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INTRODUCTION

We are pleased to present the Annual Research Report 2005 of the Research Institute of ACTA.

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

The ACTA research institute collaborates in the Netherlands Institute for Dental Sciences (Interuniversitaire Onderzoekschool Tandheelkunde, IOT). The IOT is a collaboration between the Academic Centre for Dentistry Amsterdam (’ACTA’, the combined Faculties of Dentistry of the Universiteit van Amsterdam and the Vrije Universiteit in Amsterdam), the College of Dental Science of the University Medical Center St Radboud in Nijmegen (’UMCN’), the Dental Section of the Universitair Medisch Centrum Utrecht (’UMCU’), and the Dental School of the Universitair Medisch Centrum Groningen (UMCG).

An overview of the output is presented on page 11. This table summarises for each department and section the number of publications that have appeared in 2005 in SCI-journals, the number of other scientific publications, and the number of professional publications. Data on abstracts and on popularising publications are not included in this report. Also the personnel involved in full time equivalent (fte) and the impact factor-sum (IF-sum) are included in this table. The IF-sum was calculated for each department by adding together the impact factor values of all 2005 publications according to the principle listed in the footnotes of the table.

Research Institute ACTA

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REPORT OF THE DIRECTOR

The Research Institute ACTA

• mission statement
Dental research at 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
The Research Institute ACTA is the only institute for research of the Academic Centre for Dentistry Amsterdam (ACTA). ACTA comprises the combined Faculties of Dentistry of the Universiteit van Amsterdam and the Vrije Universiteit in Amsterdam. Moreover it comprises by far the largest part of the Netherlands Institute of Dental Sciences (Interuniversitaire Onderzoekschool Tandheelkunde, IOT). The IOT as a research school was re-evaluated in the year 2000 and was given the mark of ‘Hererkenning’ (Re-recognition) from the Royal Dutch Academy of Sciences (KNAW) for a five-year period starting 2001. The most recent evaluation of dental research in the Netherlands was performed in 2004. This evaluation according to the new Standard Evaluation Protocol designed by the VSNU included a bibliometric analysis by the CTWS in Leiden. In general, the evaluation committee considered the quality, production, relevance and academic reputation of dental research in the Netherlands as very good.

• description of output, leading scientific journals in the field
The research has a very broad focus and deals with questions originating from clinical dental practice. Within the overall research programme there are large variations in the approaches taken, ranging from basic medical-biological to clinically applied. This is reflected in the type of journals where 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

• 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 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 6-12 dissertations reflects the number of PhD students ‘employed’, the total number of which was about 50 in previous years. The percentage of PhD students that finished their thesis averages at 90 % over the last 15 years, and the mean time between start of employment and defending the thesis is 4.7 years, when a correction is made for the 0.6 to 0.8 fte employment of several PhD students and for long leave of absence (e.g. illness) of some PhD students.
The main attention in the research assessment at the individual and department level is given to international publications in journals with a referee system and an impact factor (SCI publications). This category shows a slightly increasing number over the last 15 years, despite a
roughly stable input in the scientific personnel. The average quality of the publications has significantly improved over that 15-year period, as judged by the continuous increase of the impact factor sum (see figure).

- **Remarkable events in 2005**

Outstanding contributions for the year 2005 that we wish to mention are publications in high quality biomedical journals (i.e. the Proceedings of the National Academy of the United States of America, Human Genetics, Journal of Bone and Mineral Research, FASEB Journal, Antimicrobial Agents and Chemotherapy, Clinical Infectious Diseases and Journal of Proteome Research, all journals with impact factors larger than 5), and six publications in the Journal of Dental Research, which is considered the most prestigious dental journal with the highest impact factor in the category. In addition to the output indicators given, the percentage of papers in top journals in the field gives valuable information. ACTA published in total 152 scientific papers in journals with an impact factor (SCI journals). 67% of these papers appeared in journals belonging to the field “Dentistry, Oral Surgery and Medicine”. 36% of these publications were in the top 25% of the journals. 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 2005, a total of 13 awards was received by ACTA scientists for their achievements. The following individuals received a particular prestigious award:

- Prof.dr. J.M. ten Cate was chosen as Vice President of the International Association for Dental Research
- Prof.dr. C.L. Davidson received a honorary doctorate at the University of Siena in Italy
- Prof.dr. A. van Nieuw Amerongen was chosen as Researcher of the year in the field of salivary research by the International Association of Dental Research
- Prof.dr. U. van der Velden was nominated as a Honorary Member of the British Society of Periodontology
- Prof.dr. I. van der Waal was nominated as a Honorary Member of the American Academy of Oral Medicine.

- **assessment at the department level**

When the research at the department or section level is considered, a number of comments can be made. From the evaluation extending over several years it is clear that some groups perform very well and are stable in terms of input and output parameters (personnel, PhD students, publications, dissertations etc). In the evaluation report of dental research in the Netherlands performed in 2004 these groups received ratings between 4 and 5 (on a 5 point scale). On the other hand, some groups got average ratings in this evaluation. The Department of Orthodontics, which has been in a transition stage, received below average ratings. It should be noted that in 2005 this department showed a high scientific output.

The directorate holds periodic meetings with the sections to discuss the progress of the research and to express concerns such as indicated above.

**Congresses and societal activities**

- **congresses attended and organized**

In 2005 ACTA researchers have again contributed actively in internationally held meetings, workshops and symposiums, both as organisers and participants. A total of 79 lectures were given as ‘invited speaker’ at international congresses and symposia. In addition a large number of presentations were given at international congresses after selection on submission of abstracts and during congresses and symposia for a Dutch audience. Due to this large number, congress abstracts are not listed in this annual report. A total of 10 international meetings were organised by members of one of the departments of ACTA.

A special event worth mentioning is the 2005 meeting of the Central European and Scandinavian divisions of the IADR. This successful congress, organised by ACTA scientists, was attended by more than 1200 participants.
Societal activities

The prime societal value of a strong research programme is obviously its effect on the quality of the teaching given at ACTA. New findings and concepts are included in the curriculum at ACTA, but also presented to dental practitioners at frequently held continuing education activities, e.g. ACTA Quality Practice. The Research Institute has high expectations of the ACTA new curriculum with an increased focus on research and evidence based dentistry. ACTA employees take an active role as Executives in international scientific organisations (58 international functions), as members of the editorial boards of international scientific journals (58) and in being leading in ‘wetenschappelijke verenigingen’ of researchers and dental practitioners in the Netherlands. In addition it should be mentioned that many scientists are also working 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 99 professional publications. Several ACTA researchers also wrote a considerable number of popularising publications, the details of which are not included in this scientific report.

Management

Finances

The overall budget of the research institute is divided into a part controlled directly by the directorate and the remainder, which is allocated to the departments. The institute budget (senso stricto) is used for the management of the institute, the salaries of the PhD students and post doctoral employees, for travel allowances for these two groups and for the organization of courses and the annual two day research meeting. Details of the finances of the Institute are given in Table 3. The research budgets for the departments are distributed with a model primarily based on a quality assessment parameter (between 1 and 5) determined by peer review. In addition, standard bench fees are issued for the various categories of researchers (staff, post-docs, PhD students, technicians and other supporting OBP staff). For 2006 a new allocation model was made, based on several parameters, such as external peer review, bibliometric data, education, PhD theses and external funding.

personnel

The directorate of the institute comprises:

- prof.dr. J.M. ten Cate, director of research  0.5 fte
- dr. T.J.M. van Steenbergen, co-ordinator of research  0.5 fte
- mrs. F.M. Meijer, secretary  0.6 fte

The activities of the Research Institute directorate consist of organising the 2-monthly aio-refereeremiddagen, the annual two day research meeting of the IOT, the screening of new research programmes, 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, KNAW etc.

The directorate serves in many of these functions also for the Interuniversitaire Onderzoekschool Tandheelkunde (IOT).

PhD students

PhD student appointments

A constant concern is the hiring of sufficient numbers of new PhD students for all research groups (Table 4). Despite the fact that supervisors are faced with considerable difficulties in finding candidates for vacant positions, most vacancies have been filled in 2005. In Figure 1 the number of new PhD students at ACTA is shown in the years 1990 to 2005. Over the years, about 19% of all PhD students had a foreign nationality, about half of them from Europe, the rest from other continents. A mean of 8 new PhD students was appointed each year, 11 being appointed in 2005. About half of all PhD students has a dental background (see Table 5). Of all PhD students 47%
was female. In principle the Institute has the policy that each full (time) professor gets university funding for two PhD students; it is however doubtful if this policy can be retained in the coming years due to reductions in budget.

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

![Graph showing numbers of PhD students](image)

- **PhD Courses**

  The following courses were organised for PhD students: "Writing and Presenting in English", "Methodology and Statistics", "Introduction in SPSS", "Dentistry for non-dentists", and "Oral Biology". Dentistry is a multidisciplinary science and the background of the PhD students of the IOT 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 4.7 years between start and defence of the thesis within ACTA is slightly lower than the mean duration of PhD theses in research schools in the Netherlands of 5.1 years (see the report "Rendement en duur van promoties in de Nederlandse onderzoekscholen", Oost en Sonneveld, 2004). In addition, the mean duration of preparing a thesis has shown a declining tendance over the years (figure 2). To try to even diminish this time interval, the following measures were taken:
  - all PhD students and supervisors were reminded of the necessity to finish the thesis with the time of employment
  - a guideline was made for the size of the thesis; in this guideline it was argued that it is possible to finish a thesis in 4 years when a somewhat limited size - though still of sufficient scientific quality - of a thesis is accepted
  - a control system was started, in which the director of research of ACTA evaluates the progress of all PhD students

  Over the last 15 years, about 90% of all PhD students in ACTA completed their thesis (Figure 3). This high percentage is substantially larger that the mean percentage of 75% of PhD students who finish their thesis in Dutch research schools according to the report by Oost en Sonneveld mentioned above.
**Figure 2.** Mean duration of completing the thesis of ACTA PhD students related to the year of entry

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

**Points of attention**

- **HRM and Retirement**
  The research staff at ACTA has been comparatively young in the last decades. This was the result of the merging of the dental schools in the mid 1980’s. Now we are approaching a situation where heads of departments and senior scientists are retiring. In 2005 four new professors were appointed: Klein Nulend (Oral Cell Biology), Veerman (Oral Biochemistry), van Loveren (Cariology Endodontology Pedodontology) and Lobbezoo (Oral Kinesiology).
• **New building planned for 2009**
The decision for a new ACTA building located at the VU campus has finally been formalized by both Colleges van Bestuur. This will bring together groups that are currently spread out over the city at 4 different locations. Optimal research facilities at the new ACTA building were planned, to encourage collaboration between the research groups that require laboratory facilities. The increased number of scientists at one location will also facilitate to jointly take initiatives, such as in molecular aspects of dental research.

• **Future developments**
Within the Netherlands, the future of inter-university research schools such as the IOT is undecided. Graduate schools have now been formed at a local level to integrate research training both for students in the Master phase and for PhD students. In 2006 ACTA and IOT will decide about their future position as related to PhD training and research co-ordination.

