ANNUAL RESEARCH REPORT 2010

Academic Centre for Dentistry
Amsterdam
Annual Research Report 2010

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Design cover : Vormgeving en fotografie, Facilitaire Dienst, ACTA
Cover : 3-D representation of a root-filled tooth
Department of Endodontology, ACTA and Max-Planck Institute, Berlin
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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. Detailed information is given of dissertations, scientific publications in refereed journals, other scientific publications, professional publications, indicators of esteem, collaborations and societal impact.

Some issues for 2010 are specifically mentioned in this report. These include 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”, and the evaluation of the research that was performed.

An overview of the output in 2010 is presented in Table 2. This table summarises for each program the number of publications that have appeared in 2010. The personnel involved in full time equivalent (fte) and the impact factor-sum (IF-sum) are also included in this table.

We are pleased to note that the output in 2010 was high. As shown in Table 1, the number of publications in refereed journals and the IF-sum were somewhat lower than in 2009, but still higher than in all years before 2008. The number of professional publications was comparable to the high output of 2009. In 2010 a total of 18 PhD theses were published, more than in any previous year.

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 focussed. 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 aetiology, prevention and therapy of caries, and periodontal and endodontal infections. This theme has received a substantial grant from the University of Amsterdam. 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 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. 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.
In 2010 an evaluation of the research of ACTA was performed by a committee consisting of two external referees and two ACTA senior scientists. This committee concluded that ACTA has both nationally and internationally a prominent position in dental research. ACTA is strong in both clinical and fundamental research. The committee recommended continuation of the focus on the two main research themes.

- **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 2010 18 dissertations were published, more than in any previous year. The percentage of PhD students that finished their thesis averages at 90 % over the last 20 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 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 20 years, despite a relatively stable input in fte scientific personnel. The average quality of the publications has significantly improved over that 20-year period, as judged by the increase of the impact factor sum (see figure 4). In 2010 a highest number of refereed publications and a high IF sum was obtained. Also the number of professional publications was very high in 2010.

- **notable events in 2010**
Outstanding contributions for the year 2010 are publications in high ranking biomedical journals (i.e. Biomaterials, Diabetes Care, European Cells & Materials, Human Molecular Genetics, Journal of Bone and Mineral Research, Molecular Ecology and Pain, all journals with an impact factor higher than 5).

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 196 scientific papers in refereed journals, of which 168 in journals with an impact factor (SCI journals). 61% of these 168 papers appeared in journals belonging to the field “Dentistry, Oral Surgery and Medicine”. 27% of these publications were in the top 10% of the journals, 47% in the top 25% and 79% 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 2010 a total of 18 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 2010 evaluation report of research at ACTA, these groups received ratings between 4 and 5 (on a 5 point scale). Programs that have received very good ratings in 2010 (a mean score of at least 4) include those from the sections Cariology/Preventive Dentistry, Periodontology, Oral Biochemistry, and Oral Cell Biology.

**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 (70 international functions), as members of editorial boards of scientific journals (76) and in being leading in 'wetenschappelijke verenigingen' of researchers and dental practitioners in the Netherlands. Prof.dr. J.M. ten Cate is an academy professor at the Royal Academy of Arts and Sciences (KNAW).
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 164 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 2010 ACTA researchers have again contributed actively in internationally held meetings, workshops and symposiums, both as organisers and participants. A total of 129, 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 or international audience. Due to this large number, congress abstracts are not listed in this annual report. A total of 11 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€ 4010) 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€ 511, and the total amount of research contracts (3rd source) was k€ 1646.

- **personnel**
The directorate of the institute comprises:
  
<table>
<thead>
<tr>
<th>Name</th>
<th>FTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>prof. dr. V. Everts, director of research</td>
<td>0.4</td>
</tr>
<tr>
<td>dr. T.J.M. van Steenbergen, co-ordinator</td>
<td>0.6</td>
</tr>
<tr>
<td>mrs. F.M. Meijer, secretary</td>
<td>0.6</td>
</tr>
</tbody>
</table>

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
Almost all vacancies for PhD positions have been filled in 2010. In Figure 1 the number of new PhD students at ACTA is shown in the years 1990 to 2010. 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 number of 9 new PhD students were appointed per year. Despite budget restrictions 8 new PhD students could be appointed in 2010. The majority of 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 2010 five grants were awarded to the research themes; three of these in an open competition, and two personnel grants for talented PhD students. One talented post-doc was appointed. Both the open competition and the grants for talented students or post-docs 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”. Furthermore, we planned a course in grant writing. 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 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 shows 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 than 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

![Bar chart showing mean duration of thesis completion for each year of entry from 1990 to 2004.](image)

**Figure 3.** Percentage of ACTA PhD students finishing their thesis related to the year of entry

![Bar chart showing percentage of thesis completion for each year of entry from 1990 to 2010.](image)
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. Due to budget restrictions the number of persons involved in research had to be reduced slightly.

- **new building in 2010**
In 2010 ACTA moved to a new building located at the VU campus; this brings together groups that are currently spread out over the city at four different locations. Optimal research facilities at the new ACTA building are available 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 are formed at a local level to integrate research training of 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 2010 the new ACTA Graduate School of Dentistry (AGSD) was 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 to focus more on the two 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 Preventive 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 interfaculty 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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<th>2004</th>
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<th>2007</th>
<th>2008</th>
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<td>6</td>
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<td>Publications for general public</td>
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<td>61.6</td>
<td>57.9</td>
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</table>

Footnotes:
Ref publ = number of scientific papers in refereed journals.
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 refereed journals and total scientific personnel in fte.
Table 2. Summary of the number of publications, impact factor sum and academic personnel in fte (year 2010)

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<thead>
<tr>
<th>Prog</th>
<th>Dis</th>
<th>Ref publ</th>
<th>OSP</th>
<th>PP</th>
<th>PGP</th>
<th>IF</th>
<th>wp1</th>
<th>wp2</th>
<th>wp3</th>
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<td>-</td>
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<td>PAB</td>
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<td>46 (20)</td>
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<td>3</td>
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<td>SOC</td>
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<td>31</td>
<td>10</td>
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<td>OWI</td>
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<td>8 (5)</td>
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<td>4</td>
<td>-</td>
<td>6.8</td>
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<td>ACTA*</td>
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<td>196 (105)</td>
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This table summarises the number of scientific publications in refereed 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 program by adding together the impact factor values of all 2010 publications.

- **Dis** = number of dissertations
- **Ref publ** = number of scientific papers in refereed journals. Between parentheses is the number of first authors belonging to the program in question
- **OSP** = other scientific publications (international, refereed)
- **PP** = professional publications, including publications for the general public
- **PGP** = publications for the general public
- **IF** = sum of impact factors as indexed by ISI
- **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 in fte

Program acronyms and meanings:
- **PCEP** = Preventive Dentistry: Cariology Endodontology Pedodontontology
- **PAB** = Periodontology and Oral Biochemistry
- **SOC** = Social Dentistry and Behavioural Sciences
- **FRT** = Oral Function and Restorative Dentistry
- **RAO** = Oral Radiology and Orthodontics
- **MKA** = Oral and Maxillofacial Surgery
- **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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<th>2nd</th>
<th>3rd</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
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PCEP = Preventive Dentistry: Cariology Endodontology Pedodontology
PAB = Periodontology and Oral Biochemistry
SOC = Social Dentistry and Behavioural Sciences
FRT = Oral Function and Restorative Dentistry
RAO = Oral Radiology and Orthodontics
MKA = Oral and Maxillofacial Surgery

Table 4: PhD students by type of undergraduate training

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PCEP = Preventive Dentistry: Cariology Endodontology Pedodontology
PAB = Periodontology and Oral Biochemistry
SOC = Social Dentistry and Behavioural Sciences
FRT = Oral Function and Restorative Dentistry
RAO = Oral Radiology and Orthodontics
MKA = Oral and Maxillofacial Surgery
OWI = Education Institute
Preventive Dentistry Cariology Endodontology Pedodontology

Diseases of the Dental Tissues and their Prevention

Program leader
Prof.dr. W. Crielaard
Department of Preventive Dentistry
ACTA, Gustav Mahlerlaan 3004
1081 LA Amsterdam
Tel: +31-20-5980432
E-mail: w.crielaard@acta.nl

Full professors

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

Research objectives
The research program of the Departments of Preventive Dentistry, Cariology, Endodontology and Pedodontology 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
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.

- The antimicrobial resistance of microorganisms in biofilms and the polymicrobial interactions in these biofilms that modulate resistance require novel strategies to evaluate the efficacy of caries-preventive compounds. We developed a novel high-throughput active attachment model to evaluate the effects of amine fluoride (AmF) on *Streptococcus mutans* and polymicrobial biofilms. The effect of AmF on the viability of the polymicrobial biofilms was significantly less than that on the *S. mutans* biofilms, indicating a higher resistance in the complex biofilms. However, in dose-response experiments AmF reduced lactate production in both types of biofilms to the same extent. Thus, when evaluating the efficacy of caries-preventive compounds it is essential to use appropriate polymicrobial biofilm models, and to judge on the reduction of acid formation (i.e. cariogenic potential) as well as on bacterial viability.

- We investigated the effects of the probiotic bacterium *Lactobacillus rhamnosus* GG (LGG) on the cariogenic potential and microbial composition of saliva-derived microcosms. Single and dual species biofilms of LGG and *Streptococcus mutans*, and saliva-derived microcosms with or without LGG were grown in an Active Attachment Biofilm model. LGG inhibited the growth of *S. mutans* in dual species biofilms, established in saliva-derived microcosms and reduced *S. mutans* counts significantly, but did not affect pH or dentin demineralization. This suggests that other microorganisms besides *S. mutans* were responsible for increased cariogenicity of sucrose-exposed biofilms.

- To investigate if 2 versus 3 fluoride moments a day had a different effect on caries lesion progression, we designed a double-blind, randomized, cross-over in situ experiment in which sixteen participants wore an enamel and a dentine specimen with a preformed lesion placed buccally in their partial prosthesis and brushed twice a day with a 1,400 ppm amine fluoride toothpaste and rinsed once a day with either 250 amine F/NaF or a placebo rinse. There was a statistically significant increase in structurally bound fluoride in dentine, but not in enamel, when comparing the fluoride mouthrinse group with the placebo rinse group. Thus, for dentine a third fluoride moment may be beneficial in enhancing remineralisation.

- Because dentin is more caries-susceptible than enamel, its demineralization may be more influenced by additional fluoride (F). We hypothesized that a combination of professional F, as applied as acidulated phosphate F (APF), and use of 1100-ppm-F dentifrice would provide additional protection for dentin compared with 1100-ppm-F alone. Twelve adult volunteers wore palatal appliances containing root dentin slabs, which were subjected to biofilm accumulation and sucrose exposure 8x/day. The volunteers were randomly assigned to the following treatments: placebo dentifrice (PD), 1100-ppm-F dentifrice (FD), APF + PD, and APF+FD. APF and FD increased F concentration in biofilm fluid and reduced root dentin demineralization, presenting an additive protective effect.

- Orthodontic treatment with fixed appliances is considered a risk factor for the development of white spot caries lesions (WSL). We tested the hypothesis that lingual brackets result in a lower caries incidence than buccal brackets. The number of WSL that developed or progressed on buccal surfaces was 4.8 times higher than the number of WSL that developed or progressed on lingual surfaces. When measured using quantitative light-induced fluorescence (QLF), the increase in integrated fluorescence loss was 10.6 times higher buccally than lingually. This indicates that buccal surfaces are more prone to WSL development, especially when WSL existed before treatment.

- Also, the effects of casein phosphopeptide amorphous calcium fluoride phosphate (CPP-ACFP) paste vs. control paste on the remineralization of white spot caries lesions and on plaque composition were tested in a double-blind prospective randomized clinical trial. Fifty-four orthodontic patients, with multiple white spot lesions observed upon the removal of fixed appliances, used CPP-ACFP paste or control paste and were followed up for 3 months. And caries regression was assessed on quantitative light-induced fluorescence. We observed no clinical advantage for use of the CPP-ACFP paste supplementary to normal oral hygiene over the time span of 12 weeks.

- Furthermore, we investigated the effect of *Galla chinensis* on de-/re-mineralization of advanced enamel lesions by micro-CT, and showed that *Galla chinensis* could slow down the re-mineralization of enamel in the surface layer and thereby facilitate ion transport into the lesion body.

- A retrospective study was performed in sixty-six uncooperative children (4-18 years old) with at least one tooth with clinically diagnosed deep caries who underwent indirect pulp treatment. A 3-year survival analysis (Kaplan-Meier) of treated teeth was performed. The survival rate was 96% for primary molars (mean survival time, 146 weeks) and 93% for permanent teeth (mean survival time, 178 weeks), showing
that that IPT performed in primary and permanent teeth of young patients may result in a high 3-year survival rate.

- Dental decay and dental treatment are suggested to be related to body growth in children. We recorded caries prevalence and presence of dentogenic infections in three hundred eighty 6-year-old Surinam children with untreated dental decay, assigned to four different treatment groups. We observed negative correlations between anthropometric measures and the number of untreated carious surfaces and caries experience of the children. No significant differences in growth pattern between the treatment groups were observed. It is suggested that caries activity is a negative predictor for body growth in children and dental intervention does not show significant improvement within 3 years.

- Porphyromonas gingivalis is an oral pathogen strongly associated with destruction of the tooth-supporting tissues in human periodontitis. We aimed to investigate the effects of viable P. gingivalis on the expression of genes associated with inflammation and bone degradation by gingival and periodontal ligament fibroblasts. Viable P. gingivalis induced a strong in vitro inflammatory response in both GF and PDLF. Between individual donors there was large heterogeneity in responsiveness to P. gingivalis. Also, in each individual, either GF or PDLF was more responsive to P. gingivalis, which may be important for a person's susceptibility towards periodontitis.

