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### DESCRIPTION OF PROGRAMS AND RESULTS

- Cariology Endodontology Pedodontontology Microbiology
- Periodontology and Oral Biochemistry
- Social Dentistry and Behavioural Sciences
- Oral Function and Restorative Dentistry
- Oral Radiology and Orthodontics
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INTRODUCTION

The annual report starts with chapters containing the annual survey of the director, and overviews of the scientific activities. As in preceding years the scientific performance is thereafter presented for each programme per department. Detailed information is given of dissertations, publications in journals indexed in the database of the Institute of Scientific Information, other scientific publications, professional publications, indicators of esteem, collaborations and societal impact.

Some issues for 2009 are specifically mentioned in this report. These include the organization of the research of ACTA in 6 new programs, specific attention to research in education, reductions in the budget for research, and the two main research themes on which the research of ACTA is focussed: “Oral infection and immunity” and “Bioengineering, reconstruction and function of teeth and bone.”

An overview of the output is presented in Table 1. This table summarises for each program and sub-program the number of publications that have appeared in 2009 in SCI-journals, the number of other scientific publications, and the number of professional publications and popularising publications. The personnel involved in full time equivalent (fte) and the impact factor-sum (IF-sum) are also included in this table; (data on abstracts are not included in this report).

We are pleased to note that the output in 2009 was high: the number of publications in SCI indexed journals, the IF-sum and the number professional publications were substantially higher than in any of the previous years of the research institute.

Research Institute ACTA

prof.dr. V. Everts director of research
dr. T.J.M. van Steenbergen co-ordinator of research

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REPORT OF THE DIRECTOR

The Research Institute ACTA

- mission statement
Dental research at the Academic Centre for Dentistry (ACTA) focuses on the study of health and diseases of the tissues in and around the oral cavity. Beside infectious diseases like dental caries and periodontal inflammatory processes, attention is paid to the development, function and regenerative capacities of the hard tissues in general, dysfunction of the masticatory system and diseases of salivary glands and oral mucosa. It is the general aim to improve strategies for diagnosis and prevention of diseases and functional repair of the affected tissues in and around the oral cavity.
In our attempts to fulfil this mission special care is taken to establish:
- integration of basic disciplines with the clinical fields
- education and further academic training of PhD-students
- promotion and improvement of the quality of the research in ACTA with special attention to the translation of the results into applications in clinical dentistry. To this end there is a vivid interaction with professional dental organisations and industries.

- positioning of the research institute
ACTA comprises the combined Faculties of Dentistry of the University of Amsterdam and the VU University Amsterdam. The ACTA Research Institute is the only institute for research of the faculty. National collaboration is organized in the Netherlands Institute of Dental Sciences (Interuniversitair Onderzoekoverleg Tandheelkunde, IOT). The IOT organises among others a 2-day conference on dental research in the Netherlands.
ACTA has two main research themes on which research is focused. These main themes are formed around scientifically strong groups and address relevant clinical topics. The first theme is “Oral infections and immunity”; this theme focuses on the etiology, prevention and therapy of caries, periodontal and endodontal infections. The second theme is “Bioengineering, reconstruction and function repair of teeth and bone”. This theme focuses on the biological process of adaptation and repair of bone and periodontium, and on biocompatibility of dental materials. Several ACTA research groups are included in the interfacultary research institute MOVE, a collaboration between the faculty of Human Movement Sciences, the VU University Medical Center and ACTA.
In previous years, ACTA research was organised in 12 research programs. Following the suggestions of the external review committee in 2008, the research was re-organised in 2009 in 6 programs. To obtain clear management responsibilities and to be able to make budget allocations to the various departments and sections, the 6 new programs and the various sub-programs were organised according to the new departments and sections that became effective in 2008 in the faculty.

- description of output, leading scientific journals in the field
The research has a relatively broad focus and deals with questions originating from clinical dental practice. Within the overall research programme there are considerable variations in the approaches taken, ranging from basic medical-biological to applied clinical. This is reflected in the type of journals in which ACTA researchers publish. Some groups primarily present their findings in journals read in the dental research community, while others also aim for the general medical-biological literature.

Evaluation of the research program
• **external evaluation**
In 2008 an external evaluation of dental research in the Netherlands was completed according to the new Standard Evaluation Protocol designed by the VSNU. In general, the evaluation committee considered the quality, production, relevance and academic reputation of dental research at ACTA as very good. The committee has given several recommendations for future research planning. Based on this report, the director of the research institute has conceived several intentions to further strengthen the research at ACTA. For more details about this evaluation we refer to the assessment report of the committee.

• **long time performance**
The performance of the research institute and its member groups is evaluated over a longer period (see Table 1). These data show that the number of dissertations per year has fluctuated between 6 and 20. This reflects variations in external collaborations (such as non-ACTA employees receiving a PhD from our universities) and - in particular - tenure staff members finishing their PhD. The current figure of about 12 dissertations reflects the number of PhD students 'employed'. In 2009 only 6 dissertations were published. However, in 2010 a substantial higher number can be expected.
The percentage of PhD students that finished their thesis averages at 90 % over the last 15 years, and the mean time period between start of employment and defending the thesis is 4.6 years. This figure is corrected for the 0.6 to 0.8 fte employment of several PhD students and for long leave of absence (e.g. maternity and illness) of some PhD students.
The main attention in the research assessment at the individual and department level is given to international publications in journals with a peer review referee system and an impact factor (SCI publications). This category shows a slightly increasing number over the last 15 years, despite a roughly stable input in fte scientific personnel. The average quality of the publications has significantly improved over that 15-year period, as judged by the continuous increase of the impact factor sum (see figure 4). In 2009 the highest number of SCI indexed publications and the highest IF sum was obtained. Also the number of professional publications was very high in 2009.

• **remarkable events in 2009**
Outstanding contributions for the year 2009 are publications in high ranking biomedical journals (i.e. Blood, PLOS Genetics, EMBO Journal, Physical Review Letters and FASEB Journal, all journals with an impact factor higher than 7), and seven publications in the Journal of Dental Research, which is considered the most prestigious dental journal with one of the highest impact factors in the category.
In addition to the output indicators given, the percentage of papers in high impact journals in the field gives valuable information. ACTA published in total 193 scientific papers in journals with an impact factor (SCI journals). 52% of these papers appeared in journals belonging to the field “Dentistry, Oral Surgery and Medicine”. 51% of these publications were in the top 25% of the journals and 70% in the top 50%. This means that a relatively large number of publications were published in the top journals in the field.
On a personal level a considerable number of ACTA employees rank in the top of the dental and biomedical research community, as determined by the various indicators of esteem. In 2009 a total of 13 awards were received by ACTA scientists for their achievements.

• **assessment at the department level**
When the research at the department or section level is considered it is clear that some groups perform very well throughout the years and are stable in terms of input and output parameters (personnel, PhD students, publications, dissertations etc). In the 2008 evaluation report of dental research in the Netherlands, these groups received ratings between 4 and 5 (on a 5 point scale). Programs that have
received excellent ratings in 2008 include those from the sections Cariology/Experimental Preventive Dentistry, Oral Biochemistry, Oral Cell Biology, and Social Dentistry.

**Societal impact**

- **impact on teaching and dental care**
The prime societal values of a strong research program in a dental discipline are the effect on teaching and on dental care. The research improves the quality of teaching given at ACTA, both for undergraduate students, graduate students, students participating in the post-initial specialist courses, and for PhD students. New findings and concepts are included in the curriculum at ACTA, but are also presented to dental practitioners at frequently held education activities, e.g. ACTA Quality Practice. The Research Institute participates in the ACTA curriculum by offering scientific training to all ACTA dental students. The societal impact of the research of ACTA is also focussed on the influence on patient care, both within ACTA and externally. Research on different main areas of interest contributes to improved prevention, diagnosis and treatment of relevant patient groups. In this annual report the societal impact of each research program is described in more detail in the respective chapters.

- **functions in the scientific community**
ACTA employees take an active role as executives in international scientific organisations (57 international functions), as members of editorial boards of international scientific journals (70) and in being leading in ‘wetenschappelijke verenigingen’ of researchers and dental practitioners in the Netherlands. Furthermore, the societal impact is evident from the organisation of symposia and conferences in the Netherlands and abroad, presentations for dentists, medical specialists and patient groups, memberships of advisory councils, and frequent contacts with the industry. In addition many scientists are also practising as dentists in specialized clinics at ACTA or in the Amsterdam region. Obviously the societal impact of their activities, individually as clinically active professionals and leading among their peers, should be acknowledged. This is also evident from the relatively large number of 168 professional publications. Some ACTA researchers also wrote popularising publications aimed at a more general audience. Several research findings were highlighted in the general press.

- **congresses attended and organized**
In 2009 ACTA researchers have again contributed actively in internationally held meetings, workshops and symposiums, both as organisers and participants. A total of 101 lectures were given as ‘invited speaker’ at international congresses and symposia. In addition a large number of presentations were given at international congresses after selection on submission of abstracts and during congresses and symposia for a Dutch audience. Due to this large number, congress abstracts are not listed in this annual report. A total of 12 international meetings were organised by members of the different departments of ACTA.

**Management**

- **finances**
The overall budget of the research institute is divided into a part controlled directly by the directorate and another part that is allocated to the departments. The institute budget (senso stricto) of K€ 1195 is used for the management of the institute, the salaries of the PhD students and post-doctoral employees, for travel allowances for these groups, for the organization of courses and for the annual two day IOT research meeting.

The research budgets for the departments (in total being K€ 4000) are distributed based on a model containing several parameters, such as external peer review,
bibliometric data over the last 5 years, education, PhD theses and external funding. In addition, standard bench fees are issued for the various categories of researchers (staff, post-docs, PhD students, technicians and other supporting OBP staff).

In addition to the university budget (1st source) ACTA scientists were involved in many research projects with external funding. The total amount of research grants (2nd source) was K€ 821, and the total amount of research contracts (3rd source) was K€ 1894.

In 2008 an extensive reorganisation was performed within ACTA. Part of this reorganisation was a substantial reduction in the research budgets, both for PhD students and for the research programs of most departments. This reduction has been executed for the largest part in the budget restrictions in 2009.

- **personnel**
The directorate of the institute comprises:

  - prof.dr. V. Everts, director of research 0.4 fte
  - dr. T.J.M. van Steenbergen, co-ordinator of research 0.6 fte
  - mrs. F.M. Meijer, secretary 0.6 fte
The activities of the Research Institute directorate consist of organising scientific meetings with presentations of PhD students, the screening of new research projects, the day-to-day interaction with graduate students on practical matters regarding their position, compiling the annual research report, the planning of graduate courses, allocating budgets for research to the departments, controlling the institutes budget and dealing with general correspondence on research issues with UvA, VU etc.

PhD students

PhD student appointments
All vacancies for PhD positions have been filled in 2009. In Figure 1 the number of new PhD students at ACTA is shown in the years 1990 to 2009. Over the years, about 23 % of all PhD students had a foreign nationality, about half of them from Europe, the rest from other continents. A mean of number of 9 new PhD students was appointed each year. Despite budget restrictions 10 new PhD students could be appointed in 2009. About half of all PhD students have a dental background (see Table 5). Of all PhD students about 50 % is female.

The research institute has started a procedure for allocation new PhD positions for the two main research themes. In 2009 three grants were awarded to each research theme in an open competition. This open competition will be continued in the coming years.

Figure 1. Numbers of new ACTA PhD students from the Netherlands and other countries

PhD Courses
The following courses are organised for PhD students: “Dentistry for non-dentist PhD students”, “Writing and Presenting in English”, “Methodology and Statistics”, “Introduction in SPSS” and “Oral Biology”. Dentistry is a multidisciplinary science and the background of the PhD students of ACTA is diverse. Therefore, most PhD students follow external courses on specific research areas, given by experienced lecturers of research schools in other disciplines.

PhD thesis duration and completion rate
Attention has been paid to the problems related to the social security benefits of PhD students and the time that PhD students need to finish their thesis. The mean time of 4.6 years between start and defence of the thesis within ACTA is slightly lower than the mean duration of PhD theses in research schools in the Netherlands of 5.1 years (see the report “Rendement en duur van promoties in de Nederlandse onderzoekscholen”, Oost en Sonneveld, 2004). In addition, the mean duration of preparing a thesis has shown a declining tendency over the years (Figure 2).

Over the last 20 years, about 90% of all PhD students in ACTA completed their thesis (Figure 3). This high percentage is substantially larger that the mean percentage of 75% of PhD students who finish their thesis in Dutch research schools according to the report by Oost en Sonneveld mentioned above.

The external review committee noted in 2008 that they were impressed by the organisation and practice of PhD training and supervision at ACTA. They concluded that it is a well organised programme, with a remarkably high dissertation rate.

Figure 2. Mean duration of completing the thesis of ACTA PhD students related to the year of entry
Figure 3. Percentage of ACTA PhD students finishing their thesis related to the year of entry.
Points of attention

• **HRM and retirement**
The research staff at ACTA has been comparatively young in the last decades. This was the result of the merging of the dental schools in the mid 1980’s. Now we are in a situation where heads of departments and senior scientists are retiring. In 2009 ACTA has written a plan for future appointments of full professors. Due to budget restrictions the number of persons involved in research had to be reduced slightly.

• **new building planned for 2010**
The new ACTA building located at the VU campus will bring together groups that are currently spread out over the city at four different locations. Optimal research facilities at the new ACTA building are planned to encourage collaboration between the research groups that require laboratory facilities. The increased number of scientists at one location will also facilitate to jointly take initiatives, such as in molecular aspects of dental research.

• **future developments**
Within the Netherlands, graduate schools will be formed at a local level to integrate research training both Master and PhD students. In 2007 the responsibility for PhD training at ACTA was transferred from the IOT to the ACTA Research Institute. In 2009 a description was made for the new ACTA Graduate School of Dentistry (AGSD) in which the PhD training will be organized. In 2010 this graduate school will be formally installed.

The research at ACTA has always been characterized by a wide range of different topics that covered most dental disciplines. The policy for the nearby future is on one hand to maintain all good performing research programmes, but on the other hand to focus more on specific research areas with an excellent performance. Larger research groups with a good potential will focus on biofilms and oral infections (including groups such as Cariology, Periodontology, Oral Biochemistry and Social Dentistry), and on bioengineering and reconstruction of bone and teeth (including groups such as Oral Cell Biology, Oral Kinesiology, Oral Implantology, Periodontology, Dental Material Sciences and Functional Anatomy). For the later focus area, close collaboration exists in the interfacultary research institute MOVE; a collaboration between ACTA, the VU University Medical Center and the faculty of Movement Sciences at the VU University Amsterdam. In coming years the research budget from the 1st source (University budget) might be seriously diminished due to budget restrictions. It will be a big challenge to compete for 2nd and 3rd source grants and to maintain or improve the high output that ACTA has produced in the past.

**Conclusion**
The analysis of the various parameters of performance shows that the research at ACTA is, despite of budget restrictions, increasingly improving state. Future performance will be dependent among others from the success in obtaining 2nd and 3rd source grants.
### SUMMARY OF PUBLICATION OUTPUT AND INPUT

Table 1. Comparison of research indicators

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<td>84</td>
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<td>Other scientific publ.</td>
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Footnotes:
- SCI = number of scientific papers in journals indexed in the database of the Institute of Scientific Information (ISI).
- wp1 = academic personnel funded by 1st source in fte; this includes direct funding by the university.
- wp2 = academic personnel funded by 2nd source in fte; this includes research grants obtained in national competition from NWO, STW and KNAW.
- wp3 = academic personnel funded by 3rd source in fte; this includes research contracts for specific projects obtained from external organisations, such as industry, governmental ministries, European Commission and charity organisations.

**Figure 4.** Impact factor sum of ACTA publications, total scientific publications in journals indexed in the science citation index (SCI publications) and total scientific personnel in fte.
### Table 2. Summary of the number of publications, impact factor sum and academic personnel in fte (year 2009)

<table>
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<th>Prog</th>
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**ACTA***  

|       |       | 6   | 5   | 35  | 176 | 193 | 111 | 40.8 | 0    | 7.95 | 12.85 | 61.60 |

This table summarises the number of publications that have appeared in 2009 in SCI-journals, the number of other scientific publications, and the number of professional publications. Also the personnel involved in full time equivalent (fte) and the impact factor-sum (IF-sum) are included in this table. The IF-sum was calculated for each department by adding together the impact factor values of all 2009 publications.

