One-step surgical procedure

Stem cell preparation

Sinus floor elevation
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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 subsequently presented for each programme. Detailed information is given of dissertations, scientific publications in refereed journals, other scientific publications, professional publications, indicators of esteem, collaborations and societal impact.

Some issues for 2013 are specifically highlighted 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 2013 is presented in Table 1. We are pleased to note that the output in 2013 was high. The number of publications in refereed scientific journals and the IF-sum have considerably increased during the last years. In 2013 the highest number of scientific publications and the highest IF sum was accomplished. In 2013 a total of 18 PhD theses were published and defended.

Research Institute ACTA

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

Address
ACTA
Gustav Mahlerlaan 3004
1081 LA Amsterdam
The Netherlands

tel: +31-20-5980641
e-mail: tjm.vansteenbergen@acta.nl
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 fundamental 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).
  **Research themes.** ACTA has two main research themes. 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 interfacultary research institute MOVE, a collaboration between the faculty of Human Movement Sciences, the VU University Medical Center and ACTA.
  **Research programs.** Till 2008, 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, limited other research is performed, which is mainly 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 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 scientists publish. In both programs, depending on the subject, scientific findings are presented in journals read in the dental research community, or 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 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 for the years 2007-2010. It was concluded that in an international perspective ACTA has a strong position in a relatively 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, preferably in a translational way. Due to the vulnerability of small groups and to the reduction in budget it was decided to focus the research in two programs as mentioned above. To maintain the present quality of the research, ACTA will focus on the best scoring research. For more details, we refer to the self-evaluation report.

**Citation analysis.** In 2013, the CWTS in Leiden has performed a bibliometric analysis of the ACTA scientific publications over the years 2001-2011. One of the goals of this study was to identify possible benchmarks. These benchmark candidates were investigated in more detail and compared with the performance of ACTA. The conclusions of this study are as follows:

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

### Summary of research output and input

**Table 1. Comparison of research indicators 2001-2013**

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dissertations</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>
<td>18</td>
</tr>
<tr>
<td>Refereed publications</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>
<td>250</td>
</tr>
<tr>
<td>First author from ACTA</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>
<td>127</td>
</tr>
<tr>
<td>Other scientific publications</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>
<td>16</td>
</tr>
<tr>
<td>Professional publications</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>
<td>159</td>
</tr>
<tr>
<td>Publications for general public</td>
<td>8</td>
<td>14</td>
<td>9</td>
<td>12</td>
<td>9</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>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>
<td>696</td>
</tr>
<tr>
<td>Personnel WP 1</td>
<td>45.0</td>
<td>47.2</td>
<td>47.9</td>
<td>49.4</td>
<td>46.0</td>
<td>46.5</td>
<td>50.3</td>
<td>43.4</td>
<td>40.8</td>
<td>36.7</td>
<td>36.2</td>
<td>39.5</td>
<td>42.2</td>
</tr>
<tr>
<td>WP2</td>
<td>5.4</td>
<td>5.4</td>
<td>6.2</td>
<td>6.6</td>
<td>4.8</td>
<td>7.9</td>
<td>7.8</td>
<td>9.6</td>
<td>7.0</td>
<td>7.8</td>
<td>10.1</td>
<td>9.4</td>
<td>6.3</td>
</tr>
<tr>
<td>WP3</td>
<td>9.5</td>
<td>9.8</td>
<td>10.3</td>
<td>7.7</td>
<td>6.7</td>
<td>7.4</td>
<td>6.5</td>
<td>5.4</td>
<td>12.9</td>
<td>13.5</td>
<td>14.4</td>
<td>17.6</td>
<td>19.6</td>
</tr>
<tr>
<td>Guests</td>
<td>2.6</td>
<td>2.4</td>
<td>2.6</td>
<td>1.9</td>
<td>2.2</td>
<td>4.2</td>
<td>4.3</td>
<td>3.6</td>
<td>pm</td>
<td>pm</td>
<td>pm</td>
<td>pm</td>
<td></td>
</tr>
<tr>
<td>Total personnel</td>
<td>62.6</td>
<td>64.8</td>
<td>66.9</td>
<td>65.6</td>
<td>59.8</td>
<td>66.1</td>
<td>68.7</td>
<td>62.1</td>
<td>61.6</td>
<td>57.9</td>
<td>60.7</td>
<td>66.5</td>
<td>68.1</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 2013 a high number of 18 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 2013 the highest number of 250 refereed publications and the highest 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 2013 was 159.

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![Figure 1. Impact factor sum of ACTA publications, scientific publications in refereed journals, professional publications and total scientific personnel in fte.](image)

---

• **notable events in 2013**

**Publications in high ranking journals.** Outstanding contributions for the year 2013 are publications in relatively high ranking biomedical journals, i.e. Plos Pathogens, Annals of the Rheumatic Diseases, Proceedings of the National Academy Sciences of the United States of America, Molecular Biology and Evolution, all journals with an impact factor higher than 8, Nature Genetics with an impact factor of 35 and the New England Journal of Medicine with an impact factor of more than 51.

**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 250 scientific papers in refereed journals, of which 231 in journals with an impact factor (Sci journals). 47% of these 231 papers appeared in journals belonging to
the field “Dentistry, Oral Surgery and Medicine”. 23% of all publications were in the top 10% of the journals, 46% in the top 25% and 71% in the top 50% (Table 2). This means that, as in previous years, a relatively large number of publications were published in the top journals in the field, both in dental and in non-dental journals.

**Indicators of esteem.** On a personal level a number of ACTA employees rank in the top of the dental community, as determined by the various indicators of esteem, such as editorships, invited lectures, and congresses organised. In 2013 a total of 14 awards were received by ACTA scientists for their achievements. For more details we refer to the description of the two research programs.

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

**Table 2. Percentage of publications in different quartiles of dentistry and non-dental journals in 2013**

<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>25</td>
<td>23 %</td>
<td>29</td>
</tr>
<tr>
<td>Quartile 1</td>
<td>53</td>
<td>49 %</td>
<td>54</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>15</td>
<td>14 %</td>
<td>42</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>30</td>
<td>28 %</td>
<td>20</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>10</td>
<td>9 %</td>
<td>7</td>
</tr>
<tr>
<td><strong>total</strong></td>
<td><strong>108</strong></td>
<td><strong>100%</strong></td>
<td><strong>123</strong></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 parameters like input and output (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>10</td>
<td>139 (67)</td>
<td>10</td>
<td>95</td>
<td>8</td>
<td>382</td>
<td>20,10</td>
<td>4,10</td>
<td>8,05</td>
<td>34,90</td>
</tr>
<tr>
<td>ORM</td>
<td>10</td>
<td>121 (58)</td>
<td>6</td>
<td>40</td>
<td>1</td>
<td>343</td>
<td>22,15</td>
<td>2,15</td>
<td>8,35</td>
<td>32,65</td>
</tr>
<tr>
<td>OWI</td>
<td>-</td>
<td>13 (2)</td>
<td>1</td>
<td>11</td>
<td>-</td>
<td>14</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0,55</td>
</tr>
<tr>
<td>ACTA*</td>
<td>18</td>
<td>250 (127)</td>
<td>14</td>
<td>160</td>
<td>9</td>
<td>696</td>
<td>6,25</td>
<td>9,40</td>
<td>19,60</td>
<td>68,10</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 2013 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>Staff 1st</th>
<th>Staff 2nd</th>
<th>Staff 3rd</th>
<th>PhD students 1st</th>
<th>PhD students 2nd</th>
<th>PhD students 3rd</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>OII</td>
<td>13,45</td>
<td>0,70</td>
<td>4,80</td>
<td>6,65</td>
<td>3,45</td>
<td>5,90</td>
<td>34,90</td>
</tr>
<tr>
<td>ORM</td>
<td>14,70</td>
<td>0,65</td>
<td>3,10</td>
<td>7,45</td>
<td>1,50</td>
<td>5,25</td>
<td>32,65</td>
</tr>
<tr>
<td>OWI</td>
<td>-</td>
<td>-</td>
<td>0,20</td>
<td>-</td>
<td>-</td>
<td>0,35</td>
<td>0,55</td>
</tr>
<tr>
<td>Total</td>
<td>28,15</td>
<td>1,35</td>
<td>8,10</td>
<td>14,10</td>
<td>4,90</td>
<td>11,50</td>
<td>68,10</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 (87 international functions), as members of editorial boards of scientific journals (79) 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 159 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 2013 ACTA researchers have again contributed actively in internationally held meetings, workshops and symposiums, both as organisers and participants. A total of 136 lectures were given as ‘invited speaker’ at international congresses and symposia. In addition a large number of presentations were given at international congresses after selection on submission of abstracts and during congresses and symposia for a Dutch or international audience. Due to this large number, congress abstracts are not listed in this annual report. A total of 21 international meetings were organised by ACTA scientists.

**Management**

- **finances**
The overall budget of the research institute is divided into a part controlled directly by the directorate and another part that is allocated to the departments. The institute budget (senso stricto) of k€ 911 is used for the management of the institute, salaries of PhD students, for travel allowances of PhD students, for the organization of courses for PhD students and for printing PhD theses. The research budgets for the departments (in total being k€ 3472) 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€ 440, and the total amount of research contracts (3rd source) was k€ 2548.

- **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 0.3 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 2013. In Figure 2 the number of new PhD students at ACTA is shown in the years 1990 to 2013. Over the years, about 23% of all PhD students had a foreign nationality, about half of them from Europe, the rest from other continents. A mean number of about 9 new PhD students were appointed per year. Due to budget restrictions only 4 new PhD students could be appointed in 2013. 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 2013 6 new PhD students were appointed on grants awarded to the research themes. 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, the number will be limited.

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

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

Table 5: PhD students by type of undergraduate training

<table>
<thead>
<tr>
<th>Program</th>
<th>Dentistry Dutch</th>
<th>Dentistry Other</th>
<th>Biology / Chemistry</th>
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OII = 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, organized by research schools in other disciplines.

• **PhD thesis duration and completion rate**

Attention has been paid to the problems related to the social security benefits of PhD students and the time that PhD students need to finish their thesis. The mean time between start of the PhD project and the defence of the thesis within ACTA amounts 4.6 years. This is lower than the mean duration of PhD theses in research schools in the Netherlands being 5.1 years (see the report “Rendement en duur van promoties in de Nederlandse onderzoekscholen”, Oost en Sonneveld, 2004).

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 budget (1st source) had to be reduced slightly. Fortunately, the fte scientific personnel on grants (in particular 3rd source) increased in 2013. Both research priority areas received a substantial grant from the UvA, resulting in an increased 1st fte in 2012 and 2013.

• **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.

![Figure 4. Percentage of ACTA PhD students finishing their thesis related to the year of entry](image-url)
Oral Infections and Inflammation

Program Leader
Prof.dr. B.G. Loos
ACTA, Gustav Mahlerlaan 3004
1081 LA Amsterdam
Tel: +31-20-5980558
E-mail: b.loos@acta.nl

Full professors

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

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

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

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

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

The researchers within the theme “Oral Infections and Inflammation” have an international prominence in the field of oral health and have acquired a global leadership role in the emerging field of complex ecosystems such as the oral cavity; thus understanding of oral infections, inflammatory processes, oral cancer and the definition of a normal, healthy oral cavity including psychosocial factors. We have been awarded a grant from the University of Amsterdam (UvA) (starting date 1-1-2011) and we demonstrated the multiplier effect (both on the academic as well as the economic aspects) by participating in the Top Institute of Food and Nutrition (TIFN) (contract signed December 2011, first year research in 2012).

