of myocarditis, however, the pathogenesis of it remains unclear. (Cooper et al., N Engl J Med. 2009)



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Material and Methods

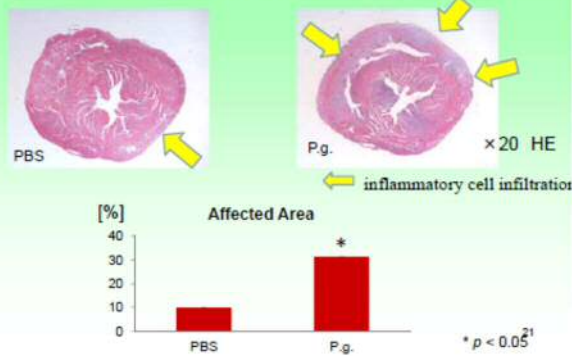
Study Design



Ashigaki N, Am J Physiol Heart Circ Physiol, 2013 ²⁰

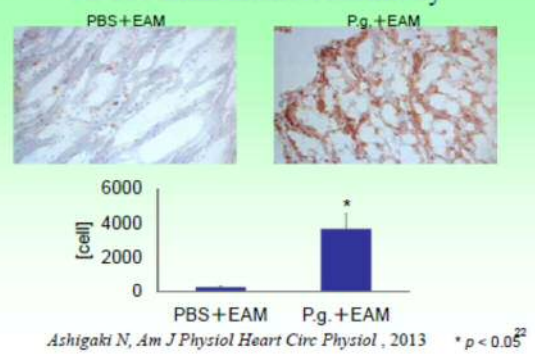
Results

Analysis of affected area



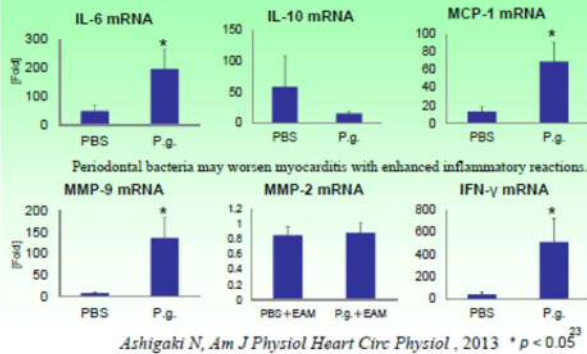
Results

CD11b Immunohistochemistry



Results

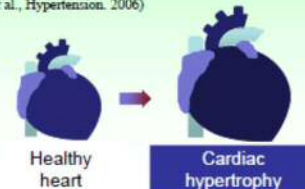
Quantitative RT-PCR



Background

Cardiac hypertrophy

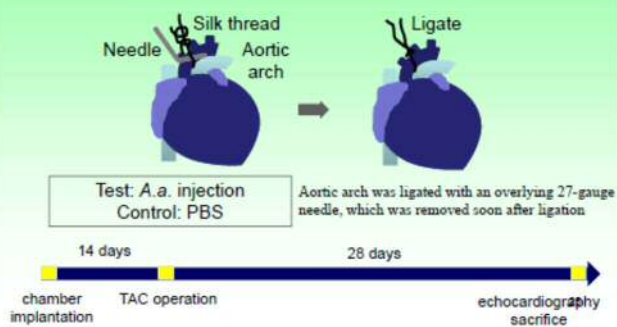
- ◆ Cardiac hypertrophy is one of the cardiovascular diseases caused by hypertension.
- ◆ Left ventricular hypertrophy (LVH) is an adaptive process that compensates for pressure overload caused by hypertension.
- ◆ But if LVH is extremely promoted, it may result in death. (Matsuoka et al., Hypertension. 2006)



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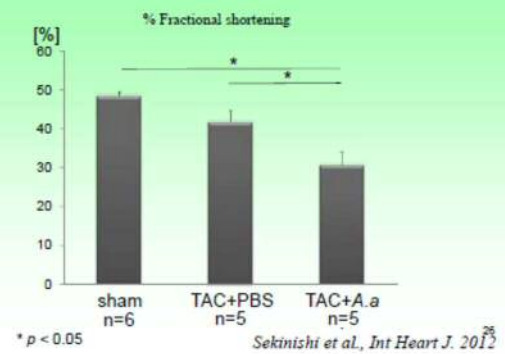
Material and Methods

