

ANNUAL  
RESEARCH  
REPORT 2006

Academic  
Centre for Dentistry  
Amsterdam

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Design cover : Vormgeving en fotografie, Facilitaire Dienst, ACTA  
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## **INTRODUCTION**

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

The ACTA research institute collaborates in the Netherlands Institute for Dental Sciences (Interuniversitaire Onderzoekschool Tandheelkunde, IOT). The IOT is a collaboration between the Academic Centre for Dentistry Amsterdam ('ACTA', the combined Faculties of Dentistry of the Universiteit van Amsterdam and the Vrije Universiteit in Amsterdam), the College of Dental Science of the Radboud University Nijmegen Medical Centre, the Dental Section of the University Medical Center Utrecht, and the Academic Mouth Care Centre Groningen.

An overview of the output is presented on page 11. This table summarises for each department and section the number of publications that have appeared in 2006 in SCI-journals, the number of other scientific publications, and the number of professional publications. Data on abstracts and on popularising publications are not included in this report. Also the personnel involved in full time equivalent (fte) and the impact factor-sum (IF-sum) are included in this table. The IF-sum was calculated for each department by adding together the impact factor values of all 2006 publications according to the principle listed in the footnotes of the table.

### **Research Institute ACTA**

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## REPORT OF THE DIRECTOR

### The Research Institute ACTA

- **mission statement**

Dental research at ACTA focuses on the study of health and diseases of the tissues in and around the oral cavity. Beside infectious diseases like dental caries and periodontal inflammatory processes, attention is paid to the development, function and regenerative capacities of the hard tissues in general, dysfunction of the masticatory system and diseases of salivary glands and oral mucosa. It is the general aim to improve strategies for diagnosis and prevention of diseases and functional repair of the affected tissues in and around the oral cavity.

In our attempts to fulfil this mission special care is taken to establish:

- integration of basic disciplines with the clinical fields
- education and further academic training of PhD-students
- promotion and improvement of the quality of the research in ACTA with special attention to the translation of the results into applications in clinical dentistry. To this end there is a vivid interaction with professional dental organisations and industries.

- **positioning of the research institute**

The Research Institute ACTA is the only institute for research of the Academic Centre for Dentistry Amsterdam (ACTA). ACTA comprises the combined Faculties of Dentistry of the Universiteit van Amsterdam and the Vrije Universiteit in Amsterdam. Moreover it comprises by far the largest part of the Netherlands Institute of Dental Sciences (Interuniversitaire Onderzoekschool Tandheelkunde, IOT). The most recent evaluation of dental research in the Netherlands was performed in 2004. This evaluation according to the new Standard Evaluation Protocol designed by the VSNU included a bibliometric analysis by the CTWS in Leiden. In general, the evaluation committee considered the quality, production, relevance and academic reputation of dental research in the Netherlands as very good. For 2007 an external evaluation is planned by an external international review committee.

- **description of output, leading scientific journals in the field**

The research has a very broad focus and deals with questions originating from clinical dental practice. Within the overall research programme there are large variations in the approaches taken, ranging from basic medical-biological to clinically applied. This is reflected in the type of journals where ACTA researchers publish. Some groups primarily present their findings in journals read in the dental research community, while others also aim for the general medical-biological literature.

### Evaluation of the research program

- **long time performance**

The performance of the research institute and its member groups is evaluated over a longer period (see Table 1). These data show that the number of dissertations has fluctuated between 6 and 20. This reflects variations in external collaborations (such as non-ACTA employees receiving a PhD from our universities) and - in particular - tenure staff members finishing their PhD. The current figure of about 11 dissertations reflects the number of PhD students 'employed'.

The percentage of PhD students that finished their thesis averages at 90 % over the last 15 years, and the mean time between start of employment and defending the thesis is 4.7 years, when a correction is made for the 0.6 to 0.8 fte employment of several PhD students and for long leave of absence (e.g. illness) of some PhD students.

The main attention in the research assessment at the individual and department level is given to international publications in journals with a referee system and an impact factor (SCI publications). This category shows a slightly increasing number over the last 15 years, despite a roughly stable input in fte scientific personnel. The average quality of the publications has

significantly improved over that 15-year period, as judged by the continuous increase of the impact factor sum (see figure 4).

- **remarkable events in 2006**

Outstanding contributions for the year 2006 that we like to mention are publications in high quality biomedical journals (i.e. Arthritis and Rheumatism Research, Journal of Bone and Mineral Research, FASEB Journal, Chemistry and Biology, Clinical Infectious Diseases and Stem Cells, all journals with impact factors higher than 5), and seven publications in the Journal of Dental Research, which is considered the most prestigious dental journal with one of the highest impact factors in the category.

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 151 scientific papers in journals with an impact factor (SCI journals). 67% of these papers appeared in journals belonging to the field "Dentistry, Oral Surgery and Medicine". 36% of these publications were in the top 25% of the journals and 67 % in top 50%. This means that a relatively large number of publications were published in the top journals in the field.

In 2006 PhD student dr. R.G. Bacabac (section Oral Cell Biology) received his doctorate with the distinction cum laude. On a personal level a considerable number of ACTA employees rank in the top of the dental and biomedical research community, as determined by the various indicators of esteem. In 2006 a total of 12 awards were received by ACTA scientists for their achievements. A particular prestigious award was received by prof.dr. I. van der Waal, who was nominated as an Honorary Member of the International Association of Oral Pathologists.

- **assessment at the department level**

When the research at the department or section level is considered it is clear that some groups perform very well throughout the years and are stable in terms of input and output parameters (personnel, PhD students, publications, dissertations etc). In the evaluation report of dental research in the Netherlands performed in 2004 these groups received ratings between 4 and 5 (on a 5 point scale). Some groups got average ratings in this evaluation. The Department of Orthodontics, which has been in a transition stage, received below average ratings. It should be noted that both in 2005 and in 2006 this department showed an improved scientific output.

The research institute has planned, together with the IOT, an external evaluation of dental research in the Netherlands. This evaluation will be performed by an international review committee in 2007.

## **Congresses and societal activities**

- **congresses attended and organized**

In 2006 ACTA researchers have again contributed actively in internationally held meetings, workshops and symposiums, both as organisers and participants. A total of 102 lectures were given as 'invited speaker' at international congresses and symposia. In addition a large number of presentations were given at international congresses after selection on submission of abstracts and during congresses and symposia for a Dutch audience. Due to this large number, congress abstracts are not listed in this annual report. A total of 7 international meetings were organised by members of one of the departments of ACTA.

A special event worth mentioning is the 2006 meeting of the European Association for Paediatric Dentistry. This successful congress, organised by ACTA scientists in Amsterdam, was attended by more than 700 participants.

- **societal activities**

The prime societal value of a strong research programme is obviously its effect on the quality of the teaching given at ACTA. New findings and concepts are included in the curriculum at ACTA, but also presented to dental practitioners at frequently held continuing education activities, e.g. ACTA Quality Practice. The Research Institute has high expectations of the ACTA new curriculum with an increased focus on research and evidence based dentistry.

ACTA employees take an active role as Executives in international scientific organisations (57 international functions), as members of the editorial boards of international scientific journals

(44) and in being leading in 'wetenschappelijke verenigingen' of researchers and dental practitioners in the Netherlands. In addition it should be mentioned that many scientists are also working as dentists in specialized clinics at ACTA or in the Amsterdam region. Obviously the societal impact of their activities, individually as clinically active professionals and leading among their peers, should be acknowledged. This is also evident from the relatively large number of 114 professional publications. Several ACTA researchers also wrote a considerable number of popularising publications, the details of which are not included in this scientific report.

## Management

### • finances

The overall budget of the research institute is divided into a part controlled directly by the directorate and another part that is allocated to the departments.

The institute budget (*sensu stricto*) is used for the management of the institute, the salaries of the PhD students and post doctoral employees, for travel allowances for these two groups and for the organization of courses and the annual two day research meeting. Details of the finances of the Institute are given in Table 3. The research budgets for the departments are distributed with a model based on several indicators. For 2006 a new allocation model was made, based on several parameters, such as external peer review, bibliometric data over the last 5 years, education, PhD theses and external funding. In addition, standard bench fees are issued for the various categories of researchers (staff, post-docs, PhD students, technicians and other supporting OBP staff).

### • personnel

The directorate of the institute comprises:

prof.dr. V. Everts, director of research	0.4 fte
dr. T.J.M. van Steenberghe, co-ordinator of research	0.5 fte
mrs. F.M. Meijer, secretary	0.6 fte

In 2006, prof.dr. V. Everts succeeded prof.dr. J.M. ten Cate as director of research. The activities of the Research Institute directorate consist of organising the 2-monthly *aiorefereermiddagen*, the annual two day research meeting of the IOT, 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.

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

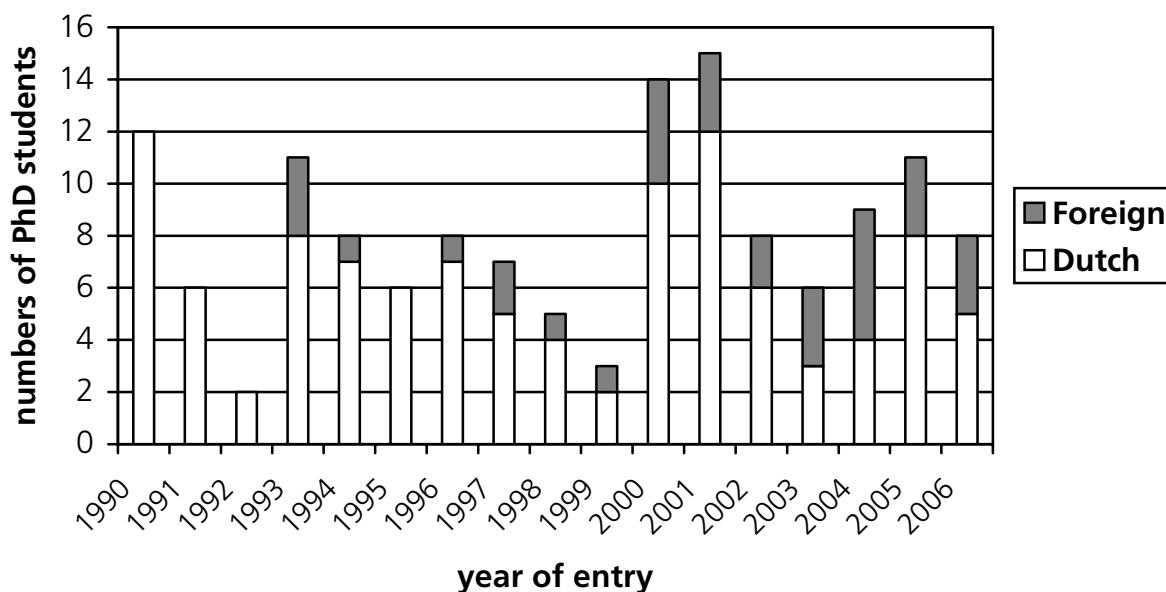
## PhD students

### • PhD student appointments

Despite the fact that some supervisors are faced with difficulties in finding candidates for vacant positions, most vacancies have been filled in 2006. In Figure 1 the number of new PhD students at ACTA is shown in the years 1990 to 2006. Over the years, about 24 % of all PhD students had a foreign nationality, about half of them from Europe, the rest from other continents. A mean of 8 new PhD students was appointed each year, 8 being appointed in 2006. About half of all PhD students have a dental background (see Table 5). Of all PhD students 50 % is female.

In principle the Institute had the policy that each full (time) professor gets university funding for two PhD students; it is however doubtful if this policy can be retained in the coming years due to reductions in budget and the appointment of new full professors. In addition, the research institute has started a procedure for allocation new PhD positions for high quality projects directed at the integration of basic and clinical science. In 2006 the first two grants for this open competition were awarded.

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



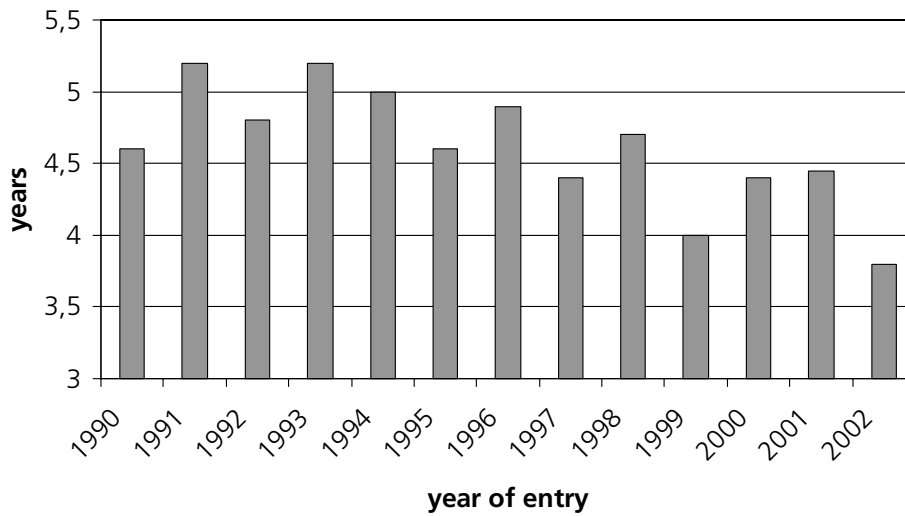
- **PhD Courses**

The following courses were organised for PhD students: "Writing and Presenting in English", "Methodology and Statistics", "Introduction in SPSS", "Dentistry for non-dentists", and "Oral Biology". Dentistry is a multidisciplinary science and the background of the PhD students of the IOT is diverse. Therefore, most PhD students follow external courses on specific research areas, given by experienced lecturers of research schools in other disciplines.

