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INTRODUCTION

ACTA is the combined Faculty of Dentistry of the University of Amsterdam (UvA) and the VU University Amsterdam. ACTA has a unique position in the Netherlands, being a combined faculty of two universities since 1984. The boards of both the University of Amsterdam and the Vrije Universiteit Amsterdam share the responsibility for the research at ACTA. Research at ACTA is organized in the ACTA Dental Research Institute.

The annual report starts with chapters containing the annual survey of the dean, and overviews of the scientific activities. As in preceding years the scientific performance is subsequently presented for each programme. Detailed information is given of dissertations, scientific publications in refereed journals, other scientific publications, professional publications, indicators of esteem, collaborations and societal impact.

Some issues for 2014 are specifically highlighted in this report. These include the evaluation of the research of ACTA over the years 2007-2013 by an international review committee. In this evaluation the two research programs of ACTA, “Oral Infections and Inflammation” and “Oral Regenerative Medicine” received a very good to excellent rating.

An overview of the output in 2014 is presented in Table 1. We are pleased to note that the output in 2014 was high. The number of publications in refereed scientific journals and the IF-sum have considerably increased during the last years. In 2014 the highest number of scientific publications and a very high impact factor sum was accomplished. In 2014 a total of 13 PhD theses were published and defended.

Research Institute ACTA

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REPORT OF THE DEAN

The Research Institute ACTA

• mission statement

Dental research at ACTA focuses on the study of health and diseases of essentially all tissues of the oral cavity, the masticatory system and of oral fluids. Besides infectious diseases like dental caries, periodontal and periapical inflammatory processes, and inflammatory processes around dental implants, attention is paid to the development, function and regenerative capacities of the hard tissues, pain and dysfunction of the masticatory system, and diseases of salivary glands and oral mucosa. It is the general aim to improve strategies for diagnosis, treatment indication and treatment planning as well as prevention of diseases, functional repair of the affected tissues in and around the oral cavity and evaluation of therapies developed to treat patients. Moreover, we aim to gain insight in the aetiology and pathology as well as the risk factors involved in these diseases. In our attempts to fulfill this mission we aim to establish:
- integration of the clinical sciences with fundamental disciplines
- education and further academic training of post-graduate and PhD-students
- knowledge transfer 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 organizations and industries.

• positioning of the research institute

National position. ACTA comprises the combined Faculties of Dentistry of the University of Amsterdam and the Vrije Universiteit Amsterdam. The ACTA Research Institute is the only institute for research of the faculty.
Research programs. In previous years, ACTA research was organized in 12 research programmes. Following the suggestions of the external review committee in 2008, the research was re-organized in 2009 in 6 programmes. To obtain more focus, starting in 2011 the research was reorganized into the two new research programmes (see below). Next to these two major programmes, some limited other research is performed, which is mainly education-related.

The programme “Oral Infections and Inflammation” (OII) focuses on (i) the aetiology, prevention and therapy of oral infections such as caries, periodontal and endodontic infections, on (ii) oral inflammatory processes, protective functions of saliva, oral cancer and on (iii) the definition of a normal, healthy oral cavity including psychosocial factors.

The programme “Oral Regenerative Medicine” (ORM) focuses on (i) the biological process of adaptation and repair of teeth, bone, mucosa and periodontium, on (ii) the biocompatibility of dental materials, and on (iii) regenerating damaged oral tissue by means of stem cell therapy and/or tissue engineering techniques, taking into account the mechanical threats of the masticatory system. ACTA research on oral regenerative medicine is also included in the interfaculty MOVE Research Institute Amsterdam, a collaboration between the faculty of Behavioural and Movement Sciences, the VU University Medical Centre (VUmc) and ACTA.

• description of output, leading scientific journals in the field

Within both research programmes considerable differences exist in the approaches used; yet, both range from fundamental medical-biological to clinical-applied science. This is reflected by the type of scientific journals in which ACTA researchers publish. Some groups primarily present their findings in journals read in the dental research community, while others also aim for the general medical-biological literature.

Evaluation of the research program

• external evaluation

SEP external evaluation. In 2014 an external evaluation of dental research of ACTA was completed according to the Standard Evaluation Protocol designed by the VSNU. Also on behalf of the Board of the Vrije Universiteit Amsterdam, the Board of the University of Amsterdam has appointed as members of the assessment committee:

Hans Marchen den Boer (Cavex Holland B.V.), Christopher McCulloch (University of Toronto), Jukka Meurman, chair (University of Helsinki), Mutlu Özcan (University of Zürich), William Wade (Queen Mary University of London). Jan Heijn (BetaText, Bergen NH) served as secretary of the assessment committee.

The two research programs of ACTA, “Oral Infections and Inflammation” and “Oral Regenerative Medicine” were evaluated separately with respect to quality of the research, relevance to society and viability.
The committee concluded about the program Oral Infections and Inflammation: “The quality of research in this programme was considered excellent. Many strong publications from the OII group have had a considerable impact in the field of dental research and have influenced opinion development on these topics in the broader scientific community. The relevance of the group’s research to society was considered to be very good. Collectively the future of the programme was considered to be very good.” The committee concluded about the program Oral Regenerative Medicine: “Because of the future trajectory and promise provided in particular by the increased integration of cell biology approaches into scaffold development and prosthodontics/implantology research, the research quality of the ORM programme was considered to be excellent. The ORM programme’s impact on society is considered to be very good. While there are some structural organizational issues that need to be resolved to ensure further integration, research success and ongoing productivity, the group’s viability is considered to be very good.” The committee gave a number of valuable recommendations that will be elaborated in the next years to further strengthen the research at ACTA. For more details about this evaluation we refer to the assessment report of the committee.

Citation analysis. In 2013, the CWTS in Leiden has performed a bibliometric analysis of the ACTA scientific publications over the years 2001-2011. One of the goals of this study was to identify possible benchmarks. These benchmark candidates were investigated in more detail and compared with the performance of ACTA. The conclusions of this study are as follows: “In this study we developed and applied a method to identify benchmark candidates for institutes with a non-mainstream research profile. These benchmarks are used to position the performance of ACTA. The outcome of this study shows an important role of ACTA in terms of output. ACTA has published an impressive amount of papers during the period studied (1,142 papers). Also the amount of number of citations received is very high (4,667) as well as the number of publications in the top 10% most highly cited (P_top10). It should be noted, however, that the latter two are size-depended: the more you publish, the more citations you will receive. If we look at the impact (MNCS and PP_top10, citations per publication normalized by field), ACTA is among the middle group. Still the impact is well above world average (10%).”

Summary of research output and input

<table>
<thead>
<tr>
<th>Table 1. Comparison of research indicators 2002-2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Dissertations</td>
</tr>
<tr>
<td>Refereed publications</td>
</tr>
<tr>
<td>First author from ACTA</td>
</tr>
<tr>
<td>Other scientific publications</td>
</tr>
<tr>
<td>Professional publications</td>
</tr>
<tr>
<td>Publications for general public</td>
</tr>
<tr>
<td>Impact factor sum</td>
</tr>
<tr>
<td>Personnel WP 1</td>
</tr>
<tr>
<td>WP2</td>
</tr>
<tr>
<td>WP3</td>
</tr>
<tr>
<td>Guests</td>
</tr>
<tr>
<td>Total personnel</td>
</tr>
</tbody>
</table>

wp1 = academic personnel funded by 1st source in fte; this includes direct funding by the university
wp2 = academic personnel funded by 2nd source in fte; this includes research grants obtained in national competition from NWO, STW and KNAW
wp3 = academic personnel funded by 3rd source in fte; this includes research contracts for specific projects obtained from external organizations, such as industry, governmental ministries, European Commission and charity organizations
**long time performance**

*Dissertations (PhD theses).* The performance of the research institute over a longer period is shown in Table 1. These data show that the number of dissertations per year has fluctuated between 6 and 18. This reflects variations in external collaborations, such as non-ACTA employees receiving a PhD from our universities and tenure staff members finishing their PhD. In 2014 13 dissertations were accomplished.

*PhD performance.* The percentage of PhD students that finished their thesis averages at 90% over the last 20 years, and the mean time period between start of employment and defending the thesis is 4.6 years. This figure is corrected for the 0.6 to 0.8 fte employment of several PhD students and for long leave of absence (e.g. maternity and illness) of some PhD students.

*Scientific publications.* The main attention in the research assessment at the individual and program level is given to publications in scientific journals with a peer review referee system. This category shows a slightly increasing number over the last 20 years, despite a relatively stable input in fte of scientific personnel. The average quality of the publications has significantly improved over the 20-year period, as judged by the increase of the impact factor sum (Figure 1). In 2014 the highest number of 255 refereed publications and a very high IF sum was obtained.

*Professional publications.* ACTA scientists are very active in communicating their research findings not only to the scientific community, but also to professionals. The number of professional publications in 2014 was 167.

Figure 1. Impact factor sum of ACTA publications, scientific publications in refereed journals, professional publications and total scientific personnel in fte.

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**notable events in 2014**

*Publications in high ranking journals.* Outstanding contributions for the year 2014 are publications in high ranking biomedical journals, i.e. the New England Journal of Medicine (impact factor 54.4), Journal of Experimental Medicine (impact factor 13.9), Biomaterials (impact factor 8.3), and Experimental Microbiology (impact factor 6.2). ACTA scientists also published many papers in the top 10% journals in dentistry, i.e. 24 papers in the 5 journals with the highest impact factor in this field, among which 5 in the Journal of Dental Research, the journal with the highest impact factor in the field.

*Impact factors.* In addition to the output indicators given, the percentage of papers in high impact journals in the field gives valuable information. ACTA published in total 255 scientific papers in refereed journals, of which
211 in journals with an impact factor (SCI journals). 49% of these 211 papers appeared in journals belonging to the field “Dentistry, Oral Surgery and Medicine”. 21% of all publications were in the top 10% of the journals, 51% in the top 25% and 75% in the top 50% (Table 2). This means that, as in previous years, a relatively large number of publications were published in the top journals in the field, both in dental and in non-dental journals.

**Indicators of esteem.** On a personal level a number of ACTA employees rank in the top of the international dental community, as determined by the various indicators of esteem, such as editorships, invited lectures, and congresses organized. In 2014 a total of 12 awards were received by ACTA scientists for their achievements. For more details we refer to the description of the two research programs.

**Grants.** As in previous years ACTA scientists obtained several important grants. An example of a successful grant is the participation of ACTA in the nationally funded and oriented Top Institute Food and Nutrition (TIFN) in 2011, where a new theme “Oral Health” has been initiated. In this theme, world players in the oral care industry, the chewing gum industry, flavour industry, food industry and (oral) care appliances industry collaborate with ACTA and with the Netherlands Organization for Applied Scientific Research (TNO). Another example is the large EU-MUNDUS project: MOVE-AGE, in which ACTA participates. At this moment two ACTA PhD students are funded by this EU-project. In 2013 a large Marie Curie ITN EU project was granted by the EU. This project, named Euroclast, is coordinated by ACTA and involves participation of seven academies and two industrial partners and a total of 11 PhD students.

**Table 2. Percentage of publications in different quartiles of dentistry and non-dental journals in 2014**

<table>
<thead>
<tr>
<th></th>
<th>dentistry journals</th>
<th>non-dental journals</th>
<th>all journals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>numbers</td>
<td>percentage</td>
<td>numbers</td>
</tr>
<tr>
<td>top 10%</td>
<td>26</td>
<td>23%</td>
<td>23</td>
</tr>
<tr>
<td>Quartile 1</td>
<td>59</td>
<td>52%</td>
<td>60</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>24</td>
<td>21%</td>
<td>33</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>23</td>
<td>20%</td>
<td>19</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>8</td>
<td>7%</td>
<td>7</td>
</tr>
<tr>
<td>total</td>
<td>114</td>
<td>100%</td>
<td>119</td>
</tr>
</tbody>
</table>

- **assessment at the program level**

When the research at the program level is considered, both programs perform over the last years in general equally well in terms of parameters like input and output (personnel, PhD students, publications, dissertations etc). In 2014 the OII output of the OII programme was higher than the ORM programme, in particular with respect to professional publications, see Table 3. Other research (OWI), not related to the two programs, is limited both in terms of input (personnel and budget), and of output. Considering the very limited financial input by ACTA, and the substantial grant for research and development for the dental simulator, the research, in particular the education related research, is considered valuable.
Table 3. Summary of the number of publications, impact factor sum and academic personnel in fte

<table>
<thead>
<tr>
<th>Program</th>
<th>Dis</th>
<th>Ref publ</th>
<th>OSP</th>
<th>PP</th>
<th>PGP</th>
<th>IF</th>
<th>wp1</th>
<th>wp2</th>
<th>wp3</th>
<th>wp tot</th>
</tr>
</thead>
<tbody>
<tr>
<td>OII</td>
<td>8</td>
<td>148 (68)</td>
<td>13</td>
<td>140</td>
<td>10</td>
<td>400</td>
<td>20,00</td>
<td>3,35</td>
<td>9,75</td>
<td>33,10</td>
</tr>
<tr>
<td>ORM</td>
<td>5</td>
<td>119 (58)</td>
<td>4</td>
<td>28</td>
<td>3</td>
<td>283</td>
<td>20,65</td>
<td>2,55</td>
<td>9,30</td>
<td>32,50</td>
</tr>
<tr>
<td>OWI</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0,55</td>
</tr>
<tr>
<td>ACTA*</td>
<td>13</td>
<td>255 (211)</td>
<td>9</td>
<td>167</td>
<td>13</td>
<td>656</td>
<td>40,65</td>
<td>5,90</td>
<td>19,60</td>
<td>66,15</td>
</tr>
</tbody>
</table>

This table summarises the number of scientific publications in refereed journals, the number of other scientific publications, and the number of professional publications. Also the personnel involved in full time equivalent (fte) and the impact factor-sum (IF-sum) are included in this table. The IF-sum was calculated for each program by adding together the impact factor values of all 2014 publications.