**Conclusion**
The analysis of the various parameters of performance shows that the research at ACTA is in a stable and - in most areas - increasingly improving state.
### SUMMARY OF PUBLICATION OUTPUT AND INPUT

#### Table 1. Comparison of research indicators

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<td>9</td>
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<td>6</td>
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<td>SCI publications</td>
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<td>105</td>
<td>122</td>
<td>119</td>
<td>146</td>
<td>126</td>
<td>133</td>
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<td>115</td>
<td>128</td>
<td>130</td>
<td>149</td>
<td>152</td>
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<td>First author from ACTA</td>
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<td>80</td>
<td>90</td>
<td>79</td>
<td>96</td>
<td>84</td>
<td>84</td>
<td>76</td>
<td>79</td>
<td>89</td>
<td>100</td>
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<td>Other scientific publ.</td>
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<td>152</td>
<td>160</td>
<td>88</td>
<td>97</td>
<td>84</td>
<td>37</td>
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<td>27</td>
<td>17</td>
<td>34</td>
<td>29</td>
<td>41</td>
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<td>Professional publ.</td>
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<td>53</td>
<td>68</td>
<td>52</td>
<td>111</td>
<td>74</td>
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<td>123</td>
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<td>131</td>
<td>198</td>
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<td>179</td>
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<td>200</td>
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<td>206</td>
<td>220</td>
<td>238</td>
<td>273</td>
<td>322</td>
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<td>53.6</td>
<td>50.6</td>
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<td>Total personnel</td>
<td>69.6</td>
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<td>68.1</td>
<td>60.7</td>
<td>63.2</td>
<td>58.1</td>
<td>54.8</td>
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**Figure 4.** Impact factor sum of ACTA publications, total scientific publications in journals indexed in the science citation index (SCI publications) and total scientific personnel in fte.
Table 2. Summary of the number of publications, impact factor sum and academic personnel in fte (year 2005)

<table>
<thead>
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<th></th>
<th>Dis</th>
<th>SCI</th>
<th>OSP</th>
<th>PP</th>
<th>IF</th>
<th>wp1</th>
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<tr>
<td>OF</td>
<td>7</td>
<td>7</td>
<td></td>
<td></td>
<td>11.6</td>
<td>3.90</td>
<td></td>
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<td>OM</td>
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<td>OR</td>
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<td>23</td>
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<td>2</td>
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<td>ST</td>
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<td></td>
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<td>0.20</td>
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<td>Total*</td>
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<td>41</td>
<td>99</td>
<td>321.5</td>
<td>46.05</td>
<td>4.80</td>
<td>6.75</td>
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</table>

This table summarises the number of publications that have appeared in 2005 in SCI-journals, the number of other scientific publications, and the number of professional publications. Also the personnel involved in full time equivalent (fte) and the impact factor-sum (IF-sum) are included in this table. The IF-sum was calculated for each department by adding together the impact factor values of all 2005 publications according to the principle listed in the footnotes of the table. In this report no information is given on abstracts and on popularising publications.

Footnotes:
- **Dis** = number of dissertations.
- **SCI** = number of scientific papers in journals indexed in the database of the Institute of Scientific Information (ISI). Between parentheses is the number of first authors belonging to the department in question.
- **OSP** = other scientific publications (international, refereed).
- **PP** = professional publications.
- **IF** = sum of impact factors as indexed by ISI. For publications with first author belonging to the department in question, 100% of the impact factor value is awarded to the department, for co-authors 50% (only one co-author per department).
- **wp1** = academic personnel funded by 1<sup>st</sup> source in fte.
- **wp2** = academic personnel funded by 2<sup>nd</sup> source in fte.
- **wp3** = academic personnel funded by 3<sup>rd</sup> source in fte.
- **wp tot** = all academic personnel.
- **CEP** = Department of Cariology Endodontology Pedodontontology.
- **OF** = Department of Oral Function.
- **PD** = Department of Periodontology, section Periodontology.
- **OC** = Department of Periodontology, section Oral Cell Biology.
- **OM** = Department of Periodontology, section Oral Microbiology.
- **OR** = Department of Orthodontics/Social Dentistry, section Orthodontics.
- **ST** = Department of Orthodontics/Social Dentistry, section Social Dentistry and Behavioural Sciences.
- **AN** = Department of Dental Basic Sciences, section Functional Anatomy.
- **MW** = Department of Dental Basic Sciences, section Dental Material Sciences.
- **OB** = Department of Dental Basic Sciences, section Oral Biochemistry.

* Total = papers co-published with members of different programs were counted only once.
### Table 3. Finances ACTA Research Institute 2005

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Note, this table is given in Dutch to avoid confusion in terminology.
**Table 4: fte of staff and PhD students (see Table 2) by type of position**

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*We note that a substantial amount of people employed by university funding (1st) are in fact employed by money earned from industrial funding (3rd).

CEP = Department of Cariology Endodontology Pedodontontology
OF = Department of Oral Function
PD = Department of Periodontology, section Periodontology
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OM = Department of Periodontology, section Oral Microbiology
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</table>

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MW = Department of Dental Basic Sciences, section Dental Material Sciences
OB = Department of Dental Basic Sciences, section Oral Biochemistry
Department of Cariology Endodontology Pedodontontology

Diseases of the Dental Tissues and their Prevention

Program leader

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

IOT senior scientists

Research objectives

The research program of the Department of Cariology Endodontology Pedodontontology 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 (CDFD) 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

In the past year the cariology group has worked on both fluoride and biofilm topics. Efforts were made to advance our expertise with the CDFF and microtiter model. The CDFF was further developed to study de- and remineralization of substratum onto which biofilms form and to evaluate the effects of substratum and the type of microbial inoculum. At a frequency of sugar pulsing of 4 times a day equilibrium was found between de- and remineralization. Pilot experiments were carried out with various communities of oral bacteria.

Studying chlorhexidine it was found that its efficacy differed when tested on single versus multispecies biofilms. Obviously this is important to explain the (limited) effects of CHX on mature dental plaque. Regarding ozone we also observed that ozone demand in the medium determined the efficacy of the treatment and that oral biofilms are highly recalcitrant to ozone. Proteome and microarray techniques were developed to gain more insight into the interactions between oral bacteria and the effect of these interactions on their virulence properties, such as resistance to antimicrobial agents. For Streptococcus mutans, several green fluorescent protein reporter and knockout strains were made which can now be used in our biofilm models and for CLSM analysis of the biofilms.

In vivo testing chlorhexidine effects on enamel and dentine were studied in various in situ experiments involving human subjects. With a similar design it was observed that omitting a water rinse after brushing did not prolong the antimicrobial effect of a toothpaste on plaque over a 6-hr period.

Two review articles on residual post-treatment endodontic disease were accepted for publication. In these articles the direction of future research projects is indicated. Previous research on the efficacy of passive ultrasonic irrigation to remove debris and microorganisms from root canals is expanded in additional in-vitro experiments. After set-up of a mono- and dual species biofilm model the ability of sodium hypochlorite to influence growth was evaluated. Differences in susceptibility were recorded and will be further evaluated in the near future. For the detection of voids along root canal fillings two fluid transport set-ups were constructed. A set-up with glucose leakage was found to be more sensitive.

A comprehensive study on the dental health effect of different packages for basic oral care in Suriname continued this year with the final evaluation. Several publications are in progress. With respect to the Atraumatic Restorative Treatment the effect of different variables on the survival rate of class II restorations are investigated in different third world countries. Four publications on this subject are accepted and some others are in progress. Beside the collaboration with universities in these countries there are also coproductions with other departments at ACTA. In particular for the research in behavioural management aspects the results are described in the program of Social Dentistry and Behavioural Sciences.

Dissertations


Academic personnel in 2005 and 2006

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Publications in journals indexed in SCI


Zaura, E., Loveren, C. van, & Cate, J.M. ten (2005). Efficacy of fluoride toothpaste in preventing demineralization of smooth dentin surfaces and narrow grooves in situ under frequent exposures to sucrose or bananas. CARIES RES, 39, 116-122.

Other scientific publications (international, refereed)


Professional publications


External reports

Crielaard, W., & Cate, J.M. ten (2005). Contract research and consultancy work. Report for Purac Biochem, NL. Amsterdam: ACTA.


Indicators of Esteem

Grants: current projects with external funding

Zaura, E., Crielaard, W. & ten Cate J.M.: Three year grant honored by STW for the project: "Probing Dynamic Microbial Community Interactions" to be started in 2006. Total of €674,448 (including €80,000 from GABA-International and €20,000 from MRC-Holland). Expected start of the project spring 2006, end 2009.

Zaura, E.: Contract research work for CurOzone USA Inc. July 2005; €5,000


Membership of international editorial boards

Amerongen, W.E.: BRAZILIAN J PED DENT
Cate, J.M. ten: EUR J ORAL SCI
Loveren, C. van: INT J DENT HYG
Peters, L.B.: INT ENDOD J
Wesselink, P.R.: DEUTSCHE ZAHNÄRTZTLICHE ZEITSCHR
Wesselink, P.R.: ENDODONTIE
Wesselink, P.R.: INT ENDOD J
Wu, M.K.: INT ENDOD J

Organisation of international congresses or symposia


Invited speakers at international congresses or symposia

Cate, J.M. ten (2005 February 01). Calcium supply and caries. Portlight, UK, Unilever, Expert Panel meeting.


Academic Centre for Dentistry Amsterdam


Other international functions

Amerongen, W.E. van: Council member. EAPD.
Amerongen, W.E. van: Council member. IAPD.
Cate, J.M. ten: President. Central European Division of the International Association for Dental Research.
Cate, J.M. ten: Elected vice president. IADR World Council.
Cate, J.M. ten: Board member. Pan European Federation / IADR.
Wesselink, P.R.: Member. Arbeitsgruppe 'Zahnmedizin' des Wissenschaftsrates Deutschland.
Wu, M.K.: Guest Professor. Peking University School of Stomatology.
Wu, M.K.: Member. Research committee ESE.

Collaborations

- Faculty of Medical Sciences, Dept. of Dentistry, University of Groningen, Prof.dr. M.C.D.N.J.M. Huysmans, R. Thomas, Groningen, The Netherlands.
- University of Nairobi, Dr. A. Kemoli, Nairobi, Kenya.
- Medische Zending, Paramaribo, Surinam.
- St. Jeugd tandverzorging, Paramaribo, Surinam.
- Royal Dental College, Dr. B. Nyvad, Århus, Denmark.
- University of Århus, Dept. of Oral Health and Paediatric Dentistry, Dr. D. Haubek, Århus, Denmark.
- Gaba International Ltd., Dr. C. Spiegelhalder, Münchenstein, Switzerland.
- Unilever Research, Dr. A.J. Roberts, Port Sunlight, UK.
- Inspektor Research Systems BV, Dr. E. de Josselin de Jong, Amsterdam, The Netherlands.
- AMC, Department of Electron Microscopy, Dr. J. van Marle, Amsterdam, The Netherlands.
- WHO Collaborating Centre Nijmegen, Dr. W. van Palenstein Helderman, Dr. J. Frencken, Nijmegen, The Netherlands.
- University of Amsterdam, SILS, Dr. B. Keijser, Dr. M de Haan, Amsterdam, The Netherlands.
- University of Dar es Salaam (MUCHS) Dr. G. Mandari, Dar es Salaam, Tanzania.
- University of Sao Paulo, Dr. M. Bönecker, Sao Paulo, Brazil.
- University of Belem, Prof. A. Nogueira, Belem, Brazil.
- Vrije Universiteit, Dr. R. van Spanning, Amsterdam.
- Wellington School of Medicine, Dr. C.H. Sissons, Wellington, New Zealand.
- European Global Health Indicators, University of Lyon, Prof. D. Bourgeois, Lyon, France.
- Queen’s University Belfast, Prof. R. Freeman, Belfast, Ireland.
- University of Liverpool, Prof. Dr. S.M. Higham, Liverpool, UK.
- University of Greifswald, Dr. Ch. Splieth, Greifswald, Germany.
- Federal University of Paraiba, Joao Pessoa, Brazil.
Annual Research Report 2005

- Universiteit van Amsterdam: F. Wittink (microarray department), L. De Jong (mass spectrometry) and H. Hoefsloot (Biosystems data analysis), SILS
- 3M Espe; Dr. I Haeberlein, Seefeld, Germany.