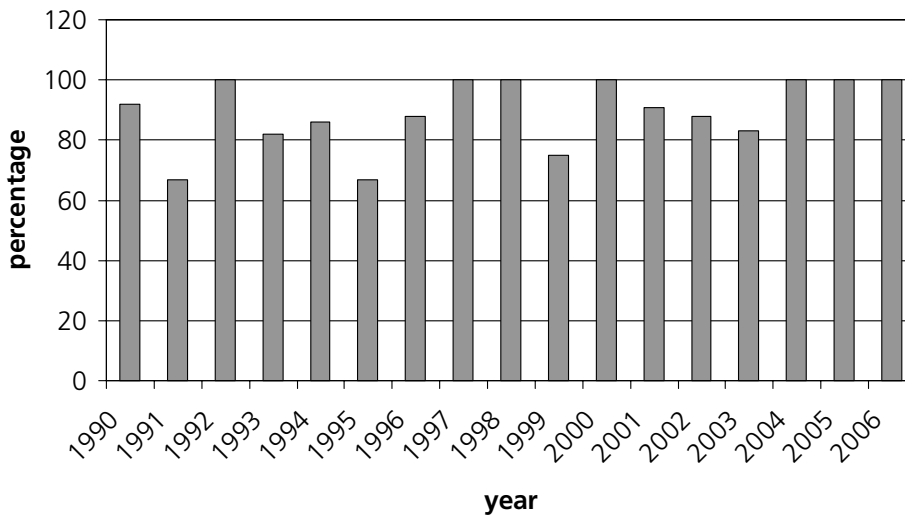
- **PhD thesis duration and completion rate**

Attention has been paid to the problems related to the social security benefits of PhD students and the time that PhD students need to finish their thesis. The mean time of 4.7 years between start and defence of the thesis within ACTA is slightly lower than the mean duration of PhD theses in research schools in the Netherlands of 5.1 years (see the report "Rendement en duur van promoties in de Nederlandse onderzoekscholen", Oost en Sonneveld, 2004). In addition, the mean duration of preparing a thesis has shown a declining tendency over the years (Figure 2). Over the last 15 years, about 90 % of all PhD students in ACTA completed their thesis (Figure 3). This high percentage is substantially larger than the mean percentage of 75 % of PhD students who finish their thesis in Dutch research schools according to the report by Oost en Sonneveld mentioned above.

**Figure 2.** Mean duration of completing the thesis of ACTA PhD students related to the year of entry



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



**Points of attention**

- **HRM and Retirement**

The research staff at ACTA has been comparatively young in the last decades. This was the result of the merging of the dental schools in the mid 1980's. Now we are approaching a situation where heads of departments and senior scientists are retiring. In 2006 three new professors were appointed: Loos (Periodontology), Van Beek (Orthodontics) and Wismeijer (Oral Implantology).

- **new building planned for 2010**

The new ACTA building located at the VU campus will bring together groups that are currently spread out over the city at four different locations. Optimal research facilities at the new ACTA building are planned to encourage collaboration between the research groups that require

laboratory facilities. The increased number of scientists at one location will also facilitate to jointly take initiatives, such as in molecular aspects of dental research.

- **Future developments**

Within the Netherlands, graduate schools will be formed at a local level to integrate research training both for students in the Master phase and for PhD students. In 2006 ACTA and IOT have decided that the responsibility for PhD training will be transferred to local graduate schools. The IOT will keep a role in co-ordination of dental research in the Netherlands.

The research at ACTA has always been characterized by a wide range of different topics that covered most dental disciplines. The policy for the nearby future is on one hand to maintain all good performing research programmes, but on the other hand to focus more on specific research areas with an excellent performance. Larger research groups with a good potential could focus on biofilms and oral infections (including groups such as Cariology, Periodontology, Oral Microbiology and Oral Biochemistry), and on bioengineering and reconstruction of bone and teeth (including groups such as Oral Cell Biology, Oral Function, Oral Implantology, Periodontology, Dental Material Sciences and Functional Anatomy).

## **Conclusion**

The analysis of the various parameters of performance shows that the research at ACTA is in a stable and - in most areas - increasingly improving state.

## SUMMARY OF PUBLICATION OUTPUT AND INPUT

Year	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Dissertations	16	20	13	15	7	7	9	11	9	12	6	12	11	11
SCI publications	105	122	119	146	126	133	116	110	115	128	130	149	152	151
First author from ACTA		66	80	90	79	96	84	84	76	79	89	100	112	104
Other scientific publ.	152	160	88	97	84	37	25	49	27	17	34	29	41	51
Professional publ.	38	53	68	52	111	74	88	107	123	75	93	91	99	114
Impact factor sum	132	131	198	171	179	167	200	176	206	220	238	273	322	344
Personnel WP 1	59.1	53.6	50.6	45.7	43.2	40.8	40.9	43.5	45.0	47.2	47.9	49.4	46.0	46.5
WP2	4.6	4.7	5.6	4.6	6.4	5.4	4.2	5.2	5.4	5.4	6.2	6.6	4.8	7.9
WP3	11.0	8.8	11.9	10.5	13.6	11.9	9.8	8.4	9.5	9.8	10.3	7.7	6.7	7.4
Guests								2.5	2.6	2.4	2.6	1.9	2.2	4.2
Total personnel	74.7	67.0	68.1	60.7	63.2	58.1	54.8	59.6	62.6	64.8	66.9	65.6	59.8	66.1

## Footnotes:

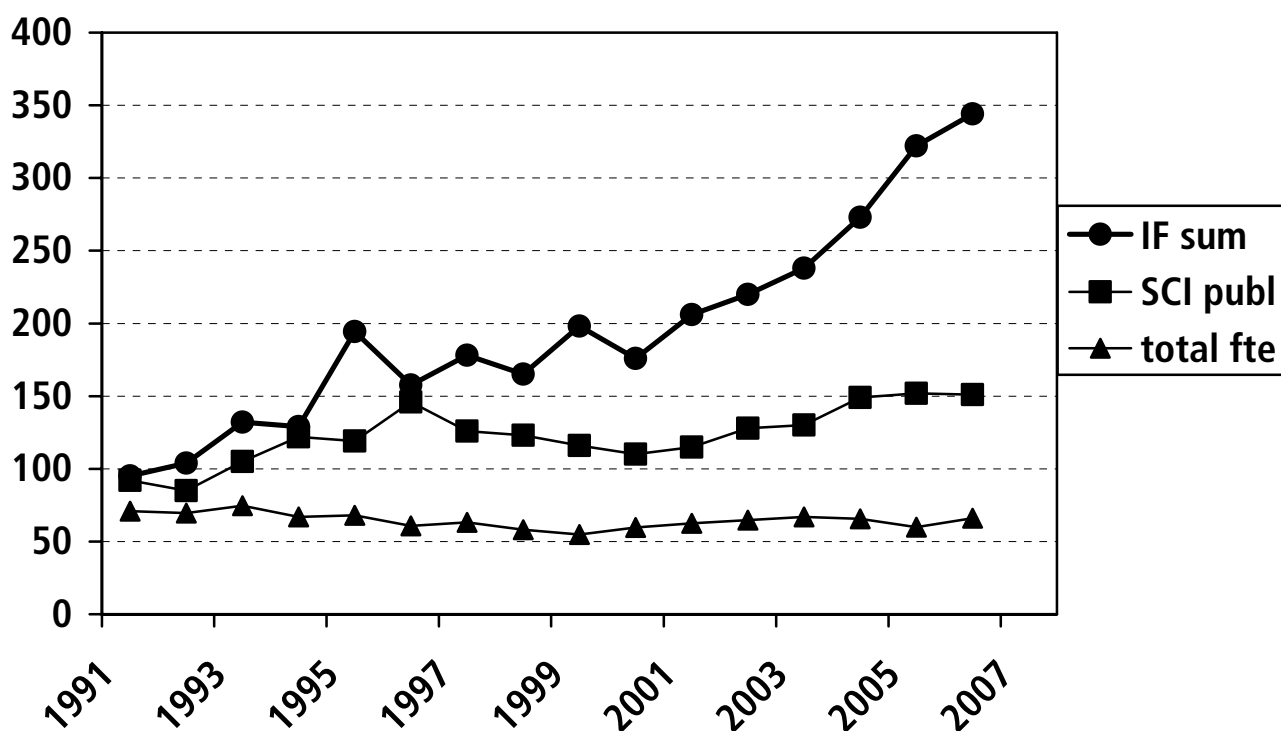
SCI = number of scientific papers in journals indexed in the database of the Institute of Scientific Information (ISI).

wp1 = academic personnel funded by 1<sup>st</sup> source in fte

wp2 = academic personnel funded by 2<sup>nd</sup> source in fte

wp3 = academic personnel funded by 3<sup>rd</sup> source in fte

Figure 4. Impact factor sum of ACTA publications, total scientific publications in journals indexed in the science citation index (SCI publications) and total scientific personnel in fte.



**Table 2. Summary of the number of publications, impact factor sum and academic personnel in fte (year 2006)**

	Dis	SCI	OSP	PP	IF	wp1	wp2	wp3	guest	wp tot
<b>CEP</b>	1	21 (12)	16	7	30.3	8.95	1.65	0.55	1.60	12.75
<b>OF</b>		8 (7)	1	9	8.2	4.30			0.50	4.80
<b>PD</b>	1	20 (13)	9	8	43.4	4.05	0.80	0.80	0.15	5.80
<b>OC</b>	1	28 (14)	12	4	77.9	3.50	5.45	0.50	1.00	10.45
<b>OM</b>	1	12 (5)	1	4	23.8	3.20				3.20
<b>MZ</b>	2	20 (13)	4	48	28.5	3.80		1.40		5.20
<b>TR</b>		3 (2)	4		1.6	2.00		1.60		3.60
<b>OR</b>	2	13 (9)	1	3	16.2	2.00		0.55		2.55
<b>ST</b>	1	13 (8)	5	19	15.7	4.20		0.40	0.10	4.70
<b>AN</b>	1	20 (11)	1	1	31.6	3.20			0.25	3.45
<b>MW</b>	1	11 (8)	1	5	18.9	3.65		1.10	0.65	5.40
<b>OB</b>	1	12 (4)	3	31	23.3	3.70		0.50		4.20
<b>Total*</b>	11	151 (104)	51	114	344.1	46.55	7.90	7.40	4.25	66.10

This table summarises the number of publications that have appeared in 2006 in SCI-journals, the number of other scientific publications, and the number of professional publications. Also the personnel involved in full time equivalent (fte) and the impact factor-sum (IF-sum) are included in this table. The IF-sum was calculated for each department by adding together the impact factor values of all 2006 publications according to the principle listed in the footnotes of the table. In this report no information is given on abstracts and on popularising publications.

## Footnotes:

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

\* Total = papers co-published with members of different programs were counted only once

Table 3. Finances ACTA Research Institute 2006

<b>Jaarrekening ACTA Onderzoekinstituut, 2006</b>			
Bedragen in €			
<b>Baten</b>		<b>Lasten</b>	
<i>Eerste geldstroom</i>		Personele lasten	6.060.714
Bijdrage CvB	5.758.388	Afschrijvingslasten	251.949
<i>2e en 3e geldstroom</i>		Inkomensoverdrachten	12.690
Baten werk iov derden	2.228.452	Kosten inventaris en apparatuur	193.080
Overige baten	378.668	Bureaunkosten	67.780
		Reis- en verblijfkosten	160.720
		Specifieke kosten (laboratorium)	1.034.987
		Overige instellingslasten	117.511
		Interne doorbelastingen	189.429
		Exploitatieresultaat	-245.648
<b>Totaal</b>	<b>8.334.509</b>	<b>Totaal</b>	<b>7.289.398</b>

Note, this table is given in Dutch to avoid confusion in terminology

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

Department/ section	Staff				PhD students				Total
	1st*	2nd	3rd	guest	1st	2nd	3rd	guest	
<b>cep</b>	6.00	1.40	0.55	1.60	2.95	0.25			<b>12.75</b>
<b>of</b>	2.10			0.50	2.20				<b>4.80</b>
<b>pd</b>	2.75	0.80	0.80	0.05	1.30			0.10	<b>5.80</b>
<b>oc</b>	1.90	1.60	0.10	0.90	1.60	3.85	0.40	0.10	<b>10.45</b>
<b>om</b>	2.10				1.10				<b>3.20</b>
<b>mz</b>	2.10		0.70		1.70		0.70		<b>5.20</b>
<b>tr</b>	1.40		1.60		0.60				<b>3.60</b>
<b>or</b>	1.50		0.55		0.50				<b>2.55</b>
<b>st</b>	1.75			0.10	2.45		0.40		<b>4.70</b>
<b>an</b>	1.80			0.25	1.40				<b>3.45</b>
<b>mw</b>	1.95		0.30	0.05	1.70		0.80	0.60	<b>5.40</b>
<b>ob</b>	2.50		0.50		1.20				<b>4.20</b>
<b>Total</b>	<b>27.85*</b>	<b>3.80</b>	<b>5.10</b>	<b>3.45</b>	<b>18.70</b>	<b>4.10</b>	<b>2.30</b>	<b>0.80</b>	<b>66.10</b>

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

CEP = Department of Cariology Endodontology Pedodontology  
 OF = Department of Oral Function  
 PD = Department of Periodontology, section Periodontology  
 OC = Department of Periodontology, section Oral Cell Biology  
 OM = Department of Periodontology, section Oral Microbiology  
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 TR = Department of Oral Surgery/Oral Radiology, section Oral Maxillofacial Radiology  
 OR = Department of Orthodontics/Social Dentistry, section Orthodontics  
 ST = Department of Orthodontics/Social Dentistry, section Social Dentistry and Behavioural Sciences  
 AN = Department of Dental Basic Sciences, section Functional Anatomy  
 MW = Department of Dental Basic Sciences, section Dental Material Sciences  
 OB = Department of Dental Basic Sciences, section Oral Biochemistry

**Table 5: PhD students by type of undergraduate training**

<b>Department / section</b>	<b>dentistry dutch</b>	<b>dentistry other</b>	<b>biology / chemistry</b>	<b>psychology</b>	<b>medicine</b>	<b>other</b>	<b>total</b>
<b>cep</b>	3	2	2	1			<b>8</b>
<b>of</b>	3	1				1	<b>5</b>
<b>pd</b>	1	4					<b>5</b>
<b>oc</b>	1		5		3	1	<b>10</b>
<b>om</b>			3				<b>3</b>
<b>mz</b>	1	1	2		1		<b>5</b>
<b>tr</b>	1	1					<b>2</b>
<b>or</b>	2			1			<b>3</b>
<b>st</b>	2			5		1	<b>7</b>
<b>an</b>	1		1			1	<b>4</b>
<b>mw</b>	3	4				2	<b>9</b>
<b>ob</b>			2				<b>2</b>
<b>Total</b>	<b>15</b>	<b>13</b>	<b>16</b>	<b>4</b>	<b>4</b>	<b>6</b>	<b>58</b>

CEP = Department of Cariology Endodontology Pedodontology  
 OF = Department of Oral Function  
 PD = Department of Periodontology, section Periodontology  
 OC = Department of Periodontology, section Oral Cell Biology  
 OM = Department of Periodontology, section Oral Microbiology  
 MZ = Department of Oral Surgery/Oral Radiology, section Oral and Maxillofacial Surgery/Oral Pathology  
 TR = Department of Oral Surgery/Oral Radiology, section Oral Maxillofacial Radiology  
 OR = Department of Orthodontics/Social Dentistry, section Orthodontics  
 ST = Department of Orthodontics/Social Dentistry, section Social Dentistry and Behavioural Sciences  
 AN = Department of Dental Basic Sciences, section Functional Anatomy  
 MW = Department of Dental Basic Sciences, section Dental Material Sciences  
 OB = Department of Dental Basic Sciences, section Oral Biochemistry

## Department of Cariology Endodontology Pedodontology

### Diseases of the Dental Tissues and their Prevention

#### Program leader

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#### IOT senior scientists and full professors



J.M. ten Cate



C. van Loveren



M.K. Wu



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P.R. Wesselink

#### Research objectives

The research program of the Department of Cariology Endodontology Pedodontology covers physico-chemical, biochemical, microbiological and clinical aspects of enamel, dentin and root caries and infection of the root canal. These aspects are studied by means of various intra-oral and in vitro models which simulate the natural processes in the oral environment and which are designed to evaluate the effects of preventive measures and restorative materials and procedures, thereby covering the field of research from the molecular level up to in situ studies.