Results obtained in 2013

Preclinical studies

• The generation of “better” antimicrobial peptides originating from natural salivary peptides is ongoing. Structural modifications varying from specific substitutions to cyclization of these peptides have increased the insight in the mode of action of these novel bactericidal and fungicidal agents. These are important and novel alternatives for conventional antibiotics. Antimicrobial properties of small peptides, derived from bacterial EDFs (Extracellular Death Factors) have been explored. It was found that these peptides reduced via a stereospecific mechanism the size of Bacillus globigii. In addition we discovered possibilities for new protective coatings on mucosal surfaces; the feasibility of “sphingoid” based components for the protection of oral surfaces against chemical and bacterial injury will be further explored.

• A novel versatile enzyme-based method was developed for in situ functionalization of biomaterial surfaces. In a proof of principle study polystyrene surface was primed with an anchoring peptide derived from salivary agglutinin and equipped with a suitable acceptor motif. This was subsequently enzymatically coupled to a bacterial repellent polyethylene (PEG)-tail. This resulted in a significant decrease of bacterial adherence to the surface.

• Characterization of bacterial surface structure is essential for fundamental research as well as for clinical purposes, such as vaccine development. With new technology we developed and established a novel and rapid method by which the presence of virulence factors on the cell walls of bacteria comprehensively can be analysed; this was validated on S. aureus. In fact, this method revealed all kinds of antigens for possible vaccine development.

• Within this –omics era, we identified in saliva with proteomics numerous (un)known molecules. Novel mathematic models are developed to comprehensively analyse the huge amount of data emerging from salivary biomarkers.

• Model systems for several oral infections were developed and exploited. The influence of oral bacteria on epithelial cell migration in vitro was established. Cytokine and matrix metalloproteinase expression in fibroblasts from peri-implantitis lesions in response to viable P. gingivalis were studied, as well as the influence of titanium on in vitro fibroblast-P. gingivalis interaction in peri-implantitis. It became clear that gingival fibroblast responsiveness is differentially affected by P. gingivalis. Further, oral implant surface roughness has a clear effect on bacterial biofilm formation (and therefore treatment efficacy). In another work, we showed that the effect of metalloporphyrins on red autofluorescence from oral bacteria; we concluded that the bacteria related to dental caries and periodontal disease exhibit red autofluorescence, but this extent is dependent on the nutrients present, such as metalloporphyrins, suggesting that the metabolic products of the oral biofilm could be responsible for red autofluorescence.

• Furthermore we explored photodynamic antimicrobial chemotherapy using five different Enterococcus faecalis strains in vitro in a root canal. In a new in vitro biofilm model we studied the possibilities for endodontic disinfection; a modified salt solution was tested for cytotoxicity, interaction with dentine and killing efficacy on multispecies biofilms: the incubation of modified vanadium chloroperoxidase in the presence of its substrates with in vitro E. faecalis biofilms showed a significant antimicrobial effect at the root canal pH. The cytotoxicity tests showed biocompatibility.
Clinical studies

- Currently research on protease based profiling crosses the borders of bacterial diagnosis expanding towards research on oral health, veterinary health (e.g. mastitis), bacterial biofilms, and even botanic research. In the search for potential biomarkers as diagnostic tools for salivary gland tumors chromosomal alterations will be investigated by array Comparative Genome Hybridization (arrayCGH). Also we are working on the generation and characterization of artificial sortase substrates to target bacterial sortase enzymes for therapeutic and diagnostic purposes.
- An important line of clinical research has been expanded. Oral infections and inflammation, in particular mucositis, has been identified as a major a side effect of hematopoietic stem cell transplant (HSCT). The oral mucositis severely comprises quality of life and recovery of such patients, and may induce fevers or even sepsis. We study oral systemic links, for example periodontal status and bacteremia, and we develop clinical protocols for oral supportive care. We investigated the relationship between oral ulcerations and bacterial species, Candida, and viruses, 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.
- The oral (microbial) ecology of the healthy oral cavity as well as several oral diseases was studied by combining expert clinical evaluations and next-generation-sequencing microbial profiling techniques. The microbiome in smokers and non-smokers with periodontitis was evaluated; patients that smoke have an even more severely disturbed microbiome than non-smoker patients; all compared to a normal healthy oral microbiome, which is diverse. The –omics approach has demanded machine learning and bioinformatics, and needs unraveling the outcome of 16S rDNA-based taxonomy analysis through mock data and simulations; thus we systematically evaluated potential bias in microbial community profiles induced by whole genome amplification.
- Systemic effects of periodontitis are being investigated with several researchers in an integrated effort. Periodontitis is epidemiologically associated with atherosclerotic forms of cardiovascular diseases (CVD) and diabetes mellitus. We explored the literature and test some aspects clinically which possible biological pathways exist to explain this relationship; and in clinical interventions studies what the effects are of periodontal intervention studies on CVD biomarkers.
- Forms of oral cancer, precursor lesions of oral cancer, particularly leukoplakia, and salivary tumours are studied. Amongst others, the prognostic value of molecular markers is examined with regard to the malignant transformation of leukoplakia. A large survey on the presence of human papilloma virus (HPV) has been performed. Also 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. The molecular genetic changes in various types of salivary gland tumours are investigated, as well as the possibility to use saliva as a tool in diagnosing salivary gland neoplasms. In fact, studies on the presence of miRNA profiles in saliva have demonstrated that differences in miRNAs can be found between patients with benign and malignant parotid neoplasms. The concept of the sentinel biopsy in staging oral cancer has also 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. Treatment of leukoplakias is been investigated. Based on a large cohort study it was demonstrated that leukoplakias after treatment, either by surgery or laser evaporation, often recurs and that the risk of future malignant transformation is not significantly reduced in these patients.
- The genetic aberrations in adenoid cystic carcinoma (ACC) of the salivary glands have been investigated, and deregulated pathways have been identified, opening future perspectives to personalized therapies. Moreover, a review of all patients with ACC treated in our institute has been performed.
- Odontogenic infections are still a point of discussion. We investigated the relationship between the spread of head and neck infections, in relation to the causal tooth. When describing the location of infection, most studies do not discriminate between maxillary and mandibular origin. Although the literature seems to be unambiguous about the predetermined spread of infection, we demonstrated that it is more difficult to predict the spread of a tooth infection than previously expected. Robust endodontic treatments will prevent odontogenic infections: this aspect is being researched including evaluation of endodontic treatments. Thus, (i) root canal fillings that are intended to prevent reinfection of the root canals were tested for their ability to prevent leakage; (ii) a novel approach for root canal disinfection was tested against biofilm as compared to chlorhexidine and sodium hypochlorite and was shown to have comparable antimicrobial properties; (iii) inter-appointment intracanal dressing with vanadium.
chloroperoxidase on in vitro *E. faecalis* biofilms was shown to be effective in the root canals; (iv) two clinical studies were performed on patients with a periapical inflammatory process to demonstrate the healing of bone lesions in 3D. The results demonstrate that 3D imaging shows a more reliable way to look at healing of periapical lesions after root canal treatments compared to traditional radiography.

- We evaluated fluoride toothpaste containing 1.5% arginine and insoluble calcium, as a new standard of care in caries prevention; despite progress, no conclusive guidelines are yet available. Other anti-caries strategies are adhesive microbeads for the targeting delivery of anticaries agents of vegetable origin. Organic acids in *Cichorium intybus* inhibit virulence-related properties of oral pathogenic bacteria and new antibacterial quaternary ammonium monomers for incorporation into CaP nanocomposite, for caries prevention, were synthesized.

- An important aspect to the translation of scientific findings to the clinic is the development of evidence-based guidelines. For example, based on a systematic review we deduced that there is not enough evidence to conclude that neither single, nor double antiplatelet therapy needs to be interrupted prior to most invasive dental procedures. Recommendations were formulated for an evidence-based guideline for dentists when performing invasive dental treatment in patients on oral antithrombotic medication. Also continuous work has been done on comprehensively summarizing the available literature with respect to various outcomes related to the prevention and therapy of gingivitis, periodontal and peri-implant diseases. For example, the use of amoxicillin and metronidazole adjunctive to supra- and subgingival debridement was summarized in a literature review: the antimicrobial therapy can enhance the clinical benefits of non-surgical periodontal therapy in adults who are otherwise healthy.

- In terms of therapy of the sequelae of caries, work has been performed on various dental materials and the Atraumatic Restorative Treatment (ART) technique. Several clinical trials evaluated the survival rate of approximal-ART restorations made with various glass-ionomer cements (GIC) using layered techniques. Layered techniques increase survival, but there was no difference in survival rate among the various GIC brands.

### Academic personnel in 2013 and 2014

#### Research staff ACTA – OII (Oral Infections and Inflammation)

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<th>(in full time equivalents)</th>
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**Output**

**Dissertations**


Scientific publications (refereed)


Epstein, J., Raber-Durlacher, J., Yurikusa, t. & Soga, Y. (2013). Dr. Yojiro Ota OBITUARY. Supportive Care in Cancer, 21(11), 2951-2952.

Flach, G.B., Tenhagen, M., Bree, R. de, Brakenhoff, R.H., Waal, I. van der, Bloemena, E., Kuik, D.J., Castelijns, J.A. & Leemans, C.R. (2013). Outcome of patients with early stage oral cancer managed by an observation strategy towards the N0 neck using ultrasound guided fine needle aspiration cytology: No survival difference as compared to elective neck dissection. Oral Oncology, 49(2), 157-164.


Loveren, C. van (2013). Exposed cervical dentin and dentin hypersensitivity summary of the discussion and recommendations. Clinical Oral Investigations, 17(S1), S73-S76.

Meleti, M. & Waal, I. van der (2013). Clinicopathological evaluation of 164 dental follicles and dentigerous cysts with emphasis on the presence of odontogenic epithelium in the connective tissue. The hypothesis of “focal ameloblastoma”. Medicina Oral Patología Oral y Cirugía Bucal, 18(1), e60-e64.


Scientific publications (non-refereed)


Doherty, R. & Cate, B. ten (2013). Bob ten Cate: 'Ninety percent of the cells in our body are bacterial cells'. British Dental Journal, 215(10), 533-535.


Professional Publications


Publications for the general public


Grants: current projects with external funding
Alvarez Rodriguez, E. The additive effects of plasma levels of omega-3 en-6 poly-unsaturated fatty acids on the response to initial periodontal therapy. A grant supplied by NVvP €4.200.--
Cate, J.M. ten, Academy Professor, Royal Netherlands Academy of Arts and Sciences (KNAW), total € 1.000.000,-period 2008-2013.
Cate, J.M. ten, Crie laard, W., Loos, B.G. & Veerman, E.C.I. “Oral health” (2011-2015) University of Amsterdam/Research Priority Area, € 1.308.000.--

Cate ten J.M. ten, Crie laard W., Soet J.J. de & Loveren C. van STW project. Seeing is believing. M.H. van der Veen & C.M.C. Volgen ant. Start October 2010 - October 2016, € 164,000.

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, Cargill, GlaxoSmithKline, TNO, WUR & ACTA (Total investment 5.2 ME).

Crielaard, W., Zaura, E. & Buijs, M.J. EU (FP7) grant for the project no. 241446: ANTIRESDEV. “The effects of antibiotic administration on the emergence and persistence of antibiotic-resistant bacteria in humans and on the composition of the indigenous microbiotas at various body sites”. Total budget for ACTA: €359.036.-- Start: November 1, 2009 – April 30, 2013. Coordinator: University College London.

Crielaard, W. & Krom, B.P. NWO Middelgroot - Studying Dynamics in complex Microbial biofilms. 2013-2017 €164,000.


Deng, D.M., Wesselink, P.R. & Crielaard, W. KNAW Grant 12CDP05 Samenwerking Guanghua school of Stomatology, Sun Yat-sen University Guang-zhou Novel molecular methods to rediscover the role of microorganisms in persistent apical periodontitis k€ 60,- 2012-2016.


Exterkate, R.A.M., Wit, W.E.A.J. de, & Crie laard W. Effect of Airfloss on interproximal plaque, a typodont study. Philips, USA (k€46,5). Report: data was reported on a weekly basis. No written report, only transfer of data.