Dis = number of dissertations
Ref publ = number of scientific papers in refereed journals. Between parentheses is the number of first authors belonging to the program in question
OSP = other scientific publications (international, refereed)
PP = professional publications
PGP = publications for the general public
IF = sum of impact factors as indexed by ISI.
wp1 = academic personnel funded by 1st source in fte
wp2 = academic personnel funded by 2nd source in fte
wp3 = academic personnel funded by 3rd source in fte
wp tot = all academic personnel in fte
OII = Oral Infections and Inflammation
ORM = Oral Regenerative Medicine
OWI = Education Institute and other research
* ACTA = the total number of dissertations and papers reflects the total for ACTA; a dissertation or paper was counted only once; the total impact factor sum is not a summation of the data from each program

Table 4: fte of staff and PhD students (see table 2) by type of position

<table>
<thead>
<tr>
<th>Program</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>OII</td>
<td>13,10</td>
<td>0,70</td>
<td>4,65</td>
<td>6,90</td>
<td>3,45</td>
<td>5,10</td>
<td>33,10</td>
</tr>
<tr>
<td>ORM</td>
<td>14,15</td>
<td>0,65</td>
<td>4,25</td>
<td>6,50</td>
<td>1,50</td>
<td>5,05</td>
<td>32,50</td>
</tr>
<tr>
<td>OWI</td>
<td>-</td>
<td>-</td>
<td>0,20</td>
<td>-</td>
<td>-</td>
<td>0,35</td>
<td>0,55</td>
</tr>
<tr>
<td>Total</td>
<td>27,25</td>
<td>1,35</td>
<td>8,90</td>
<td>13,40</td>
<td>3,55</td>
<td>10,15</td>
<td>66,15</td>
</tr>
</tbody>
</table>

OII = Oral Infections and Inflammation
ORM = Oral Regenerative Medicine
OWI = Education Institute and other Research

Societal impact

- impact on teaching and dental care

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

- **functions in the scientific and professional community**
  ACTA employees take an active role as executives in international scientific organizations (86 international functions), as members of editorial boards of scientific journals (75) and in being leading in ‘wetenschappelijke verenigingen’ of researchers and dental practitioners in the Netherlands. Prof.dr. J.M. ten Cate is appointed as an academy professor at the Royal Academy of Arts and Sciences (KNAW). Furthermore, the societal impact is evident from the organization of symposia and conferences in the Netherlands and abroad, presentations for dentists, medical specialists and patient groups, memberships of advisory councils, and frequent contacts with the industry. In addition many scientists are also practising as dentists in specialized clinics at ACTA or in the Amsterdam region. Obviously the societal impact of their activities, individually as clinically active professionals and leading among their peers, should be acknowledged. The societal impact is also evident from the relatively large number of 167 professional publications. Some ACTA researchers also wrote popularising publications aimed at a more general audience. Several research findings were high lightened in the general press.

- **invited lectures and congresses organized**
  In 2014 ACTA researchers have again contributed actively in internationally held meetings, workshops and symposiums, both as organizers and participants. A total of 136 lectures were given as ‘invited speaker’ at international congresses and symposia. In addition a large number of presentations were given at international congresses after selection on submission of abstracts and during congresses and symposia for a Dutch or international audience. Due to this large number, congress abstracts are not listed in this annual report. A total of 21 international meetings were organized by ACTA scientists.

**Management**

- **finances**
  The overall budget of the research institute is divided into a part controlled directly by the directorate and another part that is allocated to the departments. The institute budget (senso stricto) of k€ 896 is used for the management of the institute, salaries of PhD students, for travel allowances of PhD students, for the organization of courses for PhD students and for printing PhD theses. The research budgets for the departments (in total being k€ 3298) are distributed based on a model containing several parameters, such as external peer review, bibliometric data over the last 5 years, education, PhD theses and external funding. In addition, standard bench fees are issued for PhD students appointed by the research institute. In addition to the university budget (1st source) ACTA scientists were involved in many research projects with external funding. The total amount of research grants (2nd source) was k€ 676, and the total amount of research contracts (3rd source) was k€ 1840.

- **personnel**
  The directorate of the institute comprises:
  
  prof.dr. V. Everts, director of research (till December 2014) 0.40 fte
  prof.dr. A.J. Feilzer, dean and director of research ad interim p.m.
  dr. T.J.M. van Steenbergen, co-ordinator of research 0.55 fte
  mrs. F.M. Meijer, secretary 0.60 fte
  mrs. M.H.G. Piek-Backer, secretary (till April 2014) 0.30 fte
  dr. J.A.M. Korfage, research technician (starting June 2014) 0.15 fte

  The activities of the research institute directorate consist of organizing scientific meetings with presentations of PhD students, the screening of new research projects, the day-to-day interaction with graduate students on practical matters regarding their position, compiling the annual research report, the planning of graduate courses, allocating budgets for research to the departments, controlling the institutes budget and dealing with general correspondence on research issues with UvA, VU etc.
PhD students
The ACTA PhD training program is organized in the ACTA Graduate School of Dentistry (AGSD). As ACTA has no research master training, the AGSD is at the moment limited to the PhD program.

- PhD student appointments
All vacancies for PhD positions have been occupied in 2014. In Figure 2 the number of new PhD students at ACTA is shown in the years 1990 to 2014. Over the years, about 23% of all PhD students had a foreign nationality, about half of them from Europe, the rest from other continents. A mean number of about 9 new PhD students were appointed per year. Due to budget restrictions only 7 new PhD students could be appointed in 2014. About 40% of the PhD students have a dental background (see Table 5). Of all PhD students about 50% is female.

The research institute has started a procedure for allocation new PhD positions for the two main research themes. In 2014 no new PhD students could be appointed on grants awarded to the research themes, but in 2015 a limited number of new PhD students will be appointed.

Figure 2. Numbers of new ACTA PhD students from the Netherlands and other countries

![Graph showing numbers of new ACTA PhD students from the Netherlands and other countries]

Table 5: PhD students by type of undergraduate training

<table>
<thead>
<tr>
<th>program</th>
<th>dentistry</th>
<th>dentistry</th>
<th>biology / chemistry</th>
<th>psychology</th>
<th>medicine</th>
<th>other</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>OII</td>
<td>19</td>
<td>14</td>
<td>6</td>
<td>1</td>
<td>10</td>
<td>11</td>
<td>61</td>
</tr>
<tr>
<td>ORM</td>
<td>17</td>
<td>17</td>
<td>10</td>
<td>-</td>
<td>16</td>
<td>11</td>
<td>71</td>
</tr>
<tr>
<td>OWI</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>31</td>
<td>16</td>
<td>1</td>
<td>26</td>
<td>22</td>
<td>145</td>
</tr>
</tbody>
</table>

OII = Oral Infections and Inflammation
ORM = Oral Regenerative Medicine
OWI = Education Institute and other research
• **PhD Courses**
The following courses are organized for PhD students: “Dentistry for non-dentist PhD students”, “Writing and Presenting in English”, “Methodology and Statistics”, and “Oral Biology”. Dentistry is a multidisciplinary science and the background of the PhD students of ACTA is diverse. Therefore, most PhD students follow external courses on specific research areas, organized by 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 between start of the PhD project and the defence of the thesis within ACTA amounts 4.6 years. This is lower than the mean duration of PhD theses in research schools in the Netherlands being 5.1 years (see the report “Rendement en duur van promoties in de Nederlandse onderzoekscholen”, Oost en Sonneveld, 2004).

![Figure 3. Mean duration of completing the thesis of ACTA PhD students related to the year of entry](image)

Over the last 20 years, about 90 % of all PhD students in ACTA completed their thesis (Figure 4). This high percentage is substantially larger than the mean percentage of 75 % of PhD students who finish their thesis in Dutch research schools according to the report by Oost en Sonneveld mentioned above.

The external review committee evaluated the PhD programme in 2014. They concluded: “Following queries about the infrastructure and core facilities, there was strong and unanimous agreement on the effectiveness of the ACTA programme to provide excellent PhD training. The students indicated that their programmes were well-organized and were well-supported to enable fulfilment of their research goals.”
Points of attention

• HRM and retirement
In the coming years eight full professors who were active in 2013 will retire, thus giving the opportunity to appoint highly qualified researchers with a focus on one of the two programmes. Due to budget restrictions the number of persons involved in research on university budget (1st source) had to be reduced slightly. Fortunately, the fte scientific personnel on grants (in particular 3rd source) increased. Both research priority areas received a substantial grant from the UvA, resulting in an increased 1st fte in 2013 and 2014.

• new building in 2010
Since ACTA moved in 2010 to its building situated at the VU-campus the interaction between scientists from ACTA and those from other faculties that are now close-by, intensified significantly. This has resulted in an extensive collaboration between different research groups. In particular the collaboration with different departments of the VU University medical center (VUmc) has grown considerably.

• PhD training
The duration of the PhD programme is, like elsewhere in The Netherlands, in general 4 years full time. PhD students with an employee status are generally employed for 4 years full time or for 5 years during 4 days a week. PhD students funded by EU grants are appointed for 3 years. Recently, it has been decided that future PhD students funded by ACTA will also be appointed for 3 years.
The research institute has started a procedure for the allocation of new PhD positions for high quality projects which focus at the integration of fundamental and clinical science. This strategy will be continued further, concentrating on the two main research programmes.
According to the PhD regulations of both universities the course programme will be formalized with 30 ECTS points and examinations. The integration between the PhD training programme and the post-graduate clinical training programmes for dental specializations, which is limited now to the courses on statistics and oral biology, will be intensified.

Conclusion
The research at ACTA has always been characterized by a wide range of different topics that covered most dental disciplines. The present policy is to focus on the two specific research areas with an excellent performance.
The analysis of the various parameters of performance shows that the research at ACTA is, despite of budget restrictions, increasingly improving. Future performance will be dependent among others from the success in obtaining 2nd and 3rd source grants.
Oral Infections and Inflammation

Program Leaders
(starting December 2014)

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Full professors

Introduction
Oral Infections and Inflammation
The oral cavity is one of the most infected parts of man. We hardly understand why most people are completely healthy with at least a thousand different species of microorganisms in billions of numbers present...
in the mouth, while other individuals develop oral infectious diseases, chronic inflammatory processes and other pathologies, including oral cancers. The central research theme “Oral Infections and Inflammation” (OII) focuses on the pathophysiology, epidemiology and (psycho)social aspects of oral infections and inflammation and prevention and treatment of those, as well as defining and understanding the health of the mouth as a complex ecosystem, with applications far beyond the mouth alone. The four topics in this program interact with each other and can be depicted in the schematic diagram below.

Research objectives

1) The healthy oral cavity and good systemic health.
Oral health is an essential part of the general health of each person during his or her life. Poor oral health, oral infections and inflammation, oral cancer and other oral pathology, can lead to major health risks and might affect the progression of cardiovascular diseases, diabetes, cancer and cancer dissemination, systemic chronic and acute infections and vital organ failure. Poor oral health leads to a lower quality of life and economic hardship. In collaboration with several Industrial partners, the Netherlands Organization for Applied Scientific Research (TNO) and the Top Institute of Food and Nutrition (TIFN), we work on defining “normal” oral health using a molecular biology approach (-omics). At the same time, we investigate the systemic effects of oral infectious processes in relation to atherosclerotic cardiovascular disease and diabetes, both by literature review and with an intervention trial (focus is mainly on changes in the microbiome and in biomarkers of the named systemic diseases).

2) Innate immunity (cells/saliva), and susceptibility for caries and periodontal diseases.
Studies into the role of saliva and innate immune cells (salivary PMN) in the maintenance of oral health have a prominent place. Several salivary proteins have strong antimicrobial capabilities and have important protease inhibitory actions. Synthetic peptide analogues of salivary histatins are tested as broad spectrum antibiotics. The influence of saliva on the interaction of oral microorganisms with oral epithelial cells and the in vitro wound healing capacities of salivary components are also being investigated. We find PMN in rinsing samples and they have antimicrobial functionality and are thought to have an essential role in maintaining oral health. For periodontal diseases, we collaborate in a self-supported European consortium to identify genetic variations, and we model periodontal disease as a complex system (environmental, lifestyle factors, systemic factors, randomness).

3) Epidemiology and pathophysiology of oral cancer.
Forms of oral cancer, precursor lesions of oral cancer, particularly leukoplakia, and salivary tumours are studied. Amongst others, the prognostic value of molecular markers is examined with regard to the malignant transformation of leukoplakia, and the role of the human papilloma virus (HPV) has been studies. Poor oral health with its concomitant increase in the oral bacterial load, can predispose for oral cancer. Oral infections are independently associated with oral (pre)cancers. Therefore, not only the traditional risk factors smoking and alcohol usage play a role in oral cancer, but also oral bacteria, yeast and virus. Laboratory and clinical studies are ongoing. Intervention in the precursor lesions of oral cancer, particularly leukoplakia, may prevent the development of frank malignancies. Also other odontogenic tumours are studied, with emphasis on
ameloblastomas and keratocystic odontogenic tumours. Characterization is also included of salivary gland tumours at the genomic and protein level.

4) Prevention and therapy of oral infections and inflammation. The knowledge that oral infections may have systemic effects, provides a fundamental basis for new cost-effective prevention programs as well as economic and social spin-off product-innovations in the food and oral care products and dental restorative materials. The dental and medical profession is (re)educated with new knowledge on the fundamentals of normal oral health and the risks of having chronic oral inflammatory processes. The formation, structure and properties of oral and dental biofilms are studied, also in relation to tooth and implant structures. In addition, new antimicrobials and peptides have come into focus as caries and periodontitis preventive agents; emphasis is put on irrigants and ways of application to clean root canal walls from debris and biofilm. Studies into the most effective clinical measures to prevent inflammation of the gingiva and mucosa and to control oral health are being conducted, including substantial efforts to reach clinical standards for evidence based dentistry. Part of successful prevention measures is to improve and to maintain the well-being of both regular dental patients and subgroups of patients suffering from (extreme forms of) anxiety or (anticipated) pain or from physical/mental handicaps.

Within the research theme we also investigate the quality of oral health care. Currently there is limited knowledge on this topic due to the lack of a policy framework and there is limited information about which topics and measures are considered appropriate for evaluation of quality of oral health care and dentistry. To date, limited attempts on documentation of procedures have been made and the available data have a strong focus on disease oriented topics and restoration related procedures. We are setting up collaborations in an European setting to address challenges in patient centered and prevention oriented health care. The researchers within the theme “Oral Infections and Inflammation” have an international prominence in the field of oral health and have acquired a global leadership role in the emerging field of complex ecosystems such as the oral cavity; thus understanding of oral infections, inflammatory processes, oral cancer and the definition of a normal, healthy oral cavity including psychosocial factors. We have been awarded a grant from the University of Amsterdam (UvA) (starting date 1-1-2011) and we demonstrated the multiplier effect (both on the academic as well as the economic aspects) by participating in the Top Institute of Food and Nutrition (TIFN) (contract signed December 2011, first year research in 2012).