The formation, structure and properties of biofilms on hard tissue surfaces are studied extensively. The action of anticariogenic and antimicrobial agents are studied in the Constant Depth Film Fermenter (CDFF) and in a microtiter biofilm model.

Fluoride that, at present, is still the most effective caries-preventive agent is subject for further study. A better understanding of its mode of action, also on the molecular level towards microbial metabolism, as well as its possible side-effects (fluorosis and the induction of a fluoride-resistant oral microflora) will help to improve formulations and the development of fluoride-releasing devices and restorative materials.

In addition to fluoride, antimicrobials have come into focus as caries preventive agents. The efficacy alone or in combination with fluoride is still unknown and application protocols are not yet based on a critical evaluation of experimental and clinical results. The successes of antimicrobials in caries prevention are still limited.

The prevention of bacterial penetration in the root dentinal tubules and the root canal by a proper seal of the restoration is of major importance for the life expectancy of teeth. Modified disinfection methods of the root canal are studied. New filling methods and contemporary adhesive systems are tested in in vitro leakage models and in clinical studies.

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

## Results

Research in the department has focussed on various aspects of prevention and treatment of decay in the permanent and deciduous dentition. A common theme is the study of biofilms, both for caries prevention and in endodontic infections. We try to cover the entire spectrum of fundamental to translational research.

Interactions between various combinations of bacteria, as reflected in different proteome and transcriptome patterns, were studied, such as to model dental plaque. As an example we have looked at the genes and proteins that are differentially expressed in *Streptococcus mutans* when grown in the presence of *Veillonella parvula* and at the protein expression after exposure to an extract of the plant of *Psidium cattleianum*. To understand these findings various stress related regulatory systems were studied: We observed that both ClpP protease and Vic two-component system are involved in the responses of *Streptococcus mutans* to various types of stress, including acid and oxidative stress. A pilot study on dual species growth of *Porphyromonas gingivalis* and *Peptostreptococcus micros* has shown that *P. micros* can produce a red fluorescence when in close proximity of *P. gingivalis* except for a genetically modified strain of *P. gingivalis* that lacks the ability to form pigmentation. With the use of Confocal Scanning Laser Microscopy, and Live/Dead and Brightener 28 staining, we also visualized endodontic biofilm in situ in infected root canals of human teeth.

On topics closer to clinical questions we found that chlorhexidine mouthrinse did not result in a protection against demineralization of dentin and enamel. A two-year follow up of patients from the orthodontics department during the retention phase showed that caries is an important risk of orthodontic treatment while carious tissue may remain a permanent scar after the removal of fixed appliances.

In clinical aspects of endodontic treatments, we observed that the sealing ability of a new root canal filling material (GuttaFlow) was found to be significantly inferior to AH26 in straight root canals. A new study was started to study in depth the effects of ultrasound in the cleaning of endodontic canals.

A study on the health effects of four different packages of basic oral care in Suriname continued this year. Extraction with or without restoration appeared to have the best influence in the oral health with respect to caries incidence. The caries prevalence in the research group was moderate. With respect to ART there appeared to be a considerable amount of residual caries, irrespective whether they were made by means of hand instruments, with Carisolv or with burs. After three years there is, however, no significant difference in survival rate. In a study where the influence of local anaesthesia (LA) on the discomfort for the patient was investigated it was concluded that Art without LA gave the least discomfort, while the use of burs with LA gave the most discomfort. Another study dealt with a dental questionnaire to find out relations between certain questions and toothache. Eight of the twelve appeared to have a strong correlation with toothache. Also use of a LA-machine (the Wand) gave reduced pain during injection, compared to traditional LA-injection, with differences being negligible for experienced paediatric dentists.

## Academic personnel in 2006 and 2007

Research staff ACTA - CE (in full time equivalents)				
position	name	fte 2006	plan 2007	funding
Full professors	Cate, prof.dr. J.M., ten	0,50	0,50	1
	Cate, prof.dr. J.M., ten	0,15	0,30	3
	Crielaard, prof.dr. W.	0,30	0,40	1
	Loveren, prof.dr. C. van	0,50	0,50	1
	Wesselink, prof.dr. P.R.	0,20	0,20	1
Senior lecturer	Amerongen, dr. W.E. van	0,20	0,20	1
Other lecturers and tenured research staff	Luppens, dr.ir. S.B.I.	1,00	1,00	1
	Peters, dr. L.B.	0,10	0,10	1
	Sluis, drs. L.W. van der	0,40	0,40	2
	Strijp, dr. A.J.P. van	0,50	0,20	1
	Veerkamp, dr. J.S.J.	0,20	0,20	1
	Wu, dr. M.K.	0,80	0,80	1
	Zaura, dr. E.	0,50	0,50	2
Zaura, dr. E.	0,40	0,40	3	
<b>Total tenured staff</b>		<b>5,85</b>	<b>5,70</b>	
Non tenured staff	Cenci, dds. M.S.	0,50	0,50	guest
	Deng, dr. D.M.	1,00	1,00	1
	Özok, dr. A.R.	0,70	0,70	1
	Pereira, dds. T.	0,50	0,50	guest
	Terefework, dr. Z.	0,50	1,00	2
	Veen, dr.ir. M.H. van der	0,60	--	guest
	Veen, dr.ir. M.H. van der	--	0,60	1
PhD students	Gemert-Schriks, drs. M.C.M. van	0,40	0,40	1
	Gerardu, drs. V.A.M.	0,60	0,20	1
	Kara, dds. D.	0,70	0,50	1
	Klaassen, drs. M.A.	0,20	0,20	1
	Kraneveld, drs. E.	0,10	0,70	1
	Lim, drs. H.	--	0,50	1
	Pham, L.C.	0,25	0,70	2
	Shemesh H.	0,60	0,60	1
	Versloot, drs. J.	0,35	0,05	1
<b>Total non tenured staff</b>		<b>6,90</b>	<b>8,15</b>	
total 1st funding		8,95	9,55	1
total 2nd funding		1,65	2,60	2
total 3rd funding		0,55	0,70	3
total guests		1,60	1,00	guest
<b>Total research staff</b>		<b>12,75</b>	<b>13,85</b>	

## Publications in journals indexed in SCI

Cate, J.M. ten, Exterkate, R.A.M., & Buijs, M.J. (2006). The relative efficacy of fluoride toothpastes assessed with pH cycling. *CARIES RES*, 40, 136-141.

- Cimilli, H., Mumcu, G., Cimilli, T., Kartal, N., & Wesselink, P.R. (2006). The correlation between root canal patterns and interorifical distance in mandibular first molars. *ORAL SURG ORAL MED O*, 102, e16-21.
- Dijk, E.H. van, Myles, D.J., Veen, M.H. van der, & Hummelen, J.C. (2006). Synthesis and properties of an anthraquinone-based redox switch for molecular electronics. *ORG LETT*, 25, 2333-2336.
- Gerardu, V.A.M., Heijnsbroek, M., Buijs, M.J., Weijden, G.A. van der, Cate, J.M. ten, & Loveren, C. van (2006). Comparison of Clinpro Cario L-Pop estimates with CIA lactic acid estimates of the oral microflora. *EUR J ORAL SCI*, 114, 128-132.
- Gerardu, V.A.M., Loveren, C. van, Heijnsbroek, M., Buijs, M.J., Weijden, G.A. van der, & Cate, J.M. ten (2006). Effects of various rinsing protocols after the use of amine fluoride/stannous fluoride toothpaste on the acid production of dental plaque and tongue flora. *CARIES RES*, 40, 245-250.
- Heijnsbroek, M., Gerardu, V.A.M., Buijs, M.J., Weijden, G.A. van der, Cate, J.M. ten, & Timmerman, M.F. (2006). Increased salivary fluoride concentrations after post-brush fluoride rinsing not reflected in dental plaque. *CARIES RES*, 40, 444-448.
- Kamma, J.J., Bradshaw, D.J., Fulford, M.R., Marsh, P.D., Frandsen, E., Ostergaard, E., Schel, A.J., Cate, J.M. ten, Moorer, W.R., Mavridou, A., Mandilara, G., Stoesser, L., Kneist, S., Araujo, R., Contreras, N., Goroncy-Bermes, P., Burke, F., O'Mallane, D., O'Sullivan, M., & Walker, J.T. (2006). Attitudes of general dental practitioners in Europe to the microbial risk associated with dental unit water systems. *INT DENT J*, 56, 187-195.
- Kara, D., Luppens, S.B.I., & Cate, J.M. ten (2006). Differences between single- and dual-species biofilms of *Streptococcus mutans* and *Veillonella parvula* in growth, acidogenicity and susceptibility to chlorhexidine. *EUR J ORAL SCI*, 14, 58-63.
- Kraigher, A., Veen, M.H. van der, & Potocnik, I. (2006). Caries occurrence in rats after bleaching with 10% carbamide peroxide in vivo. *CARIES RES*, 40, 77-80.
- Lagerweij, M.D., & Cate, J.M. ten (2006). Acid susceptibility at various depths of pH-cycled enamel and dentine specimens. *CARIES RES*, 40, 33-37.
- Lynch, R.J., & Cate, J.M. ten (2006). Effect of calcium glycerophosphate on demineralization in an in vitro biofilm model. *CARIES RES*, 40, 142-147.
- Lynch, R.J., & Cate, J.M. ten (2006). The effect of adjacent dentine blocks on the demineralisation and remineralisation of enamel in vitro. *CARIES RES*, 40, 38-42.
- Lynch, R.J., & Cate, J.M. ten (2006). The effect of lesion characteristics at baseline on subsequent de- and remineralisation behaviour. *CARIES RES*, 40, 530-535.
- Lynch, R.J., Mony, U., & Cate, J.M. ten (2006). The effect of fluoride at plaque fluid concentrations on enamel de- and remineralisation at low pH. *CARIES RES*, 40, 522-529.
- Schel, A.J., Marsh, P.D., Bradshaw, D.J., Finney, M., Fulford, M.R., Frandsen, E., Ostergaard, E., Cate, J.M. ten, Moorer, W.R., Mavridou, A., Kamma, J.J., Mandilara, G., Stosser, L., Kneist, S., Araujo, R., Contreras, N., Goroncy-Bermes, P., O'Mullane, D., Burke, F., O'Reilly, P., Hourigan, G., O'Sullivan, M., Holman, R., & Walker, J.T. (2006). Comparison of the efficacies of disinfectants to control microbial contamination in dental unit water systems in general dental practices across the European Union. *APPL ENVIRON MICROB*, 72, 1380-1387.
- Shemesh, H., Wu, M.K., & Wesselink, P.R. (2006). Leakage along apical root fillings with and without smear layer using two different leakage models: a two-month longitudinal ex vivo study. *INT ENDOD J*, 39, 968-976.
- Sluis, L.W.M. van der, Gambarini, G., Wu, M.K., & Wesselink, P.R. (2006). The influence of volume, type of irrigant and flushing method on removing artificially placed dentine debris from the apical root canal during passive ultrasonic irrigation. *INT ENDOD J*, 39, 472-476.
- Veen, M.H. van der, Thomas, R.Z., Huysmans, M.C.D.N.J.M., & Soet, J.J. de (2006). Red autofluorescence of dental plaque bacteria. *CARIES RES*, 40, 542-545.
- Versloot, J., Veerkamp, J.S.J., & Hoogstraten, J. (2006). Dental Discomfort Questionnaire: assessment of dental discomfort and/ or pain in very young children. *COMMUNITY DENT ORAL*, 34, 47-52.
- Wu, M.K., Dummer, P.M.H., & Wesselink, P.R. (2006). Consequences of and strategies to deal with residual post-treatment root canal infection. *INT ENDOD J*, 39, 343-356.
- Wu, M.K., Sluis, L.W.M. van der, & Wesselink, P.R. (2006). A 1-year follow-up study on leakage of single-cone fillings with RoekoRSA sealer. *ORAL SURG ORAL MED O*, 101, 662-667.

### Other scientific publications (international, refereed)

- Bochove, J.A. van, & Amerongen, W.E. van (2006). The influence of restorative treatment approaches and the use of local analgesia, on the children's discomfort. *EUR ARCH PAEDIATRIC DENT*, 7, 11-16.
- Cate, J.M. ten (2006). Biofilms, a new approach to the microbiology of dental plaque. *ODONTOLOGY*, 94, 1-9.
- Cate, J.M. ten (2006). Saliva, fluoride and dental caries. In S.J. Moss (Ed.), *The benefits of Chewing II*. New York: Health Education Enterprises Inc.
- Elfrink, M.E.C., Veerkamp, J.S.J., & Kalsbeek, H. (2006). Caries pattern in primary molars. *EUR ARCH PAEDIATRIC DENT*, 7, 236-240.