- Capsular polysaccharide (CPS) of P. gingivalis is an important virulence factor. Seven capsular serotypes have been described. We used micro-array based comparative genomic hybridization analysis (CGH) to analyze a representative of each of the capsular serotypes and a non-encapsulated strain against the highly virulent and sequenced W83 strain. A conserved core P. gingivalis genome was described, which consists of 80% of the analyzed genes from the sequenced W83 strain. Among aberrant genes between the test strains and control strain many CPS biosynthesis genes were found. Furthermore, hmuS, a putative CobN/Mg chelatase involved in heme uptake, may be a more relevant virulence determinant than previously expected.

- To examine the role of the CPS in host-pathogen interactions we constructed an insertional isogenic P. gingivalis knockout in the epimerase-coding gene epsC at the end of the CPS biosynthesis locus. This mutant was non-encapsulated. capsule biosynthesis could be restored by in trans expression of an intact epsC gene. The epsC mutant induced significantly stronger inflammatory responses in gingival fibroblasts than the wild-type, whereas the complemented mutant was similar to the wild-type. This provides the first evidence that P. gingivalis CPS acts as an interface between pathogen and host, that may reduce the host's pro-inflammatory immune response.

- Through a literature review, we aimed to elucidate the feasibility of achieving protection against periodontitis though immunization against P. gingivalis, revealing that a multi-component vaccine against P. gingivalis, which includes structures shared among P. gingivalis serotypes, will be feasible to induce broad and complete protection.

- Also Tannerella forsythia is strongly associated with periodontal disease. P. gingivalis and T. forsythia are highly prevalent in humans with periodontitis, and have also been isolated from the oral cavity of cats. We investigated the prevalence of Porphyromonas gulae, P. gingivalis, and T. forsythia in the oral microflora of cats and their owners, using culture and polymerase chain reaction (PCR). All Porphyromonas isolates from cats (n=64) were P. gulae, whereas the Porphyromonas isolates from owners (n=7) were P. gingivalis. Genotyping of T. forsythia isolates (n=54) in six cat/owner couples showed that in one cat/owner couple the T. forsythia isolates (n=6) were identical, which led us to hypothesize that transmission from cats to owners had occurred and that cats may be a reservoir of T. forsythia.

- The periodontal pathogen Aggregatibacter actinomycetemcomitans comprises six serotypes (a-f), and is often identified by its 16S rRNA gene. Using 16S rRNA gene sequence analysis we revealed an aberrant cluster of 19 strains within serotype e, denoted as serotype e', with gene sequence similarities between serotype e' strains from 99.7% to 100.0%, whereas 96.8-97.5% sequence similarity was obtained with members of other serotypes. However, DNA-DNA hybridizations between a representative serotype e' strain and representative strains of serotypes b, d and e of A. actinomycetemcomitans revealed 68-75% DNA-DNA relatedness. Overall, the data obtained in this study suggest that the serotype e' strains form an evolutionary relatively stable distinct subgroup within A. actinomycetemcomitans.

- Host susceptibility is an important determinant in the development of periodontitis. We conducted a review of the literature for gene polymorphisms associated with chronic periodontitis (CP) susceptibility. Candidate gene polymorphism studies with a case-control design and reported genotype frequencies in CP patients were searched and reviewed, showing that growing evidence exists that polymorphisms in the IL1, IL6, IL10, vitamin D receptor, and CD14 genes may be associated with CP in certain populations.
However, carriage rates polymorphisms varied among studies and most studies appeared under-powered and did not correct for other risk factors. Larger cohorts, well-defined phenotypes, control for other risk factors, and analysis of multiple genes and polymorphisms are needed to get a more comprehensive insight into the contribution of gene polymorphisms in CP.

- The presence of periodontal pathogens may influence failure of dental implants after osseointegration. We assessed the prevalence of seven periodontal marker pathogens, before implant placement and 1 yr after loading, and the effect of pre-implant reduction of pathogens. In 93 individuals needing single tooth replacement the prevalence of periodontal pathogens was determined before implant treatment and 1 yr after loading, and threshold levels commonly used in Periodontology were applied. Periodontal treatment reduced pathogen levels to below threshold values in 78.3% of initially colonized subjects, however, 1 yr after loading, periodontal pathogens were present above threshold levels in 74.1% of all subjects. Thus, Long-term effectiveness of pre-implant reduction of the selected marker pathogens appeared limited in our patient population.

- Child dental anxiety and dental behavioural management problems may be related to general emotional and behavioural problems. 50 children (4-12 years old) and their parents participated in a study in which parents filled out the Child Fear Survey Schedule Dental Subscale (CFSS-DS) and the Child Behaviour Checklist (CBCL) on behalf of their child, and child behaviour during consecutive dental treatments was assessed using the Venham scale. Children aged 4 and 5 years who had sleeping problems, attention problems and aggressive behaviour, displayed more disruptive behaviour during dental treatment. Children with emotionally/ reactive and attention problems were more anxious.

- Parental attitudes likely play a role in achieving and maintaining oral health in children. To be useful in individually delivered caries prevention programmes, parental attitudes should be identified at individual level. We used Q-methodology to identify 39 parents of 6-year old children’s prevailing attitudes towards the oral health of their children. Based on their beliefs, attitudes and cognitions, five categories of parents were found: (i) conscious and responsible, (ii) trivializing and fatalistic, (iii) appearance-driven and open-minded, (iv) knowledgeable but defensive and (v) conscious and concerned. Q-methodology appears to be a fruitful way to structure the complexity of parents’ opinions and attitudes towards their children’s dental health.

- The application of cone beam computed tomography (CBCT) continued to play an important role in our endodontic research this year. In a clinical study in cooperation with the Peking University in Beijing periapical radiography (PR) was compared with the CBCT in diagnosing apical periodontitis meanwhile correlating predicting co-factors with a negative treatment outcome. PR detected periapical lesions in 13% whereas CBCT did in 26%. Density of root fillings and quality of coronal restoration appeared as predictors, which were identified with CBCT scans.

- The ability of CBCT to image root perforations in lower molars was investigated and found to be significantly better than conventional radiographs taken from 2 angles. However CBCT has limitations in detecting strip perforations in curved mesial canals.

- In a clinical study the outcome of endodontic retreatment was evaluated and the CBCT showed more periapical lesions than conventional radiographs. Also clinically the sensitivity, specificity and accuracy of CBCT in detecting vertical root fractures was assessed. The overall accuracy of the CBCT was higher than that of periapical radiographs.

- Continuing the use the dentinal defects model, it appeared that the more procedures performed, the more chance for dentinal damage: cleaning and shaping causes some damage, filling the root canals adds to the damage and retreatment procedures significantly increase the risk for vertical root fractures.

- In the irrigation studies, higher ultrasonic intensity is related to a higher oscillation amplitude of the file and resulted in a better cleaning efficacy of Passive Ultrasonic Irrigation (PUI). Using a tapered gutta-percha cone to activate the irrigant in the root canal could enhance the efficiency of the Manual-Dynamic Irrigation Technique that was more effective in removing dentin debris than the EndoVac system. Computational Fluid Dynamics is a good method to evaluate the irrigant flow in the root canal and the apical root canal needs a certain dimension for a good irrigant replacement correlated to the diameter of the needle used for syringe irrigation. Diffusion is more successful than convection in irrigant replacement in the tubules. Activation of NaOCl is a strong modulator of its reaction rate; the consumption of available chlorine increased significantly during the rest phase after activation. pH did not affect the reaction rate of 2% NaOCl.
For further disinfection the effect of hyperosmosis on a biofilm appeared in a significant reduction of the number of bacteria and seems a promising strategy in root canal treatment with a good interest of the dental industry.

In 2010 Paediatric dentistry studied more into dept the child related aspects in the treatment of young patients. Just as during the last year this year’s results concentrate on the management of child dental patients, not only their treatment approach but also the method dental caries should be looked at, its treatment and the consequences for a child’s quality of life. Several articles have been produced on the subject giving way to the understanding that full treatment includes the awareness of the caries process. This approach is to be preferred above one of just prevention or restoration and/or extraction. Dental treatment in children has a positive influence on the quality of life but treatment in general anaesthesia has no influence on development or reduction of dental anxiety. This year a thesis on this subject has been finalized. The clinical trials of the section focused this year on the child related aspects of dental treatment. Published articles and clinical trials reported on the quality of care of paediatric dentists, and dental anxiety. Three PhD theses are in process focusing on dental materials, hypomineralisation defects as an alternative caries diagnosis for caries and child dental anxiety in relation to parent’s behaviour.

All studies in paediatric dentistry focus on the child as a dental patient enabling a situation in which care can be tailor made for the child dental patient.

### Academic personnel in 2010 and 2011

<p>| Research staff ACTA - PCEP/ Preventive Dentistry Cariology Endodontontology Pedodontology (in full time equivalents) |
|---|---|---|---|
| position | Name | fte 2010 | plan 2011 | funding |
| Full professors | Cate, prof.dr. J.M., ten | 1,00 | 1,00 | 2 |
| | Crielaard, prof.dr. W. | 0,40 | 0,40 | 1 |
| | Crielaard, prof.dr. W. | 0,40 | 0,40 | 3 |
| | Loveren, prof.dr. C. van | 0,20 | 0,20 | 1 |
| | Loveren, prof.dr. C. van | 0,20 | 0,20 | 3 |
| | Wesselink, prof.dr. P.R. | 0,20 | 0,20 | 1 |
| Senior lecturer | Amerongen, dr. W.E. van | 0,15 | -- | 1 |
| | Strijp, dr. A.J.P. van | 0,10 | 0,10 | 1 |
| | Strijp, dr. A.J.P. van | 0,10 | 0,10 | 3 |
| Other lecturers and tenured research staff | Deng, dr. D.M. | 0,50 | 0,80 | 1 |
| | Deng, dr. D.M. | 0,50 | 0,20 | 2 |
| | Laine, dr. M.L. | 0,10 | -- | 1 |
| | Özok, dr. A.R. | 0,40 | 0,40 | 1 |
| | Peters, dr. L.B. | 0,10 | 0,05 | 1 |
| | Reijden, dr. W.A. van der | 0,40 | 0,20 | 1 |
| | Soet, dr. J.J. de | 0,30 | 0,20 | 1 |
| | Veerkamp, dr. J.S.J. | 0,20 | 0,20 | 1 |
| | Wu, dr. M.K. | 0,80 | 0,70 | 1 |
| | Zaura, dr. E. | 0,80 | 0,40 | 1 |
| | Zaura, dr. E. | 0,10 | 0,50 | 3 |
| Total tenured staff | 6,95 | 6,25 |</p>
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**Output**

**Dissertation**


**Scientific publications (refered)**


Scientific publications (non-refered)


Professional publications


Book editorship

Indicators of Esteem

Grants: current projects with external funding
Veen M.H. van der & Kaaij N.C. van der The use of fluoride rinse for caries prevention during the orthodontic treatment with fixed appliances. GABA. August 2009 - December 2012, €180.000,-
Cate J.M. ten, Crielaard W., Soet J.J. de & Loveren C. van STW project. Seeing is believing. M.H. van der Veen & C.M.C. Volgenant. Oktober 2010 - Oktober 2016, €500.000,-
Strijp A.J.P. van Efficacy of Hesperidin (HPN) in preventing dentine demineralization and degradation in situ. Sunstar Inc., Osaka, Japan; December 2010-May 2011, €51,000,-
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.
Deng D.M. & Crielaard W. KNAW/CAS (Chinese Academy of Sciences). Grant in the “China Exchange Programme”.
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,-
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.
Waal S.V. van der. Research grant of the European society of endodontontology €10.000,-
Wesselink P.R. et al. Ministry OCW €850.000,- Simodont project for three years (one third of this amount each year).
Zaura E. & Crielaard W. Wigley, Chicago, USA. Literature review & Clinical experiment, €70.000.

Membership of editorial boards
Cate, J.M. ten: Chinese Journal of Dental Research
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
Crielaard, W.: SGM Microbiology
Loveren, C. van: International Journal of Dental Hygiene
Loveren, C. van: Nederlands Tijdschrift voor Tandheelkunde
Peters, L.B.: International endodontic journal
Shemesh, H.: Journal of Endodontics
Sluis, L.W.M. van der: Endodontic Practice Today
Veerkamp, J.S.J.: Mondhygiënisten Vademecum
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
Zaura, E.: Caries Research

Organisation of international congresses or symposia
Annual Research Report 2010


Invited speakers at international congresses or symposia

Cate, J.M. ten (2010, September 02). 1. Dentistry in the future, are you ready? 2. Dental caries, a preventable and reversible disease (Colgate Symposium). Bahia, Brasil, FDI World meeting.


Cate, J.M. ten (2010, September 09). Biofilms. Chicago, USA, Wrigley Scientific Institute,.


Cate, J.M. ten (2010, October 15). Caries prevention, the future and today. Oslo, Norway, Norsk Tannlege Foreningen.

Cate, J.M. ten (2010, September 04). Fluoride as a public health measure: Hero or Villain. Bahia, Brasil, FDI World meeting.

Cate, J.M. ten (2010, December 09). Key note address: Fluorescence, a bright future for caries management. Liverpool, UK, ICQ congress.

Cate, J.M. ten (2010, March 26). New developments in fluoride research. New York, USA, Colgate review workshop.


Cate, J.M. ten (2010, July 15). Understanding dental caries, at the microscope and global level. Barcelona, Spain, Colgate Symposium, IADR World meeting.