Current PhD projects

Department of Oral Function

Oral Function and Oral Rehabilitation

Program leader

Prof.dr.ir. M. Naeije
Department of Oral Function
ACTA, Louwesweg 1
1066 EA Amsterdam
Tel: +31-20-5188423
E-mail: M.Naeije@acta.nl

IOT senior scientists

M. Naeije  F. Lobbezoo  M.A.J. van Waas

Research objectives

The general mission of the programme is to improve the dentist’s knowledge of the normal and the disturbed movement functions of the human masticatory system, the factors that influence these functions, and the treatment modalities that preserve or restore the patient’s function. The present research programme comprises two major research domains. One, oral kinesiology, studies (1) the influence of (experimental) orofacial pain upon the sensorimotor control of the human masticatory system; (2) the pathophysiology, diagnosis and treatment modalities of patients with a (chronic) temporomandibular disorder, (3) the pathophysiology, diagnosis and treatment modalities of patients with a (sleep-related) oral movement disorder, and (4) the development, diagnosis and treatment of internal derangements of the temporomandibular joint. Two, evaluation of implants and indirect restorations, studies the diagnosis, treatment planning, and treatment modalities of replacing lost dental tissues by removable or fixed appliances, if indicated on dental implants.

Results

Oral kinesiology

Ad 1. The influence of pain on the sensorimotor control of mandibular movements: A study conducted in close collaboration with the University of Aalborg, Denmark, showed that the fatigue- and pain-related modulation of the jaw-stretch reflex shows a time-dependent nature: intense chewing over 100 min yields a gradual, significant increase in the reflex amplitude. In a reflex study, performed in our laboratory, intense chewing was shown to cause a transient suppression of the inhibitory jaw reflex as evoked by electrical stimulation of the upper lip. This observation was highly reproducible when the experiments were repeated after one week.

Ad 2. In a multicenter study (together with prof.dr. A. De Laat, department of Stomatognathic Physiology, Catholic University of Leuven, Belgium; prof.dr. M. Nilner, department of Stomatognathic Physiology, University of Malmö, Sweden; prof.dr. A. Michelotti, department of Orthodontics, University of Naples ‘Frederico II’, Italy) on the validity of tests to classify temporomandibular disorder pain patients into several subgroups, chronic TMD patients and two
control groups (a group of chronic dental pain patients and a group of healthy pain free controls) were investigated by calibrated dentists in a single blind design.

In 2005, a Randomised Controlled Clinical Study (RCT) to the treatment effects in chronic myofascial TMD pain patients was started. In this study, the short-term and long-term effects of either 1) physical therapy, 2) stabilization splint, or 3) a self care program will be compared. Moreover, the influence of the presence of widespread pain on the treatment effects will be accounted for.

Ad 3. Bruxism and obstructive sleep apnea (OSA) are subjects of several ongoing studies. Bruxism has been suggested to cause tooth wear and temporomandibular disorder (TMD) pain. In a large-scale study, using a population sample containing community cases (about 5% of the sample) and controls between 35 and 44 years of age, that was conducted in collaboration with the University of Leipzig, Germany, no associations were found between anterior tooth wear and TMD pain. From a longitudinal, 20-week study in a sample of four sleep bruxism patients, it was shown, on the basis of time series analyses, that variations in the self-reported morning jaw muscle pain are related to variations in pain scores of the preceding evening. Further, anticipated stress, experienced stress, and self-reported diurnal clenching significantly contributed to the model, thereby explaining about 20-55% of the total variance in morning jaw muscle pain in the four patients, while objectively recorded (EMG) episodes of nocturnal masticatory muscle activity did not contribute to the model. About 30-40% of the variance in evening pain could, in turn, be predicted by variations in experienced stress and by the occlusal splint therapy that was performed during the final 13 weeks of the study.

In a polysomnographic study, and as part of an ongoing RCT study to the efficacy of different treatment modalities for nocturnal bruxism, it was estimated how much the commonly used sleep bruxism outcome variables ‘number of bruxism episodes per hour of sleep’, ‘number of bruxism bursts per hour of sleep’, and ‘percentage of total sleep time spent bruxing’ must change in an individual patient before this change can be considered statistically significant. Even though significance does not necessarily imply clinical relevance, these estimates, the so-called smallest detectable differences (SDDs), can be used as important indicators for the efficacy of a treatment modality.

Similarly, in another polysomnographic study, which is part of an ongoing RCT study to the efficacy of different treatment modalities for obstructive sleep apnea OSA, the SDD was calculated for the most frequently used OSA outcome variable ‘apnea-hypopnea index’ (AHI).

Ad 4. In a study using condylar movement recording techniques and magnetic resonance imaging techniques it was concluded that condylar position alone is not a good indicator for functional signs of TMJ hypermobility. At wide opening, it is probably the location of the condyle in front of the articular eminence in combination with a particular line of action of the masticatory muscles, which gives rise to the functional signs of hypermobility.

**Evaluation of implants and indirect restorations**

Progress is made in the efforts to evaluate adhesive partial dentures (1), and overdentures on implants (2).

Ad 1. In cooperation with the department of dental materials sciences one PhD student started a study on composite reinforced partial dentures. A survey of the literature was performed; laboratory studies with respect to the strength of partial dentures in clinical comparable circumstances was started.

Ad 2. The eight-year evaluation of a randomised controlled clinical trial, which started in 1991, and already resulted in several publications, was analysed. The conclusion is justified that with respect to patient satisfaction a simple treatment modality of two implants with a ball attachment is a good treatment option in the long run.
Academic personnel in 2005 and 2006

### Research staff ACTA - CD (in full time equivalents)

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### Publications in journals indexed in SCI


### Professional publications


External reports


Indicators of Esteem

Grants: current projects with external funding

Koutris M., Surface EMG mapping of the masseter muscle during fatiguing contractions, EU Marie Curie Fellowship, 1 fte. for four months in Aalborg, Denmark (€ 4800 plus air fares), April 15 – August 15, 2005.

Membership of international editorial boards

Lobbezoo, F.: J ORAL REHABIL
Naeije, M.: J ORAL REHABIL

Invited speakers at international congresses or symposia


Other international functions

Lobbezoo, F.: Chairman of the Research Committee. European Academy of Craniofacial Disorders (EACD).

Lobbezoo, F.: Secretary/Treasurer of the Neuroscience/TMJ Special Interest Group. International Association for Dental Research (IADR).


Collaborations

- University of Utrecht, Department of Oral Maxillofacial Surgery, Prosthodontics, and Special Dental Care, dr. H.W. van der Glas, Utrecht, The Netherlands.
- University of Halle School of Medicine, M. John, Halle, Germany.
- Université de Montréal, Faculté de médecine dentaire, Departement de santé buccale, prof.dr. G.J. Lavigne, Montréal, Quebec, Canada.
- Slotervaart General Hospital, Department of Clinical Neurophysiology and Brainmapping Laboratory, dr H.L. Hamburger, Amsterdam, The Netherlands.
- University of Washington, Departments of Oral Medicine and Psychiatry and Behavioral Sciences, prof.dr. S.F. Dworkin, Seattle (WA), USA.
- University at Buffalo, Department of Oral Diagnostic Sciences, dr. R. Ohrbach, Buffalo (NY), USA.
- University of Aalborg, Center for Sensory-Motor Interaction, Orofacial Pain Laboratory, prof.dr. P Svensson, Aalborg, Denmark.
- University of Dundee, The Dental School, dr. P. Maillou, Dundee, Scotland, United Kingdom.
- Catholic University of Leuven, Department of Stomatognathic Physiology, prof.dr. A. De Laat, Leuven, Belgium.
- University of Malmö, Department of Stomatognathic Physiology, prof.dr. M. Nilner, Malmö, Sweden.
- University of Naples ’Frederico II’, Department of Orthodontics, prof.dr. A. Michelotti, Naples, Italy.

Current PhD projects


Program leader

Prof.dr. U. van der Velden  
Department of Periodontology  
ACTA, Louwesweg 1  
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E-mail: U.vd.Velden@acta.nl

IOT senior scientists

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 bacterial and host factors involved?
   - To what extent are hereditary factors important?

2. Degradation and regeneration:
   - How is the extracellular matrix of the periodontium degraded?
   - What mechanisms are responsible for tissue homeostasis?

3. Prevention and treatment of periodontitis:
   - Which are the most effective measures to prevent and control dental plaque?

Results

Periodontitis is a complex disease because of its multifactorial etiology (bacteria, genetics and environment). We studied in an untreated Indonesian population the natural history of periodontal disease over 15 years. The results showed that with regard to the onset of periodontitis 3 risk factors could be identified: age, amount of subgingival calculus and the subgingival presence of Actinobacillus actinomycetemcomitans (odds ratio 1.2, 1.2 and 4.1 respectively).

With regard to the genetic factors we followed two strategies: 1) candidate gene approach; 2) genome wide search. The first approach has been further developed within the framework of the European Consortium and granted network INFOBIOMED; a periodontitis data-warehouse (PDWH) has been constructed and is now in its testing phase. The PDWH will be used for data-mining, visualization and cluster analysis in conjunction with the other etiological factors. The second
approach is well under way; in a multicenter European study (EPG consortium) we have now over 500 cases. A pilot on genome wide screening has been undertaken; validation studies are now being designed. Also, functional studies are undertaken which investigate the relative importance of observed genetic associations with periodontitis; we are measuring phagocytosis and neutrophil activation among patients with different genotypes for Fcgamma receptors. Further, we have investigated Th1 and Th2 responses in smoker and non-smoker patients; smokers have a predominance of a Th2 response upon stimulation, possibly explaining more periodontal destruction in smokers than non-smokers.

Periodontitis has systemic effects. In a meta analysis it was shown that C-reactive protein levels are always elevated in periodontitis in comparison to healthy controls. We have further investigated the concept that periodontitis could predispose for cardiovascular diseases. Results from a pilot study show that in periodontitis patients the intima media thickness (IMT) of the internal carotid arteries is increased in comparison to control subjects. Further, patients with periodontitis appear to have an increased pro-coagulant state and an increased insulin resistance.

Collaborative studies between Oral Cell Biology and Experimental Periodontology led to new insights into the effect of mechanostimulation on osteoclastogenesis. In collaboration with R. Oude Elferink (AMC) the lack of the anion exchanger 2 (AE2) was studied on the activity of osteoclasts and on the formation of tooth enamel. The findings show that AE2 is essential for the activity of osteoclasts; mice lacking this protein are severely osteopetrotic. The exchanger proved also to be essential for enamel formation of the mouse incisor but not for the molar. Possible similarities between osteoclasts and ameloblasts are now further explored. The interaction of osteoclast precursors with a confluent layer of bone lining cells was investigated. Attachment of a subpopulation of monocytes was followed by withdrawal of the bone lining cells. After this the monocytes migrated into the cell-free areas and fused to form multinucleated osteoclasts.

Studies on the prevention and treatment of periodontal diseases concentrate on the efficacy of electric toothbrushes, dentifrices, mouth rinses and antibiotics. Our results have shown that rinsing for 30 sec with a mouth rinse is sufficient in order to reach all intra-oral surfaces. In addition it was found that the combined use of AmF/SnF2 dentifrice and mouth rinse was more effective in plaque reduction when compared to the use of NaF dentifrice and mouth rinse. In addition the SLS in dentifrices does not seem to reduce the level of plaque inhibition offered by rinsing with chlorhexidine. Research regarding the treatment of intra-osseous defects showed that the adjunctive use of a tetracycline-coated e-PTFE membrane failed to show more attachment and bone gain.