- Gmur, R., Giertsen, E., Veen, M.H. van der, Josselin de Jong, E. de, Cate, J.M. ten, & Guggenheim, B. (2006). In vitro quantitative light-induced fluorescence to measure changes in enamel mineralization. *CLIN ORAL INVESTIG*, 10, 187-195.
- Lenters, M., Amerongen, W.E. van, & Mandari, G.J. (2006). Iatrogenic damage to the adjacent surfaces of primary molars, in three different ways of cavity preparation. *EUR ARCH PAEDIATRIC DENT*, 7, 6-10.
- Lima Targino Massoni, A.C. de, Correia Sampaio, F., Augusto Rodrigues, F., & Amerongen, W.E. van (2006). Odontologia e Letras: avaliação de um estágio supervisionado interdisciplinar internacional da UFPB. *REVISTA DE ABENO*, 6, 134-139.
- Loveren, C. van (2006). Diet and the prevention of dental health disorders. *AKTUEL ERNAEHR MED*, 31:1, 576-80.
- Loveren, C. van (2006). Ernährung und Zahnkaries. *ORALPROPHYLAXE@KINDERZAHNHK.*, 28, 76-81.
- Loveren, C. van, & Duggal, M.S. (2006). Rôle de l'alimentation dans la prévention des caries. *NUTRITION DIETETIQUE*, 41, 341-346.
- Mhaville, R.J.A., Amerongen, W.E. van, & Mandari, G.J. (2006). Residual caries and marginal integrity in relation to class II glass ionomer restorations in primary molars. *EUR ARCH PAEDIATRIC DENT*, 7, 81-84.
- Roeleveld, A.C., Amerongen, W.E. van, & Mandari, G.J. (2006). Influence of residual caries and cervical gaps on the survival rate of class II glass ionomer restorations. *EUR ARCH PAEDIATRIC DENT*, 7, 85-91.
- Sluis, L.W.M. van der (2006). Die passive Ultraschallspülung des Wurzelkanalsystems. *ENDODONTIE*, 2, 177-185.
- Veerkamp, J.S.J., Porcelijn, T., & Wennink, J.M. (2006). An audit of single drug (propofol) dental general anaesthesia in children. *EUR ARCH PAEDIATRIC DENT*, 7, 100-105.
- Versloot, J., Veerkamp, J.S.J., & Hoogstraten, J. (2006). Dental Discomfort Questionnaire for young children following full mouth rehabilitation under general anaesthesia. *EUR ARCH PAEDIATRIC DENT*, 7, 126-129.
- Wu, M.K., & Wesselink, P.R. (2006). Timeliness and effectiveness in the surgical management of persistent post-treatment periapical pathosis. *ENDOD TOPIC*, 11, 25-31.

### **Professional publications**

- Baart, J.A., Amerongen, W.E. van, Jong, K.L. de, & Allard, R.H.B. (2006). Naaldbreuk tijdens mandibulaire blok anesthesie: preventie en behandeling. *NED TIJDSCHR TANDHEELKD*, 113, 520-523.
- Cate, J.M. ten (2006). Fluoride and dental caries. In T. Takatsuka (Ed.) *The Cutting Edge of Cariology*, volume 3. Japan: Sunstar Inc..
- Cate, J.M. ten (2006). La biofilm cariogène. *SEPTODONT*, 28.
- Dinter, N. van, Maanen, E.J. van, Versloot, J., & Veerkamp, J.S.J. (2006). Ongemak van kinderen tijdens het geven van lokale anesthesie. Vergelijking van een geautomatiseerd systeem en de traditionele methode. *NED TIJDSCHR TANDHEELKD*, 113, 137-141.
- Loveren, C. van (2006). Naspoelen of niet? *PROFLAXEDIALOOG*, 1.
- Veerkamp, J.S.J., & Majstorovic, M. (2006). Angst voor tandheelkundige behandeling en naaldangst bij kinderen. *NED TIJDSCHR TANDHEELKD*, 113, 226-229.
- Zaura, E., Loveren, C. van, & Cate, J.M. ten (2006). Demineralisatie van dentine in situ bij veelvuldige blootstelling aan sacharose of banaan. *NED TIJDSCHR TANDHEELKD*, 113, 351-355.

### **External reports**

- Crielaard, W., & Cate, J.M. ten (2006). Contract research and consultancy work. Report for Purac Biochem. Amsterdam: ACTA. 17 pp.
- Zaura, E. (2006). Monthly progress reports to Work Package #1 leader of NUTRIDENT project. Amsterdam: ACTA. 4 pp.

### **Indicators of Esteem**

#### **Grants: current projects with external funding**

- Crielaard, W., Luppens S. & ten Cate J.M: NIDCR NIH Microarray grant. Stress responses of *Streptococcus mutans* in dual (& multi) species biofilms.

- Sluis, L.W.M. van der. Ivoclar-Vivodent; A new material for coronal protection of the root canal against coronal leakage (Coroseal) was tested using the Fluid Transportation model. € 6000.-
- Sluis, L.W.M. van der. Coltene-Whaledent; A new Endodontic filling material (Gutta-Flow) was tested using the Glucose Fluid Transportation model.
- Sluis, L.W.M. van der, Versluis M., D. Lohse & Wesselink, P.R. in collaboration with the University of Twente. Ultrasonic cleaning of root canals. Endodontic therapy through microstreaming and cavitation. A research proposal for the STW Open Technology Program. Physics of Fluids (POF), University of Twente, Enschede, the Netherlands. The research project will start in September 2007.
- Zaura, E. Three year grant honored by EU (FP6) for the project NUTRIDENT: "Towards functional foods for oral health care – isolation, identification and evaluation of beverage and food components with anti-caries and/or anti-gingivitis activities" started in October 2006. Coordinator: University College London. Total budget for ACTA: € 285.409.-
- Zaura, E., Crielaard, W. & ten Cate J.M. Three year grant honored by STW for the project: "Probing Dynamic Microbial Community Interactions" to be started in 2006. Total of € 674.448.- (including € 80.000.- from GABA-International and € 20.000.- from MRC-Holland).
- Zaura, E. Contract research work for CurOzone USA Inc. July 2005; € 5.000.-

### **Membership of international editorial boards**

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

### **Organisation of international congresses or symposia**

- Amerongen, W.E. van, & Veerkamp, J.S.J. (2006). Members. Local Organizing Committee, EAPD congress: Amsterdam, the Netherlands.

### **Invited speakers at international congresses or symposia**

- Amerongen, W.E. van (2006, December 02). Restorative considerations in paediatric dentistry. Antalia, Turkey, International congress of Aegean Dental Chambers.
- Cate, J.M. ten (2006, January 21). Modern concept of fluoride mechanisms. Tokyo, Japan, Symposium organized by Sunstar Company & Nagasaki University Japan at the launch of modern prevention products.
- Cate, J.M. ten (2006, January 30). Opportunities for modern oral care products. Port Sunlight, UK, Unilever.
- Cate, J.M. ten (2006, July 04). Fluoride and its role in caries prevention. Vienna, Austria, Symposium European Orthodontic Society.
- Cate, J.M. ten (2006, July 17). Caries prevention with nanoparticles hydroxyapatite. Muchenstein, Switzerland, GABA symposium.
- Cate, J.M. ten (2006, June 08). Remineralization through amine fluoride dentifrices. Toulouse, France, Pierre Fabre.
- Cate, J.M. ten (2006, June 30). Remineralization of lesions extending into dentine, keynote lecture. Brisbane, Australia, Symposium International Association for Dental Research world meeting.
- Cate, J.M. ten (2006, November 03). Modern concepts of cariology. Lima, Peru, Full day courses IADR Division meeting.
- Cate, J.M. ten (2006, November 08). Modern concepts of cariology. Maracaibo, Venezuela, Full day courses IADR Division meeting.
- Cate, J.M. ten (2006, November 22). Du risque carieux au risque parodontal. France, Association Dentaire Francaise Paris.
- Cate, J.M. ten (2006, October 28). Modern concepts of cariology. Tucuman, Argentina, Full day courses IADR Division meeting.
- Loveren, C. van (2006, March 30). The potential of sugar alcohols in caries prevention. Tampere, Finland, Research Symposium Finnish Dental Society Apollonia.
- Loveren, C. van (2006, November 24). Age-adapted caries prevention in children and adolescents. Barcelona, Spain, 6th Symposium AHIADDEC.

- Peters, L.B. (2006, June 16). An update on endodontic infection and biofilm. Toronto, Canada, Endodontic graduate alumni day.
- Peters, L.B. (2006, October 12). Biofilms and endodontic infection. Stavanger, Norway, Norwegian Dental Association meeting.
- Sluis, L.W.M. van der (2006, April 29). Ultrasonic irrigation of the root canal, a review of the literature. Germany, Köln.
- Strijp, A.J.P. van (2006, April 24). Caries management. Novi Sad, Republic of Serbia, 6th EDSA Congress.
- Strijp, A.J.P. van (2006, January 27). Caries diagnosis. When to treat? and Caries Treatment. Minimal intervention. Yangon, Myanmar, 26th Myanmar Dental conference and 7th FDI-MDA Joint educational meeting.
- Veerkamp, J.S.J. (2006, April 07). Nitrous oxide its management and safety. Helsinki, Finland, Symposium: sedation and behavioral management.
- Versloot, J. (2006, June 09). Pain: its recognition and treatment in paediatric dentistry. Amsterdam, the Netherlands, 8th congress of the European Academy of Paediatric Dentistry.
- Wesselink, P.R. (2006, June 21). Should we treat that lesion. Amsterdam, the Netherlands, ROOTS SUMMIT V.
- Wesselink, P.R. (2006, March 09). Should we treat that periapical lesion? Edinburgh, UK, Royal Odontological Society.
- Wesselink, P.R. (2006, November 22). Should gutta-percha still be compacted? Paris, France, Association Dentaire Francaise.

### **Other international functions**

- |                      |  |
|----------------------|--|
| Amerongen, W.E. van: | Council member. EAPD.  |
| Amerongen, W.E. van: | Council member. IAPD.  |
| Amerongen, W.E. van: | External examiner. Post graduate education. Gent, Belgium.   |
| Cate, J.M. ten:      | Honorary professor Universidad Peruana Cayetano Heredia, Lima, Peru.                                     |
| Cate, J.M. ten:      | Immediate past president Central European Division of the International Association for Dental Research. |
| Cate, J.M. ten:      | Management committee European Research Group Oral Biology (ERGOB).                                       |
| Cate, J.M. ten:      | Member executive committee Pan European Federation/ IADR.  |
| Cate, J.M. ten:      | Vice president IADR Board of directors.  |
| Veen, M.H. van der:  | Board member ORCA.   |
| Veen, M.H. van der:  | Honorary lecturer University of Liverpool.   |
| Veerkamp, J.S.J.:    | President European Academy for Paediatric Dentistry (EAPD).  |
| Wu, M.K.:            | Guest Professor. Peking University School of Stomatology.  |
| Wu, M.K.:            | Member. Research committee ESE.  |

### **Collaborations**

- WHO Collaborating Centre Nijmegen, Prof.dr. W. van Palenstein Helderma, Nijmegen, The Netherlands.
- Fernanda Brighenti, São Paulo State University, Araçatuba, Brazil.
- University of Nairobi, Dr. A. Kemoli, Nairobi, Kenya.
- Medische Zending, Paramaribo, Surinam.
- St. Jeugd tandverzorging, Paramaribo, Surinam.
- University of Dar es Salaam (MUCHS) Dr. G. Mandari, Dar es Salaam, Tanzania.
- University of Sao Paulo, Dr. M. Bönecker, Sao Paulo, Brazil.
- Federal University of Paraiba, J. Pessoa, Brazil.
- University of Dundee, Scotland, UK, prof. D.Evans and dr. N. Innes
- University of Melbourne, Australia, dr. D. Manton
- Gaba International Ltd., Dr. C. Weiss, Münchenstein, Switzerland.
- Vrije Universiteit, Dr. R. van Spanning, Amsterdam.
- MRC Holland, Dr. J.P. Schouten, Amsterdam.
- Wellington School of Medicine, Dr. C.H. Sissons, Wellington, New Zealand.
- NUTRIDENT consortium: Prof.dr. M. Wilson (UCL Eastman Dental Institute), Prof.dr. G. Gazzani (University of Pavia), Prof.dr. I. Ofek (University of Tel Aviv), Prof.dr. C. Pruzzo (University of Genoa), Prof.dr. P. Lingstrom (Goteborg University), Prof.dr. P. Canepari (University of Verona), Dr. D. Bradshaw (Quest International), Dr. B. McGhee (Glycologic Ltd)
- Winclove Industries, Dr. P. Pekelharing; Amsterdam TNO Kwaliteit van Leven, Dr. B. Keijser, Zeist
- Univeristé Libre de Bruxelles, Prof.dr. J. van Helden, Brussels, Belgium NIZO, Dr. M. Kleerebezem, Ede.
- Universiteit van Amsterdam F. Wittink (microarray department), L. de Jong (mass spectrometry) H. Hoefsloot (Biosystems data analysis), Dr. E. Manders (microscopy department), Dr. P. de Groot (fungal microbiology). SILS
- University of Amsterdam, SILS, Prof.dr.S. Brul & Dr. F.Klis, Amsterdam, The Netherlands.

- Unilever Research, Dr. C.Allison, Port Sunlight, UK.
- Inspektor Research Systems BV, Dr. E. de Josselin de Jong, Amsterdam, The Netherlands.
- AMC, Department of Electron Microscopy, Dr. J. van Marle, Amsterdam, The Netherlands.
- Faculty of Medical Sciences, Dept. of Dentistry, University of Groningen, Prof.dr. M.C.D.N.J.M. Huysmans, R. Thomas, Groningen, The Netherlands.
- University of Liverpool, Prof.dr.S.M. Higham, Liverpool, UK.
- Physics of Fluids (POF) group of the University of Twente, The Netherlands, (STW project). Dr. M. Versluis.
- Department of Biomedical Engineering, Erasmus University Medical Center, Rotterdam, The Netherlands, contact person: Prof.dr. Nico de Jong en Dr. D. Goertz.
- Laboratoire d'Imagerie Paramétrique CNRS UMR 7623 Université Paris 6 15 rue de l'Ecole de Médecine F - 75006 Paris, France contact person: Dr. Frédéric Padilla.
- Erasmus exchange projects:
  - Italy, Rome 'La Sapienza'. Dr. G. Gambarini
  - Italy, Verona. Prof.dr. G. Cavalieri.
  - Greece, Athens. Dr. M. Georgopoulou.
  - U.K. Cardiff. Prof.dr. P. Dummer

### **Current PhD projects**

**Gemert-Schriks, MCM van.** Aspects of an integrated package for basic oral care. Supervisor: prof.dr. J.M. ten Cate; co-supervisor: dr. W.E. van Amerongen. Start: September 2001.