- **Dis** = number of dissertations
- **SCI** = number of scientific papers in journals indexed in the database of the Institute of Scientific Information (ISI). Between parentheses is the number of first authors belonging to the department in question
- **OSP** = other scientific publications (international, refereed)
- **PP** = professional publications, including publications for the general public
- **IF** = sum of impact factors as indexed by ISI. For publications with first author belonging to the department in question, 100% of the impact factor value is awarded to the department, for publications with the last author belonging to the department, 75% is awarded, and for co-authors 50% (only one co-author per department)
- **wp1** = academic personnel funded by 1st source in fte
- **wp2** = academic personnel funded by 2nd source in fte
- **wp3** = academic personnel funded by 3rd source in fte
- **wp tot** = all academic personnel

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**CEPM** = Cariology Endodontology Pedodontology Microbiology and Microbiology  
**EN** = Endodontology  
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**OR** = Orthodontics  
**VU** = location VUmc  
**AM** = location AMC
OWI  = Education Institute
* ACTA  = the total number of dissertations and papers reflects the total for ACTA; a dissertation or paper was counted only once; the total impact factor sum is not a summation of the data from each program

Table 3: fte of staff and PhD students (see Table 2) by type of position

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CEPM  = Cariology Endodontontology Pedodontontology Microbiology
PAB   = Periodontology and Oral Biochemistry
SOC/ST= Social Dentistry and Behavioural Sciences
FRT   = Oral Function and Restorative Dentistry

CE  = Cariology and Microbiology
EN  = Endodontology
PE  = Pedodontology
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PA  = Periodontology
OI  = Oral and Implantology
OK  = Oral Kinesiology
MW  = Dental Material Sciences
OC  = Oral Cell Biology
FA  = Functional Anatomy
TR  = Oral Radiology
OR  = Orthodontics
VU  = Location VUMc
AM  = Location AMC

Prosthodontics

RAO = Oral Radiology and Orthodontics
MKA = Oral and Maxillofacial Surgery
Table 4: PhD students by type of undergraduate training

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CEPM = Cariology Endodontology Pedodontology Microbiology

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OWI = Education Institute
Cariology Endodontology Pedodontology Microbiology

Diseases of the Dental Tissues and their Prevention

Program leader
Prof. dr. J.M. ten Cate
Department of Cariology Endodontology Pedodontology Microbiology
ACTA, Louwesweg 1
1066 EA Amsterdam
Tel: +31-20-5188440
E-mail: JM.ten.Cate@acta.nl

Full professors

J.M. ten Cate  C. van Loveren  W. Crielaard  P.R. Wesselink

Research objectives
The research program of the Department of Cariology Endodontology Pedodontology Microbiology covers physico-chemical, biochemical, microbiological and clinical aspects of enamel, dentin and root caries and infection of the root canal. These aspects are studied by means of various intra-oral and in vitro models which simulate the natural processes in the oral environment and which are designed to evaluate the effects of preventive measures and restorative materials and procedures, thereby covering the field of research from the molecular level up to in situ studies.

The formation, structure and properties of biofilms on hard tissue surfaces are studied extensively. The action of anticariogenic and antimicrobial agents are studied in the Constant Depth Film Fermenter (CDFF) and in a microtiter biofilm model.

Fluoride that, at present, is still the most effective caries-preventive agent is subject for further study. A better understanding of its mode of action, also on the molecular level towards microbial metabolism, as well as its possible side-effects (fluorosis and the induction of a fluoride-resistant oral microflora) will help to improve formulations and the development of fluoride-releasing devices and restorative materials.

In addition to fluoride, antimicrobials have come into focus as caries preventive agents. The efficacy alone or in combination with fluoride is still unknown and application protocols are not yet based on a critical evaluation of experimental and clinical results. The successes of antimicrobials in caries prevention are still limited.

The prevention of bacterial penetration in the root dentinal tubules and the root canal by a proper seal of the restoration is of major importance for the life expectancy of teeth. Modified disinfection methods of the root canal are studied. New filling methods and contemporary adhesive systems are tested in in vitro leakage models and in clinical studies.

Better treatment concepts (preventive as well as conservative and in relation to behaviour management) of dental caries in children are studied. Treatment concepts like ART (Atraumatic Restorative Treatment), the influence of total rehabilitation of the children’s dentition on general and oral health, consequences of restorative treatment on the child’s coping and anxiety are under investigation.
Results
Sub-program Experimental Preventive dentistry

An in-depth insight in the commensal and pathogenic microflora of the oral cavity is essential in understanding and promoting oral health as well as preventing and combating disease. Several research lines were followed to obtain such an insight. We sampled and, using recent advances in sequencing technology, sequenced microbiomes from several intraoral niches (dental surfaces, cheek, hard palate, tongue and saliva) in three healthy individuals. Within an individual oral cavity, we found over 3600 unique sequences, over 500 different OTUs or "species-level" phylotypes (sequences that clustered at 3% genetic difference) and 88 - 104 higher taxa (genus or more inclusive taxon). Each individual sample harboured on average 266 "species-level" phylotypes with cheek samples being the least diverse and the dental samples from approximal surfaces showing the highest diversity. Principal component analysis discriminated the profiles of the samples originating from shedding surfaces (mucosa of tongue, cheek and palate) from the samples that were obtained from solid surfaces (teeth). There was a large overlap in the higher taxa, "species-level" phylotypes and unique sequences among the three microbiomes: 84% of the higher taxa, 75% of the OTUs and 65% of the unique sequences were present in at least two of the three microbiomes. The three individuals shared 1660 of 6315 unique sequences. These 1660 sequences (the "core microbiome") contributed 66% of the reads. The overlapping OTUs contributed to 94% of the reads, while nearly all reads (99.8%) belonged to the shared higher taxa. We obtained the first insight into the diversity and uniqueness of individual oral microbiomes at a resolution of next-generation sequencing. We showed that a major proportion of bacterial sequences of unrelated healthy individuals is identical, supporting the concept of a core microbiome at health.

We investigated fluorescence intensity (FI) in *Streptococcus mutans* biofilms constitutively expressing green fluorescent protein (GFP). Upon addition of glucose FI in these biofilms increased significantly to steady state levels. FI-increase could be inhibited by oral care products in a dose-responsive manner. Lactic acid produced in these biofilms was measured at the end of the FI-recording. A linear correlation was observed between FI-increase and lactate production, irrespective of the inhibitor used. The viability of biofilm cells after chlorhexidine (CHX) titration was also examined. Reduction of FI-increase was observed at low concentrations of CHX whereas a loss in viability was only seen at high concentrations. In conclusion, GFP synthesis can be used as a metabolic activity indicator in *S. mutans* biofilms.

We studied the antimicrobial activity of vanadium chloroperoxidase (VCPO) reaction products on planktonic and biofilm cells of *Streptococcus mutans* C180-2. Planktonic and biofilm cells were incubated in a buffered reaction mixture containing VCPO, halide (either chloride or bromide) and hydrogen peroxide, and the killing efficacy was assessed by CFU counts. The enzymatic products formed by VCPO significantly reduced the viability of planktonic and biofilm cells compared to their negative controls and the effect on the biofilm cells was more effective than a 0.2% CHX treatment. We conclude that VCPO and its reaction products form a potent antimicrobial system against *S. mutans*.

In a study on virulence factors of *Enterococcus faecalis* we examined its ability to form biofilms. Most studies on biofilm formation have been carried out by using *E. faecalis* monocultures. Given the polymicrobial nature of root canal infections, it is important to understand biofilm formation of *E. faecalis* in the presence of other microorganisms. Eight clinical strains of *E. faecalis* were tested for biofilm formation on hydroxyapatite disks in the presence and absence of a *Streptococcus mutans* biofilm. Significantly more *E. faecalis* viable cells were found in biofilms in the presence of *S. mutans*. This phenomenon was, however, strain-dependent. Of the 8 strains tested, biofilm formation of strains AA-OR34, ER5/1, and V583 was not influenced by *S. mutans* biofilms. The results from this study, especially the strain difference, underline the importance of studying biofilm formation in a more realistic multispecies setting.

The interaction between oral microorganism was further investigated in a study on interkingdom communication between *Candida albicans* and *S. mutans* based on the
production of secreted molecules. *C. albicans* is commonly found in the human oral cavity, where it interacts with *S. mutans*. *C. albicans* is a polymorphic fungus, and the yeast-to-hypha transition is involved in virulence and biofilm formation. *S. mutans* UA159 inhibited *C. albicans* germ tube (GT) formation in cocultures even when physically separated from *C. albicans*. Only *S. mutans* spent medium collected in the early exponential phase (4-h-old cultures) inhibited the GT formation of *C. albicans*. During this phase, *S. mutans* UA159 produces a quorum-sensing molecule, competence-stimulating peptide (CSP). The role of CSP in inhibiting GT formation was confirmed by using synthetic CSP and a comC deletion strain of *S. mutans* UA159, which lacks the ability to produce CSP. Other *S. mutans* strains and other Streptococcus spp. also inhibited GT formation but to different extents, possibly reflecting differences in CSP amino acid sequences among Streptococcus spp. or differences in CSP accumulation in the media. In conclusion, CSP, an *S. mutans* quorum-sensing molecule secreted during the early stages of growth, inhibits the *C. albicans* morphological switch.

**Sub-program Clinical cariology**

Clinical aspects of prevention focused on optimalization of frequency of fluoride use. In an in situ experiment it was found that increasing the frequency of the number of daily applications from 2 to 3 gave further protection against dentin caries but not against enamel caries. In our program on special care with patient that received bone marrow transplantation the occurrence and severity of mucositis was studied. Analyses of saliva samples rejected our hypothesis that the occurrence and severity of mucositis was related to predominance of bacteria associated with gingivitis or parodontitis. Also we were not able to find a relation with shedding of viruses. In the study on changes in the oral biofilm and the protein composition of saliva in patients being irradiated for a tumour in the head-and-neck area distinct differences were found in the proteomic profiles between saliva of radiated parotic glands and the non-radiated counterparts. Further analysis will reveal which proteins are responsible for this difference.

**Sub-program Endodontology**

The application of cone beam computed tomography (CBCT) played an important role in our endodontic research this year. In dogs conventional periapical radiography (PR) was compared with the CBCT in diagnosing apical periodontitis using histology as a gold standard. Although both techniques produced no false-positives both produced false-negatives. The percentage of false-negatives was 75% for PR, whereas 54% for CBCT. Reduction of lesion size as observed on PR was not confirmed by CBCT and 80% of the expanding lesions revealed by CBCT were not detected by PR. The number of teeth with size-reduced radiolucency (= success) seems overestimated on PR, but with size-enlarged radiolucency (= failure) underestimated. In a clinical outcome study eight years after treatment evaluated by CBCT, 85% of all teeth still showed a clear radiolucency whereas only 4% using PR.

CBCT scans were found to be significantly more accurate in detecting vertical root fractures (VRF) in extracted human teeth than PR and in a comparison of different CBCT systems regarding their accuracy in detecting VRF, Next Generation i-CAT was significantly more accurate than Scanora 3D, Accuitomo-xyz, NewTom 3G and Galileos 3D.

In the irrigation studies, during ultrasonic activation of NaOCl the direction of the oscillation towards an oval extension resulted in a better cleaning efficacy. The application of pulsed ultrasound increased the efficiency only under certain conditions. In cooperation with the university of Thessaloniki, we have further developed and validated their Computational Fluid Dynamics (CFD) which makes it possible to rebuild the fluid dynamics during an irrigation procedure in the root canal.

Resazurin, a dye indicator for the metabolism of a biofilm, has been evaluated on a dual species biofilm (for the first time) and seems applicable for studying the activity of bacteria under various circumstances.
Using optical coherence tomography (OCT) it appeared that different root canal preparation methods and filling procedures caused dentin defects procedures that may develop into root fractures. Nickel titanium rotary instruments caused more defects than hand instruments and lateral compaction of gutta percha more than non compaction.

Differences in the ability of imaging techniques to reliably assess root canal fillings has been carried out in a project with the Max Planck institute in Berlin. Micro CT, Phased enhanced CT, electron microscopy and light microscopy are compared on different parameters like percentage of gutta percha filled area, ferret diameter and voids measurements. Different preparation techniques especially for ECM seem to induce artefacts and damage the fillings possibly giving improper information.

**Sub-program Paediatric dentistry**

Paediatric dentistry mainly focuses on child related aspects in the treatment of young patients. The 2009 results concentrate, as in the former year, on the relation between dental caries, its treatment and the consequences for a child's general health. Several articles and have been produced on the subject giving way to the understanding that full treatment, including not only curative but also preventative measures, is to be preferred above an approach of just prevention or restoration and/or extraction. Dental treatment seems to have no influence on the body growth. Furthermore attention has been paid to aspects that can possibly influence the quality of restorative procedures. The skills and experience of the operator is one of these influences, but also the dental assistant has a considerable influence on the quality. Other variables had have been investigated are the size of the cavity preparation, the method of tooth isolation the difference in material brands and the consistency of the material to be applied in the cavity preparation. In the next coming two years two these investigations will be finished with two PhD thesis.

The clinical trials of the section support the paradigm that restoration and the development of dental anxiety seem to be mutually exclusive: pain related experiences cause an increased pain sensitivity during sequential treatments. Since the avoidance of treatment has comparable negative consequences the results attribute to the complex nature of managing restorative dentistry in children. About child dental fear and quality of life the preparations for a PhD thesis are finished.
## Academic personnel in 2009 and 2010

### Research staff ACTA - CEPM/ Experimental Preventive Dentistry Cariology, Microbiology
(in full time equivalents)

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<td>Fatima Faustina Pereira, dds. A. de</td>
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| total 1st funding                            | 4,60  | 4,55 | 1 |
| total 2nd funding                            | 3,10  | 2,25 | 2 |
| total 3rd funding                            | 3,55  | 2,65 | 3 |
| **Total research staff**                     | 11,25 | 9,45 | |
### Research staff ACTA – CEPM/Endodontology (in full time equivalents)

<table>
<thead>
<tr>
<th>position</th>
<th>name</th>
<th>fte 2009</th>
<th>plan 2010</th>
<th>funding</th>
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<td><strong>Full professor</strong></td>
<td>Wesselink, prof.dr. P.R.</td>
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### Research staff ACTA – CEPM/Pedodontology (in full time equivalents)

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<th>position</th>
<th>name</th>
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<th>plan 2010</th>
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<td>Veerkamp, dr. J.S.J.</td>
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Output Experimental Preventive Dentistry/Cariology, Microbiology

Publications in journals indexed in SCI


Wetensch./publ. non-refereed
Other scientific publications (international, refereed)

Cate, J.M. ten (2009). The need for antibacterial approaches to improve caries control. Advances in Dental Research, 21, 8-12.


Professional publications


External reports


Indicators of Esteem

Grants: current projects with external funding

Cate, J.M. ten. Centraal onderzoeksfonds UvA 4 jaar, €60.000, - per jaar (2007-2010)

Cate, J.M. ten. Academy professor Royal Academy of Arts and Sciences (KNAW), total €1.000.000,- period 2008-2013.

Crielaard, W. KNAW/CAS (Chinese Academy of Sciences). Grant in the “China Exchange Programme”: travel grant for lectures in Beijing, Guangzhou and Hong Kong.


Exterkate, R.A.M. & Cate, J.M. ten. Development and evaluation of relevant dental in vitro biofilm models for the screening of new active compounds. GABA, Münchenstein, Switzerland; Start: October 2007 – October 2010, €150.000,-.

Strijp, A.J.P. van. The effect of fluoride concentration and lesion type on the rate of enamel remineralisation in an in situ caries model. GSK Consumer Healthcare, Brentford, UK. Start: March 2009-October 2009, € 20,000,-.

Strijp, A.J.P. van & Laheij, A.M.G.A. Efficacy of hesperidin (hpn) in preventing dentine collagen degradation in situ. Sunstar Inc., Osaka, Japan; Start: December 2008-June 2009, €20,000,-.


Zaura, E., Cate, J.M. ten & Crielaard, W. The Oral Cavity Chip. TNO / ACTA, Ministry of Economic affairs, Industry Phase 1, approx 400 k€, 50 % industry 50 % ministry of Economic affairs. Start: 2006-2010.


Membership of international editorial boards

Cate, J.M. ten: European journal of oral sciences
Cate, J.M. ten: International Journal of Dentistry
Cate, J.M. ten: Journal of Oral Microbiology
Cate, J.M. ten: Odontology
Loveren, C. van: International Journal of Dental Hygiene
Zaura, E.: Caries Research

Organisation of international congresses or symposia


Invited speakers at international congresses or symposia

Cate, J.M. ten (2009, September 03). Developments in de science behind prevention. Singapore, FDI Colgate symposium.

Cate, J.M. ten (2009, September 06). Global actions to improve oral health, from a research perspective. Phuket, Thailand, World Conference Preventive Dentistry.


Scientific awards/honours

Other international functions
Cate, J.M. ten: Management committee. European Research Group Oral Biology (ERGOB).
Cate, J.M. ten: Immediate Past-President IADR Board of directors.
Cate, J.M. ten: Honorary professor. Universidad Peruana Cayetano Heredia, Lima, Peru.
Soet, J.J. de: Membership secretary and webmaster ORCA (European Organisation of Caries Research).
Soet, J.J. de: Secretary general ORCA (European Organisation of Caries Research).
Veen, M.H. van der: Treasurer. Diagnostic Sciences Group IADR.
Veen, M.H. van der: Secretary General European Organization for Caries Research.

Societal impact
The societal impact of the research of the sub-program of the department of Experimental Preventive Dentistry, Cariology and Microbiology is evident from the impact on patient care, and from collaborations with the industry, as is shown by for instance the grants obtained and the external reports, and from the items listed below.