Dissertations


Academic personnel in 2005 and 2006

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| total guests              | 0,15  | 0,15  | guest   |

| Total research staff      | 6,00  | 5,40  |         |

Publications in journals indexed in SCI


Other scientific publications (international, refereed)


Professional publications


Indicators of Esteem

Grants: current projects with external funding

De Vries, TJ Cellular and nuclear diversity of multinucleated osteoclasts. KNAW fellowship; 2002-2005. €250,000,-.
Van der Weijden GA & Van der Velden U: Oral-B advantage sensitive. Braun/Gilette Germany; € 48,870,-.
Van der Weijden GA & Vander Velden U: The prevention study. Braun/Gilette Germany; € 120,000,-.
Loos BG, Van Winkelhoff AI & Van der Velden U: 6th Frame work, Network of Excellence, European Commision, Section IST:INFOBIOMED 2004-2006, total buget; € 248,000,-.
Loos BG Relationship between oral and systemic health. Philips DAP Oral Health Division, 2005-2008, total budget €75,000,-.

Membership of international editorial boards

Beertsen, W.: EUR J ORAL SCI
Beertsen, W.: J CLIN PERIODONTOL
Beertsen, W.: J DENT RES
Loos, B.G.: J CLIN PERIODONTOL
Loos, B.G.: J DENT RES
Loos, B.G.: ORAL HEALTH PREV DENT
Velden, U. van der: INT J DENT HYG
Velden, U. van der: J CLIN PERIODONTOL
Weijden, G.A. van der: INT J DENT HYG

Organization of international congresses or symposia


Invited speakers at international congresses or symposia

Loos, B.G. (2005 September 22). Implants in periodontitis patients. Munich, Germany, 14th Annual scientific meeting, European Association for Osseointegration.

Scientific awards/honours

Other international functions

Beertsen, W.: Board Member. ICCBMT.
Loos, B.G.: Jury member, Meridol Research Prize.German Society of Periodontology, Germany.
Velden, U. van der: Board Member. European Federation of Periodontology.
Velden, U. van der: External examiner. European MSc programs.

Collaborations

- Universiteit van Amsterdam, Celbiologie & Histologie (dr. C.J.F. van Noorden).
- Universiteit van Amsterdam, Klinische Chemie (dr. F.J. Hoek).
- University of Sheffield (dr. D. Buttle), Sheffield, United Kingdom.
- Celltech (dr. A. Docherty), London, United Kingdom.
- Padjadjaran University, Parodontology (dr. S. Lambri), Bandung, Indonesia.
- Unilever Research (dr. D.J. Page), Port Sunlight, United Kingdom.
- Clinical & Basic Research, dept. of Bone Biology (dr. J.M. Delaisse), Ballerup, Denmark.
- Mount Sinai Hospital (dr. B. Gelb, dr. D. Brömme), New York, USA.
- Ludwig Boltzmann Institut für Osteologie (prof.dr. P. Fratzl) Vienna, Austria.
- Georg-August Universität (dr. P. Saftig) Goettingen, Germany.
- NICDR (dr. H. Birkedal-Hansen), Bethesda, USA.
- Braun Oral Research (dr. P. Warren) Baltimore, USA.
- University of Kiel, Dept of Gastro-Enterology (dr. S. Schreiber) Germany.

Current PhD projects


Section: Oral Cell Biology

Bioengineering of Bone and Periodontium

Program leader

Prof.dr. V. Everts
Oral Cell Biology
ACTA
Van der Boechorststraat 7
1081 BT Amsterdam
tel: 31-20-4448661
e-mail: v.everts@vumc.nl

IOTA senior scientists

Research objectives

The program “Bioengineering of Bone and Periodontium” of the Department of Oral Cell Biology studies the biological processes of functional adaptation and guided regeneration of bone and periodontium. Research focuses on fundamental aspects of mechanotransduction, and tissue engineering of bone 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 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, and 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. In addition, the local formation of bone and connective tissue around bone-replacing and bone-inducing grafts, and during Distraction Osteogenesis is studied, using human bone cell cultures as well as quantitative histomorphometry of human bone biopsies from augmented jaw bone. Finally, studies are performed on prevention of infections around oral and orthopaedic implants, using antimicrobial peptides combined with a bone substitute; a collaboration within the Foundation STEGA (Skeletal Tissue Engineering Group Amsterdam).
Results

Regeneration of bone and periodontium
Distraction osteogenesis is another method to augment jaw bone prior to placement of dental implants. This procedure results in bone regeneration within a fibrous gap area between two bone ends that are distracted from each other by mechanical force. Morphometric studies of jaw bone regeneration using this technique were undertaken in collaboration with the Departments of Oral & Maxillofacial Surgery (ACTA-VUMC), Alkmaar Medical Center, Gelderse Vallei Hospital, and the Department of Functional Anatomy (ACTA).

Collaborative studies between Oral Cell Biology and Experimental Periodontology led to new insights into the effect of mechanostimulation on osteoclastogenesis. In collaboration with R. Oude Elferink (AMC) the lack of the anion exchanger 2 (AE2) was studied on the activity of osteoclasts and on the formation of tooth enamel. The findings show that AE2 is essential for the activity of osteoclasts; mice lacking this protein are severely osteopetrotic. The exchanger proved also to be essential for enamel formation of the mouse incisor but not for the molar. Possible similarities between osteoclasts and ameloblasts are now further explored.

Mechanical regulation and adaptation
Building on earlier studies on mechanotransduction, we further characterized the early responses of bone cells to mechanical activation by fluid flow.

We use an in vitro model, a parallel-plate fluid flow chamber, to simulate in vivo fluid shear stresses on various cell types exposed to dynamic fluid flow in their physiological environment. The metabolic response of cells in vitro is associated with the wall shear stress. The parallel-plate flow chamber has been fully characterized for dynamic fluid flow experiments, which enables us to study the effect of physiological flow regimes on cells involving a wide range of frequencies and types of viscous fluids. Using this model, we have shown that an initial stress-kick is required for fluid shear stress-induced rate dependent activation of bone cells.

We have recently proposed that during bone remodeling, osteocyte apoptosis steers osteonal alignment in relation to mechanical loading of the whole bone. We have now shown that disuse promotes osteocyte apoptosis, while mechanical stimulation by fluid shear stress promotes osteocyte survival, by modulating the Bcl-2/Bax expression ratio.

It has been suggested that loss of estrogen during menopause alters the response of bone cells to mechanical loading, thereby contributing to the rapid loss of bone. We found that estrogen and mechanical loading have additive effects on the production of paracrine factors such as nitric oxide and prostaglandins, by bone cells from osteoporotic donors. The results suggested that estrogen and mechanical stress both promote the production of nitric oxide and prostaglandins by bone cells via independent pathways. The presence/absence of estrogen does therefore not alter the response of bone cells to mechanical loading, and the rapid loss of bone during menopause is unlikely to be caused by a change in the mechanoresponsiveness of the bone cells.

Local bone mass and architecture are affected by mechanical loading, which is thought to provoke a cellular response via loading-induced flow of interstitial fluid. For engineering bone tissue, mechanosensitive cells are needed which are able to conduct bone cell-specific functions, such as (re)modelling of bone tissue. We studied whether adipose tissue-derived mesenchymal stem cells (AT-MSCs), which are a potential source of cells for bone tissue engineering, are responsive to...
mechanical loading by pulsating fluid flow (PFF) in vitro. We found that AT-MSCs are mechano-sensitive, and might be able to conduct bone cell-specific functions during bone (re)modelling. Therefore AT-MSCs provide a promising new tool for bone tissue engineering.

Bone defects related to osteoporosis, which differs between males and females, develop with increasing age, suggesting that bone loss is related to some form of imperfect bone remodeling. Osteocytes supervise the bone remodeling process in a strain-dependent manner. The imperfect response of osteoporotic osteocytes to mechanical loading, and the reduced osteocyte density in osteoporotic patients, might relate to the imperfect bone remodeling, eventually leading to the lack of bone mass and strength in osteoporotic patients. The study results were consistent with impaired osteoblast function in osteoporotic patients, and with a different mechanism of bone loss between men and women, in which the osteocyte density might play a role.

Academic personnel in 2005 and 2006

### Research staff ACTA - OC (in full time equivalents)

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Dissertations


Publications in journals indexed in SCI


Other scientific publications (international, refereed)


Professional publications


External reports


**Indicators of Esteem**

**Grants: current projects with external funding**

Bacabac RG, Klein-Nulend J: Physics Development Project grant # PHL-146: Development of an optical tweezer setup (€ 63,000)

Bronckers ALJJ and Jansen J.: Project grant STW-NWO (#NK 6099) Tissue Engineering of the Periodontal Ligament 2004-2008: 1 OIO (ACTA) , 0.4 fte technician (ACTA) and 1 OIO (KUN)

Bronckers AL: NIH (USA) RO1-project: "Enamel fluorosis; Mechanisms of Action" (September 2005-September 2010). Co-PI: Prof. P. DenBesten (University of California San Francisco). (total amount $1,400,000; for ACTA: $ 586,000).


Klein-Nulend J, Noote PJ, Korstjens CM: Smith & Nephew Project: Effect of low intensity pulsed ultrasound on established delayed union or nonunion of the fibula, after a high tibial osteotomy. (Participation Oral Cell Biology, 1 fte AIO for 2 yrs, 0.2 fte postdoc for 1 yr), 2005-2007.


**Membership of international editorial boards**

Bronckers, A. L. J. J.: EURL ORAL SCI
Bronckers, A. L. J. J.: ODONTOLOGY
Everts, V.: EUR J ORAL SCI
Everts, V.: EUR J MORPHOL
Klein Nulend, J.: J MUSCULOSKELETAL RES
Loon, J. J. W. A. van: BIOL SCI SPACE
Lyaruu, D. M.: CONNECT TISSUE RES
Lyaruu, D. M.: EUR J ORAL SCI

**Organisation of international congresses or symposia**


**Invited speakers at international congresses or symposia**

Everts, V. (2005 May 01). Bone resorption: an interplay between bone lining cells and osteoclasts. Sheffield, UK, Seminar at the University of Sheffield.


Scientific awards/honours


Other international functions

Bronckers, A.L.J.J.: Member of working committee. COST-action B23.
Everts, V.: Member. Bone Quality Club, Procter and Gamble.
Klein Nulend, J: Member. ESA workshop on Life Sciences.
Loon, J.J.W.A. van: Management Board member. American Society for Gravitational and Space Biology, ASGSB.
Loon, J.J.W.A. van: Vice-President. European Low Gravity Research Association, ELGRA.
Loon, J.J.W.A. van: Member. Topical Team Low Back Pain, European Space Agency.