Transverse aortic constriction



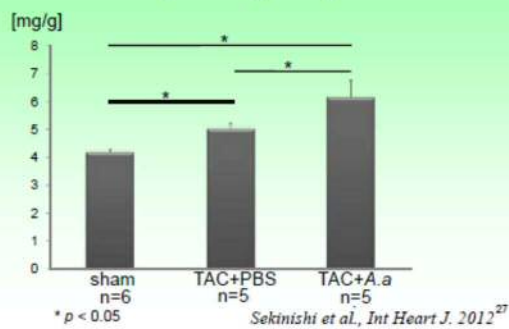
Results

Echocardiography



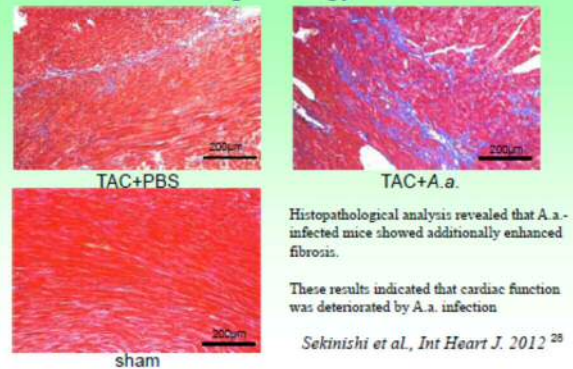
Results

Heart weight/body weight ratio

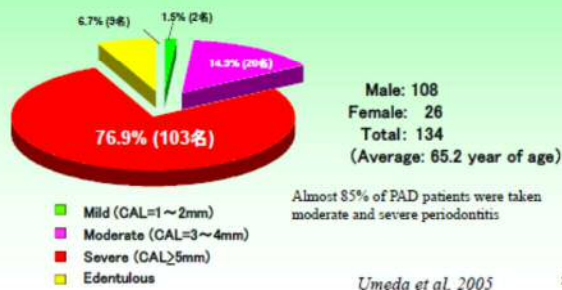


Results

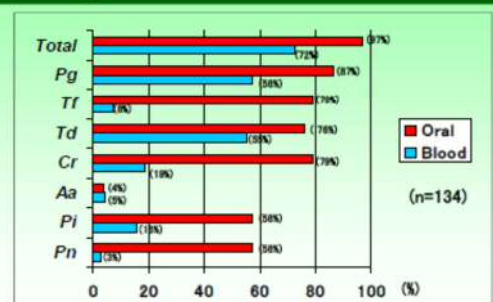
Histopathology × 200



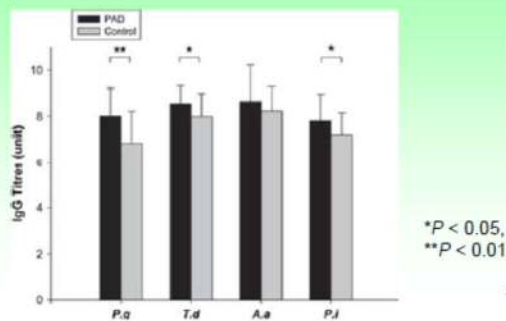
Prevalence of Periodontitis in Peripheral artery disease



Periodontopathic bacteria from Oral or Arterial samples



Serum IgG titers against *P. gingivalis*, *T. denticola*, *A. actinomycetemcomitans* and *P. intermedia* in PAD patients and control subjects.



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Association of several risk factors with peripheral arterial disease in logistic regression model

| Dependent variable: PAD | | |
|-------------------------|--------------------|---------|
| Independent variables | Odds Ratio(95% CI) | P value |
| Periodontitis | 5.45 (1.57-18.89) | 0.007* |
| Smoking | 0.75 (0.13-4.43) | 0.754 |
| Age | 0.99 (0.94-1.05) | 0.813 |
| Gender | 1.65 (0.18-15.61) | 0.661 |
| Diabetes | 0.18 (0.03-1.12) | 0.065 |

95% CI: 95% confidence interval

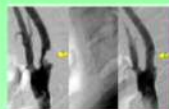
* $P < 0.05$ represents significant difference

Yi-Wen Chen et al, Eur J Vasc Endovasc Surg, 2008

32

Background

Arterial injury



- ◆ Balloon angioplasty and stent implantation are the most widely used techniques for treating coronary arterial stenosis.
- ◆ Mechanical injury to the vascular lumen occurs during angioplasty and causes neointimal hyperplasia and vascular remodeling, resulting in restenosis of the culprit lesion.

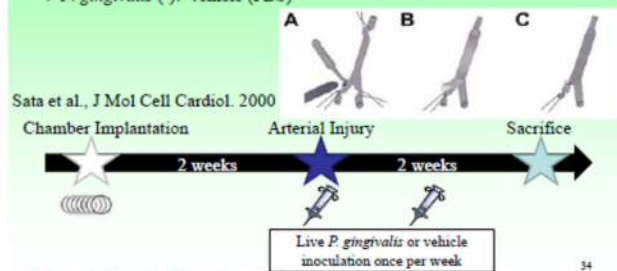
(Yamamoto et al., Hypertens Res. 2008)

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Materials and Methods

Arterial Injury Model

- *P. gingivalis* (+): live *P. gingivalis* (CFU 10^7 /mouse)
- *P. gingivalis* (-): vehicle (PBS)

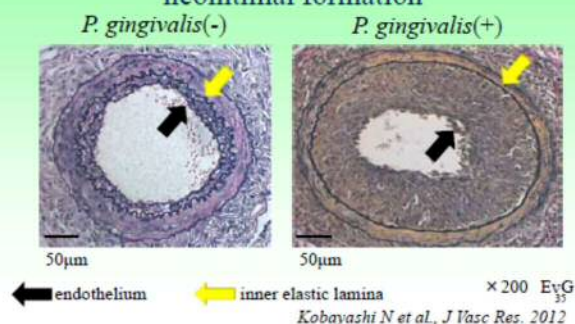


Kobayashi N et al., J Vasc Res. 2012

34

Results

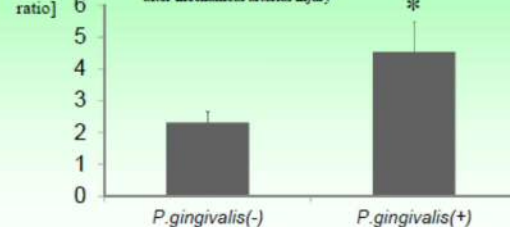
P. gingivalis infection enhanced neointimal formation



Results

P. gingivalis infection accelerated Intima/Media (I/M) ratio

It was confirmed that *P. gingivalis* promoted neointimal formation after mechanical arterial injury



Each group N=11

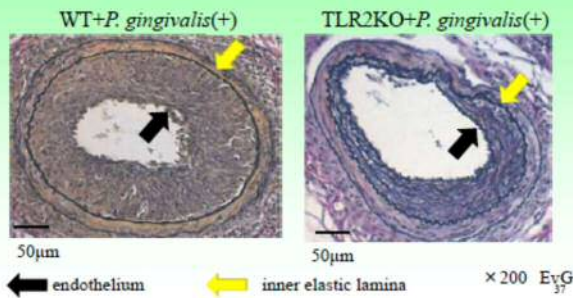
Kobayashi et al., J Vasc Res. 2012

* $p < 0.05$ ³⁶

Results

Suppressed neointimal hyperplasia in TLR-2 KO mice

TLR-2 deficiency negated *P. gingivalis* induced neointimal formation.