Results obtained in 2014

Preclinical studies

• The possibilities for point of care saliva diagnostics has been further expanded. The application of a rapid and simple diagnostic technology (FRET [Fluorescence Resonance Energy Transfer] technology) could enable the medical and dental practitioners to perform a “point of care” test to identify the presence of bacterial pathogen proteases. So far this research line has proven its applicability in the field of oral pathogens, e.g. for *P. gingivalis* and periodontitis. But it appeared that this technology has also potential for applications beyond the oral cavity, resulting in a review on bacterial proteases in general and the potential applications of the FRET technology in, for example, veterinary healthcare for diagnosis of bovine mastitis.

• In the oral cavity, the salivary proteins and peptides are selectively adsorbed to the enamel surface to form a proteinaceous film called the acquired salivary pellicle. This pellicle is composed of peptides and (glycosylated) proteins. Some domains of the salivary pellicle-forming proteins serve as receptors for adherence of colonizing bacteria during dental-biofilm formation. Although in vitro studies with antimicrobial oral care products active on dental biofilm models showed antimicrobial efficacy, they did not completely remove the biofilms. We developed. We used synthetic combinatorial technologies, i.e. peptide phage display, to make a library of new antimicrobial peptides with potential antibiofilm activity. From this library we identified a decapeptide (KKVVFVKFK), named KSL. This patented compound has a broad range microbicidal activity, and also inhibits biofilm development, and is not only applicable in oral preventive care but also for other usage where biofilm formation needs inhibition.

• Saliva is one of the most important factors responsible for maintaining the oral ecological equilibrium. Saliva harbors a large panel of antimicrobial proteins and peptides which directly and indirectly inhibit uncontrolled outgrowth of bacteria. Various antimicrobial peptides were characterized for their antimicrobial- and immunomodulatory activity. In particular, we were one of the first to discover a way to incorporate molecular vehicles into the bacterial cell wall by using bacterial-own enzymes. Furthermore, we were the first to discover the effect of a specific class of antimicrobial peptides i.e. the “extracellular death factors”, to affect bacterial cell size.
Clinical studies

- The cause of salivary stones formation remains unclear. In addition to local factors, such as calcification of a mucus plug and micro-sialoliths produced by the salivary gland itself, several systemic diseases have been
suggested to play a role in the development of salivary stones. However, in a large multicenter case-control study we showed that systemic diseases, use of medication, smoking and use of alcohol do not increase the risk of developing a salivary stone.

- A cross-sectional, observational study was conducted to evaluate inter-individual biochemical variation in unstimulated whole saliva in a population of 266 healthy young adults. Salivary flow rate, protein content, pH, buffering capacity, mucins MUC5B and MUC7, albumin, secretory-IgA, S-cystatin, lactoferrin, chitinase, amylase, proteases and lysozyme were determined. Using spectral clustering, we identified 2 clusters of individuals. One group (8.3% of the subjects) was characterized by having low salivary pH values and high lysozyme activity and MUC7. The large group contained 3 subclusters of subjects, characterized as follows: (i) normal salivary pH, high amylase and lysozyme activity; (ii) normal salivary pH and low salivary flow rate; (iii) high salivary pH, high flow rate and low protein content. However, these 3 sub-clusters were not sufficiently differentiated to allow rigorous statistical comparisons.

- The oral (microbial) ecology of the healthy oral cavity as well as several oral diseases and preventive strategies were studied by combining expert clinical evaluations and next-generation-sequencing microbial profiling techniques. The potential antimicrobial selectivity of an oxygenating mouthwash, Ardox-X® (AX) was determined and the effects of a twice-daily oral AX-rinse on dental plaque composition evaluated. AX showed high inter-species variation in microbial growth inhibition. During a period of 7-days non-brushing but twice daily rinsing, a significant microbial shift in composition was observed. Therefore, AX has the potential for selective inhibition of oral bacteria. In another clinical trial, the 6-week use of a 5,000-ppm fluoride (F) toothpaste on caries-related factors in dental plaque and saliva was studied. The toothpaste increased the interdental fluid F concentration and there was a decrease in lactic acid production rate on the tongue. This was accompanied by changes in interdental biofilm acidogenicity. Also, an increase in the salivary buffer capacity and a reduction of the salivary mutans streptococci were observed. This latter study clearly demonstrated the ability of 5,000-ppm F toothpaste to modify caries-related factors in dental plaque and saliva.

- Human papilloma virus (HPV) induced head and neck squamous cell carcinomas (HNSCC) proved to be different from non HPV induced squamous cell carcinoma with regard to genetics and prognosis.

- P16 was shown to be a good surrogate marker for HPV, but p16 positive, HPV negative tumors occur and have as bad a prognosis as HPV negative tumors.

- In a well-defined cohort of 144 cases, the malignant transformation rate of oral leukoplakia was 1-2% on a yearly basis, independent of the treatment of the leukoplakia.

- Human papilloma virus (HPV) induced head and neck squamous cell carcinomas (HNSCC) proved to be different from non HPV induced squamous cell carcinoma with regard to genetics and prognosis.

- An important line of clinical research has been expanded. Oral inflammation (mucositis) and oral infections have been identified as major side effects of cancer treatments. Oral mucositis severely comprises quality of life, and may induce fevers or even life-threatening sepsis in these patients. We co-authored the evidence-based MASCC/ISOO Clinical Practice Guidelines for the management of mucositis, and two papers proposing new mechanisms (including those associated with oral pathologies) for the pathogenesis and consequences of therapy-induced inflammatory responses in cancer patients.

- The systemic effects of oral infections, in particular periodontitis have been further described in reviews and experimentally evaluated. Periodontitis is epidemiologically associated with atherosclerotic forms of cardiovascular diseases (CVD) and diabetes mellitus. We performed a comprehensive systematic review to ascertain the effects of periodontal intervention studies on CVD biomarkers. Moreover we studied the effects of the treatment of periodontitis in patients already having CVD. It was found that periodontal treatment improves endothelial function of major arteries and reduces biomarkers of atherosclerotic disease, especially C-reactive protein (CRP), and especially in those already suffering from CVD and/or diabetes.

- We evaluated genetic studies in periodontitis and concluded pleitropy for risk genes involved in various inflammatory diseases. Based on this concept we searched for new genetic risk factors for periodontitis by the candidate gene approach based on 47 risk genes of genome-wide significance for RA and SLE. Variants at IRF5 and PRDM1 showed association with periodontitis. Both genes are implicated in beta-interferon signalling and are also genome-wide associated with SLE and inflammatory bowel disease. In addition, we identified a genetic variant within gene SLC23A1, coding for a vitamin C transporter protein, further implicating a role for vitamin C in the pathogenesis of periodontitis.

- We explored mathematical modeling to predict the diagnosis of periodontitis by applying artificial neural networks trained by immunologic parameters. ANNs can be employed for accurate diagnosis of aggressive
periodontitis or chronic periodontitis by using relatively simple and conveniently obtained parameters, like leukocyte counts in peripheral blood.

- In a narrative review article frequently encountered oral complications were presented, being associated with hematopoietic stem cell recipients focusing on the inflammatory pathways and inflammatory mediators involved in their pathogenesis.
- In the project family matters it turned out that family functioning and nurturing strategies were significantly related to the caries prevalence in 5- to 8-year-old children. These findings open new strategies in dental health education.
- Deciduous Molar Hypomineralization (DMH) is a developmental disturbance in primary teeth. Possible determinants of DMH were studied in a prospective cohort study among 6-year-old children. Dutch ethnicity, low birth weight, alcohol consumption by the mother during pregnancy and any fever in the first year of the child's life are associated with DMH.
- In a randomized clinical trial pit and fissure sealants were compared to partial excavation and restorative treatment in primary teeth in arresting dentinal caries lesions. The latter treatment group showed significantly better clinical survival after 18 months. In both groups no caries progression was observed.
- Various preventive measures against gingival inflammation were evaluated by gathering the scientific evidence in the manner of systematic reviews. A summary of case reports showed that manual toothbrushes can be associated with serious accidents. The efficacy of powered toothbrushes in plaque removal was found to be on average 46%. Chlorhexidine dentifrices/gels were found to be more effective than regular dentifrices, however compared to chlorhexidine mouthwashes they are less effective. For the comparison of dentifrices containing triclosan and stannous fluoride inconclusive evidence was found and most likely the minor differences were clinically insignificant. An essential oils mouthrinse was found to be more effective than its placebo.
- Several clinical studies were performed. With respect to treatment of periodontal disease a diode laser did not improve the effect of non-surgical periodontal therapy. Further, the effect of ultrasonic scalers on temperature changes inside the tooth were evaluated; the results show that care should be taken that the cooling water has room temperature and that, dependent on the scaler system, the proper amount of water is supplied.
- For the cleaning of implant surfaces the air polisher was found to provide the best potential with respect to titanium surface changes, cleaning efficacy and biocompatibility. The latter results were also the basis for a clinical practice guideline which was developed in conjunction with the Dutch Society for Periodontology and the Dutch Society for Oral Implantology.
- A 6-month trial showed that a cetylpyridinium chloride mouthwash was significantly more effective in reducing plaque scores than the vehicle control. However this was not substantiated in gingival inflammation score. A 3-week trial evaluated the effect of sugar-free chewing gum sweetened with xylitol or maltitol. In circumstances where regular brushing is performed, no effect of chewing gum was observed on bleeding and plaque scores. Based on systematic literature analyses, evidence emerged for the use of chewing gum containing chlorhexidine. Also, meta-analyses and individual results indicate a beneficial effect of chlorhexidine-gum on plaque inhibition, however, the level of evidence to recommend the use a chlorhexidine gum is considered weak.
- Patient centered outcomes to dental treatment have been studied using the Oral Health Impact Profile NL version; the quality of life for edentulous persons wearing prostheses was assessed. Also, the quantitative and qualitative variations in levels of care for patients with cancer of the head and neck were analysed retrospectively using international and national databases.
## Academic personnel in 2014 and 2015

### Research staff ACTA – OII (Oral Infections and Inflammation) (in full time equivalents)

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Dissertations


Metska, M.E. (2014, March 04). Diagnosis and decision making in endodontics with the use of cone beam computed tomography. Universiteit van Amsterdam (149 pag.). Prom./coprom.: prof.dr. P.R. Wesselink & dr. A.R. Ozok.


Scientific publications (refereed)


Hoogenkamp, M.A. & ten Cate, J.M. (2014). Determination of arginine catabolism by salivary pellet. MethodsX, 1, 1-5. doi: 10.1016/j.mex.2014.01.001


Slot, D.E. & van der Weijden, F. (2014). Insufficient evidence to determine the effects of routine scale and polish treatments. Evidence-Based Dentistry, 15 (3), 74-75. doi: 10.1038/sj.sbd.6401039


Scientific publications (non-refereed)


**Professional Publications**


36


Publications for the general public

Grants: current projects with external funding
Ten Cate, J.M., Crielaard, W., de Soet, J.J., van Loveren, C., van der Veen, M.H. & Volgenant, C.M.C. (2014). Seeing is believing. STW project; granted € 500.000: (2010, October 01 - 2016, October 01).


Indicators of Esteem

Editorship book


Memberships editorial board
Aartman, I.H.A.: European Journal of Dental Education.
Bloemena, E.: ISRN Gastroenterology.
Brand, H.S.: Nederlands Tijdschrift voor Tandheelkunde.
Crielaard, W.: Microbiology - SGM.
Gorter, R.C.: European Journal of Dental Education.
Raber-Durlacher, J.E.: Mediterranean Oncology Journal.
Scientific awards/honours

Organization of (inter)national congresses and symposia
Krom, B.P. (2014). Organizer. Fall-symposium Royal Dutch Society for Microbiology, Section General and Molecular Microbiology: Artis, Amsterdam, the Netherlands (2014, October 31).

Invited speakers at (inter)national scientific congresses or symposia
Research on Medical Countermeasures Against Biological Agents. NATO Science and Technology Organization.


**Boutsioukis, C.** (2014, January 08). Root canal irrigation, Part II: irrigants. Thessaloniki, Greece, Postgraduate program, Department of endodontontology, Dental School, Aristotle University.


**Crielard, W. & de Jager, M.** (2014, April 01). The oral health theme. Amsterdam, the Netherlands, Amsterdam Life Science Café.


**De Jongh, A.** (2014, June 06). Een "Spotlight mind": Fictie of realiteit? Deventer, the Netherlands, KOP scientific meeting.


**Krom, B.P.** (2014, May 13). Wound ecology. MECC Maastricht, the Netherlands, 11th VEC.

**Krom, B.P.** (2014, May 22). *Candida* and other fungi, forgotten players in the oral ecology. Aarhus, Denmark, 11th EOMW.


**Loos, B.G.** (2014, May 23). Systemic benefits of periodontal therapy. Periodontal therapy is especially beneficial for the patient with cardio-vascular disease (CVD) and the patient with diabetes: The dentist and oral hygienist play an important role. Valladolid, Spain, Spanish Society of Periodontontology (SEPA).

**Loos, B.G.** (2014, September 10). Periodontitis is a complex disease and is linked with cardiovascular diseases (CVD) and diabetes. Dubrovnik, Croatia, IADR/PER.

**Loos, B.G.** (2014, October 03). Genetics and inflammation, the periodontal-genetic connection. Elsinore, Denmark, Danish Society of Periodontology.


**Raber-Durlacher, J.E.** (2014, May 05). The importance of excellent supportive care for treatment compliance and effectiveness. Milaan, Italy, Consensus Conference of Supportive Care in concurrent chemo-radiation treatment of head and neck cancer; Fondazione IRCCS ISTUTUTO NAZIONALE DEI TUMORI.

**Raber-Durlacher, J.E.** (2014, June 02). The importance of multiprofessional and international cooperation. Okayama University, Japan, National Conference Division of Hospital Dentistry, Oral Supportive Care in Cancer.


Ten Cate, J.M. (2014, March 03). Mondgezondheid. Amsterdam, the Netherlands, Amsterdamlzeizing, Universiteit van Amsterdam.


Ten Cate, J.M. (2014, June 06). New approaches, what is there beyond fluoride? Gdansk, Poland, European Academy for Pediatric Dentistry.


Ten Cate, J.M. (2014, September 16). Biofilms, more than just a different name for dental plaque. Ann Arbor, Dental School, Michigan University.

Ten Cate, J.M. (2014, October 23). Capita selecta in biofilm research. Chengdu, China, West China School of Stomatology.


Zaura, E. (2014, October 31). Acquiring and establishing a healthy oral microbiome. Amsterdam, the Netherlands, KNVM-Section General and Molecular Microbiology.

Other (inter)national scientific functions

Crielaard, W.: Visiting professor - Oral Microbiology School of Stomatology, Sun Yat Sen University, Guangzhou, China.

