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INTRODUCTION

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

Some issues for 2012 are specifically mentioned in this report. These include the two main research themes, i.e. research programs, on which the research of ACTA is focussed starting 2011: “Oral Infections and Inflammation” and “Oral Regenerative Medicine”.

An overview of the output in 2012 is presented in Table 1. We are pleased to note that the output in 2012 was high. The number of publications in refereed journals and the IF-sum have considerably increased over a long period; they are in 2012 comparable to those in recent productive years. In 2012 a total of 13 PhD theses were published.

Research Institute ACTA

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REPORT OF THE DIRECTOR

The Research Institute ACTA

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

- **positioning of the research institute**
  National position. ACTA comprises the combined Faculties of Dentistry of the University of Amsterdam and the VU University Amsterdam. The ACTA Research Institute is the only institute for research of the faculty. National collaboration is organized in the Netherlands Institute of Dental Sciences (Interuniversitair Onderzoekoverleg Tandheelkunde, IOT). The IOT organises among others once a year a 2-day conference on dental research in the Netherlands.

  Research themes. ACTA has two main research themes on which research is focussed. These main themes are formed around scientifically strong groups and address relevant clinical topics. The first theme is “Oral Infections and Inflammation”; this theme focuses on the aetiology, prevention and therapy of caries, and periodontal and endodontal infections. The second theme is “Oral Regenerative Medicine”. This theme focuses on the biological process of adaptation and repair of teeth, bone and periodontium, and on biocompatibility of dental materials. Both themes have received a substantial grant from the University of Amsterdam. The ACTA research on oral regenerative medicine is also included in the interfaculty research institute MOVE, a collaboration between the faculty of Human Movement Sciences, the VU University Medical Center and ACTA.

  Research programs. In previous years, ACTA research was organised in 12 research programs. Following the suggestions of the external review committee in 2008, the research was re-organised in 2009 in 6 programs.
  To obtain more focus, starting 2011 the research was reorganised into two new research programs, according to the two main themes: “Oral Infections and Inflammation” and “Oral Regenerative Medicine”. Next to these two major programs, some limited other research is performed, which is education related.

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

Evaluation of the research program

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

Semi-internal evaluation. In 2010 an evaluation of the research of ACTA was performed by a committee consisting of two external referees and two ACTA senior scientists. This committee concluded that ACTA has both nationally and internationally a prominent position in dental research. ACTA is strong in both clinical and fundamental research. The committee recommended continuation of the focus on the two main research themes.

SEP internal evaluation. In 2011 an internal evaluation of the ACTA research was performed over the years 2007-2010. It was concluded that in an international perspective ACTA has a strong position in a relative large number of dental disciplines. Based on the recommendations outlined in that evaluation and on the internal evaluation in 2010 several strategies were made for the future research policy of ACTA. The general strategy is to maintain both fundamental and clinically applied research, preferentially in a translational way. Due to the vulnerability of small groups and to the reductions in budget it was decided to focus the research in two programmes as mentioned above. To preserve the present quality of the research, ACTA will focus on the strongest research. For more details, we refer to the self-evaluation report.

Summary of research output and input

Table 1. Comparison of research indicators 2000-2012

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
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</tr>
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<tbody>
<tr>
<td>Dissertations</td>
<td>11</td>
<td>9</td>
<td>12</td>
<td>6</td>
<td>12</td>
<td>11</td>
<td>11</td>
<td>12</td>
<td>13</td>
<td>6</td>
<td>18</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>Refereed publications</td>
<td>135</td>
<td>130</td>
<td>137</td>
<td>152</td>
<td>170</td>
<td>166</td>
<td>189</td>
<td>185</td>
<td>214</td>
<td>216</td>
<td>196</td>
<td>199</td>
<td>208</td>
</tr>
<tr>
<td>First author from ACTA</td>
<td>107</td>
<td>86</td>
<td>85</td>
<td>106</td>
<td>111</td>
<td>130</td>
<td>131</td>
<td>117</td>
<td>159</td>
<td>132</td>
<td>105</td>
<td>103</td>
<td>117</td>
</tr>
<tr>
<td>Other scientific publications</td>
<td>24</td>
<td>12</td>
<td>8</td>
<td>12</td>
<td>8</td>
<td>17</td>
<td>13</td>
<td>6</td>
<td>24</td>
<td>12</td>
<td>18</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Professional publications</td>
<td>107</td>
<td>123</td>
<td>75</td>
<td>93</td>
<td>91</td>
<td>99</td>
<td>114</td>
<td>113</td>
<td>98</td>
<td>168</td>
<td>164</td>
<td>169</td>
<td>132</td>
</tr>
<tr>
<td>Publications for general public</td>
<td>8</td>
<td>14</td>
<td>9</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impact factor sum</td>
<td>176</td>
<td>206</td>
<td>220</td>
<td>238</td>
<td>273</td>
<td>322</td>
<td>344</td>
<td>354</td>
<td>435</td>
<td>509</td>
<td>434</td>
<td>503</td>
<td>493</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 organisations, such as industry, governmental ministries, European Commission and charity organisations

• 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 2012 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 2012 a high number of 208 refereed publications and a 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 2012 was 132.

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

- Notable events in 2012

Publications in high ranking journals. Outstanding contributions for the year 2012 are publications in relatively high ranking biomedical journals, i.e. Nucleic Acids Research, Cytokine & Growth Factor Reviews, Annals of Surgery, British Journal of Psychiatry and Allergy, four journals with an impact factor higher than 6 and one journal, Nucleic Acids Research, higher than 8.

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 208 scientific papers in refereed journals, of which 193 in journals with an impact factor (SCI journals). 53% of these 193 papers appeared in journals belonging to the field “Dentistry, Oral Surgery and Medicine”. 20% of all publications were in the top 10% of the journals, 43% in the top 25% and 81% 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 considerable number of ACTA employees rank in the top of the dental and biomedical research community, as determined by the various indicators of esteem, such as editorships, invited lectures, and congresses organised. In 2012 a total of 21 awards were received by ACTA scientists for their achievements. For more details we refer to the description of the two research programs.
Table 2. Percentage of publications in different quartiles of dentistry and non-dental journals

<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>25%</td>
<td>13</td>
</tr>
<tr>
<td>Quartile 1</td>
<td>43</td>
<td>42%</td>
<td>33</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>37</td>
<td>36%</td>
<td>35</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>13</td>
<td>13%</td>
<td>17</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>10</td>
<td>10%</td>
<td>5</td>
</tr>
<tr>
<td>total</td>
<td>103</td>
<td>100%</td>
<td>90</td>
</tr>
</tbody>
</table>

- assessment at the program level

When the research at the program level is considered, both programs perform in general equally well in terms of most input and output parameters (personnel, PhD students, publications, dissertations etc); 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>5</td>
<td>119 (58)</td>
<td>10</td>
<td>95</td>
<td>6</td>
<td>281</td>
<td>19,10</td>
<td>6,05</td>
<td>8,05</td>
<td>33,20</td>
</tr>
<tr>
<td>ORM</td>
<td>9</td>
<td>98 (60)</td>
<td>4</td>
<td>40</td>
<td>5</td>
<td>224</td>
<td>20,15</td>
<td>3,35</td>
<td>9,20</td>
<td>32,70</td>
</tr>
<tr>
<td>OWI</td>
<td>-</td>
<td>3 (2)</td>
<td>-</td>
<td>11</td>
<td>1</td>
<td>4</td>
<td>0,30</td>
<td>-</td>
<td>0,35</td>
<td>0,65</td>
</tr>
<tr>
<td>ACTA*</td>
<td>13</td>
<td>208 (117)</td>
<td>14</td>
<td>132</td>
<td>12</td>
<td>493</td>
<td>39,55</td>
<td>9,40</td>
<td>17,60</td>
<td>66,55</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 2011 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>12.20</td>
<td>2.60</td>
<td>3.45</td>
<td>6.90</td>
<td>3.45</td>
<td>1.65</td>
<td>33.20</td>
</tr>
<tr>
<td>ORM</td>
<td>12.05</td>
<td>1.45</td>
<td>4.45</td>
<td>8.10</td>
<td>1.90</td>
<td>5.35</td>
<td>32.70</td>
</tr>
<tr>
<td>OWI</td>
<td>0.30</td>
<td>-</td>
<td>0.35</td>
<td>-</td>
<td>-</td>
<td>0.20</td>
<td>0.65</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>24.55</strong></td>
<td><strong>4.05</strong></td>
<td><strong>8.25</strong></td>
<td><strong>15.00</strong></td>
<td><strong>5.35</strong></td>
<td><strong>9.35</strong></td>
<td><strong>66.55</strong></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 organisations (61 international functions), as members of editorial boards of scientific journals (77) 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 organisation of symposia and conferences in the Netherlands and abroad, presentations for dentists, medical specialists and patient groups, memberships of advisory councils, and frequent contacts with the industry. In addition many scientists are also practising as dentists in specialized clinics at ACTA or in the Amsterdam region. Obviously the societal impact of their activities, individually as clinically active professionals and leading among their peers, should be acknowledged. The societal impact is also evident from the relatively large number of 134 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 2012 ACTA researchers have again contributed actively in internationally held meetings, workshops and symposiums, both as organisers and participants. A total of 120 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 7 international meetings were organised by ACTA scientists.
Annual Research Report 2012

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€ 948 is used for the management of the institute, the salaries of PhD students and post-doctoral employees, for travel allowances for these groups, for the organization of courses and for the annual two day IOT research meeting.
The research budgets for the departments (in total being k€ 3616) 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€ 1357, and the total amount of research contracts (3rd source) was k€ 1790.

• personnel
The directorate of the institute comprises:
prof.dr. V. Everts, director of research 0.4 fte
dr. T.J.M. van Steenbergen, co-ordinator of research 0.6 fte
mrs. F.M. Meijer, secretary 0.6 fte
mrs. M.H.G. Piek-Backer, secretary 0.4 fte

The activities of the research institute directorate consist of organising scientific meetings with presentations of PhD students, the screening of new research projects, the day-to-day interaction with graduate students on practical matters regarding their position, compiling the annual research report, the planning of graduate courses, allocating budgets for research to the departments, controlling the institutes budget and dealing with general correspondence on research issues with UvA, VU etc.

PhD students
The ACTA PhD training program is organised 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 2012. In Figure 2 the number of new PhD students at ACTA is shown in the years 1990 to 2012. Over the years, about 23 % of all PhD students had a foreign nationality, about half of them from Europe, the rest from other continents. A mean number of 9 new PhD students were appointed per year. Despite budget restrictions 14 new PhD students, many of them part-time, could be appointed in 2012. 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 2012 five new PhD students were appointed on grants awarded to the research themes in an open competition. Both the open competition and the grants for talented students or post-docs will be continued in the coming years, however due to budget reductions, in a limited number.
Figure 2. 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>
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<td></td>
<td>Dutch</td>
<td>other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OII</td>
<td>17</td>
<td>14</td>
<td>17</td>
<td>4</td>
<td>13</td>
<td>7</td>
<td>72</td>
</tr>
<tr>
<td>ORM</td>
<td>9</td>
<td>10</td>
<td>10</td>
<td>-</td>
<td>19</td>
<td>14</td>
<td>62</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>28</td>
<td>24</td>
<td>27</td>
<td>4</td>
<td>32</td>
<td>21</td>
<td>136</td>
</tr>
</tbody>
</table>

Oil = Oral Infections and Inflammation
ORM = Oral Regenerative Medicine
OWI = Education Institute and other research

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

- **PhD thesis duration and completion rate**
  Attention has been paid to the problems related to the social security benefits of PhD students and the time that PhD students need to finish their thesis. The mean time of 4.6 years between start and defence of the thesis within ACTA is lower than the mean duration of PhD theses in research schools in the Netherlands of 5.1 years (see the report “Rendement en duur van promoties in de Nederlandse onderzoekscholen”, Oost en Sonneveld, 2004). In addition, the mean duration of preparing a thesis shows a slightly declining tendency over the years (Figure 3).
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 noted in 2008 that they were impressed by the organisation and practice of PhD training and supervision at ACTA. They concluded that it is a well organised programme, with a remarkably high dissertation rate.
Points of attention

- **HRM and retirement**
The research staff at ACTA has been comparatively young in the last decades. This was the result of the merging of the dental schools in the mid 1980’s. Now we are in a situation where heads of departments and senior scientists are retiring. Due to budget restrictions the number of persons involved in research on university (1st source) had to be reduced slightly. Fortunately, the fte scientific personnel on grants (2nd and 3rd source) increased in 2012. Both research priority areas received a substantial grant from the UvA, resulting in an increased 1st fte on 2012.