**Gerardu, VAM.** Acidogenicity of dental plaque and antimicrobial intervention. Supervisor: prof.dr. J.M. ten Cate; co-supervisor: prof.dr. C. van Loveren. Start: March 2001.

**Kara, D.** Structure and properties of multi-species biofilms. Supervisor: prof.dr. J.M. ten Cate. Start: November 2002.

**Klaassen, M.A.** Quality of life, oral health and dental anxiety in children. Supervisors: prof.dr. J. Hoogstraten & prof.dr. J.M. ten Cate, co-supervisor: dr. J.S.J. Veerkamp. Start: December 2005.

**Pham, C.** Probing dynamic microbial community interactions. Supervisors: dr. E. Zaura, prof.dr. JM ten Cate & prof.dr. W. Crielaard. Start: September 2006.

**Ramirez, A.** Development and evaluation of fatty acid based antimicrobials targeted to (oral) biofilm-infections. Supervisors: prof.dr. W. Crielaard & dr. R. Otto. Start: September 2006.

**Schel, AJ.** Microbial risk assessment of dental unit water supplies in general practices. Supervisors: prof.dr. J.M. ten Cate & prof.dr. C. Vandenbroucke-Grauls. Start: October 2001.

**Shemesh, H.** Treatment of the root canal wall. Supervisor: prof.dr. P.R. Wesselink; co-supervisor: dr. M-K. Wu. Start November 2004.

**Versloot, J.** Recognition, prevention and treatment of pain in child dental patients. Supervisors: prof.dr. J. Hoogstraten & prof.dr. J.M. ten Cate; co-supervisor: dr. J.S.J. Veerkamp. Start: December 2002.

## Department of Oral Function

### Oral Function and Oral Rehabilitation

#### Program leader

Prof.dr.ir. M. Naeije  
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E-mail: M.Naeije@acta.nl

#### IOT senior scientists and full professors



M. Naeije



F. Lobbezoo



D. Wismeijer

#### Research objectives

The general mission of the programme is to improve the dentist's knowledge of the normal and the disturbed movement functions of the human masticatory system, the factors that influence these functions, and the treatment modalities that preserve or restore the patient's function. The present research programme comprises two major research domains, ***Oral Kinesiology*** and ***Oral Implantology and Prosthetic Dentistry***.

#### Results

##### ***Oral Kinesiology***

*Influence of (experimental) orofacial pain upon the sensorimotor control of the human masticatory system:*

In a collaborative study with the Aalborg University, it was found that subsequent bouts of intense gum chewing can induce jaw muscle hyperalgesia to pressure stimuli, and even (transient) signs of myofascial pain in healthy individuals. This finding corroborates the suggestion that muscle hyperactivity plays an important role as a contributing factor to the etiology of myogenous temporomandibular disorders (TMD).

*Pathophysiology, diagnosis and treatment modalities of chronic temporomandibular disorders:*

In a collaborative study, performed together with the Universities of Leuven, Malmö, and Naples, the concurrent validity of two diagnostic systems for TMD, viz., the Research Diagnostic Criteria (RDC) and the dynamic/ static pain tests, is being investigated. A preliminary analysis shows the validity to be only moderate. Interestingly, when a combination of both systems is used, the validity seems to improve to more acceptable levels.

In a 6-months treatment follow-up study in a group of myogenous TMD patients, it was shown that an individually-tailored treatment modality caused a persisting reduction in pain and a ditto improvement in functional impairment. However, in patients with high somatization scores at baseline (i.e., before the start of the treatment), these positive treatment effects tended to dissolve during the follow-up period.

A new scale for the quantification of occlusal and non-occlusal tooth wear was developed and tested for its reliability. The scale was found to be reliable for the assessment of occlusal wear,

both clinically (i.e., chair-side) and on dental casts. For non-occlusal wear, however, clinical assessment was found to be more reliable than that on dental casts.

In a randomised clinical trial, the effectiveness of three different therapies for patients with myogenous TMD-pain is being studied. The therapies involved are: 1) counseling, 2) counseling combined with a stabilization splint, and 3) counseling combined with physical therapy. After 8 weeks of treatment, treatment success will be evaluated with a patient specific approach, which was adapted for its use in TMD patients. Furthermore, follow-up measurements over a period of 1 year will be performed. So far, 25 patients have entered the study.

*Pathophysiology, diagnosis and treatment modalities of (sleep-related) oral movement disorders:*

As part of an ongoing RCT study to the efficacy of mandibular advancement devices (MAD) for obstructive sleep apnea (in collaboration with the Slotervaart General Hospital), a polysomnographic study was performed to the most effective mandibular protrusion position, dictated by a MAD, in the treatment of obstructive sleep apnea (OSA). It was found that a MAD must be set at least at 25% of the maximal protrusion position of the mandible to have a therapeutic effect in OSA patients.

*The development, diagnosis and treatment of internal derangements of the temporomandibular joint:*

In close collaboration with the section of Pedodontology of Acta, a clinical and kinematic follow-up study to the development and the natural course of anterior disk displacements with reduction (ADDR's) has started. A group of 200 children between 12 and 16 years of age will be investigated twice a year during the follow-up period of 2 years.

In an ongoing follow-up study to the natural course of ADDR's in adults (students and TMD patients) it was shown that most ADDR's remain stable in time. However, in 2 patients, the ADDR had progressed into a closed lock condition, despite the fact that the patients reported no or only minimal clinical symptoms. This may explain the discrepancy which exists between the outcome of MRI studies to ADDR's and that of clinical studies.

**Oral Implantology and Prosthetic Dentistry:**

*Incorporation of proteins in biomimetic coatings (dr. Y. Liu):*

A slow release of BMP's (bone morphogenetic proteins) from the implant coatings is thought to have a stimulating effect on bone growth. Besides oral implants, bone filling osseointegrative materials and membranes have also been coated and have become integrated in the department's research projects.

As part of a new experimental dental-implant model for the in-vivo testing of functionalized surfaces within unfavourable bony environments, thirty-four goats were implanted with 4 implants per animal (in collaboration with Bern and Inner Mongolia Agriculture University China). All animals have been sacrificed and the histological analysis is currently being evaluated.

Ca/P ratio influences biomimetic coatings formation on implants and bone fillers. Three different kinds of coating materials for titanium, zirconia, Bio-Osis, bioceramics and membranes were developed.

The improvements of the osteoconductive and osteoinductive properties of Zirconia implants by additional CaP coatings and bone growth factors. Zirconia discs and invitro characteristics of the implant material have successfully been coated.

*Evaluation of patient treatment where oral implants are incorporated (prof.dr. D. Wismeijer):*

A number of these projects involve CAD-CAM patient analysis and treatment. We are also interested in evaluating procedures where complications involved with dental implants are treated.

BIOS-2. The Breda Implant overdenture study. An evaluation after 8 years. This project has run since 1992. This year the variables concerning the hard and soft periimplant tissues 8 years after the initial treatment have been evaluated. In cooperation with the department of oral microbiology we are also looking at genetic factors related to bone loss and smoking.

Pre-surgical CAD/CAM planning and fabricating surgical guide and suprastructure on dental implants in order to restore fully edentulous mandible/maxilla, an in vitro and a clinical study. A MEC approval has been asked for. An in vitro analysis of forces on the bone and the implants is being developed. A number of patients have been treated in a pilot study.

A multi centre randomised controlled clinical trial comparing conventional loading of an overdenture on two implants with a bar to immediate loading of an overdenture on two implants with a bar. Patient treatment starts in February 2007. Forty-three patients have already been treated in a pilot study in 2006.

Single tooth replacement in the esthetic zone. Comparing three different implant systems in immediate and conventional loading protocols. This project is being carried out in conjunction with the AMPHIA teaching hospital in Breda. All the patients have been treated, the last in the trimester of 2006.

Implants supporting free end sadels. A multi center clinical trial. All the patients have been treated and the 6 month evaluation has been carried out. In 2007, the material of the three treatment centers will be combined.

### Academic personnel in 2006 and 2007

Research staff ACTA - CD (in full time equivalents)				
position	name	fte 2006	plan 2007	funding
Full professors	Lobbezoo, prof.dr. F.	0,50	0,50	1
	Naeije, prof.dr.ir. M.	0,40	0,40	1
	Wismeijer, prof.dr. D.	0,10	0,30	1
Lecturers and other tenured staff	Denissen, dr. H.W.	0,10	0,10	1
	Liu, dr. Y.	0,20	0,60	1
	Meulen, drs. M.J., van der	0,10	0,10	1
	Selms, drs. M.K.A., van	0,20	0,50	1
	Visscher, dr. C.M.	0,50	0,40	1
<b>Total tenured staff</b>		<b>2,10</b>	<b>2,90</b>	
Non tenured staff	Buchem, drs. J. van	--	0,20	guest
	Klenke, drs. F.	--	0,20	guest
	Koutris drs. M.	0,20	0,20	guest
	Stoker, drs.ir. G.T.	0,10	0,10	guest
	Tahmaseb, A.	0,20	0,30	guest
	Uilenbroek, H.	--	0,20	guest
PhD students	Aarab, drs. G.	0,40	0,40	1
	Kalaykova, dds. S.I.	0,50	0,30	1
	Rollman drs. A.	0,60	0,60	1
	Selms, drs. M.K.A., van	0,50	--	1
	Tuyt, drs. M.	--	0,25	1
	Zaag, drs. J., van der	0,20	0,20	1
<b>Total non tenured staff</b>		<b>2,70</b>	<b>3,45</b>	
total 1st funding		4,30	5,15	1
total guests		0,50	1,20	guest
<b>Total research staff</b>		<b>4,80</b>	<b>6,35</b>	

### Publications in journals indexed in SCI

Feine, J., Jacobs, R., Lobbezoo, F., Sessle, B.J., Steenberghe, D. van, Trulsson, M., Fejerskov, O., & Svensson, P. (2006). A functional perspective on oral implants. State-of-the-science and future recommendations. *J ORAL REHABIL*, 33, 309-312.

Kalaykova, S.I., Naeije, M., Huddleston Slater, J.J.R., & Lobbezoo, F. (2006). Is condylar position a predictor for functional signs of TMJ hypermobility? *J ORAL REHABIL*, 33, 349-355.

- Liu, Y., Huse, R.O., Groot, K. de, Buser, D., & Hunziker, E.B. (2006). The degradation rate and osseointegrative efficacy of BMP-2 bearing biomimetic coatings vary as a function of the drug delivery mode. *KEY ENG MATER*, 309-311, 969-972 part 1-2.
- Liu, Y., Li, J.P., Hunziker, E.B., & Groot, K. de (2006). Incorporation of growth factors into medical devices via biomimetic coatings. *PHILOS T ROY SOC A*, 364, 233-248.
- Lobbezoo, F., Brouwers, J.E.I.G., Cune, M.S., & Naeije, M. (2006). Dental implants in patients with bruxing habits. *J ORAL REHABIL*, 33, 152-159.
- Lobbezoo, F., Selms, M.K.A. van, & Naeije, M. (2006). Masticatory muscle pain and disordered jaw motor behaviour: Literature review over the past decade. *ARCH ORAL BIOL*, 51, 713-720.
- Lobbezoo, F., Zaag, J. van der, & Naeije, M. (2006). Bruxism: its multiple causes and its effects on dental implants. An updated review. *J ORAL REHABIL*, 33, 293-300.
- Meulen, M.J. van der, Lobbezoo, F., Aartman, I.H.A., & Naeije, M. (2006). Self-reported oral parafunctions and TMD pain intensity in temporomandibular disorder patients. *J OROFAC PAIN*, 20, 31-35.

### **Other scientific publications**

- Buser, D., Belser, U., & Wismeijer, D. (2006). Implant therapy in the esthetic zone. Single tooth replacements. The ITI treatment guide volume 1. 268 pp. Berlin, Germany: Quintessence.

### **Professional publications**

- Eijkman, M.A.J., & Loon, L.A.J. van (2006). Claims: onaangename wenssen. *ACTA QP*, 2, 102-109.
- Huddleston Slater, J.J.W., Huddleston Slater, J.J.R., & Naeije, M. (2006). Behandeling van temporomandibulaire dysfunctie in de algemene praktijk. Een inventarisatie aan de hand van declaratiecodes. *NED TIJDSCHR TANDHEELKD*, 113, 10-13.
- Kalaykova, S.I. (2006). Does ADHD, or rather ADH-medication cause bruxism? *NVGPT BULLETIN*, 24, 11.
- Kalaykova, S.I., Naeije, M., Huddleston Slater, J.J.R., & Lobbezoo, F. (2006). Is er een relatie tussen de positie van het kaakopje bij maximale mondopening en symptomen van hypermobiliteit in het kaakgewricht? *NED TIJDSCHR TANDHEELKD*, 113, 391-396.
- Lobbezoo, F. (2006). Tussen slijten en verbijten. Inaugurele rede. Amsterdam, the Netherlands: Vossiuspers UvA.
- Lobbezoo, F. (2006). Tussen slijten en verbijten. *NED TIJDSCHR TANDHEELKD*, 113, 282-283.
- Lobbezoo, F., & Naeije, M. (2006). Wetenschappelijk gefundeerde behandeling van temporomandibulaire dysfunctie. Bezint eer ge begint. *NED TIJDSCHR TANDHEELKD*, 113, 14-17.
- Lobbezoo, F., Zaag, J. van der, Visscher, C.M., Meulen, M.J. van der, Stofkoper, J.W., & Naeije, M. (2006). Het postinitiële masterprogramma Orale Kinesiologie van ACTA: Van Bruegelsyndroom tot stralende glimlach. *NED TIJDSCHR TANDHEELKD*, 113, 387-390.
- Wetselaar, P., & Koutris, M. (2006). What are the effects of occlusal forces on periodontal tissues? *NVGPT BULLETIN*, 24, 6-7.