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

Krom, B.P. ERC starting grant collaborator, QuorumProbes, Dr. Michael Meijler PI, € 80. Start: October 2013, end: October 2014.


Loos, B.G. “Regenerative surgical treatment of peri-implant osseous defects - a multicenter randomized prospective clinical study” (2011-2013). A grant supplied by Tigran AB, Sweden, € 20,000,-.


Loos, B.G. “The effect of daily dietary intake of dried juice concentrates of fruit, vegetables and berries (Juice Plus+) upon periodontal outcomes in chronic periodontitis: a multi-centre RCT” (2010-2013) A grant supplied by JuicePlus, USA, (ENURGISE) € 71,830,-.


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

Sluijs, E. van der. (2012-2013) The effect of rinsing or drinking water on morning bad breath. A grant supplied by NVvP € 2.400,-


Veerman, E.C.I. & Brand, H.S. Topschool Institute of Food and Nutrition. Saliva and oral health: 1 AIO, 0.05 UD.


Weijden, G.A. van der & Loos, B.G. TIFN WP1 en WP2 clinical studies, € 139.000,-

Weijden, G.A. van der. Unrestricted Educational Grant € 74.940,-

Weijden, G.A. van der. TNO Roquette / Baker € 60.306,-

Weijden, G.A. van der. TNO Sunstar / Sorbet € 56.520,-

Weijden, G.A. van der. GABA, Halitosis € 10.478,-

Weijden, G.A. van der. P&G “ERBA” € 21.924,-

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

Book editorship

Memberships of editorial board
Aartman, I.H.A.: European Journal of Dental Education.
Bloemena, E.: ISRN Gastroenterology.
Brand, H.S.: Nederlands Tijdschrift voor Tandheelkunde.
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.
Cate, J.M. ten: The Chinese Journal of Dental Research.
Crielard, W.: Microbiology - SGM.
Gorter, R.C.: European Journal of Dental Education.
Heijden, G.J.M.G. van der: Journal of Medical Case Reports.
Jongh, A. de: Journal of EMDR Practice and Research.
Loveren, C. van: Nederlands Tijdschrift voor Tandheelkunde.
Özen, B.: American Journal of Medical Sciences and Medicine.
Raber-Durlacher, J.E.: Mediators of Inflammation, special issue Alimentary Mucositis: Mediators, Mechanisms and emerging therapies.
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: Nederlands Tijdschrift voor Geneeskunde.
Waal, I. van der: Oral Oncology.
Wesselink, P.R.: Deutsche Zahnärztliche Zeitschrift.
Invited speakers at (inter)national scientific congresses or symposia


Brand, H.S. (2013, April 12). De tandarts in beeld. Amsterdam, the Netherlands, Nederlands Filmmuseum.


Cate, J.M. ten (2013, September 26). Mode of action of fluorides. Shanghai, China, Unilever caries prevention symposium.


Cate, J.M. ten (2013, June 27). Rational use of effective therapeutics. Seefeld, Germany, 3MESPE.


Cate, J.M. ten (2013, August 01). Theoretical aspects of enamel remineralization. Cincinnati, USA, P&G.


Loos, B.G. (2013, March 13). Oral infections, i.e. periodontitis, affect general health. Rome, Italy, School of Dentistry, Sapienza University.


Loos, B.G. (2013, October 15). Periodontitis and other oral infections are risk factors for cardiovascular diseases and diabetes. Academic Medical Center, University of Amsterdam, AMC Ruysch lecture.


Slot, D.E. & Weijden, G.A. van der (2013, April 05). How to perform a systematic review? Cairo, Egypt, 2 day workshop Cairo University.


Slot, D.E. (2013, October 30). Dentistry is teamwork! St. Petersburg, Russia, Russische mondhygiënisten vereniging.


Waal, I. van der (2013, September 05). Lichen planus and lichenoid lesions; leukoplakia; histopathology of odontogenic cysts and tumors. European Meeting of Oral Diseases. Amsterdam, the Netherlands, European Meeting Oral Diseases.


Annual Research Report 2013


Wesselink, P.R. (2013, June 21). The role of CBCT in endodontic treatment planning and outcome. Toronto, Canada, Annual Symposium, University of Toronto.


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

Scientific awards/honours
Cate, J.M. ten (2013). Honorary professor. West China School of Stomatology: (2013, February 01).

Organisation of (inter)national congresses and symposia
Brand, H.S.: Board member Salivary Research Group, International Association of Dental Research (IADR).
Raber-Durlacher, J.E.: Organizer MASCC/ISOO Annual Symposium Berlin, Germany, June 23-26, 2013.

Other (inter)national scientific functions
Bloemena, E.: Member ESP Working Group Head and Neck Pathology.
Brand, H.S.: Board member Salivary Research Group, International Association of Dental Research (IADR).
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.
Gorter, R. C.: Executive board member ADEE (since 2013).
Heijden, G.J.M.G. van der: Member working group GRADE.
Houtem, C.M.H.H.: Member congress committee Nederlandse Vereniging voor Kindertandheelkunde (NVvK) en Vereniging tot Bevordering der Tandheelkundige Gezondheid voor Gehandicapten (VBTGG).
Krom, B.P.: Reviewer Atip-Avenir Programme, France, April.
Laine, M.L.: External reviewer for international grant application Hong Kong Scientific Evaluation Board.
Laine, M.L.: External reviewer of appointment of senior lecturer P. Mäntylä University of Helsinki, Finland.
Loos, B.G.: Member international scientific committee 46th meeting of the Continental European Division of the International Association for Dental Research (CED-IADR), September 4-7-2013, Florence, Italy.
Loos, B.G.: Councilor Board CED (Continental European Division) and CED representative PER (Pan European Region) International Association of Dental Research (IADR).
Loos, B.G.: Ad hoc reviewer Polish Institute of Sciences.
Loos, B.G.: Board member Society for the advancement of Natural Sciences, Medicine and Surgery, University of Amsterdam, the Netherlands.
Loos, B.G.: Examiner PhD committee Faculty of Dental Medicine, Sapienza University, Rome, Italy.
Raber-Durlacher, J.E.: Board member Multinational Association for Supportive Care in Cancer (MASCC).
Raber-Durlacher, J.E.: Section Head "Cytokine and Growth Factors Section" MASC/ISSO Mucositis Study Group.

Raber-Durlacher, J.E.: Founding member International Group for Light in Oncology Barcelona (iGLOB).

Raber-Durlacher, J.E.: International reviewer Italian Scientific Societies of Oncology and Radiotherapy (AIOM and AIRO) Consensus Statements about head and neck supportive care.

Rosema, N.A.M.: Advisory board member Glaxo Smith Kline (GSK).

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


Soet, J.J. de: Membership secretary and webmaster European Organization for Caries Research (ORCA).

Soet, J.J. de: Member working group to develop new guidelines for Infection Prevention in dentistry for the NMT Nederlandse Vereniging voor Medische Microbiologie. September 2013-2014.

Slot, D.E.: Advisory board member Global Dental Hygiene.


Veen, M.H. van der: Immediate 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.

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


Societal impact

Oral infections and oral cancer have a substantial impact on the society. Oral infectious diseases are the most frequent infections in the western society and have important consequences, both medically and economically. Head and neck squamous cell carcinomas (HNSCC) and specifically oral squamous cell carcinomas (OSCC) are the most prevalent forms of head and neck cancer. The general aim of the program is to understand the normal healthy oral cavity and to understand links with general health, to study oral innate immunity and susceptibility to caries and periodontal diseases, to study prevention and treatment options for the oral infectious and inflammatory processes and to study the epidemiology and pathogenesis of oral cancers, in particular in relation to good/poor oral health. In addition, attention is paid to social and psychological aspects of dental treatment, such as dental anxiety.

Through education, a new generation of dentists and researchers in the Netherlands, Europe and the world are trained to implement a radical shift from mechanistically and (invasive) treatment oriented professionals to 21st century oral physicians focused on diagnosis and prevention of dental and of oral infections and maintenance of the quality of life. Over the last 5 years it has become increasingly clear that oral infections are having negative impact on cardiovascular health, diabetic status and quality of life. The researchers in this theme focus on this aspect.

The members of our priority area have had a relative large number of invitations to give lectures at dental congresses, and to educate the dental profession on fundamental understanding of oral health. Moreover, we experienced increased interest from newspapers, magazines and radio programs on the above subjects, in which we participated. The link oral health - general health is actively communicated by the researchers. Notably, the Dutch Dental Association has announced this link as their anniversary theme for 2014.
Important for the dental profession and the general public, is the substantial number of published and accessible systematic reviews (and meta-analyses) on the various modes of prevention and oral hygiene measures. These contribute to clinical protocols for the dental profession and form the basis for evidence based dentistry.

Ongoing clinical research on oral and head/neck cancer contributes to improved prevention, diagnosis and treatment of relevant patient groups. New plans are developed to bring together knowledge on oral microbiomes and salivary innate immune peptides with oral cancer diagnosis and pathophysiology. The program has strong links with all players in the oral care industry; this not only results in “contract research”, but also in industrial co-funding of grants (STW) and has led to participation of ACTA in the Top Institute Food and Nutrition (TIFN), where the theme “Oral Health” has been initiated. In this theme, world players in the oral care industry, the chewing gum industry, flavour industry, food industry and (oral) care appliances industry collaborate with the University of Wageningen, TNO and ACTA.

The societal impact of the research is evident from the impact on patient care and public dental health, and from collaborations with the industry, as is shown by for instance the grants obtained and the external reports. The societal impact of the clinical research contributes to improved prevention, diagnosis and treatment of relevant patient groups. The societal impact is evident from the items listed below.

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

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

**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.


*Dekker, J. den*: Branche moet anders gaan denken. DFA Magazine 2013, (26), 3-5.


*Le Roos, B.G.* Poets je gezond, interview Algemeen Dagblad (AD), Saturday March 2, 2013, Weekend page 17.


**Impact of the research on professionals**

Patients are referred by their dentists to the various specialized clinics of the clinicians participating in the program for diagnosis and treatment based on the latest scientific evidence. Several scientists of the program had interviews in Dutch dental Journals. A total of 95 professional publications were written.


*Loos, B.G.* Bewustwording van mondgezondheid gaat toenemen, interview Quality Practice (QP) Tandheelkunde, 8 (6): page 4-6.


Louropoulou, A. Interview NMT journal, November 2013.


Organization of congresses and symposia for (health care) professionals


Strijp, A.J.P. van: Co-organizer. ACTA symposium Diagnostic codes in Dentistry: Amsterdam, the Netherlands, November 03, 2013.

Invited speakers at professional congresses or symposia

Bloemena, E. (2013, June 14). Basale Oncologie. Figi Zeist, the Netherlands, NMT congres.


Brand, H.S. (2013, April 12). De tandarts in beeld. Amsterdam, the Netherlands, Nederlands Filmmuseum.


Jongh, A. de (2013, August 27). Psychische problemen met consequenties voor de praktijk. Amsterdam, the Netherlands, VMTI congres "Tussen de Oren".


Krom, B.P. (2013, January 30). Schimmels in de mond bij geriatrische patiënten. Amsterdam, the Netherlands, Studiegroep voor Geriatrische Tandheelkunde.


Loos, B.G. (2013, November 14). Parodontitis bij 55+. Rotterdam, the Netherlands, De Tand in al zijn facetten, National scientific congress, WTA, NVT, NVvE, NVVRT.


Louropoulou, A. (2013, November 22). De reiniging van implantaat-gedragen constructies. Utrecht, the Netherlands, NvVP najaarscongres parallelprogramma.

Louropoulou, A. (2013, February 07). Hoe tandheelkundige implantaten te reinigen. Apeldoorn, the Netherlands, Oral B up to date events.