Collaborations

- AMC, Dept Cell Biology and Histology (Prof. dr. C. van Noorden), Amsterdam, NL.
- AMC, Dept Experimental Hepatology (Prof. dr. R. Oude Elfrink), Amsterdam, NL.
- City University of New York, Dept Mechanical Engineering (Prof.dr.ir. S.C. Cowin), New York, NY, USA.
- Erasmus University Rotterdam, Dept Orthopaedics (Dr.ir. H. Weinsans), Rotterdam, NL.
- Eindhoven University of Technology, Dept Biomedical Engineering (Prof.dr.ir. R. Huiskes), Eindhoven, NL.
- Hospital Hilversum, Dept Orthopaedics (Dr. G.H.R. Albers), Hilversum, NL.
- Keele University, Centre for Science and Technology in Medicine (Prof.dr A. El Haj), Stoke-on-Trent, UK.
- Penn State University College of Medicine, Dept Cell and Molecular Physiology (Dr. Q. Chen), Hershey, PA, USA.
- Spaarne Hospital Heemstede, Dept Orthopaedics (Dr. P. A. Nolte), Heemstede, NL.
- University of Texas, Dept. Orthodontics (Dr. R.N.D’Souza, Dr. P.J. Duke), Houston, TX, USA.
- University of Helsinki, Dept Biosciences, Division Biochemistry (Dr. H. Rauvala), Helsinki, Finland.
- University of Aberdeen Medical School, Dept Medicine and Therapeutics (Dr. M.H. Helfrich), Aberdeen, Scotland.
- Utrecht University Medical Center, Dept Orthopaedic Surgery (Dr. W.J.A. Dhert), Utrecht, NL.
- VUmc, Dept Endocrinology (Prof dr. P. Lips), Amsterdam, NL.
- VUmc, Dept Orthopaedics (Prof.dr. P.I.J.M. Wuisman, Dr. M.N. Helder), Amsterdam, NL.
- VUmc, Dept Clinical Physics and Engineering (Prof.dr. R.M. Heethaar, Dr.ir. Th.H. Smit), Amsterdam, NL.
- VUmc, Dept Pathology (Dr. F. van Milligen), Amsterdam, NL.
- VUmc, Dept Haematology (Dr. G.J. Schuurhuis), Amsterdam, NL.
- VUA, Dept Biophysics and Complex Systems (Prof.dr. C.F. Schmidt), Amsterdam, NL.
- Radboud University Nijmegen, NL, Dept Orthodontics and Oral Biology, Prof.dr. A.M. Kuijpers-Jagtman, Dr. J.C. Malthe; Department of Biomaterials, Prof. dr. J. Jansen and Dr. X.F. Walboomers
- University of Kiel. Dept. Biochemistry, Prof.dr. P. Saftig, Kiel, Germany.
- NIDR, Prof.dr. H. Birkedal Hansen, Bethesda, Washington, USA.
- Nordic Bioscience, dr. M. Karsdal, Herlev, Denmark.

Current PhD projects


Bloemen, V. The role of cell-cell interactions in the modulation of bone resorption during tooth movement. Supervisors: Prof.dr. V. Everts and Prof.dr. A. Zentner; co-supervisor: Dr. T. de Vries. Start: October 2005.

Faber, C. Antimicrobial peptides (AMPs) linked to polymethyl-methacrylate (PMMA) beads for the prevention and treatment of osteomyelitis. Supervisors: Prof.dr. A. van Nieuw Amerongen, Prof.dr. P.I.J.M. Wuisman; Co-supervisor: Dr. DM Lyaruu. Start: July 2000.


Section: Oral Microbiology

Microbiological Aspects of Oral Infections

Program leader

Prof.dr. A.J. van Winkelhoff
Oral Microbiology
ACTA
Van der Boechorststraat 7
1081 BT Amsterdam
Tel: +31-20-444 8677
E-mail: AJ.vanWinkelhoff@vumc.nl

IOT senior scientists

Research objectives

One research objective is to study the role of K antigens in the virulence of Porphyromonas gingivalis. The genetic basis of the different K antigens of this pathogen is currently under investigation.

Periodontal damage is caused by the interaction of the host and the parasites. Therefore, host-parasite interactions have become a major part of our research aims. The interaction is studied by microbiological analysis of the subgingival plaque of well described periodontitis patients and by identification of gene polymorphisms in innate immunity genes. In this way, the relationship between genetic features of the host and the subgingival microflora in periodontitis is studied.

The microbial colonisation of dental implants (Department of Oral and Maxillofacial Surgery and Maxillofacial Prosthetics, University Hospital Groningen) is subject of scientific research.

Research in Cariology involves the development of a molecular approach to determine the role of glycosyltransferase genes in the pathogenesis of dental caries.

Results

A study on the antimicrobial resistance among bacteria involved in destructive periodontal diseases has revealed significantly higher MIC values among bacterial isolates from Spanish patients in comparison to Dutch patients. Antimicrobial resistance towards multiple antibiotics was noted for F. nucleatum, P. intermedia and A. actinomycetemcomitans. In the development of molecular diagnosis in oral infection, the Real Time (RT) PCR Taqman technique has been validated in a study of a large amount of subjects representing periodontal health and disease. Comparison between anaerobic culture and RT PCR has shown the superiority of the RT PCR technique, however, the observed differences in detection did not exceed the 15% level. The efficacy of universal primer/probe sets to determine total bacterial load has been studied using laboratory strains as well as human plaque samples. It was found that none of the tested sets were able to reliable detect and quantify oral pathogens such as P. gingivalis and T. forsythensis.

In collaboration with researchers of the Queen Mary London Hospital (Prof.dr. M.A. Curtis) the locus responsible for the capsule production (K antigens) has been investigated. Differences in
the construction of this locus in different serotypes have been found. Restriction Fragment Length Polymorphism analysis of the locus in all serotypes demonstrated significant variation between serotypes and limited conservation within serotypes.

In relation to the genetic background of periodontal diseases the candidate gene approach has revealed several polymorphisms in innate immunity genes. The most recent finding is the association of a polymorphism (-260C>T) in the gene encoding for CD14, a co-receptor involved in the recognition of bacterial lipopolysaccharide. Logistic regression analysis adjusted for gender, age, smoking and prevalence of *P. gingivalis* and *A. actinomycetemcomitans* showed an association between the CD14 -260 T/T genotype and periodontitis (P=0.004, OR 3.0, 95% CI 1.4-6.9).

### Academic personnel in 2005 and 2006

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### Publications in journals indexed in SCI


### Professional publications


External reports


Indicators of Esteem

Grants: current projects with external funding


Membership of international editorial boards

Winkelhoff, A.J. van: CLIN ORAL IMPLAN RES
Winkelhoff, A.J. van: EVID DENT PRACT
Winkelhoff, A.J. van: J CLIN PERIODONTOL
Winkelhoff, A.J. van: J PERIODONTAL RES
Winkelhoff, A.J. van: J PERIODONTOL

Invited speakers at international congresses or symposia

Winkelhoff, A.J. van (2005 September 15). Antibiotic resistance in the subgingival microflora. A comparison between The Netherlands and Spain. Amsterdam, the Netherlands, IADR/CED.


Scientific awards/honours


Other international functions

Soet, J.J. de: Secretary General. ORCA (European Organisation of Caries Research).
Winkelhoff, A.J. van: Visiting Professor. University of London, Eastman Dental Hospital, Department of Periodontology.

Collaborations

- University Complutense Madrid, Dept of Periodontology, Prof.dr. M. Sanz, Madrid, Spain.
- University of Oslo, Dept. Microbiology, Prof.dr. I. Olson, Oslo, Norway.
- University of Gothenburg, Dept. Oral Microbiology, Prof.dr. G. Dahlén, Gothenburg, Sweden.
- University College of London, Queen Mary's School of Medicine and Dentistry, Prof.dr. M.Curtis, London, UK.
- Department Medical Microbiology and Infection prevention, VU University Medical Center, Prof.dr. C.M.J.E. Vandenbroucke-Grauls, Amsterdam, The Netherlands.
- Laboratory of Immunogenetics, VU University 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 Health Sciences, Kristianstad University, Prof.dr. S. Renvert, Kristianstad, Sweden.
- Department of Informatics, VU University Medical Center, dr. C.J.N.M. van der Palen, 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.
- Ablynx, Gent, Belgium. Prof.dr. H. de Haard.

Current PhD projects


Department of Oral and Maxillofacial Surgery / Oral Pathology

Oral and maxillofacial disorders: diagnosis and treatment

Program leader

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

IOT senior scientists

I. van der Waal
D.B. Tuinzing
E. Bloemen

Research objectives

The research of the Department of Oral and Maxillofacial Surgery / Oral Pathology consists of four main areas of interest, being:
1. Early diagnosis of oral cancer and precancer, including cancer of the salivary glands.
2. Surgical orthopedics of the maxillofacial skeleton.
3. The rationale of removing asymptomatic impacted wisdom teeth and some other dental alveolar subjects.
4. Inflammatory and inflammatory-like diseases of the oral and perioral structures, including the jaw bones and the lymph nodes of the neck.

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).

The research on surgical orthopedics is focused on maxillofacial function and healing capacity after treatment of acquired and congenital jaw deformities. Attention is focused on the indications/counter-indications and preventive measures in surgical-orthodontic treatment of dentofacial deformities.

A second aspect of the program deals with the dynamics of the surrounding tissues after corrective surgery of maxillofacial bones e.g. the musculature, the temporal mandibular joint and bone(-substitutes) in cleft and oro-implantology cases. In the studies mentioned before there is a close collaboration with the Department of Orthodontics and the section Oral Cell Biology. Furthermore, there is collaboration with the Department of Surgical Orthopedics of the VUmc. The program is related to the recently established Onderzoeksinstuut MOVE of the VUmc.

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, particularly in aggressive or recurrent giant...
cell granulomas. Furthermore, a study is undertaken about the treatment of non-tuberculous mycobacterial lymphadenitis in children, comparing surgical versus medical treatment.

**Results**

The study on early diagnosis of oral cancer, including the salivary glands, is ongoing. In the international literature some interesting papers had been published about the prognostic value of DNA ploidy measurement in oral leukoplakia. However, recently it has been disclosed that those papers were based on fraud. Since we had not adjusted our research strategy to those falsified figures, no delay in the progress of our own study has been caused.

The project on the possible value of markers for the diagnosis and prognosis of salivary gland tumours has been focused until now on adenoid cystic carcinoma and myoepithelioma, but will be expanded to other tumour types.

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.

The randomized study on the removal of asymptomatic lower wisdom teeth has been closed. A manuscript has been submitted.

Several multi-center studies are running concerning new implant surfaces and new implant designs. In the line of bone and bone substitute research in the sinus floor elevation model, there are several studies running. The most recent study is on the clinical and histological results on SBC (Straumann Bone Ceramic) in sinus floor elevation. Early clinical and histological results are promising.

The study on inflammatory and inflammatory-like diseases of the oral and perioral structures, including the jaw bones, has been running well. A thesis on various aspects of central giant cell granuloma is expected in 2006.

**Dissertations**

### Academic personnel in 2005 and 2006

#### Research staff ACTA - MZ (in full time equivalents)

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### Publications in journals indexed in SCI


Other scientific publications (international, refereed)


Professional publications


Indicators of Esteem

Grants: current projects with external funding

Bruggenkate, C.M. ten: SBC (Straumann Bone Ceramic) bone substitute for sinus floor elevation (2005-2006) Straumann; € 52.000,-


Membership of international editorial boards

Bruggenkate, C.M. ten; CLIN ORAL IMPLAN RES
Waal, I. van der: ACTA STOMATOLOGICA CROATICA
Waal, I. van der: EUR J CANCER
Waal, I. van der: J DENT UNIV SAO PAOLO
Waal, I. van der: MEDICINA ORAL
Annual Research Report 2005

Waal, I. van der: MUND, KIEFER-, GESICHTSCHIRURGIE
Waal, I. van der: ORAL HEALTH PREV DENT
Waal, I. van der: ORAL ONCOLOGY

Scientific awards/honours


Organisation of international congresses or symposia


Invited speakers at international congresses or symposia


Other international functions

Bruggenkate, C.M. ten: Regular teacher. Basel University, Switzerland.
Bruggenkate, C.M. ten: Delegate for Belgium. ITI.
Bruggenkate, C.M. ten: Delegate for Finland. ITI.
Bruggenkate, C.M. ten: Board member. ITI (International Team for Implantology).
Bruggenkate, C.M. ten: Chairman. ITI Development Committee.
Bruggenkate, C.M. ten: Member. ITI Expert Pool.
Bruggenkate, C.M. ten: Regular ITI teacher. ITI Germany.
Waal, I. van der: Member. Scientific Committee STOMA.
Waal, I. van der: Expert for the UICC. Telepathology Consultation Center for odontogenic tissue. International Union Against Cancer (UICC).