Sluis, L.W.M. van der (2010, June 03). How to improve your irrigation procedure. Lebanon, Beirut, Middle East Dental Conference.


Scientific awards/honours


Veen, E.S. (2010). De kwaliteit van tandartsunitwater. 2nd prize. NT-GSK Bachelorscriptie Award 2010. GSK-congres Talking Points in Dentistry: Beurs van Berlage, Amsterdam, the Netherlands (2010, June 05).

Other international functions
Amerongen, W.E. van: Board member. IAPD.
Cate, J.M. ten: Member management committee. European Research Group Oral Biology (ERGOB).
Cate, J.M. ten: Honorary professor. Universidad Peruana Cayetano Heredia, Lima, Peru.
Cate, J.M. ten: Honorary professor. University of Hong Kong, China.
Cate, J.M. ten: Member advisory panel. Wrigley Scientific Institute, Chicago, USA.
Crietlaard, W.: Member research advisory committee University of Hong Kong Dental School.
Crietlaard, W.: Honorary professor. University of Hong Kong, China.
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: President-Elect. Diagnostic Sciences Group IADR.
Wu, M.K.: Member. European Society of Endodontics (ESE).

Membership academies

Societal impact
The societal impact of the research is evident from the impact on patient care and public dental health, 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. Furthermore, the societal impact is evident from the existence of three-year postdoctoral programs in Endodontology and Pedodontontology and from lectures for dental professionals, as listed below.

Interactions and collaborations with the industry and other non-university groups
For current grants from the industry, see ‘Indicators of Esteem”. In addition, the following collaborations with the industry exist.
Crietlaard, W. Biological Safety Officer at Purac Biochem.
Laheij, A.M.G.A., van Loveren, C. de Soet, J.J & 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, Therwill. Switzerland
Soet, J.J. de Biosafety Officer platform, together with VROM: project for database on disinfection.
Strijp, A.J.P. van Sunstar Inc., Osaka, Japan.
Zaura, E. & Crietlaard W. Wrigley, Chicago, USA.
Interactions with the general public

Impact of the research on professionals
J.J. de Soet has been interviewed by Nederlands Tandartsenblad in Infection Prevention in dentistry, together with an inspector of Medical Health (June 2010).
Post-initial training and various courses were given on Cariology, Endodontology and Pedodontology.

Organization of national conferences and symposia
W.A. van der Reijden organized the Microbial Diversity Symposium during the Spring Meeting NVvMM.

Invited speakers at national congresses or symposia
A total of 16 lectures were given by Cristescu, Metska, Peters, Shemesh, Veerkamp, Elfrink and Van Dijk.

Other national functions
W. Crielaaard is cluster coordinator in the Netherlands Systems Biology Institute for the cluster “Microbial Communities”.
C. van Loveren is chairman of the scientific Advisory Board Preventive Dentistry and Oral Diseases of Ivoren Kruis.
J.J. de Soet is a member of committee of disinfection agents of Biosafety Officers Platform.
J.S.J. Veerkamp is chairman of the Consilium Pedodontologicum.

Courses organised for dental and medical professionals
More than 13 courses were given for dental professionals on prevention, diagnostics and treatment.

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

Collaborations
- AMC Research Landsteiner Laboratory, Academic Medical Center.
- AMC, Department of Biomedical Optical, Amsterdam, the Netherlands.
- AMC, Department of Electron Microscopy, Amsterdam, the Netherlands.
- Erasmus MC, Rotterdam-Dep. of Biomedical Engineering.
- Federal University of Paraíba, 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, Ziest, 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 Medical Microbiology and Infection prevention, Vrije Universiteit, prof.dr. C.M.J.E. Vandenburgue-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-Vrielin, University of Utrecht, the Netherlands.
- Department of Health Sciences, Kristianstad University, prof.dr. S. Renvert, Kristianstad, Sweden.
- Department of Informatics, VU University Medical Center, Amsterdam, the Netherlands.
- Department of Dentistry and Oral Hygiene and Department of Biomedical Engineering. Faculty of Medical sciences, University of Groningen, Groningen, the Netherlands. prof.dr. M.C.D.N.J.M. Huysmans.
- Division of Biological Chemistry and Drug Discovery, School of Life Sciences, University of Dundee, Dundee, UK.
- Department of Medical Microbiology and National Reference Center for Systemic Mycoses, University Medical Center Göttingen, Göttingen, Germany.
- Department of Pediatric and Social Dentistry, São Paulo State University (UNESP), Araçatuba, Brazil.
- Department of Prosthodontics and Periodontology, Dental School of Piracicaba, State University of Campinas, SP, Brazil.
- Institute of Computer Science, FORTH Vassiliki Vouton, Heraklion, Greece, prof.dr. V. Moustakis.
- University of Kiel, Institute for Clinical Molecular Biology, Kiel, Germany, dr. A. Scheafer.
- Laboral Diagnostics CV, Houten, the Netherlands.
- 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, Göl, Germany, Synchrotron based nano-tomography.
- University of Thessaloniki. Dental faculty, dept. of endodontics, Thessaloniki, Greece.
- University of Toulouse Dental faculty.
- 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).
- Medische Zending, Paramaribo, Surinam.
- São Paulo State University Department of Pediatric and Social Dentistry, (UNESP), Araçatuba, Brazil.
- St. Jeugdstandverzorging, Paramaribo, Surinam.
- University of Nairobi, Nairobi, Kenya.
- WHO Collaborating Centre Nijmegen, Nijmegen, the Netherlands.

Current PhD projects
Annual Research Report 2010


Metska ME. Cone beam CT in endodontic diagnostic Supervisor: prof.dr. P.R. Wesselink; co-supervisor: dr. A.R. Özok Start: October 2008


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, Gustav Mahlerlaan 3004
1081 LA Amsterdam
Tel: +31-20-5980558
E-mail: B.Loos@acta.nl

Full professors
B.G. Loos  U. van der Velden  G.A. van der Weijden  E.C.I. Veerman

Research Objectives
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?

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 immuno-neuro-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 micrororganisms with oral epithelial cells.

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 cannot 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 (M2) and dizygotic (D2) 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 M2 and D2 twins were discordant regarding attachment loss and bone loss. The discordance was greater in D2 compared to M2 twins. In M2 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 straight forward 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 and importantly 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 (pH) 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 SIRPα, a potential regulator of osteoclast activity, was elucidated. Osteoclast formation was not changed in SIRPα 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.

Cell-activating properties of salivary histatins. We have compared the effect of histatin and LL-37, another wound healing peptide, on several wound-healing related activities. This revealed that in contrast to LL-37, histatin had no pro-inflammatory or cytotoxic effects. We have found that cyclic histatin is 1000-fold more active than the natural linear peptide stimulation with regard to its wound healing properties. We now have found that cyclic histatin has a 100-fold higher affinity for cellular receptor, strongly suggesting that the increased activity of the cyclic variant is due to a better recognition by its cognate receptor on the cell membrane. In collaboration with the Dr. Martin and Dr. Van Ameijde (dept. of Medicinal Chemistry, University of Utrecht) the intracellular signalling route which is activated by histatin will be explored. Using a novel efficient enzymatic procedure for cyclization of peptide (developed in collaboration with Prof HJ Ploegh, Whitehead Institute, USA), we are now able to produce large quantities of cyclic histatin peptides that are required for analysis of peptide structure using high-resolution spectroscopic techniques. In collaboration with prof. Hans Vogel (Calgary, Canada) a start will be made with the structure analysis of cyclic and linear histatin peptides using NMR and CD spectroscopy.

Design of protective coatings. In a project funded by the Technology Foundation we aim to develop a new class of enamel-protecting compounds that mimic and enhance the protective features of the natural saliva components. Using Phage Display peptides were selected with affinity to hydroxyapatite, saliva and mucins, the main constituents of the acquired pellicle covering the tooth surface in situ. In addition, hydroxyapatite-binding domains in salivary agglutinin and statherin have been identified. In future work we will explore the feasibility of these peptides for enhancement of the barrier function of the natural pellicle, with as final aim to develop products which enhance its protective function against dental erosion.

Saliva and dental erosion. Hard candy often contains citric acid and/or other acids, which may contribute to the development of dental erosion. In collaboration with the Bambodino Pediatric Dental Clinic (D.L. Gambon, DDS) in Rotterdam, the effects of acidified hard candy on the secretion rate and the pH of saliva are studied. These studies have shown that different types of hard candy show considerable variation in their in vivo erosive potential.

Diagnosis and treatment of saliva-related oral problems. Lactoferrin-derived peptide. We have designed a chimeric peptide in which the spatial orientation of two antimicrobial domains of bovine lactoferrin is mimicked. This chimera exhibits enhanced antimicrobial activity against both yeasts and a variety of Gram-positive and Gram-negative bacteria compared. The interaction of the chimera with model membranes is
further investigated using several biophysical methods including Differential Scanning Calorimetry, Circular dichroism and NMR analysis. In ongoing collaborative studies with a number of research institutes the efficacy is explored of above mentioned lactoferrin peptides and the human cathelicidin peptide LL-37 against several notorious multidrug-resistant bacteria, e.g. *Burkholderia pseudomallei* (Dept of Oral Diagnosis and Tropical Diseases, University of Khon Kaen, Thailand) and *Vibrio haemolyticus, Vibrio cholerae*, MRSA, *Escherichia coli* and parasites like *Entamoeba histolytica* (University of Culliacan Sinaloa, Mexico). Focus will be put on the potency to attack biofilms of *Burkholderia pseudomallei*. Moreover the effects on the type-III secretory system via which the bacteria cause lesion on enterocytes will be studied.

Interaction of salivary agglutinin with microorganisms, its role in innate immunity. In case of mucosal damage mixing of saliva and serum may occur. In collaboration with Sanquin (dr. D.Wouters; prof.dr. T. van de Berg) was shown that salivary agglutinin (SAG) activates the serum complement system, a cascade of serum proteins meant to kill bacteria and activate immune cells. SAG activates the complement through binding to mannose-binding lectin. This interaction depends on the presence of carbohydrates in SAG. Mannose-binding lectin presumably binds to fucose residues on SAG. In collaboration with Niclas Karlsson (University of Goteborg) was shown that the carbohydrate chains on SAG are highly fucosylated. In future research we will investigate whether interindividual differences in fucose content lead to differences in complement activation.

Extracellular death factors. Variants of the antimicrobial peptide Chicken Cathelicidin 27 (CMAP27) were studied for their broad spectrum antimicrobial activity against Methicillin resistant *Staphylococcus aureus*, *Yersinia pestis*, *Bacillus anthracis* and *Vibrio cholerae* (in collaboration with M. Molhoek, TNO and prof. H.P. Haagsman, University of Utrecht). Substitution of single and multiple phenylalanine (Phe) residues to tryptophan (Trp) resulted in variants with improved antibacterial as well as decreased salt sensitivity. In addition, these peptides exhibited enhanced neutralisation of lipopolysaccharide-induced release of pro-inflammatory cytokines in human peripheral blood mononuclear cells. Research in the near future will focus on the stability of CMAP27 variants in serum. Besides porcine antimicrobial peptide PMAP23 and variants of a potential novel class of antimicrobial (penta)peptides, *i.e.* Extracellular Death Factors, will be studied for their antimicrobial spectrum, immunomodulatory properties and anti-biofilm activities.

Sortase-targeting peptides. In 2011 a project, funded by NOW-ZONMW, will start, focused on the bacterial enzyme sortase as a target for antimicrobial intervention. Aim of the study is to generate sortase-targeting peptides which inhibit the expression of virulence factors on the cell wall of *S. aureus*.

Salivary Statherin effects on *C. albicans*. Salivary statherin inhibits hyphen formation of *C. albicans*. We have narrowed down the active domain on this peptide. Future research will focus on the mode of action of statherin and statherin derived peptides.

Impact of systemic diseases on saliva. Saliva as diagnostic fluid. One of the diseases on which we focus in this part 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.

Development of highly specific diagnostic tools based on peptides. By using highly specific fluorogenic substrates we have been able to detect bacterial enzyme activity of *B. anthracis in vivo* (in collaboration with Mw W. Kaman - van Zanten, ErasmusMC, Rotterdam). In parallel, specific substrates were developed for *P. gingivalis*. Using these substrates we have been able to detect the presence of *P. gingivalis* in saliva and crevicular fluid within minutes, without the need for sample pre-treatment or enzyme isolation. In ongoing collaborative studies with a number of research institutes we explore the potential of these fluorogenic substrates to detect various bacteria, including *Tannerella forsythus, Pseudomonas aeruginosa* (Dept. Medical Microbiology and Infectious Diseases, ErasmusMC, Rotterdam and Department of Biomedical Engineering, University Medical Center Groningen), *Burkholderia spp.*, (Dept of Oral Diagnosis and Tropical Diseases, University of Khon Kaen, Thailand) and *Helicobacter pylori* (dr. Tinoco, Rio de Janeiro) directly in patient material.

Dry mouth and systemic disease. This line of research examines the relationships between systemic diseases, saliva secretion, xerostomie and oral health. This is studied in patients with inflammatory bowel diseases (dr. A.A. van Bodegraven, VUMc; Dutch Federation of Crohn and Colitis Ulceroza) and liver transplant patients (dr. E. Davidovich, Jerusalem). Other groups of patients are those receiving stem-cell transplantation for malignant diseases (dr. J. Raber-Durlacher, ACTA). The results of these studies indicate that the level of xerostomia is related to the severity of the systemic disease. The level of xerostomia is also associated with the severity of chronic oral complaints. In collaboration with the saliva clinic of the Centre of Special Dental Care (dr. C.P. Bots) the saliva of patients referred to this clinic is analyzed. These data will be used to provide more evidence-based treatments for the alleviation of xerostomia.
## Academic personnel in 2010 and 2011

### Research staff ACTA – PAB (in full time equivalents)

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Output

Dissertations


Scientific publications referred

Berchier, C.E., Slot, D.E. & Weijden, G.A. van der (2010). The efficacy of 0.12% chlorhexidine mouthrinse compared with 0.2% on plaque accumulation and periodontal parameters: a systematic review. Journal of Clinical Periodontology, 37(9), 829-839.