- **new building in 2010**
In 2010 ACTA moved to a new building located at the VU campus; this brought together groups that were spread out over the city at four different locations. Optimal research facilities at the new ACTA building are available to encourage collaboration between the research groups that require laboratory facilities. The increased number of scientists at one location facilitates to jointly take initiatives, such as in molecular aspects of dental research.

- **future developments**
Within the Netherlands, graduate schools are formed at a local level to integrate research training of both Master and PhD students. In 2007 the responsibility for PhD training at ACTA was transferred from the IOT to the ACTA Research Institute. In 2010 the new ACTA Graduate School of Dentistry (AGSD) was formally installed.

The research at ACTA has always been characterized by a wide range of different topics that covered most dental disciplines. The present policy is to focus on the two specific research areas with an excellent performance. Collaboration will be increased in the interfacultary research institute MOVE, a collaboration between ACTA, the VU University Medical Center and the faculty of Movement Sciences at the VU University Amsterdam. In coming years the research budget from the 1st source (University budget) might be seriously diminished due to budget restrictions. It will be a big challenge to compete for 2nd and 3rd source grants and to maintain or improve the high output that ACTA has produced in the past.

**Conclusion**
The analysis of the various parameters of performance shows that the research at ACTA is, despite of budget restrictions, increasingly improving. Future performance will be dependent among others from the success in obtaining 2nd and 3rd source grants.
Oral Infections and Inflammation

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G.A. van der Weijden

Introduction
Oral Infections and Inflammation
Oral health is an essential part of the general health of each person during his or her lifetime. Poor oral health, oral infections and inflammation, oral cancer and untreated oral diseases can lead to major health risks such as an increased risk of heart disease, cancer and cancer dissemination, systemic chronic infections and vital organ failure. Poor oral health leads to a lower quality of life and economic hardship.

The oral cavity is one of the most infected parts of the body. Most people are completely healthy while thousands of species of microorganisms thrive in their mouth while some develop oral diseases. This research theme of ACTA is involved in (i) many aspects of oral infections and inflammation, (ii) prevention of those, and (iii) understanding the health of the oral cavity as a complex ecosystem, with applications far beyond the oral cavity alone.

Translational research and understanding of the functioning of the healthy state of the oral cavity are giving promising perspectives on both new cost-effective prevention programs for the population as well as economic and social spin-off product-innovations in the food sector, 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.

In the past years, we have gone through a transition period: the process of integration and subversion of various areas of expertise towards a common theme with clearly more focus and mass: the research priority area “Oral Infections and inflammation”. Our group has demonstrated the international prominence of ACTA in the field of oral health and has acquired a global leadership role in the emerging field of complex ecosystems such as the oral cavity; thus understanding oral infections, inflammatory processes, oral cancer and the definition of a normal, healthy oral cavity including psychosocial factors. We have been awarded a 5 year 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 researchwork in 2012).

Research objectives
Important aspects of the central theme have been studied, in essence with half the scientific community of ACTA, on integrated research areas. These can be grouped as preclinical and clinical objectives.

Preclinical objectives
An important area concerns the physico-chemical, biochemical and microbiological aspects of enamel, dentin, dental caries, and infections of the root canal system. The formation, structure and properties of oral and dental biofilms are studied extensively. These aspects are studied by means of various in vitro models which simulate the natural processes in the oral environment and which are designed to evaluate the effects of preventive measures and restorative materials and procedures, thereby covering the field of research from the molecular level up to ex vivo studies.

Fluoride that, at present, is still the most effective caries-preventive agent is subject of study. Research is aimed at a better understanding of its mode of action, also on the molecular level towards microbial metabolism, as well as its possible side effects. In addition to fluoride, antimicrobials have come into focus as caries preventive agents. The efficacy alone or in combination with fluoride is still unknown and application protocols are not yet based on a critical evaluation of experimental and clinical results. The success of antimicrobials in caries prevention is still limited.

Modified desinfection methods of the root canal system are studied. New filling methods and contemporary adhesive systems are tested in in vitro leakage models and in clinical studies.

The biological functions of the salivary (glyco) proteins are studied and the variation in glandular (glyco) proteins from the submandibular, sublingual and parotid glands. Furthermore there is focus on the biological significance of the whole set of salivary proteinase inhibitors. Synthetic peptide analogues of salivary histatins as broad spectrum antibiotics are developed, particularly to Candida albicans and other selected oral pathogens. Influence of saliva on the interaction of oral microorganisms with oral epithelial cells and the in vitro wound healing capacities of salivary components are measured.

Clinical objectives
Several studies into pre-caries and dental erosive lesions involve the role and characteristics of enamel, dentin, and the effects of fluoride, foods and candy. Research is aimed to obtain an in-depth modern insight in the commensal and pathogenic microflora of the oral cavity, oral infectious processes and diseases, including caries, gingivitis, periodontitis and peri-implantitis, and its interactions with host cells. A major clinical study to this end has been started in 2012 (to be continued in 2013) with healthy subjects aged 18-30, to define the “normal” oral cavity. Individual characteristics and specific dental and periodontal characteristics are being recorded. Moreover this has been combined with salivary, blood and plasma parameters, dietary habits and psychosocial factors.

Better treatment concepts of dental caries in children are studied, both preventive as well as conservative and in relation to behaviour management. These concepts include ART (Atraumatic Restorative Treatment), the influence of total rehabilitation of the children’s dentition on general and oral health, and consequences of restorative treatment on the child’s coping and anxiety.

To study the susceptibility to periodontitis, questions are addressed on the relative role of genetic, environmental and life style factors in the overall initiation and progression of periodontal diseases. Common disease genes are now specially in focus, and various mathematical models to describe the disease have been developed.
Systemic effects of oral infections are still an important topic. Periodontitis is epidemiologically associated with atherosclerotic forms of cardiovascular diseases (ACVD). We study possible causal relationships to explain this association and the effects of periodontal intervention studies on ACVD biomarkers. And vice versa, which are the effects of the treatment of periodontitis in patients already having ACVD or diabetes. Studies are conducted on the prevention and treatment of gingivitis, periodontitis, and peri-implantitis. These involve the most effective measures to prevent and control oral health including substantial efforts to reach clinical standards for evidence based dentistry.

The effect of conditions known for their potential to impair oral health (such as the use of medical drugs, systemic diseases and psychological stress) on the quality and quantity of saliva is studied. Oral health-related well-being and behaviour is studied in dental patients. We aim to improve and to maintain the well-being of both regular dental patients and subgroups of patients suffering from (extreme forms of) anxiety or (anticipated) pain or from physical/mental handicaps. Moreover, since the well-being of patients is highly dependent on the treatment they receive from dental professionals, our efforts are also aimed at these dental professionals, lowering stress levels and preventing burnout, helping them in communicating adequately with their patients.

Forms of oral cancer, precursor lesions of oral cancer, particularly leukoplakia, odontogenic tumours and salivary gland tumours are studied. Amongst others, the prognostic value of molecular markers is examined with regard to the malignant transformations. A study on peri-implantitis, implant loss and osteoradionecrosis after irradiation in oral cancer patients focuses on the (long) term complications after oral cancer treatment. A study on the effect of a low intensity laser on intra oral radiation mucositis has been started and participation in a multicenter study to predict clinical outcomes after orofacial tumour resection has been initiated. This last project is a collaboration with AVL/NKI, UMCN and the University of Twente.

Clinical outcome studies of root canal treatments in infected root canals using an innovative approach with 3D CBCT scans could give valuable information on different disinfection protocols.

Results obtained in 2012

Preclinical studies

- Studies are ongoing on antimicrobial peptides derived from salivary peptides, to combat a variety of pathogens. This are important and novel alternatives for conventional antibiotics. Variants of lactoferrin, a salivary protein i.e. lactoferricin, lactoferrampin and a peptide composed of a combination of both peptides (Chimera), were studied for their antimicrobial and antymycobial activity and toxicity.
- Effects of salivary peptides on oral soft and hard tissue cells are studied. Since LL-37 deficiency has been related to aggressive periodontitis, the effect of LL-37 on osteoclastogenesis was studied. It was found LL-37 indeed exerts an inhibitory effect on in vitro osteoclastogenesis, as evidenced by the inhibition of a number of processes including formation of multinucleated cells and TRAP expression.
- Bacterial proteases play an important role in a broad spectrum of processes, including colonization, proliferation, and virulence. In this respect, bacterial proteases are potential diagnostic biomarkers for bacterial diagnosis and targets for novel therapeutic protease inhibitors. To investigate these potential functions, we designed and used a protease substrate fluorescence resonance energy transfer (FRET) library comprising 115 short d- and l-amino-acid-containing fluorogenic substrates as a tool to generate proteolytic profiles for a wide range of bacteria. Bacterial specificity of the D-amino acid substrates was confirmed using enzymes isolated from both eukaryotic and prokaryotic organisms. Overall, the specific characteristic of our substrate peptide library makes it a rapid tool to high-throughput screen for novel substrates to detect bacterial proteolytic activity.
- Next-generation sequencing (NGS) technologies enable deep microbiome profiling. However, selecting the right gene region for sequencing is important. We therefore developed TaxMan: a web-based tool that trims reference sequences based on selected primer pairs, and returns an assessment of primer specificity, allows taxa plotting, and improves sequence matching algorithms speed. http://www.ibi.vu.nl/programs/taxmanwww/. We further found that, for clustering oral microbial sequence data, pre-processing steps by both denoising and chimera checking led to best cluster accuracy.
- Interactions between oral microbes, and microbes and host, are crucial in disease development. Host-P. gingivalis interactions play an important role in periodontitis. We showed that encapsulated as well as non-encapsulated P. gingivalis invade host cells, and thereby resist in vitro antibiotic treatment.
- Cariogenic biofilms may be influenced by the introduction of fluoride, some chemical agents or probiotic bacteria. Using an Active Attachment Biofilm model, we found that the probiotic bacterium L. Rhamnosus GG (LGG) established in saliva-derived microcosms and reduced S. mutans counts significantly, but did not
Clinical studies

- We initiated several clinical studies applying new molecular open-ended techniques, which do not preselect for certain species, to study the composition of occlusal and supragingival dental plaque, the cariologic microbiota, the subgingival microbiota in periodontal health and disease, the microbiology of endodontic infections. All dental plaques are much more complex than previously thought. Clearly, results point to new, non-cultivable, fastidious species and these are now recognized also to associated with infectious processes in the oral cavity. Interestingly, we investigated the salivary Candida abundance relative to the bacterial load: microbiomes with high Candida load were less diverse and appeared dominated by saccharolytic, acidogenic streptococci.

- In oral infections, interactions between oral pathogens and host cells are crucial in the development of disease. We showed that periodontal fibroblasts from patients appeared more prone to recognize and respond to the periodontal pathogen *P. gingivalis*, and that cells from *P. gingivalis* culture-positive persons responded more strongly to *P. gingivalis* than cells from *P. gingivalis*-negative persons.

- We expand our salivary diagnostic capabilities. From the the knowledge on detecting bacterial enzyme activity of *B. anthracis* in vivo, we investigate in parallel, specific substrates for *P. gingivalis*. Using these substrates we have been able to detect the presence of *P. gingivalis* in saliva and crevicular fluid within minutes, without the need for sample pre-treatment or enzyme isolation. This was tested in health, periodontitis and peri-implantitis.