Background

Abdominal Aortic Aneurysm (AAA)



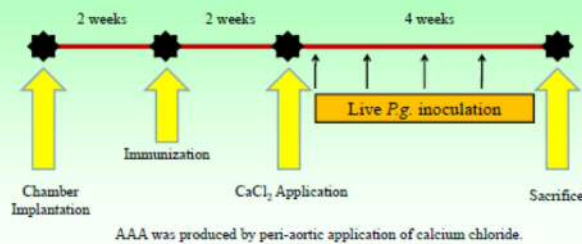
- ◆ Common and life-threatening vascular disease.
- ◆ Inflammation appears to play a fundamental role in AAA development and progression.
- ◆ MMPs, particularly MMP-2 and MMP-9, are expressed and produced in increased amounts in human aneurysm tissue.

(Thompson et al., Ann N Y Acad Sci. 1996)

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Material and Methods

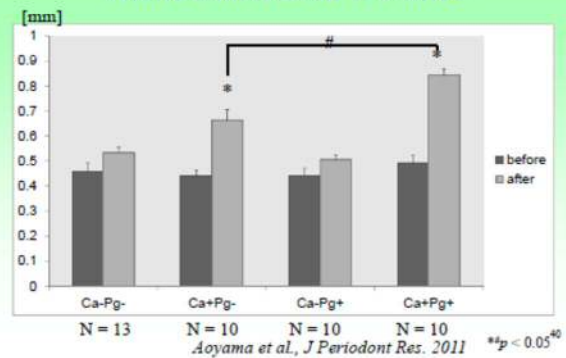
Time Schedule



Aoyama N et al, J Periodont Res, 2011 ³⁹

Results

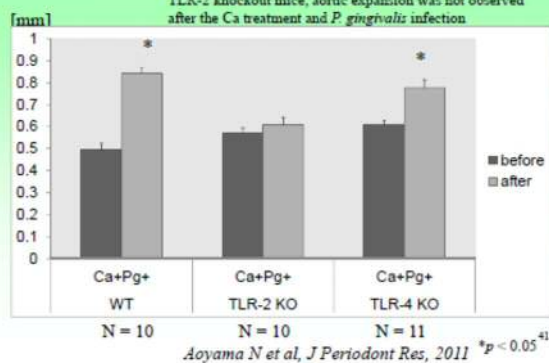
Aortic Diameter in WT Mice



Results

Comparison of Aortic Diameters

TLR-2 knockout mice, aortic expansion was not observed after the Ca treatment and *P. gingivalis* infection



Aoyama N et al, J Periodont Res, 2011

Results

Histopathological Analysis

P. gingivalis infection could accelerate the progression of AAA with TLR-2 signaling.

EvG staining x 200 100µm

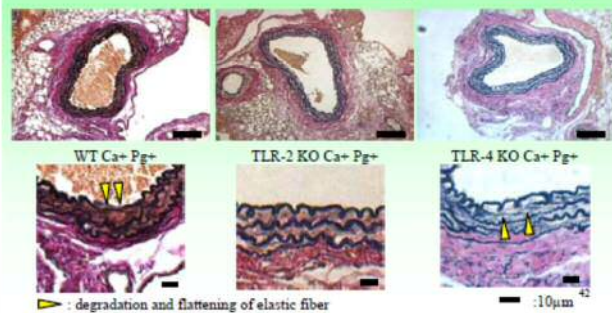


Table 3 Presence of periodontopathic bacteria in an oral sample, arterial (aneurysmal) wall and mural thrombus of AAA patients. Bacteria are detected by a polymerase chain reaction assay.

| Bacteria | Oral sample (n = 32) | Aneurysmal wall | Mural thrombus |
|--|----------------------|-----------------|----------------|
| All bacteria studied | 28 (88) | 24/26 (92) | 14/14 (100) |
| <i>Aggregatibacter actinomycetemcomitans</i> | 1 (3) | 0/1 (0) | 0 |
| <i>Campylobacter rectus</i> | 11 (34) | 5/11 (45) | 1/7 (14) |
| <i>Porphyromonas gingivalis</i> | 26 (81) | 22/26 (85) | 12/15 (80) |
| <i>Prevotella intermedia</i> | 13 (41) | 4/13 (31) | 0/7 (0) |
| <i>Prevotella nigrescens</i> | 4 (10) | 1/4 (25) | 0/3 (0) |
| <i>Tannerella forsythia</i> | 23 (72) | 5/23 (22) | 0/13 (0) |
| <i>Tropaeolum denticola</i> | 19 (59) | 12/19 (63) | 3/10 (30) |

Oral samples: bacterial positive numbers (percentage). Arterial (aneurysmal) wall, Mural thrombus: bacterial positive ratio to positive finding of these in oral samples (percentage).

Periodontopathic bacteria were present in 86% of disease arteries of AAA patients, whose oral samples were positive for periodontopathic bacteria.

P. gingivalis and *T. denticola* were frequently detected among aneurysmal walls and oral samples.

These results suggested that periodontitis might be associated with AAA

Kurihara et al. Eur J Vasc Endovasc Surg 2004 43

Periodontitis and Buerger disease

Buerger disease is characterized by the absence or minimal presence of atheromas, segmental vascular inflammation, vasoocclusive phenomenon, and involvement of small-and medium-sized arteries and veins of the upper and lower extremities

(Iwai T et al. J Vasc Surg 42: 107-115, 2005)

(Chen Y-W et al. Int J Cardiol 122: 79-81, 2007)

Tabacco smoking is the only indisputable etiologic factor of Buerger disease. The various features of Buerger disease might be better explained by considering the disease as a systemic reaction to bacterial infection or to an antigen originating from bacteria rather than as an immunologic disorder.