Interactions and collaborations with the industry and other non-university groups
Laheij, A.M.G.A., Loveren, C., van, Soet, J.J. de & Balm, A.J. (Netherlands Cancer Institute/Antonie van Leeuwenhoek Hospital), Rasch, C. (Netherlands Cancer Institute/Antonie van Leeuwenhoek Hospital), Schipper, R. (Laboratorium Wageningen Universiteit en Researchcentrum). Prospective study of changes in the oral biofilm and the protein composition of saliva in patients, being irradiated for a tumour in the head-and-neck area. GABA International AG. Dept. Scientific Affairs, Therwil, Switzerland.
Loveren, C., van, Buijs, M. & Kleverlaan, C.J. The addition of small amounts of calcium lactate to fruit juices reduces the risk of dental erosion. Friesland Foods.

Impact of the research on professionals
A total of 6 courses were given for dental professionals.

Memberships of national editorial boards
Loveren, C. Van is editor of the Nederlands Tijdschrift van Tandheelkunde.

Invited speakers at national congresses or symposia
A total of 9 lectures were given.

**Other national functions**

W. Crielaard is cluster coordinator in the Netherlands Systems Biology Institute.
Collaborations

- AMC Research Landsteiner Laboratory, Academic Medical Center.
- AMC, Department of Biomedical Optics, Amsterdam, the Netherlands.
- AMC, Department of Electron Microscopy, Amsterdam, the Netherlands.
- Erasmus MC, Rotterdam - Dep. of Biomedical Engineering.
- Federal University of Paraiba, Joao Pessoa, Brazil.
- Gaba International Ltd, Therwil, Switzerland.
- Inspektor Research Systems BV, Amsterdam, the Netherlands.
- Josephine Bay Paul Center, Marine Biological Laboratory, Woods Hole, MA, USA.
- LUMC kindergeneeskunde.
- MRC-Holland BV, Amsterdam, the Netherlands.
- NIZO, Ede
- NUTRIDENT consortium: (UCL Eastman Dental Institute), (University of Pavia), (University of Tel Aviv), (University of Genoa), (Goteborg University), (University of Verona), (Quest International), (Glycologic Ltd)
- Sanquin; Phagocyte Laboratory; Department of Blood Cell Research
- Saxion University of Applied Sciences, Deventer.
- State University of Campinas, Dental School of Piracicaba, SP, Brazil.
- Sunstar Inc., Osaka, Japan.
- TNO Quality of Life, Business Unit Food and Biotechnology Innovations, Microbial TNO, Genomics Group, Zeist, the Netherlands.
- Unilever Research, Port Sunlight, UK.
- Université Libre de Bruxelles, Brussels, Belgium.
- Université Paris 6 : Laboratoire d'Imagerie Paramétrique CNRS UMR 7623 Université Paris 6 15 rue de l'Ecole de Médecine F - 75006 Paris, France.
- Universiteit van Amsterdam Department of Molecular Microbial Physiology, Swammerdam Institute for Life Sciences, Faculty of Science, Amsterdam, the Netherlands.
- University Medical Center Göttingen Department of Medical Microbiology and National Reference Center for Systemic Mycoses, Göttingen, Germany.
- University of Amsterdam (microarray department (mass spectrometry) (Biosystems data analysis), (microscopy department), (fungal microbiology).
- University of Amsterdam Centre for Advanced Microscopy, Section of Molecular Cytology, Swammerdam Institute for Life Sciences, Amsterdam, the Netherlands.
- University of Amsterdam Microarray Department & Integrative Bioinformatics Unit, Faculty of Science, Amsterdam, the Netherlands.
- University of Amsterdam, Van 't Hoff Institute for Molecular Sciences.
- University of Bath, Bath, United Kingdom.
- University of Birmingham, Dental School, Birmingham UK.
- University of Dar es Salaam (MUCHS), Dar es Salaam, Tanzania.
- University of Dundee, Division of Biological Chemistry and Drug Discovery, School of Life Sciences, UK.
- University of Groningen, Faculty of Medical Sciences, Dept. of Dentistry.
- University of Groningen, Department of Biomedical Engineering.
- University of Liverpool, Liverpool, UK.
- University of Melbourne, Australia.
- University of the Mediterranean, Marseille, France.
- VU University Amsterdam, Department of Molecular Cell Physiology, the Netherlands.
- Wellington School of Medicine, Wellington, New Zealand.
- University of Oslo, Dept. Microbiology, prof.dr. I. Olson, Oslo, Norway.
- University College of London, Queen Mary's School of Medicine and Dentistry, prof.dr. M.Curtis, London.
- Department of Medical Microbiology and Infection prevention, Vrije Universiteit, prof.dr. C.M.J.E. Vandenbroucke-Grauls, Amsterdam, the Netherlands.
- Laboratory of Immunogenetics, Vrije Universiteit Medical Center, prof.dr. A.S. Peña, Amsterdam, the Netherlands.
- Department of Oral and Maxillofacial Surgery and Maxillofacial Prosthetics, University of Groningen, prof.dr. B. Stegenga, Groningen, the Netherlands.
- Department of Microbiology, Ghent University, Dr. S. van trappen and prof.dr. P. de Vos.
- Department of MicroArrayFacility, dr. T. Breit, Universiteit van Amsterdam, the Netherlands.
- Faculty of Veterinary Medicine, dr. H. Booij-Vrielings, University of Utrecht, the Netherlands.
- Department of Health Sciences, Kristianstad University, prof.dr. S. Renvert, Kristianstad, Sweden.
Current PhD projects


Output Endodontontology

Dissertations

Publications in journals indexed in SCI

Other scientific publications (international, refereed)

Indicators of esteem
Grants: current projects with external funding
Macedo R. French Dutch Academy exchange program. €2500,-
Wesselink, P.R. et al. Ministry OCW €850.000,-. Simodont project for three years (one third of this amount each year).

Membership of international editorial boards
Peters, L.B. International endodontic journal
Shemesh, H. Journal of Endodontics
Sluis, L.W.M. van der Endodontic Practice Today
Wesselink, P.R. Deutsche Zahnärztliche Zeitschrift
Wesselink, P.R. Endodontic Practice Today
Wesselink, P.R. Endodontie
Wesselink, P.R. International endodontic journal
Wu, M.K. International endodontic journal

Invited speakers international congresses or symposia
Sluis, L.W.M. van der (2009, May 27). Success and failure in endodontics, a critical review and an overview of the irrigant activation systems in endodontics. Mexico City, Mexico., International Meeting of the Mexican Endodontic Society.

Other international functions
Wu, M.K.: Member. Research committee ESE.

Societal impact
The societal impact of the research of the sub-program of the department of Endodontology is evident from the impact on patient care and from the lectures for dental professionals, as listed below.

Impact of the research on professionals
A total of 21 courses and master classes were given for dental professionals. In addition, 15 presentations were given to various dental organisations.

Organization of national congresses and symposia
L.W.M. van der Sluis organised the congress of the NVVE. ’Desinfectie gewoon doen’.

Invited speakers at national congresses or symposia
A total of 4 lectures were given.

Collaborations
- Erasmus MC, Rotterdam, Optical Coherence Tomography.
- Hebrew university, school of dental medicine, dept of endodontics, Jerusalem, Israel.
- Laboratoire de Sonochimie des Fluides Complexes ; Institut de Chimie Séparative de Marcoule, France.
- Max Planck institute for colloids and interfaces , Potsdam, Germany.
- Max Planck Institute, Golm, Germany, Synchrotron based nano- tomography.
- University of Thessaloniki. Dental faculty, dept. of endodontics, Thessaloniki, Greece.
- University of Twente Physics of Fluids (POF) group of the Netherlands, (STW project: Ultrasonic irrigation of root canals: Endodontic therapy through micro streaming and cavitation).

Current PhD projects
Jiang LM. Ultrasonic cleaning of the root canals. Supervisor: prof.dr. P.R. Wesselink; co-

Output Pedodontology

Publications in journals indexed in SCI


Other scientific publications (international, refereed)


Professional publications


Indicators of esteem
Grants: current projects with external funding
Amerongen, W.E. van & Kemoli, A. Nuffic fellowship, PhD project, total €75.000,-, since 2005.


Membership of international editorial boards
Amerongen, W.E.: Brazilian Journal of Pediatric Dentistry
Amerongen, W.E.: Pediatric Dentistry
Veerkamp, J.S.J.: Brazilian Journal of Pediatric Dentistry

Invited speakers international congresses or symposia
Other international functions
Amerongen, W.E. van: Board member. IAPD.

Societal impact
The societal impact of the research of the sub-program of the department of Pedodontontology is focussed on the impact on patient care.

Other national functions
J.S.J. Veerkamp is Chairman of the Consilium Pedodontologicum.

Invited speakers at national congresses or symposia
A total of 3 lectures were given.

Impact of the research on professionals
Several courses were given for dental professionals.

Collaborations
- Medische Zending, Paramaribo, Surinam.
- São Paulo State University Department of Pediatric and Social Dentistry, (UNESP), Araçatuba, Brazil.
- St. Jeugd tandverzorging, Paramaribo, Surinam.
- University of Nairobi, Nairobi, Kenya.
- WHO Collaborating Centre Nijmegen, Nijmegen, the Netherlands.

Current PhD projects
Periodontology and Oral Biochemistry

Biology, Physiology and Pathophysiology of the Periodontium
Protective Functions of Saliva for the Oral Cavity

Program leader
Prof. dr. B.G. Loos
Department of Periodontology
ACTA, Louwesweg 1
1066 EA Amsterdam
Tel: +31-20-5188558
E-mail: B.Loos@acta.nl

Full professors

B.G. Loos  U. van der Velden  W. Beertsen  E.C.I. Veerman

Research Objectives Periodontology
Periodontitis is a destructive inflammatory disease of the supporting tissues of the teeth. It is caused by bacteria and affects a substantial part of the human population. Over the age of 45 years it is a major cause for tooth loss. This research program is devoted to clarify the individual differences in susceptibility to periodontitis and to investigate the mechanisms involved in periodontal breakdown and repair/regeneration. In addition the evaluation of the efficacy of new preventive and therapeutic measures is part of the program.

The following questions are addressed:
1. Susceptibility to periodontitis and systemic effects:
   - Which are the host factors involved?
   - To what extent are hereditary factors important?
   - What are the systemic effects of periodontitis?
2. Bone degradation:
   - How is the osteoclast formed and how is its activity regulated?
3. Prevention and treatment of gingivitis and periodontitis:
   - Which are the most effective measures to prevent and control oral health?

Results
Periodontitis is a complex disease because of its multifactorial etiology (bacteria, genetics and life style factors). A limited number of family studies suggested that periodontitis aggregates in families. Although family studies might give a first impression of familial aggregation, they can not distinguish between the influence of genetic and shared environmental effects as an explanation for the familial clustering of periodontitis. In this respect twin studies are especially useful. For chronic periodontitis relatively few twin studies have been carried out, but the results suggest a substantial role of genetic factors in the etiology. However these studies have limitations because they were not based on selected periodontitis patients. Therefore a twin study was performed to assess, in monozygotic (MZ) and dizygotic (DZ) twin pairs selected on the basis of one sib of a twin pair suffering from moderate to severe chronic adult periodontitis, the contribution of genetics, life style factors and periodontal pathogens to the clinical phenotype of the
disease. The results showed that both MZ and DZ twins were discordant regarding attachment loss and bone loss. The discordance was greater in DZ compared to MZ twins. In MZ twins the discordance could not be explained by education, smoking, body mass index and periodontal pathogens. Therefore, the factors that play an important role in the development of chronic adult periodontitis are not straightforward pathogenic bacteria and genetics. We concluded that perhaps also epigenetic changes are important. New studies on the role of epigenetics in periodontitis will be initiated.

Regarding gaining further insight in genetic factors for the susceptibility of periodontitis we are still following two strategies: 1) candidate gene approach; 2) genome wide search. In 2008 and 2009 both the Departments of Periodontology and Oral Microbiology have joined forces with the European Periodontal Genetics (EPG) consortium of which we are one of three founding partners. Genetic epidemiology with the candidate gene approach was applied to the 600+ patients with aggressive periodontitis (AgP), 300+ patients with chronic periodontitis (CP) and 800+ controls that are part of EPG. We have found no associations between periodontitis and SNP’s in the genes encoding for IL-1 (publication late 2008), NOD-1 (publication 2009), IL-6 (publication 2010), but we did find significant associations between periodontitis and SNP’s for the COX1 and B-defensin genes (both 2010 pubs). Moreover we found a genetic relationship between periodontitis and cardiovascular disease.

The second approach (genome wide search) has now been applied (publication 2010): we found AgP to be strongly associated with the intronic SNP rs1537415, which is located in the glycosyltransferase gene GLT6D1. We replicated the association in a panel of Dutch generalized and localized AgP patients. In the combined analysis including 1758 subjects, rs1537415 reached a genome-wide significance level of P= 5.51 x 10^-9. We are currently still expanding our biobank of AgP patients; a new genome wide search is planned with newly developed gene chips, containing 1 million gene polymorphisms dispersed over total genome. The Institute for Clinical Molecular Biology from the Medical Center University of Kiel (P.I. prof. S. Schreiber) is financing these efforts.

The systemic effects of periodontitis are still being investigated. A pro-coagulant state in periodontitis may also be related to activated platelets. We have demonstrated for the first time that blood platelets in periodontitis are present in vivo in an activated form. Moreover, specifically $P$. gingivalis and $A$. actinomycetemcomitans can activate blood platelets ex vivo. We will continue this work by further studying the role of platelets in periodontal disease and health. The systemic effects of periodontitis will further be studies: we have initiated an ambitious intervention study, where we apply various antimicrobial regimens in conjunction with traditional scaling and rootplaning. The effects of therapy on acute phase proteins, white blood cells and pro-coagulant state will be investigated.

Osteoclasts are multinucleated cells specialized in bone resorption. Extracellular acidification by these cells is essential for this process. Chloride/bicarbonate exchange by anion exchanger 2 (Ae2) is involved to maintain a near-neutral intracellular pH (pHi) during proton pumping. In mice deficient for Ae2 the long bone osteoclasts were not active. Surprisingly, calvaria osteoclasts expressed a normal activity. We found that the sodium dependent co-transporter Slc4a4 was expressed in calvaria osteoclasts but not in long bone osteoclasts. Calvaria osteoclasts employ both Ae2 and Slc4a4, whereas osteoclasts present in the long bones make use only of Ae2. These data provide strong support for the functional diversity between different osteoclast populations.

Multinucleated osteoclasts can form from diverse cell types of the myeloid lineage such as macrophages, monocytes and bone marrow precursors. It is unclear, however, which developmental stage of the lineage present in bone marrow are more prone to become osteoclasts. The differentiation potential of early blasts, myeloid blasts and monocytes, successive stages of myeloid differentiation, was compared. We could identify myeloid blasts as the precursor which is equipped to become an osteoclast within a short period of time. The osteoclast is the cell type responsible for the unwanted bone degradation in periodontitis. Therefore, agents that specifically interfere with the osteoclasts
without leading to undesired side effects such as osteonecrosis of the jaw in case of bisphosphonates are desired. AstraZeneca inhibitor c-Src inhibitor AZD0530, which has been used in clinical trials without reported side effects, is such a candidate. c-Src is highly expressed in osteoclasts and their precursors. AZD0530 interfered with osteoclast formation and activity, most strikingly when added early in osteoclastogenesis.

Transcription factor C/EBPβ is present in various isoforms. In collaboration with dr. J. Smink, Max Delbrueck Center for Molecular Medicine, Berlin, Germany, it was established that the balance of expression of isoforms of transcription factor C/EBPβ turned out to be crucial in osteoclast differentiation. Increased osteoclast activity was found in C/EBP knock-out mice and in mice expressing the short isoform of C/EBP.

In collaboration with drs. E. van Beek and T. van den Berg, Department of Molecular Immunology and Cell Biology, VU University, Amsterdam/ Sanquin Research Laboratory, Amsterdam, the role of SIRPa, a potential regulator of osteoclast activity, was elucidated. Osteoclast formation was not changed in SIRPa knock-out mice, but the resorption was markedly reduced.

Studies on the prevention and treatment of periodontal diseases concentrate on the efficacy of electric/manual toothbrushes, dentifrices, mouth rinses, antibiotics and techniques for professional debridement. One 6-months study showed that a CPC-mouthrinse significantly reduced the amount of dental plaque. However this was not reflected in a significant improvement of the gingival condition of the panelists. A study with an oral irrigator showed that 4-weeks of interdental irrigation resulted in a significant improvement of the gingival condition however not in a reduction of the amount of visible plaque. Furthermore the outcome of systematic reviews indicates that a tongue-cleaner may reduce bad breath. However this effect is transient. The comparison of 0.12% and 0.2% shows a significant difference in favor of 0.2%. However the difference is clinically negligible. For hexetidine and hydrogen peroxide there is limited scientific evidence to draw conclusions of their effect on plaque and gingivitis. Consequently there appears to be no indication to advice patients using these products to improve the gingival condition or reduce plaque accumulation.