### **Indicators of Esteem**

#### **Grants: current projects with external funding**

- Lobbezoo, F. Senior Visiting Research Fellowship, Faculty of Health Sciences, Medical School, University of Adelaide, Australia, 2006.
- Lobbezoo, F. Distinguished Visitors Fellowship, Faculty of Sciences, University of Adelaide, Australia, 2006.
- Wismeijer, D. Straumann AG Switzerland. Immediate loading of two implants connected by a bar and an overdenture. A RCT comparing immediate loading with conventional loading. 140.000 euro.
- Wismeijer, D. ITI Foundation, Basel, Switzerland. In vivo degradability and osteoconductivity of calcium phosphate coatings with different crystalline properties. Sum awarded: 193.000 CHF.

#### **Membership of international editorial boards**

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

## Invited speakers at international congresses or symposia

- Klenke, F.M., Liu, Y., Siebenrock, K.A., & Hofstetter, W. (2006, June 06). The biological properties of calcium phosphate bone substitutes are influenced by the biomaterials' pore sizes. Bologna, Italy, Europe Orthopedic Research Society.
- Liu, Y. (2006, May 05). Enhanced bone apposition to BMP-coated implants: Tissue Integration of Dental Implants. Bern, Switzerland, Andre Schroeder Memorial Symposium.
- Liu, Y. (2006, November 08). Surface functionalization of devices for maxillofacial surgery. Hong Kong, China, 7Th Asia Oral and Maxillofacial Surgery Society Meeting.
- Liu, Y. (2006, October 20). Bone formation enhancement by BMP-2-functionalized implant coatings- A study in miniature pigs. Lausanne, Switzerland, AO Symposium Biomaterials, Cell-, Tissue and Gene based Therapies: From Basic Research to Clinical Applications.
- Liu, Y., Enggist, L., Kuffer, A., Wismeijer, D., Buser, D., & Hunziker, E.B. (2006, oktober 20). Osteoinductive efficacy of BMP-2-functionalized dental-implant coatings. Zurich, Switzerland, EAO.
- Lobbezoo, F. (2006, August 17). Management of 'Gnawing' Jaw Pain: The Dutch Approach. Adelaide, Australia, Public lecture University of Adelaide.
- Lobbezoo, F. (2006, August 25). Bruxism is a contraindication for oral implant treatment: True or False. Adelaide, Australia, Seminar Dental School, University of Adelaide.
- Lobbezoo, F. (2006, February 22). Loading and overload of dental implants. Chicago, USA, American Equilibration Society (AES).
- Lobbezoo, F. (2006, June 27). Movement disorders in the dental office. Brisbane, Australia, International Mastication Symposium (IMS).
- Lobbezoo, F. (2006, June 28). Classification of TMD pain. Recent insights into the etiology of bruxism and its effects on dental implants. Brisbane, Australia, Australian New Zealand Academy of Orofacial Pain (ANZAOP).
- Lobbezoo, F. (2006, June 28). Report of an ongoing multicenter study to the classification of TMD pain. Brisbane, Australia, RDC/TMD Consortium.
- Lobbezoo, F. (2006, September 29). Human oral movement disorders. Barcelona, Spain, Voordracht Open Meeting EACD.

## Other international functions

- Lobbezoo, F.: President-Elect. European Academy of Craniomandibular Disorders (EACD).
- Lobbezoo, F.: Member. Research Committee European Academy of Craniomandibular Disorders (EACD).
- Lobbezoo, F.: Secretary/Treasurer. Neuroscience Group. International Association for Dental Research (IADR).
- Visscher, C.M.: International board member. Physical Therapy Board of Craniofacial and Cervical Therapeutics.
- Wismeijer, D.: Member. Education Committee of the ITI (CH).

## Collaborations

### *Oral Kinesiology:*

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

### *Oral Implantology and Prosthetic Dentistry:*

- Inner Mongolia Agriculture University, Huhehot, China.

- Department of Nuclear Medicine and School of Dentistry, University of Nijmegen, the Netherlands: (dr. O. Bormen and prof.dr. J. Jansen)
- Department of Prosthetic Dentistry of the University of Dunedin Dental School (A. Payne)
- Department of MFP and Special Dental Care of the AMPHIA teaching hospital Breda (NL).
- Department of Oral and Maxillofacial Surgery of the AMPHIA teaching hospital Breda (NL).
- Hospital of Stomatology, Dental School of Zhejiang University, Huangzhou, China.
- Maxillofacial Surgery Department, University of Bern, Bern, Switzerland.

### **Current PhD projects**

**Aarab G.** The dental treatment of obstructive sleep apnea syndrome and snoring. Supervisors: prof.dr.ir. M. Naeije and prof.dr. F. Lobbezoo: Start: 2002.

**Kalaykova, SI.** Internal derangements in the temporomandibular joint. Supervisors: prof.dr.ir. M. Naeije and prof.dr. F. Lobbezoo: Start: 2004.

**Klenke F.** Development of biomaterial – growth factor constructs for use as bone substitutes. Supervisor: prof.dr. D. Wismeijer: Start: 2005.

**Rollman A.** Chronic myogenous CMD: diagnostic, etiology en treatment. Supervisor: prof.dr.ir. M. Naeije; co-supervisor; dr. C.M. Visscher: Start: 2004.

**Selms MKA van.** Myogenous temporomandibular disorder pain: diagnosis, etiology, motor consequences, and treatment follow-up. Supervisors: prof.dr.ir. M. Naeije and prof.dr. F. Lobbezoo: Start: 2000.

**Stoker GT.** BIOS-2 The Breda implant overdenture study part two. Comparing three different treatment modalities for implant supported overdentures. An eight year evaluation. Supervisor: prof.dr. D. Wismeijer: Start 2002.

**Zaag J. van der.** A polysomnographic study to the efficacy of treatment modalities of nocturnal bruxism. Supervisors: prof.dr.ir. M. Naeije and prof.dr. F. Lobbezoo; Start: 1998.

## Department of Periodontology

### Biology, Physiology and Pathophysiology of the Periodontium

#### Program leader

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#### IOT senior scientists and full professors



U. van der Velden



W. Beertsen



B.G. Loos



G.A. van der Weijden

#### Research objectives

Periodontitis is a destructive inflammatory disease of the supporting tissues of the teeth. It is caused by bacteria and affects a substantial part of the human population. Over the age of 45 years it is a major cause for tooth loss. This research program is devoted to clarify the individual differences in susceptibility to periodontitis and to investigate the mechanisms involved in periodontal breakdown and repair/regeneration. In addition the evaluation of the efficacy of new preventive and therapeutic measures is part of the program.

The following questions are addressed:

1. *Susceptibility to periodontitis and systemic effects:*

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

2. *Degradation and regeneration:*

- How is the extracellular matrix of the periodontium degraded?
- What mechanisms are responsible for tissue homeostasis?

3. *Prevention and treatment of periodontitis:*

- Which are the most effective measures to prevent and control dental plaque?

#### Results

Periodontitis is a complex disease because of its multifactorial etiology (bacteria, genetics and environment). We studied in an untreated Indonesian population the natural history of periodontal disease over 15 years. The results showed that with regard to the onset of periodontitis, the subgingival presence of calculus and *Actinobacillus actinomycetemcomitans* could be identified as risk factors and age as a risk determinant. Regarding disease progression, the number of sites with a probing depth  $\geq 5$  mm and the number of sites with recession were identified as risk predictors and male gender as risk determinant. At present the relationship between dietary intake of vitamin C and the periodontal status is studied in this population.

With regard to the genetic factors we are still following two strategies: 1) candidate gene approach; 2) genome wide search. The first approach has been further developed within the framework of the European Consortium and granted network INFOBIOMED; a periodontitis data-

warehouse (PDWH) has been constructed and now datamining and biomedical informatics tools are used to explore complex relationships between genes and other etiological factors. The second approach is well under way; in a multicenter European study (EPG consortium) we have now over 600 cases. A pilot on genome wide screening has been undertaken among 200 cases; a confirmation study to validate new candidate genomic loci associated with periodontitis is now being designed. Also, functional studies are undertaken which investigate the relative importance of observed genetic associations with periodontitis; preliminary results indicate differences in phagocytosis and neutrophil activation among patients with different genotypes for Fc $\gamma$  receptors. Further, we have investigated Th1 and Th2 responses in smoker and non-smoker patients; smokers have a predominance of a Th2 response upon stimulation, possibly explaining more periodontal destruction in smokers than non-smokers.

Periodontitis has systemic effects. In a meta analysis it was shown that C-reactive protein levels are always elevated in periodontitis in comparison to healthy controls. We have further investigated the concept that periodontitis has systemic effects and may predispose to cardiovascular diseases (CVD). In particular, we have investigated biomarkers of CVD, related to a prothrombotic state and related to metabolic syndrome. Patients with periodontitis appear to have an increased pro-coagulant state and an increased insulin resistance.

Collaborative studies between Oral Cell Biology and Experimental Periodontology led to new insights into the involvement of different fibroblast populations in the formation of osteoclasts. In the presence of gingival fibroblasts osteoclastogenesis was lower compared to the formation induced by periodontal fibroblasts. This study strongly indicates that fibroblasts modulate osteoclastogenesis and thereby the level of bone resorption. In addition, preliminary results indicate that periodontitis patients may have a (acquired?) resistance to osteoclastogenesis stimulating cytokines; monocytes from patients differentiate less abundant to tartrate resistant acid phosphatase (TRACP) positive cells (indicative for osteoclast, see below).

Tartrate resistant acid phosphatase (TRACP) is found primarily in osteoclasts. We have shown considerable differences in the expression of the enzyme by osteoclasts of long bone versus those of the skull. It appeared that the latter osteoclasts expressed a 25 fold higher level of TRAP activity. In addition huge differences in the proteolytic enzymes used by the different osteoclast subpopulations was found by making use of mice deficient for various cysteine proteinases.

Studies on the prevention and treatment of periodontal diseases concentrate on the efficacy of electric toothbrushes, dentifrices, mouth rinses and antibiotics. Our results have shown that rinsing for 30 sec with a mouth rinse is sufficient in order to reach all intra-oral surfaces. In addition it was found that the combined use of AmF/SnF<sub>2</sub> dentifrice and mouth rinse was more effective in plaque reduction when compared to the use of NaF dentifrice and mouth rinse. In addition the SLS in dentifrices does not seem to reduce the level of plaque inhibition offered by rinsing with chlorhexidine.

Research regarding the treatment of periodontal pockets showed that the subgingival mechanical cleaning in itself, had limited effect, in actually removing bacteria. However during follow-up the mean total CFU tended to increase, whereas the prevalence of periodontopathogens further reduced. This showed that it is apparently difficult for these species to survive in treated pockets.

## Academic personnel in 2006 and 2007

Research staff ACTA - PD (in full time equivalents)				
position	name	fte 2006	plan 2007	funding
Full professors	Beertsen, prof.dr. W.	0,05	0,05	1
	Loos, prof.dr. B.G.	0,50	0,50	1
	Velden, prof.dr. U., van der	0,50	0,50	1
Senior lecturer	Weijden, dr. G.A., van der	0,50	0,50	3
Lecturers and other tenured staff	Bos, dr. T., van den	1,00	1,00	1
	Schoonheim-Klein drs. M.E.	0,40	0,40	1
	Timmerman, dr. M.F.	0,10	--	1
	Timmerman, dr. M.F.	0,30	--	3
	Vries, dr. T.J., de	0,80	0,40	2
	Vries, dr. T.J., de	--	0,40	3
<b>Total tenured staff</b>		<b>4,15</b>	<b>3,75</b>	
Non tenured staff	Bizarro, dds.msc. S.	0,20	0,20	1
	Raber-Durlacher, dr. J.E.	0,05	0,05	guest
PhD students	Barendregt, drs. D.S.	0,05	0,05	guest
	Comandasu, dds. E.A.	0,70	0,70	1
	Paraskevas, drs. S.P.	--	0,05	1
	Torres, dds. G.L.	0,60	0,60	1
	Van Strydonck, drs. D.A.C.	0,05	0,05	guest
<b>Total non tenured staff</b>		<b>1,65</b>	<b>1,70</b>	
total 1st funding		4,05	4,00	1
total 2nd funding		0,80	0,40	2
total 3rd funding		0,80	0,90	3
total guests		0,15	0,15	guest
<b>Total research staff</b>		<b>5,80</b>	<b>5,45</b>	

## Dissertations

Paraskevas, S.P. (2006, January 25). The effect of mouthrinses and dentifrices on plaque and periodontal diseases. UvA Universiteit van Amsterdam (191 pag.). Prom./coprom.: prof.dr. U. van der Velden, & dr. G.A. van der Weijden.

## Publications in journals indexed in SCI

Barendregt, D.S., Velden, U. van der, Timmerman, M.F., & Weijden, G.A. van der (2006). Comparison of two automated periodontal probes and two probes with a conventional readout in periodontal maintenance patients. *J CLIN PERIODONTOL*, 33, 276-282.

Bültzingslöwen, I. Von, Brennan, M.T., Spijkervet, F.K.L., Logan, R., Stringer, A., Raber-Durlacher, J.E., & Keefe, D. (2006). Growth factors and cytokines in the prevention and treatment of oral and gastrointestinal mucositis. *SUPPORT CARE CANCER*, 14, 519-527.

Everts, V., Korper, W., Hoeben, K.A., Jansen, I.D., Bromme, D., Cleutjens, K.B.J.M., Heeneman, S., Peters, C., Reinheckel, T., Saftig, P., & Beertsen, W. (2006). Osteoclastic bone degradation and the role of different cysteine proteinases and matrix metalloproteinases: differences between calvaria and long bone. *J BONE MINER RES*, 21, 1399-1408.

Gerardu, V.A.M., Heijnsbroek, M., Buijs, M.J., Weijden, G.A. van der, Cate, J.M. ten, & Loveren, C. van (2006). Comparison of Clinpro Cario L-Pop estimates with CIA lactic acid estimates of the oral microflora. *EUR J ORAL SCI*, 114, 128-132.