- Oral microflora may be involved in oral mucositis, a side effect of hematopoietic stem cell transplant (HSCT). We investigated the relationship between oral ulcerations and bacterial species, Candida, and viruses. Oral rinses from HSCT patients were assessed for microbial presence by real-time PCR, which revealed that mainly *P. gingivalis*, and *P. micra, T. denticola, F. nucleatum, C. glabrata, C. kefyr*, and HSV-1 and EBV may play a role in ulcerative oral mucositis. Furthermore HSV-1 is a predictor of ulcerations of oral mucosa following HSCT.

- We continued genetic studies in periodontitis and reviewed the literature. Genetic studies of aggressive periodontitis showed that TLR2 gene variants cannot be considered as a candidate gene.
The life style factor diet, in particular vitamin C and fruit supplements, is becoming more and more a part of our focus. In a clinical study we found lower vitamin C plasma levels in periodontitis, but intracellular stores of vitamin C are not different between patients and controls.

Studies have been performed to systematically evaluate the clinical evidence with respect to the effect of chewing gum on oral health, mouth rinses and bad breath, toothbrush design on plaque removal and various mechanical instruments on the cleaning of dental implant surfaces. The results show that the use of sugar-free chewing gum as an adjunct to toothbrushing provides a small but significant reduction in plaque scores. The most compelling evidence was provided for chlorhexidine mouthwashes, and those that contained a combination of cetyl pyridinium chloride and zinc provided the best evidence profile on oral malodor. The available evidence indicates that bristle tuft arrangement (flat trim, multilevel, angled) contributes to the variation in observed efficacy.

Several projects have focused on evidence based dentistry related to the prevention and therapy of periodontal diseases and oral halitosis. After validation experiments in assessing oral malodour by organoleptic measures and by using the oral chroma and halimeter, we performed a clinical study assessing the effect of the drinking of a glass of water or the rinsing with water on morning bad breath. Both interventions have an impact on oral malodour outcomes. Using a representative sample from the Dutch population, we examined some psychosocial aspects of halitosis. The results showed that almost 90% of the Dutch population aged 16 years and older were regularly faced with halitosis.

A clinical trial was performed on caries-preventive properties of shiitake mushroom, in which volunteers rinsed with a solution of shiitake fractions, placebo, or active caries inhibitory rinse (Meridol®). Plaque, acidogenicity, and microbial composition were determined. Rinses with shiitake reduced metabolic activity of plaque, but not plaque scores or acidogenicity, indicating an anticariogenic effect of shiitake extract but less potent than Meridol®.

Dental treatment of young children is difficult and sometimes children are referred to a specialist pediatric dentist. Parents of non-referred and referred paediatric dental patients were asked to fill out the Child Rearing Practices Report (CRPR) and the Child Fear Survey Schedule Dental Subscale (CFSS-D5) on behalf of their children. Results show that referral status and dental anxiety of 4-12 year old children were not associated with parental rearing style.

The association between complete absence of post-treatment periapical lesion and the quality of root canal filling was studied with a clinical study in cooperation with the Peking University in Beijing China. This is one of two studies we conducted on the healing of periapical periodontitis. These studies are important in that for the first time 3D CBCT scans are utilized for most higher resolution.

Human papilloma virus (HPV) is present squamous cell carcinomas of the oropharynx. We studied the epidemiology and have shown that the incidence of HPV related tumors is increasing over the last 20 years. In general, the prognosis of HPV positive carcinomas is better than the HPV negative tumors. A prognostic model was developed in which patients were classified into three risk groups according to HPV-status, nodal stage and comorbidity. The concept of the sentinel biopsy in staging oral cancer has been demonstrated and validated in a large multicentre trial. To firmly establish the diagnosis of oral leukoplakia the histopathological examination of (part of) the lesion should be included. It was shown that DNA ploidy can be of prognostic value in the progression of oral leukoplakia.

There is 40-years experience with the treatment of ameloblastomas. Retrospective study showed that in none of the patients treated by radical surgery a recurrence was observed with a mean follow-up period of 10.5 years. In 50% of patients treated by enucleation only a recurrence developed in an average period of five years. The histological subtype of ameloblastoma did not influence the treatment outcome. This also applied to the unicystic type.

We are further exploring oral health-related quality of life in people addicted to alcohol or other drugs. If people do not perceive to have oral problems, they will likely not comply with dental treatment and advice.

The well-being of oral surgeons and other dental staff was assessed, looking at levels of burn-out, job demands and general psychological distress. One quarter of the dental professionals were categorized as having a serious burnout risk. Dentists appeared to have most trouble with work environment aspects: time pressure and financial worries.

Studies are ongoing on the efficacy of eye movement desensitization and reprocessing (EMDR), a trauma-focused intervention method. EMDR appeared to be effective in post-traumatic stress disorder (PTSD) symptom severity, and led to a significantly faster recovery than those who received brief eclectic psychotherapy.
In collaboration with TNO, ACTA once again reported on child dental health in the Netherlands, based on a large scale epidemiologic study that was funded by the Dutch Health Insurance Counsel (TZ report). It appeared the oral health of children was better in 2011 than in 2005, but that there still is much room for oral health improvement. The Dutch minister of health has expressed her appreciation of our studies and committed to financing further studies in this area.

### Academic personnel in 2012 and 2013

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<thead>
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<th>Research staff ACTA – OII (Oral Infections and Inflammation)</th>
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<td>Full professors</td>
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<td>Bloemena, prof.dr. E.</td>
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<td>Cate, prof.dr. J.M. ten</td>
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<td>Senior lecturers</td>
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<td>Other lecturers and tenured research staff</td>
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<td>Aartman, dr. I.H.A.</td>
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<td>Allard, mr.dr. R.H.B.</td>
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**Other lecturers and tenured research staff**

**PhD students**
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### Output

#### Dissertations


**Weijers, M.** (2012, October 29). Oral squamous cell carcinoma; some epidemiological and clinicopathological aspects. VU University Amsterdam (93 pag.). Prom./coprom.: prof.dr. I. van der Waal.

#### Scientific publications (referred)


Tariq, M., Bruijs, C., Kok, J. & Krom, B.P. (2012). Link between culture zeta potential homogeneity and Ebp in Enterococcus faecalis. Applied and Environmental Microbiology, 78(7), 2282-2288.


Scientific publications (non-referred)


Professional Publications


Publications for the general public


Patents


Indicators of Esteem

Grants: current projects with external funding


Bloemena, E. ICTO grant: Meer (web)micro. € 10.000

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

Cate ten J.M. ten, Crielaard W., Soet J.J. de & Loveren C. van STW project. Seeing is believing. M.H. van der Veen & C.M.C. Volgenant . Start October 2010 - October 2016, € 500.000,-


Crielaard, W., Preventive Dentistry, Periodontology, Oral Biochemistry, Cariology,, TIFN Oral Health (2012-2016): Public Private Partnership funded by the Dutch Ministry of Economic Affairs, Wrigley, Philips Research, Gargill, GlaxoSmithKline, TNO, WUR & ACTA (Total investment 5.2 M€).


Exterkate, R.A.M. & Cate, J.M. ten. Short report on the anti-bacterial effect of 4 test rinses in an Active Attachment Biofilm model. GABA, Switzerland €15.000.

Exterkate, R.A.M. & Cate, J.M. ten. Short report on the anti-bacterial effect of 6 test rinses in an Active Attachment Biofilm model. GABA, Switzerland €15.000.


Krom, B.P. Interspecies interactions as targets to fight burnwound infections, Nederlandse Brandwonden Stichting, € 194.162,00, start 01-09-2012, end 31-8-2014.

Laheij, A.M.G.A., Loveren, C. van, Soet, J.J. de & Balm, A.J. (Netherlands Cancer Institute/Antonie van Leeuwenhoek Hospital). Prospective study of changes in the oral biofilm and the protein composition of saliva in patients, being irradiated for a tumour in the head-and-neck area. GABA International AG. Dept. Scientific Affairs, Therwill, Switzerland.


Loos, B.G. “Microbiome of periimplant sulcus/pocket: A pyrosequencing study on the microflora of periimplant health and disease” (2011-2012). A grant by the Deutsche Gesellschaft fur Parodontologie, € 50,000.-

Loos, B.G. “Oral health” (2011-2015) University of Amsterdam/focuspoint. Joint effort Prof.dr J.M. ten Cate, prof. W. Crielaard, Prof. dr. B.G. Loos, Prof. dr. E. Veerman. Dept. of Conservative and Preventive Dentistry, ACTA. €1,308,000.-

Loos, B.G. “Regenerative surgical treatment of peri-implant osseous defects - a multicenter randomized prospective clinical study” (2011-2012) A grant supplied by Tigran AB, Sweden, € 20,000.-


Matse, J.H. Rene Vogels reisbeurs € 2400 and KWF Reisbeurs voor Academici € 2100 of a project between 01/01/2012 - 16/3/2012.

Schoonheim-Klein, M.E. NIH (2011-2016) in cooperation with Harvard, UCSF and Creighton US$ 100.000,-.


Strijp van A.J.P., Extraction of intra-oral plaque samples by wearing an in situ device. Philips Research, the Netherlands. March 2011- April 2012. € 5.000,-

Veen van der, M.H. & Kaaij van der N.C., The use of fluoride rinse for caries prevention during the orthodontic treatment with fixed appliances. GABA. Start August 2009-december 2012, €180.000,-.


Wesselinck, P.R., Ministry OCW € 850.000,-. Simodont project for three years 2008-2010. Extended till 2013 by decision of OCW in October 2011.

Book editorial


Membership of international editorial boards

Bloeumen, E.: ISRN Gastroenterology.
Bonifacio, C.C.: APCD journal.
Cate, J.M. ten: Chinese Journal of Dental Research.
Cate, J.M. ten: European Journal of Oral Sciences.
Cate, J.M. ten: International Journal of Dentistry.
Cate, J.M. ten: Journal of Dental Research.
Cate, J.M. ten: Journal of Oral Microbiology.
Cate, J.M. ten: Odontology.
Crielarda, W.: Microbiology - SGM.
Gorter, R.C.: European Journal of Dental Education.
Jongh, A. de: Journal of EMDR Practice and Research.
Loos, B.G.: Journal of Dental Research.
Raber-Durlacher, J.E.: Mediterranean Oncology Journal.
Raber-Durlacher, J.E.: Supportive Care in Cancer.
Raber-Durlacher, J.E.: Mediators of Inflammation, special issue Alimentary Mucositis: Mediators, Mechanisms and emerging therapies.
Schoonheim-Klein, M.E.: European Journal of Dental Education.
Waal, I. van der: Journal of Dentistry University of Sao Paolo.
Waal, I. van der: Medicina Oral.
Waal, I. van der: Minerva Stomatologica.
Waal, I. van der: Oral Oncology.
Wesselink, P.R.: Deutsche Zahnärztliche Zeitschrift.
Wesselink, P.R.: Endodontic Practice Today.
Wesselink, P.R.: Endodontie.
Zaura, E.: Caries Research.

Invited speakers at international congresses or symposia
Cate, J.M. ten (2012, February 14). Diversity in dental biofilms. Chicago, USA, MARS.
Cate, J.M. ten (2012, April 17). Fluoride and biofilms. Weybridge, UK, GSK.
Cate, J.M. ten (2012, September 14). How tooth structure and its associated biofilms are modified by age, erosion and attritional wear. Helsinki, Finland, Symposium IADR PER.
Cate, J.M. ten (2012, September 06). Remineralization through biofilms. Chicago, USA, Wrigley Oral Care.
Cate, J.M. ten (2012, October 15). The dental plaque biofilm, a new target for prevention of oral diseases. Chengu, China, West China School of Stomatology.
Cate, J.M. ten (2012, January 05). The numerous microbial species in oral biofilms: how could antibacterial therapy be effective? Vina del Mar, Chile, ICNARA2.


Rosema, N.A.M. (2012, June 08). Toothbrushes to improve gingival health- what advances have been made? Vienna, Austria, Euro Perio.