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Table II. Results of periodontal examination and PCR detection of patients with Buerger disease and of controls

| Subject No. | Periodontitis grade | Artery | Oral cavity |
|-------------|---------------------|----------------|------------------------|
| Patient 1 | C | Td | Td, Td, Cr, Ps |
| Patient 2 | B | Td, Cr | Ps, Td, Td, Cr, Ps, Ps |
| Patient 3 | C | Td, Td, Cr, Ps | Ps, Td, Td, Cr, Ps, Ps |
| Patient 4 | C | Td, Cr, Ps | Ps, Td, Td, Cr, Ps |
| Patient 5 | C | Td, Td, Cr, Ps | Ps, Td, Td, Cr, Ps, Ps |
| Patient 6 | B | Td, Td, Cr, Ps | Ps, Td, Td, Cr, Ps, Ps |
| Patient 7 | C | Ps, Td, Cr, Ps | Ps, Td, Td, Cr, Ps, Ps |
| Patient 8 | D | Ps, Td, Cr | Ps, Td, Cr |
| Patient 9 | C | Ps, Td | Ps, Td, Td, Cr, Ps, Ps |
| Patient 10 | C | Td | Ps, Td, Td, Cr, Ps |
| Patient 11 | C | Ps | Ps, Td, Td, Cr, Ps |
| Patient 12 | C | None | Ps, Td, Td, Cr, Ps, Ps |
| Patient 13 | B | Td | Ps, Td, Td, Cr, Ps, Ps |
| Patient 14 | C | Td | Ps, Td, Td, Cr |
| Control 1 | — | None | — |
| Control 2 | — | None | — |
| Control 3 | — | None | — |
| Control 4 | — | None | — |
| Control 5 | — | None | — |
| Control 6 | — | None | — |
| Control 7 | — | None | — |

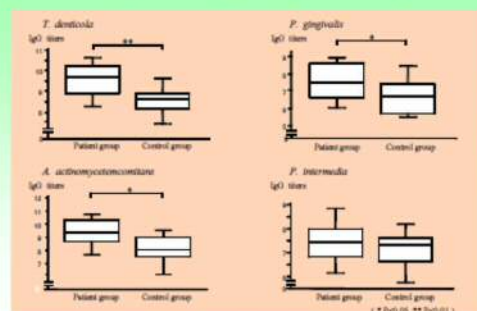
PCR, Polymerase chain reaction; Ps, *Porphyromonas gingivalis*; Td, *Tannerella forsythia*; Cr, *Campylobacter rectus*; Ps, *Prevotella intermedia*; Ps, *Prevotella nigrescens*.

All patients with Buerger disease were male, and their ages are shown in Table I. The ages of the control patients were 69, 62, 25, 72, 77, 78, and 65 years.

The recorded sites were distal, splenic, anteroposterior malformation, distal, distal, femoral, and splenic arteries, respectively.

Grade A was normal (pocket depth on probing, <2 mm); grade B, moderate periodontitis (pocket depth, 2-5 mm); grade C, severe periodontitis (pocket depth, >5 mm); and grade D, sclerodentulous.

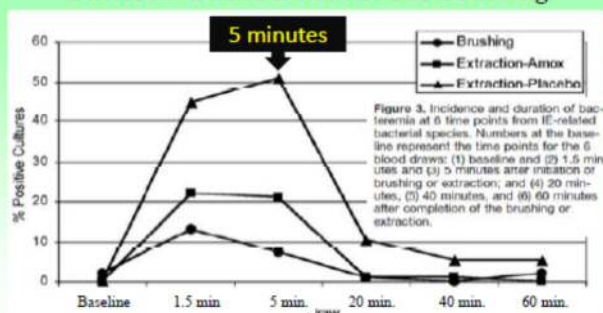
Comparison of IgG titers against periodontopathic bacteria



Chen Y-W et al. Int J Cardiol, 2007

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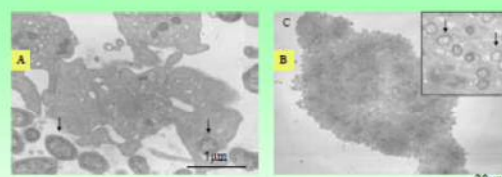
Bacteremia after Extraction or Brushing



Lockhart et al., Circulation. 2008

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Platelet aggregation induced by *P. gingivalis*