**Research objectives Oral Biochemistry**

Without saliva all oral tissues will be affected by exogenous factors as microorganisms and aggressive nutritional components. Saliva apparently protects oral surface tissues against harmful attacks. The primary aim of the research of the Department of Oral Biochemistry is to analyse the contribution of the individual salivary components, particularly of the (glyco) proteins to maintain oral tissues healthy, also in relation to microbiological aspects of oral infections. The research is focussed on answering the following questions:

1. What are the biological functions of the salivary (glyco) proteins and subsequently what is the biological significance of the variation in glandular (glyco) proteins from the submandibular, sublingual and parotid glands?
2. What is the biological significance of the whole set of salivary proteinase inhibitors, particularly the specific salivary cystatins? Are they involved in the regulation of oral inflammatory processes? What is the relation between immunoneuro-regulatory processes in the periodontium and mucosa and the expression of inhibitory proteins in the salivary glands?
3. Can synthetic peptide analogues of histatins be applied as broad spectrum antibiotics, particularly to *Candida albicans* and other oral pathogens? In future such peptides might be useful in newly developed saliva substitutes.
4. The effect of conditions known for their potential to impair oral health (such as the use of medical drugs, systemic diseases and psychological stress) on the quality of saliva.
5. Influence of saliva on the interaction of oral microorganisms with oral epithelial cells.

**Results**

**Properties and working mechanism of antimicrobial peptides**
Previously we have designed a chimeric peptide in which the spatial orientation of two antimicrobial domains of bovine lactoferrin is mimicked as confirmed by NMR structural analysis (in collaboration with Dr. H. Vogel, Univ. of Calgary, Canada). This chimera exhibits enhanced antimicrobial activity against both yeasts and a variety of Gram-positive and Gram-negative bacteria compared to the individual peptides. The interaction of the chimera with model membranes is currently further investigated using several biophysical methods including Differential Scanning Calorimetry, Circular dichroism and NMR analysis (In collaboration with Dr. M. Bastos, Univ. Porto, Portugal and Dr. H. Vogel, Univ. of Calgary, Canada). In ongoing collaborative studies with a number of research institutes the efficacy is explored of antimicrobial peptides against several notorious multidrug-resistant bacteria, e.g. *Vibrio haemolyticus, Vibrio cholerae, MRSA* (University of Culiacán Sinaloa, Mexico), *Microbacterium tuberculosis*, *Helicobacter pylori*, *Pseudomonas aeruginosa* (Dept Medical Microbiology, Vumc), *Burkholderia pseudomallei*,(Dept. of Oral Diagnosis and Tropical Diseases, University of Khon Kaen, Thailand).
New developments
- Oral Biochemistry has become involved as partner in the Consortium Partner Immunovalley. This consortium is aimed at enhancing economic and scientific activities in the field of veterinary infection diseases.
- A novel PhD project will start in 2010, in which will be investigated the application of antimicrobial peptides in fighting anti-warfare agents has been (collaboration with Department of Defense and TNO).

Saliva as diagnostic fluid
Currently we explore the potential of saliva as diagnostic fluid for monitoring various diseases. One of the diseases which potentially can be diagnosed using saliva is Idiopathic Nephropathy (IgAN). This disease is caused by deposition in the kidney of aberrantly glycosylated IgA. We have developed compounds to facilitate detection of aberrantly glycosylated IgA molecules in patient saliva. In collaboration with dr. I. van Die, Dept. of Molecular Celbiology and Immunology, VUMC, Amsterdam this line of investigation will be continued.

New developments
- Dr. F.J. Bikker who has been appointed as post-doc in 2009, will explore in collaboration with TNO the feasibility of peptide substrates for diagnosis of periodontitis and halitosis.
- In addition, via dr. F.J. Bikker we have become partner in the European IMPOCT consortium, aiming to develop new technologies for diagnosis.

Saliva, epithelia and microorganisms
This line of research is focused on the role of saliva in protection and maintenance of oral epithelia. It was already found that salivary histatin enhances in vitro wound closure of epithelial cells. We now have found that histatin enhances re-epithelialization in a 3D-wound model. In addition, we have determined the minimal domain and were able to enhance the potency of histatin 1,000-fold by cyclization. Future studies are designed to identification of the cellular receptor and elucidation of signaling pathways. In collaboration with prof. H.J. Ploegh, Whitehead Institute, USA) a novel enzyme-based procedure for efficient cyclization of peptides has been developed giving yields > 90%, much higher than those obtained with classical organic chemical methods (2-10%).

Interactions of salivary agglutinin with microorganisms, its role in innate immunity
In previous research the bacteria binding domains of Salivary Agglutinin (SAG) has been mapped. Recent research is focusing on the role of SAG in the innate immune system. In collaboration with Sanquin (Diana Wouters, Timo van de Berg) SAG has been shown to activate the complement system through the lectin pathway by binding to mannose binding lectin (MBL). In collaboration with dr K. Hartshorn (New York) was shown that salivary agglutinin bind influenza A viruses and enhances its uptake in neutrophils. In collaboration with Niclas Karlsson (University of Goteborg, Sweden) and Anthony Moran (University of Galway, Ireland) glycosylation of SAG is studied. Glycosylation of SAG is different from the homologous protein in tears an lung. Helicobacter pylori bound to carbohydrate residues on SAG. SAG of different donors showed glycosylation dependent differences in affinity for H. pylori.

Interaction of statherin with microorganisms
It was demonstrated that salivary statherin peptide inhibits in C. albicans the transition of yeast to the more infectious hyphal form. In future research is aimed at the identification of the minimal active domain. In collaboration with dr. David Beighton (King’s College London, Dental institute) adhesion of Actinomyces ssp. to statherin will be studied.

Impact of systemic diseases on saliva
This line of research, which examines the impact of systemic diseases on the composition and properties of saliva, focuses on patients with kidney disease (prof.dr. P.M. ter Wee, VUMC), patients with gastrointestinal diseases (dr. A.A. van

43
Bodegraven, VUmc), and patients receiving stem-cell transplantation for malignant diseases (dr. J. Raber-Durlacher, LUmc). Results indicate that the level of xerostomia is associated with the severity of the systemic disease.
Diagnosis and treatment of saliva-related oral problems
Since May 2007 dr. C.P. Bots, dentist, has joined the saliva clinic at ACTA, which guides patients suffering from saliva-related problems. More than 150 patients have been diagnosed and provided with advice. In addition, patient oriented research has been undertaken to evaluate the efficacy of oral moisturizing gels for the alleviation of xerostomia. In another project it was investigated whether the level of oral dryness can be estimated by judging the appearance of the tongue.

Academic personnel in 2009 and 2010

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### Output Periodontology

**Dissertations**


**Publications in journals indexed in SCI**


Other scientific publications (international, refereed)

Professional publications
Academic Centre for Dentistry Amsterdam

recessievorming. In W. Beertsen, M. Quirynen, D. van Steenberghe & U. van der Velden (Eds.), Parodontologie (pp. 455-472).


External reports


Membership of international editorial boards
Beertsen, W.: European journal of oral sciences
Loos, B.G.: Journal of Clinical Periodontology
Loos, B.G.: Journal of Dental Research
Loos, B.G.: Oral Health and Preventive Dentistry
Slot, D.E.: International Journal of Dental Hygiene
Velden, U. van der: Journal of Clinical Periodontology
Weijden, G.A. van der: International Journal of Dental Hygiene

Scientific awards/honours


Invited speakers at international congresses or symposia


Other international functions
Loos, B.G.: Board member. Continental European Division (CED).
Loos, B.G.: External examiner MSc. EFP Graduate programs in periodontology.
Loos, B.G.: Member publications committee. International Association of Dental Research (IADR).
Raber-Durlacher, J.E.: Member advisory board. MASCC/ISOO Mucositis Study Group.
Raber-Durlacher, J.E.: Chair section Dysphagia. MASCC/ISOO Oral Care Study Group.
Raber-Durlacher, J.E.: External assesor for promotion of dr. Logan to associate professor. School of Dentistry, University of Adelaide, Australia.
Velden, U. van der: External examiner MSc. EFP Graduate programs in periodontology.
Velden, U. van der: Chairman post graduate education committee. European Federation of Periodontology.
Velden, U. van der: Board Member. European Federation of Periodontology.

Societal impact
The societal impact of the research of the sub-program of the department of Periodontology is evident from the impact on patient care, and from collaborations with the industry, as is shown by for instance the grants obtained.

Interactions and collaborations with the industry and other non-university groups
Several collaborations exist with the industry, evident from grants obtained over the years from among others Philips and Proctor % Gamble.

Impact of the research on professionals
G.A. van der Weijden gave interviews for the Nederlands Tandartsenblad.

Invited speakers at national congresses or symposia
Several presentations were given for dental professionals.

Other national functions
B.G. Loos is a member of the Concilium Parodontologicum.

Courses for dental and medical professionals
Scientists of the department participated in courses in the Netherlands for dentists and oral hygienists.

Lectures during courses for dental and medical professionals in the Netherlands
Several presentations were given for dentists and oral hygienists in the Netherlands.

Interactions with the general public
N.A.M. Rosema gave a radio interview for the program Atlas, autumn 2009.

Collaborations
- Universiteit van Amsterdam, Klinische Chemie (prof.dr. A. Sturk, dr. R. Nieuwland), Amsterdam, NL.
- ACTA, Dept. Oral Microbiology (prof.dr. W. Crielaerd), Amsterdam, NL.
- Department of Molecular Medicine and Gene Therapy, Lund University, Lund, Sweden (dr. J. Richter).
- University of Sheffield (dr. D. Buttle), Sheffield, United Kingdom.
- Celltech (dr. A. Docherty), London, United Kingdom.
- Padjadjaran University, Dept. Periodontology (dr. S. Lambr), Bandung, Indonesia.
- Unilever Research (dr. D.J. Page), Port Sunlight, United Kingdom.
- Ludwig Boltzmann Institut fur Osteologie (prof.dr. P. Fratzl) Vienna, Austria.
Current PhD projects


Output Oral Biochemistry

Publications in journals indexed in SCI


Other scientific publications (international, refereed)

Professional publications

Publications aimed at the general public

Publications aimed at the general public
Patents
Indicators of Esteem
Grants: current projects with external funding

Bikker F.J. & Veerman, E.C.I. Defensie/TNO. Application of antimicrobial peptides as anti-warfare therapeutics. Total amount: € 280,000,-.

Bolscher J.G.M. Co-investigator of research project on the "Antimicrobial peptides against Burkholderia pseudomallei". Grant from Thailand government, covering PhD-student, visits to foreign research labs and visits of co-investigator to Khon Kaen University (2006-2010). Principal Investigator: prof.dr. Suwimol Taweechaisupapong, Department of Oral Diagnosis, Khon Kaen University, Thailand.


Invited speakers at international congresses or symposia


Other international functions


Societal impact
The societal impact of the research of the sub-program of the department of Oral Biochemistry is evident from the impact on patient care, and from collaborations with the industry, as is shown by for instance the grants obtained.

Lectures during courses for dental and medical professionals in the Netherlands

Brand H.S. participated in 5 courses

Other national functions

H.S. Brand is a contributor for the Nederlands Tijdschrift voor Tandheelkunde. E.C.I Veerman is member of a user committee for ZON-MW.

Invited speakers at national congresses or symposia

Two presentations were given at a symposium in the Netherlands.

Collaborations
- ACTA, Orale Microbiologie (dr. J.J. de Soet)
- ACTA, afdeling Mondziekte en Kaakchirurgie (prof.dr. E. Bloemena).
- VUmc, afdeling Medische Microbiologie (prof.dr. C.M.J.E Vandenbroucke-Grauls, dr. B. Appelmelk).
- VUmc, Afdeling Moleculaire Celbiologie en Immunogenetica, sectie Immunomodulatie (prof.dr Y. van Kooyk, Dr. T.B.H. Geijtenbeek).
- VUmc, Afdeling Moleculaire Celbiologie en Immunogenetica, sectie Glycoimmunologie (dr. I van Die).
- VUmc, afd Dematologie (dr. S. Gibbs, prof.dr. R. Schepers)
- Universiteit van Amsterdam, AMC, Afdeling Celbiologie en Histologie (dr. J. van Marle).
- Universiteit van Amsterdam, AMC, Afdeling Humane Retrovirologie (prof.dr. B. Berkhout).
Current PhD projects


Social Dentistry and Behavioural Sciences

Oral Health-related Well-being and Behaviour

Program leader
Prof. dr. J. Hoogstraten
Social Dentistry and Behavioural Sciences
ACTA, Louwesweg 1
1066 EA Amsterdam
Tel: +31-20-5188 247/246
Fax: +31-20-5188 233
E-mail: J.Hoogstraten@acta.nl

Full professors

J. Hoogstraten  A. de Jongh  G.H.W. Verrips

Research objectives
In line with recent developments within the section and ACTA, concerning both staff-composition and research reorientation, and stimulated by the very good/excellent rating of the section’s research efforts received from the International Review Committee, research is now focused on Oral Health-related Well-being and Behaviour, of both patients and general dental practitioners and their staff. Three general objectives are guiding the section’s research efforts now: one, to monitor and improve the oral health of the Dutch population and to increase patients’ quality of life and satisfaction and the public trust in dentistry; two, to assess the determinants and general consequences of occupational stress and well-being of general dental practitioners and their staff; three, to study dental anxiety and pain, two major barriers to seek and maintain dental care, of both adult and child-patients, from a multidimensional perspective and with the help of psychologists, dentists, and double-trained staff-members.

Results
A survey of Dutch adults (n=1959) showed that the prevalence of dental fear was 24.3%. Among phobias, dental phobia was the most common (3.7%), followed by height and spider phobia. Fear of dental treatment was associated with female gender and intrusive re-experiencing. Findings suggest that dental fear is a remarkably severe condition with a long duration.

Data from a sample of dental patients (n= 1462) indicate that a wide variety of dental experiences are related with both high dental anxiety and dental phobia, while general traumatic experiences were not.

Research findings also indicate that anxious patients felt more pain during a dental injection than less anxious patients. In fact, 28 % of variance of pain felt was accounted for by fear of dental pain, the use of surface anaesthesia and gender.

Concerning treatment of an anxiety disorder it was shown that questions about the relative efficacy of EMDR- a promising treatment option- for the treatment of anxiety disorders remain still largely unanswered. A behaviour checklist meant to be used to raise awareness for toothache of very young children among parents and healthcare providers was presented: “a Toothache traffic light” based on the earlier developed Dental Discomfort Questionnaire.
Results of research do show that short-term consequences of third molar surgery have a strong effect on patients’ quality of life. Experiencing postoperative complications substantially amplifies this effect. It appeared, in another study, that a high information text prior to alleged third molar extraction was rated as indeed more informative, requiring less additional information, and led to higher satisfaction by all participants. Follow-up research implying actual TME-patients is planned.

The hypothesis that young children’s oral health-related quality of life improves after oral rehabilitation under general anaesthesia was tested. This hypothesis was empirically confirmed in a randomized controlled trial. In a theoretical paper – published as a Focus-article in EJOS – it was argued that existing oral health-related quality of life questionnaire are a mix of both a formative measurement model and a reflective measurement model whereas the instruments are usually analyzed as if they are based on a reflective model only. Implications are serious.

Research findings do suggest that body dysmorphic disorders (BDD) are relatively common among patients attending cosmetic clinics. Collaborative research effects with other ACTA-departments were extensive. We refer to the research results sections of these departments (Oral Function, Oral and Maxillofacial Surgery, Pedodontology, and Orthodontics).

### Academic personnel in 2009 and 2010

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### Dissertations
Publications in journals indexed in SCI


Other scientific publications (international, refereed)


Professional publications


Indicators of Esteem
Membership of international editorial boards
Gorter, R.C.: European Journal of Dental Education
Jongh, A. de: Journal of EMDR Practice and Research

Invited speakers at international congresses or symposia

Gorter, R.C. (2009, April 23). Burnout and job engagement in veterinary professional career: risks and challenges. Amsterdam, the Netherlands, European Veterinary Conference.


Organization of international congresses or symposia

Other international functions
Jongh, A.de: Treasurer. EMDR European Association.
Jongh, A. de: Member scientific committee. EMDR International Association.

Societal impact
The societal impact of the research of the sub-program of the department of Social Dentistry is evident from the impact on patient care and from the items listed below.

**Interactions with the general public**
A. de Jongh gave about 30 interviews for radio broadcasting and Dutch magazines and journals, most of these about the prevalence of dental fear. R.C. Gorter gave 3 interviews about burn-out. M.A.J. Eijkman had one interview. M.A.J. Eijkman wrote 7 articles in the Dutch newspaper NRC/Handelsblad.

**Invited speakers at national congresses or symposia**
A total of 10 presentations were given.

**Other national functions**
A. de Jongh, R.C. Gorter and A.J. van Wijk are members of a total of 4 national committees and advisory councils.

**Courses for dental and medical professionals**
A total of 5 courses were given in the Netherlands for dental professionals. A. de Jong is supervisor of the post-initial training for "tandarts-angstbegeleiding".

**Lectures during courses for dental and medical professionals in the Netherlands**
A total of more than 20 presentations were given for dentists in the Netherlands.

**Organization of national congresses and symposia**
R.C. Gorter was involved in the organization of two symposia in the Netherlands.