Crielaard, W.: Visiting professor - Oral BioSciences, Hong Kong University, Hong Kong, China.

De Jongh, A.: Member scientific committee - EMDR Europe Association.
De Jongh, A.: Honorary Professor - School of Health Sciences. Salford University, Manchester, United Kingdom.


De Soet, J.J.: Treasurer - Stichting Orale Biologie.

Gorter, R.C.: Executive board member - Association for Dental Education in Europe (ADEE), since 2013.

Gorter, R.C.: Member - Platform for better oral health in Europe.

Loos, B.G.: Board member - International Association for Dental Research (IADR), Continental European Division (CED).

Loos, B.G.: Invited expert - Xith European workshop in Periodontology: Effective prevention of periodontal and peri-implant diseases. EFP (European Federation of Periodontology) and AAP (American Academy of Periodontology), La Granja (Segovia), Spain, November 9-12.

Loos, B.G.: Member scientific planning committee - International Association for Dental Research-Pan European Region (IADR-PER) congress, September 10-13, Dubrovnik, Croatia.

Raber-Durlacher, J.E.: External assessor promotion committee - Promotion Dr. Farah Mougeot Research Group Director Carolinas Health Care System. Charlotte, USA.

Raber-Durlacher, J.E.: External member promotion committee - Dr. Rachel Gibson to Associate Professor level D, University of Adelaide, Australia.

Raber-Durlacher, J.E.: External member - European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Group Brussel.

Raber-Durlacher, J.E.: Member board of directors - Multinational Association Supportive Care Cancer MASCC/ISOO; Mucositis Study Group Chair Cytokines and Growth Factor Section.

Shemesh, H.: Member scientific committee Dutch Society of Endodontology (NVvE).


Slot, D.E.: Member congress committee - Nederlandse Vereniging voor Parodontologen (NVvP).


Slot, D.E.: Workshop initiator contributor - Russian Dental meeting for dental hygienists, Moscow, Russia.

Ten Cate, J.M.: Member Accreditatie van het onderwijs van de opleiding, October 21-24 - West China School of Stomatology, Chengdu, China.


Van der Veen, M.H.: Honorary lecturer - University of Liverpool, UK.

Van der Veen, M.H.: Immediate past president - Diagnostic Sciences Group, International Association for Dental Research (IADR).

Van der Waal, I.: Secretary general - European Organization for Caries Research (ORCA).

Van der Weijden, G.A.: Member scientific committee STOMA.

Van der Weijden, G.A.: Chairman commissie richtlijn Peri-Implantitis - NVOI/NVvP.


Van der Weijden, G.A.: Member - Benoemingscommissie KIMO.

Van der Weijden, G.A.: Member stuurgroep 2, kamer mondzorg - NMT & ACTA.


Van Diermen, D.E.: Board member - Dutch Dental Society.

Van Loveren, C.: Member advisory board - Sugar Bureau UK.
Van Loveren, C.: Member advisory board - Tooth Friendly Society.
Wesselink, P.R.: Chairman - Task force Prevention of mouth injuries in field hockey for the Royal Netherlands field hockey association (KNHB).

Supervisor of an external PhD student

Societal impact
Oral infections and oral cancer have a substantial impact on the society. Oral infectious diseases are the most frequent infections in the western society and have important consequences, both medically and economically. Head and neck squamous cell carcinomas (HNSCC) and specifically oral squamous cell carcinomas (OSCC) are the most prevalent forms of head and neck cancer. The general aim of the program is to understand the normal healthy oral cavity and to understand links with general health, to study oral innate immunity and susceptibility to caries and periodontal diseases, to study prevention and treatment options for the oral infectious and inflammatory processes and to study the epidemiology and pathogenesis of oral cancers, in particular in relation to good/poor oral health. In addition, attention is paid to social and psychological aspects of dental treatment, such as dental anxiety.
Through education, a new generation of dentists and researchers in the Netherlands, Europe and the world are trained to implement a radical shift from mechanistically and (invasive) treatment oriented professionals to 21st century oral physicians focused on diagnosis and prevention of dental and of oral infections and maintenance of the quality of life. Over the last 5 years it has become increasingly clear that oral infections are having negative impact on cardiovascular health, diabetic status and quality of life. The researchers in this theme focus on this aspect.
The members of our priority area have had a relative large number of invitations to give lectures at dental congresses, and to educate the dental profession on fundamental understanding of oral health. Moreover, we experienced increased interest from newspapers, magazines and radio programs on the above subjects, in which we participated. The link oral health - general health is actively communicated by the researchers. Notably, the Dutch Dental Association has announced this link as their anniversary theme for 2014.
Important for the dental profession and the general public, is the substantial number of published and accessible systematic reviews (and meta-analyses) on the various modes of prevention and oral hygiene measures. These contribute to clinical protocols for the dental profession and form the basis for evidence based dentistry.
Ongoing clinical research on oral and head/neck cancer contributes to improved prevention, diagnosis and treatment of relevant patient groups. New plans are developed to bring together knowledge on oral microbiomes and salivary innate immune peptides with oral cancer diagnosis and pathophysiology.
The program has strong links with all players in the oral care industry; this not only results in “contract research”, but also in industrial co-funding of grants (STW) and has led to participation of ACTA in the Top Institute Food and Nutrition (TIFN), where the theme “Oral Health” has been initiated. In this theme, world players in the oral care industry, the chewing gum industry, flavour industry, food industry and (oral) care appliances industry collaborate with the University of Wageningen, TNO and ACTA. The societal impact of the research is evident from the impact on patient care and public dental health, and from collaborations with the industry, as is shown by for instance the grants obtained and the external reports. The societal impact of the clinical research contributes to improved prevention, diagnosis and treatment of relevant patient groups. The societal impact is evident from the items listed below.

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

Several collaborations exist with the industry, evident from grants obtained over the years; see the list of current grants in the paragraph of indicators of esteem above.

- **Crielaard, W.** As part of TIFN interactions with Wrigley, GSK, Philips Research & Cargill.
- **Krom, B.P.** Brandwondencentrum, Beverwijk, Isala Klinieken, Zwolle, Lallemand Health Solutions, Canada.
- **Van Strijp, A.J.P. & Lagerweij, M.D.** 3M ESPE, Seefeld.

**Interactions with the general public**


**Impact of the research on professionals**

Patients are referred by their dentists to the various specialized clinics of the clinicians participating in the program for diagnosis and treatment based on the latest scientific evidence. Several scientists of the program had interviews in Dutch dental Journals. A total of 167 professional publications were written.


Organization of congresses and symposia for (health care) professionals


Wesselink, P.R. (2014). Organizer. Leergang (Master class) endodontology for ACTA Dental education BV.

Invited speakers at professional congresses or symposia


De Jongh, A. (2014, June 06). De revanche van het systeemdenken. Utrecht, the Netherlands, Congres Sociale psychiatrie.


Krom, B.P. (2014, October 07). Ecologie van de wond. Haarlem, the Netherlands, NOVW/NTVW 9de Nationaal multidisciplinair congres voor wondprofessionals.


Loos, B.G. (2014, May 16). Een gezonde mond is goed voor de cardio-vasculaire patiënt en voor de diabeet: de tandarts heeft hierin een rol. Amsterdam, the Netherlands, NMT Jubileumcongres.


Other professional functions

**Bruers, J.J.M.**
- Adviseur - Commissie Onderzoeksbegeleiding (COB), KNMT.
- Secretaris - Nederlandse Vereniging voor de studie van Sociale Tandheelkunde (NVSSST).

**Danser, M.M.**
- Chairman - Dutch Society of Periodontology (NVvP).
- Board member - Bestuur Vereniging EMDR Nederland.

**De Jongh, A.**
- Lid Kamer GZ-psycholoog (vertegenwoordiger voor het Nederlands Instituut van Psychologen, NIP).
- Lid klankbordcommissie - Screening en Diagnostiek van psychische problematiek bij volwassen in relatie tot Vroegkinderlijke Chronische Traumatisering in de Geestelijke Gezondheidszorg (GGZ) en in de medische (huisartsen)- verpleegkundige- en agogische (GGZ) pr.
- Lid werkgroep accreditatie psychotraumatherapeut - Nederlandstalige Vereniging voor Psychotrauma (NtVP).
- Chair - Consilium Chirurgicum Oris.
- Chair IT-advisory Committee (Data analysis) - International Association of Oral and Maxillofacial Surgery (IAOMS).
- Chair commissie - Landelijke richtlijn Antibioticaprofylaxe bij tandheelkundige ingrepen bij patiënten met een gewrichtsprothese NOV.

**Raber-Durlacher, J.E.**
- Lid expert group - Nederlandse Vereniging van Tandartsen. Landelijke richtlijn orale mucositis bij patiënten met kanker 2014 V&VN en IKNL.

**Rozema, F.R.**
- Chair - Consilium Chirurgicum Oris.
- Chair IT-advisory Committee (Data analysis) - International Association of Oral and Maxillofacial Surgery (IAOMS).
- Chair commissie - Landelijke richtlijn Antibioticaprofylaxe bij tandheelkundige ingrepen bij patiënten met een gewrichtsprothese NOV.

**Slot, D.E.**
- Chair accreditation committee bachelor mondzorg, 2 nieuw te starten opleidingen - NVAO.
- Initiator contributor - Workshop European Federation of Periodontology (EFP), 9-12 November, Segovia, Spain.
- Member lustrum commissie 2016 - Nederlandse Vereniging voor Parodontologie (NVvP).

**Van der Heijden, G.J.M.G.**
- Member Epidemiology Educational Programs Audit Committee - Netherlands Epidemiology Society.

**Van der Waal, I.**
- External evaluator - School of Health Sciences, School of Health, Athens, Greece.

**Van der Weijden, G.A.**
- Member Epidemiology Educational Programs Audit Committee - Netherlands Epidemiology Society.

**Van der Weijden, G.A.**
- Chairman commissie richtlijn parodontale behandeling in de algemene praktijk - Nederlandse Vereniging voor Parodontologie (NVvP).

**Van Diermen, D.E.**
- Member Regio-overleg - ASK Antistolling, regio Amsterdam.

**Van Houtem, C.M.H.H.**
- Vice voorzitter - VBTGG.

**Van Loveren, C.**
- Chairman scientific advisory board - Preventive Dentistry and Oral Diseases, Ivoren Kruis.

**Van Wijk, A.J.**
- Board member - Dutch Pain Society.

Courses organized for dental and medical professionals

Scientists of the program participated in courses in the Netherlands for dentists and oral hygienists. More than 20 courses were given in the Netherlands for dentists, medical specialists and oral hygienists by the following scientists:
Lectures given during courses for dental and medical professionals in the Netherlands

A large number of lectures were given during courses for dentists, medical specialists and oral hygienists in the Netherlands by the following scientists:

Aartman, I.H.A.:

Baart, J.A.:
- Infectieleeer, lokale anesthesie en gebitsextractie voor tropenartsen, VUmc, 13-03-2014

Brand, H.S.:
- Sikkelscelanemie. Stichting Jeugdtandverzorging Amsterdam. 23 May 2014
- Acute immunologische reacties in de tandheelkundige praktijk. PAOT-cursus Acute Medische Situaties in de tandheelkunde. ACTA Dental Education BV. 6 June 2014

Crielard W.:
- The Future of Microbiology, Mondhygiënisten Noord Oost Nederland Groningen, the Netherlands, 20 September 2014.

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Crielard W.:
- The Future of Microbiology, Mondhygiënisten Noord Oost Nederland Groningen, the Netherlands, 20 September 2014.
Eijkman, M.A.J.:

Rozena, F.R.:
- Update rondom tandheelkundig en medisch handelen, Quality Practice, Utrecht, 2 en 6 June 2014.
  Medische anamnese en implicaties voor het handelen in de mondzorg, Quality Practice, Amsterdam, 8 November 2014.

Teeuw, W.J.:
- Parodontitis en diabetes mellitus, Quallity Practice Mondhygiënisten, ACTA, Amsterdam, the Netherlands, November 8, 2014.
- The periodontal clinic as a location for diabetes screening Perio-workshop ACTA, Amsterdam, the Netherlands, October 23, 2014.
- Het gewicht telt ook mee! Verwijzersavond afdeling Parodontologie, ACTA, Amsterdam, the Netherlands, October 1, 2014.
- Parodontitis en algemene gezondheid. Hart- en vaatziekten en Diabetes mellitus PPI Hoorn, the Netherlands, September 17, 2014.
- Het paro-protocol Glimlach! Tandzorg, Gouda, the Netherlands, September 1, 2014.
- Een zwaarwegend probleem? Mondgezondheid en overgewicht, Quality Practice Tandartsen, ACTA, Amsterdam, the Netherlands, June 21 & 28, 2014.
- Heeft parodontitis invloed op de algemene gezondheid van de mens? Dentamed Haaglanden, Den Haag, the Netherlands, May 27, 2014.
- Microbiologie. Als het beestje maar een naam heeft. Seminar NVM, Breukelen, the Netherlands, April 14, 2014.

Ten Cate, J.M.:

Van der Heijden, G.J.M.G.:
- (2014, March 29). Toepassing van richtlijnen. Amsterdam, the Netherlands, ADE.

Van der Waal, I.:
- Mondzakten en Kaakchirurgie bij kinderen; een cursus voor orthodontisten, tandartsen en kindertandartsen. ACTA Dental Education. Amsterdam, 11 April 2014.
- Mondpathologie; een cursus voor parodontologen. Organisatie NVVP. Driebergen, 7 November 2014.

Van der Weijden, G.A.:
- Nazorg van Implantaten, NVOI, Putten, the Netherlands, December 12, 2014
- Nazorg van Implantaten & Air Polisher, Utrecht, the Netherlands, November 20, 2014
- Workshop Air Polisher, Rotterdam, the Netherlands, October 28, 2014
- Workshop Air Polisher, Utrecht, the Netherlands, April 14, 2014

Van Diermen, D.E.:
- De medisch spannende patient. Voordracht op symposium “De medisch spannende patient” voor tandartsen en mondfhygiënisten, Benecke, Amsterdam 18 March 2014
- Richtlijn antistolling. wordshop bij Quality Practice dag voor tandartsen op 29 March en 4 April 2014
- De medische anamnese en de consequenties voor de tandarts, Voordracht Tandartsenkring Zuid-Oost Drenthe, 21 November 2014, Emmen
- Medische anamnese en antistolling. Voordracht bij Masterclass Implantologie, ADE, 26 November 2014, ACTA
- Medische interactie en medicatie. Voordracht en 3 workshops Quality Practice Assistenten. 12 December 2014, Utrecht
- Medische aspecten van de Lachgas. PAOT Lachgascursus. Amsterdam, 3 September 2014
- De medische anamnese. Preventietour. Lezingen voor tandart-assistenten via KNMT op 8 oktober (Schiphol), 3 November 2014 (Nieuwegein)

Van Loveren, C.:

Van Strijp A.J.P.:

Van Wijk, A.J.:
- Het beoordelen van richtlijnen. 4 April 2014, ADE, Utrecht, the Netherlands.
- Psychologie van pijn. 13 June 2014, Endo leergang dag, ACTA, Amsterdam, the Netherlands.