Scientific publications non-referred

Professional publications


Publications aimed at the general public


Veerman, E.C.I. (27-10-2010). Een speekselenzym bevordert wondgenezing. NRC Handelsblad

Patents

Indicators of Esteem
Grants: current projects with external funding
Bikker, F.J. STW Valorisatie Grant. Rapident : Substrates for rapid oral diagnosis. € 25,000.
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. S.Taweechaisupapong, Department of Oral Diagnosis, Khon Kaen University, Thailand.
Bolscher, J.G.M. Co-investigator of research project on the "Inhibition of Burkholderia pseudomallei biofilm formation by the Lactoferrin peptide LFchimera." Grant from Thailand government, covering PhD-student, visits to foreign research labs and visits of co-investigator to Khon Kaen University (2010-2014). Principal Investigator: prof.dr. S. Taweechaisupapong, Department of Oral Diagnosis, Khon Kaen University, Thailand.

Membership of editorial boards
Brand, H.S.: Nederlands Tijdschrift voor Tandheelkunde
Loos, B.G.: Journal of Clinical Periodontology
Loos, B.G.: Journal of Dental Research
Loos, B.G.: Oral Health and Preventive Dentistry
Schoonheim-Klein, M.E.: European Journal of Dental Education
Slot, D.E.: International Journal of Dental Hygiene
Annual Research Report 2010

Velden, U. van der: Journal of Clinical Periodontology
Weijden, G.A. van der: International Journal of Dental Hygiene

Organization of international congresses or symposia

Scientific awards/honours

Invited speakers at international congresses or symposia

Other international functions
Loos, B.G.: Outside examiner, oral final examination. Post graduate program in periodontology.

Raber-Durlacher, J.E.: Expert reviewer information summary about oral complications in cancer. (Contribution to NCI PDQ (National Cancer Institute Physician Data Query).


Velden, U. van der: EFP representative for the accreditation of the postgraduate in periodontology. Dental Faculty and Hospital, University of Strasbourg, France, September 28-29.

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.


Societal impact
The societal impact of the research 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, Proctor & Gamble and Wrigley.

Impact of the research on professionals
W.J. Teeuw gave interviews for Dutch journals.

Invited speakers at national congresses or symposia
A total of 5 presentations were given by W.J. Teeuw and B.G. Loos.

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

U. van der Velden is chairman of the Concilium Parodontologicum and a member of the raad van commissarissen Nederlands Tijdschrift voor Tandheelkunde.

E.C.I. Veerman is a expert reviewer for Programme Translationeel Onderzoek, ZONMW.

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.

Collaborations
- Universiteit van Amsterdam, Klinische Chemie (prof.dr. A. Sturk, dr. R. Nieuwland), Amsterdam, NL.
- Department of Molecular Medicine and Gene Therapy, Lund University, Lund, Sweden (dr. J. Richter).
- University of Sheffield (dr. D. Battle), Sheffield, United Kingdom.
- Celltech (dr. A. Docherty), London, United Kingdom.
- Padjadjaran University, Dept. Periodontology (dr. S. Lambri), Bandung, Indonesia.
- Unilever Research (dr. D.J. Page), Port Sunlight, United Kingdom.
- Ludwig Boltzmann Institut fur Osteologie (prof.dr. P. Fratzl) Vienna, Austria.
- Universität Kiel (dr. P. Saftig) Kiel, Germany.
- Braun Oral Research (dr. P. Warren) Baltimore, USA.
- University of Kiel, Dept of Gastro-Enterology (prof.dr. S. Schreiber) Germany.
- University of Bonn, Dept of Periodontology (prof.dr. S. Jepsen), Germany.
- VUMc, Medische Microbiologie (dr. B. Appelmelk).
Current PhD projects

Aekkalak S. Inhibition of *Burkholderia pseudomallei* biofilm formation by Lactoferrin peptide LFchimera. Supervisor: prof.dr. Suwimol Taweechaisupapong, Department of Oral Diagnosis, Faculty of Dentistry, and Melioidosis Research Center, Khon Kaen University, Thailand. co-supervisor: dr. J.G.M. Bolscher, The Academic Centre for Dentistry Amsterdam (ACTA), the Netherlands. Start: August 2010.


- VUmc, Orthopedie (dr. T. Smit).
- VUmc, Moleculaire Celbiologie en Immunogenetica, sectie Immunomodulatie (prof.dr.Y. van Kooyk).
- VUmc, Moleculaire Celbiologie en Immunogenetica, sectie Glycoimmunologie (dr. I. van Die).
- VUmc, Dermatologie (dr. S. Gibbs, prof.dr. R. Schepers).
- Universiteit van Amsterdam, AMC, Celbiologie en Histologie (dr. J. van Marle).
- Universiteit van Amsterdam, AMC, Humane Retrovirologie (prof.dr. B. Berkhour).
- Rijksuniversiteit Groningen, Afdeling Mondzienken en Kaakchirurgie (prof.dr. A. Vissink).
- Sanguin, Departments of Immunopathology (dr. D. Wouters) and Blood Cell Research (prof.dr. T. van den Berg).
- Kindertandheelkundepraktijk Bamabodino. Rotterdam (drs. D. Gambon)
- University of Chile, Santiago, Institute of Biomedical Sciences (prof.dr. M. González).
- University of Madrid, Centro de Investigaciones Biologicas (prof. dr. L. Rivas).
- University of Oporto, Portugal, Dept of Chemistry (dr. M. Bastos).
- UAS, Faculty of Medicine, Hospital Pediatrico de Sinaloa, Mexico (dr. Nidia León Sicairos).
- University of Chiang Mai, Thailand, Dept of Odontology and Oral Pathology (dr. S. Krisanaprakornkit).
- Mahidol University, Bangkok, Thailand, Fac Science and Fac of Tropical Medicine (prof.dr. S. Sirisinha and dr. N. Chantarita).
- University of Aquila (Italy), Dept. of Biomedical Sciences and Technology (dr. A. Bozzi).
- Deutsche Krebsforschungszentrum Division of Molecular Genome Analysis, Heidelberg (dr. C. End).
- University of Calgary, Calgary, Canada. Dept. of Biological Sciences (prof.dr. H.J. Vogel).
- Whitehead Institute and MIT, Cambridge, MA, USA (prof.dr. H.L. Ploegh).
- The Hebrew University, Hadassah School of Dental Medicine, Department of Pediatric Dentistry, Jerusalem, Israel (dr. E. Davidovich).
- University of Goteborg, Sweden (dr. Niclas Karlsson).
- Erasmus Medisch Centrum. Medical Microbiology (prof dr A van Belkum, Dr W. Wamel)
- Universiteit of Utrecht, Medicinal Chemistry (Dr N. Martin)
- Rapid Pathogen Screening (RPS), Sarasota, Florida, USA (Dr B. van Dine)
- University of Utrecht. Faculty of Veterinarian Medicine (Prof Dr H. Haagsman)


Social Dentistry and Behavioural Sciences

Oral Health-related Well-being and Behaviour

Program leader
Prof.dr. J. Hoogstraten
Social Dentistry and Behavioural Sciences
ACTA, Gustav Mahlerlaan 3004
1081 LA Amsterdam
Tel: +31-20-5980246/247
E-mail: J.Hoogstraten@acta.nl

Full professors

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 in 2007, and advices given by a recent self-organized ACTA review-committee, section’s research efforts are now focused on Oral Health-related Well-being and Behaviour, of both patients and general dental practitioners and their staff.
As for dental patients we aim to improve and to maintain the well-being of both regular dental patients and subgroups of patients suffering from (extreme forms of) anxiety or (anticipated) pain or from physical/mental handicaps. Moreover, since the well-being of patients is highly dependent on the treatment they receive from dental professionals who are often working solo and limited in their career-possibilities, our efforts are also aimed at these dental professionals, keeping them away from stress and burnout, and helping them in communicating adequately with their patients.

Results
For patients suffering from chronic phantom limb pain preliminary findings suggest that substantial reductions of this pain can be achieved, using a psychological intervention focused on trauma or pain-related memories. People who are intellectually disabled (ID) seem to have poorer oral hygiene and a higher prevalence of oral health problems compared to the general population. The hypothesis that the availability of comprehensive information prior to a dental appointment would enhance cooperative behaviour of these patients, had to be rejected, however. For patients with ID it was shown, based on a literature-review that these patients seem to have a predisposition to the development of a Post Traumatic Stress Disorder (PTSD). Four persons with mild ID were subsequently successfully treated with an evidence-based treatment (EMDR). Using EMDR, a Two-Method Approach was outlined in order to be able to use EMDR for a broad spectrum of symptoms and problems.
For patient with non-syndromic severe hypodontia common patterns of tooth agenesis were successfully identified, using the recently introduced Tooth Agenesis Code (TAC) procedure.
Joint research efforts with the Department of Oral and Maxillofacial Surgery showed that anxiety sensitivity does not predict anxiety and pain related to third molar removal, and that surgical removal of a third molar by use of local anaesthesia has minimal impact on the development of dental anxiety or symptoms of psychological trauma.
In a study comparing flapless implant surgery with the traditional flap access approach, findings suggest that the non-traditional procedure does result in less favourably results regarding well-being and feelings of pain than the flap access approach.

Bitewings radiographs of young children can reveal a considerable amount of caries surfaces and inadequate restorations, but it was also shown that the country of birth of the child’s mother does play a role in the prevalence of dental caries. Indeed, parental attitudes are likely to play a role in achieving and maintaining a desired level of oral health- related well-being in children. Using Q-methodology five profiles of parents were identified to be used in developing tailor-made strategies in caries prevention.

Well-being of dental staff in the western part of Northern Ireland seems seriously threatened because of job demands and limited job resources.

One – quarter of the dentists were categorized as having a serious burnout risk and the proportion of dentists suffering from psychological distress was also unusually high. It is recommended that attention for burnout risk is given priority by dental associations. It must be noted that in the Netherlands many dental hygiene students work in a dental practice during their study, taking over several tasks usually performed by the dentist, including so-called reserved procedures. Indeed, professional behaviour in the medical/ dental educational context is currently a major issue, since patient safety and well-being is involved. Staff members should therefore be particularly trained in dealing with students showing unprofessional behaviour.

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, Center for Special Dental Care (SBT), Pedodontology and Orthodontics).
Dissertations


Scientific publications (refereed)


Meurs, D., Rutten, M. & Jongh, A. de (2010). Does information about patients who are intellectually disabled translate into better cooperation during dental visits? Special Care in Dentistry, 30(5), 200-205.


Professional publications


Langetermijn effecten van de gebitsontwikkeling na stamceltransplantatie. Nederlands Tijdschrift voor Tandheelkunde, 117, 331-335.


Annual Research Report 2010


Book editorship

Indicators of Esteem

Membership of editorial boards
Jongh, A. de: European Journal of Psychotraumatology
Jongh, A. de: Journal of EMDR Practice and Research

Invited speakers at international congresses or symposia
Gorter, R.C. (2010, August 26). Professional behaviour in dental education. Amsterdam, the Netherlands, Association for Dental Education in Europe (ADEE), workshop.

Organization of international congresses or symposia

Scientific awards/honours

Societal impact
The societal impact of the research of the 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 7 interviews for radio broadcasting and Dutch magazines and journals, most of these about the prevalence of dental fear. F.M.D. Oosterink-Wubbe gave 7 interviews about dental fear. J. Poorterman had one interview. M.A.J. Eijkman wrote 10 articles in the Dutch newspaper NRC/Handelsblad.

Invited speakers or moderators at national congresses or symposia
A total of 11 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. de Jongh is supervisor of the post-initial training for "tandarts-angstbegeleiding".

Lectures during courses for dental and medical professionals in the Netherlands
A total of 6 presentations were given for dentists 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.

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**Current PhD projects**


Oral Function and Restorative Dentistry

Loading and Tissue Regeneration

Program leader
Prof.dr. F. Lobbezoo
Department of Oral Kinesiology
ACTA, Gustav Mahlerlaan 3004
1066 EA Amsterdam
Tel: +31-20-5980412
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Full professors

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Introduction

Loading and Tissue Regeneration

The human masticatory system has several important functions that determine an individual’s general health and well-being, like biting, chewing, swallowing, talking, laughing, and yawning. Sometimes, patients are confronted with problems in performing these functions. This may have various causes. On the one hand, chemical and bacteriological factors may hamper a healthy functioning of the masticatory system by causing infection and inflammation. On the other hand, mechanical overloading as well as “underloading” or disuse of the constituent structures of the masticatory system (viz., teeth, bone, cartilage, muscles, and joints) may yield functional oromandibular impairments. The research of ACTA’s research program “Loading and Tissue Regeneration” (LTR-ACTA) focuses on the mechanical threats for the masticatory system, on the resulting clinical problems, as well as on the solutions for these clinical problems. Groups that are currently involved in LTR-ACTA are Oral Kinesiology (OKI), Oral Implantology and Prosthodontics (IMP), Dental Materials Sciences (DMS), Oral Cell Biology (OCB), and Functional Anatomy (FA).