Louropoulou, A. (2013, October 03). Hoe tandheelkundige implantaten te reinigen. Heerlen, the Netherlands, Oral B up to date events.

Rozema, F.R. (2013, June 06). Capita Selecta 1, Tandheelkunde vs. Geneeskunde: De mond openbaart. Amsterdam, the Netherlands, Medisch Tandheelkundige Interactie VMTI.

Rozema, F.R. (2013, October 03). Quality control integrated in EHR? Amsterdam, the Netherlands, Symposium Diagnostische codes voor de Mondzorg, ACTA.


Slot, D.E. (2013, February 07). Hoe kan een patiënt zijn implantaat het beste reinigen? Apeldoorn, the Netherlands, Oral B up to date events.


Slot, D.E. (2013, October 03). Hoe kan een patiënt zijn implantaat het beste reinigen? Heerlen, the Netherlands, Oral B up to date events.

Waal, I. van der (2013, November 01). De mond als spiegel van de gezondheid. Rotterdam, the Netherlands, Afscheidssymposium A.G. Dumans.


Other professional functions:

Bloemena, E.: Member committee Beroepuitoefening en Kwaliteit NVVP.
Bloemena, E.: Member committee Kwaliteit en Capaciteit Bevolkingsonderzoek Darmkanker.
Bloemena, E.: Member committee Kwaliteitseisen Pathologie Bevolkingsonderzoek Darmkanker.
Bloemena, E.: Member committee Richtlijn Hepatocellulair Carcinoom.
Bloemena, E.: Member committee Richtlijn Hoofd Hals Kanker.
Bloemena, E.: Chair Wetenschappelijke Raad PALGRA.
Danser, M.M.: Chairman Dutch Society for Periodontology.
Diermen, D.E. van: Member Education committee (Vereniging Medisch Tandheelkundige Interactie (VMTI)).
Diermen, D.E. van: Secretary Nederlands Taalkundig Genootschap, Nieuwegein.
Diermen, D.E. van: Member Working group 2 Kamer Mondzorg.
Gorter, R. C.: Executive board member ADEE (since 2013).
Heijden, G.J.M.G. van der: Member Epidemiology Educational Programs Audit Committee Netherlands Epidemiology Society.
Loveren, C. van: Member working group 2 Foundation Kennis Instituut Mondzorg.
Loveren, C. van: Member Guidelines Committee Richtlijn Mondzorg voor jeugdigen.
Loveren, C. van: Chairman scientific advisory board Preventive Dentistry and Oral Diseases, Ivoren Kruis.
Rosema, N.A.M.: Member Accreditatie-Commissie KwaliteitsRegister mondhygiënisten (KRM).
Rozema, F.R.: Member COK.
Rozema, F.R.: Chair Consilium Chirurgicum Oris.
Rozema, F.R.: Councillor IAOMS.
Slot, D.E.: Member Commissie Richtlijn parodontale behandeling in de algemene praktijk, Nederlandse Vereniging voor Parodontologie (NVvP).
Slot, D.E.: Member Congres Commissie Nederlandse Vereniging voor Parodontologie (NVvP).
Slot, D.E.: Member Lustrum Commissie Nederlandse Vereniging voor Parodontologie (NVvP).
Strijp, A.J.P. van: Advisor Guidelines Committee Mondzorg voor jeugdigen.
Weijden, G.A. van der: Member Commissie richtlijn mankrachtplanning Nederlandse Vereniging voor Parodontologie (NVvP).
Weijden, G.A. van der: Member Commissie Richtlijn parodontale behandeling in de algemene praktijk, Nederlandse Vereniging voor Parodontologie (NVvP).
Weijden, G.A. van der: Member Commissie richtlijn Peri-Implantitis NVOI/NVvP.
Weijden, G.A. van der: Member Redactieraad allesoverhetgebit.nl.
Weijden, G.A. van der: Board member Dutch Society for Periodontology.
Courses organized for dental and medical professionals
Scientists of the program participated in courses in the Netherlands for dentists and oral hygienists. More than 16 courses were given in the Netherlands for dentists, medical specialists and oral hygienists by:

- **Deng, D.** (2013, October 28 - November 8). Training course on dental education. This course is organized for 18 teachers from Shanghai Jiao Tong University College of Stomatolgy.
- **Diermen, D.E. van.** Moderator bij Quality Practice voor mondhgyeniësten: Medische situaties in de Mondhygienepraktijk, 13 April 2013 (200 deelnemers)
- **Diermen, D.E. van.** Cursus "Alles over de medische anamnese" voor Mondhygiënisten via DCM, 14 June 2013 (12 deelnemers)
- **Diermen, D.E. van.** PAOT cursus Acute Medische situaties in de tandartspraktijk" op vrijdag 31 mei 2013 (16 deelnemers)
- **Diermen, D.E. van.** Moderator bij najaarscongres NVM: "The circle of life" op zaterdag 9 november 2013 in Den Haag (500 deelnemers)

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

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

- **Aartman, I.H.A.** April 20 and May 18 2013, ACTA Quality Practice, “Hoe waarschijnlijk is mijn diagnose?”
- **Aartman, I.H.A.** November-December 2013, Statistics for Periodontology MSc.
- **Bizzarro, S.** Parodontale chirurgie bij de behandeling van parodontitis, Paroprotocol on road, ACTA Dental Education, Apeldoorn, the Netherlands, June 7, 2013.
- **Bizzarro, S.** Parodontale chirurgie bij de behandeling van parodontitis, Paroprotocol on road, ACTA Dental Education, Breda, the Netherlands, October 4, 2013.
- **Bloemena, E.** Wat doet een patholoog? Opleiding tot oncoloogisch verpleegkundige. Amstel academie, VU, Amsterdam, the Netherlands 12-11-2013.
- **Bloemena, E.** Histology of head and neck squamous cell carcinoma, OOA Course, VUmc, Amsterdam, the Netherlands. 31-1-2013
- **Bloemena, E.** Cytology of salivary gland tumors, AISOS course, AMC, Amsterdam, the Netherlands. 29-1-2013
- **Brand, H.S.** De tandarts in beeld. Nederlands Filmmuseum, Amsterdam.
- **Brand, H.S.** Accidents can happen. Afscheidssymposium professor C. de Baat. Stichting Beeld en Geluid, Hilversum.
- **Danser, M.M.** ACTA QP dag, “Röntgendiagnostiek”, April 20 and May 18, 2013.
- **Danser, M.M.** Moderator ACTA-QP + lecture “AB + CHX, wat is de meerwaarde”, Amsterdam, June 8, 2013.
- **Danser, M.M.** Parodontale nazorg en antibiotica gebruik bij paro-patiënten, Paroprotocol on road, ACTA Dental Education, Breda, the Netherlands, October 4, 2013.
Diermen, D.E. van. 9 January 2013: college Medische Anamnese voor 1e jaars thk studenten en staf.
Diermen, D.E. van. 4 September 2013: “De medische aspecten van lachgas”, voordracht bij ACTA lachgascursus.
Huffels, R.A.M. Effecten van de initiële behandeling, Paroprotocol on road, ACTA Dental Education, Breda, the Netherlands, October 4, 2013.
Jong, T.M.H. de. Effecten van de initiële behandeling, Paroprotocol on road, ACTA Dental Education, Apeldoorn, the Netherlands, June 7, 2013.
Laine, M.L. Hoe om te gaan met slechte adem?, Paroprotocol on road, ACTA Dental Education, Apeldoorn, the Netherlands, June 7, 2013.
Laine, M.L. Hoe om te gaan met slechte adem? Paroprotocol on road, ACTA Dental Education, Breda, the Netherlands, October 4, 2013.
Loos, B.G. Masterclass to medical PhD students (preceeding Ruysch Lecture), Academic Medical Center (AMC), University of Amsterdam, the Netherlands, October 15, 2013.
Loos, B.G. Nieuwe inzichten in de etiologie en epidemiologie van parodontitis, Paroprotocol on road, ACTA Dental Education, Breda, the Netherlands, October 4, 2013.
Loos, B.G. Nieuwe inzichten in de etiologie en epidemiologie van parodontitis, Paroprotocol on road, ACTA Dental Education, Apeldoorn, the Netherlands, June 7, 2013.
Loos, B.G. Post-adolescente parodontitis en ons dilemma wel/niet systemische antibiotica, Department of Periodontology Verwijzersavond, April 10, 2013.
Paraskevas, S. Parodontale herbeoordeling, Paroprotocol on road, ACTA Dental Education, Apeldoorn, the Netherlands, June 7, 2013.
Paraskevas, S. Parodontale herbeoordeling, Paroprotocol on road, ACTA Dental Education, Breda, the Netherlands, October 4, 2013.
Rosema, N.A.M. Update Parodontologie workshop, Quality Practice ACTA, Amsterdam, 8 June 2013.
Slot, D.E. “Do lasers/photodynamic therapy have a role in Non surgical periodontal treatment?” ACTA QP, 8 June 2013.
Academic Centre for Dentistry Amsterdam

Strijp, A.J.P. van. QP Tandheelkunde Themadag Modern Cariësmanagement in restauratief perspectief. Moderne inzichten in de Cariologie (30-11-2013 and 7-12-2013).
Teeuw, W.J. Parodontale screening in de algemene praktijk, Paroprotocol on road, ACTA Dental Education, Apeldoorn, the Netherlands, June 7, 2013.
Teeuw, W.J. Parodontale screening in de algemene praktijk, Paroprotocol on road, ACTA Dental Education, Breda, the Netherlands, October 4, 2013.
Velden, U. van der. Voeding: de verwaarloosde factor in de Parodontologie, Paroprotocol on road, ACTA Dental Education, Apeldoorn, the Netherlands, June 7, 2013.
Velden, U. van der. Voeding: de verwaarloosde factor in de Parodontologie, Paroprotocol on road, ACTA Dental Education, Breda, the Netherlands, October 4, 2013.
Waal I. van der. Oncologie voor de tandarts.. Amsterdam (ACTA). 5 April 2013.
Weijden, G.A. van der. Workshop Air polisher, Utrecht, the Netherlands, February 13.
Weijden, G.A. van der. Workshop Air polisher, Hechten, Amsterdam, the Netherlands. March 7.
Weijden, G.A. van der. Seminar Paro-Restauratief, Amsterdam, the Netherlands, March 7.
Weijden, G.A. van der. Tandhalsgevoeligheid, Den Bosch, the Netherlands, March 11.
Weijden, G.A. van der. Tandhalsgevoeligheid, Amsterdam, the Netherlands, March 12.
Weijden, G.A. van der. Tandhalsgevoeligheid, Zwolle, the Netherlands, March 13.
Weijden, G.A. van der. Workshop Air polisher, Drachten, the Netherlands, February 13.
Weijden, G.A. van der. Seminar Periodontal maintenance, Amsterdam, the Netherlands, May 23.
Weijden, G.A. van der. Workshop air polisher, Amsterdam, the Netherlands, May 23.
Weijden, G.A. van der. Seminar mouthrinses and interdental cleaning, Amsterdam, the Netherlands, May 30.
Weijden, G.A. van der. Moderator ACTA-QP, Amsterdam, the Netherlands, June 15.
Weijden, G.A. van der. Workshop air polisher, Utrecht, the Netherlands, September 2.
Weijden, G.A. van der. Workshop air polisher, Utrecht, the Netherlands, October 23.
Weijden, G.A. van der. Tandhalsgevoeligheid, Regiobijeenkomst NVM, Utrecht, the Netherlands, October 31.
Weijden, G.A. van der. Alles over Mondhygiëne, Compact Clinic KPA, Amsterdam, the Netherlands, November 12.
Weijden, G.A. van der. Mondhygiëne, Ivoren Kruis symposium, Amsterdam, the Netherlands, November 16.
Wesselink, P.R. Twee klinische avonden voor tandheelkundige professionals.
Wesselink, P.R. Tooth injury (Tandletsel). September 28 and October 11 Moderator and speaker ACTA QP Acta dental education BV.
Zerbo, I.R. Implanteren bij de paro-patiënt, Paroprotocol on road, ACTA Dental Education, Apeldoorn, the Netherlands, June 7, 2013.
Zerbo, I.R. Implanteren bij de paro-patiënt, Paroprotocol on road, ACTA Dental Education, Breda, the Netherlands, October 4, 2013.