Weijden, G.A. van der (2012, June 07). 1. Interdental oral hygiene, the evidence. 2. Mouthrinse, the evidence. Vienna, Austria, European Federation of Periodontology (EFP), EuroPerio VII.


Weijden, G.A. van der (2012, July 06). Interdental oral hygiene, the evidence. Stuttgart, Germany, Summer-Academy FZ.


Wesselink, P.R. (2012, June 15). 1. What have we achieved the last 20 years. 2. What will we achieve the coming 20 years. Berlin, Germany, 25 Jahre Endodontie, Quintessenz Symposium.


Membership academies
Cate, J.M. ten (2008, January 01 - 2013, December 31). Academy professor. Royal Netherlands Academy of Arts and Sciences (KNAW).

Scientific awards/honours

Cate, J.M. ten (2012, February 01). Honorary professor. West China School of Stomatology.


Organisation of international congresses and symposia


Cate, J.M. ten (2012, January 02). Organizing committee. International Conference on Novel Anticaries and Remineralizing agents ICNARAA2: Chile.


Other international functions


Bolscher, J.G.M.: Co-investigator of research project on the "Inhibition of Burkholderia pseudomallei" biofilm formation by the Lactoferrin peptide LFchimera. Principal Investigator: prof.dr. S.Taweelahpsapong Department of Oral Diagnosis, Khon Kaen University, Thailand.

Brandt, B.W.: Invited opponent at thesis defense Departamento de Tecnologías del Medio Ambiente, Universidad de Cádiz.

Cate, J.M. ten: Honorary professor Universidad Peruana Cayetano Heredia, Lima, Peru.

Cate, J.M. ten: Honorary professor University of Hong Kong, China.

Cate, J.M. ten: Member advisory panel Wrigley Science Institute, Chicago, USA.


Krom, B.P.: Reviewer Atip-Avenir Programme, April, France.


Loos, B.G.: Invited expert at the IXth European Workshop in Periodontology. Theme: 1st Joint EFP/AAP workshop on periodontal and systemic diseases EFP (European Federation of Periodontology) and AAP (American Academy of Periodontology), La Granja, Madrid, Spain.

Loos, B.G.: Opponent of M. Yakob with the PhD thesis “Associations between oral biofilm, periodontal disease, and systemic health; with focus on atherosclerosis and breast cancer”, February 13, 2012 Karolinska Institute of Odontology and University of Helsinki, Faculty of Medicine, Stockholm, Sweden.

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

Raber-Durlacher, J.E.: Editorial consultant Mediterranean Oncology Journal.

Raber-Durlacher, J.E.: Board member Multinational Association for Supportive Care in Cancer (MASCC).

Schoonheim-Klein, M.E.: Chair Advisory committee the excellence in Dental Education Advisory Committee (EDEAC).
Schoonheim-Klein, M.E.: External examiner Dental School, Trinity College, Dublin, Ireland
Shemesh, H.: Country representative European Society of Endodontology, General assembly meeting, Barcelona, Spain.
Soet, J.J. de: Membership secretary and webmaster European Organization for Caries Research (ORCA).
Veen, M.H. van der: Past president Diagnostic Sciences Group, International Association for Dental Research (IADR).
Veen, M.H. van der: Secretary general European Organization for Caries Research (ORCA).
Veen, M.H. van der: Honorary lecturer University of Liverpool, UK.
Velden, U. van der: Chairman postgraduate education committee European Federation of Periodontology (EFP).
Velden, U. van der: Executive board member European Federation of Periodontology (EFP).
Waal, I. van der: Member scientific committee STOMA.
Weijden, G.A. van der: Board member Advisory board DentalCare.com.

Supervisor of an external PhD student
Krom, B.P.: Supervisor of external PhD student Jarosz with thesis: "Molecular unracling of interspecies crosstalk". Supervisor: Prof.dr. H.C. van der Mei University Medical Center Groningen, the Netherlands, 2012, February 01.

Societal impact
Oral infections, in particular caries, root canal infections and periodontal diseases, have a substantial impact on the society. They are the most frequent infections in the western society and have important consequences, both medically and economically. The general aim of the program is to understand the normal healthy oral cavity and thus to better understand the causes and circumstances of the oral infections, to investigate preventive measures, and to develop treatment strategies. The program also contains research projects on oral cancer and precancerous lesions. In addition, attention is paid to social and psychological aspects of dental treatment, such as dental anxiety, a condition which, if not treated properly, automatically develops into a self-reinforcing spiral of negative thoughts, avoidance, tooth decay, oral infections, and pain. We are currently investigating the effectiveness of a range of treatment methods to alleviate people’s fear and anxiety responses and to improve quality of life. We focus on measuring the patient’s perception and valuation of their oral health, since evidently these are major drivers of oral health care consumption.
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. Interestingly, 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.

Our finding that salivary peptides promote wound healing has attracted much attention and interest from industry to apply these peptides, which have been patented by us, for healing of chronic wound and skin burns. The role of saliva as a medium for non-invasive diagnostics is internationally a “hot topic”.

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 burden of dental caries in young Lao children is high. As a result, these children suffer from toothache, and school absenteeism is very common. ACTA researchers helped to develop strategies on dental health care.

Likewise, ACTA researchers evaluated the gingival health in young children in Burma, who participated in a school-based toothbrushing programme. Also sodium fluoride toothpaste were collected in various countries and the fluoride content was assessed. All samples from the Netherlands complied with ISO labelling requirements and there were no differences between the fluoride content declared and that found to be present on analysis. In samples purchased in various other countries, sodium monofluorophosphate toothpastes predominantly showed a low percentage of free available fluoride and the majority of toothpastes did not follow standard labeling guidelines. These results have big societal impact beyond The Netherlands and contribute to our role in helping developing countries.

Interactions and collaborations with the industry and other non-university groups
Several collaborations exist with the industry, evident from grants obtained over the years from among others Philips, Proctor & Gamble, Gaba (Colgate); see the list of current grants in the paragraph of indicators of esteem above.

In addition the following interactions can be mentioned:
Shemesh, H. In relation to the STW project with Satelec, ACTEON group, Mergignac, France.

In addition the following advisory functions can be mentioned:
Cate, J.M. ten; Wrigley Science Institute, member Advisory panel, 2010-2013.
Loveren, C. van; Advisory function for the Dutch Consumers Organization and the Dutch Dental Association about free dental care fees.

Interactions with the general public
Several scientists had interviews with the Dutch general press in journals, radio and television or wrote papers for the general public. More details are listed below.
Eijkman, M.A.J; Four articles for the general public in the Dutch newspaper NRC (see also the paragraph on Publications for the general public)
Jongh, A. de; One article for the general public in Folia Magazine.
Strijp, A.J.P. van; Zo zorg je voor een stralende lach zonder gaatjes. Interview J/M Ouders.

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 patient treatment related to the sub-programme Oral and Maxillofacial Surgery were adopted by the Dutch Society for Oral and Maxillofacial Surgery. Several scientists of the program had interviews in Dutch dental Journals. A total of 95 professional publications were written. In addition, the following items can be mentioned:
Krom B.P. (2012, August) Interview Nederlands Tijdschrift voor Wondzorg, nr. 8: 10-11, NTVW.
Shemesh, H. Richtlijn gebruik van CBCT in tandheelkunde, Endodontologie – NMT.
Strijp, A.J.P. van (2012, September 21). “Niets is zo moeilijk als gedragsverandering”. Dental Tribune

Warnsinck, C.J. Richtlijn aangezicht pijn – Nederlandse Vereniging voor Endodontologie (NVvE), Amsterdam, the Netherlands.

Weijden, G.A. van der (March 2012). “Nazorg van implantaten”, College van adviserend tandartsen, Zeist, the Netherlands.


Organisation of national congresses and symposia


Jongh, A. de Organizer 5 symposia.

Shemesh, H. Lustrum congress Nederlandse Vereniging voor Endodontologie (NVvE), Amsterdam, the Netherlands.


Memberships of national editorial boards

Brand, H.S.: Nederlands Tijdschrift voor Tandheelkunde.

Loveren, C. van: Nederlands Tijdschrift voor Tandheelkunde.

Waal, I. van der: Nederlands Tijdschrift voor Geneeskunde.

Other national functions

More than 25 memberships of national committees and advisory councils can be mentioned. The following scientists were members of these committees: Allard, R.H.B., Bloemena, E., Loos, B.G., van Loveren, C., Shemesh, H., de Soet, J.J., van Strijp, A.J.P., Veerman, van der Velden, U., E.C.I., van der Waal, I., van der Waal, S.V., Wesselink, P.R., Wu, M.K.

Invited speakers at national congresses or symposia

More than 65 presentations were given for professionals at congresses and symposia in the Netherlands by the following scientists:


Courses organised for dental and medical professionals

Scientists of the program participated in courses in the Netherlands for dentists and oral hygienists. A total of 13 courses were given in the Netherlands for dentists, medical specialists and oral hygienists.


Lectures during courses for dental and medical professionals in the Netherlands

More than 45 lectures were given during courses for dentists, medical specialists and oral hygienists in the Netherlands.