**Collaborations**
- **Gorter, R.C.:** University of Dundee, Dental Health Services Research Unit, Prof. R. Freeman, Dundee, Scotland.
- **Gorter, R.C.:** University of St Andrews, Butt Medical School, Prof. G. Humphries, St Andrews, Scotland.

**Current PhD projects**
Oral Function and Restorative Dentistry

Oral MOVE

Program leader
Prof.dr. F. Lobbezoo
Department of Oral Kinesiology
ACTA, Louwesweg 1
1066 EA Amsterdam
Tel: +31-20-5188412
E-mail: F.Lobbezoo@acta.nl

Full professors

Research Program “Oral Move”
MOVE is an Interfaculty Research Institute of the VU University Amsterdam: a joint venture of the Faculty of Human Movement Sciences, and parts of the VU University Medical Center and of the Academic Centre for Dentistry Amsterdam (ACTA). MOVE covers a broad spectrum of research. Within MOVE, fundamental as well as applied human movement research is performed, with a strong integrative and translational signature. The focus of the research is on healthy and pathological movement, as well as on the musculoskeletal system and its disorders. The MOVE-related research of ACTA is organized in the Research Program “Oral MOVE”. Pivotal in Oral MOVE is a healthy oral system, which is essential for an unhampered execution of functions like biting, chewing, swallowing, talking, laughing, and kissing, thereby determining an individual’s general health and well-being.

Currently, three out of the five sub-programs of Oral MOVE are officially part of the Interfaculty Research Institute MOVE, viz., Oral Cell Biology, Functional Anatomy, and Oral Kinesiology. The sub-programs “Oral Cell Biology” and “Functional Anatomy” are embedded in the MOVE program “Loading and Tissue Regeneration” of the MOVE theme “Musculoskeletal Biology”. The sub-program “Oral Kinesiology” is part of the MOVE program “Systems Physiology” of the MOVE theme “Structure and Motion”. In the next coming years, the other two sub-programs of ACTA’s MOVE-related research (Oral Implantology and Dental Material Sciences) will be admitted to the Interfaculty Research Institute MOVE as well. From the below-given descriptions of the five sub-programs, it can be learnt which specific research topics are being addressed and how the research of the ACTA Research Program Oral MOVE is related to that of the Interfaculty Research Institute MOVE.

Research Priority Area “Oral Regenerative Medicine”
The Interfaculty Research Institute MOVE has chosen ‘Regenerative Medicine’ as one of its Domains (i.e., a collaboration of researchers on a key topic). Likewise, Oral Regenerative Medicine (ORM) has been formulated as the Research Priority Area of the Oral MOVE program, in which parts of the Oral MOVE research activities take place. A healthy oral system is characterized not only by sound dental and periodontal tissues, but also by a healthy musculoskeletal system (muscle and bone/cartilage). Musculoskeletal tissues can be affected by numerous pathologies and conditions. In case of tissue loss, the replacement or regeneration
of degenerating/degenerated cells, tissues, or organs is needed to restore or establish normal function (Mason A, Dunnill PA. A brief definition of regenerative medicine. Regen Med 2008; 3(1):1-5). ORM studies these processes both fundamentally and translationally in multidisciplinary settings, in which dentistry/oral medicine closely collaborate with medical disciplines like orthopedics and neurology, both within and outside The Netherlands. The main objectives of ORM-related research are: (1) to develop better strategies to prevent degeneration of oral tissues and/or organs; and (2) to develop minimally invasive, regenerative treatment strategies when prevention fails and treatment is required. Both the prevention of degeneration and minimally invasive, regenerative treatments illustrate the ongoing shift from curing diseases to preventing them. Clearly, a focus on early diagnosis will play an important role in enabling this shift. The outcome of all ORM’s research efforts will be an increased understanding of degenerating/degenerated oral tissues and an improved ability to replace or regenerate these tissues, thereby restoring oral function. From the below-given descriptions of the five sub-programs of Oral MOVE, it can be learnt which research activities take place within the framework of the ORM Research Priority Area.

Sub-program Oral Kinesiology

Research objectives
Chewing, laughing, smiling, talking, yawning etc. are important movement functions of the human masticatory system. Sometimes patients are confronted with problems in performing these functions, which are related to a malfunction of the jaw muscles and/or the temporomandibular joint. This program studies the normal and disturbed functions of the jaw muscles and the temporomandibular joint, the factors that influence these functions and the treatment modalities that preserve or restore these functions.

Results

Influence of (experimental) orofacial pain upon the sensorimotor control of the human masticatory system:
In a collaborative study with the departments of Physiology and Biophysics, Faculty of Medicine, Ege University, Bornova, Izmir, TURKEY, it was shown that intense eccentric contractions of the human jaw-closing muscles can provoke symptoms of delayed-onset-muscle-soreness in the jaw muscles. This suggests that the conclusions drawn from pain and fatigue inducing experiments performed so far, viz., that the jaw-closing muscles are rather fatigue resistant, may be due to difficulties imposing eccentric contractions upon these muscles. These new findings open the possibility to further study the onset and aetiology of myofascial TMD pain.

Pathophysiology, diagnosis and treatment modalities of chronic temporomandibular disorders (TMD):
For musculoskeletal disorders like low back pain and fibromyalgia, evidence is growing for fear of movement to play an important role in the development of chronic pain. In temporomandibular disorder (TMD) patients, however, this construct has not received any attention yet. Therefore, 1) a generally used instrument to measure fear of movement, the Tampa Scale for Kinesiophobia (TSK), was adapted for its use in TMD patients, 2) the psychometric properties of this TSK-TMD were assessed, and 3) the degree of fear of movement in various subgroups of TMD (i.e. pain, joint sounds, and limited movements) was evaluated. In a sample of TMD patients and consistent with prior evaluations of the original TSK, confirmatory factor analysis indicated a two-factor model to provide the best fit of the TSK-TMD, with activity avoidance and somatic focus as its subscales. This two-factor solution also shows generally good reliability and convergent validity. A moderate association was found between the presence of TMD pain and the degree of fear of movement, while, especially for activity avoidance, strong associations were found with TMD sounds and limited mandibular movements. These results provide a basis for use of the TSK-TMD in future clinical research.
The role of ethnic background upon the level of pain and psychological distress was studied in a group of 504 TMD patients. Ethnic background turned out to be associated with the psychological distress of TMD patients, regardless of their socioeconomic status, but not with the level of their TMD pain or with their oral parafunctional activities. This indicates that in TMD patients with psychological distress, ethnic background should be taken into account.
Pathogenesis, diagnosis and treatment modalities of internal derangements of the temporomandibular joint:
Since it is still unknown which factors are responsible for closed locking in the temporomandibular joint (TMJs) with a reducing anterior disc displacement (ADDR), it was experimentally tested whether TMJ loading by intensive gum chewing could influence disc reduction. Fifteen ADDR patients with complaints of intermittent locking and 15 ADDR patients without intermittent locking (controls) participated in the study. The amount of mouth opening (RDR), expressed as a percentage of the maximum mouth opening, at which the disc reduction takes place, was quantified using the sagittal condylar movement traces. RDR was recorded at baseline, after max. 60 minutes of gum chewing at a constant, habitual pace, after 20 minutes rest, and, if necessary, after 72 hours. The smallest detectable difference in RDR was 10%. While the post-chewing RDR didn't differ from its baseline value in the patients without intermittent locking, it did differ significantly in patients with intermittent locking. In two of these subjects, the RDR had increased, and in four subjects, a temporary locking was observed. The locking resolved within 72 hours after the chewing exercise. Thus, while TMJ loading by means of intensive gum chewing does not influence the disc reduction in ADDR patients without intermittent locking, it can delay, or even prevent a disc reduction in patients with complaints of intermittent locking.

Pathophysiology, diagnosis and treatment modalities of (sleep-related) oral movement disorders:
In an RCT-design, the treatment effects of a mandibular advancement device (MAD) were compared with those of nasal CPAP (nCPAP) and an intra-oral placebo device. Sixty-four OSA patients (52.0 ± 9.6 years) were randomly assigned to three parallel groups: MAD, nCPAP, and placebo device. From all patients, two polysomnographic (PSG) recordings were obtained at the hospital: one before treatment and one after approx. 6 ± 2 months of treatment. After treatment, the MAD group and the nCPAP group showed similar, but significantly larger reductions in the AHI than the placebo group. In conclusion; MAD seems equally effective as nCPAP in the treatment of OSA. Therefore, MAD may be considered as the primary treatment for OSA.

Sub-program Oral Implantology and Prosthodontics
Research objectives
The general mission of the program is to improve the dentist’s knowledge of the treatment modalities that preserve or restore the patient’s function. This with special emphasis on Oral Implantology. The present research program comprises three major research domains, Stimulation of bone growth around Oral Implants, Oral Implants used in prosthetic dentistry and Peri-implantitis.

Results
Stimulation of bone growth around oral implants
A slow release of BMP’s (bone morphogenetic proteins) from the implant coatings is thought to have a stimulating effect on bone growth. Besides oral implants, bone filling osseoconductive materials and membranes have also been coated and have become integrated in the department’s research projects.
As part of a new experimental dental-implant model for the in-vivo testing of functionalized surfaces within unfavourable bony environments, thirty-four goats were implanted with 4 implants per animal (in collaboration with Bern University, Switzerland and Inner Mongolia Agriculture University China). All animals have been sacrificed and the histological analysis has been evaluated. The results have been evaluated and now in the preparation for publication.
The Ca/P ratio influences biomimetic coating formation on implants and bone fillers. Three different kinds of coating materials for titanium, zirconia, Bio-Oss, bio-ceramics and membranes were developed in our group.
In a sinus lift model (clinical trial), 22 patients have been treated with Bio-Oss functionalized with BMP-2. The histology results have been analysed. This study
results have been presented at various scientific meetings. They are now in preparation for publications. The use of tissue expanders to expand the mucosa in areas where bone augmentation is the indicated treatment. 28 goats have been treated and slaughtered, histology analysis has been carried out and the results have been evaluated. The first report has been submitted for publication. A clinical trial is now being carried out in an external dental practice. Osteoclast-Controlled Protein Release from Calcium-Phosphate-Based Bone-Substitute Materials: A Biomimetic Coating Technique. This project in collaboration with Frank Kleinke, Clinical Research Department, University of Bern Switzerland has finished. The PhD thesis titled “Angiogenesis in bone: Implications for bone tumor therapy and bone tissue engineering” will be defended in January 2010. In 2009, we have developed a new product which we think will have a future in bone regeneration therapy. This calcium phosphate material has BMPs incorporated in it and is expected to totally resorb within a number of weeks during which the BMP’s will be released. This product is now under research in our department (in vitro with cell cultures) and an animal experiment is carried out in collaboration with Zhejiang University, China. The human study has been designed. Oral Implants used in prosthodontic dentistry Pre-surgical CAD/CAM Planning and Fabricating Surgical Guide and Superstructure on Dental Implants in order to restore the fully edentulous mandible/maxilla. A total of 35 patients have been treated. The in vitro stress and misfit analysis have been carried out. It seems that the misfit of the CAD/CAM planned and fabricated superstructure is less than that which can be acquired using the conventional impression technique. Two articles have been accepted for publication, one of which is in press. Second technique has been developed for the treatment of patients who are partially dentate. The first results are in a write up stage.

BIOS-2. The Breda Implant (BIOS) overdenture study. An evaluation after 8 years. This project has run since 1992. This year the variables concerning the hard and soft peri-implant tissues after 8 years after the initial treatment have been evaluated. In cooperation with the department of oral microbiology, we are also looking at genetic factors related to bone loss and smoking. The microbiology has been evaluated. The DNA analysis has been carried out All OPT’s has been evaluated with the radiology department. The statistical analysis is now being carried out. An article on the clinical results is in press. This progress of this project remains rather slow. GT Stoker has personal problems making it difficult for him to find time to work on the project. A multi centre randomized controlled clinical trial comparing conventional loading of an overdenture on two implants with a bar to immediate loading of an overdenture on two implants with a bar. Patient treatment started in February 2007 and up till now all of the patients have been treated. The project is now being carried by one of the Oral Implantology (OI) master students. The first article has been submitted for publication. Implants supporting free end saddles. A multi center clinical trial was carried out internationally (Breda, Colombia and New Zealand). All the patients have been treated and the 6 month evaluation has been carried out. In 2007 the second patient evaluation has taken place. The third evaluation was carried out in 2008. The material is now being analyzed in the Dunedin Dental School (NZ). Our department is analyzing the patient satisfaction. The results are in a write-up stage. A new project which is being carried out in our department together with the department of experimental Dermatology of the VUMC (Dr. Susan Gibbs) is “Developing an autologous full thickness graft which can be used in the oral cavity. A.P. Vriens (Tio,). No fundamental progress can be reported on this project this year. As the Tio working on it finds most of his time consumed by his training. Peri-implantitis In 2009, we have started a research project on peri-implantitis together with the section of oral microbiology. The idea behind this project is that to look at peri-implantitis from various angles. One of them is the type of bacteria and the colonization thereof that we see in peri-implant defects; the second angle is to look at the debris on the contaminated implant surface and to look for a method in which
we can clean the surface in vitro and later on in vivo. A third approach is to find a way to change the surface tension of the implant surface, which lasts long enough to enhance the bone regeneration process and as a therapy can be carried out in vivo. The fourth angle is to find a way to change the surface tension of the implant surface which lasts long enough to enhance the bone regeneration process and as a therapy can be carried out in vivo. We have one PhD student from our department (Oral Implantology and Prosthetic Dentistry) and one from Oral Cell Biology working on this project. We further have two guests who look at the surface tension and the bone regeneration.
Sub-program Dental Material Sciences

Research objectives
The general objective of this program is to predict and improve the clinical performance of dental restorative materials covering the complete range of materials involved in the procedures of creating restorations with direct or indirect techniques. Composition, structure and fabrication of the materials as well as their handling and application techniques are studied in vitro as well as in vivo. The increasing trend to replace the difficult and costly manual procedures by automated procedures with information technology is being studied on its merits. In particular the possible advantages of the automated production of indirect restorations by CAD/CAM technology are evaluated. The physical properties and quality of restorations, as well as the esthetic properties, influenced by digital color measurement and reproduction, are subject of our attention. CAD/CAM technology offers the possibility to use new strong ceramic materials as a base for all-ceramic restorations. Mainly the research into Y-TZP zirconia indicates that its excellent physical properties make it an alternative for metal alloys in stress-bearing substructures. Apart from basic scientific research, a substantial part of the research involves the development of laboratory experiments and equipment that simulates the clinical conditions as closely as possible, ultimately to be used as standard quality control tests (so-called accelerated tests).

Since 2002 the research area of the section includes clinical research on dental materials. For instance a study into the performance of indirectly made resin composite crown restorations has been started. In 2003 in the department clinic a start was made with special consulting hours where patients with suspected health effects of metals used in dental restorative materials, can be referred to. This project has developed both clinically and on basic science aspects quite well.

Results
Substantial progress has been made in revealing the mechanisms that play a role in the stress distribution in specimens exposed to tensile stresses in bond strength tests. For this research FEA was used to demonstrate the stress distributions in test specimens in more detail. It was shown that specimen size and shape had a significant influence on the bond strength. Based on this knowledge new studies towards the bonding properties, strength and design properties were started. Special attention was paid to (i) core build-up and post systems, (ii) orthodontic bracket systems, and (iii) cantilevered teeth and (pre)molars. Furthermore, fracture toughness and fatigue of model systems were investigated. Various experimental and new commercial versions of low shrinking restorative monomer systems were tested in our department.

The development of ‘smart’ ceramics such as Y-TPZ-Zirconia is of main interest as a strong base for full ceramic restorations that might replace the use of metal-based materials in restorative dentistry. In applied science nano-technology is an example of a field of increasing interest, which has been introduced in dentistry. The CAD/CAM-technology in dentistry has reached a stage that can compete with all manual restorative methods. This fast-growing technique becomes a main area of interest in the field of quality assessment. The main challenges are now in developing a reliable bond between as Y-TPZ-Zirconia and dentine or enamel. Another clinical problem of major concern is still the veneer chipping.

Color measurements and automated color reproduction with the aid of CAD/CAM are of great scientific and commercial interest. A number of color measurement devices were tested and their clinical performance has been evaluated. Interestingly, due to shift from metal-based materials to Y-TPZ-Zirconia the color of restorations are again problematic because of the completely different background color. A PhD-grant on the topic “The Science of Creating Tooth Color” was obtained.

In 2003 a laboratory test was developed to determine intra-orally the composition of metal alloys used for indirect restorations. In the last 2 years, together with the departments of clinical immunology, pathology and dermatology of the academic hospital (VUmc) a clinical study was conducted. Seventy patients with suspected health effects on dental materials were evaluated, while 30 healthy patients were
included as control. Patch test, lymphocyte transformation tests, and cytokine production of immunologic reactions of the T-lymphocytes were investigated. The incidence of metal-ion release by the use of metal-based restorative materials is a topic of main interest. However, in spite of an extensive amount of literature, there is a lack of overview on the dental consequences of these effects.