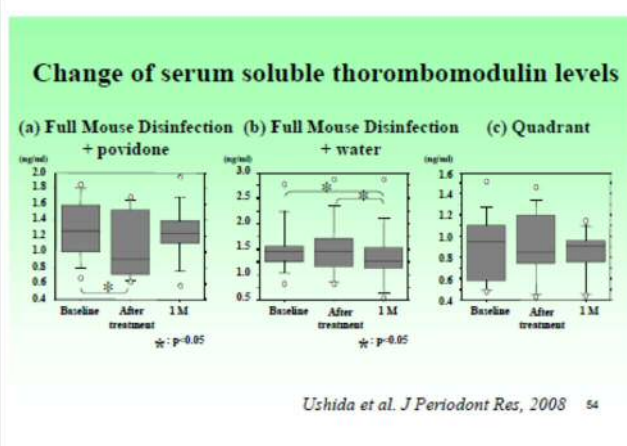
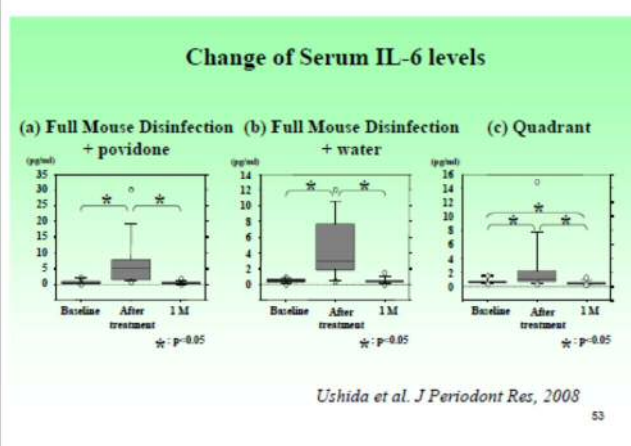
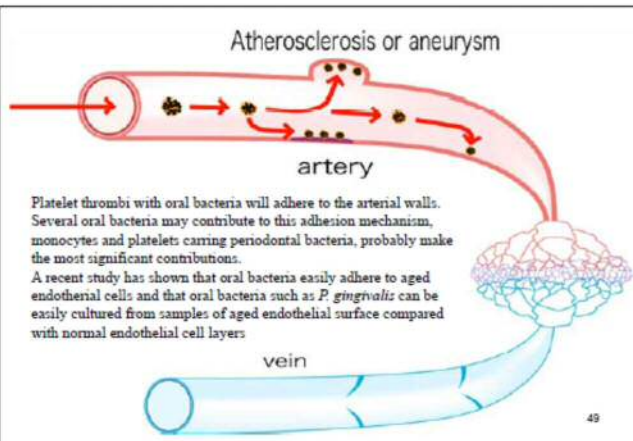
Small aggregation after 5 minutes; Activated platelets are surrounding bacteria

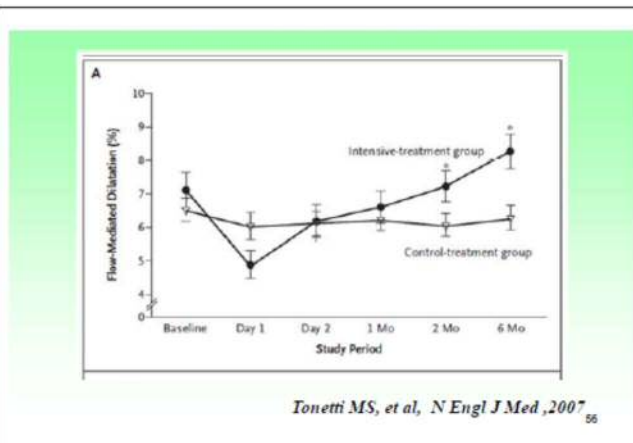
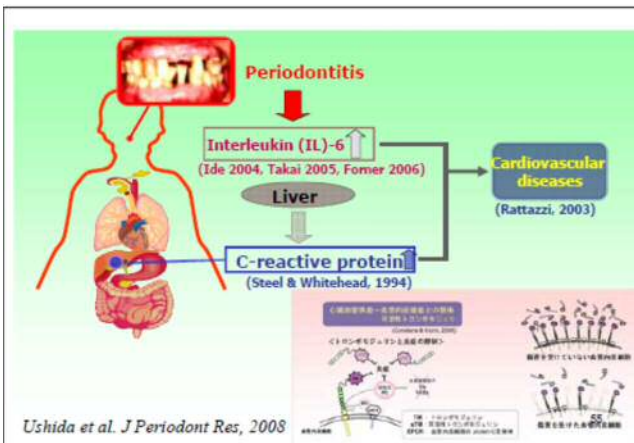
Large aggregation after 10 minutes; Bacteria are wrapped in the aggregation

Platelets may play a vital role in the transportation of oral bacteria!

X Li et al. Thrombosis Research 2008

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Influence of periodontal infection on circulation

Basic studies

- Abdominal aortic aneurysm
P. gingivalis promotes aortic aneurysms
Inhibition of aneurysms by MMP regulation
TLR-2 plays a role in aneurysm development
Aoyama N et al., J Periodont Res. 2011
Aoyama N et al., J Periodont Res. 2012
Aoyama N et al., Circ J. 2013
- Arterial injury
P. gingivalis promotes neointimal formation
Kobayashi N et al., J Vasc Res. 2012
- Myocardial infarction
A. actinomycetemcomitans deteriorates remodeling after MI
Hanatani T et al., Int Heart J. 2012
- Myocardial hypertrophy
Periodontal infection promotes myocardial hypertrophy
Sekizuchi A et al., Int Heart J. 2012
- Myocarditis
P. gingivalis deteriorates myocarditis
Achigaki N et al., AJP Heart Circ Physiol. 2012

Influence of periodontal infection on circulation

Clinical studies

- Atherosclerosis and hypertension
Level of serum antibody against a periodontal pathogen is associated with atherosclerosis and hypertension
Hanaoka T et al., Hypertension Research 2013
- Ischemic stroke
Association of serum anti-periodontal pathogen antibody with ischemic stroke
Hosomi N et al., Cerebrovasc Dis. 2012
- Atherosclerosis
Detection of periodontal bacteria in atherosclerotic lesion
Toyofuku T. et al., Surg Today. 2011
- Coronary Heart Disease
Prediagnostic plasma antibody levels to periodontopathic bacteria and risk of coronary heart disease
Ueno M et al., Int Heart J. 2012
Periodontal status and *Prevotella intermedia* antibody in acute coronary syndrome
Soejima H. et al., Int J Cardiol. 2008

Three potential mechanisms of the association between periodontitis and CVD include:

- Direct bacterial effects on platelets and host cells
- Systemically or locally induced inflammatory mediators
- Autoimmune responses