- Gerardu, V.A.M., Loveren, C. van, Heijnsbroek, M., Buijs, M.J., Weijden, G.A. van der, & Cate, J.M. ten (2006). Effects of various rinsing protocols after the use of amine fluoride/stannous fluoride toothpaste on the acid production of dental plaque and tongue flora. *CARIES RES*, 40, 245-250.
- Haar, S.F. de, Hiemstra, P.S., Steenberghe, T.J.M. van, Everts, V., & Beertsen, W. (2006). Role of polymorphonuclear leukocyte-derived serine proteinases in defense against *Actinobacillus actinomycetemcomitans*. *INFECT IMMUN*, 74, 5284-5291.
- Haar, S.F. de, Tigchelaar-Gutter, W., Everts, V., & Beertsen, W. (2006). Structure of the periodontium in cathepsin C-deficient mice. *EUR J ORAL SCI*, 114, 171-173.
- Heijnsbroek, M., Gerardu, V.A.M., Buijs, M.J., Loveren, C. van, Cate, J.M. ten, Timmerman, M.F., & Weijden, G.A. van der (2006). Increased salivary fluoride concentrations after post-brush fluoride rinsing not reflected in dental plaque. *CARIES RES*, 40, 444-448.
- Lent, P.L. van, Grevers, L., Lubbers, E., Vries, T.J. de, Nabbe, K.C., Verbeek, S., Oppers, B., Sloetjes, A., Blom, A.B., & Berg, W.B. van den (2006). Fcγ receptors directly mediate cartilage, but not bone, destruction in murine antigen-induced arthritis: uncoupling of cartilage damage from bone erosion and joint inflammation. *ARTH RHEUM/AR C RES*, 54, 3868-3877.
- Palenstein Helderma, W.H. van, Kyaing, M.M., Aung, M.T., Soe, W., Rosema, N.A.M., Weijden, G.A. van der, & Hof, M.A. van 't (2006). Plaque removal by young children using old and new toothbrushes. *J DENT RES*, 85, 1138-1142.
- Paraskevas, S.P., & Weijden, G.A. van der (2006). A review of the effects of stannous fluoride on gingivitis. *J CLIN PERIODONTOL*, 33, 1-13.
- Paraskevas, S.P., Timmerman, M.F., Velden, U. van der, & Weijden, G.A. van der (2006). Additional effect of dentifrices on the instant efficacy of toothbrushing. *J PERIODONTOL*, 77, 1522-1527.
- Perez Amodio, S.G., Jansen, D.C., Schoenmaker, A.M., Vogels, I.M., Reinheckel, T., Hayman, A.R., Cox, T.M., Saftig, P., Beertsen, W., & Everts, V. (2006). Alveolar osteoclasts express a higher level of tartrate-resistant acid phosphatase than long bone osteoclasts and activation does not depend on cathepsin K or L activity. *CALCIFIED TISSUE INT*, 79, 245-254.
- Perez Amodio, S.G., Jansen, D.C., Tigchelaar-Gutter, W., Beertsen, W., & Everts, V. (2006). Endocytosis of tartrate-resistant acid phosphatase by osteoblast-like cells is followed by inactivation of the enzyme. *CALCIFIED TISSUE INT*, 78, 248-254.
- Rhemrev, G.E., Timmerman, M.F., Veldkamp, I., Winkelhoff, A.J. van, & Velden, U. van der (2006). Immediate effect of instrumentation on the subgingival microflora in deep inflamed pockets under strict plaque control. *J CLIN PERIODONTOL*, 33, 42-48.
- Sanz, M., Velden, U. van der, Steenberghe, D. van, & Baehni, P. (2006). Periodontology as a recognized dental speciality in Europe. *J CLIN PERIODONTOL*, 33, 371-375.
- Strijdonck, D.A. Van, Timmerman, M.F., Velden, U. van der, & Weijden, G.A. van der (2006). Chlorhexidine mouthrinse in combination with an SLS-containing dentifrice and a dentifrice slurry. *J CLIN PERIODONTOL*, 33, 340-344.
- Timmerman, M.F., & Weijden, G.A. van der (2006). Bone level around endodontically treated teeth in periodontitis patients. *J CLIN PERIODONTOL*, 33, 620-625.
- Velden, U. van der, Abbas, F., Armand, S., Loos, B.G., Timmerman, M.F., Weijden, G.A. van der, Winkelhoff, A.J. van, & Winkel, E.G. (2006). Java project on periodontal diseases. The natural development of periodontitis: risk factors, risk predictors and risk determinants. *J CLIN PERIODONTOL*, 33, 540-548.
- Vries, T.J. de, Schoenmaker, A.M., Wattanaroonwong, N., Hoonard, M., Nieuwenhuijse, A., Beertsen, W., & Everts, V. (2006). Gingival fibroblasts are better at inhibiting osteoclast formation than periodontal ligament fibroblasts. *J CELL BIOCHEM*, 98, 370-382.

### Other scientific publications (international, refereed)

- Loos, B.G. (2006). Systemic effects of periodontitis. *INT J DENT HYG*, 4, 1:34-38 discussion 50-52.
- Loos, B.G. (2006). Systemic markers of inflammation in periodontitis. In H. Tanyeri, S. Multlu, C. Scully, & E. Kürklü (Eds.), *Periodontology: Oral medicine interactions* (pp. 137-143). Istanbul, Turkey: Oral Medicine Society, Ozkaracan Matbaacilik Ltd.
- Loos, B.G., Laine, M.L., Palen, C. van der, Lessmann, F., Winkelhoff, A.J. van, Velden, U. van der, Crusius, J.B.A., Morree, S.A., Pena, A.S., Brooks, A.J., Pereira, A.S., Moor, G. de, Maoj, V., & Sanchez, F.M. (2006). Biomedical Informatics in chronic infectious and inflammatory disease research: periodontitis as a case study. In *PROCEEDINGS MIE* (pp. 77-83).
- Mattheos, N., Attström, R., Fundak, A., Knutsson, K., Padrutt, S., Polychronopoulou, A., Schoonheim-Klein, M., & Saxer, U.P. (2006). Assessing behavioural change support abilities of the oral healthcare team. *ORAL HEALTH PREV DENT*, 4, 71-77.
- Schoonheim-Klein, M., Habets, L.L.M.H., Aartman, I.H.A., Vleuten, C.P.M. van der, Hoogstraten, J., & Velden, U. van der (2006). Implementing an objective structured clinical examination (OSCE) in dental education: effects on students' learning strategies. *EUR J DENT EDUC*, 10, 226-235.
- Timmerman, M.F., & Weijden, G.A. van der (2006). Risk factors for periodontitis. *INT J DENT HYG*, 4, 2-7.

- Velden, U. van der (2006). The significance of supragingival plaque accumulation in periodontal disease. *INT J DENT HYG*, 4, 1:11-14.
- Versteeg, P.A., Timmerman, M.F., Paraskevas, S.P., & Weijden, G.A. van der (2006). Evaluation of several brushing motion combinations in relation to plaque-removing efficacy with Oral-B CrossAction Power: a professional brushing study. *INT J DENT HYG*, 4, 204-208.
- Weringh, M. van, Barendregt, D.S., Rosema, N.A.M., Timmerman, M.F., & Weijden, G.A. van der (2006). A thin or thick probe handle: does it make a difference? *INT J DENT HYG*, 4, 140-144.

### **Professional publications**

- Danser, M.M., Barendregt, D.S., & Weijden, G.A. van der (2006). Parodontale nazorg. In M. Quirynen, D. van Steenberghe, W. Beertsen, & U. van der Velden (Eds.), *Handboek Parodontologie*, 1st edition (pp. C3:1-34). Houten/Diegem: Bohn Stafleu Van Loghum.
- Dijkstra, J.C., Raber-Durlacher, J.E., & Loos, B.G. (2006). Veranderingen in geslachtshormonen. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene Ziekteleer voor Tandartsen*, 2nd edition (pp. 231-237). Houten/Diegem: Bohn Stafleu Van Loghum.
- Hoesel, Q.G.C.M. van, Raber-Durlacher, J.E., & Rietveld, D.H.F. (2006). Oncologie. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene Ziekteleer voor Tandartsen*, 2nd edition (pp. 49-52). Houten/Diegem: Bohn Stafleu Van Loghum.
- Loos, B.G., & Velden, U. van der (2006). Vatbaarheid voor parodontitis. In M. Quirynen, D. van Steenberghe, W. Beertsen, & U. van der Velden (Eds.), *Handboek Parodontologie*, 1st edition (pp. C3:1-34). Houten/Diegem: Bohn Stafleu Van Loghum.
- Raber-Durlacher, J.E. (2006). Kan een zwangere met een gezonde gingiva ook zwangerschapsgingivitis krijgen? *MONDHYG VADEMECUM*, 4, 10.
- Raber-Durlacher, J.E., & Loos, B.G. (2006). Wat is de invloed van hormonen (bijvoorbeeld overgang, pilgebruik, zwangerschap) op het tandvlees? *MONDHYG VADEMECUM*, 4, 4.
- Velden, U. van der (2006). Refractaire parodontitis. In M. Quirynen, D. van Steenberghe, W. Beertsen, & U. van der Velden (Eds.), *Handboek Parodontologie*, 1st edition (pp. B2.7:1-13). Houten/Diegem: Bohn Stafleu Van Loghum.
- Versteeg, P.A., Timmerman, M.F., Piscaer, M., Velden, U. van der, & Weijden, G.A. van der (2006). Tandenspoetsen en gingivalaesies. *NED TIJDSCHR TANDHEELKD*, 113, 268-272.

### **External reports**

- Hoenderdos, N.L., Rosema, N.A.M., Timmerman, M.F., Versteeg, P.A., Velden, U. van der, & Weijden, G.A. van der (2006). Different brushing times of an oscillating rotating electric toothbrush. Report for Procter & Gamble. Amsterdam: ACTA.
- Hoenderdos, N.L., Rosema, N.A.M., Timmerman, M.F., Versteeg, P.A., Velden, U. van der, & Weijden, G.A. van der (2006). Evaluation of manual toothbrushes with regular and soft filament designs in relation to gingival abrasion and plaque removal. Report for GABA. Amsterdam: ACTA.

### **Indicators of Esteem**

#### **Grants: current projects with external funding**

- Loos, B.G., Winkelhoff, A.J. van & Velden, U. van der. 6th Frame work, Network of Excellence, European Commission, Section IST INFOBIOMED 2004-2006, total budget; €248.000,-.
- Loos, B.G. Relationship between oral and systemic health. Philips DAP Oral Health Division, 2005-2008, total budget €75.000,-.
- Vries, T.J., de. Cellular and nuclear diversity of multinucleated osteoclasts. KNAW fellowship; 2002-2007. €250.000,-.
- Weijden, G.A., van der & Velden, U. van der. EB25 vs Stratus prototypes Braun/Gillette Germany; €24.900,-.
- Weijden, G.A., van der & Velden, U. van der. Filament design GABA Int. €58.390,-.
- Weijden, G.A., van der & Velden, U. van der. Oral-B advantage sensitive. Braun/Gillette Germany; €48.870,-.
- Weijden, G.A., van der & Velden, U. van der. The prevention study. Braun/Gillette Germany; €40.000,-.

## Membership of international editorial boards

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

## Invited speakers at international congresses or symposia

- Loos, B.G. (2006, June 29). An overview of genetic polymorphisms and periodontal status and CRP and other systemic markers in patients with periodontal diseases. Are these risk factors for cardiovascular diseases? Madrid, Spain, European Federation of Periodontology (EFP), EuroPerio V.
- Loos, B.G. (2006, March 08). CRP and other systemic markers in patients with periodontal diseases. Are these risk factors for cardiovascular diseases? Emerging trends in oral healthcare. Amsterdam, The Netherlands, Philips Oral Healthcare Symposium.
- Loos, B.G. (2006, December 09). Genetic factors as prognostic indicators for therapeutic success. Berlin, Germany, Current controversies in periodontology (Aktuelle Kontroversen in der Parodontologie).
- Loos, B.G. (2006, September 03). Periodontitis and atherosclerosis; Genetics in relation to periodontology, parts 1 and 2; Systemic markers of inflammation in periodontitis, parts 1 and 2; Immunological events and markers in periodontitis; Implants in periodontitis patients. Sidney, Australia, Current controversies in periodontology (Aktuelle Kontroversen in der Parodontologie).
- Velden, U. van der (2006, March 24). Can we predict future periodontal destruction from clinical findings or the microflora. Oxford, British Society of Periodontology, spring meeting.
- Velden, U. van der (2006, June 29). Strategies on prevention of periodontal diseases: importance of diagnosis and home care. Madrid, Spain, European Federation of Periodontology (EFP), EuroPerio V.
- Velden, U. van der (2006, June 22). The significance of supragingival plaque accumulation in periodontal disease. Leuven, Belgium, Symposium Parodontologen.
- Velden, U. van der (2006, March 08). The significance of supragingival plaque accumulation in periodontal disease. Emerging trends in oral healthcare. Amsterdam, The Netherlands, Philips Oral Healthcare Symposium.
- Weijden, G.A. van der (2006, March 17). Paradigm shifts in mechanical plaque control. Goteborg, Sweden, 1st Jan Lindhe symposium.

## Other international functions

Loos, B.G.:	External examiner. European MSc programs, Göteborg.
Velden, U. van der:	Board Member. European Federation of Periodontology.
Velden, U. van der:	Chairman Post Graduate Education Committee. European Federation of Periodontology.
Velden, U. van der:	External examiner. European MSc programs. Leuven.

## Collaborations

- University of Sheffield (dr. D. Buttle), Sheffield, United Kingdom.
- Celltech (dr. A. Docherty), London, United Kingdom.
- Padjadjaran University, Parodontology (dr. S. Lambri), Bandung, Indonesia.
- Unilever Research (dr. D.J. Page), Port Sunlight, United Kingdom.
- Ludwig Boltzmann Institut für Osteologie (prof.dr. P. Fratzl) Vienna, Austria.
- Universität Kiel (dr. P. Saftig) Kiel, Germany.
- Braun Oral Research (dr. P. Warren) Baltimore, USA.
- University of Kiel, Dept of Gastro-Enterology (dr. S. Schreiber) Germany.
- University of Oslo, Dept of Oral Biology (dr. K. Schenck) Norway.

## Current PhD projects

**Barendregt DS.** Periodontal probing. Supervisor: prof.dr. U. van der Velden; co-supervisor: dr. G.A. van der Weijden. Start: September 2002.