Collaborations
- Ben Gurion University of the Negev, Beer Sheva, Israel, Dr. M. Meijler.
- Brandwondencentrum Beverwijk, Dr. B. Boekema, Brandwonden project.
- Cairo University, Egypt, Oral Medicine and Periodontology Department, Faculty of Dentistry, Clinic for Conservative Dentistry and Periodontology, Uniklinikum Schleswig-Holstein-Campus, Kiel, Germany, Karim M. Fawzy El-Sayed
- Common Wealth University, Virginia, Prof.dr. H.A. Schenkein
- Dr. Y. Iijima. University of Nagasaki, Japan.
- Erasmus medisch Centrum, Dr. M. van Zelm
- ERC starting grant. UMCG Groningen, Brandwonden project.
- Indiana University-Purdue University, Fort Wayne, IN, USA, Health Science Research Center, Mark Putt
- Interleukin Genetics, USA: Prof. dr. K. Kornman
- Isala Klinieken Zwolle, Algemene Chirurgie, Dr. J. Oskam.
- Prof.Dr. W.H. van Palenstein Helderman, Utrecht
- Tigran, Malmö, Sweden, U. Lundgren
- TNO, Zeist, Dr. E. Tsivtsivadze
- UMCG Groningen, Dr. L.U. Lahoda
- Uniklinikum Schleswig-Holstein-Campus, Kiel, Germany, Clinic for Conservative Dentistry and Periodontology, Christof Doerfer
- Universiteit van Amsterdam, AMC, Dept. of Clinical Chemistry
- Universiteit van Groningen, Dept. of Periodontology
- University Federico II, Naples, Italy. Department of Periodontology, Andrea Blasi
- University of Bandung, Indonesia, Amaliya
- University of Bonn, Dept. of Periodontology, Prof.dr. S. Jepsen
- University of Kiel, Germany, Dept. of Gastro-Enterology, Prof.dr. S. Schreiber
- University of Kiel, Germany, Institute for Clinical Molecular Biology, Dr. A. Scheafer
- University of Kristianstad, Sweden, Prof. dr. S. Renvert
- University of Madrid, Spain, Prof. dr. M. Sanz
- University of Malaya, Malaysia, Faculty of Dentistry, Dr. Rathna Devi Vaithilingam
- University of Maryland Dental School, Baltimore, USA, Dr. M.A. Jabra-Rizk.
- University of Milan, Italy, Unit of Periodontology, Giulio Rasperini
- University of Missouri-Kansas City, USA, Dept. of Periodontics, School of Dentistry, Charles Cobb
- University of Patras, Greece, Prof.dr. T. Bountis
- University of Rome, Italy, Prof. dr. Pilloni
- AMC: Dept of microscopy. Dr. J. Stap, Amsterdam
- Birkhoven zorggoed. Vakgroep medische dienst. Dr. G.J. van der Putten. Amersfoort
- Centre for Integrative Bioinformatics (IBIVU), VU Amsterdam, Prof. J. Heringa, Dr. S. Abeln.
- Department of Farm Animal Health, Faculty of Veterinary Medicine, Utrecht University, Utrecht, the Netherlands. Dr. Gerrit Koop.
- Department of Oral Medicine, Charlotte, NC, USA. Mike Brennan and Peter Lockhart.
- Dr. Alex Mira, Center for Advanced Research in Public Health, Valencia, Spain.
- Dr. Wilfred Röling, Molecular Cell Physiology, FALW, VU.
- Erasmus MC, Department of Medical Microbiology and Infectious Diseases, Rotterdam, the Netherlands. Mw. W.E. Kamar-van Zanten, dr. J.P. Hays, dr. Willem van Wamel
- Fong Moy MD, Prof. Awang Bulgiba, MSc PhD, Medical School, University of Malaysia, Kuala Lumpur, Malaysia
- Hebrew University-Hadasah. Dr. Davidovich, Jerusalem, Israel
- Khon Kaen University, Dept. Of Oral Diagnosis. Dr. S. Taweewchaisupapong, Khon Kaen, Thailand.
- Kindertandheelkundepraktijk Bambodino. Dr. D.L. Gambon, Rotterdam
- Max Planck Institute for Chemical Ecology, Department of Bioorganic Chemistry, Jena, Germany. Prof Dr Axel Mithoefer,
- Max Planck Institute for Chemical Ecology, Department of Bioorganic Chemistry, Prof. dr. Axel Mithoefer, Jena, Germany
- Medical School, Prof. van Laar, Newcastle upon Tyne, U.K.
- Medisch Centrum Leeuwarden. Dr. De Visscher, Leeuwarden
- Nederlands Speekselcentrum. Dr. C.P. Bots, Hilversum
- Paul Glasziou, Centre for Research in Evidence-Based Medicine, Faculty of Health Sciences and Medicine, Bond University, Queensland, Australia, and Centre for Evidence-Based Medicine & Department of Primary Care, Oxford University, Oxford UK
- Peking University School of Stomatology. Prof. Hong Hua, Beijing, China
- Prof. Helen Worthington, PhD; Paul Brocklehurst PhD; Prof Iain Tickle, PhD; School of Dentistry, The University of Manchester, Manchester, UK
Current PhD projects


Macedo, RG de. Aspect of sodium hypochlorite as a root canal irrigant. Supervisor: prof.dr. P.R. Wesselink; co-
supervisor: dr. L.W.M van der Sluis, start: October 2010.


Oral Regenerative Medicine

Program Leader
Prof. dr. V. Everts
Department of Oral Cell Biology
ACTA Gustav Mahlerlaan 3004
1081 LA Amsterdam
Tel: +31-20-5980882
E mail: V.Everts@acta.nl

Full professors

A.G. Becking  C.M. ten Bruggenkate  A.J. Feilzer  S. Gibbs  J. Klein-Nulend
J. de Lange  F. Lobbezoo  M. Naeije  F.J.M. Roeters  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. Importantly, trauma or disease may result in damaged tissues which in turn result in functional oromandibular impairments. The research of ACTA’s research program “Oral Regenerative Medicine” (ORM) focuses on regenerating damaged oral tissue by means of stem cell therapy or tissue engineering techniques, taking into account the mechanical threats for the masticatory system and inflammatory reactions involved in tissue repair. Relevant clinical problems are used to guide the research
 aimed at developing novel solutions for these clinical problems. Groups that are involved in ORM-ACTA are Oral Kinesiology (OKI), Oral Implantology and Prosthodontics (IMP), Dental Materials Sciences (DMS), Oral Cell Biology and Functional Anatomy (OCB/FA), Oral Radiology (ORA), Orthodontics (ORT), and Oral and Maxillofacial Surgery (OMS), both of the Academic Medical Center (AMC) and of the VU Medical Center (VUmc).

The Interfaculty MOVE Research Institute has chosen “Regenerative Medicine” as one of its domains (i.e., a collaboration of researchers within the VU campus on a key topic). Likewise, ORM has been formulated as one of the two priority areas (“zwaarte punt”) of ACTA. As implied above, a healthy oral system is characterized not only by the absence of infection and/or inflammation of dental and periodontal tissues, but also by a healthy musculoskeletal system and oral mucosa. Musculoskeletal tissues (i.e., bone, cartilage, muscles, and joints) and mucosa (epithelium and underling connective tissue) can be damaged or even destroyed by, for example, mechanical overloading, disuse, disease or trauma. In case of tissue loss, the replacement or regeneration of degenerating/degenerated cells, tissues, or organs is needed to restore or establish normal function (Mason A, Dunnill PA. A brief definition of regenerative medicine. Regen Med 2008;3(1):1-5). ORM studies these processes both at a fundamental and translational level in multidisciplinary settings, in which dentistry/oral medicine closely collaborates with medical disciplines like orthopaedics, neurology and dermatology/ plastic surgery, both within and outside The Netherlands. The main objectives of ORM-related research are: (1) to develop strategies to prevent degeneration of oral tissues and/or organs by understanding the mechanisms of tissue homeostasis and repair, and (2) to develop minimally invasive, regenerative treatment strategies when prevention fails and treatment is required. Clearly, a focus on early diagnosis will play an important role in repairing tissue damage before it becomes too extensive.

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 and biomaterials together with the impact of mechanical loading and their interaction with the implanted area which is essential if optimal tissue regeneration and vascularized graft take without adverse reactions 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/degenerated oral tissues and an improved ability to replace or regenerate these tissues, thereby restoring oral function and thus oral health-related quality of life.

**Research objectives**

**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 treatment and 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 and rehabilitation of impaired or lost ortho-mandibular function. Two main approaches can be distinguished. First, fundamental studies are conducted to develop novel advanced techniques, prior to clinical testing in patient studies (phase 1), taking into account all the regulatory issues within NL and Europe for “advanced therapy medical products” (ATMPs) and medical devices. Noteworthy in this context are studies to:

- a) stimulate bone growth around dental implants and into bone defects;
- b) close oral mucosa lesions with tissue engineered mucosa when native autograft mucosa is limiting;
- c) study of the interaction of the cells and biomaterials to be implanted with wound healing mediators derived from the implant site (wound bed) as the inflammatory status will influence graft take and vascularization;
- d) fabricate dental restorations using computer-aided design and manufacturing (CAD/CAM);
- e) use tissue engineering and regenerative medicine techniques, focussing on the collagen network and adipose stem cells;
- f) use tissue engineering techniques, focussing on the collagen network and adipose stem cells;
- and g) improve the microcirculation in patients undergoing, for example, radiotherapy for malignancies.

Second, phase 1 (safety and 1st efficacy) and phase 2 randomized clinical trials are performed to test novel constructs described above and to add 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 2013

Tissue regeneration and engineering

- A novel role for CD27 in osteoclast formation was established. Bone marrow osteoclast precursors express this molecule. Interaction with CD70, which is expressed on activated immune cells, skews differentiation towards dendritic cells.
- Osteonecrosis is a common side-effect of high dosage bisphosphonate use. Bisphosphonates are commonly used drugs that inhibit osteoclasts by causing osteoclast apoptosis. Long bones are not prone to this side effect. It was now shown that mouse jaw marrow cells that are driven towards osteoclast differentiation take up more bisphosphonate than long bone marrow cells, thus indicating bone-site specific responses to bisphosphonates.
- Dietary magnesium deficiency could cause osteoclasts to resorb bone, thus compensating for the deficiency. The effect of magnesium deprivation on osteoclasts was studied in vitro. Deficiency caused an increased osteoclastogenesis, both from long bone and from jaw bone marrow cells.
- We studied how cultured stem cells and keratinocytes will interact with soluble wound healing mediators present within the wound bed after transplantation. Upon transplantation keratinocytes are primarily activated to promote wound closure. In contrast, dermal fibroblasts and in particular adipose derived stem cells (ASC) respond vigorously to factors present in the wound bed leading to increased secretion of angiogenesis/granulation tissue formation factors. These findings have implications for the choice of cell type (ASC or dermal fibroblast) to be used in regenerative medicine strategies and indicates the importance of taking into account interactions with the wound bed when developing advanced therapies for difficult to close cutaneous wounds (eg burns and ulcers).
- We have described human maxillary sinus floor elevation as a model for bone regeneration enabling the application of one-step surgical procedures. In addition, we reported a novel approach revealing the effect of a collagenous membrane on osteoconductivity in maxillary sinus floor elevation with β-tricalcium phosphate. We reported growth factor gene expression profiles of bone morphogenetic protein-2-treated human adipose stem cells seeded on calcium phosphate scaffolds in vitro. Finally, we reported important differences in proliferation, differentiation, and cytokine production by bone cells seeded on titanium-nitride and cobalt-chromium-molybdenum surfaces.
- A model for cell-mechanics studies has been published for testing the influence of nanostructural environment and fluid flow on osteoblast-like cell behavior. Using this model, we found that endothelial nitric oxide synthase is not essential for nitric oxide production by osteoblasts subjected to fluid shear stress in vitro. A review paper on nitric oxide signaling in mechanical adaptation of bone is published. We also used the model for cell-mechanics to show that strontium ranelate, an anti-osteoporotic drug, affects signaling from mechanically-stimulated osteocytes towards osteoclasts and osteoblasts.
- In collaboration with researchers from different institutes, among which VUmc, it was found that X-linked PLS3 mutations cause osteoporosis and fractures. This finding has attracted much attention, and has been

- Developmental defects in pH-regulating transmembrane molecules can affect the structure of enamel and bone. We recently detected in mouse ameloblasts (the cells that produce enamel) several new pH-regulating molecules including NKCC1, NKCC2, Slc26A3 and Slc26A6. These molecules are well known pH-regulators and ion-transporters in pancreatic and renal tubular epithelium. A transmembrane molecule (SPPL2a) isolated from brain and present in B-cells was also expressed by mouse ameloblasts. Disruption of the Sppl2a gene in mice caused severe enamel defects, indicating the relevance of this protein for formation of enamel.