Collaborations

- Advisory board DentalCare.com.
- AMC Research Landsteiner Laboratory, Academic Medical Center, Amsterdam, the Netherlands.
- AMC, Department of Biomedical Optics, Amsterdam, the Netherlands.
- AMC, Department of Electron Microscopy, Amsterdam, the Netherlands.
- AMC: Dept. of microscopy: dr. J. Stap.
- Bambodino Kinderpraktijk, dr. Gambon, Rotterdam, the Netherlands.
- Braun Oral Research (dr. P. Warren) Baltimore, USA.
- Charite University, Berlin, Germany.
- Charles Cobb, Department of Periodontics, School of Dentistry, University of Missouri-Kansas City, USA.
- Christof Doerfer, Clinic for Conservative Dentistry and Periodontology, Uniklinikum Schleswig-Holstein-Campus Kiel-Germany.
- Department Medical Microbiology and Infection prevention, Vrije Universiteit, prof.dr. C.M.J.E. Vandenbroucke-Grauls, Amsterdam, the Netherlands.
- Department of Clinical Epidemiology and Biostatistics, VUmc Amsterdam, the Netherlands.
- Department of Clinical Genetics, VUmc Amsterdam, the Netherlands.
- Department of Dentistry and Oral Hygiene and Department of Biomedical Engineering. Faculty of Medical sciences, University of Groningen, Groningen, the Netherlands. prof.dr. M.C.D.N.J.M. Huysmans.
- Department of Dermatology, Sint Antonius Ziekenhuis, Nieuwegein, the Netherlands.
- Department of ENT, Dental Ophthalmological, and Cervicofacial Sciences, University of Parma, Unit of Oral Pathology and Medicine, section of Odontostmatology, Parma, Italy.
- Department of Health Sciences, Kristianstad University, prof.dr. S. Renvert, Kristianstad, Sweden.
- Department of Informatics, VU University Medical Center, Amsterdam, the Netherlands.
- Department of Medical Microbiology and National Reference Center for Systemic Mycoses, University Medical Center Göttingen, Göttingen, Germany.
- Department of MicroArrayFacility, dr. T. Breit, Universiteit van Amsterdam, the Netherlands.
- Department of Microbiology, Ghent University, Dr. . S. van trappen and prof.dr. P. de Vos.
- Department of Oral and Maxillofacial Surgery and Maxillofacia Prosthetics, University of Groningen, prof.dr. B. Stegenga, Groningen, the Netherlands.
- Department of Oral and Maxillofacial Surgery, Leids Universitair Medisch Centrum, Leiden.
- Department of Oral Medicine, Carolina Medical Center, Carolina, USA.
- Department of Oral Surgery, University of Porto, Porto, Portugal.
- Department of Otolaryngology/Head and Neck Surgery, VUmc, Amsterdam, the Netherlands.
- Department of Pediatric and Social Dentistry, São Paulo State University (UNESP), Araçatuba, Brazil.
- Department of Prosthodontics and Periodontology, Dental School of Piracicaba, State University of Campinas, SP, Brazil.
- Deutsche Krebsforschungszentrum Division of Molecular Genome Analysis, Heidelberg (dr. C. End).
- Division of Biological Chemistry and Drug Discovery, School of Life Sciences, University of Dundee, Dundee, UK.
- EMEA Oral Health Advisory Council.
- Erasmus MC, Department of Medical Microbiology and Infectious Diseases, mw. W.E. Kaman-van Zanten, Willem van Wamel, Rotterdam, the Netherlands.
- Erasmus MC, Dept. of Biomedical Engineering, Rotterdam, the Netherlands.
- Faculty of Veterinary Medicine, dr. H. Booij-Vrieling, University of Utrecht, the Netherlands.
- Federal University of Paraiba, Joao Pessoa, Brazil.
- Gaba International Ltd. Therwil, Switzerland.
- Global Dental Hygiene Advisory Board.
- Hebrew University-Hadassh, dr. Davidovich, Jerusalem, Israel.
- Inspektor Research Systems BV, Amsterdam, the Netherlands.
- Institute of Computer Science, FORTH Vassilika Vouton, Heraklion, Greece, prof.dr. V. Moustakis.
- Josephine Bay Paul Center, Marine Biological Laboratory, Woods Hole, MA, USA.
- Karim M. Fawzy El-Sayed, Oral Medicine and Periodontology Department- Faculty of Dentistry- Cairo University- Egypt, Clinic for Conservative Dentistry and Periodontology, Uniklinikum Schleswig-Holstein-Campus Kiel-Germany.
- Laboral Diagnostics CV, Houten, the Netherlands.
- Laboratoire de Sonochimie des Fluides Complexes; Institut de Chimie Séparative de Marcoule, France.
- Laboratory of Immunogenetics, Vrije Universiteit Medical Center, prof.dr. A.S. Peña, Amsterdam, the Netherlands.
- Ludwig Boltzmann Institut fur Osteologie (prof.dr. P. Fratzl) Vienna, Austria.
- LUMC kindergeneeskunde.
- Mahidol University, Bangkok, Thailand, Fac Science and Fac of Tropical Medicine (prof.dr. S. Sirisiha and dr. N. Chantharita).
- Mark Pot, Health Science Research Center, Indiana University-Purdue University, Fort Wayne, IN, USA.
- Max Planck Institute for Chemical Ecology, Department of Bioorganic Chemistry, prof.dr. Axel Mithoefer, Jena, Germany.
- Max Planck Institute, Dept. of intrfaces and colloids, Potsdam, Germany.
- Medical School, Prof. van Laar, Newcastle upon Tyne, U.K.
- Medisch Centrum Leeuwarden, dr. De Vischer, Leeuwarden, the Netherlands.
- MRC-Holland BV, Amsterdam, the Netherlands.
- Netherlands Cancer Institute, Amsterdam, the Netherlands.
- NIZO, Ede, the Netherlands.
- NUTRIDENT consortium: (UCL Eastman Dental Institute), (University of Pavia), (University of Tel Aviv), (University of Genoa), (Goteborg University), (University of Verona), (Quest International), (Glycologic Ltd).
- Padjadjaran University, Dept. Periodontology (dr. S. Lambri), Bandung, Indonesia.
- Peking University School of Stomatology, Beijing, China.
- Peking University School of Stomatology, prof. Hong Hua, Beijing, China.
- Philips Research, the Netherlands, B. Gottenbos.
- Prasanna Neelakantan, Saveetha Dental College and Hospitals, Saveetha University, Chennai, India.
- Rajiv Ghandhi University of health sciences, Karnakata, Bangalore, India.
- Rapid Pathogen Screening (RPS), Sarasota, Florida, USA (dr. B. van Dine).
- Rijksuniversiteit Groningen, Afdeling Mondzientes en Kaakchirurgie (prof.dr. A. Visserink).
- Sanguin, Departments of Immunopathology (dr. D. Wouters) and Blood Cell Research (prof.dr. T. van den Berg).
- Sanquin; Phagocyte Laboratory; Department of Blood Cell Research.
- Sao Paulo State University, Araraquara, Brazil (dr. M.M. Bellucci and dr. P. de Souza).
- Saxion University of Applied Sciences, Deventer, the Netherlands.
- State University of Campinas, Dental School of Piracicaba, SP, Brazil.
- Sunstar Inc., Osaka, Japan.
- Swammerdam Institute for Life Sciences, University of Amsterdam, Amsterdam, the Netherlands.
- The Hebrew University, Hadassah School of Dental Medicine, Department of Pediatric Dentistry, Jerusalem, Israel (dr. E. Davidovich).
- TNO Quality of Life, Business Unit Food and Biotechnology Innovations, Microbial TNO, Genomics Group, Zeist, the Netherlands.
- Top Institute of Food and Nutrition (TIFN) project TNO, Zeist, the Netherlands.
- UAS, Faculty of Medicine, Hospital Pediatrico de Sinaloa, Mexico (dr. Nidia Leon Sicairos).
- UAS, Faculty of Medicine, Hospital Pediatrico de Sinaloa, Mexico (dr. Nidia Leon Sicairos).
- Unilever Research (dr. D. J. Page), Port Sunlight, United Kingdom.
- Unilever Research, Port Sunlight, UK.
- Université Libre de Bruxelles, Brussels, Belgium.
- Universitary Medisch Centrum Utrecht, dr. Dijkema, Utrecht, the Netherlands.
- Universität Kiel (dr. P. Saftig) Kiel, Germany.
- Université Paris 6; Laboratoire d’Imagerie Paramétrique CNRS UMR 7623 Université Paris 6 15 rue de l’École de Médecine F - 75006 Paris, France.
- Universiteit of Utrecht. Medicinal Chemistry (dr. N. Martin).
- Universiteit Twente, Fluid dynamics Lab, Enschede, the Netherlands.
- Universiteit van Amsterdam, AMC, Celbiologie en Histologie (dr. J. van Marle).
- Universiteit van Amsterdam, AMC, Humane Retroviroleiology (prof.dr. B. Berkhout).
- University of Amsterdam, Department of Molecular Microbial Physiology, Swammerdam Institute for Life Sciences, Faculty of Science, Amsterdam, the Netherlands.
- University of Amsterdam, Klinische Chemie (prof. dr. A. Sturk, dr. R. Nieuwland), Amsterdam, NL.
- University College of London, Queen Mary's School of Medicine and Dentistry, prof. dr. M. Curtis, London.
- University Medical Center Göttingen, Department of Medical Microbiology and National Reference Center for Systemic Mycoses, Göttingen, Germany.
- University of Chiang Mai, Thailand, Dept of Odontology and Oral Pathology (dr. S. Krisanaprapornkit).
- University of Amsterdam (microarray department (mass spectrometry) (Biosystems data analysis), (microscopy department), (fungal microbiology), Amsterdam, the Netherlands.
- University of Amsterdam Centre for Advanced Microscopy, Section of Molecular Cytology, Swammerdam Institute for Life Sciences, Amsterdam, the Netherlands.
- University of Amsterdam Microarray Department & Integrative Bioinformatics Unit, Faculty of Science, Amsterdam, the Netherlands.
- University of Amsterdam, Van 't Hoff Institute for Molecules Sciences, Amsterdam, the Netherlands.
- University of Aquila (Italy), Dept. of Biomedical Sciences and Technology (dr. A. Bozzi).
- University of Bath, Bath, United Kingdom.
- University of Birmingham, Dental School, Birmingham UK.
- University of Bonn, Dept. of Periodontology (prof. dr. S. Jepsen), Germany.
- University of Calgary, Calgary, Canada. Dept. of Biological Sciences (prof. dr. H.J. Vogel).
- University of Calgary, Calgary, Canada. Dept. of Biological Sciences (prof. dr. H.J. Vogel).
- University of California Los Angeles (UCLA), School of Dentistry, Los Angeles, CA, USA: dr. David T. Wong.
- University of Chiang Mai, Thailand, Dept of Odontology and Oral Pathology (dr. S. Krisanaprapornkit).
- University of Chile, Santiago, Institute of Biomedical Sciences (prof. dr. M. González).
- University of Dar es Salaam (MUCHS), Dar es Salaam, Tanzania.
- University of Dundee, Division of Biological Chemistry and Drug Discovery, School of Life Sciences, UK.
- University of Goeteborg, Sweden (dr. Niclas Karlsson).
- University of Gothenburg, Dept. of Oral Microbiology, prof. dr. G. Dahlén, Gothenburg, Sweden.
- University of Groningen, Department of Biomedical Engineering.
- University of Groningen, Faculty of Medical Sciences, Dept. of Dentistry.
- University of Kiel, Dept. of Gastro-Enterology (prof. dr. S. Schreiber), Germany.
- University of Kiel, Institute for Clinical Molecular Biology, Kiel, Germany, dr. A. Scheafer.
- University of Liverpool, Liverpool, UK.
- University of Madrid, Centro di Investigaciones Biologicas (prof. dr. L. Rivas).
- University of Melbourne, Australia.
- University of Oporto, Portugal, Dept of Chemistry (dr. M. Bastos).
- University of Oporto, Portugal, Dept of Chemistry (dr. M. Bastos).
- University of Oslo, Dept. of Microbiology, prof. dr. I. Olson, Oslo, Norway.
- University of the Mediterranean, Marseille, France.
- University of Utrecht. Faculty of Veterinarian Medicine (prof. dr. H. Haagsman).
- University of Zurich, Switzerland, dept. of Endodontology, dr. Frank Paque.
- UNPAD in Bandung.
- Utrecht University, Department of Infectious Diseases and Immunology, prof. dr. H.P. Haagsman, Utrecht, the Netherlands.
- VU University Amsterdam, Department of Molecular Cell Physiology, the Netherlands.
- VUMc, Dermatologie (prof.dr. S. Gibbs, prof.dr. R. Schepers).
- VUMc, Medische Microbiologie (dr. B. Appelmelk).
- VUMc, Moleculaire Celbiologie en Immunogenetica, sectie Glycoimmunologie (dr. I. van Die).
- VUMc, Moleculaire Celbiologie en Immunogenetica, sectie Immunomodulatie (prof.dr. Y. van Kooyk).
- VUMC, Molecular Cell Biology and Immunology: dr. M.Boks.
- VUMc, Orthopedie (prof.dr.ir. T.H. Smit).
- VUMC. Dept. of Dermatology, professor S Gibbs.
- Wellington School of Medicine, Wellington, New Zealand.
- Whitehead Institute and MIT, Cambridge, MA, USA (prof.dr. H.L. Ploegh).
- Wim van Palenstein Helderman, Utrecht, the Netherlands.
Current PhD projects


Oral Regenerative Medicine

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J. Klein-Nulend  J. de Lange  M. Naeije  F.J.M. Roeters  F.R. Rozema  P.F. van der Stelt
D.B. Tuinzing  E.A.J.M. Schulten  D. Wismeijer

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. 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. 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
The Interfaculty MOVE Research Institute has chosen “Regenerative Medicine” as one of its domains (i.e., a collaboration of researchers 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 underlying connective tissue) can be damaged or even destroyed by, for example, mechanical overloading, disuse, or disease. In case of tissue loss, the replacement or regeneration of degenerating/regenerated cells, tissues, or organs is needed to restore or establish normal function (Mason A, Dunnill PA. A brief definition of regenerative medicine. Regen Med 2008;3(1):1-5). ORM studies these processes both fundamental and translational in multidisciplinary settings, in which dentistry/oral medicine closely collaborates with medical disciplines like orthopaedics and neurology, both within and outside The Netherlands. The main objectives of ORM-related research are: (1) to develop strategies to prevent degeneration of oral tissues and/or organs, and (2) to develop minimally invasive, regenerative treatment strategies when prevention fails and treatment is required. Both the prevention of degeneration and minimally invasive, regenerative treatments illustrate the ongoing shift from curing diseases to preventing them. Clearly, a focus on early diagnosis will play an important role in enabling this shift.