Wesselink, P.R. :
- at least 10 lectures during 2014.

Zaura, E.:
- (2014, 17 May). Quality Practice day “Ongelijke behandeling; de tandheelkundige zorg van de toekomst?” for dentists, ACTA, Amsterdam, lecture entitled: ‘Cariologie en erfelijkheid’.

Inaugural lectures


Collaborations

- Ben Gurion University of the Negev, Beer Sheva, Israel, Dr. M. Meijler
- Brandwondencentrum Beverwijk, Dr. B. Boekema, Brandwonden project.
- Cairo University, Egypt, Oral Medicine and Periodontology Department, Faculty of Dentistry, Clinic for Carolinas Health Care System Charlotte, North Carolina, USA Professor Michael Brennan
- Centre for Integrative Bioinformatics (IBIVU), VU Amsterdam, Prof. J. Heringa, Dr. S. Abeln.
- Center for Zoonotic Diseases, University of Bern, Switzerland, Dr. S. Rodriguez Campos.
- Christof Doerfer,
- Clinic for Conservative Dentistry and Periodontology, Uniklinikum Schleswig-Holstein-Campus Kiel-Germany
- College of Dentistry, New York University, USA, Richard Niederman
- Common Wealth University, Virginia, Prof.dr. H.A. Schenkein
- Conservative Dentistry and Periodontology, Uniklinikum Schleswig-Holstein-Campus, Kiel, Germany, Karim M. Fawzy El-Sayed
- Department of Conservative Dentistry, University of Groningen, NL.
- Department of Endodontology, Universidad DeLaSalle Bajo, Leon, Mexico
- Department of Periodontics, School of Dentistry, University of Missouri-Kansas City, USA, Charles Cobb
- Department of Periodontology, University Federico II, Naples, Italy, Andrea Blasi
- Diderot University, Paris, France
- D. Duijster, Research Fellow, Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ), Eschborn, Germany
- Dr. Alex Mira, Center for Advanced Research in Public Health, Valencia, Spain.
- Dr. Joost Teixeira de Matos, Swammerdam Institute for Life Sciences, UvA.
- Dr. Wilfred Röling, Molecular Cell Physiology, FALW, VU.
- Erasmus medisch Centrum, Dr. M. van Zelm
- Dr. Y. Iijima. University of Nagasaki, Japan.
- Department of Periodontology, University Federico II, Naples, Italy, Andrea Blasi
- Diderot University, Paris, France
- D. Duijster, Research Fellow, Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ), Eschborn, Germany
- Dr. Alex Mira, Center for Advanced Research in Public Health, Valencia, Spain.
- Erasmus medisch Centrum, Dr. M. van Zelm
- F. van Lenthe, Associate Professor of Social Epidemiology, Department of Public Health, Erasmus MC, University Medical Center Rotterdam, the Netherlands
- H. Whelton, Professor of Dental Public Health and Preventive Dentistry, Dean School of Dentistry, University of Leeds, Leeds, United Kingdom
- Health Science Research Center, Indiana University-Purdue University, Fort Wayne, IN, USA, Mark Putt
- Indiana University-Purdue University, Fort Wayne, IN, USA, Health Science Research Center, Mark Putt
- Interleukin Genetics, USA: Prof. dr. K. Kornman
- Isala Klinieken Zwolle, Algemene Chirurgie, Dr J. Oskam.
- J. Mackenbach, Professor of Public Health, Chair of Department of Public Health, Erasmus MC, University Medical Center Rotterdam, the Netherlands
- King’s college, London, UK
- LUMC, Dorine Bresters. Late effecten na oncologische behandeling en stamceltransplantatie op kinderleeftijd.
- Max Planck Institute, Berlin, Germany
- M. Bots, Professor of Cardiovascular Epidemiology, Department of Epidemiology, Julyus Center, University Medical Center Utrecht, Utrecht, the Netherlands
- Oral Diagnostic Sciences University of Adelaide, Adelaide Australia Professor Richard Logan
- Oral Medicine and Periodontology Department- Faculty of Dentistry- Cairo University- Egypt, Clinic for Conservative Dentistry and Periodontology, Uniklinikum Schleswig-Holstein-Campus Kiel-Germany Karim M. Fawzy El-Sayed
- Physics of Fluids, University of Twente, NL.
- Prof. Li J, Dr. Cheng L, West China School of Stomatology, Sichuan University, China
- Prof.dr. C. van Loveren, member advisory board of sugar bureau; member of advisory board tooth friendly society.
- Radboud University Medical Center Prof. dr Nicole Blijlevens
- Radboud University Medical Center Prof. dr. W.H. van Palenstein Helderman
- Regional Center for Biomedical Research, Albacete Science & Technology Park, University of Castilla-La Mancha, Albacete, Spanje, Dr. P.W.J. de Groot.
- Saveetha University, Chennai, India
- S. Listl, Associate Professor, Translational Health Economics, Dental School, Heidelberg University, Heidelberg, Germany
- Tel Aviv University, Tel Aviv, Israel
- Tigran, Malmö, Sweden, U. Lundgren
- TNO, Zeist, Dr. E. Tsivtsivadze
- UMCG Groningen, Dr. L.U. Lahoda
- Uniklinikum Schleswig-Holstein-Campus, Kiel, Germany, Clinic for Conservative Dentistry and Periodontology, Christof Doerfer
- Unit of Periodontology University of Milan, Milan, Italy, Giulio Rasperini
- Universiteit van Amsterdam, AMC, Dept. of Clinical Chemistry
- Universiteit van Groningen, Dept. of Periodontology
- University of Bandung, Indonesia, Amaliya
- University of Bonn, Dept. of Periodontology, Prof.dr. S. Jepsen
- University of Cagliari, Italy
- University of Gothenburg Sweden Professor Inger von Bültzingslöwen
- University of Kiel, Germany, Dept. of Gastro-Enterology, Prof.dr. S. Schreiber
- University of Kiel, Germany, Institute for Clinical Molecular Biology, Dr. A. Scheafer
- University of Kristianstad, Sweden, Prof. dr. S. Renvert
- University of Madrid, Spain, Prof. dr. M. Sanz
- University of Malaya, Malaysia, Faculty of Dentistry, Dr. Rathna Devi Vaithilingam
- University of Maryland Dental School, Baltimore, USA, Dr. M.A. Jabra-Rizk.
- University of Milan, Italy, Unit of Periodontology, Giulio Rasperini
- University of Missouri-Kansas City, USA, Dept. of Periodontics, School of Dentistry, Charles Cobb
- University of Patras, Greece, Prof.dr. T. Bountis
- University of Rome, Italy, Prof. dr. Pilloni
- Van Minnen, A. Radboud University Nijmegen Behavioral Science Institute, NijCare, the Netherlands, Nijmegen (Van Minnen): Mental Health Organization “Pro Persona,” Center for Anxiety Disorders Overwaal, Nijmegen, the Netherlands
- Van der Gaag. Department of Clinical Psychology, VU University Amsterdam and EMGO+ Institute for
Current PhD projects


Oral Regenerative Medicine

Program Leaders
(starting December 2014)

Prof.dr. D. Wismeijer
Department of Oral Implantology and
Prosthodontics
ACTA Gustav Mahlerlaan 3004
1081 LA Amsterdam
Tel: +31-20-5980297
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Dr. C.J. Kleverlaan
Department of Dental Materials Sciences
ACTA Gustav Mahlerlaan 3004
1081 LA Amsterdam
Tel: +31-20-5980882
E mail: c.kleverlaan@acta.nl

Full professors

A.G. Becking  C.M. ten Bruggenkate  V. Everts  A.J. Feilzer  T. Forouzanfar

S. Gibbs  J. Klein-Nulend  J. de Lange  F. Lobbezoo  F.J.M. Roeters

E.A.J.M. Schulten  P.F. van der Stelt  D.B. Tuinzing

Introduction
The human masticatory system has several important functions that determine an individual’s general health and well-being, like biting, chewing, swallowing, talking, laughing, and yawning. Sometimes, patients are
confronted with problems in performing these functions. This may have various causes. On the one hand, chemical and bacteriological factors may hamper a healthy functioning of the masticatory system by causing infection and inflammation. On the other hand, mechanical overloading as well as underloading or disuse of the constituent structures of the masticatory system (viz., teeth, bone, cartilage, muscles, and joints) may yield functional oromandibular impairments. Importantly, trauma or disease may result in damaged tissues which in turn result in functional oromandibular impairments. The research of ACTA's research program “Oral Regenerative Medicine” (ORM) focuses on regenerating damaged oral tissue by means of stem cell therapy or tissue engineering techniques, taking into account the mechanical threats for the masticatory system and inflammatory reactions involved in tissue repair. Relevant clinical problems are used to guide the research aimed at developing novel solutions for these clinical problems. Groups that are involved in ORM-ACTA are Oral Kinesiology (OKI), Oral Implantology and Prosthodontics (IMP), Dental Materials Sciences (DMS), Oral Cell Biology and Functional Anatomy (OCB/FA), Oral Radiology (ORA), Orthodontics (ORT), and Oral and Maxillofacial Surgery (OMS), both of the Academic Medical Center (AMC) and of the VU Medical Center (VUmc).

The Interfaculty MOVE Research Institute Amsterdam has chosen “Regenerative Medicine” as one of its domains (i.e., a collaboration of researchers within the VU campus on a key topic). Likewise, ORM has been formulated as one of the two priority areas (“zwaartepunt”) of ACTA. As implied above, a healthy oral system is characterized not only by the absence of infection and/or inflammation of dental and periodontal tissues, but also by a healthy musculoskeletal system and oral mucosa. Musculoskeletal tissues (i.e., bone, cartilage, muscles, and joints) and mucosa (epithelium and underling connective tissue) can be damaged or even destroyed by, for example, mechanical overloading, disuse, disease or trauma. In case of tissue loss, the replacement or regeneration of degenerating/degenerated cells, tissues, or organs is needed to restore or establish normal function. ORM studies these processes both at a fundamental and translational level in multidisciplinary settings, in which dentistry/oral medicine closely collaborates with medical disciplines like orthopaedics, neurology and dermatology/plastic surgery, both within and outside The Netherlands.

The main objectives of ORM-related research are the degenerating/degenerated oral tissues and an improved ability to replace or regenerate these tissues, thereby restoring oral function and thus oral health-related quality of life. The ultimate goal of oral regenerative medicine is to regenerate parts of the masticatory system, e.g. teeth, jaw bone and/or mucosa. Since this dot on the horizon is far away, we now concentrate on:

A. Regeneration of jaw bone and oral mucosa.
B. Tissue response of the host to implant materials and restoratives.
C. Gaining in-depth knowledge of non-infectious diseases of the masticatory system.

Research objectives

A. Regeneration of jaw bone and oral mucosa
Stem cells and smart substrates
Adipose tissue derived stem cells have been used to heal bone defects in human jaws. The application of these cells proved to result in an improved healing of the bone defects. In the coming period this will be further explored making use of different types of biological and non-biological substrates (see B).

3D printing and biomimetic coating - CAD/CAM
By making use of 3D bioprinters and the biomimetic coating developed in this research program, scaffolds containing (stem) cells and proteins will be constructed that can be implanted. The biomimetic coating involves the use of different growth factors that modulate cell behaviour and activity. By combining these different modalities it will be possible to finely tune tissue formation at sites wished for.

Computer Aided Design/Computer Aided Manufacturing (CAD/CAM) of tooth replacement, crown and bridgework and guided implant placement devices used to insert both tooth root implants as well as implants used to substitute bone loss based on CBCT scans combined with planning and designing software also being developed in this research program. In a joint project with industry the technology used to 3D print composite, PMMA and ceramics in crown and bridgework is being refined.

A project focussed on the milling / printing of full tooth implants has shown that we can print teeth in titanium and zirconium within the same dimensions as the tooth scanned with CBCT. This technology makes it possible to design and fabricate one off implants for the specific bone volume in the individual patient.
B. Tissue response of the host to implant materials and restoratives

Tissue response of the host

Tissue lost after trauma or surgical intervention should be replaced or, most preferably, regenerate. In this part of the programme regeneration is induced by making use of a wide variety of scaffold materials, different cell types (e.g. stem cells) and a variety of growth factors and cytokines. The collaboration between clinical and non-clinical scientists from different departments and backgrounds (dental material sciences, implantology, oral cell biology) ensures a multi-disciplinary approach. It becomes more and more clear that implant materials long thought being harmless are now found to evoke an immunological response. Since the use of implant material increases tremendously knowledge about the response of these materials is of crucial importance. Whereas in the majority of cases, implants remain inert in the host, in some cases adverse events are observed e.g. host responses can include bioreabsorption (breakdown) of the implant material resulting in leachables, an inflammatory response leading to adjacent mucosa and bone degradation, irritation to the surrounding tissues and sensitization of the host. It is of utmost importance to develop safe biomaterials and implants for oral regenerative medicine. For this topic scientists with different background join forces in order to tackle these issues. Two approaches to this research line are investigated:

1) Safety assessment of dental implants. For this the Adverse Outcome Pathway (AOP) approach is used to investigate potential inflammatory responses in full compliance with the 3Rs. Toxicity, irritation and sensitization are the focus. Both organotypic in vitro tissue engineered oral mucosa and bone constructs are used as healthy and disease models with integrated immune cells (e.g. Langerhans Cells) as well as traditional cell cultures.

2) Improved diagnostic testing of questionable adverse events to dental materials. Currently the skin patch is used to identify an allergic response of the individual to a dental implant. Due to differences in skin and oral immunity as well as cutaneous penetration, often false negatives are diagnosed. Improved patch testing methods, (eg use of microneedles and different salts) as well as in vitro lymphocyte proliferation and cytokine tests are being investigated a alternatives.

Biological response to loading

The maintenance and survival of tissues like bone and cartilage largely depend on mechanical loading exerted upon these tissues. The different cell types that harbour these tissues are mechanosensitive and respond to mechanical loading. Also the stiffness of the substrate the cells live on, has profound effects on their metabolic activities. A combination of substrate stiffness and mechanical loading will make it possible to direct the cells in such a way that they generate tissues wished for, such as bone and cartilage.