MOVE

In part, the research of LTR-ACTA is integrated in the Interfaculty Research Institute MOVE; a joint venture of the VU University Amsterdam that includes the Faculty of Human Movement Sciences and parts of the VU University Medical Center and of ACTA. MOVE covers a broad spectrum of fundamental and applied human movement research, with a strong integrative and translational signature. The focus of the research is on healthy and pathological movements, as well as on the musculoskeletal system and its disorders. The research is organized in three themes: Musculoskeletal Biology, Structure and Motion, and Motor Control. The aim of the research within the theme “Musculoskeletal Biology” is to prevent or recover damage to the motor system, due to disposition, ageing, inadequate nutrition, incorrect movement, or loading habits. This is found in patients with osteoporosis, arthrosis, and discus degeneration, as well as in patients with damaged bone, cartilage, or muscle tissues. The research program within the theme “Musculoskeletal Biology” is called “Loading and Tissue Regeneration”. Tissue regeneration is possible by means of mechanical loading and through growth factors, hormones, and medication. An important tool for the regeneration of tissue is the use of stem cells which are able to differentiate into bone, cartilage, and muscle cells. Insight into tissue regeneration is obtained by comparing results from tissue culture and animal models to computer simulations.
of the motor system and to biomechanical research in clinical trials with patients. The MOVE-related research of LTR-ACTA is part of this latter, equally named research program.

**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 priority area (“zwaartepunt”) of LTR-ACTA. As implied above, a healthy oral system is characterized not only by the absence of infection and/or inflammation of dental and periodontal tissues, but also by a healthy musculoskeletal system. Musculoskeletal tissues (i.e., bone, cartilage, muscles, and joints) can be affected adversely by, for example, mechanical overloading or by disuse. 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 collaborates with medical disciplines like orthopaedics 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 and thus oral health-related quality of life.

**Research objectives**

**Oral Kinesiology**

Two main categories of threats compromise the health of the human masticatory system, viz., chemical/bacteriological threats and mechanical threats. Chemical/bacteriological threats are responsible for diseases within and around the teeth (e.g., caries and periodontitis), while mechanical threats (‘over’- or ‘under’ loading) may compromise the health of the muscles (painful hyper- or hypotrophic muscles), joints (internal derangements or osteoarthrosis), bones (hyper- or hypotrophic jaws) and teeth (attrition) of the masticatory system. The Oral Kinesiology program focuses on the mechanical threats for the muscles and joints of the human masticatory system. Its aim is to prevent damage and promote recovery from damage to the muscles and joints due to adverse oral habits, such as clenching and grinding (bruxism).

The research lines of the program of Oral Kinesiology are clinically oriented and the following questions are being addressed:

1. Bruxism (clenching and grinding habits):
   a. What is the pathophysiology of bruxism?
   b. How can bruxism be influenced?
2. Masticatory muscle pain:
   a. What are the relationships between bruxism and masticatory muscle pain?
   b. What is the pathophysiology of masticatory muscle pain?
   c. How can masticatory muscle pain be diagnosed and differentiated from other orofacial pain conditions?
   d. What are the most effective treatment modalities for masticatory muscle pain?
3. Temporomandibular joint pathology:
   a. What are the relationships between bruxism and temporomandibular joint pathology?
   b. How can temporomandibular joint pathology best be diagnosed?
   c. What is the natural course of temporomandibular joint pathology?
   d. What are the most effective treatment modalities for temporomandibular joint pathology?
4. Sleep apnea:
   a. What is the pathophysiology of sleep apnea?
   b. Can sleep apnea be influenced by imposing different static (occlusal) loadings upon the masticatory system during sleep?

Cause-and-effect relationships are studied, taking important cofactors like age, gender, ethnic background, psychosocial factors and genetic factors into account.
Oral Implantology and Prosthodontics

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.

1. Stimulation of bone growth in general and specifically around Oral Implants,
   A slow release of BMP’s (bone morphogenetic proteins) from the implant coatings is shown to have a stimulating effect on bone growth. Besides oral implants, bone filling osseointegrative materials and membranes have also been coated and have become integrated in the department’s research projects. Moreover, an osteointegrative bone filling material has been developed and under evaluation in vitro and in vivo.

2. Oral Implants used in prosthetic dentistry
   The department of Oral Implantology and Posthetic Dentistry has directed it’s research toward the evaluation of different treatment options for prosthetic patients using dental implants. Being aware of the expected impact digitalization will have on dentistry as well as oral implantology it is also evaluating new digital tools in oral implantology. Working together with industry we are focusing on the precision of planning tools as well as digital scanning as an alternative for impression taking.
   Together with the technical university of Eindhoven we share a post doc with whom we are looking at workflow mining in the digital environment. Together with the department of social dentistry we are designing a study looking at the impact of digital dentistry on the dental workforce.

3. Peri-implantitis
   In 2008, we have started a research project on peri-implantitis together with the section of oral microbiology and periodontology joined us in 2009.
   The idea behind this project is that to look at peri-implantitis from various angles. One of them is to analyze 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.
   In vitro and in vivo treatment evaluations are under way.

Dental Materials Sciences

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.

Oral Cell Biology

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.

Functional Anatomy
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

Oral Kinesiology
Bruxism. To further unravel the pathophysiology of bruxism, a series of twin cohort studies was performed in young and middle-aged adults. A dose-response relationship was observed between tobacco use and sleep grinding. Further, nicotine dependence was found to be an important predisposing factor for sleep grinding. In a nine-year follow-up study, the long-term natural course of bruxism was assessed. Self-reported sleep grinding and awake clenching were found to fluctuate considerably over time between the ages of 14 and 23 years. In a case-control study using full-night polysomnography, the observed highly significant associations between sleep-related motor events (periodic leg movements and sleep bruxism) and EEG arousals from sleep suggest that both types of motor events are the result of the same underlying neurophysiologic mechanism. This underlines the recent insight that sleep bruxism is a sleep-related movement disorder rather than an oral parafunction.

Masticatory muscle pain. In a systematic literature review, positive associations were found between TMD pain and self-reported/clinically diagnosed bruxism, while no such associations were observed in studies employing instrumental diagnoses of bruxism (e.g., polysomnography). Interestingly, a questionnaire study revealed that TMD patients believe that bruxism is harmful for their masticatory system. Fortunately, they also believe that they can actively reduce their purportedly adverse bruxing behaviour themselves (“self-efficacy”). Further, in a multicenter questionnaire study, associations were found between pain-related disability on the one hand and depression and somatization levels and pain duration on the other. Experimentally induced jaw-muscle fatigue/pain by means of an accelerated gum-chewing task caused a decrease in the inhibitory jaw reflex activity, suggesting that jaw-muscle fatigue/pain might contribute to jaw-closing-muscle hyperactivity. In order to come to a better pain model for jaw muscle pain, a new instrumental technique was developed which can
successfully provoke a delayed-onset muscle soreness in the human jaw muscles. This pain model opens new possibilities in the study to the relationship between jaw muscle overloading and jaw muscle pain. In order to study the role of genetic factors in the onset and maintenance of chronic musculoskeletal pain in general, and of TMD pain in particular, and in collaboration with the Netherlands Twin Register and the department of Social Dentistry, a questionnaire study to a large sample of twins and their family members was started. The current scientific diagnostic standard for temporomandibular disorders, the Research Diagnostic Criteria for TMD (RDC/TMD), is in the process of being updated. Earlier results of our diagnostic validity research line will be incorporated in this updated version. At the same time, new concepts (like the use of familiar pain on clinical tests) will be introduced in the RDC/TMDv2. To further strengthen our frontier role in supplying evidence for the validity of diagnostic tests for TMD, we have started a new clinical study (in collaboration with the department of Endodontics) that incorporates these new concepts. Furthermore, a questionnaire to kinesiophobia (fear of movement) was adapted for its use in TMD patients (the Tampa Scale for Kinesiophobia for TMD). In other musculoskeletal pain conditions like low back pain, kinesiophobia has been related to an increased risk to develop chronic complaints. In a current follow-up study, where TMD patients from 7 Dutch Orofacial Pain Clinics are enrolled, the role of kinesiophobia in the development of chronic complaints is further evaluated.

Temporomandibular joint pathology. In a biomechanical study to the loading of the temporomandibular joint during lower jaw movements it was shown that the joint reaction forces are larger during opening than during closing. This may explain the important diagnostic finding that ADDR clicking sounds during opening are louder than during closing. A two-year follow-up study to anterior disc displacements with reduction (ADDR) has shown that an ADDR is usually a stable condition of the human temporomandibular joint. Only in patients who also report complaints of intermittent locking, the ADDR has a tendency to develop into a disc displacement without reduction. Surprisingly, and adding unique information to current knowledge of the progress of intermittent locking, this loss of capacity of the disc to reduce is only rarely accompanied by the classical symptoms of lower jaw locking (inability to open the mouth, pain).

Sleep apnea. A polysomnographic study has shown that a mandibular occlusal position of 50% of the maximum protrusion is to be recommended as a weighted compromise between efficacy and side effects when starting a treatment with a mandibular advancement device (MAD) for the management of obstructive sleep apnea (OSA). Further, in a large-scale randomized clinical trial with a placebo-controlled parallel design, we found that an MAD is equally effective, but less invasive, in the management of mild/moderate OSA as the “gold standard” treatment for OSA, viz., continuous positive airway pressure (CPAP). In the long-term follow-up of that trial, the positive effects were maintained for both active treatment conditions.

Perspectives. A world-wide consortium of temporomandibular disorder experts has taken the initiative to come to a new, thoroughly updated version of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD). Two of our researchers actively participate in this consortium and the results of our multi-center study to the diagnostic accuracy of temporomandibular pain tests are incorporated in the new revised version of the RDC/TMD.

**Oral Implantology and Prosthodontics**

Stimulation of bone growth in general and specifically 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 osseoductive materials and membranes have also been coated and have become integrated in the department’s research projects. Based on our previous findings, an osteoinductive bone filling material has been developed and in vitro and in vivo test are under taken. One PhD project is carried out by Mr. Tie Liu as well as other researchers in this topic.

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 the publication is in the preparations.

In a sinus lift model (clinical trial), 22 patients have been treated with Bio-Oss functionalized with BMP-2. The histology results have been analyzed. This study results have been presented at various scientific meetings. The two years clinical follow up by CBCT is ongoing together with the radiology department.

The use of tissue expanders to expand the mucosa in area’s where bone augmentation is the indicated treatment. 28 goats have been treated and slaughtered, histological analysis has been carried out and the results have been evaluated. 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 was 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 it 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 vitro in our department in collaboration with cell biology department. An animal experiment is carried out in collaboration with Zhejiang University, China. The human study has been designed. We are now in discussion with the patent bureau of the VU to patent this product and treatment objective it can be used for. Following the advice of the bureau a publication is on hold until the paperwork has been done. This material is now being analysed in a bench study where we are looking at it’s cleaning property and the depth into which it will penetrate the implant surface when using airflow.

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. Mr. Vriens has decided to put is Implant training on hold and starting form November he is promoting his time to this project.

Oral Implants used in prosthetic 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. A second technique has been developed for the treatment of patients who are partially dentate.

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 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 have 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. G.T. 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 and a second is in preparation. This project is being extended with the evaluation of the fit of the bar when comparing digital impressions with analogue impressions.

Implants supporting free end saddles. A multi center clinical trial was carried out as a multycentre study. (The Netherlands Colombia and New Zealand). Our department has analyzed the patient satisfaction and the results have been submitted for publication.

We have started a new project together with industry looking at several aspects of digital imaging, digital treatment planning and oral implant scanning. This study is being carried out together with the radiology department and the section of functional anatomy. We are evaluating the precision of a digital planning instrument, the precision of the oral scanning of new scanning abutments on the implants and a scanning and printing procedure where we scan teeth prior to extraction and print an implant to replace the tooth immediately. 20 human cadaver mandibles are being used for this project. A second project here is the evaluation of three different intraoral scanners (3M Itero and Cerec). We are looking t the preciseness of analogue impressions compared to digital impressions made with three different intraoral scanners in a student patient group. Using digital subtraction methods the differences are being analyzed and we hope to be able to introduce guidelines for clinical use.

Peri-implantitis. In 2008, we have started a research project on peri-implantitis together with the section of oral microbiology. The idea behind this project is to look at peri-implantitis from various angles (bacteria types, colonization of the implant surface, cleaning of the implant surface, the surface tension of the implant and bone regeneration onto the implant surface.

Dental Materials Sciences

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.

**Oral Cell Biology**

Regeneration of bone and periodontium. For engineering bone tissue to restore, for example, maxillofacial defects, mechanosensitive cells are needed to conduct bone cell-specific functions, such as bone remodeling. Mechanical loading affects local bone mass and architecture in vivo by initiating a cellular response via loading-induced flow of interstitial fluid. After surgical removal of ectopically impacted third molars, human dental pulp tissue is an easily accessible and interesting source of cells for mineralized tissue engineering. We found that human dental pulp cells, like osteogenic cells, acquire responsiveness to pulsating fluid shear stress in mineralizing conditions. Thus dental pulp cells might be able to perform bone-like functions during mineralized tissue remodeling in vivo, and therefore provide a promising new tool for mineralized tissue engineering to restore maxillofacial defects. We also found that pulp-derived mesenchymal stem cells (PDSCs) with a mature phenotype are more responsive to pulsating fluid shear stress than osteogenically immature PDSCs and produce more bone in vivo. Thus PDSCs with a mature osteogenic phenotype might be preferable for bone tissue engineering to restore, for example, maxillofacial defects, because they might be able to perform mature bone cell-specific functions during bone adaptation to mechanical loading in vivo.