Tissue regeneration is possible by means of guiding stem cells and differentiated cells to repair and regenerate damaged tissue with the aid of custom-designed biomaterials (matrices), mechanical loading, and nutrients (viz., growth factors, hormones, and medication). Stem cells can be differentiated into bone, cartilage, muscle cells, and oral mucosa and it is the understanding of the interactions between these different cell types together with the impact of mechanical loading which is essential if optimal tissue regeneration is to be achieved in the future. Insight into tissue regeneration is obtained by comparing results from tissue culture and animal models to computer simulations of the motor system and to biomechanical research in clinical trials with patients.

The outcome of all ORM’s research efforts will be an increased understanding of degenerating/regenerated oral tissues and an improved ability to replace or regenerate these tissues, thereby restoring oral function and thus oral health-related quality of life.

Research objectives

Overview

The research of ORM focuses on the effects of events that damage or even destroy oral tissue (e.g., tumor removal, trauma accidents), including the effects of mechanical overloading or underloading on the tissues of the masticatory system, on the resulting clinical problems, as well as on the solutions for these clinical problems. These events have detrimental consequences for the constituent structures of the masticatory system (viz., the teeth, the periodontal tissues, the alveolar bone, the skeletal bone, cartilage, the mucosa, and the jaw musculature). Tissue damage and breakdown can occur, which may in turn cause clinical signs and symptoms of the intra-oral structures and/or of the maxillo-mandibular structures. For example, patients may report to the clinic of the dentist, orthodontist, or oral and maxillofacial surgeon with symptoms like tooth wear, tooth mobility, tooth loss with or without bony defects, pain in the masticatory muscles or in the temporomandibular joints, or dysfunction of the musculoskeletal structures (e.g., a reduced maximal mouth opening). Hard to heal lesions may develop in the oral mucosa as a result from radiation/ chemotherapy after tumor removal, extensive tooth extraction, or trauma. All of these signs and symptoms may yield complaints of a reduction or even a loss of normal oral and mandibular functions. Apart from these physical complaints, comorbid factors like an impaired psychosocial functioning and a reduced oral health-related quality of life are commonly found in patients with pain and dysfunction of the masticatory system as well. After a proper diagnostic procedure, the health care professionals involved in the care of these patients may indicate rehabilitation strategies with the aim to restore normal oral and mandibular functions, following the principles of evidence-based dentistry.

Treatment planning and rehabilitation

Much research of ORM focuses on treatment planning and actual rehabilitation of impaired or lost oromandibular function. Two main approaches can be distinguished. First, fundamental studies are conducted to
develop new techniques for application, after proper clinical testing, in patient populations. Noteworthy in this context are studies to: a) stimulate bone growth around dental implants and into bone defects; b) fabricate dental restorations using computer-aided design and manufacturing (CAD/CAM); c) use tissue engineering and regenerative medicine techniques, focussing on the collagen network and adipose stem cells; and d) improve the microcirculation in patients undergoing, for example, radiotherapy for malignancies. Second, randomized clinical trials are performed to add to the evidence base of treatment modalities. In this context, systematic reviews and meta-analyses are regularly performed. In addition, evidence-based guidelines are developed for application in clinical practice.

Results obtained in 2012

Loading and tissue damage

- As it is generally thought that bacteria are a possible cause of peri-implantitis we focussed on the detection of an alleged marker for pathogenic microbiota, the bacteria P. gingivalis. Using a wide variety of techniques we found that P. gingivalis was not as specific as thought in peri-implantitis patients.
- In a literature review on the general decontamination of diseased implant surfaces we concluded that the mechanical and chemical decontamination should be combined to create an optimal environment for tissue regeneration. One of our ideas when treating contaminated implant surfaces is to work with airflow and calcium phosphate powder enriched with BMP's. We did a literature review on airflow abrasion and we concluded that this might prove to be an good approach.
- We reviewed the use of heterodimeric BMPs in osteogenesis and concluded that they have more distinct signaling and bio-functions than homodimeric BMP's have. They are characterized by more a faster effect, can be used at lower concentration and have a higher efficiency than homodimeric BMPs. Consequently, heterodimeric BMPs bear promising application potential in inducing osteogenesis.
- The BMP heterodimers BMP2/7 of 5-150 ng/mL were shown to enhance osteoclastic CaP resorption to a similar level as the two homodimers but at a much lower concentration. Low-concentration of BMP2/7 heterodimer may favor a rapid remodeling of bone and, thus, bear a promising potential in cytokine-based tissue engineering.
- Using CBCT we managed to distract STL files of single teeth which were printed into titanium. The teeth were extracted and using subtraction techniques we proved that the printed teeth had the same dimensions as the extracted teeth. The fit into the extraction sockets was perfect. This opens new possibilities to print dental implants that fit the patient’s individual situation.
- Bonding to dentin is still a challenge, especially in difficult accessible areas like the root channel system. Some fundamental aspects and novel bonding procedures were investigated. Furthermore, the strength, and fatigue- and the bonding properties of zirconia were investigated. Zirconia can be used as restorative material for dental crowns and bridges, but it can also be an alternative for metal implants. Understanding the surface properties of zirconia is therefore ongoing research.
- Bone loss at inflamed sites in i.e. periodontitis and Crohn’s disease is likely dependent on the inflamed state of peripheral blood, which contains both osteoclast precursors and inflammatory mediators such as T-lymphocytes. We established that osteoclasts form only in the presence of monocytes and T-lymphocytes, and that more osteoclasts are formed from Crohn’s disease peripheral blood.
- Osteoclasts are multinucleated cells that form through fusion of mononuclear precursors. Using time-lapse imaging we found that precursors fuse with each other or with existing multinucleated cells. We also found that osteoclasts split into separate syncitiae, which occurred after separation of different compartments containing multiple nuclei connected by a cytoplasmic tube.
- Jaw joint degeneration is often preceded by anterior disk displacement (ADD). In a biomechanical analysis we have demonstrated that increased friction does not result in ADD, but to increased shear loading in the cartilage layer on the mandibular condyle. This makes the cartilage layer vulnerable for damage, which ultimately could lead to arthritis/arthritis in the jaw joint.
- Lack of physical activity results in muscle atrophy and bone loss, which can be counteracted by mechanical loading. Similar molecular signalling pathways are involved in the adaptation of muscle and bone mass to mechanical loading. We studied whether anabolic and metabolic factors regulating bone mass are also produced by osteocytes in bone in response to mechanical loading. We found that muscle and bone possibly communicate via endocrine and/or paracrine signaling pathways in response to mechanical loading.
• Mehanosensing by osteocytes is a determining factor in bone adaptation. We found that MT1-MMP modulates the mehanosensitivity of osteocytes. In addition, we observed that mechanical loading prevents the stimulating effect of IL-1β on osteocyte-modulated osteoclastogenesis. Finally, we obtained important new insight in the mechanism of mehanosensing by osteocytes after microscale fluid flow analysis in a human osteocyte canalculus using a realistic high-resolution image-based three-dimensional model.

• Our research focuses on the understanding and stimulation of the differentiation of (adipose) stem cells into tissue-specific cell types for the formation of jaw bone, cartilage, and soft periodontal tissue. Crucial in these processes is a.o. the effects of (growth)factors on stem cell proliferation and differentiation. We have shown that a short (15 minutes only) bone morphogenetic protein-2 treatment is sufficient to stimulate osteogenic differentiation of human adipose stem cells seeded on calcium phosphate scaffolds. This short pre-treatment is a very promising tool for use in a clinical one-step surgical procedure, e.g. the clinical maxillary sinus floor elevation model.

• Related to the development of enamel fluorosis we found that a single high dose of fluoride in hamster pups induced subameloblastic cysts in the late secretory stage of enamel formation. These cysts posteruptively become enamel defects. Monofluoro phosphate (MFP) was more potent in inducing these defects than NaF. After several weeks of functioning, many white spots eroded into enamel pits.

• Microcirculation processes are paramount in wound healing and can be seriously damaged by various forms of therapy, especially in patients with a malignancy. The monitoring of microcirculation in these groups of patients gives insight in the aetiology of complications that are often seen after applying tumour therapy or after bone grafts. In two articles, the alternations in microcirculation have been described in patients who underwent radiation therapy.

• The treatment of patients with a midfacial hypothyrosis who underwent radiotherapy in their youth is very challenging. Distraction osteogenesis seems a good option. Several patients have been documented and described showing good functional and aesthetic results.

Clinical signs, symptoms and diagnosis

• A review of the literature has shown that there is no evidence for a possible causal association between bruxism (teeth clenching and grinding) and occlusal factors. This was further corroborated in a cross-sectional study, where the contribution of occlusion to the differentiation between bruxers and non-bruxers was found to be negligible.

• A large-scale clinical and population questionnaire study has shown that pain intensity and fear of jaw movements play an important role in the decision to seek care for orofacial pain. The continuous search for help is associated with catastrophizing and the use of painkillers.

• Abbreviated versions of the frequently used Oral Health Impairment Profile (OHIP) questionnaire were shown to have good psychometric properties for use in TMD populations. A new questionnaire was developed to enable the assessment of the influence of social support in chronic pain. This Social support and Pain Questionnaire (SPQ) also showed good psychometric properties.

• Using Xray subtraction techniques for measuring changes in bone along dental implants were depicted on non-standardized panoramic radiographs. We concluded that the measuring method is a helpful tool to monitor changes around implants even when non-standardized radiographs are being used. Whereas changes of marginal bone level are increased five to eight times during the first year after surgery, the presented method shows gradual loss of bone during 15 years after surgery.

• The clinical success of a restoration is partly dependent on the acceptance of the patient. Colour and translucency play of the restoration an important role in this acception. Unfortunately circa one out of three restorations are clinically not acceptable and the research in this field was focused on the colour determination by the classical shade guides and electronic measurements.

• Adverse reactions of metals to the skin are common. Also adverse oral reactions can be related to the use of metals. The use of the palladium salt, sodium tetrachloropalladate, showed that Pd allergy is much more common than previously assumed. Based on the high incidence of Pd and Ni allergy, which are also cross-reactive, it is advisable to ban Pd out of dental applications.

• Voxel gray values from CBCT ( Cone-Beam CT) deviate from actual HUs (Hounsfeld Units). This affects usefulness for bone density measurements. However, a strong linear correlation exists, which may permit deriving actual HUs from CBCT scanners.

• Two reviews were performed on the use of anticonvulsants and antidepressants in orofacial pain disorders. In both studies a ‘15-item checklist’ was used to assess the methodological quality of each
study. The limited evidence of their effectiveness in pain management and their side effects, make the administration of anticonvulsants and antidepressants in the treatment of pain in patients with orofacial pain questionable. It is important to develop a consensus on the treatment of these disorders using these medications.

- In a study on pain assessment it was demonstrated that, in contrast to chronic pain patients, a single rating of pain ‘on average’ is not an accurate predictor of the actual ‘average’ pain in patients with pain after surgical removal of the third lower molar. A single pain rating cannot replace a multiple pain rating in these kind of patients. Furthermore, a relative pain reduction of 69% or more was experienced as a ‘successful’ reduction in patients with third molar removal.

- We analysed the effects of change of direction of masseter (MAS) and medial pterygoid muscles (MPM) and changes of moment arms of MAS, MPM and bite force on static and dynamic loading of the condyles after surgical mandibular advancement. The results do not support the idea that increased postoperative condylar loading is a serious cause for condylar resorption or relapse.

- We evaluated whether surgical mandibular advancement procedures induced a change in the direction and the moment arms of the masseter (MAS) and medial pterygoid (MPM) muscles. This study demonstrated that bimaxillary surgery in patients with an mpa >39° leads to a significant change of direction of MAS and MPM in the sagittal plane.

**Treatment planning and rehabilitation**

- A technique was developed to determine the direction of tooth grinding in vitro, using scratched enamel specimens and scanning electron microscopy. When applied to clinical samples, this technique will be of great value when planning restorative rehabilitation procedures of tooth wear in bruxism (teeth clenching and grinding) patients.