The department has 3 PhD-students who are in their last phase of their training. This asks much time and effort of the staff. These students will defend their thesis in 2010. Moreover an equal amount of thesis is expected to be defended in 2011. The overall scientific output in terms of citation and publishing rate is rather high. The chairman of the department, Prof.dr. A.J. Feilzer, became in June 2009 dean of the faculty. The board of ACTA is still deliberating on the opening of a vacancy for a successor.

**Sub-program Oral Cell Biology**

**Research objectives**

The program "Bioengineering of Bone and Periodontium" of the Department of Oral Cell Biology studies the biological processes of functional adaptation and guided regeneration of bone and periodontium. Research focuses on fundamental aspects of mechanotransduction, and tissue engineering of bone, cartilage, and periodontium. The results are used in more applied research towards repair and regeneration of jawbone and periodontium, and prevention/treatment of infections around implants.

Mechanical stress is capable of modulating the activity of osteoblasts and osteoclasts, which are orchestrated in their activity by the mechanosensitive osteocytes, and the activity of periodontal fibroblasts, which mediate adaptation of the tissue to a changing force regime. To clarify the cell biological processes of mechanical adaptation, in vitro experiments are performed in which the reaction of bone and connective tissue cells to mechanical stress is studied in cell and organ culture, and at the single cell level. The results are verified in studies of bone under weightlessness conditions during space flight, and in disuse osteoporosis. Bone growth factors are locally produced growth factors, which can be used for clinical regeneration of bone and cartilage. They are involved in fracture repair and in the regulation of normal bone growth, but they also play a role in pattern formation of the dentition and the skeleton in the early embryonic phase. Their role in regeneration of bone and periodontium is studied using cell and animal experiments.

The tissue engineering part of the research is focused around (1) the synthesis, deposition, and degradation of the collagen network in bone and cartilage, (2) the use of adipose tissue-derived mesenchymal stem cells in combination with injectable scaffolds (hydrogels) or resorbable scaffolds and growth factors for tissue engineering of a.o. jaw bone augmentation by sinus floor elevation and the intervertebral disc, (3) the role of mechanical factors in stem cell differentiation,(4) the intercellular communication between bone cells and stem cells, and (5) the mechanisms of bone degradation by bone-site specific osteoclasts.

**Results**

**Regeneration of bone and periodontium**

Adipose tissue-derived mesenchymal stem cells (ASCs) in combination with bone morphogenetic protein-2 (BMP-2) or transforming growth factor-β1 (TGF-β1) are under evaluation for bone tissue engineering. We found that ASCs modify collagen-I to form a functional bone extracellular matrix for tissue engineering, dependent on the growth factor added.

Tumor cells in the bone microenvironment initiate a vicious cycle of bone degradation by osteoclasts. c-Src is highly expressed in tumors and osteoclasts, and therefore drugs like AZD0530, designed to inhibit Src activity, might selectively interfere with both tumor and osteoclast activity. We found a reversible effect of AZD0530 on osteoclast formation and activity, which makes it a promising candidate to temper osteoclastic bone degradation in bone diseases with enhanced osteoclast activity such as osteolytic metastatic bone disease.
Mechanical adaptation and regeneration

Adaptation of bone mass is brought about by the coordinated actions of osteoclasts and osteoblasts, orchestrated by signalling factors produced by osteocytes in response to mechanical loading. In patients with systemic inflammatory diseases, the balance between bone formation and resorption is often disturbed resulting in bone loss. We found that the cytokines TNFα and IL-1β inhibit mechanical loading-induced NO production by osteocytes via abrogation of PFF-stimulated [Ca2+]. We thus identified a novel pathway by which cytokines could affect bone mass in inflammatory diseases by reducing the physiological response of osteocytes to mechanical loading.

Stochastic resonance is exhibited by many biological systems, where the response to a small stimulus is enhanced with the aid of noise. We found that the bone cell response to a small periodic fluid shear stress was increased with the addition of noise, which suggests that noise enhances the activity of bone cells in driving the mechanical adaptation of bone.

Matrix strains due to external loading are different in bones of different pathologies with different bone mineral density (BMD), and are sensed by the osteocytes. The mechanosensitivity of osteocytes is strongly influenced by their morphology. We explored whether osteocyte morphology plays a role in various bone pathologies with different BMD using confocal laser scanning microscopy and nano-CT, in osteopenic, osteoarthritic, and osteopetrotic bone. We found that osteopenic osteocytes were relatively large and round, osteopetrotic osteocytes were small and discoid shaped and osteoarthritic osteocytes were large and elongated. These differences might reflect an adaptation to matrix strain due to different external loading conditions, and indicate differences in osteocyte mechanosensitivity.

Nitric oxide is produced by osteocytes through the activity of constitutive endothelial nitric oxide synthase (eNOS) or inducible nitric oxide synthase (iNOS). We investigated eNOS and iNOS expression in osteocytes during orthodontic force application, and found that eNOS mediates bone formation in the tension area, while iNOS mediates inflammation-induced bone resorption in the compression area.

Wnts are involved in mechanical adaptation of bone, but whether mechanical loading modulates Wnt signaling in osteocytes is unclear. We found that loading activates the Wnt canonical pathway through functional Wnt production in osteocytes, and that NO might play a role in PFF-induced Wnt production. We also found that mechanical loading activates the beta-catenin signaling pathway by a mechanism involving nitric oxide, focal adhesion kinase, and the Akt signaling pathway. This provides a framework for understanding the role of beta-catenin in mechanical adaptation of bone.

A problem worldwide is the increase in enamel fluorosis, a developmental defect in enamel due to ingestion of too much fluoride (F) during childhood. We postulated that the primary effect of enamel fluorosis was transient overproduction of protons in developing enamel by F-stimulated apatite formation. We speculate that the buffering capacity of ameloblasts was not sufficient of neutralizing this excess of protons which induces many secondary changes. Using pH sensitive fluorescent dyes we showed that osteoclast cell cultures deficient in three out of five isoforms of Ae2 are indeed insufficient in (intracellular) pH regulation when secreting protons during pit formation. These data suggests that partly the same molecular mechanisms operate in osteoclasts and in ameloblasts but for different purposes. Ameloblasts secrete bicarbonates to neutralise acids in forming enamel, whereas osteoclasts secrete protons to acidify and degrade bone. Partial inactivation of isoforms Ae2a, b1 and b2 impaired osteoclastic bone resorption of long bones but not in orofacial bone. The data confirmed previous findings that there are probably different populations of osteoclasts, one class operating in orofacial bone and another in long bones. Such differences may eventually lead to development of therapeutics selective for osteoclasts in particular anatomical areas (orofacial bone) but not in other areas throughout the body.

Sub-program Functional Anatomy
Research objectives
The research program deals with the general question of how histological, anatomical, (neuro-) physiological and mechanical properties of the jaw muscles, jaws and jaw joints affect the development, maintenance and degradation of form and function of the masticatory system. The mission is to obtain fundamental knowledge to enable prevention of oral dysfunction and recovery of pathologic structure and function in the masticatory system.

The research is concentrated at the following three themes:
1: Unraveling of the mechanisms of bone adaptation to its mechanical function with emphasis to (1) architecture, structure and mechanical loading, (2) tensions and deformations at the tissue and cellular level and (3) the response of bone cells to tensions and deformations controlling growth and adaptation.
2: Testing of hypotheses regarding bone adaptation by analysis of the effects of experimentally altered loading on shape and structure of bone using animal models.
3: Application of biomechanical models in clinical situations to predict risks of aberrant loading patterns and loss of tissue in relation to muscle atrophy, loss of dental elements, jaw joint dysfunction, oral implants, orthodontic treatment and oral surgery.

Results
An animal model to assess the relationship between masticatory muscle activation and mechanical loading of the mandibular bone has been applied successfully. For the first time long term (up to 48 hours) bone strain has been measured concomitant with EMG elicited in adjacent masticatory muscles in freely moving rabbits. Herewith the full spectrum of daily loading of the mandibular bone can be analyzed. In order to compare this spectrum with bones that bear the weight of the body similar data has been obtained from the tibia. Preliminary analysis has shown that compared to the tibia, the daily loadings in the mandible are larger in number, especially at frequencies of about 5 Hz. Their peak amplitudes, however, are lower. These loading patterns have been linked to the local architecture of the mandibular bone. Remarkable variations in the degree of mineralization were found and could be, at least partially, associated with the function of the adjacent musculature.

Analysis of the quality and quantity of the cartilaginous structures in normal and arthrotic temporomandibular joints has been performed with MicroCT. To that aim cadaverous joints were treated with a contrast medium. Using this technique enables to relate the characteristics of the cartilage to those of the adjacent subchondral bone. Methods to reconstruct all relevant shapes and their mutual position are in progress. These are necessary to enable the construction of biomechanical models to study the mechanical interaction of the bone-cartilage interface in the joint dynamically.

To predict the external and internal behavior of trabecular bone during loading Finite Element Analysis (FEA) can be applied. To that aim a geometrical model, reflecting the fine architecture of the relevant structure is composed of a large number of regularly shaped elements. As each of these elements is assumed to have a certain stiffness (the stiffness of bone tissue) the transfer of external loads to internal tensions and deformations can be predicted. As it has been demonstrated earlier this stiffness varies with the local mineral content, but such variation is generally neglected. For the first time it could be demonstrated that in
the mandibular condyle this simplification leads to an overestimation of the local
tensions, while local deformations are hardly affected. Furthermore, it has been
shown that the observed mineral distribution in the trabeculae of the mandibular
condyle leads to a construction that is more compliant to bending and more stable
in compression than was considered before. This knowledge will be applied to
analyze the altered biomechanical interaction between the articular cartilage and
the subchondral bone during progress of osteoarthritis.
Using biomechanical modeling the question whether or not the temporomandibular
joint is loaded during jaw opening has been clarified. With an extensive sensitivity
analysis it has not been appeared possible to load the joint more heavily during
unloaded jaw closing than during jaw opening. The underlying biomechanical model
will be further adapted to predict mechanical causes for the occurrence of
difficulties in closing the jaw in subjects with a so-called hypermobile joint.
The collagenous fibers in the articular disc of the temporomandibular joint have a
distinct orientation. It has been shown using dynamical FEA that these orientations
coincide with the tensile strain patterns that can be predicted during habitual jaw
open-close movements. It was striking that, even though this structure is relatively
thin, these patterns differed between the superior and inferior layers. The
perspectives are that these consequences can be applied for tissue engineering of
this structure which is intended to repair or replace deteriorated joints.
### Academic personnel in 2009 and 2010

#### Research staff ACTA – FRT/Oral Kinesiology (in full time equivalents)

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### Research staff ACTA – FRT/Oral Cell Biology (in full time equivalents)

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Output Oral Kinesiology

Publications in journals indexed in SCI


Other scientific publications (international, refereed)
Academic Centre for Dentistry Amsterdam


Scientific publications (non-refereed)

Professional publications

Indicators of Esteem

Membership of international editorial boards
Lobbezoo, F.: Journal of Craniomandibular Function
Lobbezoo, F.: Journal of Oral Rehabilitation
Visscher, C.M.: Journal of Craniomandibular Function

Invited speakers at international congresses or symposia
Koutris, M. (2009, April 01). Voyage to the East Mediterranean. Izmir, Turkye, Center for Brain Research, Department of Physiology, Faculty of Medicine, Ege University Bornova.
Annual Research Report 2009


Scientific awards/honours

Other international functions
Koutris, M.: Member of the Research Committee. European Academy of Craniomandibular Disorders (EACD).
Lobbezoo, F.: Member of the Research Committee. European Academy of Craniomandibular Disorders (EACD).

Societal impact
The societal impact of the research of the department of Oral Kinesiology is focused on the influence on patient care, both within the department and externally. Research contributes to improved prevention, diagnosis and treatment of relevant patient groups. The societal impact is evident from the items listed below.

Interactions and collaborations with the industry and other non-university groups
Lobbezoo F. Member of the International Clinical Advisory Board of Medotech, a Danish company that produces biofeedback devices for the treatment of sleep bruxism.

Invited speakers at national congresses, symposia
Two presentations were given at symposia in the Netherlands.

Other national functions
F. Lobbezoo, C.M. Visscher and S.I. Kalaykova were members of a total of four national committees and advisory councils related to oral kinesiology.

Courses for dental and medical professionals
Two courses were organized for dentists in the Netherlands.

Lectures during courses for dental and medical professionals in the Netherlands
A total of 32 presentations were given for dentists, medical specialists, and physiotherapists in the Netherlands.

Collaborations
- Slotervaart General Hospital, Department of Clinical Neurophysiology and Brain Mapping Laboratory, dr. H.L. Hamburger, Amsterdam, the Netherlands.
- Slotervaart General Hospital, Department of Radiology, dr. J.P. Klein, Amsterdam, the Netherlands.
Current PhD projects


Output Oral Implantology and Prosthodontics

Publications in journals indexed in SCI


Other scientific publications (international, refereed)

Professional publications
Indicators of Esteem

Grants: current projects with external funding

Liu, Y. & Wismeijer, D. Koninklijke Nederlandse Akademie van Wetenschappen (KNAW), Samenwerkingsproject 08CDP043, 2008 (€69,690,-) for three years.


Liu, Y. & Wismeijer, D. In vivo degradability and osteoconductivity of calcium phosphate coatings with different crystalline properties. ITI Foundation, Basel, Switzerland. Sum awarded: 193,000 CHF.

Wismeijer, D. Immediate loading of two implants connected by a bar and an overdenture. A RCT comparing immediate loading with conventional loading. Straumann AG, Switzerland, €140,000,-.

Wismeijer, D. & Tahmaseb A. Evaluation of the EXE plan CAD/CAM system. Straumann AG, Switzerland, €200,000,-.

Invited speakers at international congresses or symposia


Other international functions

Liu, Y.: Honorary professor. Hospital of Stomatolgy, Dental School of Zhejiang University, Huangzhou, China.

Liu, Y.: Scientific advisor. Maxillofacial surgery department, University of Bern, Bern, Switzerland.

Wismeijer, D.: Member. Education Committee of the ITI (CH).

Wismeijer, D.: Member. Education Core group of the ITI (CH).

Wismeijer, D.: Honorary professor. Zhejiang University, China.

Societal impact

The societal impact of the research of the department of Oral Implantology and Prosthodontics is focussed on the influence on patient care, both within the department and externally. Research contributes to improved treatment of relevant patient groups. The societal impact is evident from the items listed below.

Interactions and collaborations with the industry and other non-university groups

Collaboration exists on research related to dental implants, as is shown for instance in the grants obtained from leading companies in this field such as Straumann and Geistlich.

Impact of the research on professionals

D. Wismeijer is as a member of the ITI (International Team on Implantology) group involved in developing teaching tools for implant dentistry. Recent publications are the ITI treatment guides of which he is an editor.

Invited speakers at national congresses or symposia

A total of 3 presentations were given.

Other national functions

D. Wismeijer is a member of four national committees and advisory councils.
Lectures during courses for dental professionals in the Netherlands
A total of more than 10 presentations were given for dentists, medical specialists and oral hygienists in the Netherlands.

Collaborations
- Department of Product & Process Engineering, DelftChemTech, Delft University of Technology.
- Zhejiang-California Nano Systems Institute, Hangzhou, China.
- Department of life sciences, Inner Mongolia Agriculture University, Huhehot, China.
- Department of Nuclear Medicine and School of Dentistry, University of Nijmegen, the Netherlands: (Dr. Otto Bormen and Prof. J. Jansen).
- Department of Prosthetic Dentistry of the University of Dunedin Dental School (Alan Payne).
- Department of restorative dentistry and biomaterial sciences. Harvard University, Boston, USA (German Gallucci).
- Dipartimento di Medicina, Chirurgia e Odontoiatria – A.O. San Paolo, Università degli Studi di Milano. Matteo Chiapasco / Paolo Cassentini.
- Department of MFP and Special Dental Care of the AMPHIA teaching hospital Breda (NL).
- Hospital of Stomatology, Dental School of ZheJiang University, Huangzhou, China.
- Clinical Research Department (dkf), University of Bern, Bern, Switzerland.
- University of Utrecht, Department of Oral Maxillofacial Surgery, Prosthodontics, and Special Dental Care, dr. M.C. Cune, Utrecht, the Netherlands.

Current PhD projects

Output Dental Material Sciences

Dissertations

Publications in journals indexed in SCI


Other scientific publications


Professional publications


External reports

Indicators of Esteem
Grants: current projects with external funding
Signum-Neco follow up study.
3M-ESPE. Learning curve traditional versus digital impressions, € 90.000,- 2009.

Membership of international editorial boards
Feilzer, A.J.: American Journal of Dentistry
Feilzer, A.J.: Odontology
Zel, J.M. van der: Digital Dental Journal

Invited speakers at international congresses or symposia
Muris, J. (2009, September 25). Exposure to oral metal allergens; with a focus on palladium allergy testing. Amsterdam, the Netherlands, 22nd European Research Group on Experimental Contact Dermatitis (ERGECD) Congress.

Scientific awards/honours

Other international functions

86
Societal impact
The societal impact of the research of the sub-program of the department of Dental Materials Sciences is evident from the impact on patient care and from the items listed below.

Interactions and collaborations with the industry and other non-university groups
In total 16 collaborations exist with industrial groups.