Studies have suggested that potential links between periodontitis and CVD include direct effects from bacteria and indirect effects through host inflammatory responses as well as autoimmune responses. Since DNA of *P. gingivalis* has been detected in atherosclerotic plaques; and periodontal infections can result in bacteremias and endotoxemias in the patients, systemic effects on the cardiovascular system through these exposures seem biologically reasonable. Three potential mechanisms of the association between periodontitis and CVD include: direct bacterial effects on platelets and host cells systemically or locally induced inflammatory mediators autoimmune responses

CLINICAL CARDIOLOGY heart.org

Our new clinical theme C in Cardiovascular

ACS Arrhythmia/EP Brain/Kidney/Peripheral Clinical cardiology Heart failure Imaging Interventional/Burgery Lipid/Metabolic Prevention

heartwire

CLINICAL CARDIOLOGY

AHA: No evidence that gum disease causes CHD

APRIL 16, 2012, San Diego

Charlotte, NC: A new scientific statement from the **American Heart Association (AHA)** says it agrees with the conclusions of the **ADA** statement, which is that periodontal disease contributes to atherosclerosis, heart disease, or stroke [1].

The statement, in a paper published online in *Circulation* on April 16, 2012, says that although observational studies support an association between periodontal disease and atherosclerotic vascular disease independent of known confounders, they do not support a causative relationship.

The American Dental Association Council on Scientific Affairs says it agrees with the conclusions of the AHA statement.

Lead author of the statement, Dr. Peter Lackhart (Cardiovascular Center, Charlotte, NC), commented to heartwire: "We were aware of concerns that have been reported in the lay press about the idea that gum disease can lead to heart disease, and there was an overwhelming consensus that the AHA should look into it to assess whether the science supported such a conclusion."

Not worth stressing out about

He added: "After extensive review of all the literature in this field, we were not able to find any real scientific evidence

AHA Scientific Statement

Periodontal Disease and Atherosclerotic Vascular Disease: Does the Evidence Support an Independent Association?

A Scientific Statement From the American Heart Association

The American Dental Association Council on Scientific Affairs Concurs With the
Conclusions of This Report

Endorsed by the World Heart Federation

Peter B. Lockhart, DDS, Co-Chair; Ann F. Bolger, MD, FAHA, Co-Chair;
Panos N. Papapanou, DDS, PhD; Olusegun Osipowale, MD; Maurizio Trevisan, MD;
Matthew F. Trevisan, MD; Kathryn A. Twardert, PhD, FAHA; Isaac W. Nwachugwu, MD, MPH, FAHA;
Heather L. Gornik, MD, MHS, FAHA; Michael H. Gewitz, MD, FAHA; Walter R. Wilson, MD;
Sidney C. Smith, Jr, MD, FAHA; Larry M. Badier, MD, FAHA;
on behalf of the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease
Committee of the Council on Cardiovascular Disease in the Young, Council on Epidemiology and
Prevention, Council on Peripheral Vascular Disease, and Council on Clinical Cardiology

Circulation. 2012;125:2520-2544

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Abstract—A link between oral health and cardiovascular disease has been proposed for more than a century. Recently, concern about possible links between periodontal disease (PD) and atherosclerotic vascular disease (ASVD) has intensified and is driving an active field of investigation into possible association and causality. The 2 disorders share several common risk factors, including cigarette smoking, age, and diabetes mellitus. Patients and providers are increasingly presented with claims that PD treatment strategies offer ASVD protection; these claims are often endorsed by professional and industrial stakeholders. The focus of this review is to assess whether available data support an independent association between ASVD and PD and whether PD treatment might modify ASVD risks or outcomes. It also presents mechanistic details of both PD and ASVD relevant to this topic. The correlation of PD with ASVD outcomes and surrogate markers is discussed, as well as the correlation of response to PD therapy with ASVD event rates. Methodological issues that complicate studies of this association are outlined, with an emphasis on the terms and metrics that would be applicable in future studies. Observational studies to date support an association between PD and ASVD independent of known confounders. They do not, however, support a causative relationship. Although periodontal interventions result in a reduction in systemic inflammation and endothelial dysfunction in short-term studies, there is no evidence that they prevent ASVD or modify its outcomes. (Circulation. 2012;125:2520-2544.)

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February 4, 2013, Tokyo

Acknowledgement

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- Center for Cooperative Education Research, Kyushu Dental University
Tomoya Hanatani DDS PhD

Periodontal condition in CHD patients

We are now performing a clinical research to analyze the association between the infection of periodontal bacteria and coronary heart disease (CHD).

The results we have already obtained are following.

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Materials and Methods

Subjects

- Five hundreds and six subjects were recruited from patients with cardiovascular diseases in Tokyo Medical and Dental University Hospital from May 2012 to April 2013.
- The subjects were divided into six groups according to age and the existence of CHD.

| GROUPS | 31-60 years | 61-70 years | Over 70 years |
|--------------|-------------|-------------|---------------|
| CHD positive | YC (n=27) | MC (n=61) | EC (n=94) |
| CHD negative | YN (n=129) | MN (n=108) | EN (n=87) |

Materials and Methods

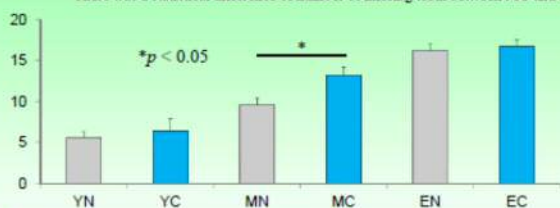
Analyses

- Clinical measurements
 - Missing teeth number
 - Probing depth
 - Clinical attachment level
 - Bleeding on probing
- Anti-periodontal bacterial antibody by ELISA
- Amount of periodontal bacteria by real-time PCR
P. gingivalis, *A. actinomycetemcomitans*, *P. intermedia*