Stem cells offer an interesting tool for tissue engineering, but the clinical applications are limited by donor-site morbidity and low cell number upon harvest. Recent studies have identified an abundant source of stem cells in subcutaneous adipose tissue. Adipose stem cells (ASCs) present in adipose tissue are able to differentiate to several lineages and express multiple growth factors, which makes them suitable for clinical application. Buccal fat pad (BFP), an adipose-encapsulated mass found in the oral cavity, could represent an easy access source for dentists and oral surgeons. We found that BFP contains a population of stem cells that share a similar phenotype with ASCs from abdominal subcutaneous fat tissue, and are also able to differentiate into the chondrogenic, adipogenic, and osteogenic lineage. These results define BFP as a new, rich, and accessible source of ASCs for tissue engineering purposes.

Human (h) adipose tissue-derived mesenchymal stromal cells (ASC) constitute an interesting cellular source for bone tissue engineering applications. Wnts, for example Wnt5a, are probably important regulators of osteogenic differentiation of stem cells, but the role of Wnt5a in hASC lineage commitment and the mechanisms activated upon Wnt5a binding are unknown. Our data illustrate the importance of Wnt5a as a stimulator of hASC osteogenic differentiation, and show that changes in actin cytoskeleton controlled by ROCK are determinants for Wnt5a-induced osteogenic differentiation of hASC.

Mechanical adaptation and regeneration. Bone is a specialized connective tissue that tolerates mechanical loads derived from weight bearing and from muscle contractions. In regions of high bone loading, the
mechano-responsive osteocytes inhibit osteoclastic bone resorption by producing signaling molecules. We found that mechanical loading induced changes in gene expression by osteocytes, which likely contribute to the inhibition of osteoclastogenesis after mechanical loading of bone. Because mechanical loading upregulated gene expression of MEPE but not PHEX, possibly resulting in the upregulation of OPG gene expression, we speculated that MEPE is a soluble factor involved in the inhibition of osteoclastogenesis by osteocytes.

Bone mechanotransduction is vital for skeletal integrity. Osteocytes are thought to be the cellular structures that sense physical forces and transform these signals into a biological response. The Wnt/beta-catenin signaling pathway has been identified as one of the signaling pathways that is activated in response to mechanical loading, but the molecular events that lead to an activation of this pathway in osteocytes are not well understood. We found that mechanical loading activates the beta-catenin signaling pathway by a mechanism involving nitric oxide, focal adhesion kinase, and the Akt signaling pathway. These data provide a framework for understanding the role of beta-catenin in mechanical adaptation of bone.

We hypothesized that the failure to regulate pH in the enamel space is one of the mechanisms that leads to development of enamel fluorosis after excess intake of fluoride. We localised the cystic fibrosis transmembrane regulator (Cftr, a chloride channel) in the apical membranes and the sodium bicarbonate exchanger 1 (Nbce1) in basolateral membranes of maturation ameloblasts. Disruption of the gene coding for Cftr impaired completion of enamel mineralization. The data so far support the concept that maturation ameloblasts regulate pH by secreting bicarbonrates into the forming enamel. Several of these pH regulators have also been found in osteoclasts suggesting that mutation of pH regulators may also function of both cell types.

Recent work with the Ae2 knock-out mouse reinforces that heterogeneity of osteoclasts exists. Markedly, these mice present with severe osteopetrosis of long bones, whereas normal tooth eruption occurred in these mice. Since osteoclasts are formed through fusion of local precursors present in bone marrow, this could imply that local differences, for instance differences in bone marrow composition, could be causative for the existence of different osteoclast. A.P de Souza Faloni, a Brazilian exchange student from the Federal University of Sao Paulo and the Dental School of Universidade Estadual Paulista at Araraquara described that jaw and long bone marrow have a different osteoclastogenesis potential. Bone marrow differentiated into osteoclasts in a faster way than mandibular marrow, possibly due to a higher percentage of osteoclast precursors, in particular myeloid blasts that can differentiate more rapidly into osteoclasts, present in long bone marrow. In a follow-up study, A. Azari showed that jaw and long bone marrow derived osteoclasts differ in size and shape and that they respond differently to bone and dentin. Jaw derived osteoclasts were primarily round, whereas the majority of long bone derived osteoclasts was star shaped.

Different bones evoke different osteoclastogenesis responses. When osteoclastogenesis is performed on femoral cortical bone slices, osteoclast formation is markedly increased compared to osteoclast formation assays on plastic or on calvarial bone. Expression of various pro-osteoclastogenesis signals (RANK, c-fms, NFATc1, c-fos, IL-1β, TNF-α) was increased compared to cultures on plastic or calvarial bone, whereas expression of an inhibitor of osteoclast formation, MafB, was increased on calvarial bone.

Infantile osteopetrosis is a disease caused by defective osteoclasts that lack an essential subunit of a proton pump, eventually leading to early death in man and mouse. In collaboration with Dr. J. Richter, University of Lund, Sweden, it was shown in a mouse model for infantile osteopetrosis that wild-type cells could rescue these mice, even without leading to blindness and deafness. We showed that osteoclasts from the rescued mice contained wild type fusion partners, thereby restoring their bone degrading capacity.

**Functional Anatomy**

Adaption. During function the various anatomical structures experience forces. They are a dominant determinant for maintenance and adaptation. They are subject to ongoing analysis to unravel on the one side the influence of daily or incidental loads and on the other side the underlying mechanisms. The mechanical properties of the mandibular condyle and their consequences for habitual loading and deformation have been analyzed. Using MicroCT large scale Finite Element Models have been constructed which were subjected to compression and shear tests. It was predicted that although the cortex may be stronger than the cancellous bone, the latter plays a dominant role in the transfer of loads to the body of the mandible.

As it had been demonstrated earlier that the cores of the trabeculi generally are more mineralized and herewith stiffer than the outer layers, this property was included in the models. It appeared that if such were neglected (as had been the case in other studies) the apparent stiffness of the structure would be overestimated. Consequently, the trabecular bone of the mandibular condyle appeared to be more compliant that had been predicted before.
The amount of collagen in porcine condylar bone was demonstrated to increase with age, but their mature cross-links decreased. As the latter is associated with bone turnover, the relatively low number of mature cross-links after the age of 40 weeks suggests that bone turnover rate continues to be high.

In an animal model the relationship between the daily activation of the masseter muscle and the concomitant deformations in the mandible were assessed. Furthermore these deformations were compared with those occurring in leg bone. The spectrum of strain amplitudes in the mandible appeared to be much wider than in the leg bone. Furthermore, in the mandible they occurred with preferences for certain frequencies, whereas such preferences were absent in the leg bone.

The mineral density distribution in the mandible has been considered to reflect the local differences in deformation. The latter may relate to the sites where muscles attach. However, analysis of the mineral density distribution in human mandibles with MicroCT did not confirm this consideration. Despite this fact the patterns in the various mandibles were very similar, suggesting that either other factors than muscle attachments are responsible for the major differences in deformation, or that there are other factors that determine the mineral density distribution in this bone more profoundly. By drastically changing the function of the jaw muscles, two studies examined the adaptive capabilities of the rabbit masticatory system. A decrease of the daily occlusal forces was achieved by lowering the consistency of food, resulting in a reduction of the total daily muscle use especially in the weeks following the change. The decrease seems to be limited to activity levels normally generated during mastication. These changes in neuromuscular activity might cause adaptational modifications in the masticatory system, e.g. the fiber type composition of the jaw muscles and the degree of mineralization of the muscle attachment sites. Adaptation of masticatory muscles has been analyzed in rabbits. After three months of disuse caused by temporary disablement with Botox, the cross-sections of the fibres in these muscles had been decreased. Also their fibre types had been altered. It was striking that not only the treated muscles were affected, but also the other ones, indicating that their function had been changed. Most probably they have had to work harder due to the disabling of the normally co-contracting treated ones.

Preliminary results in this area give perspectives on how normal and altered muscle function contribute to bone loading near the attachments and beyond, and herewith on bone growth and resorption.

Biomechanics. It has been suggested that impaired lubrication of the temporomandibular joint can lead to joint deterioration and herewith to dysfunction. However, the mechanism by which this deterioration is initiated is unknown. Applying biomechanical modeling it has been predicted that increased friction between the articulating cartilaginous structures in this joint primarily affects the shearing stresses in the articular layers on the condyle and articular eminence.

The suspected increase of stress in the articular disc was hardly present, although the most heavily stressed areas had been relocated. Subjects with a hypermobile jaw joint are suspected to be vulnerable for joint degradation also. As the biomechanics of a hypermobile joint are presently ill understood. Neither is known how such an in it self relatively harmless affliction could lead to a severely painful joint. To analyse and enable prediction of the consequences of jaw joint hypermobility a biomechanical model has been developed in which the morphology can be fitted to healthy subjects either with or without this affected type of jaw joints.

Perspectives in this area include assessment of the influences of aging on jaw joint function. Furthermore, the analysis of the relevant factors that discriminate between normal and hypermobility of the jaw joint starts to give insights in the etiology of the latter.
## Academic personnel in 2010 and 2011

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

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## PhD students

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### Total non tenured staff

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## Output

### Dissertations


**Bloemen, V.** (2010, July 01). Cell-cell interactions during osteoclastogenesis. VU University Amsterdam (164 pag.). Prom./coprom.: prof.dr. V. Everts & dr.ir. T.J. de Vries.


Scientific publications (non-referred)


Loon, J.J.W.A. van (2010). Mechanomics and physicomics in gravity related research. In M. Monici & J.J.W.A. van Loon (Eds.), Cell Mechanochemistry, biological systems and factors inducing mechanical stress, such as light, pressure and gravity (pp. 1-22). Kerala, India: Transworld research network.


Vatsa, A., Smit, T.H. & Klein-Nulend, J. (2010). Mechanobiology of bone: from cell to organ. In M. Monici & J.J.W.A. van Loon (Eds.), Cell Mechanochemistry, biological systems and factors inducing mechanical stress, such as light, pressure and gravity (pp. 131-152). Kerala, India: Transworld research network.


Professional publications


62


Publications aimed at the general public

Book editorship


Indicators of Esteem
Grants: current projects with external funding
Bank, R. & Everts, V. TNO beurs Kenniscentrum, NITE project; AIO (1 fte, 4 year) 2007-2011.

Bronckers, AL. NIH grant on dental fluorosis.a 1 year extension to end of 2012 (87 k US $).

Dozic, A. Forensic Dentistry research “Federalno Ministarstvo za Obrazovanje i Nauku u Bosni i Hercegovini” (Grant “N 05-39-8398” 01/2010).

Everts, V. Grant to Marina Belucci, Brazilian postdoc CAPES (Coordenação de Aperfeiçoamento Pessoal de Nivel Superior) and the program is called PDEE - sandwich (Programa de Doutorado no País com Estágio no Exterior - sanduiche). September 2010- August 2011. €16,460. -

Everts, V. KNaw grant for collaboration with China on a 2-year project, €45,170. - 2010-2011.

Everts, V. KNaw grant for collaboration with China on a 10 months project, €13,925.- 2010-2011.


Klein-Nulend, J. & Helder, M.N.: Effect of low intensity pulsed ultrasound (LUPUS) on chondrogenic differentiation of adipose tissue-derived mesenchymal stem cells with or without coculture with chondrons. (1 fte AIO, 0,5 yr).


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. Analyzing digital workflow. A project together with the Technical University of Eindhoven (prof.dr. M. van Genuchten & dr.ir. H.A. Reijers) 125000 CHF.

Wismeijer, D. & Tahmaseb, A. Evaluation of the EXE plan CAD/CAM system. Straumann AG, Switzerland, €200.000,-

Membership of editorial boards
Bronckers, A.L.J.J.: Odontology
Dozic, A.: Journal of Dentistry
Everts, V.: International Journal of Dentistry
Everts, V.: The Open Bone Journal
Feilzer, A.J.: American Journal of Dentistry
Feilzer, A.J.: Odontology
Klein Nulend, J.: Journal of Musculoskeletal Research
Klein Nulend, J.: Nederlands Tijdschrift Calcium en Botstofwisseling
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
Koolstra, J.H.: Journal of Dental Biomechanics
Lobbezoo, F.: Journal of Cranioandibular Function
Lobbezoo, F.: Journal of Oral Rehabilitation
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
Visscher, C.M.: Journal of Cranioandibular Function

Scientific awards/honours
Veen, E.S. (2010). De kwaliteit van tandartsuniswiter. 2nd prize. NT-GSK Bachelorscriptie Award 2010. GSK-congres Talking Points in Dentistry: Beurs van Berlage, Amsterdam, the Netherlands (2010, June 05).

Organization of international congresses or symposia

Invited speaker at international congresses or symposia
Annual Research Report 2010


Everts, V. (2010, July 05). Series of lectures on bone and connective tissue remodeling. Bangkok, Thailand, Department of Anatomy, Chulalongkorn University.

Feilzer, A.J. (2010, March 20). Digietaal afdruken. Amsterdam, the Netherlands, Symposium at Dental Expo, RAI.

Feilzer, A.J. (2010, March 19). Panel discussion at the opening ceremony. Amsterdam, the Netherlands, Dental Expo, RAI.


Klein Nulend, J. (2009, October 26). Bone augmentation with autologous adipose tissue-derived mesenchymal stem cells, BMP-2, and calcium phosphate carrier in the human maxillary sinus floor elevation model. The Hague, NL, Symposium ZonMW program “Translational Adult Stem Cell Research (TAS)”.


Klein Nulend, J. (2010, December 16). The role of osteocytes in mechnano-adaptive bone remodeling. Cebu City, Philippines, College of Arts and Sciences, SMED-AVR, University of San Carlos, Talamban Campus.