- Muscle fibers adapt to functional demands. In a study to unravel the mechanism behind this adaptation process it has been demonstrated that in particular so-called hybrid fibers adapt more easily to their mechanical environment than other fibers.

- In order to quantify the local deformation of bone, electronic speckle pattern interferometry has been successfully applied as a new technique to approximate the deformations of the whole cortex under influence of bone loading. This enables to validate finite element models that had been constructed to predict the relationship between bone loading and deformation.

- A considerable heterogeneity of the cortical bone-mineral density was found in the mandibles of adult rabbits. The heterogeneous mineral-density distribution might serve to suppress bone-strain amplitudes in regions architecturally susceptible to larger deformations during loading.

- Biomechanical analysis of the effects of a fractured mandibular neck and its treatment by maxillomandibular fixation have demonstrated that altered articulation in the temporomandibular joint may give rise to disturbances in mandibular movements and dysocclusion. Furthermore, the treatment does not necessarily prevent the mandibular condyle to dislocate.

- 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 be also an alternative for metal implants. Understanding the surface properties of zirconia is therefore ongoing research.

**Clinical signs, symptoms and diagnosis**

- Two systematic reviews of the literature assessed the prevalence of (sleep-related) bruxism in adults and children, respectively. Both studies suggest that bruxism is a common condition in both populations. However, there is a high variability in findings due to methodological shortcomings. Both papers provide suggestions for future studies on this topic.

- Polysomnographically recorded sleep bruxism and periodic limb movements during sleep were shown to have a common underlying neurophysiological mechanism associated with arousals in the electroencephalogram. While polysomnography is the gold-standard diagnostic tool for sleep bruxism, self reports and clinical assessments for this condition were only poorly correlated.

- A research protocol was developed for the assessment of associations between masticatory activity and quality of life in elderly persons with a dementia. For the assessment of masticatory activity, a two-colour chewing gum test was developed and tested for its reliability and feasibility for use in this difficult and fragile patient population.

- For the assessment of pain in patients with Down syndrome, modified versions of the facial affect scale and of the numeric rating scale are recommended. Any application must be preceded by a comprehension assessment. A systematic assessment of the literature could not identify a specific pattern of behavioural pain indicators in people with intellectual disabilities.

- An experimental study suggested that temporomandibular disorder (TMD) pain is a manifestation of delayed-onset muscle soreness. When myogenous TMD pain is provoked by means of hypertonic saline injections, a reorganization of increasing and decreasing muscle activities occurs. For the clinical diagnosis of TMD pain, a finding of familiar pain on dynamic/static testing yields diagnoses that are the least influenced by comorbidities like depression and somatisation.

- Tooth wear rather than TMD pain has a negative impact on a patient’s quality of life. This impact is comparable with that of edentulousness.

- Adverse reactions of metals to the skin are common. Also adverse oral reactions can be related to the use of metals. The use of palladium (Pd) 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.
• A survey amongst Dutch Dentists showed large differences in the motivation to adopt and use digital technologies in everyday practice. There were only a few enthusiastic early adaptors meaning that there is a distinct role for those involved in teaching in dentistry to take this into account.

• Preclinical safety testing of new (and existing) biomaterials is essential before these substances are used in humans. If such prior safety testing is not performed, implanted biomaterials may result in an inflammatory reaction eg. allergy or irritancy. Within a European and American collaboration, and in full compliance with the 3Rs, an in vitro human epithelial equivalent model has been developed (in our laboratory) and tested internationally to identify potentially sensitizing from irritant or non-irritant substances and to determine the potency (strength) of the sensitizer/irritant.

• Field of View in CBCT influences the depiction of trabecular microstructure in human mandible.

• Grey values in CBCT systems significantly deviated from Hounsfield unit values measured with MSCT. Field of View FOV and spatial resolution and number of projections had a significant influence on grey valu measurements in CBCT images.

• Cephalometric soft-tissue evaluation from a recording of a patient in supine position is generally reliable, except for the throat-chin area where a clinically relevant difference was found. The contour of the submandibular tissues in supine position causes the chin to appear more prominently. This may cause incorrect orthodontic diagnosis and treatment planning.

Treatment and rehabilitation
• 83 patients with 99 therapy resistant ulcers were treated with a novel full thickness tissue engineered skin construct in an extensive phase 1 multicentre study. No related adverse events occurred and wounds became revitalized resulting in healing. A hospital exemption has now been given by IGZ to treat all patients with chronic skin wounds with this ATMP skin construct in NL who cannot be included in a clinical study.

• In a community dental care population, mandibular advancement devices could be indicated and monitored successfully in patients with obstructive sleep apnea (OSA) and snoring. At the same time, a randomized clinical trial with occlusal stabilization splints were shown to worsen an existing OSA in some, but not all patients. The findings of both studies have immediate clinical implications.

• Care-seeking of patients with temporomandibular disorder (TMD) pain is mainly determined by person-related characteristics, like catastrophizing, assertiveness, and a critical attitude towards healthcare. Improvement of TMD-pain complaints over a 6-month period is best predicted by the number of care practitioners attended (positive) and the degree of hindrance on function (negative).

• Tooth colour and the colour and discolouration of restorations are still a challenge for the dentist and scientist. The focus of the research was on the perceptibility and acceptability thresholds for colour differences.

• Research on the efficacy and precision of intra oral scanners as a substitute for non-digitized impression techniques shows that there is still a lot to win in the precision and time involved when using these techniques.

• In a literature review on the use of digital implant planning tools the precision of these show a high variety of results and these are user and system dependent. We found that patients with an overdenture in the maxilla supported by two implants prefer to have the palate uncovered by the denture base when taking aesthetics and taste into account.

• We found that patients fitted with an overdenture on two implants in the maxilla show an increased satisfaction level, less psychological discomfort, less physical and social disability as well as increased chewing ability, speech and general satisfaction (OHIP).

• We introduced a new classification of peri-implant bone defects in implant patients based on a long term radiological follow-up of 110 patients over 16 years.

• We showed in a multi-center trial that the function of bilateral distal extension removable partial dentures supported by distally placed implants significantly increased patient satisfaction during function.

• We showed that long term outcomes of crowns supported by short implants in the posterior regions of the jaw can be a predictable treatment outcome.

• An anatomically shaped cranial collimator was designed to reduce radiation exposure in cephalomatric imaging. The shape of the area shielded by this collimator was based on mean measurements of cephalometric landmarks of 100 orthodontic patients. The collimator reduces the irradiated area by almost one-third without interfering with the imaging system or affecting the image quality.
## Academic personnel in 2013 and 2014

### Research staff ACTA – ORM Oral Regenerative Medicine

(in full time equivalents)

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<tr>
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Total non tenured staff

| Total 1st funding | 19.20 | 16.10 |
| Total 2nd funding | 22.15 | 19.45 |
| Total 3rd funding | 2,15  | 2,15  |
| Total research staff | 8,35 | 6,85 |
| Total 3rd funding | 32.65 | 28,45 |

Output

Dissertations


Scientific publications (referred)


in osteoclast development by CD70 on activated immune cells. Proceedings of the National Academy of Sciences of the United States of America, 110(30), 12385-12390.


Scientific publications (non refereed)


Professional publications


Publications aimed at the general public

Grants: current projects with external funding
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).

Bronckers, A.L.J.J.: NIH grant for joint collaboration between Oral Cell Biology ACTA, Amsterdam, Oral Biology, Semmelweis University of Medicine, Budapest, Hungary and UCSF School of Dentistry, USA (US$ 52.000).

Chen, H. PhD project is financially supported by the China Scholarship Council (CSC).


Dental Oy Instrumentarium lends a OP300 CBCT unit for research and clinical purposes. Expected term: 3 years. Annual worth: ± € 20.000.

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.

Everts, V. Coordinator of FP7-PEOPLE-2013-Marie Curie ITN project EUROCLAST. Project with 7 academies and two private companies. 11 ES Rs € 3.100.000, September 2013-September 2017.

Feilzer, A.J., Klein Nulend, J., Kleverlaan, C.J. & Everts V. Research priority grant, University of Amsterdam, €1.650.000,,- 2012-2016.


Gorter R.C. & Wismeijer, D. International Team for Implantology (ITI): Digital dentistry in practice; on dentists’ interaction with technological transformations. First part of PhD project funding, collaboration of Social Dentistry and Oral Implantology. February 2012 – December 2013: € 110.000,-.

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.


Wismeijer, D. 2012. 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.

Indicators of Esteem
Editorship book

Memberships of editorial board
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 Reconstructive Dentistry.
Lobbezoo, F.: Journal of Craniomandibular Function.
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
Organization of (inter)national scientific congresses and symposia

Everts, V. (2013). Organizer. Two day conference Dutch Society Calcium and Bone Metabolism: Woudschoten, the Netherlands (2013, November 14 - 2013, November 15).


Invited speakers at (inter)national congresses or symposia


Delwel, S. (2013, October 12). Challenges of orofacial pain assessment in elderly with dementia. 2nd Amsterdam Symposium on Palliative Care, Vrije Universiteit, Amsterdam, the Netherlands, Research meeting.


Everts, V. (2013, November 21). Bone remodeling, recent insights. Istanbul, Turkye, Yeditepe University, Dental Faculty.

Gibbs, S. (2013, March 13). Allergenicity testing of chemicals from an innate immunology perspective. Amsterdam, the Netherlands, European Immunology workshop.


Kuijts, R.H. (2013, September 06). Tooth wear, to treat or not to treat. What are the questions? Eye, Amsterdam, the Netherlands, ACTA-DE International Tooth Wear Congress: 4 clinical approaches 4 tooth wear.


Lobbezoo, F. (2013, September 27). The DC/TMD expanded. Bordeaux, France, EACD.


Wismeijer, D. (2013, October 17). What have we learned and where are we going to. Dublin, Ireland, EAO Dublin, satellite symposium Camlog.