Impact of the research on professionals
A total of 7 courses were given for dental professionals.

Impact of the research on the general public

Organization of national congresses and symposia
A.J. Feilzer organized one national symposium.

Invited speakers at national congresses or symposia
One presentation was given during a national symposium.

Other national functions
A.J. Feilzer is a member of three national committees.

Collaborations
- Albert Schweitzer Ziekenhuis, Afdeling dermatologie, dr. R Laeijendekker, the Netherlands.
- VUMc, Afdeling Pathologie, prof.dr. R.J. Scheper, the Netherlands.
- VUMc, Laboratorium voor klinische immunologie, dr. M. von Blomberg, the Netherlands.
- VUMc, Afdeling dermatologie, dr. Th Rustemeyer, the Netherlands.
- UMCG, Conservative dentistry, prof.dr. M.C.D.N.J.M. Huysmans, prof.dr. M. Ozcan, the Netherlands.
- Laborzentrum Bremen, dr. E. Valentine-Thon, Germany.
- University of Turku, prof.dr. P. Vallittu, Finland.
- University of Geneva, prof.dr. I. Krejci, Switzerland.
- Universität Regensburg, prof.dr. M. Behr, Germany.
- University of Tennessee, Clinical Research Center, College of Dentistry, dr. F. Garcia Godoy, Memphis, USA.
- Division of Biomaterials, Department of Restorative Dentistry, UTHSC Dental School, 7703 Floyd Curl Drive, S. Wendt, San Antonio, Texas, USA.
- University of Tanta, dr. A.I. Abdallah, Egypt.
- University of Alexandria, dr. M.M. Aboushelib, Egypt.
- University of Cairo, dr. A. el Zohairy, Egypt.
- King Saud University, dr. Z. Salameh, Riyadh, Saudi Arabia.
- Health Sciences University of Hokkaido, dr. M. Hashimoto, Hokkaido, Japan.

Current PhD projects
Publication Oral Cell Biology

Publications in journals indexed in SCI


Ae2(a,b)-Deficient mice exhibit osteopetrosis of long bones but not of calvaria. The FASEB Journal, 23, 3470-3481.


Academic Centre for Dentistry Amsterdam


Other scientific publications (international, refereed)

Other scientific publications (non-refereed)


Professional publications


External reports

Indicators of Esteem
Grants: current projects with external funding
Bank R. & Everts, V: TNO beurs Kenniscentrum, NITE project; AIO (1 fte, 4 jaar) 2007-2011.
Bronckers AL: SRON: Osteoclast formation under microgravity and hypergravity. (June 2009-Jan 2011) Postdoc, 1.5 years and bench fee (total amount €150).
Everts, V: Grant to Renata Neves, Brazilian PhD student awarded a scholarship from the CAPES Foundation, a federal agency under the Ministry of Education of Brazil, to develop part of her PhD research as a special student at Academic Centre of Dentistry Amsterdam (ACTA), under supervision of V. Everts and R. Bank (Nov 2007-May 2008).


Membership of international editorial boards
Bronckers, A.L.J.J.: Odontology
Everts, V.: International Journal of Dentistry
Everts, V.: The Open Bone Journal
Everts, V.: The Open Enzyme Inhibition Journal
Klein Nulend, J.: Journal of musculoskeletal research
Klein Nulend, J.: The Open Biology Journal
Klein Nulend, J.: The Open Nitric Oxide Journal
Klein Nulend, J.: The Open Tissue Engineering and Regenerative Medicine Journal
Loon, J.J.W.A. van: Biological Sciences in Space
Loon, J.J.W.A. van: Microgravity Science and Technology
Lyaruu, D.M.: Connective Tissue Research

Scientific awards/honours

Organisation of international congresses or symposia

Invited speakers at international congresses or symposia
Klein Nulend, J. (2009, April 17). Role of osteocytes in strain-adapted bone remodeling. Tunis, Tunisia, Meeting on Osteoporosis: from cells to therapy.

Other international functions
Everts, V.: External reviewer. EU FP6 project: Eurogrowth, Berlin, Germany.
Loon, J.J.W.A. van: Member. Co-I ESA pan-European ground based research experiments.
Loon, J.J.W.A. van: Member evaluation board. ESA Fly-your-thesis student program for parabolic flight campaign.
Societal impact
The societal impact of this sub-program is focused on the effect of the research on the advancement of science in general and on the education courses for dental students. One lecture in the Netherlands is listed below.

Interactions and collaborations with the industry and other non-university groups
Institut de Recherches Internationales Servier: Effects of strontium ranelate on the response of osteocytes to mechanical loading and osteocyte-signalling towards osteoclasts and osteoblasts (PI: Klein-Nulend J, Co-PI: Bakker AD)
Geistlich Pharma AG: Histology and histomorphometry on human biopsies from patients after sinus floor elevation (PI: Klein-Nulend J, Co-PI: de Lange G)

Organization of national congresses and symposia
J. Klein-Nulend organized two symposia were in the Netherlands.

Invited speakers at national congresses, symposia
A total of 5 presentations were given for professionals and patients in the Netherlands.

Other national functions
V. Everts and J. Klein-Nulend participated in 17 national research committees.

Collaborations
- VU, Movement Sciences (prof.dr. A. de Haan, dr. R. Jaspers, dr. H.L. Gerrits)
- City University of New York, dr.ir. S.C. Cowin, New York, NY, USA.
- Erasmus University Rotterdam, prof.dr.ir. H. Weinans, Rotterdam, NL.
- Hospital Hilversum, dr. G.H.R. Albers, Hilversum, NL.
- Keele University, prof.dr. A. El Haj, Stoke-on-Trent, UK.
- Spaarne Hospital Heemstede, dr. P.A. Nolte, Heemstede, NL.
- Utrecht University Medical Center, dr. W.J.A. Dheret, Utrecht, NL.
- VUMC, Dept. of Endocrinology, prof.dr. P. Lips, dr. N. Bravenboer, Amsterdam, NL.
- VUMC, Dept. of Plastic Surgery (prof.dr. M. Ritt), Amsterdam, NL.
- Göttingen University, prof.dr. C.F. Schmidt, Göttingen, Germany.
- VUA, Dept. of Theoretical Physics (prof.dr. F.C. MacKintosh), Amsterdam, NL.
- UMCG (prof.dr. R.A. Bank), Groningen, NL.
- Kyoto University, prof.dr.ir T. Adachi, dr. M. Tanaka, Kyoto, Japan.
- Okayama University, dr. H. Kamioka, Okayama, Japan.
- AMOLF, dr. G. Koenderink, dr. R.G. Bacabac, Amsterdam, NL.
- Harvard University, Boston, MA, USA (dr. R. Krishnan).
- Radboud University Nijmegen, NL, prof.dr. A.M. Kuijpers-Jagtman, dr. J.C. Maltha, dr. R. van 't Hoff.
- Radboud University Nijmegen, prof.dr. J. Jansen and dr. X.F. Walboomers.
- Univ. Madrid, Spain, prof. J. Medina.
- Univ Oulu Finland: dr. S. Kellokumpu.
- Univ. Madrid, Spain, prof. R. Marco.
- Univ. Madrid, Spain, prof. Medina.
- Univ. Milaan, Italy, prof. S. Bradamante.
- Univ. Groningen, dr. H. Harmsen.
- Univ. of Connecticut, USA, M. Musgrave.
- VU Amsterdam, Fact. Physics, D. Iannuzzi.
- Nordic Biosciences, Herlev, Denmark, dr. K. Henriksen.
- University of Aberdeen, UK, prof. M. Helfrich.
Current PhD projects

Output Functional Anatomy

Dissertations

Publications in journals indexed in SCI


Indicators of Esteem

Grants: current projects with external funding


Invited speakers at international congresses or symposia


Scientific awards/honours


Membership of international editorial board

Koolstra, J.H.: Journal of Dental Biomechanics

Other international functions


Societal impact

The societal impact of this sub-program is limited to the effect of the research on the advancement of science in general and on the education courses for dental students.

Collaborations

- ACTA, Department of Orthodontics (prof. dr. A. Zentner), Amsterdam, the Netherlands.
- ACTA, Department of Oral Function (prof. dr. F. Lobbezoo, prof. dr. ir. M. Naeije), Amsterdam, the Netherlands.
- ACTA, Department of Dental Material Sciences (prof. dr. A.J. Feilzer), Amsterdam, the Netherlands.
- ACTA, Department of Dental Radiology (dr. W.G.M. Geraets, prof. dr. P.F. van der Stelt), Amsterdam, the Netherlands.
- ACTA, Department of Oral Cell Biology (dr. D.M. Lyaruu, dr. R.A. Bank, dr. ir. T.J. de Vries, prof. dr. V. Everts), Amsterdam, the Netherlands.
- Eindhoven University of Technology, Department of Materials Technology (prof. dr. ir. J.M.J. den Toonder), Eindhoven, the Netherlands.
- Hiroshima University, Department of Orthodontics (dr. N. Kawai), Hiroshima, Japan.
- University of Tokushima, Department of Orthodontics and Dentofacial Orthopedics (prof. E. Tanaka), Tokushima, Japan.
- Kyushu University, Department of Oral and Maxillofacial Radiology (dr. T.K. Goto), Fukuoka, Japan.
- University of Naples, Department of Orthodontics (I. Cioffi, dr. M. Farella), Naples, Italy.
- The Fourth Military Medical University, Department of General Dentistry (prof. Y. Chen), Xi’an, China.

Current PhD projects


Tuijt M. The role of muscle function on internal derangements’ of the TMJ. Supervisors: prof. dr. F. Lobbezoo & prof. dr. ir. M. Naeije; co-supervisor: dr. ir. J.H. Koolstra. Start:
2007.

Oral Radiology and Orthodontics

Diagnostic Imaging of the Tissues in the Maxillo-facial Complex
Craniofacial development, psychosocial aspects and biomaterials in orthodontics

Program leader
Prof. dr. P.F. van der Stelt
Oral and Maxillofacial Radiology
ACTA, Louwesweg 1
1066 EA Amsterdam
Tel: +31-20-5188 262
E-mail: P.vd.Stelt@acta.nl

Full professors

P.F. van der Stelt  H. van Beek  A. Zentner

Research objectives Radiology
The research of the Department of Oral and Maxillofacial Radiology is focused on the development and improvement of diagnostic methods for the visualization of normal and abnormal structures in the maxillofacial complex. This is realized from different perspectives including fundamental and applied (clinical) components:
The application of advanced digital image processing procedures enables the recognition of specific features in radiographic images of normal and abnormal structures being characteristic for the condition of these structures. Typically, these features are either used for the quantitative assessment of tissue characteristics (density, homogeneity, etc.) or they add a new dimension to the description of the (patho)physiology of the tissue structures under investigation. Commonly the order of magnitude of this description is between the microscopic (micro; e.g., connectivity, density) and the anatomic (macro; e.g., texture, entropy) level.
2. Three dimensional visualization of radiographic information.
An important aspect of the research objectives is the visualization of radiographic image data into 3D-space. The purpose of 3D imaging is to overcome the inherent drawbacks of projection radiography, such as the lack of information about the third dimension. We try to achieve this goal by the use of specific 3D reconstruction techniques called Local CT and Cone Beam CT, which results in a much lower dose and a higher resolution than conventional CT. This makes the technique a better choice for many common dental diagnostic tasks than conventional CT.

Results
Computer aided analysis of digital radiographic images.
Our contribution to the Osteodent project (see annual report 2006) was focused on the quantitative analysis of the radiographic trabecular pattern on intra-oral radiographs and panoramic radiographs. We were able to demonstrate that quantitative analysis of the radiographic trabecular pattern is able to predict between 70 and 80% of the osteoporotic subjects. Several papers were published in 2007 and 2008. The large database of images and clinical parameters is further explored and several publications are in progress.
Another implementation of computer aided analysis of digital images is the quantitative assessment and colour coded visualisation of bone quality around implants. A large study is in progress based on the analysis of longitudinal data of panoramic images of implant patients. The amount of bone loss and percentage of implants that are failing is correlated with several social and clinical parameters of these patients. The first results will be available and published in 2009.

*Three dimensional visualization of radiographic information*

Several studies based on CBCT data sets, both clinical and fundamental, are on the way. The CBCT facilitates many opportunities for collaboration with other dental disciplines, such as orthodontics (interactive location of cephalometric points in 3D), CMD-treatment (TMJ disorders), Implantology (templates for guided surgery based on series of axial slices and 3D reconstructions), oral surgery (impacted third molars) and endodontology (number of root canals; vertical root fractures). The first publications of the endo-studies were accepted.

The work on virtual 3D data using a 3D wand, shutter glasses and mini LCD screens with left and right perspective are making progress. One dissertation was published based on this study. Lack of time keeps the progress at a slow pace, but nevertheless some new developments were achieved. The purpose of these studies is to develop the optimum system for the display of 3D information in a clinical environment.

Within the framework of 3D reconstruction and volume rendering we contributed to the Simodont project. The feasibility of 3D volume rendering of objects to be used in a virtual learning environment was shown. The virtual learning environment consists of a haptic device with realistic 3D feedback to train students in cavity preparations on simulated teeth.

**Research objectives Orthodontics**

The research activities at the Department of Orthodontics focus on basic and clinical research in orthodontics and related disciplines. Three main themes exist:

1. Basic and clinical description of environmentally and genetically induced aberrations of facial form.
2. To determine the impact of Orthodontics on the quality of life.
3. To optimize orthodontic material properties and procedures for clinical use.

**Results**

The research activities at the department of Orthodontics focus on basic and clinical research in orthodontics and related disciplines, and the following directions were pursued in the year 2009.

1. Growth and growth regulation during normal and abnormal craniofacial development. A number of projects were carried out within this larger theme, which for a long time has been the department’s major research field. Strong collaboration links have been established with the Section of Functional Anatomy ACTA. Animal experimental set-ups with soft diet elucidate the function-morphology interrelation with regard to facial form and function.

   The treatment of cleft patients remains under scientific scrutiny and multicenter growth/development/treatment outcome is charted in collaboration with Nijmegen University.

2. Orthodontics and quality of life. This research theme has now been expanded and new projects have been started on the basis of previous work. In particular collaborative work with the section of Social Dentistry has been intensified.

3. Biomaterials. Studies were carried out in collaboration with the section of Dental Material Sciences ACTA. Bond strength and setting characteristics of glass ionomer cements and fatigue fracture of orthodontic arch wires were investigated.
## Academic personnel in 2009 and 2010

<table>
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Research staff ACTA – RAO/OR (in full time equivalents)

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Output Oral Radiology

Publications in journals indexed in SCI


Nackaerts, O., Horner, K., Jacobs, R., Karayianni, K., Mitsea, A., Berkas, L., Masteris, M., Lindh, C., Stelt, P.F. van der, Marjanovic, E., Adams, J.E., Pavitt, S. & Devlin, H.

Other scientific publications (international, refereed)

Professional publications

Indicators of Esteem
Membership of international editorial boards
Stelt, P.F. van der: Clinical Oral Implants Research
Stelt, P.F. van der: Dento-Maxillo-Facial Radiology
Stelt, P.F. van der: European Journal of Dentistry
Stelt, P.F. van der: Odontology
Stelt, P.F. van der: Oral surgery, oral medicine, oral pathology, oral radiology and endodontics

Invited speakers at international congresses or symposia

Other international functions
Berkhout, W.E.R.: Member. Research and Scientific committee EADMFR.

Organization of international congresses or symposia

Societal impact
The societal impact of the research of the department of Oral and Maxillofacial Radiology is focused on the improvement of diagnostic imaging procedures. This relates to not only technical parameters, but also other factors that influence the
diagnostic performance of radiodiagnostic procedures, such as the effect of viewing conditions and observer characteristics. Part of the activities include continuing education courses on the safe use of radiation in dental practice and application of digital imaging in dentistry.
Interaction and collaboration with the industry and other non-university groups
Within the framework of the VU Imaging Centre, collaboration has been established with QR-Imaging and Morita (both CBCT) and Duerr (digital sensor system) as well as Unfors (dosimetry) as preferred partners.

Interaction with the general public
Regularly, the department is contacted by members of the public with questions about the use of radiographs in dentistry.

Impact of the research on professionals
More than 20 courses were given for professionals. The department provides service to dental clinics in carrying out a "stralingsrisicoanalyse" (radiation risk analysis; this is a legal requirement for the certification.

Lectures during courses for dental and medical professionals in the Netherlands
Several lectures were given during courses.

Invited speakers at national congresses and symposia
A total of 7 presentations were given.

Other national functions
P.F. van der Stelt is director of the Nederlands Tijdschrift voor Tandheelkunde BV and chairman of Stichting Tandheelkundige Kennis.

Collaborations
- Prof. S.M. Dunn, Rutgers University Dept. of Biomedical Engineering, Piscataway NJ, USA.
- Prof. R. Jacobs, Imaging Sciences, Katholieke Universiteit Leuven, Belgium

Current PhD projects

Output Orthodontics

Dissertations

Publications in journals indexed in SCI


Other scientific publications (international, refereed)


Professional publications


Indicators of Esteem
Membership of international editorial boards
Zentner, A.; European Journal of Orthodontics
Zentner, A.; Journal of Dental Biomechanics
Zentner, A.; Journal of orofacial orthopedics
Zentner, A.; Orthodontia

Invited speakers at international congresses or symposia


Winter, F.R. de (2009, June 10). An introduction to ESAS (EFOSA’s Self Assessment System), Helsinki, Finland, EFOSA (European Federation of Orthodontic Specialists Association) General Assembly Meeting.