Lobbezoo, F. (2010, March 01). Bruxism & Implants. Aarhus, Denmark, School of Dentistry, Aarhus University.


Loon, J.J.W.A. van (2010, March 02). The ESA ESTEC-TEC-MMG lab and hypergravity facility (The Large Diameter Centrifuge, LDC). Noordwijk, NL, Rodent research investigator working group meeting, (ESTEC).


Wismeijer, D. (2010, August 26). The ACTA approach. Amsterdam, the Netherlands, ADEE Post graduate implant dentistry.

Other international functions


Klein Nulend, J.: Visiting professorship. San Carlos University, Department of Physics, Cebu City, Philippines.


Liu, Y.: External reviewer. AO foundation grant in the field of bone regeneration, biomaterials and dental implant.
Liu, Y.: Honorary professor. Hospital of Stomatology, Dental School of Zhejiang University, Huangzhou, China.
Liu, Y.: Scientific advance. Maxillofacial surgery department, University of Bern, Bern, Switzerland.
Lobbezoo, F.: Member. Grindcare Clinical Advisory Board (CAB).
Loon, J.J.W.A. van: Chair person. Bone & Muscle expert group of the EC-Theseus project (run by ESF as coordinator).
Loon, J.J.W.A. van: Member. Co-I ESA Topical team on Animal Development. Coordinator prof. M. Jamon, University Marseille, France.
Loon, J.J.W.A. van: Member. Co-I ESA Topical team on Geomicrobiology for Space Settlement and Exploration (GESSE). Coordinator prof. Kai Finster, Aarhus University, DE.
Loon, J.J.W.A. van: Member evaluation board ESA Fly-your-thesis student program for parabolic flight campaign.
Loon, J.J.W.A. van: Member. PI ESA Topical Team on Human Centrifuge.
Visscher, C.M.: International board member. Physical Therapy Board of Craniofacial and Cervical Therapeutics (PTBCC), USA.
Wissemeijer, D.: Member. Education Committee ITI (CH).
Wissemeijer, D.: Member. Education Core Group ITI (CH).
Wissemeijer, D.: Honorary professor. Zhejiang University, China.

**Supervisor of an external PhD student**


**Societal impact**

The societal impact of the clinical research is focused on the influence on patient care, both within the department and externally. Research contributes to improved treatment of relevant patient groups. The research program also contributes to the master program of Oral Kinesiology, in which post graduate dental student are trained to become a "tandarts gnatholog/kinesioloog".

The BIOS research project has had it’s impact on the acceptance of the treatment of edentulous patients with oral implants by the Dutch Health Insurance companies. For edentulous patients the treatment with two implants and an overdenture has been accepted as the treatment of choice for edentulous patients.

The results of the research on bone adaptation and regeneration will offer multiple opportunities for the development of new therapeutic agents to prevent (inflammation-associated) unwanted clinical bone loss, thereby preventing a.o. mobility loss with aging.

Enamel fluorosis is an increasing esthetic problem in several countries. The project on mechanism of enamel fluorosis adds to our understanding how these defects develop which will help to prevent these defects in future.

The societal impact is furthermore evident from the items listed below.

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

- Elephant Industries, Hoorn, the Netherlands.
- Degudent GmbH, Hanau.
- 3M-ESPE, Zoeterwoude.
- Cavex Holland B.V., Haarlem.
- Melisa.org, (Prof.dr V. Stejskal), Stockholm, Sweden.
- Laborzentrum Bremen, dr E. Valentine-Thon PhD.
- Servier, strontium ranelate & osteocyte mechanosensitivity.
- Smith @ Nephew, low intensity pulsed ultrasound effects on stem cells.
- Friesland-Campina, Physical activity, nutrition and bone metabolism.
- Straumann
- Geistlich
Annual Research Report 2010

The research project “Pre-surgical CAD/CAM Planning and Fabricating Surgical Guide and Superstructure on Dental Implants in Order to Restore the Fully Edentulous Mandible/Maxilla” has pathed the way to industry who have decided to by the patients that belong to Tahmaseb en de Cleck. Two industrial partners now own the patents and will bring the system to the market. ACTA will conduct a multi center clinical trial to expand the research on this novel tool.

Interactions with the general public
Feilzer A.J. Prof.dr. Albert Feilzer over digitaal afdrukken, YouTube (2:39 min).
Van Calcar N. Nieuwslicht Digitaal scannen, VARA, Amsterdam, February 2010.

Impact of the research on professionals
D.Wismeijer is a member of the ITI education Core group and of the ITI education Committee. ITI is an international team of researchers and clinicians who stimulate research and education in the field of oral implantology. He is one of the editors’ of the ITI treatment guides which have been published in 9 languages. He is the first author and editor of treatment guide 4 which is published in 2010 in already 5 languages. In September of this year he was leader of an ITI committee working on a literature review on novel treatments in oral which will be available on line for the dental community.

Wismeijer was interviewed for the industrial partners magazine starget on the topic of Digital implantology, also printed in the British journal of dentistry. He was also interviewed by an independent journalist as a expert for Straumann’s 2010 Annual report. In a Dutch dental journal he was interviewed together with prof. Van Winkelhoff on the subject “do implants have big disadvantages” where both interviewees gave their opposite opinions on the subject.

Lobbezoo F. & Visscher C.M. Members of the Dutch Society of Headache Patients Committee that develops a Guideline for the Diagnosis and Treatment of Orofacial Pain.

Organization of national congresses or symposia

Invited speakers at national congresses, symposia
A total of more than 12 presentations were given for professionals and patients in the Netherlands by Visscher, Van Dalen, Kleverlaan, Muris, Khashayar and Wismeijer.

Other national functions
V. Everts and J. Klein-Nulend participated in 3 national research committees.
Lobbezoo F. Chairman of the Netherlands Institute for Dental Sciences (IOT).
Visscher CM. Chairman of the Jaco den Dekker scriptieprijs (KNF).
Feilzer A.J. Chairman of Normcommissie Tandheelkunde, Nederlands Normalisatie Instituut.
Feilzer A.J. Member beleidscommissie Medische hulpmiddelen, Nederlands Normalisatie Instituut.
Feilzer A.J. Chairman of ISO TC 106, SC2, WG 19.
Feilzer A.J. Chairman Nederlandsch Tandheelkundig Genootschap.
Kleverlaan C.J. Member of Normcommissie Tandheelkunde, Nederlands Normalisatie Instituut.
Kleverlaan C.J. Member of ISO TC 106.
Mirus J. Vice-voorzitter Vereniging Medisch Tandheelkundige Interactie (VMTI) Amsterdam 2010-heden.
D.Wismeijer is a member of four national committees and advisory councils.

Courses organized for dental and medical professionals
J.H. Koolstra organized one course in the Netherlands.
F. Lobbezoo & CM. Visscher organized two courses for dentists in the Netherlands.
Feilzer A.J. and Kleverlaan C.J. Digitaal afdrukken in de tandheelkundige praktijk, ADE.
Kleverlaan C.J. Succesvol kiezen uit composieten en bondingsystemen, BSL.

Lectures given during courses for dental and medical professionals in the Netherlands
A total of more than 14 lectures were given by Everts, Klein Nulend, Lobbezoo, Feilzer, Kleverlaan, Khashayar, Van Calcar, Van Dalen, Dozic, and Wismeijer.

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Collaborations

- VUMc, Afdeling Pathologie, prof.dr. R.J. Scheper, the Netherlands.
- VUMc, Afdeling dermatologie, dr. Th Rustemeeyer.
- Universitair medisch Centrum St. Radboud/Radboud Universiteit Nijmegen, Cariologie en Endodontologie, prof.dr. M.C.D.N.J.M. Huysmans
- University of Zurich, Center for Dental and Oral Medicine, Dental Materials Unit, prof.dr. M. Özcan.
- University of Turku, Department of Prosthetic Dentistry and Biomaterials research, prof. dr. Pekka Vallittu, Turku, Finland.
- University of Tanta, Department of Restorative Dentistry, dr. Al Abdalla, Tanta, Egypt.
- University of Cairo, Department of Operative Dentistry, dr. AA. El Zohairy, Cairo, Egypt.
- Regensburg University Medical Center, Department of Prosthetic Dentistry, prof.dr. M Behr, Regensburg, Germany.
- Universiteit van Genève, Division of Cariology and Endodontology, prof.dr. I. Krejci, Genève, Swiss.
- University of Tennessee, Clinical Research Center, dr. F. Garcia Godoy, Memphis, USA.
- UTHSC Dental School, Department of Restorative Dentistry, S. Wendt, San Antonio, Texas, USA.
- King Saud University, dr. Z. Salameh, Riyadh, Saudi Arabia.
- Health Sciences University of Hokkaido, dr. M. Hashimoto, Hokkaido, Japan.
- 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. Dhert, Utrecht, NL.
- VUMC, Dept. Endocrinology, prof.dr. P. Lips, Dr. N. Bravenboer, Amsterdam, NL.
- VUMC, Dept. Plastic Surgery (prof.dr. M. Ritt, dr. M.G. Mullender), Amsterdam, NL.
- VUMC, Dept. Rheumatology, prof.dr. W.F. Lems, Amsterdam, NL.
- Göttingen University, prof.dr. C.F. Schmidt, Göttingen, Germany
- VUA, Dept. 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. Wulboomers.
- Univ. Madrid, Spain, prof. J. Medina.
- Univ. Oslo Finland: dr. S. Kellokumpu.
- Univ. Madrid, Spain, prof. R. Marco.
- Univ. Milaan, Italy, prof. S. Bradamante.
- 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
- University of Lund, Sweden, prof. J. Richter.
- University of Umea, Sweden, prof. U. Lerner.
- University of Helsinki, Finland, prof. K.Vaananen
- University of Kiel, Germany, prof. P. Saftig.
- University of Stockholm, prof. G. Andersson.
- University of Leuven, Dept. Rheumatology, prof.dr F. Luyten, Leuven, Belgium.
- Philippines, Cebu City, San Carlos University, Talamban Campus, dr. R.G. Bacabac.
- Eindhoven University of Technology, Department of Materials Technology (prof.dr.ir. J.M.J. den Toonder), TU 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

Aarab G. Oral appliance treatment for obstructive sleep apnea  
Supervisors: prof.dr.ir. M. Naeije & prof.dr. F. Lobbezoo:  

Barbery H el. Titanium-allergy: a cause of oral implant failure?  

Blaauboer ME. Myofibroblasts. Supervisor: prof.dr. V. Everts;  
co-supervisors: dr.ir. T.H. Smit & dr. R. Stoop. Start: October  
2007.


Haaren EM van. Clinical, mechanical and biological aspects of impaction bone grafting in orthopaedic revision implantology  


Juffer P. Biological pathways for regulation of muscle fiber size and bone mass. Supervisors: prof.dr. J. Klein Nulend &  


Manfredini D. The triangle "bruxism, pain, and psychosocial factors". Supervisor: Prof. dr. F. Lobbezoo; co-supervisors: dr. J. Ahlberg (University of Helsinki, Finland), dr. E. Winocur (University of Tel Aviv, Israel). Start: 2009.


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, Gustav Mahlerlaan 3004
1081 LA Amsterdam
Tel: +31-20-5980262
E-mail: P.vd.Stelt@acta.nl

Full professors

P.F. van der Stelt  H. van Beek

Research objectives
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 both fundamental and applied (clinical) components:

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. The studies undertaken currently focus on the quantitative analysis of bone density and bone architecture.

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
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. The purpose of these studies is to develop the optimum system for the display of 3D information in a clinical environment.
In the last year, much effort is put into the transformation of the two-dimensional quantitative description of the trabecular pattern into a three-dimensional approach. The software to do this is currently in the last phase of testing.

Three-dimensional data-sets were obtained from cadaver specimens, using several different CBCT machines, a medical CT-machine (MSCT) and micro-CT. The purpose is to optimize the imaging characteristics of CBCT using MSCT as the clinical reference and MicroCT as the gold standard for the visualization of the trabecular architecture.

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 2010.