Other (inter)national scientific functions
Aarab, G.: Member research committee American Academy of Dental Sleep Medicine (AADSM).
Disse, M.: Member EFOSA on behalf of the NVvO.
Gibbs, S.: Member European Research Group for Experimental Contact Dermatitis (ERGCD).
Gibbs, S.: Member and principal investigator NIRM.
Goené, R.J.: President Post-Academic Education Committee NVvO.
Klein Nulend, J.: Directory board member of the MOVE Research Institute Amsterdam, VU University Amsterdam, the Netherlands.
Klein Nulend, J.: Member scientific board Department of Regenerative Medicine, Research Centre for New Technologies in Life Science EngineerinKleing, University of Tehran, Iran.
Klein Nulend, J.: Member research assessment committee Group Biomedical Sciences (Dept. Oral Health Sciences and Dept. Development and Regeneration), KU Leuven, Belgium.
Koutris, M.: Chair research committee European Academy of Craniomandibular Disorders (EACD).
Kramer, G.J.C.: Chair Wetenschap en Accreditatie commissie NVvo.
Kuitert, R.B.: Member Richtlijncommissie NVvo.
Lobbezoo, F.: Member management committee .EU-COST Action TD-1005 (Pain assessment in patients with impaired cognition, especially dementia).
Lobbezoo, F.: Member working group 1 Psychometrics and Algesimetry .EU-COST Action TD-1005 (Pain assessment in patients with impaired cognition, especially dementia).
Lobbezoo, F.: Member Grindcare Clinical Advisory Board (CAB) of the Danish company Medotech, Denmark.
Loon, J.J.W.A. van: Member scientific and program committee ELGRA Biennial Symposium and General Assembly, Vatican City, Rome, Italy, 11-14 September 2013.
Loon, J.J.W.A. van: Member review board ESA Spin-Your-Thesis (SYT) and Drop-Your-Thesis (DYT) educational programs; March 2013.
Loon, J.J.W.A. van: Member ESA Topical Team Advanced Compound Microscopy (From Molecules to Organism Morphology). Coordinators Jürgen Bereiter-Hahn (Goethe University Frankfurt am Main) and David Jones (Philippus University Marburg), February 2013.
Loon, J.J.W.A. van: Member management committee European Low Gravity Research Association (ELGRA).

Prahl, C.: Board member NVOS.
Prahl, C.: Board member Stichting ter bevordering van de orthodontie.
Prahl, C.: Member study group USA: Angle Society North Atlantic Component.
Sanderink, G.C.H.: Chairman Trustfund IADMFR.
Stelt, P.F. van der: Scientific advisor Kuwait University.
Visscher, C.M.: Board member Physical Therapy Board of Craniofacial and Cervical Therapeutics (PTBCCT), USA.
Wetselaar, P.: Member committee Tandartsen Nauta Nederlandse Vereniging voor Gnathologie en Prothetische Tandheelkunde.
Wismeijer, D.: Chairman 5th ITI consensus conference group, Kursaal, Berne (CH): Clinical guidelines as produced on the topics of CAD/CAM, implant abutment materials and complications involving implant abutments and abutment material.
Wismeijer, D.: Member Consensus conference Camlog Rome: 'Effect of the dept of implant placement on boneloss around implants.
Wismeijer, D.: Honorary consultant Dental Clinic, School of Stomatology, Zhejing Chinese Medical University, Hangzou.
Wismeijer, D.: Member scientific advisory board International Association of Digital Dentistry (IADD).
Wismeijer, D.: Member ITI Education Committee.
Wismeijer, D.: Member ITI Research Committee.
Wismeijer, D.: Examiner Royal College of Surgeons of Scotland.
Zandieh Doulabi, B.: Visiting professor Research Center for New Technologies in Life Sciences Engineering, University of Tehran, Iran.
Zandieh Doulabi, B.: Head Department Regenerative Medicine Research Centre for New Technologies in Life Science Engineering, University of Tehran, Iran.

Supervisor of an external PhD student
Societal impact
The societal impact of the programme is evident by, among others, the impact on patient care, interactions with the industry and other non-university groups, the impact on professionals, and relevant (inter-)national functions. The research program also contributes to the post-graduate training programs.
The research on overloading and pain of the musculoskeletal structures of the masticatory system has direct impact on the quality of diagnostic procedures and of patient care, and extends its influence towards an improvement of the (oral-) health-related quality of life. The implications of this research are not only important for general orofacial pain patient groups, but also for more vulnerable populations like those suffering from dementias and otherwise impaired cognitive abilities.
An ambitious future goal of the program is to improve health care and treatment of patients with juvenile idiopathic arthritis. Diagnosis of arthritis of the jaw joint is commonly missed by clinicians, eventually possibly leading to progressive pain and malfunctioning of the joint. Research started in 2012 is focused on learning the biological parameters of the three types of cartilage present in the jaw joint. Inflammation will be mimicked in vitro and it will be determined whether mechanical loading will lead to a decreased inflammation.
Special focus is on orthodontic patients with cranio-facial deformities and/or related malocclusions. A program of quality of life related to this topic is carried out.
During the last couple of years it became clear that implanted materials like metals can have adverse effects like allergy. This last subject is now an important issue of investigation. An improved understanding how metals may induce an allergic reaction will have an enormous impact on the society.
The societal impact of the research on oral and maxillofacial radiology is focused on the improvement of diagnostic imaging procedures. This relates to not only technical parameters, but also other factors that influence the diagnostic performance of radio-diagnostic procedures, such as the effect of viewing conditions and observer characteristics. Part of the activities includes continuing education courses on the safe use of radiation in dental practice and application of digital imaging in dentistry.
Enamel fluorosis is an increasing aesthetic problem in several countries. The project on mechanism of enamel fluorosis adds to our understanding how these defects develop which will help to prevent these defects in future. The results of our research on bone adaptation and regeneration will offer multiple opportunities for the development of new therapeutic agents to prevent (inflammation-associated) unwanted clinical bone loss, thereby preventing among others mobility loss with aging.
The societal impact of the clinical research on oral and maxillofacial surgery is focussed on the influence on patient care, both within the department and externally. Research contributes to improved treatment of relevant patient groups.
More details of the societal impact of the program are listed below.

Radiology
The societal impact of the research on oral and maxillofacial radiology is focused on the improvement of diagnostic imaging procedures and radiation safety. 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 ConebeamCT in dentistry. In 2013 the Ministries of Social Affairs and Public Health officially recognized the ConebeamCT course of the department of Oral Radiology as a “Radiation Protection course”.

Oral and Maxillofacial Surgery/Oral Pathology VUmc
The societal impact of the research of the department of Oral and Maxillofacial Surgery/Oral Pathology is focussed on the influence on patient care, both within the department and externally. Research on all main areas of interest contributes to improved prevention, diagnosis and treatment of relevant patient groups. The societal impact is evident from the items listed below.

Interactions and collaborations with the industry and other non-university groups
Several scientists of the program have contacts with the industry, see the list of current grants in de paragraph of indicators of esteem above.
The department of Oral and Maxillofacial Surgery/Oral Pathology has collaborations with the firms Straumann and Biohorizons related to maxillofacial implantology (Ten Bruggenkate, Schulten, Forouzanfar).
Department of Radiology: Instrumentarium Dental Oy, Finland.
Disse, M. Orthodontist in het schisisteam.
Kramer, G.J.C. Orthodontist schisisteam MCA.
Kramer, G.J.C. Voorzitter/secretaris Special Interest Group Orthodontics NVSCA.
Lobbezoo, F. Member of the Grindcare Clinical Advisory Board (CAB) of the Danish company Medotech.
Prahl, C. Orthodontist in het schisisteam VUmc.
Visscher, C.M. Board member of the Physical Therapy Board of Craniofacial and Cervical Therapeutics (PTBCCT), USA, 2003-present.

Impact of the research on the general public

Impact of the research on professionals
Patients are referred by their dentists to the various specialized clinics of the departments participating in the program for diagnosis and treatment based on the latest scientific evidence. The guidelines for diagnosis and treatment of patients have been adopted by the Dutch association for Oral and Maxillofacial Surgery (Nederlandse Vereniging voor Mondziekten, Kaak- en Aangezichtschirurgie, NVMKA).
Lobbezoo, F. Member of the Dutch Society of Headache Patients Committee that develops a Guideline for the Diagnosis and Treatment of Orofacial Pain.
Visscher, C.M.: Member of the Dutch Society of Headache Patients Committee that develops a Guideline for the Diagnosis and Treatment of Orofacial Pain.

Organization of congresses and symposia for (health care) professionals
Klein Nulend, J. (2013). Organizer. Osteo-Artrose Refeereravond (3x) under auspices of the MOVE Research Institute Amsterdam, VU University Medical Center, Amsterdam, NL; co-organizer: Prof.dr. W.F. Lems (VUmc, Dept. Rheumatology); Amsterdam, the Netherlands (2013, November 14 - 2013, November 15).
Wismeijer, D. 10-10-2013 Voorzitter studie club ITI Gelderland Hotel Avegoor te Ellecom 19.00 – 22.30 Peri-implantitis.
Wismeijer, D. 17-12-2013 Voorzitter studie club ITI Gelderland Hotel Avegoor te Ellecom 19.00 – 22.30 Calcium Phosphate bone substitutes.

Invited speakers at professional congresses or symposia
Baart, J.A. (2013, November 15). De tand in al zijn facetten II. Rotterdam, the Netherlands, Congres de Doelen.
Bruggenkate, C.M. ten (2013, March 16). Augmentation. Amsterdam, the Netherlands, Implantologie à VU.
Bruggenkate, C.M. ten (2013, March 26). Implant success or failure. Gorinchem, the Netherlands, Course on Implantology.


Bruggenkate, C.M. ten (2013, September 13). Sinuslifting. Putten, the Netherlands, NVOI het Fundament.

Bruggenkate, C.M. ten (2013, December 03). Stem cell project. Amsterdam, the Netherlands, CTRM congress ACTA.


Goené, R.J. (2013, March 08). Teamwork: all of us know more than one of us. Amsterdam, the Netherlands, ITI Thema-avond.

Karssemakers, L.H.E. (2013, August 14). Een nieuw gezicht voor Nv assisterenden in MKA. CT bij UCH. Assen, the Netherlands, 57e Najaarsvergadering NvMKA.


Lobbezoo, F. (2013, April 12). Slaapstoornissen, snurken en slaapapneu. ACTA, Amsterdam, the Netherlands, WTA Spring Congress 2013 “Slaapstoornissen”.


Other professional functions

Baart, J.A.: Member scientific advisory board Geneesmiddelen Bulletin (GeBu).
Bruggenkate, C.M. ten: Chair Nederlandse ITI sectie.
Lobbezoo, F.: Advisory board member ACTA Quality Practice.
Lobbezoo, F.: Chairman The Netherlands Institute for Dental Sciences (IOT).
Wetselaar, P.: Member committee Tandarts Gnathologen Nederlandse Vereniging voor Gnathologie en Prothetische Tandheelkunde.

Visscher, C.M.: Chair science committee Nederlandse Vereniging voor Orofaciale Fysiotherapie (NVOF).

Courses organized for dental and medical professionals

More than 46 courses were given in the Netherlands for dentists, medical specialists and oral hygienists by the following scientists:

A total of more than 30 courses were given by staff members of the dept. of Oral Radiology: W.E.R. Berkhout, R.C. Hoogeveen, G.C.H. Sanderink and P.F. van der Stelt.


Goené, R.J. Implantologie: Het Fundament, NVOI, Putten, 22 & 23-03-2013
Goené, R.J. Implantologie voor praktijkmedewerkers, NVOI Jubileumcongres, 16/19-05-2013
Goené, R.J. Implantologie: Het Overzicht, NVOI, Utrecht 16-06-2013
Goené, R.J. Implantologie: Het Fundament, NVOI, Putten, 13-14-09-2013
Goené, R.J. Person to Person, Biomet/3i Tendenstandartsen, Amsterdam, Live surgery, 21-09-2013
Goené, R.J. Implantologie Integraal, NVOI, Putten, 4-10-2013
Goené, R.J. Implantologie De Verdieping, NVOI, Putten, 21 & 22-11-2013

Koolstra, J.H. Organizer, ACTA-QP-cursus “TMD-Doedag” (Amsterdam, March 2013).

Tahmaseb, A. 21-01-2013: Cadaver Course Rotterdam.