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Number of missing teeth

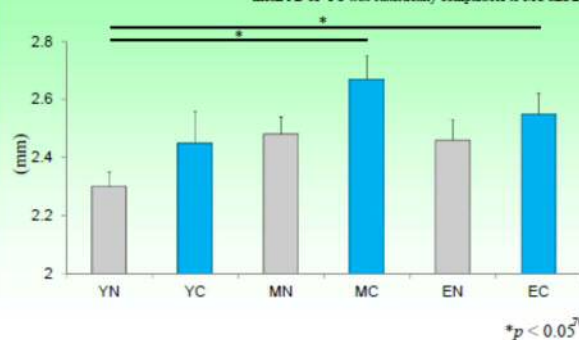
There was a statistical difference of number of missing teeth between MC and MN.



| GROUPS | 31-60 years | 61-70 years | Over 70 years |
|--------------|-------------|-------------|---------------|
| CHD positive | YC (n=27) | MC (n=61) | EC (n=94) |
| CHD negative | YN (n=129) | MN (n=108) | EN (n=87) |

Average PD

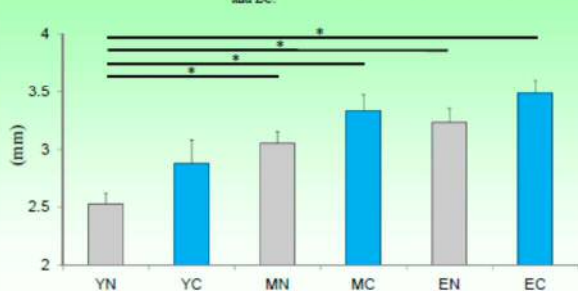
The mean PD of YN was the smallest of the six groups. The mean PD of MC and EC was higher than YN, although the mean PD of YC was statistically comparable to MC and EC.



*p < 0.05⁷⁰

Average CAL

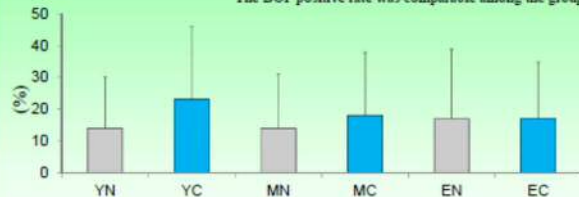
The mean CAL of YN was also the smallest of the six groups. The mean CAL of MN, MC, EN and EC was higher than YN, while the mean CAL of YC did not statistically differ from MC and EC.



*p < 0.05⁷¹

BOP positive rate

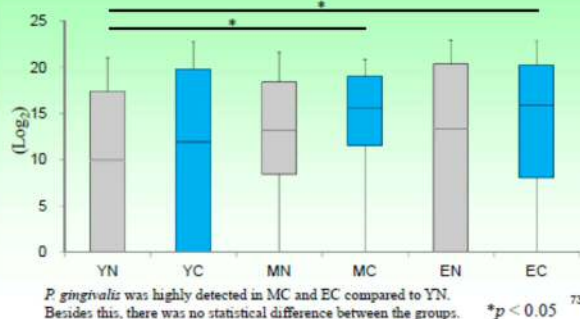
The BOP positive rate was comparable among the groups



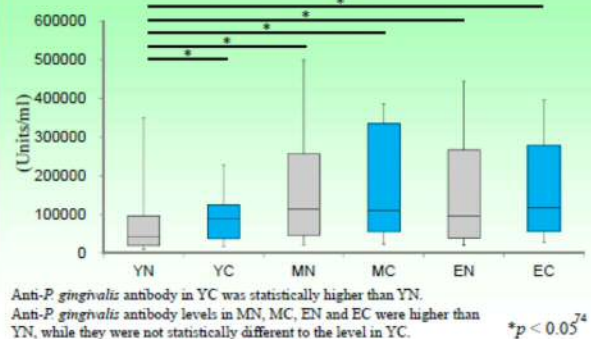
| GROUPS | 31-60 years | 61-70 years | Over 70 years |
|--------------|-------------|-------------|---------------|
| CHD positive | YC (n=27) | MC (n=61) | EC (n=94) |
| CHD negative | YN (n=129) | MN (n=108) | EN (n=87) |

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P. gingivalis counts in 1ml of saliva



Anti-*P. gingivalis* antibody level



Summary of this clinical study

- CHD patients in relatively young age groups had a high level of anti-*P. gingivalis* antibody, although the amount of *P. gingivalis* was comparable to the non-CHD subjects.
- Continuous inflammatory reaction induced by *P. gingivalis* infection may influence to CHD.

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6. 聴講者による評価（フォーム）

LECTURE EVALUATION FORM

Professor Yuichi IZUMI

On March 21, 2014 : 10.30-11.30 A.M.

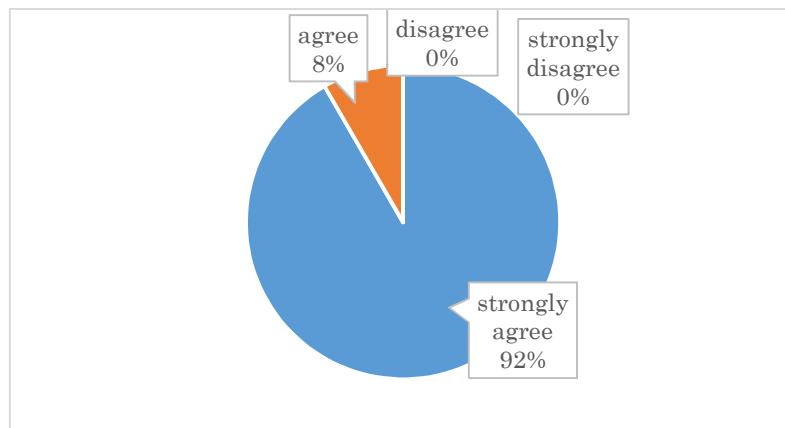
**Lecture on “Periodontitis and Cardiovascular Disease z The Link and Relevant”
At the Faculty of Dentistry, Khon Kaen University, Thailand**