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 2010 and 2011

<table>
<thead>
<tr>
<th>Research staff ACTA – RAO- OR/TR (in full time equivalents)</th>
<th>fte 2010</th>
<th>plan 2011</th>
<th>funding</th>
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</thead>
<tbody>
<tr>
<td><strong>Full professor</strong></td>
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<tr>
<td>Beek, prof.dr. H. van</td>
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<td>Prahl-Andersen, B.</td>
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<td>pm</td>
<td>guest</td>
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<tr>
<td>Stelt, prof.dr. P.F. van der</td>
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<tr>
<td>Zentner, prof.dr. A.</td>
<td>pm</td>
<td>pm</td>
<td>guest</td>
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<tr>
<td><strong>Senior lecturer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Habets, dr. L.L.H.M.</td>
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<td>Sanderink, dr. G.C.H.</td>
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<td>0,10</td>
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<tr>
<td><strong>Lecturers and other tenured research staff</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Algera, dr. T.J.</td>
<td>pm</td>
<td>pm</td>
<td>guest</td>
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<tr>
<td>Berkhout, dr. W.E.R.</td>
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<td>0,10</td>
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<td>Geraets, dr. W.G.M.</td>
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<tr>
<td>Hassan, dr. B.A.</td>
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<tr>
<td>Kuitert, dr. R.B.</td>
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<td>0,20</td>
<td>1</td>
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<tr>
<td>Mileman, dr. P.A.</td>
<td>pm</td>
<td>pm</td>
<td>guest</td>
</tr>
<tr>
<td>Prahl, dr. C.</td>
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<td>0,05</td>
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<tr>
<td>Verheij, dr. H.</td>
<td>0,30</td>
<td>0,30</td>
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</tr>
<tr>
<td><strong>Total tenured staff</strong></td>
<td>2,45</td>
<td>2,45</td>
<td></td>
</tr>
</tbody>
</table>
position | name | fte 2010 | plan 2011 | funding |
--- | --- | --- | --- | --- |
Non tenured staff | Beerens, drs. M.W. | -- | pm | |
| Bos, dr. A. | 0,40 | 0,40 | 1 |
| Disse, drs. M. | 0,05 | pm | 1 |
| Elmi, P. | -- | pm | |
| Fabels, L.N.J. | -- | pm | |
| Graven, drs. K.M.L. | pm | pm | |
| Hiemstra, drs. R.E.I. | pm | -- | |
| Kaaij, drs. N.C.W., van der | pm | pm | |
| Keles, drs. F. | pm | pm | |
| Nijkamp, drs. P.G. | 0,05 | -- | 1 |
| Noverraz, R.L.M. | -- | pm | |
| Parys, drs. K. van | pm | -- | |
| Reitsma, drs. J.H. | pm | pm | |
| Vermeulen, F.M.J. | -- | pm | |
| Vlag, drs. J., van der | pm | pm | |
| Vreeke, drs. M. | pm | -- | |
| Vries, L. de | -- | pm | |
| Westing, drs. K., van | pm | -- | |
| Wezel, msc. N.A. van | -- | pm | |
PhD students | Hassan, drs. B.A. | 0,40 | -- | 1 |
| Ibrahim, dds. N. | 0,75 | 0,75 | 3 |
| Parsa, dds. A. | 0,75 | 0,75 | 3 |
| Willems, drs. N.M.B.K. | pm | pm | |
Total non tenured staff | 2,40 | 1,90 | |

| | total 1st funding | 2,45 | 1,95 | 1 |
| | total 3rd funding | 2,40 | 2,40 | 3 |

Total research staff | 4,85 | 4,35 | |

Output

Dissertations

Scientific publications ( refereed)


Professional publications


Indicators of Esteem

Membership of editorial boards
Beek, H. van: Nederlands Tijdschrift voor Tandheelkunde
Stelt, P.F. van der: Clinical Oral Implants Research
Stelt, P.F. van der: Dento-Maxillo-Facial Radiology
Stelt, P.F. van der: Odontology
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


Organization of international congresses or symposia
Hassan, B.A. (2010). Member organizing committee. 1st Cone Beam Computed Tomography Certification Course: Western Cape University, Cape Town, South Africa (2010, November 19 - 2010, November 21).
Other international functions
Berkhout, W.E.R.: Member research and Scientific committee EADMFR.
Stelt, P.F. van der: Member scientific committee Society of Computer Aided Radiology.
Winter, F.R. de.: Honorary secretary European Federation Orthodontic Specialists Associations (EFOSA).
Winter, F.R. de.: Chairman quality committee European Federation Orthodontic Specialists Associations (EFOSA).
Zentner, A.: Honorary treasurer European Orthodontic Society.
Zentner, A.: Election member Kammerversammlung der Zahnärztekammer Nordrhein.

Societal impact
The societal impact of the research on 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 includes continuing education courses on the safe use of radiation in dental practice and application of digital imaging in dentistry.

The societal impact of the research on 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.

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.

Habets, L.L.M.H. et. al.: collaboration on “3D” research related to dental plaster models together with an interuniversity work group (KUN, RUG, ACTA).

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

Impact of the research on professionals
Berkhout WE.R. Member “Werkgroep Ministerie van VWS; aanpassing besluit stralingsbescherming ten aanzien van Conebeam CT”.
Van der Stelt P.F. Member “Werkgroep Ministerie van VWS; aanpassing besluit stralingsbescherming ten aanzien van Conebeam CT”.

Courses given for dental and medical professionals in the Netherlands
More than 26 courses were given.

Lectures giving during courses for dental and medical professionals in the Netherlands
A large number of lectures were given during courses.

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


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: +31-20-4441023
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 prosthesis 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).

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.

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, interferon or denosumab, particularly in aggressive or recurrent giant cell granulomas.

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
The research on surgical orthopedics is focused on maxillofacial function and healing capacity after treatment of acquired and congenital jaw deformaties. Attention is focused on the indications/contra-indications and preventive measures in surgical-orthodontic treatment of dentofacial deformaties. 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 BSSO is the most frequently used method for lengthening of the mandible. Distraction osteogenesis (DOG) is more recently introduced for the same indication. The aim of the study is to compare both treatment modes on several aspects in a RCT.

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.

Dental implants are commonly used for replacement of teeth or as an anchorage for prostheses. The number of implants and the system of anchorage used in this last group of patients can vary in different clinics. The aim of the study is to compare these different systems and evaluate the use of peri-operative antibiotics. 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 antithrombotic 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 project is carried out in close collaboration with the department of Social Dentistry and Behavioural Sciences, ACTA.

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 clopidroge, 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.

Arthrosclerosis and rheumatoid arthritis are probably both related to periodontitis. In this study, the effect of the treatment of periodontitis in relation to AS en RA is evaluated.

Results
Research on oral cancers, including tumours of the salivary glands, and odontogenic tumours is ongoing. Early diagnosis of oral squamous cell carcinoma focuses on molecular characterization of leukoplakia. Research on diagnosis and prognosis of salivary gland tumours focuses at present on mucin expression in situ and in saliva of patients. In odontogenic tumours interesting results were obtained with regard to the expression of COX-2. Furthermore, the 40-years experience with the treatment of ameloblastomas has been evaluated. Interesting results were obtained with regard to the expression of COX-2 in odontogenic tumours. Furthermore, the 40-years experience with the treatment of ameloblastomas has been evaluated.

In 2010, D.M.J. Milstein successfully finished his PhD thesis on oral microcirculation. 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, among others on the clinical, histological and histomorphometrical aspects of different bone substitutes, e.g. Straumann Bone Ceramic. The most recent study is on the use of adipose-derived mesenchymal stem cells in sinus floor elevation procedures. In 2010 a study started on peri-implantitis, implant loss and osteoradionecrosis after irradiation in oral cancer patients. In addition, two new PhD projects on oral implantology were started.

Projects investigating the relation between periodontitis and arthrosisclerosis and rheumatoid arthritis were initiated. The PhD projects on distraction osteogenesis and Giant cell granulomas are developing according to plan.
In the project on the evidence-based guideline development a questionnaire study amongst Dutch dentists has been performed in collaboration with the NMT (Dutch Dental Association) as well as a survey in Dutch oral and maxillofacial surgeons. A study that evaluated the quality of existing guidelines from the USA and UK has been performed. Furthermore, the incidence of bleeding after dental extractions at ACTA has been established.

Academic personnel in 2010 and 2011

<table>
<thead>
<tr>
<th>Research staff ACTA – MKA- AMC / VUmc (in full time equivalents)</th>
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<tr>
<td><strong>position</strong></td>
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<td>__________</td>
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<td>total 3rd funding</td>
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80
Dissertations

Scientific publications (referred)


Scientific publications (non-referred)


Professional publications


Publications aimed at the general public


Indicators of Esteem

Grants: current projects with external funding

Bruggen, C.M. ten. Research on maxillofacial implantology. (2008-2012) Straumann; € 50.000,-


Lange J. de, Apperloo R. Dental implants as anchorage for prostheses; number, configuration and suprastructure. Straumann. Duration of the project 2010-2015.

Membership of editorial boards

Brand, H.S.: Nederlands Tijdschrift voor Tandheelkunde
Bloemena, E.: ISRN Gastroenterology.
Bloemena, E.: World Journal of Gastrointestinal Oncology
Bruggenkate, C.M. ten: Clinical Oral Implants Research
Goené, R.J.: European Journal of Oral Implantology
Goené, R.J.: Journal of Implant and Reconstructive Dentistry
Waal, L. van der: Acta Stomatologica Croatica
Waal, L. van der: European Journal of Cancer
Waal, L. van der: Journal of Dentistry University of Sao Paolo
Waal, L. van der: Medicina Oral
Waal, L. van der: Minerva Stomatologica
Waal, L. van der: Oral Health and Preventive Dentistry
Waal, L. van der: Oral Oncology
Waal, L. van der: Padjadjaran Journal of Dentistry
Waal, L. van der: Nederlands Tandartsenblad
Waal, L. van der: Nederlands Tijdschrift voor Geneeskunde

Invited speakers at international congresses or symposia

Becking, A.G. (2010, November 18). Digital planning incl 3D. Amsterdam, the Netherlands, Wales in Walls orthognathic meeting VUMc.
Bruggenkate, C.M. ten (2010, January 15). Implant structures. Helsinki, Finland, Kick of meeting ITI.
Teeseling, R.A. van (2010, June 01). Orthognatic course. Belek, Turkey, SORG.
Waal, L. van der (2010, June 05). Oral cancer; diagnosis and treatment; Oral leukoplakia; diagnosis and management. University of Parma, Italy, European Master Degree on Oral Laser Application (EMDOLA).


Scientific awards/honours


Other international functions


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: 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
C.M. ten Bruggenkate: collaboration with the Straumann company on research related to dental implants.

J. de Lange, R.C. Apperloo and B. Eggermont: collaboration with the Straumann company on research related to dental implants.

J. de Lange: collaboration with the Martin company on research related to distraction.

Interactions with the general public
H.S. Brand gave a presentation about oral health for Sjögren patient, J.A. Baart gave a presentation about schisis and E.A.J.M. Schulten gave a presentation about reconstructive oral surgery.

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

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 18 presentations were given.
Other national functions
A total of 24 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, J.A. Baart, A.G. Becking, E. Bloemen, H.S. Brand, C.M. ten Bruggenkate, D.E van Diermen, R.J. Goené, H.S. Schouten, E.A.J.M. Schulten, I. Van der Waal and S.A. Zijlerveld.

Courses for dental and medical professionals
A total of 29 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 30 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
- Department of Oral and Maxillofacial Surgery, Leids Universitair Medisch Centrum, Leiden
- Department of Oral and Maxillofacial Surgery, Rijnland Ziekenhuis, Leiderdorp
- Netherlands Cancer Institute, Amsterdam, the Netherlands
- Department of Dermatology, Sint Antonius Ziekenhuis, Nieuwegein
- Swammerdam Institute for Life Sciences, University of Amsterdam, Amsterdam, the Netherlands
- Department of ENT, Dental Ophthalmological, and Cervicofacial Sciences, University of Parma, Unit of Oral Pathology and Medicine, section of Odontostomatology, Parma, Italy
- Department of Oral Surgery, University of Porto, Porto, Portugal
- Department of Oral Medicine, Carolina Medical Center, Carolina, USA
- Department of Nuclear Medicine and PET research, VUMc, Amsterdam
- Department of Clinical Epidemiology and Biostatistics, VUMc, Amsterdam
- Department of Clinical Genetics, VUMc, Amsterdam
- Department of Endocrinology, VUMc, Amsterdam
- Department of Otolaryngology/Head and Neck Surgery, VUMc, Amsterdam
- Department of Oral and Maxillofacial Surgery, Isala Klinieken, Zwolle
- Department of Cardiology, Isala Klinieken, Zwolle
- Department of Rheumatology, LUMC, Leiden
- Department of Otolaryngology, Sint Lucas Andreas ziekenhuis, Amsterdam
- Department of Pulmonary Diseases, Academic Medical Center, Amsterdam
- Department of Children Oncology, Emma Kinderziekenhuis, Amsterdam

Current PhD projects


Education Institute

Research on Dental Education

Program leader

Dr. J.M. Vervoorn
Education Institute
ACTA, Gustav Mahlerlaan 3004
1081 LA Amsterdam
Tel: +31-20-5980438
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), 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 2010 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.

Academic personnel in 2010 and 2011

<table>
<thead>
<tr>
<th>position</th>
<th>name</th>
<th>fte 2010</th>
<th>plan 2011</th>
<th>funding</th>
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<td>pm</td>
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<td>institute</td>
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<td>pm</td>
<td>pm</td>
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<td>Boer, drs. I.R. de</td>
<td>pm</td>
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<tr>
<td></td>
<td>Buis, drs. J.</td>
<td>pm</td>
<td>pm</td>
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<tr>
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<td>Wesselink, prof.dr. P.R.</td>
<td>pm</td>
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<td>PhD students</td>
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<td>pm</td>
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<td></td>
<td>Koopman, P.</td>
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Output

Scientific publications (refereed)


Scientific publications (non-refereed)


Professional publications


Indicators of Esteem

Grants: current projects with external funding

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

Membership of editorial boards

Schoonheim-Klein, M.E.: European Journal of Dental Education

Other international functions


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

Organisation of international congresses or symposia


Invited speakers at international congresses or symposia


Boer, I.R. de (2010, August 26). Creation of tooth pathology in a virtual world. Amsterdam, the Netherlands, ADEE 2010, Special Interest Group "Virtual Reality in Dental Education".

Koopman, P. (2010, August 26). Realisation of the virtual clinical lab with the Simodont. Amsterdam, the Netherlands, ADEE 2010, Special Interest Group "Virtual Reality in Dental Education".


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
Standby, nr. 4, interview ACTA August 2010: De werkelijkheid achter de onwerkelijkheid van de toekomstige opleiding tandheelkunde.

Current PhD projects
Appendix

List of SCI journals, their impact factors and the number of ACTA publications in 2010 in each journal

<table>
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<tr>
<th>Journal</th>
<th>IF</th>
<th>Number of publications</th>
<th>Journal</th>
<th>IF</th>
<th>Number of publications</th>
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<td>BIOCHEM BIOPH RES CO</td>
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