Insight in the interaction between implanted material either being of biological non-biological origin and the surrounding tissues is of crucial importance for the understanding how the host respond to the implanted material. Special attention is paid to the response of the tissue under conditions of mechanical loading or unloading.

Response of oral mucosa to injury

Oral mucosa in contrast to skin heals rapidly and with almost scar free healing. With the aid of physiologically relevant tissue engineered oral mucosa and skin constructs, mechanisms of healing are compared in vitro. In particular, differences in proliferation, migration and differentiation of the epithelium and the deposition of extracellular matrix by (myo-)fibroblasts is investigated. Trafficking of immune cells involved in determining the quality of scar formation is the focus as well as the impact of the environment e.g. air versus saliva. Once normal healing mechanisms are established, the models can be used to investigate the mode of action of novel therapeutic compounds in vitro.

C. Gaining in depth knowledge of non-infectious diseases of the masticatory system.

Pain, trauma and dysfunction

Overloading of the constituent tissues of the masticatory system, notably cartilage, bone, muscle tissue, periodontal tissues, and hard dental tissues due to bruxism (i.e., tooth grinding and clenching) and adverse oral habits (e.g., nail biting and excessive gum chewing) may lead to pain and dysfunction of the chewing apparatus. In turn, such conditions may yield risks for the individual’s general health and cognitive abilities. A threat to the success of dental implants is peri-implant disease which is characterised by bone loss around the individual implants. The secondary cause of this bone loss is infection. The primary cause of peri-implant bone loss can be overloading, immunological response to the implant material.

Within the framework of ORM, the causes, consequences, and management of pain, trauma and dysfunction of the masticatory system are studied in multiple international and multidisciplinary settings.
The following items are studied:
- diagnosis, epidemiology, pathophysiology, and management of bruxism and obstructive sleep apnea
- diagnosis, epidemiology, and treatment of orofacial pain, including psychosocial aspects and the relationship between genetic factors, mastication and cognition in elderly institutionalized persons with different types of dementia
- surgical treatment strategies for orthognatic defects
- incidence and treatment of maxillofacial trauma
- peri-implantitis

Results obtained

A. Regeneration of jaw bone and oral mucosa

Stem cells and smart substrates
- Six studies were published in which the release was investigated of bone morphogenetic protein (BMP) incorporated into Calcium Phosphate as a carrier. This technology known as biomimetic coating has been the basis for research at ACTA during the last 8 years. It has been shown to be an effective bone substitute in critical size defects promoting osteogenesis and enhancing bone growth.
- The gain of mineralized bone has been compared between deproteinized bovine bone allograft (DBA) and biphasic calcium phosphate (BCP) for dental implant placement. Patients with atrophic maxillae underwent bilateral sinus elevation with DBA and BCP. After 3 to 8 months, implants were placed, and biopsies were retrieved. The BCP and DBA materials showed similar osteoconductive patterns and mineralized bone, although signs of more active bone formation and remodeling were observed in BCP-than in DBA-grafted biopsies. It has been demonstrated that malocclusion which often remains after conservative treatment of fractures of the collum mandibulae most probably are created due to an altered articulation in the temporomandibular joint.

3D printing and biomimetic coating - CAD/CAM
- A study on the precision of intraoral scanners as new instruments that could be used in operative dentistry showed that there is still improvement possible in this area as the precision of the instruments analysed vary considerably.
- A series of CAD/CAM materials were investigated with the focus on the influence of restoration thickness and bonding related to the fracture resistance. The in vitro study showed that thickness above 0.5 mm could afford the normal bite force and proficient bonding is required for most materials.

B. Tissue response of the host to implant materials and restoratives

Tissue response of the host
- A study on annual bone loss around dental implants in a 16 year followup study introduced a new index to catagorize bone loss measured on radiographs.
- A study one the accuracy of CBCT scans in which we analysed the trabecular bone in implant sites has given us more insight into the precision of this radiological tool and its application in dental implant planning. In this same area another study showed the influence of the reduction of artefacts produced by CBCT scans around dental implants on the precision of this same tool. We also investigated the influence of the Fields of View of CBCT scans and the influence on its precision.
- A clinical study showed that oral lesions and Pd-induced immune responses are associated with the presence of dental alloys. However, most oral disease patients did not show positive patch test results or in vitro signs of specific immunoreactivity, suggesting local toxic reactions or the involvement of innate immune responses
- Our epidermal equivalent assay for identifying and labelling sensitizers was investigated in an international multi centre study.

Biological response to loading
- Research on the use of 2 implants supporting an overdenture in the upper jaw showed encouraging results when evaluating patients quality of life. A multi center overdenture evaluation study in the lower jaw showed long term positive results as well.
- We published two papers showing that mechanically loaded muscle cells produce factors that are very similar to the factors produced by mechanically loaded bone cells. These factors were shown to be able
to affect the formation of bone resorbing osteoclasts in culture. It is thus possible that bone mass is affected by muscle loading e.g. during mastication.

- Aging reduces bone mass as well as the anabolic response of bone to mechanical stimuli, resulting in osteopenia. Endoplasmic reticulum (ER) stress impairs the response of myogenic cells to anabolic stimuli, and is involved in sarcopenia, but whether ER stress also contributes to osteopenia is unknown. We found that the expression of several ER stress markers was higher in osteocytes from bones of old compared to adult mice. Since ER stress altered the response of osteocytes to mechanical loading, it could be a novel factor contributing to osteopenia.

- Skeletal muscle fibers have the ability to increase their size in response to a mechanical overload. Finite element modeling data suggest that mechanically loaded muscles in vivo may experience not only tensile strain but also shear stress. However, whether shear stress affects biological pathways involved in muscle fiber size adaptation in response to mechanical loading is unknown. We found that shear stress exerted on myofiber extracellular matrix plays an important role in mechanotransduction in muscle.

- Mechanical stimulation reduces sclerostin expression in rodents. However, few data are available about the effect of physical stimuli in human systems. We explored the effect of mechanical loading on SOST expression by subjecting Azadc-treated human bone cells to pulsating fluid flow (PFF). Our results suggest that NO and other soluble factors are involved in the inhibition of SOST expression by PFF.

- In response to mechanical loading skeletal muscle produces numerous growth factors and cytokines that enter the circulation. We hypothesized that myotubes produce soluble factors that affect osteoclast formation and aimed to identify which osteoclastogenesis-modulating factors are differentially produced by mechanically stimulated myotubes. We showed that mechanically loaded myotubes secrete soluble factors, among others IL-6, which affect osteoclast formation. These results suggest that muscle could potentially affect bone homeostasis in vivo via production of growth factors and/or cytokines.

- The combination of cytokines present in the circulation of patients with active rheumatoid arthritis might contribute to the generalized bone loss that commonly occurs in these patients, by directly inhibiting osteoblast proliferation and differentiation, but especially by enhancing endogenous cytokine (RANKL) and interleukin-6 (IL-6) production by osteoblasts, thereby stimulating osteoclastogenesis. We found that active RA sera contains circulating factors, likely cytokines and chemokines, that might contribute to bone loss by directly inhibiting osteoblast proliferation and differentiation, but especially, these factors modulate endogenous cytokine production by osteoblasts, thereby affecting osteoclastogenesis.

- Mechanosensitive osteocytes regulate bone mass in adults. Interleukin 6 (IL-6), such as present during orthodontic tooth movement, also strongly affects bone mass, but little is known about the effect of IL-6 on osteocyte function. Therefore we determined in vitro whether IL-6 affects osteocyte mechanosensitivity, and osteocyte regulation of osteoclastogenesis and osteoblast differentiation. Our results suggest that IL-6 is produced by shear-loaded osteocytes and that IL-6 may affect bone mass by modulating osteocyte communication toward osteoblasts.

**Response of oral mucosa to injury.**

- Tissue engineered skin and mucosa equivalents have been established from TERT immortalized cell lines and validated against the primary cell counterparts. The models consist of reconstructed epithelium on a fibroblast populated dermis or lamina propria. Inflammatory responses during wound healing and scar formation were investigated.

**Gaining in depth knowledge of non-infectious diseases of the masticatory system.**

**Pain, trauma and dysfunction**

- The long-term research line on the diagnostics of orofacial pain and temporomandibular disorders was acknowledged by several co-authorships related to the international classification system for Temporomandibular Pain (the DC/TMD).

- Research on genetics provided novel insights in the role of heritability in bruxism and orofacial pain.

- Studies on the recognition of pain in persons with impaired cognition (like people with dementia or Down syndrome) are ongoing. For example, the reliability of an Orofacial Pain Scale for Non-Verbal Individuals (OPS-NVI) was tested, as well as the use of facial pictograms to assess pain intensity.

- In a series of experimental and clinical studies, a positive association between mastication and cognition was found. These results may have important consequences for daily care of elderly persons.
• Several studies on bruxism have contributed to an improved insight into the pathophysiology, diagnosis, and consequences of sleep bruxism.
• Ongoing studies on the different types of cartilage in the temporomandibular joint aim to explain the clinical observation that condylar cartilage is more vulnerable for remodelling than the cartilage of the disc and fossa. The role of mechanical loading in this process is being studied as well.
• A review of published studies of the last 30 years on traumatology showed that in American, African and Asian studies road traffic crashes were the predominant cause. In European studies the aetiology varied, with assaults and road traffic crashes being the most important factors. In Oceania assaults were the most important.
• We found that measurements of the height of the ramus on orthopantomographic (OPT) images cannot be relied on as an absolute indication for surgical intervention in patients with mandibular condyle fracture.

### Academic personnel in 2014 and 2015

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### PhD students

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**Total non tenured staff**: 20,30
**total 1st funding**: 20,65
**total 2nd funding**: 2,55
**total 3rd funding**: 9,30
**Total research staff**: 32,50

### Output

#### Dissertations


Scientific publications (refereed)


Scientific publications (non refereed)


Professional publications


Publications aimed at the general public


Grants: current projects with external funding


Scherder, E.J.A. & Lobbezoo, F. (2014). Diagnostiek en behandeling van pijn bij mensen met een dementia die thuis wonen of in het verpleeghuis zijn opgenomen. F. Lobbezoo responsible for the dental part of this project which equals approx. 1/3 of the total amount granted €126.667, -: NutsOHRA, RCOAK, SBOH, Henriëtte Hofje as sources for the funding of three PhD projects (NutsOHRA €150.000, -: RCOAK €160.000, -: Henriëtte Hofje €40.000, -: Alzheimer Nederland €30.000, -: total = €380.000, (2012, January 01 - 2017, December 31).

Scherder, E.J.A. & Lobbezoo, F. (2014). Pijn bij volwassenen met een verstandelijke beperking. F. Lobbezoo responsible for the dental part of this project which equals approx. 1/4 of the total amount granted €53.750, -: NutsOHRA, Fonds Verstandelijk Beperken and Innovatiefonds as sources of funding for one PhD project (NutsOHRA, €150.000, -: Fonds Verstandelijk Gehandicapten €15.000, -: Innovatiefonds €50.000, -: Total €215.000, (2010, January 01 - 2015, December 31).


Indicators of Esteem
Editorship book
Dozic, A. Jaarboek Esthetische Tandheelkunde, Member Editorial Board, since 2009.
Feilzer, A.J. Praktijkboek Tandheelkunde, Member Editorial Board, since 2008.
Memberships of editorial board

Aarab, G.: Journal of Dental Sleep Medicine.
Everts, V.: The Open Bone Journal.
Everts, V.: The Open Enzyme Inhibition Journal.
Feilzer, A.J.: Odontology.
Goené, R.J.: Journal of Implant and Reconstructive Dentistry.
Lobbezoo, F.: Journal of Craniomandibular Function.
Poorterman, J.H.G.: Nederlands Tijdschrift voor Tandheelkunde
Van Calcar, N.P.: De Tandartspraktijk.
Van der Stelt, P.F.: Dentomaxillofacial Radiology.
Van der Stelt, P.F.: Journal of Dentistry Shiraz University of Medical Sciences.
Van der Stelt, P.F.: Odontology.

Scientific awards/honours


Organization of (inter)national scientific congresses and symposia


Bakker, A.D. (2014). Organizing committee. Yearly Symposium, Centre for Translational Regenerative Medicine, Vumc: Amsterdam, the Netherlands (2014, October 09).


Invited speakers at (inter)national congresses or symposia


Bakker, A.D. (2014, April 07). Effect of IL-6 on osteocyte mechanosensitivity. Melbourne, Australia, University of Melbourne, Department of Medicine.

Bakker, A.D. (2014, November 17). Culture and application of mesenchymal stem cells for regeneration of mesenchymal tissues. Ghent, Belgium, AMBA winter school on polymers for biomedical applications.

Bakker, A.D. (2014, November 15). Cytokines and growth factors affect osteogenic differentiation of adipose tissue derived mesenchymal stem cells. Amsterdam, the Netherlands, IFATS.

Bakker, A.D. (2014, December 11). Is it possible to cure osteoporosis by altering bone cell mechanosensitivity? Sneekkersten, Denmark, Annuals symposium of the Faculty of Health and Medical Sciences, University of Copenhagen.

De Vries, T.J. (2014, December 06). De rol van tandfibroblasten met de FOP-mutatie in botvorming en botafbraak. Amsterdam Marriot Hotel, the Netherlands, Fybrodysplasia ossificans progressiva patients society.


Klein Nulend, J. (2014, October 28). Mechanosensation by osteocytes and bone adaptation, and regeneration. Wenzhou, Zhejiang, China, Wenzhou Medical University, School of Pharmacy.


Visscher, C.M. (2014, March 28). Orofaciale pijn en fysiotherapie. Amsterdam, the Netherlands, Symposium VU.

Visscher, C.M. (2014, April 30). The role of the physical therapist in the multidisciplinary treatment of headache. Las Vegas, USA, PhysicalTherapy Board of Craniofacial & Cervical Therapeutics Pre-Conference Course of the AAOP/ICOT meeting.

Visscher, C.M. (2014, May 01). Temporomandibular pain is partly heritable. Las Vegas, USA, American Academy of Orofacial Pain (AAOP) 38th scientific meeting and International Conference on Orofacial Pain and Temporomandibular Disorders (ICOT).