Collaborations

- De Ottenhorst, Clinic for companion animal medicine, Terneuzen (J.P. de Vos, A.G.D. Burm, A.P. Focker)
- Eemland, Clinic for companion animal medicine, Amersfoort (H. Boschloo, M. Karsijns)
- Erasmus MC Rotterdam, Department of Oral and Maxillofacial Surgery (E.H. van der Meij/K.P. Scheeman)
- MRC-Holland (H.M.B. Duarte)
- School voor Tandheelkunde, Mondzienken en Kaakchirurgie, afdeling Parodontologie, Leuven. België (K.N.A. Michiels)
- UMC Groningen, afdeling Mondzienken, Kaakchirurgie en Bijzondere Tandheelkunde (A. Vissink, F.K.L. Spijkervet)
- University of Malaya, Oral Medicine, Oral Pathology & Periodontology Department, Faculty of Dentistry, Kuala Lumpur, Malaysia (Ajura Abdul Jalil, Rosnah Binti Zain)
- University of Bonn (Germany), Department of Oral and Maxillofacial Surgery
- University of Freiburg (Germany), Department of Oral and Maxillofacial Surgery
- University of Bern (Switzerland), Department of Oral and Maxillofacial Surgery
- VUMc, afdeling plastische chirurgie (H.A.H. Winters), Amsterdam
- VUMc, Department of Clinical Epidemiology and Biostatistics (J. Berkhof, D.J. Kuik), Amsterdam
- VUMc, Department of Haematology (P.C. Huygens), Amsterdam
- VUMc, Department of Nuclear Medicine, Amsterdam
- VUMc, Department of Otolaryngology/Head and Neck Surgery (C.R. Leemans, B.J.M. Braakhuis, H.J. Ruiter-Schippers, A. Brink, R.H. Brakenhoff), Amsterdam
- VUMc, Department of Radiation Oncology (J.A. Langendijk, B.J. Slotman), Amsterdam
- VUMc, Department of Radiology, Amsterdam
- VUMc, Institute of Pathology (P. van der Valk), Amsterdam
- Zaans Medisch Centrum, afdeling Mondzienken en Kaakchirurgie (Th.B.M. de Rijcke)

Current PhD projects


Section: Oral and Maxillofacial Radiology

Diagnostic Imaging of the Tissues in the Maxillo-facial Complex

a. Computer aided analysis of digital radiographic images
b. Three dimensional visualization of radiographic information
c. Diagnostic performance of radiographic systems

Program leader

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

IOT senior scientist

P.F. van der Stelt

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 fundamental as well as applied (clinical) components:


The application of advanced digital image processing procedures enables the recognition of specific features in radiographic images of normal and abnormal structures being characteristic for the condition of these structures. Typically, these features are either used for the quantitative assessment of tissue characteristics (density, homogeneity, etc.) or they add a new dimension to the description of the (patho)physiology of the tissue structures under investigation. Commonly the order of magnitude of this description is between the microscopic (micro; e.g., connectivity, density) and the anatomic (macro; e.g., texture, entropy) level.

2. Three dimensional visualization of radiographic information.

An important aspect of the research objectives is the visualization of radiographic image data into 3D-space. The purpose of 3D imaging is to overcome the inherent drawbacks of projection radiography, such as the lack of information about the third dimension. We try to achieve this goal by the use of specific 3D reconstruction techniques called Local CT and Cone Beam CT, which results in a much lower dose and a higher resolution than conventional CT. This makes the technique a better choice for many common dental diagnostic tasks than conventional CT.

3. Diagnostic performance of radiographic systems.

Once a new image analysis system has been developed and validated, it is important to know its value for the diagnostic process. The relevant performance of a diagnostic method not only depends on its technical sophistication, but also on such factors as the incidence and clinical variability of the disease under examination, the perceptive abilities of the diagnostician and the utility of the diagnostic outcome. These factors together form the diagnostic system. Consequently, this part of the research is aiming at evaluation and improvement of image analysis procedures from the system perspective.
Results

Computer aided analysis of digital radiographic images.
Digital subtraction radiography is a sensitive method for the detection of small changes in mineralized tissues. Two images of the same region of interest taken with identical projection geometry are required for this technique. We further developed software programs to match non-identical image projections. A new module is under investigation which applies statistical models to the images to predict the best match. This approach seems to be very promising because of its robustness. Testing is undertaken at this moment. This technique has also been applied in a study as part of the I-Imas project (EU Framework 6). We were able to predict an optimised image based on a low dose scout image. A complete system including the image optimisation software is currently under construction by other partners in the project. The first images have been taken with the new sensor. Two publications have been completed and are submitted. The Osteodent project (EU Framework 5), aiming at the early diagnosis of osteoporosis using dental radiography techniques, finished by the end of 2005. This project was done in collaboration with groups in Manchester (coordinator), Malmö, Athens and Leuven. It involved 600 osteoporotic patients and controls. Our contribution was focused on the quantitative analysis of the radiographic trabecular pattern on intra-oral radiographs and panoramic radiographs. We were able to demonstrate that quantitative analysis of the radiographic trabecular pattern is able to predict between 70 and 80% of the osteoporotic subjects. Several publications are in different stages at this moment.

Three dimensional visualization of radiographic information
Two projects related to Local CT have been undertaken. These projects were set up to study the clinical application of Local CT and 3D visualisation. The results indicate that Local CT provides more information that can not be produced by conventional projection techniques. The results will be published. In summer a Cone Beam CT device was installed. Several studies, both clinical and fundamental, have been started since then.

Diagnostic performance of radiographic systems
The PhD-project on the implementation of digital radiography in general dental practice is making good progress and has resulted in some more papers. Erwin Berkhout will present his thesis about this subject in the first half of 2006.

Research personnel in 2005 and 2006

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Publications in journals indexed in SCI


Professional publications


External reports


Indicators of Esteem

Grants: current projects with external funding


Invited speakers at international congresses or symposia

Stelt, P.F. van der (2005 July 02). Bone, architectural and radiographic structure explained. Athens, Greece, Symposium on ‘Bone Quality: implications for osteoporosis diagnosis and implantology’.

Stelt, P.F. van der (2005 December 02). Image optimization and advanced imaging. Glasgow, UK, NHS.


**Other international functions**


Mileman, P.A.: Member. IADR Diagnostic Systems Group Constitution and Byelaws Committee.


**Collaborations**

- Karolinska Institutet Huddinge.
- Universiteit Leuven
- University Medical College, Medical Decision Making Unit, Department of General Surgery, Dr. W. van den Hout, Leiden, The Netherlands.
- Dept. of Biomedical Engineering, Rutgers University, Piscataway, NJ, USA, Prof. S.M. Dunn.
- Dept. of Oral Radiology, University of Manchester, UK, Prof. Keith Horner.
- Dept. of Medico-Physics, University College of London, UK, Prof. R. Speller.

**Current PhD projects**

Section: Orthodontics

Craniofacial development, psychosocial aspects and biomaterials in orthodontics

Program leader

Prof. dr. A. Zentner
Orthodontics
ACTA, Louwesweg 1
1066 EA Amsterdam
Tel: +31-20-5188 415
E-mail: A.Zentner@acta.nl

Research objectives

The research activities at the Department of Orthodontics focus on basic and clinical research in orthodontics and related disciplines. Three main themes exist:
1. Growth and growth regulation during normal and abnormal craniofacial development. Several questions are studied in this larger theme, which for a long time has been the department’s major research field.
2. Orthodontics and quality of life. Projects related to this research theme involve psychosocial impacts of dental aesthetics psychosocial characteristics of orthodontic treatment.
3. Biomaterials. Studies are directed at biologically active molecules, bond strength of glass ionomer cements and fatigue fracture of orthodontic arch wires

Results

The following directions were pursued in the year 2005.
1. Growth and growth regulation during normal and abnormal craniofacial development. A number of projects were carried out within this larger theme.
2. Orthodontics and quality of life. Projects related to this research theme were carried out in collaboration with the Universities of New Jersey, USA, and Mainz, Germany. In particular, this work involved development and testing of questionnaires for assessment in children of oral health-related quality of life and of psychosocial impacts of dental aesthetics on the latter in adults. Furthermore, the effects of dental esthetics and orthodontic treatment on oral health attitudes and the role of dental aesthetics and some psychosocial characteristics in the perception of oral health-related quality of life were studied. In addition, the influence of a number of psychosocial characteristics on orthodontic treatment demand was investigated.
3. Biomaterials. Studies were carried out in collaboration with the Section of Oral Biochemistry of the Department of Dental Basic Sciences, ACTA, and The University of Mainz, Germany, which were directed at the development of novel techniques of covalent immobilization on the surface of various biomaterials of biologically active molecules such as antimicrobial peptides, cell-attachment and mineralization promoting molecules. In addition, in collaboration with the Section Dental Material Sciences of the Department of Dental Basic Sciences, ACTA, bond strength and setting characteristics of glass ionomer cements and fatigue fracture of orthodontic arch wires were investigated.
Dissertations


Academic personnel in 2005 and 2006

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Publications in journals indexed in SCI


Other scientific publications (international, refereed)


**Professional publications**


**Indicators of Esteem**

**Membership of international editorial boards**

Zentner, A.: AM J ORTHOD DENTOFAC  
Zentner, A.: EUR J ORTHODONT  
Zentner, A.: J OROFAC ORTHOPED  
Zentner, A.: ORTHODONTIA

**Invited speakers at international congresses or symposia**


**Other international functions**


**Current PhD projects**


Section: Social Dentistry and Behavioural Sciences

Dental Care and Dental Care Systems: Quality and Efficiency

Program leader

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

IOT senior scientists

Research objectives

There are two major research domains for the department of Social Dentistry and Behavioural Sciences. One domain concerns the quality and efficiency of dental care and dental care systems. Basically, our department’s research efforts in this field have three general goals. First, development of a quality assurance system that covers all aspects of dental care and potentially assures the continuous improvement of all practitioners and the quality of dental care by adequate assessment methods identifying strengths and weaknesses. Second, stimulating the implementation and assessing the effects of a quality system in dentistry in order to actually improve the oral health of the Dutch population and to increase patient satisfaction and the public trust in dentistry. Third, assessing the determinants and general consequences of occupational stress among general dental practitioners.

The second major research interest of the department concerns dental anxiety and pain. It goes without saying that dental anxiety and anticipating pain constitute major barriers to seek dental care. For that reason our department wishes to extensively study these concepts of both adults and children from a multidimensional perspective and with the help of psychologists, dentists, and double-trained staff-members.

The second major research interest of the department concerns dental anxiety and pain. It goes without saying that dental anxiety and anticipating pain constitute major barriers to seek dental care. For that reason our department wishes to extensively study these concepts of both adults and children from a multidimensional perspective and with the help of psychologists, dentists, and double-trained staff-members.