Wismeijer, D. 21-11-2013. NVOI de verdieping. 1) Implantologie in een digitale omgeving. 1 hr. 2) Bruggen op implantaten 1 hr. 14 November.

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


Baart, J.A. Antibiotica en pijnstellers. Patiënten en hun pillen: the big four try out NVT-NVMKA-VMTI, ACTA Amsterdam; 6 February 2013
Baart, J.A. Wilt u de mond focusvrij maken? QP oncologie ACTA Amsterdam, 2 February 2013
Baart, J.A. Mondziekten en kaakchirurgie voor huisartsen. VUmc Amsterdam; 7 February 2013
Baart, J.A. Kaakchirurgie bij kinderen. RAAK kinderartsen AMC-VUmc; 19 February 2013
Baart, J.A. Locale anesthesie voor assisterenden. Dental education ACTA/VUmc 7 March 2013
Baart, J.A. Uitbreiding dentogene ontstekingen, lokale anesthesie en extracties voor tropenartsen. VUmc Amsterdam 14 March 2013
Baart, J.A. Beroep kaakchirurgie. Weekend academie Amsterdam, ‘t Koggeschip Amsterdam, 16 March 2013
Baart, J.A. Medische situaties in de mondhygiënepraktijk. Pijnbestrijding tijdens en na de behandeling. Quality Practice, ACTA dental education; 13 April 2013
Baart, J.A. Atraumatisch extraheren en ridge preserveren. Obdam 5 April 2013
Baart, J.A. Koester je patiënten, ook als ze pillen gebruiken. Klinische avond, Leiderdorp; 9 April 2013
Baart, J.A. Antibiotica en pijnstillers. Patiënten en hun pillen: the big four try out NVT-NVMKA-VMTI, Den Haag; 17 April 2013
Baart, J.A. Antibiotica en pijnstillers. Patiënten en hun pillen: the big four try out NVT-NVMKA-VMTI, VUmc Amsterdam; 24 April 2013
Baart, J.A. Pain management during and after treatment. Russian society of dental hygienists. ACTA InHolland; 2-4 May 2013
Baart, J.A. De kaakchirurg in het schisisteam. Schisisdag ACTA dental education, Amsterdam; 17 May 2013
Baart, J.A. Autotransplantatie van een premolaar na een fronttrauma. QP ACTA; 28 September 2013
Baart, J.A. Weefselsparende kaakchirurgie. NVT/WTA Amsterdam; 4 oktober 2013
Baart, J.A. Autotransplantatie van een premolaar na een fronttrauma. QP ACTA; 12 October 2013
Baart, J.A. Radiologie: straling, diagnostiek en verantwoordelijkheden. QP ACTA; 2 November 2013
Baart, J.A. E-learning “pijnstilling in de tandartspraktijk” live online BSL; 19 november 2013
Baart, J.A. Wintersymposium. Aangezichtstrauma: epidemiologie en algemene principes. VUmc/ACTA; 13 December 2013
Baart, J.A. Schisisdag voor tandartsen. Kaakchirurgie bij schisiskinderen. ACTA-VUmc Amsterdam; 7 May 2013
Baart, J.A. Lokale anesthesie voor assisterenden. IJburg-tandheelkundig centrum Amsterdam; 17 May 2013
Baart, J.A. Lokale anesthesie voor assisterenden. Alkmaar 8 June 2013
Baart, J.A. Weefselsparende tandheelkunde. WTA-cursus. ACTA; 4 October 2013
Baart, J.A. Lokale anesthesie voor assisterenden. ACTA-VUmc; 7 November 2013
Forouzanfar, T. Bloedverdunners in de tandartspraktijk. Themaproject NVT-NVMKA-MTI, Alkmaar en Maastricht 8 February and 2 May 2013
Forouzanfar, T. Pijnstillers in de tandartspraktijk. Themaproject NVT-NVMKA-MTI, Alkmaar en Maastricht 8 February and 2 May 2013
Goené, R.J. Atraumatisch extraheren en ridge preserveren. Obdam 5 April and 10 October 2013
Lobbezoo F. Kauwen op bruxisme. Contribution to ACTA-QP Course “TMD-Doedag” (Amsterdam, 2 & 9 March 2013).
Lobbezoo F. All you need to know about pain! Bijdrage ACTA-DE Course “Pijn, een verwarrend dilemma” (Amsterdam, March 2013).
Lobbezoo F. Moderator WTA Spring Congress 2013 “Slaapstoornissen” (Amsterdam, April 2013).
Schulten, E.A.J.M. Reconstructie van kaakdefecten na chirurgische tumorbehandeling: chirurgische en
prothetische mogelijkheden. Themadag Quality Practice: Mondafwijkingen - de rol van de tandarts. ACTA 26-01 and 02-02-13


Vervoorn-Vis G.M.G.J. Workshop ‘TMD-functieonderzoek’. Contribution to ACTA-QP Course “TMD-Doedag” (Amsterdam, 2 & 9 March 2013).

Vervoorn-Vis G.M.G.J. Workshop ‘Vervaardigen wasindex & oefentherapie’. Contribution to ACTA-QP Course “TMD-Doedag” (Amsterdam, 2 & 9 March 2013).


Wismeijer, D. 14-11-2013. A car is not just a faster bicycle. Voordracht voor klinische avond praktijk voor Implantologie Daan Kruger Nieuw Vennep. 1,5 hrs.


Collaborators
- AMOLF (Prof.dr. G. Koenderink), Amsterdam, NL.
- Biofarmind, The Hague, the Netherlands
- City University of New York (Dr.ir. S.C. Cowin), New York, 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 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 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)
Annual Research Report 2013

- University of Aberdeen (Prof. dr. M. Helfrich), Aberdeen, UK.
- University of Cairo, Department of Operative Dentistry, dr. AA. El Zohairy, Cairo, Egypt.
- University of California San Francisco (Prof. dr. P. DenBesten), San Francisco, USA.
- University of Connecticut (Dr. M. Musgrave), Connecticut, USA.
- University of Groningen, Department of Prosthodontics, Prof dr M.C. Cune, Prof H Meijer Groningen, The Netherlands.
- University of Helsinki (Prof. dr. K. Vaananen), Helsinki, Finland.
- University of Helsinki, Department of Stomatognathic Physiology & Prosthetic Dentistry, dr. J. Ahlberg, Helsinki, Finland.
- University of Hong Kong, Dept Oral Diagnosis and Polyclinics (Dr. T.K. Goto), Hong Kong, China.
- University of Hull, Dept Engineering (Prof. dr. M. Fagan), Hull, Great Britain.
- University of Kiel (Prof. dr. P. Saftig), Kiel, Germany.
- University of Madrid, (Prof. dr. R. Marco), Madrid, Spain.
- University of Milan (Prof. dr. S. Bradamante), Milan, Italy.
- University of Montreal. Faculty of Dentistry, prof dr Gilles Lavigne, Montreal, PQ, Canada.
- University of Naples, Dept Orthodontics (Dr. I. Cioffi, Dr. M. Farella), Naples, Italy.
- University of Navarra, School of Medicine (Prof. dr. J.F. Medina), Pamplona, Spain.
- University of 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. dr. G. Andersson), Stockholm, Sweden.
- University of Sydney, Faculty of Dentistry, Jaw Function and Orofacial Pain Research Unit, prof dr Greg Murray, Sydney, Australia.
- University of Tanta, Department of Restorative Dentistry, dr. A. Abdalla, Tanta, Egypt.
- University of Tennessee, Clinical Research Center, dr. F. Garcia Godoy, Memphis, USA.
- University of Tokushima, Dept Orthodontics and Dentofacial Orthopedics (Prof. dr. E. Tanaka, Dr. N. Kawai), Tokushima, Japan.
- University of Turku, Department of Prosthetic Dentistry and Biomaterials research, Prof. dr. Pekka Vallittu, Turku, Finland.
- University of Umea (Prof. dr. U. Lerner), Umea, Sweden.
- University of Umea, Faculty of Medicine, department of Clinical Oral Physiology, prof dr A. Wännman, Umea, Sweden.
- University of Zurich, Center for Dental and Oral Medicine, Dental Materials Unit, prof. dr. M. Özcan.
- UTHSC Dental School, Department of Restorative Dentistry, S. Wendt, San Antonio, Texas, USA.
- Utrecht University Medical Center (Prof. dr. W.J.A. Dhert, Prof. dr. H. Weinaus), Utrecht, NL.
- Vrije Universiteit, Department of Clinical Neuropsychology, prof. dr. E.J.A. Scherder, Amsterdam, The Netherlands.
- Vrije Universiteit, Nederlands Tweelingen Register (NTR), prof. dr. D.I. Boomsma, Amsterdam, the Netherlands.
- VU Amsterdam, Dept Movement Sciences (Prof. dr. J. van Dieën, Prof. dr. A. de Haan, Dr. R. Jaspers, Dr. K. Gerritsen), Amsterdam, NL.
- VU Amsterdam, Dept Theoretical Physics (Prof. dr. F.C. MacIntosh, Prof. dr. G. Wuitte), Amsterdam, NL.
- VU Amsterdam, Physics (Prof. dr. D. Iannuzzi), Amsterdam, NL.
- VUMc, Afdeling dermatologie, dr. Th. Rustemeyer.
- VUMC, Depr Physiology (Prof. dr V. van Hinsberg), Amsterdam, NL.
- VUMC, Dept Dermatology (Prof. dr. R. Hoekzema), Amsterdam, NL.
- 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. T.H. Smit), Amsterdam, NL.
- VUMC, Dept Pathology (Dr. I. van Hoogstraten), Amsterdam, NL.
- VUMC, Dept Plastic Surgery (Dr. Frank Niessen), Amsterdam, NL.
- VUMC, Dept Plastic Surgery (Prof. dr. M. Ritt, Dr. M.G. Mullender), Amsterdam, NL.
- VUMC, Dept Rheumatology (Prof. dr. W.F. Lems), Amsterdam, NL.
- Zhejiang-California Nano Systems Institute, Hangzhou, China.
Current PhD projects


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


Damaskos, S. The reliability an accuracy of Cone Beam Computed Tomography in detecting calcified atheromatous lesions within the lumen of the internal carotid artery. Project leaders: dr. W.E.R. Berkhout & dr. T. Forouzanfar


Education related research, including other research

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

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

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

Results
In 2013 further experiments have been carried out on training behaviour of students preparing for practical examinations. It appeared that students who were in control of their training program and decided on their own testing moments performed better than students that had to follow the test schedule of the faculty. The possibility to collect data on training and testing behaviour in such a controlled environment offers the opportunity to compare performance of various groups of students using similar exercises. For the use of a virtual learning environment for dental students, virtual teeth have been developed. The created models appear feasible for use in dental education and a useful learning asset in addition to human extracted teeth and as a possible replacement of plastic teeth (Frasaco).

Academic personnel in 2013 and 2014

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Output

Scientific publications (refereed)

Scientific publications (non refereed)

Professional publications

Grants: current projects with external funding
Schoonheim-Klein, M.E. NIH (2011-2016) in cooperation with Harvard, UCSF and Creighton US$ 100.000,- .
Wesselink, P.R., Ministry OCW € 800.000,-. Simodont project for three years 2008-2010. Extended till 2013 by decision of OCW in October 2011.
Wismeijer, D. & Gorter R.C. International Team for Implantology (ITI): Digital dentistry in practice; on dentists’ interaction with technological transformations. First part of PhD project funding, collaboration of Social Dentistry and Oral Implantology. February 2012 – December 2013: 110.000,- euro.

Indicators of Esteem
Invited speakers at (inter)national congresses or symposia

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

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.

Organization of congresses and symposia for (health care) professionals

Other professional functions
Gorter, R. C.: Executive board member ADEE (since 2013).

Current PhD projects
List of SCI journals, their impact factors and the number of ACTA publications in 2013 in each journal

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