- A review of the literature has provided clinicians with suggested clinical approaches for the management of implant prostheses in bruxism patients.

- A multi-center investigation showed that TiZr small-diameter bone level implants had at least the same outcomes after 12 months as Ti Grade IV bone level implants. The improved mechanical properties of TiZr implants may extend implant therapy to more challenging clinical situations.

- Reporting on “Oral function after maxillectomy and reconstruction with an obturator’” we concluded that the size of the maxillectomy defect did not significantly influence the functional outcome, but adjuvant radiotherapy resulted in worse mouth opening and oral and swallowing problems. Residual dentition had a positive influence on mastication and subjective outcomes.

- Evaluation of implant and superstructure survival by using a reference-based guided surgery seems to be a reliable treatment option for edentulous patients. The CAD/CAM superstructure, inserted and loaded immediately after guided implant insertion, demonstrated acceptable fit to the underlying implants.

- In an in vitro pilot study the aim was to assess the accuracy of the preemptive individually fabricated root analogue implant (RAI) based on three-dimensional (3D) root surface models obtained from a cone beam computed tomography (CBCT) scan, computer-aided designing (CAD), and computer-aided manufacturing (CAM) technology and to measure the discrepancy in congruence with the alveolar socket subsequent to placement of the RAI. We managed to obtain a very high precision when we subtracted scans from the printed RAI from scans of the extracted tooth. We concluded that the preemptive CAD/CAM-based RAI technique might offer promising features for immediate implant placement.

- Clinical and laboratory evaluations of composite materials as restoratives are still important, especially for the long term. Different composites were evaluated in the lab and in vivo after 6 years and the clinical behaviour. Although in vitro differences were found, clinical outcome for both resin composite materials over 6 years of clinical service was similar. Full composite crown were also clinically evaluated after 3 years. Their survival rate dependent on the cement which was used to lute the crown to the tooth.

- Lengthening of the mandible is one of the most frequently performed procedures in maxillofacial surgery. There are two different operation options to achieve this goal, namely, a BSSO and Distraction (DOG) procedure. In a case control study as well as in a RCT, both options have been compared. There is no difference in outcome of therapy between the two groups.

- Obstructive sleep apnoea (OSA) is a common affliction. Several therapy options are available. In maxillofacial surgery, the oral appliance is very often used. Moreover, maxillo-mandibular advancement (MMA) shows good results in patients with severe OSA with a success rate of more than 90%. 

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• Giant cell granuloma of the jaw bone is a rare and sometimes aggressive disease. The research is focused on the possible value of the use of calcitonin, interferon or denosumab, in aggressive or recurrent giant cell granulomas. Treatment with denosumab shows excellent results in these patients.
• The incidence of maxillofacial fractures and accompanied complications was investigated in Amsterdam. The study population consisted of 408 males and 171 females with a mean age of 35.9 years. The most common cause of the fractures was traffic related, followed by violence. There were mainly mandibular and zygomatic bone fractures in both males and females (80% of all fractures). The main fracture site of the mandible was the combination of mandibular body with mandibular condyle (66 patients; 26.8%). In fractures of the upper 2/3 of the face, zygomatic bone fractures were most common. The complications consisted of inaccurate reposition and infections.
• The incidence of venous thromboembolism (VTE) and the need for thromboembolism prophylaxis was investigated in patients undergoing surgery for oral and maxillofacial trauma. Of the 479 patients included in the study, one presented with VTE (0.2%). Surgery time classification proved to have a significant relationship with VTE.
• For evidence-based recommendation, a review was performed on clinical trials concerning third molar surgery reporting the use of antibiotic prophylaxis compared with no treatment or placebo with "infection" as outcome. There is limited evidence supporting the efficacy of commonly used antibiotics in preventing complications after lower third molar removal.

### Academic personnel in 2012 and 2013

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|                  | Kuitert, dr. R.B.        | 0,20 | 0,20 | 1 |
|                  | Sanderink, dr. G.C.H.    | 0,10 | 0,05 | 1 |
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## Lecturers and other tenured staff

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### Total tenured staff

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## Non tenured staff

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Output

Dissertations


Scientific publications (referred)


Scientific publications (non refereed)


Professional publications


Publications aimed for the general public

Eijkman, M.A.J. (28-01-2012). Implantaat sneuvelt niet vaak. NRC Handelsblad
Eijkman, M.A.J. (08-12-2012). Kaakproblemen door een slecht passend mondstuk. NRC Handelsblad
Eijkman, M.A.J. (06-03-2012). Tandenknarsen verwant aan been bewegen. NRC Handelsblad

Patents

Book editorship

Indicators of Esteem

Grants: current projects with external funding
Bank, R.A. & Everts V: TNO beurs Kenniscentrum, NITE project; AIO (1 fte) 2007-2012.
Boer, S. de, Koolhaas, J.M. & Loon, J.J.W.A. van: NWO-ALW a 4 years PhD Grant: Title: “Coping with altered gravity: orchestrating role of brain serotonin”.
Bronckers, A.L.J.J.: NIH grant on dental fluorosis a 3 year extension to end of 2014 (87 k US $ per year)
Christiansen, C., Svensson, P. & Lobbezoo, F. Development of a user-friendly bruxism treatment device.
Everts, V. KNAW grant for collaboration with China on a 2-year project. Postdoc Q. Wong, €45,170.-. December 2010-2011.
Everts, V. NIRM grant on multinucleated giant cells. PhD student, €280.000,-. September 2011-2015.
Everts, V., Lenthe, H. van, Koolstra, J.H. & Lobbezoo, F. Biomechanical changes in articulation of the jaw joint due to aging. EU-MOVE-AGE PhD Program.
Gorter, R.C. & Wismeijer, D. “Digital dentistry in practice; On dentists’ interaction with technological transformations” to be led by dr. Gorter with an ITI research grant to the amount of CHF 123’821. Granted.
Gucht, J. van der & Loon, J.J.W.A. van: NWO-ALW: 4 years PhD Grant: Title: “Self-organization and dynamics of actin networks under microgravity conditions”.


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


Loon, J.J.W.A. van: NWO PhD-project, 2011-2015,


Wismeijer, D. & Eekeren, P. van. The comparison of osseointegration of Apliquiq implants with immediate vs delayed loading. A split mouth design. Thommen medical. Granted 80.000.

Wismeijer, D. & Liu, Y. Peri-implantitis project 46 Straumann implants. Granted inkind.

Wismeijer, D. A pilot study looking at the treatment of edentulous patients with mini implants. Granted 22.000.

Wismeijer, D. Comparing the immediate loading (within 48 hours) of two interconnected implants with an overdenture to the immediate loading of 4 Mini Dental implants and an overdenture in a Randomized Controlled Clinical trial. Granted 213.727.


Membership of international editorial boards
Aarab, G.: Journal of Dental Sleep Medicine.
Bruggenkate, C.M. ten: Clinical Oral Implants Research.
Everts, V.: The Open Bone Journal.
Everts, V.: The Open Enzyme Inhibition Journal.
Feilzer, A.J.: Odontology.
Forouzanfar, T.: Medicina Oral
Goené, R.J.: Journal of Implant and Reconstrucive Dentistry.
Stelt, P.F. van der: Dentomaxillofacial Radiology.
Stelt, P.F. van der: Journal of Dentistry Shiraz University of Medical Sciences.
Stelt, P.F. van der: Odontology.

Scientific awards/honours

Organisation of international congresses and symposia
Invited speakers at international congresses or symposia


Everts, V. (2012, June 01). Bone remodeling, recent insights. Istanbul, Turkey, Yeditepe University, Dental Faculty.


Goené, R.J. (2012, December 14). Mastering esthetics in post extraction sites, TEAMWORK: all of us know more than one of us. Istanbul, Turkey, Dental Institute Association, IDED, 3rd Int. Congress.


Goené, R.J. (2012, April 13). Teamwork: all of us know more than one of us. Portugal, Universidade de Lisboa.


Klein-Nulend, J. (2012, July 04). How our bones sense mechanical loading and transduce this information at the cellular level. London, UK, Seminar at Department of Bioengineering & Kennedy Institute of Rheumatology Division, Imperial College.


Liu, Y. (2012, November 02). Osteointegration in implant dentistry. Taipei, Taiwan, Taiwan University.


Overman, J.R. (2012, November 20). Adipose stem cell application in sinus floor elevation. Hampton, VA, USA, Hampton University, School of Engineering & Technology, Department of Chemical Engineering.


Stelt, P.F. van der (2012, April 14). Radiation protection and health safety regulations. Dubai, UAE.


Wismeijer, D. (2012, October 13). 20 Years of implantology. What have we learned? Copenhagen, Denmark, European Association for Osseointegration (EAO), 21st annual scientific meeting.


**Supervisor of an external PhD student**

**Bronckers, A.L.J.J.**
Co-supervisor of external PhD student D. Oortgiesen with thesis: "A tissue engineering approach to the regeneration of periodontal tissues" Supervisors: Prof.dr. J.A. Jansen and Prof.dr G.J. Meijer; co-supervisor: Dr. X.F. Walboomers Radboud University Nijmegen, 24-12-2012.

**Everts, V.:**
Supervisor of external PhD student K. Kanjanamekanant with thesis: "Roles of adenosine triphosphate (ATP) and gap junction hemichannels in mechanically-stimulated human periodontal ligament cells" Supervisor: Prof.dr. P. Pavasant Chulalongkorn University, Bangkok, Thailand, 23-11-2012.

**Other international functions**

**Aarab, G.:**
Board member American Academy of Dental Sleep Medicine (AADSM).

**Berkhout, W.E.R.:**
Member Research and Scientific Committee European Academy of Dento-Maxillo-Facial Radiology (EADMFR).

**Berkhout, W.E.R.:**
Member Central Council European Academy of Dento-Maxillo-Facial Radiology (EADMFR).

**Berkhout, W.E.R.:**
Member Selection criteria and radiation protection committee European Academy of Dento-Maxillo-Facial Radiology (EADMFR).

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

**Feilzer, A.J.:**
Chairman ISO TC 106, SC2, WG 19.

**Klein Nulend, J.:**
Founding member Micro-mechanical Tissue Repair Society.

**Kleverlaan, C.J.:**
Member ISO TC 106.

**Koutris, M.:**
Chair research committee European Academy of Craniomandibular Disorders (EACD).

**Liu, Y.:**
External reviewer AO foundation grant in the field of bone regeneration, biomaterials end dental implant.

**Liu, Y.:**
Honorary professor Hospital of Stomatlogy, Dental School of Zheijang University, Huangzhou, China.

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

**Lobbezoo, F.:**
Member management committee EU-COST Action TD-1005 (Pain assessment in patients with impaired cognition, especially dementia).

**Lobbezoo, F.:**
Member Grindcare Clinical Advisory Board (CAB), Medotech Denmark.

**Lobbezoo, F.:**
President-Elect International RDC/TMD Consortium Network, International Association of Dental Research (IADR).

**Lobbezoo, F.:**

**Lobbezoo, F.:**
External examiner PhD thesis B. Craane, September 2012 University of Leuven, Belgium.

**Lobbezoo, F.:**
External examiner PhD thesis N.N. Zhao, May 2012 University of Sydney, Australia.

**Lobbezoo, F.:**
Member Working Group 1 “Psychometrics and Algesimetry”, EU-COST Action TD-1005 (Pain assessment in patients with impaired cognition, especially dementia).

**Sanderink, G.C.H.:**
Chairman Trustfund IADMFR.

**Visscher, C.M.:**
Board member Physical Therapy Board of Craniofacial and Cervical Therapeutics (PTBCCT), USA.

**Wismeijer, D.:**
Member Education Committee of the ITI (CH).
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.
The BIOS research project has had its impact on the acceptance of the treatment of edentulous patients with oral implants by the Dutch Health Insurance companies. For edentulous patients, the treatment with two implants and an overdenture has been accepted as the treatment of choice for edentulous patients. The results of the research on bone adaptation and regeneration will offer multiple opportunities for the development of new therapeutic agents to prevent (inflammation-associated) unwanted clinical bone loss, thereby preventing among others mobility loss with aging.
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.
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.