Results

The section’s research on compliance in orthodontics, carried out in close cooperation with the department of orthodontics of ACTA, resulted in a completed PhD thesis. It was shown that subjects who had undergone orthodontic treatment appeared to have a more positive attitude towards orthodontics than untreated subjects, but this attitude seemed to be predicted by the orthodontic experience itself, and not by any specific aspect of the treatment. Moreover,
previously treated females evaluated their experiences with orthodontics more positively than previously treated males. In another study it was found that all subjects preferred attractive teeth over success in sports, but high grades in school, a slim body figure, a lot of friends and a good general health were preferred over attractive teeth. Research also showed that the assumption that patients’ personality characteristics alone can predict patient compliance to a clinically useful degree is no longer tenable, and that the level of compliance, as indicated by orthodontic residents during treatment, is not a determinant of patient satisfaction in the long run. The most important factor contributing to patient satisfaction was the patient’s satisfaction with the doctor-patient relationship. Finally it was found that the extended version of the TRA explained 20% of the variance in the patients’ intention to comply. The patients’ anticipated regret, attitude and motivation to comply were significant determinants of the patients’ intention to comply. In the context of the section’s activities on work stress and dentist-assistant communication it appeared that there is a lack of recent data on burnout among dental hygienists. Although some knowledge is available on work stressors, a thorough investigation on burnout incidence, risk factors, as well as job resources is needed. It was shown that male and female dentists perceive their communication with the assistant differently; male dentists tend to be influenced by the gender differences, female dentists by striving for friendliness. A major development was the introduction of the so-called Stress Thermometer, an easily accessible Internet-based instrument for feedback on work stress and burnout. Results indicate the applicability of the Stress Thermometer to a representative variety of dentists.

As for the section’s anxiety and pain research-line, it appears that particularly the implementation of a high level of predictability during treatment; the training of patients in the use of coping skills, and the application of in vivo exposure to anxiety provoking stimuli are the most appropriate options for the management of anxious dental patients and the reduction of their anxiety level. Furthermore results suggest that fear of dental pain is a highly important covariate in dental pain research, i.e., less fear is reported when the pain has been experienced personally. It also appeared the dental treatment of children leads to reduced toothache-related behaviours and that the Dental Discomfort Questionnaire is a useful instrument for acquiring insight into the behavioural aspects of young children as a consequence of toothache or dental treatment, thereby underlining the importance of a behavioural approach in young children. The behavioural reaction of children who receive local anesthesia with a traditional syringe or with a computerized device (Wand) was analyzed. Within the high-anxious group no differences were found. It was concluded that low-anxious children seem to benefit from the use of the Wand instead of the traditional syringe in receiving local anesthesia. Finally, researchers of our department are also involved in the research activities of several other ACTA departments. We refer to the Results-sections elsewhere.

Dissertations

Academic personnel in 2005 and 2006

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Publications in journals indexed in SCI


Other scientific publications (international, refereed)


Professional publications


Indicators of Esteem

Grants: current projects with external funding


Membership of international editorial boards

Aartman, I.H.A.: COMMUNITY DENT ORAL
Gorter, R.C.; EUR J DENT EDUC

Collaborations

- School of Dentistry, Queen’s University Belfast, Dental Public Health. Professor Ruth Freeman. Belfast. Northern Ireland.

Current PhD projects


Section: Dental Material Sciences

Dental Restorations

Program leader

Prof.dr. A.J. Feilzer
Dental Material Sciences
ACTA, Louwesweg 1
1066 EA Amsterdam
Tel: +31-20-5188335
E-mail: A.Feilzer@acta.nl

IOT senior scientists

Research objectives

The general objective of this program is to predict and improve the clinical performance of dental restorative materials covering the complete range of materials involved in the procedures of creating restorations with direct or indirect techniques. Composition, structure and fabrication of the materials as well as their handling and application techniques are studied in vitro as well as in vivo. The increasing trend to replace the difficult and costly manual procedures by automated procedures with information technology is being studied on its merits. In particular the possible advantages of the automated production of indirect restorations by CAD/CAM technology are evaluated on the physical properties and quality of restorations, as well as the esthetic properties like digital color measurement and reproduction. CAD/CAM technology offers the possibility to use new strong ceramic materials as base for all-ceramic restorations. Mainly the research into Y-TZP zirconia indicates that its excellent physical properties makes 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 simulate the clinical conditions as closely as possible, ultimately to be used as standard quality control tests (so-called accelerated tests). Examples of such equipment are the 'ACTA-wear machine', the 'ACTA-intense' and the 'ACTA-fatigue device'.

Since 2002 the research area of the section includes clinical research on dental materials. For instance a European granted project on the clinical behavior of large class I and II glass-ionomer cement restorations is finished and a clinical study into the performance of a new denture resin base material is under investigation. In 2003 in the department clinic a start was made with a special consulting hours where patients with suspected the health effects of metals used in dental restorative materials can be referred to. This project has developed clinically as well as on basic science aspects quite well.

More specifically, the following aspects were investigated:
1. The effect of various agents on the morphology of dentin surfaces and the consequence on the quality of the bond with restorative materials.
2. The effect of test setup design on the results of the (micro and macro) tensile bond strength tests.

3. The operator independent determination of optical properties of resin-based composites and ceramics in relation to composition and the effect of aging on color.

4. The effect of ultrasound on the reaction rate of glass-ionomers.

5. The effect of the design of core build-up constructions on the resistance to premature failure during fatiguing.

6. The effect of water sorption of adhesives and resin cements on the adhesion to ceramics and the occurrence of fractures in ceramic crowns and inlays.

7. The effect of fatigue loading on the cohesive and adhesive properties of bonded restorations.


10. The effect of restorations under stressed conditions studied by three-dimensional finite elemental analysis (3D FEA).

11. The effect of surface defects on the strength of ceramics.

12. The thermal compatibility of dental ceramic systems.

13. The effect of design parameters on the survival rate of adhesive bridges.

14. The applicability of glass ionomer cement for orthodontic purposes.

15. The effects on general health of metal based restorative materials.

Results

Substantial progress has been made in revealing the mechanisms that play a role in the stress distribution in specimens exposed to tensile stresses in bond strength tests. For this research FEA was used to demonstrate the stress distributions in test specimens in more detail. It was shown that specimen size and shape had a significant influence on the bond strength.

A number of devices has been tested and modified to make them suitable for color, opacity and translucency measurements on resin composites and ceramics. The applicability of standard digital cameras for color determination of teeth was studied. With this method a significant relation of the color of different segments of teeth was demonstrated, which can be used to reconstruct the tooth color of missing parts of the tooth.

A standardized preparation and restoration technique of human premolars to test core built-up systems was developed. Preliminary tests showed that properly selected adhesive systems make post consolidation in build-up constructions superfluous.

The stress generated at the interface of the restoration and the cavity walls due to water sorption and mismatch of mechanical properties of the different materials, measured in a specially designed device could be confirmed with FEA.

A clinical study into the use of ultrasound for the accelerated set of glass-ionomer cement restoratives was finished with a PhD-thesis. It was shown that ultrasound dramatically increased the rate of setting of glass-ionomer cements, and in addition improved the surface hardness. A study into the applicability of this method in orthodontic bracket cementation is in progress.

In 2003 a start was made to develop a laboratory test to determine the composition of metal alloys used intra-orally for indirect restorations. This test is of main interest, as only traces of the metals need to be collected in situ to be analyzed on allergenic substances. Because of the medical aspects involved, cooperation has been sought with the department of allergic and skin diseases of the AMC and of the VUmc. Clinically, more than a 300 patients with suspected side-effects on dental materials were evaluated, while with a modified lymphocyte transformation test immunologic reactions of the T-lymphocytes on the metals of which their dental restorations are composed of the latter patients was screened.

Developments in the field of dental materials science made great strides forward. Experimental versions of low shrinking restorative monomer systems are recently introduced in dentistry and 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 metallic 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. A new technique in CAD/CAM is the rapid fabrication technique, which opens
new opportunities for homemade indirect ceramic restorations and introduction of new ceramic materials. The department is closely involved in these developments. The incidence of metal-ion release by the use of metallic 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. 

In 2005 three PhD-students, G. Isgrö, A. Dozic and R.N.B. van Duinen obtained their PhD degree. The department has 3 PhD-students who are in their last phase of their training. This asks much time and effort of the staff. Nevertheless, new steps in the clinical research development of the department were taken. The overall scientific output in terms of citation and publishing rate is rather high. Many manuscripts were accepted but not published yet.

**Academic personnel in 2005 and 2006**

| Research staff ACTA - MW (in full time equivalents) |
|-----------|----------------|----------------|----------------|
| position  | name            | fte 2005 | plan 2006 | funding |
| Full professors | Feilzer, prof.dr. A.J. | 0.40 | 0.40 | 1 |
|            | Zel, prof.dr.ir. J.M., van der | 0.30 | 0.30 | 3 |
| Senior lecturer | Kleverlaan, dr. C.J. | 0.60 | 0.60 | 1 |
|            | Gee, dr. A.J. de | 0.05 | 0.05 | guest |
| Lecturers and other tenured research staff | Pallav, dr. P. | 0.20 | 0.20 | 1 |
|            | Paridon, drs. M.W., van | 0.05 | 0.05 | 1 |
|            | Bolhuis, dr. H.P.B. | 0.10 | 0.10 | 1 |
|            | Dozic, dr. A. | 0.60 | 0.60 | 1 |
| Total tenured staff | | 2.30 | 2.30 |
| Non tenured staff | Jager, dr.ir. N., de | 0.10 | -- | 1 |
| PhD students | Abou Shelib, dds. M.N.M. | 0.80 | 0.80 | 3 |
|            | Algera, drs. T.J. | 0.20 | 0.20 | 1 |
|            | Dalen, drs. A., van | 0.10 | 0.10 | 1 |
|            | Kler, ing. M., de | 0.05 | 0.05 | guest |
|            | Keulemans, drs. F. | 0.40 | 0.40 | 1 |
|            | Meegdes, ing. M. | 0.05 | 0.05 | guest |
|            | Muris, drs. J. | 0.10 | 0.50 | 1 |
|            | Wang, dds. H. | 0.50 | -- | 1 |
| Total non tenured staff | | 1.70 | 2.50 |
| total 1st funding | | 2.85 | 3.65 | 1 |
| total 3rd funding | | 1.10 | 1.10 | 3 |
| total guests | | 0.15 | 0.15 | guest |
| Total research staff | | 4.10 | 4.90 |

**Dissertations**


Duinen, R.N.B. van (22-11-2005). A study into the prospects of traditional glass ionomer cement as a universal direct restorative material. UvA Universiteit van Amsterdam Prom./coprom.: Feilzer, prof.dr. A.J., & Kleverlaan, dr. C.J.

Publications in journals indexed in SCI


Other scientific publications (international, refereed)


Professional publications


External reports


Patents

European Patent nr 02077661.3 -1265/1378735: Method for determining a colour of a segment for a position in a set of teeth.

Indicators of Esteem

Grants: current projects with external funding


Membership of international editorial boards

Feilzer, A.J.: AM J DENT
Feilzer, A.J.: ODONTOLOGY

Invited speakers at international congresses or symposia

Scientific awards/honours


Other international functions

Zel, J.M. van der.: Chairman. ISO/TC106 adhoc group on Dental CAD/CAM systems.

Collaborations

- Elephant Industries, Hoorn, the Netherlands.
- DeguDent GmbH, Hanau, Germany.
- Melisa.org, (prof.dr. V. Stejskal), Stockholm, Sweden.
- Department of Material Science, Imperial College, (D.r R. Hill), London, UK.
- Queens Mary College, (Prof.dr. G. Pearson), London, UK.
- MIRC, (Prof.dr. S. Hampshire), Limerick, Ireland.
- Dental Biomaterials Department, Faculty of Dentistry, Alexandria University, Egypt.
- Department of Prosthodontics, West China College of Stomatology, Sichuan University, Sichuan, China.
- Department of Prosthodontics, Faculty of Dentistry, Hacettepe University, Samanpazari/Ankara, Turkey.
- Nova Southeastern University, College of Dental Medicine, Health Professions Division (dr. F. Garcia-Godoy), Nova Southeastern University, Fort Lauderdale, Florida.
- Advanced Dental Technology Center.

Current PhD projects


Meegdes, M. Esthetic CAD-CAM restorations by computer modeled layer build-up. Supervisor: prof.dr.ir. J.M. van der Zel, start January 2005 (guest).