Please take a minute or two to complete this questionnaire by ticking your response to the statements.

| | Strongly Agree | Agree | Disagree | Strongly Disagree |
|--|----------------|-------|----------|-------------------|
| 1. The choice of topic was relevant me. | | | | |
| 2. The Lecturer had a) good knowledge of subject | | | | |
| b)Presented it well | | | | |
| 3. There was sufficient opportunity for open discussion/questions. | | | | |
| 4. Did the Lecturer meet your expectations? | | | | |
| 5. Overall, I would rate this session as being | Excellent | Good | Average | Poor |
| | | | | |
| 6. Do you wish the Lecturer to be invited here again? | Yes | | No | |
| | | | | |
| 7. Any comments? | | | | |

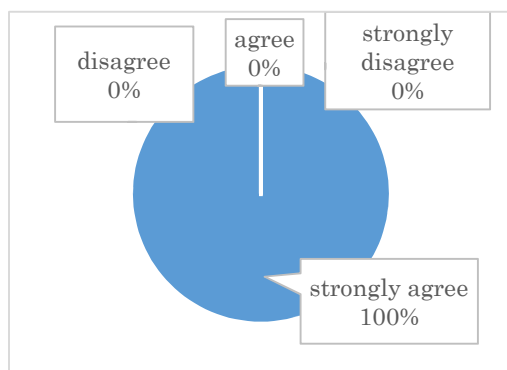
聴講者による評価結果（グラフ）

1. The choice of topic was relevant me.

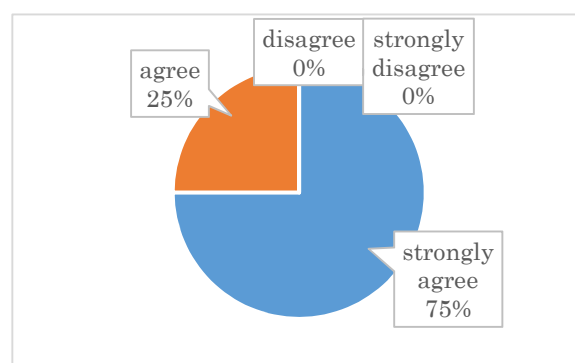


2. The Lecturer had

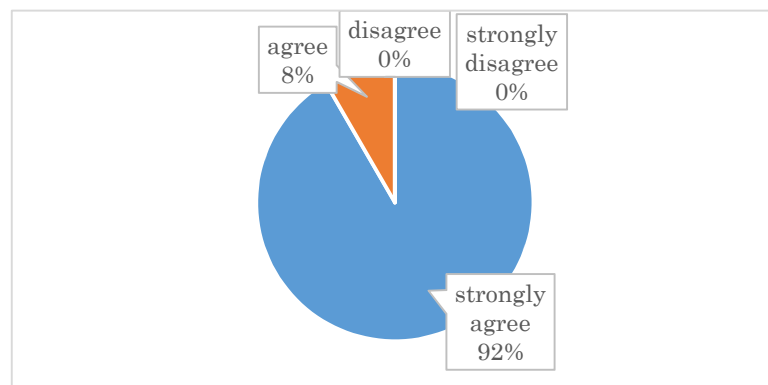
a) good knowledge of subject



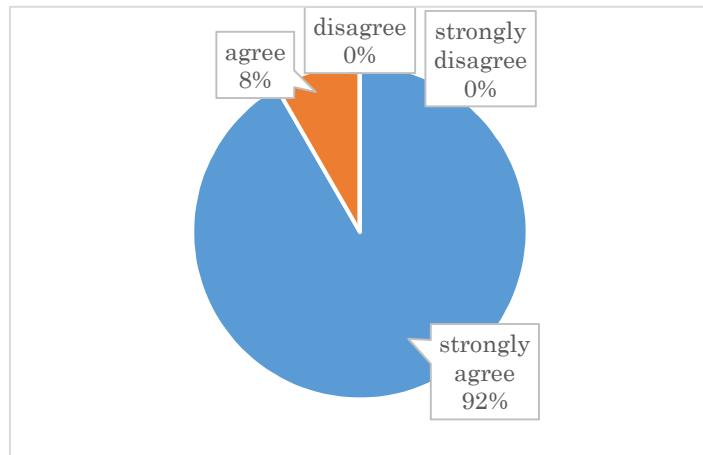
b) Presented it well



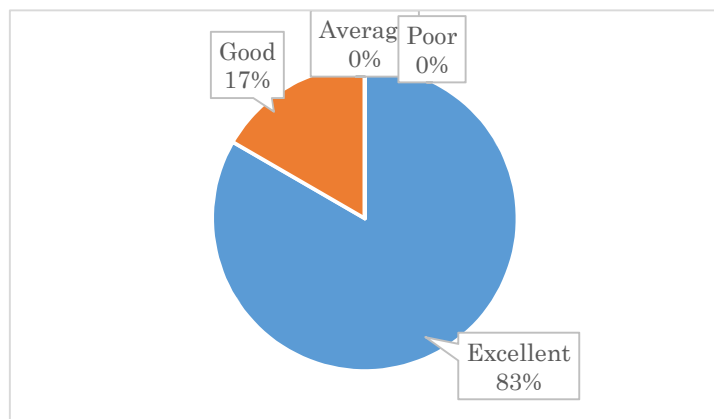
3. There was sufficient opportunity for open discussion/questions.



4. Did the Lecturer meet your expectations?



5. Overall, I would rate this session as being



6. Do you wish the Lecturer to be invited here again?