Interaction 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 the paragraph of indicators of esteem above.
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 patient treatment related to the sub-programme Oral and Maxillofacial Surgery were adopted by the Dutch Society for Oral and Maxillofacial Surgery. The guidelines for diagnosis and treatment of orofacial pain related to the sub-programme Oral Kinesiology were developed by the Dutch Society of Headache Patients. Several scientists of the program had interviews in Dutch dental Journals. A total of 40 professional publications were written.

Membership of editorial board of national journals
Calcar, N.P. van: Member Editorial Board. Praktijkboek Tandheelkunde.
Dozic, A.: Member Editorial Board. Jaarboek Esthetische Tandheelkunde.
Feilzer, A.J.: Member Editorial Board. Praktijkboek Tandheelkunde.
Stelt, P.F. van der: Director Ned Tijdschrift voor Tandheelkunde BV (Dutch Dental Journal Inc).
Lobbezoo, F.: Member of the advisory editorial board of “ACTA Quality Practice

Organization of national congresses and symposia
Everts, V.: Organisation of 2 day Conference in Woudschoten of the Dutch Society of Calcium and Bone Metabolism (November 2012).

Invited speakers at national congresses or symposia

Other national functions
More than 24 memberships of national committees and advisory councils can be mentioned for the following individuals: Baart, J.A., Bruggenkate C.M. ten, Diermen, D.E. van, Everts, V., Feilzer, A.J., Goené, R.J., Klein-Nulend, J., Kleverlaan, C.J., Lobbezoo, F., Muris, J., Schulten, E.A.J.M., Stelt, P.F. van der, Visscher, C.M.

Courses for dental and medical professionals

Lectures given during courses for dental and medical professionals in the Netherlands

Collaborations
- AMOLF, Dr. G. Koenderink, Dr. R.G. Bacbac, Amsterdam, NL.
- Amsterdam Medical Center, Amsterdam, Prof. G. de Lange. the Netherlands.
- Biofarmind, The Hague, the Netherlands
- City University of New York, dr.ir. S.C. Cowin, New York, NY, USA.
- Clinical Research Department (dkf) , University of Bern, Bern, Switzerland.
- 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 life sciences, Inner Mongolia Agriculture University, Huhehot, China.
- Department of maxillofacial surgery Prof. Dr. G. Juodzbalys., Lithuanian University of Health sciences.
- Department of MFP and Special Dental Care of the AMPHIA teaching hospital Breda (NL).
- Department of Nuclear Medicine and PET research, VUmc, Amsterdam
- Department of Nuclear Medicine and School of Dentistry, University of Nijmegen, the Netherlands: (Dr. Otto Bormen and Prof. J. Jansen)
- Department of oral and maxillofacial radiolog; prof. ME Parker., University of Western Cape, South Africa.
- Department of Oral and Maxillofacial Surgery, Leids Universitair Medisch Centrum, Leiden
- Department of Oral and Maxillofacial Surgery, Rijnland Ziekenhuis, Leiderdorp
- Department of Oral Surgery, University of Bern, Bern, Switzerland. (Daniel Buser)
- Department of Product & Process Engineering. DelftChemTech, Delft University of Technology
- Department of prosthodontics , University of Bern, Bern, Switzerland. (Urs Braegger)
- Department of prosthodontics, University of Zurich, Zurich, Switzerland. (Frauke Muller)
- Department of restorative dentistry and biomaterial sciences. Harvard University, Boston USA (German Gallucci)
- Dipartimento di Medicina, Chirurgia e Odontoiatria – A.O. San Paolo, Università degli Studi di Milano. Matteo Chiapasco / Paolo Cassetinti
- Ege University, Faculty of Medicine, Center for Brain Research & Department of Physiology, prof dr K. Türker, Bornova, Izmir, Turkey.
- Eindhoven University of Technology Dr ir H.A Reijers, Den Dolech 2, PO Box 513, 5600 MB, The Netherlands
- Eindhoven University of Technology, Department of Materials Technology (prof. dr. ir. J.M.J. den Toonder), Eindhoven, the Netherlands.
- Erasmus University Rotterdam, Prof. dr.ir. H. Weinans, Rotterdam, NL.
- Göteborg University, Sweden. Grethe Jonasson; a) Research & Development Unit in Southern Ålvsborg County, Sweden; b) Research Center, Public Dental Service, Gothenburg, Sweden; c) Department of Orthodontics
- Göttingen University, Prof.dr. C.F. Schmidt, Göttingen, Germany
- Harvard University, Boston, MA, USA (Dr. R. Krishnan).
- Health Sciences University of Hokkaido, dr. M. Hashimoto, Hokkaido, Japan.
- Hiroshima University, Department of Orthodontics (dr. N. Kawai), Hiroshima, Japan.
- Hospital Hilversum, Dr. G.H.R. Albers, Hilversum, NL.
- Hospital of Stomatology, Dental School of Zhejiang University, Huangzhou, China.
- Imaging Sciences, prof. R. Jacobs, Katholieke Universiteit Leuven, Belgium.
- Institut für Anatomie, Zentrum für Experimentelle Medizin, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany
- 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.
- Kyushu University, Department of Oral and Maxillofacial Radiology (dr. T.K. Goto), Fukuoka, Japan.
- Margareta Ahlqwist; Department of Oral and Maxillofacial Radiology Institute of Odontology - University of Gothenburg, Gothenburg, Sweden.
- Nordic Biosciences, Herlev, Denmark. Dr. K. Henriksen
- Okayama University, Dr. H. Kamioka, Okayama, Japan.
- Philippines, Cebu City, San Carlos University, Talamban Campus, Dr. R.G. Bacabac
- Radboud University Nijmegen, NL, Prof.dr. A.M. Kuipers-Jagtman, Dr. J.C. Maltha, Dr. R. van ’t Hoff;
- Radboud University Nijmegen, Prof. dr. J. Jansen and Dr. X.F. Walboomers
- Regensburg University Medical Center, Department of Prosthetic Dentistry, Prof. dr. M Behr, Regensburg, Germany.
- 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.
- Straumann AG, Basel Zwitserland. R Willie head of Prosthodontics
- Techn. Univ. Eindhoven, Prof. M. Rautenberg
- UMCG (Prof.dr. R.A. Bank), Groningen, NL.
- Univ. Madrid, Spain, Prof. R. Marco.
- Univ. Milaan, Italy, Prof. S. Bradamante.
- Univ. of Connecticut, USA, M. Musgrave
- Universitair Medisch Centrum St. Radboud/Radboud Universiteit Nijmegen, Cariologie en Endodontologie, prof. dr M.C.D.N.J.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 of Aberdeen, UK, Prof. M. Helfrich
- University of Cairo, Department of Operative Dentistry, dr. AA. El Zohairy, Cairo, Egypt
- University of California San Francisco (Prof DenBesten)
- University of Groningen, Department of Prosthodontics, Prof dr M.C. Cune, Prof Dr H Meijer Groningen, The Netherlands.
- University of Helsinki, Department of Stomatognathic Physiology & Prosthetic Dentistry, dr J. Ahlberg, Helsinki, Finland.
- University of Helsinki, Finland, Prof. K.Vaananen
- University of Kiel, Germany, Prof. P. Saftig
- University of Leuven, Dept Rheumatology, Prof.dr F. Luyten, Leuven, Belgium
- University of Naples, Department of Orthodontics (I. Cioffi, dr. M. Farella), Naples, Italy.
- University of Navarra School of Medicine, Pamplona, Spain (Prof dr JF Medina)
- University of Nijmegen, Department of Prosthodontics, dr C Kreulen Nijmegen, The Netherlands
- 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. G. Andersson
- University of Tanta, Department of Restorative Dentistry, dr. Al Abdalla, Tanta, Egypt.
- University of Tennessee, Clinical Research Center, dr. F. Garcia Godoy, Memphis, USA.
- University of Tokushima, Department of Orthodontics and Dentofacial Orthopedics (prof. E. Tanaka), Tokushima, Japan.
- University of Turku, Department of Prosthetic Dentistry and Biomaterials research, Prof. dr. Pekka Vallittu, Turku, Finland.
- University of Umeå, Sweden, Prof. U. Lerner
- 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, Dr. W.J.A. Dhert, 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, Fact. Physics, D. Iannuzzi
- VUA, Dept Movement Sciences, Prof.dr. J. van Dieën, Prof.dr A. de Haan, Dr. R. Jaspers, Dr. K. Gerritsen, Amsterdam, NL.
- VUMc, Dept Theoretical Physics (Prof.dr. F.C. MacKintosh), Amsterdam, NL.
- VUMc, Afdeling dermatologie, dr. Th. Rustemeyer.
- VUMc, Afdeling Pathologie, prof.dr. R.J. Scheper.
- VUMC, Dept Endocrinology, Prof dr. P. Lips, Dr. N. Bravenboer, 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 Plastic Surgery (Prof.dr. M. Ritt, Dr. M.G. Mullender,), Amsterdam, NL.
- VUMC, Dept Rheumatology, Prof. Dr. W.F. Lem's, Amsterdam, NL.
- Zhejiang-California Nano Systems Institute, Hangzhou, China

**Current PhD projects 2012**

Apperloo, RC. Dental implants as anchorage for prostheses, number, configuration and suprastructure.


Bromoosh P. Diagnostic value of Cone Beam CT for the assessment of erosive lesions of the TMJ. Supervisors: prof.dr. P.F. van der Stelt and prof.dr. F. Lobbezoo, start: September 2012.


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), 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 2012 experiments have been carried out on training behaviour of students preparing for practical examinations. It appeared that behaviour of students shows a relationship with results of their examinations. Also it turned out that students who are in control of their program and deciding of testing moments performed better. The possibility to collect data on training behaviour in such a controlled environment offers the opportunity to compare performance of various groups of students even from separate universities using similar exercises.

Academic personnel in 2012 and 2013

| Research staff ACTA - OWI and other research (in full time equivalents) |
|-------------------------------------------------|---|---|---|
| Position                                         | name                        | fte 2012 | plan 2013 | funding |
| Staff members education institute              | Gorter, dr. R.C.           | 0,10     | pm         | 1       |
|                                                | Vervoorn, dr. J.M.         | 0,05     | 0,10       | 3       |
|                                                | Schoonheim-Klein, dr. M.E. | 0,20     | --         | 1       |
|                                                | Schoonheim-Klein, dr. M.E. | 0,05     | --         | 3       |
|                                                | Wesselink, prof.dr. P.R.  | 0,05     | 0,10       | 3       |
| PhD students                                    | Bakker, drs. D.R.         | 0,10     | 0,15       | 3       |
|                                                | Boer, drs. I.R. de        | 0,10     | 0,20       | 3       |
|                                                | Koopman, P.               | pm       | 0,15       | 3       |
| total 1st funding                              | 0,30                       | --       | 1         |
| total 3rd funding                              | 0,35                       | 0,70     | 3         |
| Total research staff                           | 0,65                       | 0,70     | 3         |
Output
Scientific publications (refereed)


Professional publications


Professional publications not included in the Annual Research Report 2011


Publications aimed for the general public

Indicators of Esteem
Grants: current projects with external funding
Wesselink P.R. & Vervoorn J.M. A grant of € 800.000,- (2008-2010) was obtained from the Ministry of Education for "Simodont, virtuele realiteit de werkelijkheid". This grant was obtained together with the department of Preventive Dentistry Cariology Endodontology Pedodontontology. This grant has been extended for unlimited time and finished in 2012.

Membership of international editorial boards
Gorter, R.C.: Associate editor European Journal of Dental Education.

Other international functions
Schoonheim-Klein, M.E.: Chair Advisory committee the excellence in Dental Education Advisory Committee (EDEAC).

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.

Current PhD projects
### Appendix 2012

List of SCI journals, their impact factors and the number of ACTA publications in 2012 in each journal

<table>
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<th>Journal</th>
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