Other (inter)national scientific functions

Bakker A.D.: Board member - European Calcified Tissue Society
Bakker A.D.: Co-chair new investigator committee - European Calcified Tissue Society
Bakker A.D.: Board member - Dutch Society for Calcium and Bone Metabolism
Disse, M.A.: Member - RTS.
Everts, V.: Member and principal investigator - NIRM.
Everts, V.: Visiting professor - Chulakorn University, Bangkok, Thailand, September-November 2014.
Gibbs, S.: Member. European Research Group for Experimental Contact Dermatitis (ERGECD).
Gibbs, S.: Member and principal investigator - NIRM.
Goené, R.J.: Member Clinical Advisory board - Biomet/3i, West Palm Beach, Florida.
Klein Nulend, J.: Member scientific board - Department of Regenerative Medicine, Research Centre for New Technologies in Life Science Engineering, University of Tehran, Iran.
Klein Nulend, J.: Directory board member - MOVE Research Institute Amsterdam, VU University Amsterdam, the Netherlands.
Klein Nulend, J.: External professor - San Carlos University, Dept. Physics, Cebu City, Philippines.
Klein Nulend, J.: Outer board member - Irish Research Council Postdoctoral International Assessment 2014 (Fellowships in Science, Engineering and Technology), Royal Irish Academy.
Kuitert, R.B.: Member - Richtlijncommissie NVvO.
Lobbezoo, F.: NYU visiting Guest Faculty Recipient 2014-2015 - College of Dentistry, New York University, New York, NY, USA.

Lobbezoo, F.: Member - Task Force Global Year Against Orofacial Pain, International Association for the Study of Pain (IASP).

Sanderink G.C.H.: Executive committee International Association of DentoMaxilloFacial Radiology

Van der Stelt, P.F.: External examiner. PhD examination Jose Hidalgo Rivas, Facuculty of Medical and Human Sciences, University of Manchester, Manchester, UK.

Van Loon, J.J.W.A.: Guest professor - State Key Laboratory of Space Medical Fundamentals and Application of the Astronaut Research and Training Center of China, Beijing, China.


Van Westing, K.: Member - Richtlijnencommissie NVvO.

Zandieh Doulabi, B.: Visiting professor - Research Center for New Technologies in Life Sciences Engineering, University of Tehran, Iran.

Zandieh Doulabi, B.: Head Department Regenerative Medicine - Research Centre for New Technologies in Life Science Engineering, University of Tehran, Iran.

Supervisor of an external PhD student


Societal impact

The societal impact of the programme is evident by, among others, the impact on patient care, interactions with the industry and other non-university groups, the impact on professionals, and relevant (inter-)national functions. The research program also contributes to the post-graduate training programs.

The research on overloading and pain of the musculoskeletal structures of the masticatory system has direct impact on the quality of diagnostic procedures and of patient care, and extends its influence towards an improvement of the (oral-) health-related quality of life. The implications of this research are not only important for general orofacial pain patient groups, but also for more vulnerable populations like those suffering from dementias and otherwise impaired cognitive abilities.

An ambitious future goal of the program is to improve health care and treatment of patients with juvenile idiopathic arthritis. Diagnosis of arthritis of the jaw joint is commonly missed by clinicians, eventually possibly leading to progressive pain and malfunctioning of the joint. Research started in 2012 is focused on learning the biological parameters of the three types of cartilage present in the jaw joint. Inflammation will be mimicked in vitro and it will be determined whether mechanical loading will lead to a decreased inflammation.

Special focus is on orthodontic patients with cranio-facial deformities and/or related malocclusions. A program of quality of life related to this topic is carried out.

During the last couple of years it became clear that implanted materials like metals can have adverse effects like allergy. This last subject is now an important issue of investigation. An improved understanding how metals may induce an allergic reaction will have an enormous impact on the society.

The societal impact of the research on oral and maxillofacial radiology is focused on the improvement of diagnostic imaging procedures. This relates to not only technical parameters, but also other factors that influence the diagnostic performance of radio-diagnostic procedures, such as the effect of viewing conditions and observer characteristics. Part of the activities includes continuing education courses on the safe use of radiation in dental practice and application of digital imaging in dentistry.

Enamel fluorosis is an increasing aesthetic problem in several countries. The project on mechanism of enamel fluorosis adds to our understanding how these defects develop which will help to prevent these defects in future. The results of our research on bone adaptation and regeneration will offer multiple opportunities for
the development of new therapeutic agents to prevent (inflammation-associated) unwanted clinical bone loss, thereby preventing among others mobility loss with aging.

The societal impact of the clinical research on oral and maxillofacial surgery is focussed on the influence on patient care, both within the department and externally. Research contributes to improved treatment of relevant patient groups.

More details of the societal impact of the program are listed below.

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

Several scientists of the program have contacts with the industry, see the list of current grants in de paragraph of indicators of esteem above.

**Dental Material Sciences:**
- Elephant Industries, Hoorn, the Netherlands, ISO TC106
- Vertex, zeist, the Netherlands, ISO TC106
- Degudent GmbH, Hanau, joint research projects
- Heraeus Kulzer GmbH, Wehrheim, joint research projects
- 3M-ESPE, Zoeterwoude / seefeld, joint research projects
- GC Europe, Leuven Belgium, joint research projects
- Saremco, Rebstein, Switzerland, joint research projects
- Cavex Holland B.V., Haarlem, joint research projects

**Oral Kinesiology:**
- Lobbezoo, F. Member - Grindcare Clinical Advisory Board (CAB) of Sunstar Suisse.
- Visscher, C.M. Board member - Physical Therapy Board of Craniofacial and Cervical Therapeutics (PTBCCT), USA.

**Oral Radiology:**
- Instrumentarium Dental Oy –CBCT and Panoramic unit placed at department for testing and patient care.
- Newtom QR – (2014, April- 2014 July) Invitation of students (F. San Giorgi and A. Nieuwland) to prepare their mastertheses in Newtoms headquarters – Verona, Italy.

**Interactions with the general public**


**Impact of the research on professionals**

Patients are referred by their dentists to the various specialized clinics of the departments participating in the program for diagnosis and treatment based on the latest scientific evidence.

The guidelines for diagnosis and treatment of patients have been adopted by the Dutch association for Oral and Maxillofacial Surgery (Nederlandse Vereniging voor Mondziekten, Kaak- en Aangezichtschirurgie, NVMKA).


Organization of congresses and symposia for (health care) professionals

Invited speakers at professional congresses or symposia
Baart, J.A. (2014, May 08). Printen in de MKA-chirurgie. Amsterdam, the Netherlands, AMC.
Goené, R.J. (2014, December 11). Mastering esthetics in post-extraction sites. Nieuwegein, the Netherlands, Landelijke studiedag AIOS-MKA.
Rollman, A. (2014, March 28). Behandeling bij TMD: to seek or not to seek? ...that’s the question! Nijmegen, the Netherlands, Studiedag Nederlandse Vereniging voor Orofaciaal Fysiotherapeuten (NVOF) en NVGPT.
Van der Stelt, P.F. (2014, September 10). CBCT: is meer altijd beter? Rotterdam, the Netherlands, Erasmus University, Landelijke onderwijsdag AIOS MKA.

Other professional functions
Aarab, G.: Member research committee - American Academy of Dental Sleep Medicine (AADSM).
Berkhout, W.E.R.: Coördinerend stralingsdeskundige ACTA - Raad van Bestuur VU.
Berkhout, W.E.R.: Lid - Raad van Advies ACTA-Dental Education.
Berkhout, W.E.R.: Lid - Raad van Commissarissen NTvT.
Courses organized for dental and medical professionals

A large number of courses were given in the Netherlands for dentists, medical specialists and oral hygienists by the following scientists:

Berkhout W.E.R.:
- Course coordinator Radiation protection courses ACTA, officially accredited by the Ministry of Social Affairs:
  - Stralingshygienisch Gekwalificeerd Beroepsbeoefenaar – Tandheelkunde
  - Stralingshygienisch Gekwalificeerd Beroepsbeoefenaar – Conebeam CT
  - (2014, April – May) KNMT Iqual themaprogramma Beeldvormende technieken – KNMT

Goené R.J.:
- NVOI: Implantologie Het Overzicht, Utrecht 14 June 2014
- NVOI: Implantologie Integraal 13 October
- NVOI: Implantologie de Verdieping, 27 en 28 November
- NVOI: Implantologie Het Fundament, Putten 15 March & 19 September 2014
- NVOI Implantologie Het Vervolg, Putten 13 December 2014
- NVOI: De Hoofdzaak, UMCG Groningen 15 & 16 May 2014

Lobbezoo, F. & Visscher, C.M.:
- Organizers. TMD Doe Dag. ACTA-QP Course, Amsterdam. (February 13, 2014).
- Organizers. TMD Doe Dag voor mondhygiënisten. ACTA-QP Course, Amsterdam. (April 12, 2014).

Van der Stelt, P.F.:
- KNMT Iqual themaprogramma Beeldvormende technieken – KNMT. (2014, April – May)
Lectures given during courses for dental and medical professionals in the Netherlands

Aarab G.:
- Slaapapneu: red alerts en consequenties voor de dagelijkse praktijk. ACTA-QP Course ‘TMD-Doedag voor mondhygiënisten’ Amsterdam (April 12, 2014).

Baart, J.A.:
- Veilig werken in de tandheelkunde. Opgaan met vreemd gedrag van de patiënt. Quality Practice, ACTA dental education Amsterdam, 25-01-2014
- Veilig werken in de tandheelkunde. Opgaan met vreemd gedrag van de patiënt. Quality Practice, ACTA dental education Amsterdam, 31-01-2014
- Chirurgie in de dagelijkse praktijk, Benecke Amsterdam, 04-12-2014
- Lokale anesthesie voor assisterenden, Tilburg, 08-02-2014
- Lokale anesthesie voor assisterenden, ACTA-VUmc, 06-03-2014
- Symptomen en syndromen, ACTA-VUmc, 15-05-2014
- Lokale anesthesie voor assisterenden, ACTA-VUmc, 06-06-2014
- QP chirurgie in de algemene praktijk, ACTA dental education, 20-06-2014
- Lokale anesthesie voor assisterenden, ACTA-VUmc, 11-09-2014
- Lokale anesthesie voor assisterenden, Garderen, 04-10-2014
- Atraumatisch extraheren en socket preserveren, Obdam, 31-10-2014
- Lokale anesthesie voor tandartsassistenten, Garderen, 01-11-2014
- Lokale anesthesie voor assisterenden, ACTA-VUmc, 06-11-2014
- QP chirurgie in de algemene praktijk, ACTA dental education, 28-11-2014

Berkhout, W.E.R.:
- 10 lectures during several courses for medical professional

Gilijamse, M.:
- Cursus dentoalveolaire chirurgie voor tandartsen
- Behandeling van TMD: de rol van de kaakchirurg. TMD-DOE symposium 13-2-2014, ACTA DE

Goené, R.J.:
- Implantologie: Het Fundament, NVOI, Putten, 15 March
- Implantologie: de Hoofdzak, NVOI, Groningen, 15 & 16 mei
- Person to Person, Tenden tandartsen, Amsterdam, Live surgery, 7 June
- Peri-Implantitis, Biomet/3i, Antwerpen
- Implantologie: Het Fundament, NVOI, Putten, 19 September
- Person to Person, Tendenstandartsen, Amsterdam, Live surgery, 21 September
- Het Overzicht, NVOI, Utrecht 14 June

Hoogeveen, R.C.:
- 10 lectures during several courses for medical professionals

Jongsma, L.A.:

Kleverlaan, C.J.:

Knibbe W.:
- Behandeling van TMD: de rol van de psycholoog. ACTA-QP Course ‘TMD-Doedag’ Amsterdam (February 13, 2014)

Koutris M.:
- Workshop ‘Vervaardiging wasindex t.b.v. opbeetplaat’. ACTA-QP Course ‘TMD-Doedag’ Amsterdam (February 13, 2014).
  
Lobbezoo F.:  
- Diagnostiek van TMD. ACTA-QP Course ‘TMD-Doedag’ Amsterdam (February 13, 2014)  
- Workshop ‘Vervaardiging wasindex t.b.v. opbeetplaat’. ACTA-QP Course ‘TMD-Doedag’ Amsterdam (February 13, 2014)  

Lobbezoo, F. & Feilzer, A.J.:  

Muris, J.:  

Roeters, F.J.M.:  

Rollman A.:  

Sanderink, G.C.H.:  
- 10 lectures during several courses for medical professionals

Tuinzing, D.B.:  
- Introduction Wooley/Hickmann/Richardson/Morris Amsterdam Wales ad Amstel 27-11-2014  
- Clinical demonstrations Paramaribo 28 April -2 May 2014  
- Lectures Planning by numbers? Clinical demonstrations Cipto Mangugusumo Hospital, 18 June  
- Lecture Planning Surg Orthod for beginners Makassar 6-14 December 2014

Van Daelen, A.C.L.:  
- Person to person, klinische cursus implantologie chirurgie en prothetiek (live surgery), Tendens tandartsen, Amsterdam, 07 June 2014  
- Implantologie Integraal, NVOI, Putten, 3 October 2014  
- Person to person, klinische cursus implantologie chirurgie en prothetiek (live surgery), Tendens tandartsen, Amsterdam, 29 November 2014

Van Dalen, A.:  
- (2014, November 01). Wanneer faalt een restauratie? Amsterdam, Symposium De gefaalde restauratie-2, ACTA Dental Education (ADE).

Van der Stelt, W.E.R.:  
- 10 lectures during several courses for medical professionals
Visscher CM.:
- Behandeling van TMD: de rol van de fysiotherapeut. ACTA-QP Course ‘TMD-Doedag’ Amsterdam (February 13, 2014).
- Fysiotherapie voor patiënten met kaakklachten. Quality Practice Assistenten. Update dag 1, Utrecht (December 12, 2014).

Warnsink J.:

Wetselaar P.:
- Workshop ‘Vervaardiging wasindex t.b.v. opbeetplaat’. ACTA-QP Course ‘TMD-Doedag’ Amsterdam (February 13, 2014).
- Slapen en slijten. ACTA-QP Course ‘TMD-Doedag voor mondhygiënisten’ (Amsterdam, April 2014).

Wetselaar, P. & Koutris M.:
- Behandeling van TMD: rol van de tandarts. ACTA-QP Course ‘TMD-Doedag’ Amsterdam (February 13, 2014).

Willems, N.M.B.K.:
- ACTA Dental Education, 8th of March 2014, Orthodontie: wanneer en waarom?