Scientific awards/honours
Zentner, A. (2009). Award of the Order of Candle. International Association of Dental Promotion, Supporting Member of FDI.

Other international functions
Winter, F.R. de: Chairman quality committee European Federation Orthodontic Specialists Associations (EFOSA).
Zentner, A.: Honorary treasurer European Orthodontic Society.
Zentner, A.: Member expert committee. German Orthodontic Society (DGKFO) on benefits and Effects of Orthodontic Treatment.
Zentner, A. Election member Kammerversammlung der Zahnaerztekammer Nordrhein.

Societal impact
The societal impact of the research of the department of Orthodontics is focussed on the influence on patient care, both within the department and externally. Special focus is on orthodontic patients with cranio-facial deformities and/or related malocclusions. A program of quality of live related to this topic is caring out.

Interactions and collaborations with the industry and other non-university groups
Habets, L.L.M.H. et. al.: collaboration with “3Dshape” on research related to dental plaster models.

Interactions with the general public
R. Kuitert gave interviews for broadcasting “Network” (NCRV) on orthodontic treatment and for the consumer program “Radar” (TROS).

Organization of national congresses and symposia
H. van Beek organised one national symposium.

Invited speakers at national congresses or symposia
A total of 4 presentations were given at symposia in the Netherlands.

Other national functions
Three national functions can be mentioned.

Courses for dental and medical professionals
Seven courses and workshops were given in the Netherlands and Belgium for dentists, medical specialists, oral hygienists and auxiliary personal.

Current PhD projects
Oral and Maxillofacial Surgery / Oral Pathology

Oral and maxillofacial disorders: diagnosis and treatment

Program leader
Prof. dr. I. van der Waal
Department of Oral and Maxillofacial Surgery/Oral Pathology
ACTA
VU Medical Center
P.O. Box 7057
1007 MB Amsterdam
Tel: +31-20-444 1023
E-mail: i.vanderwaal@vumc.nl

Full professors

Research objectives
The research of the Department of Oral and Maxillofacial Surgery/Oral Pathology of ACTA is focussed on early diagnosis of oral cancer and precancer, including cancer of the salivary glands, on surgical orthopedics of the maxillofacial skeleton and on maxillofacial implantology and reconstructive preprosthetic surgery. In addition research is performed on other aspects of oral and maxillofacial surgery, such as osteoradionecrosis and antithrombotic medication. The research is performed at the locations of the VU University Medical Center (VUmc) and the Academic Medical Center (AMC).

Research at the VUmc location
A substantial percentage of oral cancer is preceded by so-called precursor lesions, particularly leukoplakia. Intervention in the precursor stage may prevent the development of frank malignancy. The ongoing intervention study of oral leukoplakia is being continued both in a retrospective and prospective manner. Amongst others, the prognostic value of the DNA content is examined with regard to the predictive value of malignant transformation. There is a close collaboration with both the General Pathology Department and the ENT-Department of the VU University Medical Center (VUmc) in Amsterdam, both being related to the VUmc-Institute for Cancer and Immunology (V-ICI).

Salivary gland tumours are a very heterogeneous group of tumours, with more than 40 subtypes recognised in the most recent WHO classification. Classification is based solely on histopathology. Sometimes, correct classification and prediction of biological behaviour is difficult. Therefore, our studies aim to better characterize these tumours at the genomic and protein level. There is a close collaboration with the General Pathology Department, related to the VUmc-Institute for Cancer and Immunology (V-ICI), and with the Department of Oral Biochemistry of ACTA.

The research on surgical orthopedics is focused on maxillofacial function and healing capacity after treatment of acquired and congenital jaw deformities. Attention is focused on the indications/contraindications and preventive measures in surgical-orthodontic treatment of dentofacial deformities. In addition, the
dynamics of the surrounding tissues after corrective surgery of maxillofacial bones is studied, e.g. the musculature and the temporal mandibular joint. In these studies there is a close collaboration with the department of Orthodontics. The research on maxillofacial implantology and reconstructive preprosthetic surgery deals primarily with bone and bone-substitutes in maxillofacial implantology. Research includes a number of investigations on the maxillary sinus floor elevation model, where bone grafts and bone substitutes are investigated. Apart from that, the patient material in general and of post-oncological patients in particular form a valuable source for research. In the studies mentioned before there is a close collaboration with the department of Oral Cell Biology of ACTA, the department of Endocrinology of the VUmc and the departments of Oral and Maxillofacial Surgery at the Rijnland Hospital, Leiderdorp and the St Antonius Hospital, Nieuwegein. The research on surgical orthodontics and on maxillofacial implantology is included in the recently established Research Institute MOVE of the VUmc. Implantology research at the AMC location is focussed on the clinical usefulness of Implant Stability Quotient (ISQ) measurements in implant stability and osseointegration, and on the effect of different fixation techniques on the bone quality in buccal onlay bone grafting. The aim of the study on evidence-based guideline development on the management of invasive dental procedures in patients using antithrombotic medication is to assess the best available evidence on the risks and benefits of withholding or continuing antitrombotic medication during invasive dental procedures, assess the current practice by dentist, general practitioners, and oral surgeons, and to develop a multidisciplinary practice guideline on this topic. This research program is carried out in close collaboration with the department of Social Dentistry and Behavioural Sciences, ACTA.

Results
The study on early diagnosis of oral cancer, including the salivary glands, is ongoing. The project on the possible value of markers for the diagnosis and prognosis of salivary gland tumours has been focused until now on adenoid cystic carcinoma with mucinous differentiation and myoepithelioma, which has been the topic of a thesis completed in 2008. Presently, the focus is on mucin expression in situ and in saliva of patients with mucoepidermoid carcinoma. The group on surgical orthopedics of the maxillofacial skeleton has been making steadily progress, focusing on condylar hyperplasia and on the use of imaging techniques on soft tissue changes after orthognatic surgery. Several multi-centre studies are running concerning new implant surfaces and new implant designs. In the line of bone and bone substitute research in the sinus floor elevation model, there are several studies running. The most recent study is on the clinical and histological results on SBC (Straumann Bone Ceramic) in sinus floor elevation. Clinical and histological results are promising. In the project on the evidence-based guideline development a questionnaire study has been performed in collaboration with the NMT (Dutch Dental Association). A study that evaluated the quality of existing guidelines from the USA and UK has been performed.

Research at the AMC location
Giant cell granuloma of the jaw bone is a rare, but sometimes aggressive disease. The research is focused on the possible value of the use of calcitonin or interferon, particularly in aggressive or recurrent giant cell granulomas. In a spin-off of the study of the optimal treatment of non-tuberculous mycobacterial lymphadenitis, children were treated with antibiotics or a wait and see policy. Bisphosphonates are commonly prescribed for treatment and prevention of osteoporosis, and they are also used in combination with chemotherapy and radiotherapy to treat cancers that are metastatic to bone. Recent publications describe a condition, known as osteonecrosis of the jaw, in which patients receiving bisphosphonates while undergoing chemotherapy develop avascular necrosis of the jaw either spontaneously, due to oral trauma or following dental extraction. The aim
of this study is to elucidate the effects of chemotherapy and bisphosphonates on the oral microcirculation of breast cancer and multiple myeloma patients. Furthermore, the effects of cytotoxic chemotherapy on the microvasculature, morphology and capillary density of the oral mucosa are evaluated. This research project is conducted in collaboration with the Departments of Internal Medicine, Division of Hematology and Oncology, Translational Physiology and Clinical Epidemiology and Biostatistics, Academic Medical Center, Amsterdam.

The aim of the study on anticoagulant medication is to evaluate the effect of low dose regimes of aspirin, as well as the effect of ticlopidine and clopidrogel, on bleeding in patients undergoing oral surgical procedures. This research project is performed in close collaboration with the Department of Internal Medicine, Vascular Medicine, Academic Medical Center Amsterdam.

The research on anxiety and third molar surgery investigates the relation between anxiety sensitivity, dental anxiety, expected pain and experienced pain following third molar surgery. This research program is conducted in collaboration with the department of Social Dentistry and Behavioural Sciences, ACTA.

**Results**

The two implantology research projects at the AMC location were completed. The studies on inflammatory and inflammatory-like diseases of the oral and peri-oral structures, including the jaw bones and the lymph nodes of the neck, have been running well. The results of the antibiotic versus conservative wait and see study for treatment of non-tuberculous mycobacterial lymphadenitis in children will be published in 2010.

In the study on the effect of chemotherapy on the oral microcirculation several articles have been published in 2009. Three remaining papers are expected to be published in 2010.

**Academic personnel in 2009 and 2010**

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Output VUmc location

Dissertations

Publications in journals indexed in SCI


Other scientific publications (international, refereed)


Professional publications


Publications aimed at the general public


Indicators of Esteem

Grants: current projects with external funding


Membership of international editorial boards

Becking, A.G.: Orthodontics and Craniofacial Research
Bloemena, E.: World Journal of Gastrointestinal Oncology
Bruggenkate, C.M. ten: Clinical Oral Implants Research
Goené, R.J.: European Journal of Oral Implantology
Waal, I. van der: Acta Stomatologica Croatica
Waal, I. van der: European Journal of Cancer
Waal, I. van der: Journal of Dentistry University of Sao Paolo
Waal, I. van der: Journal of Stomatological Investigation
Waal, I. van der: Medicina Oral
Waal, I. van der: Minerva Stomatologica
Waal, I. van der: Oral Health and Preventive Dentistry
Waal, I. van der: Oral Oncology
Waal, I. van der: Padjadjaran Journal of Dentistry

Invited speakers at international congresses or symposia


Waal, I. van der (2009, June 30). Diseases of the jaws with emphasis on the clinicoradiographic aspects. Amsterdam, the Netherlands, 17th International Congress of DentoMaxilloFacial Radiology.


Waal, I. van der (2009, August 27). Leukoplakia. Amsterdam, the Netherlands, European Meeting on Oral Diseases; diagnosis and management.


Organization of international congresses and symposia


Scientific awards/honours


Other international functions
Becking, A.G.: Member scientific committee. European Association Craniomaxillofacial Surgery.

Becking, A.G.: Member. ITI.

Becking, A.G.: Member. Strasbourg Osteosynthesis Research Group

Bruggenkate, C.M. ten: Delegate. ITI Finland

Bruggenkate, C.M. ten: Member expert pool. ITI Straumann

Waal, I. van der: Register of external evaluation experts. Hellenic Quality Assurance Agency for Higher Education (HQAA)

Waal, I. van der: Expert for the UICC. Telepathology Consultation Center for odontogenic tissue. International Union Against Cancer (UICC)

Waal, I. van der: Member scientific committee. STOMA

Societal impact
The societal impact of the research of the department of Oral and Maxillofacial Surgery/Oral Pathology is focussed on the influence on patient care, both within the department and externally. Research on all main areas of interest contributes to improved prevention, diagnosis and treatment of relevant patient groups. The societal impact is evident from the items listed below. For more detailed information we refer to the annual reports of the departments in the VU University Medical Center and the Academic Medical Center.
Interactions and collaborations with the industry and other non-university groups
Bruggenkate ten C.M.: collaboration with the Straumann company on research related to dental implants.

Interactions with the general public
H.S. Brand gave a presentation about oral health for Sjögren patients

Impact of the research on professionals
R.H.B. Allard participated in the preparation committee for a guideline for smoking cessation.

Memberships of national editorial boards
Waal, I. van der: Member Editorial Board Nederlands Tandartsenblad
Waal, I. van der: Member Editorial Board Nederlands Tijdschrift voor Geneeskunde

Organization of national congresses and symposia
R.H.B. Allard is co-organiser of the WTA-cursus “Geweld”.

Invited speakers at national congresses or symposia
A total of 10 presentations were given.

Other national functions
A total of 28 memberships of national committees and advisory councils related to oral and maxillofacial surgery can be mentioned. The following scientists were members of these committees: R.H.B. Allard, A.G. Becking, E. Bloemena, H.S. Brand, D.E van Diermen, R.J. Goené, H.S. Schouten, E.A.J.M. Schulten, I. Van der Waal and S.A. Zijderveld.

Courses for dental and medical professionals
A total of 20 courses were given in the Netherlands for dentists, medical specialists and oral hygienists

Lectures during courses for dental and medical professionals in the Netherlands
A total of more than 65 presentations were given for dentists, medical specialists and oral hygienists in the Netherlands

Collaborations
- Biofarmind, The Hague, the Netherlands
- Crucell, Leiden, The Netherlands
- Institut für Anatomie, Zentrum für Experimentelle Medizin, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany
- Leids Universitair Medisch Centrum, afdeling mondziekten en kaakchirurgie, Leiden
- Rijnland Ziekenhuis, afdeling Mondziekten en kaakchirurgie, Leiderdorp
- Netherlands Cancer Institute, Amsterdam, The Netherlands
- Sint Antonius Ziekenhuis, afdeling dermatologie, Nieuwegein
- Swammerdam Institute for Life Sciences, University of Amsterdam, Amsterdam, The Netherlands
- University of Parma, Unit of Oral Pathology and Medicine, Section of Odontostomatologie, Department of ENT, Dental Ophthalmological, and Cervicofacial Sciences, Parma, Italy
- University of Porto, Department of Oral Surgery, Porto, Portugal
- VUmc, afdeling Nucleare Geneeskunde en PET research, Amsterdam
- VUmc, Department of Clinical Epidemiology and Biostatistics, Amsterdam
- VUmc, Department of Clinical Genetics
- VUmc, Department of Endocrinology, Amsterdam
- VUmc, Department of Otolaryngology/Head and Neck Surgery, Amsterdam
- VUmc, Department of Pathology, Amsterdam
Current PhD projects


Output ACTA/AMC location

Publications in journals indexed in SCI


Other scientific publications (international, refereed)

Professional publications

Indicators of Esteem
Grants: current projects with external funding

Membership of international editorial boards

Scientific awards/honours

Societal impact
The societal impact of the research of the department of Oral and Maxillofacial Surgery/Oral Pathology at the AMC location is focussed on the influence on patient care

Current PhD projects

Education Institute

Research on Dental Education

Program leader
dr. J.M. Vervoorn
Education Institute
ACTA, Louwesweg 1
1066 EA Amsterdam
Tel: +31-20-5188438
E-mail: J.Vervoorn@acta.nl
Research objectives
In the ACTA faculty of Dentistry research is performed on several aspects of education in dentistry. This includes research on the evaluation of courses within the curriculum, research on new teaching methods, such as the Objective Structured Clinical Examination (OSCE), and development and evaluation of a computed aided digital teaching system of pre-clinical skills (the Simodont), and comparison with biomedical education elsewhere in Europe.

The input of academic personnel is limited to staff of the education institute, and to some staff members of the various departments. The research should not be considered as a separate programme; however it is intended that this research will increase in the coming years.

Results
In 2009 several experiments have been carried out on transfer of skills. First results are exciting and confirm the assumption that skills, developed in virtual reality, are transferred to reality. Also data on the acceptance of new developments in education have been collected; first results show that the higher realism of the virtual system is percept, the higher the acceptance. Papers on research projects have been submitted to scientific journals.

Academic personnel in 2009 and 2010

<table>
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<th>Research staff ACTA - OWI (in full time equivalents)</th>
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Publications in journals indexed in SCI
**Other scientific publications (international, refereed)**


**Professional publications**


**Publications aimed at the general audience**


**Indicators of Esteem**

**Grants: current projects with external funding**

**Wesselink P.R. & J.M. Vervoorn.** A grant of € 800.000,- (2008-2010) was obtained from by the Ministry of Education for "Simodont, virtuele realtime de werkelijkheid". This grant was obtained together with the department of Cariology, Endodontology and Pedodontology.

**Memberships of international editorial boards**

**Gorter, R.C.** European Journal of Dental Education

**Schoonheim, M.E.** European Journal of Dental Education

**Other international functions**

**Kersten, H.W.:** Secretary General of the ADEE.

**Vervoorn, J.M.:** Board member of the ICOND.

**Organisation of international congresses or symposia**


**Invited speakers at international congresses or symposia**

Societal impact
The societal impact of the research is focused on the effect of the education courses for dental students, not only within the own faculty, but also in a world-wide perspective. This involves in particular, the research on computed aided digital teaching system of pre-clinical skills (the Simodont).

Interactions and collaborations with the industry and other non-university groups
MOOG inc. Development of the Simodont, a haptic dental trainer.

Interactions with the general public
Folia, interview ACTA November 2009.
Ad Valvas, interview ACTA September 2009.
NRC wetenschap bijlage, interview ACTA September 2009.
De Volkskrant, interview ACTA October 2009.
Dentz, interview ACTA June 2009.

Current PhD projects
# Appendix

List of SCI journals, their impact factors and the number of ACTA publications in 2009 in each journal

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