Section: Functional Anatomy

Oral Function and Oral Rehabilitation: Functional Anatomy

Program leader

Prof. dr. T.M.G.J. van Eijden
Functional Anatomy
ACTA
Meibergdreef 15
1105 AZ Amsterdam
Tel: +31-20-5665 374
E-mail: T.M.vanEijden@amc.uva.nl

IOT senior scientists

Research objectives

The research program deals with the general question of how histological, anatomical, (neuro-)physiological and mechanical properties of the jaw muscles, jaws and jaw joints affect the development of normal and abnormal form and function of the masticatory system. The research is performed in a multidisciplinary way and mainly focussed on the mechanisms that determine the capacity for adaptational changes of these structures. Both analytical (morphometry, immunohistochemistry, electromyography, force registration) and predictive (biomechanical modeling) methods are applied for this purpose.

The masticatory muscles have many different properties that determine their possibilities for force generation and that vary across and among muscles. Among these are the variation in myosin heavy chain (MHC) isoform content, important for the velocity of muscle contraction. Muscle activation determines the amount of force produced by the muscles. Thus far muscle activation has predominantly been studied for specific motor tasks, not representative for normal daily behavior. Information on variation of muscle properties as well as daily muscle use is important for three reasons. First, it can shed light on the mechanisms that determine the physiological properties of masticatory muscles, because muscle fibers adapt to the frequency and intensity of activation. Second, it can be expected that adaptational changes (of, for example, MHC content) could occur in clinical situations, such as bruxism, aberrant dental occlusion, orthodontic and gnathosurgical interventions, abnormal craniofacial morphology, and age-related or edentulous masticatory muscle and jaw bone atrophy. Third, the muscles determine to a large extent the loading of jaws, teeth and joints. As a consequence of these loadings bone and cartilage deform. These deformations play a dominant role in the development, maintenance, and degradation of bone and cartilage. In bone the relationship between loading and deformation is predominantly determined by its (micro)architecture. Furthermore, the quality of this architecture determines the capacity to prevent failure. Thus far, it is unknown to what extent and by what mechanisms these processes are influenced.
Results

Using telemetry we have examined the circadian variation and intermuscular correlation of rabbit jaw muscle activity. Muscle use was assessed as the relative time per hour (duty time) during which predefined levels of the day’s peak EMG were exceeded. The various jaw muscles exhibited a circadian covariant pattern of duty time. The activation of pairs of jaw-closing muscles was more highly correlated than that of pairs consisting of a jaw-closing and a jaw-opening muscle. The mutual dependence of hourly muscle activity increased with the activity level, suggesting that the jaw muscles are more independently controlled during non-powerful than during powerful motor behaviour. In a separate study the daily muscle use of a jaw-closing muscle (masseter) and a jaw opening muscle (digastric) was examined during postnatal development (age 3-8 weeks), during the transition from suckling to chewing. For both muscles, muscle use (i.e. duty times, burst numbers, burst lengths) did not change during postnatal development. This suggests that the amount of jaw muscle activation is already established before chewing develops and remains the same until adult age.

Using microCT we have been able to determine the degree and distribution (DMB) of mineralization in the cortical and trabecular bone of the human mandibular condyle. Within the cortical bone the DMB increased with the distance from the cortical canals to the periphery. Similarly, the DMB of the trabecular bone increased with the distance from the surface of the trabeculae to their cores. This heterogeneity is likely to have an important influence on the mechanical quality (stiffness, strength) of the condyle. This influence was further examined in a finite element analysis of the condyle. It appeared from this analysis that heterogeneity in mineralization increases both the mean stresses and strains in cortical bone. In trabecular bone, however, the mean strains increase whereas the mean stresses decrease. In a separate study it was demonstrated that during mandibular development both architecture, degree and composition of mineralization of bone changes drastically. In a subsequent analysis the mechanical consequences of these changes will be further examined.

Using a combined finite element and rigid body analysis the stresses and strains in the cartilages of the condyle, the glenoid fossa and in the articular disc during jaw movement have been further analysed. The results showed e.g. that during jaw movement the pressure gradient in the disc is heterogeneous. In order to evaluate the effect of overloading and abnormal disc position, finite element models were compared of joints with or without disc displacement. In the symptomatic model, large stresses were observed in the posterior part of the disc and in the retrodiscal tissue, while the stress level kept constant during sustained clenching. It was concluded that in the symptomatic joint the function of the disc as a stress absorber was impaired and that the
retrodiscal tissue was subject to excessive stress. As this structure is less suitable to bear large stresses this might result in tissue damage.

**Academic personnel in 2005 and 2006**

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**Publications in journals indexed in SCI**


Professional publications


Indicators of Esteem

Grants: current projects with external funding


Collaborations

- University of Naples, Department of Orthodontics (dr. M. Farella), Naples, Italy.
- University of Washington, Department of Orthodontics (prof.dr. S.W. Herring), Seattle, USA.
- Kyushu University, Department of Oral and Maxillofacial Radiology (dr. T.K. Goto), Fukuoka, Japan.
- Århus University, Department of Orthopaedics (dr.ir. M. Dalstra), Århus, Denmark.
- Hiroshima University, Department of Orthodontics (dr. E. Tanaka, dr. N. Kawai), Hiroshima, Japan.
- University of British Columbia (prof.dr. A.G. Hannam), Vancouver, Canada.

Current PhD projects


Section: Oral Biochemistry

Protective Functions of Saliva for the Oral Cavity

Program leader
Prof.dr. A. van Nieuw Amerongen
Oral Biochemistry
ACTA
Van der Boechorststraat 7
1081 BT Amsterdam
Tel: +31-20-444 8675
E-mail: A.vanNieuwAmerongen@VUmc.nl

IOT senior scientists

Research objectives

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.

Results

The microbicidal effects of LL-37 and truncated variants were studied against a variety microorganism, including C. albicans, E. coli, P. gingivalis, and S. mutans. Each peptide exhibited a specific spectrum of activity against these microorganisms, which was partly related to a matching in physico-chemical features such as charge and hydrophobicity, between peptide and the target. For a number of truncated LL-37 peptides the membrane effects were studied in C. albicans. Like the parent molecule LL-37, these peptides induced a phase separation in the membrane, leading to a segregation in both the lipid and membrane proteins, and subsequently leakage of series of intracellular proteins.
Perspectives.

In 2006 a new PhD project will start, which is focussed on the mutual interplay between saliva(ry components), epithelial cells and microorganisms, to increase our understanding of the role of salivary components, including antimicrobial peptides, under conditions that resemble more the physiological situation.

Xerostomia, saliva and oral health in relation to systemic diseases

The ongoing longitudinal study on the effects of haemodialysis on salivary parameters and oral health was concluded. The collected data show that in general the oral health of patients on haemodialysis is comparable to control subjects. Only increases in dental calculus, TMJ complaints and bad taste were reported. Haemodialysis patients that received a kidney transplant showed increases in unstimulated saliva secretion and decreases in the level of xerostomia and thirst.

Another systemic disease investigated is Crohn’s Disease, a chronic inflammatory bowel disease. Using a questionnaire, we demonstrated that the incidence of xerostomia and other oral complaints are increased in patients with Crohn’s disease, especially in female patients. Both the level of xerostomia and the number of oral complaints showed significant correlations with intestinal disease activity.

Finally, we developed a method to quantify the concentration of uric acid in saliva of patients with rheumatic diseases. This method will be used to examine the use of saliva as diagnostic fluid for monitoring uric acid levels.

Binding characteristics of salivary agglutinin.

For salivary agglutinin it was demonstrated that for binding of IgA and S. mutans the same sequence on the SRCR domains was responsible. By an alanine scan it was demonstrated that within this peptide other residues were critical compared to bacteria binding. It is now planned to investigate a large number of bacteria for the binding of salivary agglutinin and which residues are critical for binding.

Academic personnel in 2005 and 2006

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Dissertations


Publications in journals indexed in SCI


Other scientific publications (international, refereed)


Professional publications


Patents

Indicators of Esteem
Grants: current projects with external funding

Membership of international editorial boards
Brand, H.S.: J DENT RES
Nieuw Amerongen, A. van: ODONTOLOGY
Nieuw Amerongen, A. van: ORAL BIOSCI MED.

Organization of international congresses or symposia

Invited speakers at international congresses or symposia

Scientific awards/honours

Other international functions
Nieuw Amerongen, A. van: Visiting professor. Dental Schools of Khon Kaen, Bangkok and Chiang Mai.
Collaborations

- Dept. of Periodontology, Katholieke Universiteit Leuven (prof.dr. M. Quirynen).
- Dept. of Medical Microbiology and Infection Prevention, VUMc, Amsterdam (dr. F. Namavar, dr. B.J. Appelmelk, prof.dr. C.M.J.E. Vandenbroucke-Grauls).
- Dept. of Medical Microbiology and Immunology, Universiteit Aarhus.
- Dept. of Biological Psychology, Vrije Universiteit, Amsterdam (dr. E.J.C. de Geus, dr. G. Willemsen).
- EU-Consortium on: Mucins in the pathophysiology of inflammatory diseases of the broncial and gastrointestinal epithelia. (prof.dr. D.M. Swallow and seven individual laboratoria in Europe).
- Universiteit Utrecht, Faculty of Social Sciences, Capaciteitsgroep Health Psychology (prof.dr. L.J.P. van Dooren en dr. J. Roose).
- University of Innsbruck, Austria (prof.dr. B. Redl).
- VU University Medical Center, Medical Chemistry, Amsterdam (dr. B. Overdijk).
- VU University Medical Center, Pathology, Amsterdam (dr. E. Bloemena and prof.dr. R. Schepers).
- Rijksuniversiteit Groningen, Mondheelkunde en Kaakchirurgie (prof.dr. J. Schuitemaker and F. van Engelenburg).
- University of Manchester, School of Biological Sciences, Manchester, United Kingdom (dr. J.K. Sheehan).
- University of Turku, Finland (dr. J. Tenovuo).
- Landbouw Universiteit Wageningen (dr. T. Abee).
- Rijksuniversiteit Groningen, Materia Technica (dr. H.J. Busscher).
- Universiteit Maastricht, dept. of Internal Medicine and dept. of Microbiology (dr. A. van der Ven and dr. E.E. Stoberbering).
- Katholieke Universiteit Nijmegen, Revalidatie (dr. P. Jongerius).
- Universiteit van Amsterdam, Academisch Medisch Centrum dept. of Clinical Chemistry (mw.dr. Y.M.C. Henskens).
- VU University Medical Center, dept. of Nefrologe (prof. dr. P.M. ter Wee).
- Institute of Medical Biology, dept. of Immunology and Microbiology, Odense, Denmark (dr. U. Holmkov).
- Deutsche Krebsforschungszentrum, Division of Molecular Genome Analysis, Heidelberg, Germany (Dr. J. Mollenhauer).
- Göteborg University, dept. of Oral Microbiology, Sweden (dr. A. Almståhl).
- Dept. of Biophysics, Netherlands Cancer Institute, (dr. L.C.J.M. Oomen).
- Dept. of Electronen Microscopie, AMC, Amsterdam (dr. J. van Marle).
- University of Mainz, Medizinische Mikrobiologie und Hygiene, Germany (dr. M. Sapp).
- Institute of Molecular Pathology and Immunology of the University of Porto, IPATIMUP, Porto, Portugal (dr. L. David).
- Unilever Research, Vlaardingen (Dr. H. de Haard).
- University of Jena, dept. of Preventive Dentistry (dr. S. Kneist).
- Prof.dr. B. Berkhout, dept. of Human Retrovirology, Universiteit van Amsterdam.

Current PhD projects


## Appendix

List of SCI journals, their impact factors and the number of ACTA publications in 2005 in each journal

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