Collaborations
- ACT, Dept Oral & Maxillofacial Surgery, VUMC (Prof.dr. C.M. ten Bruggenkate, Prof.dr. E.A.J.M. Schulten, Dr. T. Forouzanfar), Amsterdam, NL.
- AMOLF (Prof.dr. G. Koenderink), Amsterdam, NL.
- Autonomic Technologies Inc. (California, V.S.), de afdeling MKA van de Universiteit van Turijn (Italië)
- A-Skin BV (Prof R Scheper), Amsterdam, NL.
- Biofarmind, The Hague, the Netherlands
- City University of New York (Dr.ir. S.C. Cowin), New York, USA.
- Crucell, Leiden, the Netherlands
- Department of Clinical Epidemiology and Biostatistics, VUmc, Amsterdam
- Department of Clinical Genetics, VUmc, Amsterdam
- Department of Endocrinology, VUmc, Amsterdam
- Department of Nuclear Medicine and PET research, VUmc, Amsterdam
- Department of Oral and Maxillofacial Surgery, Leids Universitair Medisch Centrum, Leiden
- Department of Oral and Maxillofacial Surgery, Rijnland Ziekenhuis, Leiderdorp
- Dutch Polymere Institute, TU Eindhoven en TU Delft; DSM.
- Ege University, Faculty of Medicine, Center for Brain Research & Department of Physiology, prof.dr. K. Türker, Bornova, Izmir, Turkey.
Annual Research Report 2014

- Eindhoven University of Technology, Dept Materials Technology (Prof.dr.ir. J.M.J. den Toonder), Eindhoven, NL.
- Göttingen University (Prof.dr. C.F. Schmidt), Göttingen, Germany.
- Harvard University (Dr. R. Krishnan), Boston, USA.
- Health Sciences University of Hokkaido, dr. M. Hashimoto, Hokkaido, Japan.
- Heelkunde/Traumatologie en Anesthesiologie van VUmc, EMGO, de Boerhaave kliniek in Amsterdam.
- Hiroshima University, Dept Orthodontics (Prof.dr. Tanne, Dr. R. Sano), Hiroshima, Japan.
- Hospital Hilversum (Dr. G.H.R. Albers), Hilversum, NL.
- Institut für Anatomie, Zentrum für Experimentelle Medizin, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany.
- Katholieke Universiteit Leuven, Dept Biomechanics (Prof.dr. P. van Lenthe, Prof.dr. D. Vanderschueren), Leuven, Belgium.
- Katholieke Universiteit Leuven, Dept Physiology (Prof.dr. P. Hespel, Prof.dr. L. Deldicque, Prof.dr. S. Boonen, Dr. R. Manders), Leuven, Belgium.
- Katholieke Universiteit Leuven, Dept Rheumatology (Prof.dr F.P. Luyten, Prof.dr. P. Vanderschueren), Leuven, Belgium.
- Keele University (Prof.dr A. El Haj), Stoke-on-Trent, UK.
- King Saud University, dr. Z. Salameh, Riyadh, Saudi Arabia.
- Kyoto University (Prof.dr.ir T. Adachi, Dr. M. Tanaka), Kyoto, Japan.
- Linköping University, Dept Clinical Experimental Medicine, Div Orthopaedics (Dr. A. Fahlgren), Linköping, Sweden.
- Linköping University, Dept Physics, Chemistry and Biology (Dr. E. Jager), Linköping, Sweden.
- Netherlands Cancer Institute, Division of Immunology (Dr. Y. Xiao, Dr. J. Borst), Amsterdam, the Netherlands.
- Nordic Biosciences (Dr. K. Henriksen), Herlev, Denmark.
- Okayama University (Prof.dr. H. Kamioka), Okayama, Japan.
- Radboud University (Prof.dr. A.M. Kuipers-Jagtman, Dr. R. van ’t Hoff), Nijmegen, NL.
- Radboud University (Prof.dr. J. Jansen and Dr. X.F. Walboomers), Nijmegen, NL.
- Radboudumc, IQ-healthcare, prof.dr. R. Nijhuis, Nijmegen, the Netherlands.
- Regensburg University Medical Center, Department of Prosthetic Dentistry, Prof. dr. M Behr, Regensburg, Germany.
- San Carlos University, Dept Physics, Cebu City (Prof.dr. R.G. Bacabac), Philippines.
- Slotervaart General Hospital, Department of Clinical Neurophysiology and Brain Mapping Laboratory, dr. H.L. Hamburger, Amsterdam, the Netherlands.
- Spaarne Hospital Heemstede (Dr. P.A. Nolte), Heemstede, NL.
- Technical University Eindhoven (Prof.dr. M. Rauterberg), Eindhoven, NL.
- TNO Life Style - Behavioral and Societal Sciences, dr. E. Vermeiren and A. Schuller, Leiden, the Netherlands.
- UMCg (Prof.dr. R.A. Bank), Groningen, NL.
- Università degli Studi di Milano, Laboratory of Toxicology, DiSeF (Prof.dr. E. Corsini), Milan, Italy.
- Universitair Medisch Centrum St Radboud/de Radboud Universiteit Nijmegen, Cariologie en Endodontologie, prof. dr M.C.D.N.I.M. Huysmans.
- Universiteit van Genève, Division of Cariology and Endodontology, prof. dr. I. Krejci, Genève, Swiss.
- University at Buffalo, Department of Oral Diagnostic Sciences, dr. R. Ohrbach, Buffalo (NY), USA.
- University Estadual Paulista (UNESP), Department of Dental Materials and Prosthodontics, prof.dr. Daniela Aparecida de Godoi Gonçalves and prof.dr. Cinara M. Camparis, Araquara School of Dentistry, Araquara, Brazil.
- University Medical Center (UMC) Utrecht and Radboudumc, IQ-healthcare, dr. CM Speksnijder, Nijmegen, the Netherlands.
- University of Aberdeen (Prof.dr. M. Helfrich), Aberdeen, UK.
- University of Cairo, Department of Operative Dentistry, dr. AA. El Zohairy, Cairo, Egypt.
- University of California San Francisco (Prof.dr. P. DenBesten), San Francisco, USA.
- University of Cardiff (Prof.dr. B. Evans), Cardiff, UK.
- University of Connecticut (Dr. M. Musgrave), Connecticut, USA.
- University of Helsinki (Prof.dr. K. Vaananen), Helsinki, Finland.
- University of Helsinki, Department of Stomatognathic Physiology & Prosthetic Dentistry, dr. J. Ahlberg, Helsinki, Finland.
Academic Centre for Dentistry Amsterdam

- University of Hong Kong, Dept Oral Diagnosis and Polyclinics (Dr. T.K. Goto), Hong Kong, China.
- University of Kiel (Prof. dr. P. Saftig), Kiel, Germany.
- University of Madrid, (Prof.dr. R. Marco), Madrid, Spain.
- University of Milan (Prof.dr. S. Bradamante), Milan, Italy.
- University of Montreal, Faculty of Dentistry, prof.dr. Gilles Lavigne, Montreal, PQ, Canada.
- University of Naples, Dept Orthodontics (Dr. I. Cioffi, Dr. M. Farella), Naples, Italy.
- University of Navarra, School of Medicine (Prof.dr. J.F. Medina), Pamplona, Spain.
- University of Padova, TMD Clinic, dr. D. Manfredini, Padova, Italy.
- University of São Paulo State (UNESP), Department of Dental Materials and Prosthodontics, F. Trindade, LF and Valandro, São Paulo, Brazil.
- University of Stockholm (Prof.dr. G. Andersson), Stockholm, Sweden.
- University of Sydney, Faculty of Dentistry, Jaw Function and Orofacial Pain Research Unit, prof.dr. Greg Murray, Sydney, Australia.
- University of Sydney, Faculty of Dentistry, Department of Orthodontics, prof.dr. Ali M Darendeliler, Sydney, Australia.
- University of Tanta, Department of Restorative Dentistry, dr. AI Abdalla, Tanta, Egypt.
- University of Tennessee, Clinical Research Center, dr. F. Garcia Godoy, Memphis, USA.
- University of Tokushima, Dept Orthodontics and Dentofacial Orthopedics (Prof.dr. E. Tanaka, Dr. N. Kawai), Tokushima, Japan.
- University of Turku, Department of Prosthetic Dentistry and Biomaterials research, Prof. dr. Pekka Vallittu, Turku, Finland.
- University of Umea (Prof.dr. U. Lerner), Umea, Sweden.
- University of Umea, Faculty of Medicine, department of Clinical Oral Physiology, prof.dr. A. Wännman, Umea, Sweden.
- University of Zurich, Center for Dental and Oral Medicine, Dental Materials Unit, prof. dr. M. Özcan.
- UTHSC Dental School, Department of Restorative Dentistry, S. Wendt, San Antonio, Texas, USA.
- Utrecht University Medical Center (Prof.dr. W.J.A. Dher, Prof.dr.ir. H. Weinans), Utrecht, NL.
- Vrije Universiteit, Department of Clinical Neuropsychology, prof.dr. E.J.A. Scherder, Amsterdam, the Netherlands.
- Vrije Universiteit, Nederlands Tweelingen Register (NTR), prof.dr. D.I. Boomsma, Amsterdam, the Netherlands.
- VU Amsterdam, Dept Movement Sciences (Prof.dr. J. van Dieën, Prof.dr. A. de Haan, Dr. R. Jaspers, Dr. K. Gerritsen), Amsterdam, NL.
- VU Amsterdam, Dept Physics (Prof.dr. F.C. MacKintosh, Prof.dr. G. Wuitte, Prof.dr. E. Peterman), Amsterdam, NL.
- VU Amsterdam, Physic (Prof.dr. D. Iannuzzi), Amsterdam, NL.
- VUMc, Dept Dermatology (Prof T Rustemeyer, Prof.dr R. Hoekzema), Amsterdam, NL
- VUMc, Dept Endocrinology (Prof.dr. P. Lips, Dr. N. Bravenboer), Amsterdam, NL.
- VUMC, Dept Medical Oncology (Prof T de Grujilj), Amsterdam, NL
- VUMc, Dept Orthopaedics (Prof.dr. B.J. van Royen, Dr. M.N. Helder, Prof.dr.ir. T.H. Smit), Amsterdam, NL.
- VUMc, Dept Pathology (Dr. I. van Hoogstraten), Amsterdam, NL
- VUMc, Dept Pathology, prof.dr. R.J. Scheper.
- VUMc, Dept Physiology (Prof.dr V. van Hinsberg, Dr P Koolwijk), Amsterdam, NL
- VUMc, Dept Plastic Surgery (Dr. Frank Niessen), Amsterdam, NL
- VUMc, Dept Plastic Surgery (Prof.dr. M. Ritt, Dr. M.G. Mullender), Amsterdam, NL.
- VUMc, Dept Rheumatology (Prof.dr. W.F. Lems), Amsterdam, NL.

Current PhD projects


Apperloo, RC. Dental implants as anchorage for prostheses, number, configuration and suprastructure. Supervisor: prof. dr. J. de Lange, start: June 2010.


Zamani Y. Development of functional scaffolds for bone tissue engineering using 3D printing of cells and biomaterials. Supervisors: Prof. G. Amoabediny (Tehran University, Iran) & Prof.dr. J. Klein-Nulend, co-supervisors: Dr. B. Zandieh Doulabi & Dr. M.N. Helder.


Education related research, including other research

Research on Dental Education
Associate dean of educational research and development
Dr. J.M. Vervoorn
Education Institute
ACTA, Gustav Mahlerlaan 3004
1081 LA Amsterdam
Tel: +31-20-5980438
E-mail: J.Vervoorn@acta.nl

Research objectives
In the ACTA faculty of Dentistry research is performed on several aspects of education in dentistry. This includes research on the evaluation of courses within the curriculum, research on new teaching methods, such as the Objective Structured Clinical Examination (OSCE), development and evaluation of a computer aided digital teaching system creating a virtual learning environment including the application of haptics (the Simodont Dental Trainer), the development of virtual teeth and jaws and comparison with biomedical education elsewhere in Europe.

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

Results
In 2014 several experiments have been carried out with respect to choices in the development of the virtual dental trainer. It appeared that students performed better and were more satisfied working with 3D than with 2D vision; also availability of force feedback turned out to be essential for good performance. The amount of force feedback affected the results of students as well as their satisfaction.

Data on inter and intra observer reliability of assessment showed that including calibration in the workflow of an assessment procedure improved the reliability of the assessments.

Academic personnel in 2014 and 2015

<table>
<thead>
<tr>
<th>Position</th>
<th>Name</th>
<th>fte 2014</th>
<th>plan 2015</th>
<th>funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staff members education institute</td>
<td>Gorter, dr. R.C.</td>
<td>pm</td>
<td>pm</td>
<td>guest</td>
</tr>
<tr>
<td></td>
<td>Vervoorn, dr. J.M.</td>
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<td>0,10</td>
<td>3</td>
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<td></td>
<td>Wesselink, prof.dr. P.R.</td>
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<td>0,15</td>
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<tr>
<td></td>
<td>Boer, drs. I.R. de</td>
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<td>0,20</td>
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<tr>
<td>total 3rd funding</td>
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<td>0,55</td>
<td>3</td>
</tr>
<tr>
<td>Total research staff</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Output

Scientific publications (non refereed)

Professional publications

Indicators of Esteem

Invited speakers at (inter)national congresses or symposia

Memberships of (inter)national editorial board
Gorter, R.C.: European Journal of Dental Education.

Other (inter)national scientific functions
Gorter, R.C.: Executive board member - Association for Dental Education in Europe (ADEE), since 2013.
Gorter, R.C.: Member - Platform for better oral health in Europe.
Vervoorn, J.M.: Chair special interest group since 2009 - ADEE: Virtual reality in dental education.
Vervoorn, J.M.: Chair - Simodont Users Meeting.

Societal impact
The societal impact of the research and development is focused on the effect of learning behaviour on learning outcomes and on the implementation of new technologies in education. This involves in particular the research on a computer aided digital learning environment (the Simodont dental trainer).

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

Other professional functions
Gorter, R.C.: Lid Commissie Onderzoeksbegeleiding (COB) - KNMT.
Gorter, R.C.: Lid Algemene Interfacultaire Ethische Commissie - UvA.

Courses organized for dental and medical professionals
Vervoorn, J.M.:
- Course (2 days) on Virtual reality in Dentistry to the faculty of Shanghai Institute of Stomatology.
- Approximately 15 presentations for faculty members of various dental schools as an introduction to the Simodont Dental Trainer.

**Current PhD projects**


### Appendix 2014

List of SCI journals, their impact factors and the number of ACTA publications in 2014 in each journal

<table>
<thead>
<tr>
<th>Journal</th>
<th>IF</th>
<th>Number of publications</th>
<th>Journal</th>
<th>IF</th>
<th>Number of publications</th>
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<td>ACTA ODONTOL SCAND</td>
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<tr>
<td>ALTEX-ALTERN ANIM EX</td>
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