**Comandasu EA.** Genetically determined heterogeneity of Fc-gamma receptor function may result in differential responsiveness and activity of neutrophils, monocytes and platelets. Supervisor: prof.dr. U. van der Velden; co-supervisor: prof.dr. B.G. Loos. Start February 2004.

**Rosema M.** Efficacy of toothbrushing. Supervisor: prof.dr. U. van der Velden; co-supervisor: dr. G.A. van der Weijden. Start: September 2006.

**Schoonheim-Klein ME.** Objective Structured Clinical Examination (OSCE) in dental education. Supervisors: prof.dr. U. van der Velden and prof.dr. J. Hoogstraten. Start: June 2004.

**Torres GL.** Periodontitis in twins and their spouses. Supervisor: prof.dr. U. van der Velden; co-supervisor: prof.dr. B.G. Loos. Start September 2002.

**Van Strijdonck, DAC.** Chlorhexidine use. Supervisor: prof.dr. U. van der Velden; co-supervisor: dr. G.A. van der Weijden. Start: September 2001.

## Section: Oral Cell Biology

### Bioengineering of Bone and Periodontium

#### Program leader

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#### IOT senior scientists and full professors



V. Everts



A.L.J.J. Bronckers



J. Klein Nulend



R.A. Bank

#### Research objectives

The program “Bioengineering of Bone and Periodontium” of the Department of Oral Cell Biology studies the biological processes of functional adaptation and guided regeneration of bone and periodontium. Research focuses on fundamental aspects of mechanotransduction, and tissue engineering of bone, cartilage, and periodontium. The results are used in more applied research towards repair and regeneration of jawbone and periodontium, and prevention/treatment of infections around implants.

Mechanical stress is capable of modulating the activity of osteoblasts and osteoclasts, which are orchestrated in their activity by the mechanosensitive osteocytes, and periodontal fibroblasts, which mediate adaptation of the tissue to a changing force regime. To clarify the cell biological processes of mechanical adaptation, in vitro experiments are performed in which the reaction of bone and connective tissue cells to mechanical stress is studied in cell and organ culture, and at the single cell level. The results are verified in studies of bone under weightlessness conditions during space flight, and in disuse osteoporosis. Bone growth factors are locally produced growth factors, which can be used for clinical regeneration of bone and cartilage. They are involved in fracture repair and in the regulation of normal bone growth, and also play a role in pattern formation of the dentition and the skeleton in the early embryonic phase. Their role in regeneration of bone and periodontium is studied using cell and animal experiments. In addition, the local formation of bone and connective tissue around bone-replacing and bone-inducing grafts, and during distraction osteogenesis is studied, using human bone cell cultures as well as quantitative histomorphometry of human bone biopsies from augmented jaw bone. Finally, studies are performed on prevention of infections around oral and orthopaedic implants, using anti-microbial peptides combined with a bone substitute; a collaboration within the Foundation STEGA (Skeletal Tissue Engineering Group Amsterdam).

The tissue engineering part of the research is focused around (1) the synthesis, deposition and degradation of the collagen network in bone and cartilage, (2) the use of adipose tissue-derived stem cells in combination with injectable scaffolds (hydrogels) and growth factors for tissue engineering of the intervertebral disc, and (3) the role of mechanical factors in stem cell differentiation.

## Results

### ***Regeneration of bone and periodontium***

Collaborative studies between Oral Cell Biology and Experimental Periodontology led to new insights into the involvement of different fibroblast populations in the formation of osteoclasts. In the presence of gingival fibroblasts osteoclastogenesis was lower compared to the formation induced by periodontal fibroblasts. This study strongly indicates that fibroblasts modulate osteoclastogenesis and thereby the level of bone resorption.

Tartrate resistant acid phosphatase (TRACP) is found primarily in osteoclasts. We have shown considerable differences in the expression of the enzyme by osteoclasts of long bone versus those of the skull. It appeared that the latter osteoclasts expressed a 25 fold higher level of TRAP activity. In addition huge differences in the proteolytic enzymes used by the different osteoclast subpopulations was found by making use of mice deficient for various cysteine proteinases.

Transitional ameloblasts in neonatal hamsters appeared to be very sensitive to a single short lasting fluoride exposure; the fluoride induced a cystic lesion that may be associated with the formation of surface pits in enamel of fluorotic teeth. In vitro the deposition of fluorotic non-mineralizing matrix in hamster matrix was counteracted by a high calcium supply given just before the fluoride insult. Fluorotic enamel also recovered faster in vitro when after fluoride insult calcium supply was high. High calcium levels in vitro enhanced secretion of amelogenins and it was speculated that it was the buffering capacity of the amelogenins that counteracted a fluoride-induced local pH drop in the forming enamel that might be responsible for fluorosis. Thus, high dietary calcium uptake preceding or following fluoride insult is likely beneficial in reducing the fluorotic changes in forming enamel.

Distraction osteogenesis is a technique to augment bone tissue by gradual distracting two bone ends. In the gap between the bone ends new bone will form. Bone formation during distraction osteogenesis in the lower human jaw was slightly faster at a distraction rate of 0.5 mm/day than 1.0 mm/day. This effect was likely associated with blood vessel formation in the distraction gap which was slightly higher at the lower distraction rate. Morphometric studies of jaw bone regeneration using this technique were undertaken in collaboration with the Departments of Oral & Maxillofacial Surgery (ACTA-VUMC), Alkmaar Medical Center, Gelderse Vallei Hospital, and the Department of Functional Anatomy (ACTA).

To treat or prevent bacterial infections in bone defects bone substitutes can be loaded with antibiotics or antimicrobial peptides. The release characteristics of the antibiotic gentamycin were tested for a series of commercially available synthetic bone substitutes clinically used to fill bone defects.

The collagen meshwork of long bones were compared with that in calvariae; major differences were found in levels of lysyl hydroxylation and cross-links. The collagen meshwork of the different compartments of the intervertebral disc were analyzed as well, and compared with cartilage derived from the meniscus and articular joints. We have developed quantitative real-time PCR of the 23 collagen-modifying enzymes (goat; human) in order to investigate the expression of these enzymes in osteoblasts and chondrocytes and to follow stem cell differentiation.

### ***Mechanical adaptation and regeneration***

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

Mechanosensing by bone cells directs changes in bone mass and structure, in response to the challenges of mechanical loading. Low-amplitude, high-frequency loading stimulates bone growth by enhancing bone formation and inhibiting disuse osteoporosis, but how bone cells sense vibration stress is unknown. We have now shown that correlations of nitric oxide and prostaglandin production with the maximum acceleration rate relate to nucleus oscillations, providing a physical basis for cellular mechanosensing of high-frequency loading.

Loading frequency is an important parameter for the stimulation of bone formation in vivo. It is still unclear how the information of external loading characteristics is conveyed to osteoblasts and osteoclasts. We have shown that pulsatile fluid flow with different frequencies stimulates the release of nitric oxide by osteoblasts in a dose-dependent manner. In contrast, prostaglandin E2 production was enhanced uniformly by all fluid flow regimes, independent of flow frequency. This implies that the NO response may play a role in mediating the differential effects of the various loading patterns on bone.

We have recently proposed that during bone remodeling, osteocyte apoptosis steers osteonal alignment in relation to mechanical loading of the whole bone. Bone tissue can adapt to orthodontic load. Mechanosensing in bone occurs by osteocytes, which translate the canalicular flow resulting from bone loading into osteoclast and osteoblast recruiting signals. Apoptotic osteocytes attract osteoclasts, and inhibition of osteocyte apoptosis can therefore affect bone remodeling. Since TNF- $\alpha$  is a pro-inflammatory cytokine with apoptotic potency, and elevated levels are found in the gingival sulcus during orthodontic tooth movement, we investigated if mechanical loading by pulsating fluid flow affects TNF- $\alpha$ -induced apoptosis in chicken osteocytes, osteoblasts, and periosteal fibroblasts. We have shown a key regulatory role for osteocyte apoptosis in bone remodeling after application of an orthodontic load.

Osteocytes are thought to orchestrate bone remodeling by producing factors that influence other cell populations during bone homeostasis. However, it is unclear exactly how osteocytes are able to influence neighboring bone cells. We have shown that osteocytes subjected to mechanical loading by pulsating fluid flow inhibit proliferation but stimulate differentiation of osteoblasts in vitro via soluble factors and that the release of these factors was at least partially dependent on the activation of an NO pathway in osteocytes in response to pulsating fluid flow. Thus, the osteocyte appears to be more responsive to pulsating fluid flow than the osteoblast or periosteal fibroblast with respect to the production of soluble signaling molecules affecting osteoblast proliferation and differentiation. These findings provide further insight into how osteocytes influence bone cell populations during bone loading.

Imperfect bone remodeling might relate to an imperfect response of osteocytes to mechanical loading. We found subtle differences in the mechanoresponse of bone cells from 9 osteoporotic and 9 osteoarthritic donors, measured as nitric oxide and prostaglandin E2 production. These results might relate to the lack of bone mass in osteoporotic patients, or the excess thereof in osteoarthritic patients.

Bone morphogenetic proteins (BMPs) initiate, promote, and maintain chondrogenesis and osteogenesis. We hypothesized that BMP-2 induces an osteogenic, and BMP-7 a chondrogenic phenotype in adipose tissue-derived mesenchymal stem cells (AT-MSCs). We have shown that BMP-2 treatment for 15 min induces osteogenic differentiation, whereas BMP-7 stimulates a chondrogenic phenotype of AT-MSCs. Therefore, AT-MSCs triggered for only 15 min with BMP-2 or BMP-7, provide a feasible tool for bone and cartilage tissue engineering.

For bone tissue engineering, it is important that mesenchymal stem cells (MSCs) display a bone cell-like response to mechanical loading. We have shown earlier that this response includes increased nitric oxide production and cyclooxygenase-2 (COX-2) gene expression, both of which are intimately involved in mechanical adaptation of bone. COX-2 gene expression is likely regulated by polyamines, which are organic cations implicated in cell proliferation and differentiation. This has led to the hypothesis that polyamines may play a role in the response of adipose tissue-derived MSCs (AT-MSCs) to mechanical loading. We have shown that mechanical loading by pulsating fluid flow modulates polyamine levels. Our findings did suggest that polyamines modulate the response of human AT-MSCs to mechanical loading. This was the first study implicating polyamines in the response of human AT-MSCs to mechanical loading, creating opportunities for the use of polyamines in tissue engineering approaches targeting skeletal defects.

We have shown the intracellular upregulation of nitric oxide production after mechanical stimulation, an essential chemical signal in bone remodeling. This was done in real time using the fluorescent chromophore DAR-4M AM. Differences in cellular response to mechanical stimulation of different regions of a single cell were observed. This opens up the possibility to uncover the complexities and function of single osteocytes in the dynamic process of bone remodeling.

**Academic personnel in 2006 and 2007**

<b>Research staff ACTA - OC (in full time equivalents)</b>				
<b>position</b>	<b>name</b>	<b>fte 2006</b>	<b>plan 2007</b>	<b>funding</b>
Full professors	Bank, prof.dr. R.A.	0,20	0,30	guest
	Everts, prof.dr. V.	0,40	0,30	1
	Klein Nulend, prof.dr. J.	0,70	0,70	1
Senior lecturer	Bronckers, dr. A.L.J.J.	0,40	0,40	1
	Bronckers, dr. A.L.J.J.	0,10	0,10	2
Lecturers and other tenured staff	Loon, dr. J.J.W.A., van	0,70	--	guest
	Loon, dr. J.J.W.A., van	--	0,70	2
	Lyaruu, dr. D.M.	0,40	0,40	1
	Lyaruu, dr. D.M.	0,50	0,50	2
<b>Total tenured staff</b>		<b>3,40</b>	<b>3,40</b>	
Non tenured staff	Bakker, dr. A.D.	--	0,80	1
	Korstjens, dr. C.M.	0,10	0,20	3
	Zandieh Doulabi, dr. B.	1,00	1,00	2
PhD students	Bacabac, dr.ir. R.G.	0,70	0,70	1
	Berendsen, drs. A.D.	0,70	0,70	2
	Bloemen, drs. V.	0,70	0,70	1
	Knippenberg, drs. M.	--	0,70	1
	Knippenberg, drs. M.	0,35	--	2
	Kraft, drs. D.	0,05	--	guest
	Kroeze, drs. R.J.	0,70	0,70	2
	Lu, msc. Z.	--	0,35	3
	Rutten, drs. S.	0,40	0,40	3
	Santos, drs. A.	0,70	0,70	2
	Silva, drs. V.C.	0,05	0,40	guest
	Tan, drs. S.D.	0,20	0,15	1
	Vatsa, drs. A.V.	0,70	0,70	2
Vonk, ing. L.A.	0,70	0,70	2	
<b>Total non tenured staff</b>		<b>7,05</b>	<b>8,90</b>	
total 1st funding		3,50	4,85	1
total 2nd funding		5,45	5,80	2
total 3rd funding		0,50	0,95	3
total guests		1,00	0,70	guest
<b>Total research staff</b>		<b>10,45</b>	<b>12,30</b>	

**Dissertations**

Bacabac, R.G. (2006, January 24). Bone cell mechanosensitivity and microgravity. Vrije Universiteit Amsterdam (194 pag.). Prom./coprom.: prof.dr. J. Klein Nulend, prof.dr.ir. R.M. Heethaar, dr.ir. T.H. Smit, & dr. J.J.W.A. van Loon.

**Publications in journals indexed in SCI**

Amir, L.R., Becking, A.G., Jovanovic, A., Perdijk, F.B.T., Everts, V., & Bronckers, A.L.J.J. (2006). Formation of new bone during vertical distraction osteogenesis of the human mandible is related to the presence of blood vessels. CLIN ORAL IMPLAN RES, 17, 410-416.

- Amir, L.R., Becking, A.G., Jovanovic, A., Perdijk, F.B.T., Everts, V., & Bronckers, A.L.J.J. (2006). Vertical distraction osteogenesis in the human mandible: a prospective morphometric study. *CLIN ORAL IMPLAN RES*, 17, 417-425.
- Bacabac, R.G., Smit, T.H., Loon, J.J.W.A. van, Zandieh Doulabi, B., Helder, M.N., & Klein Nulend, J. (2006). Bone cells responses to high frequency vibration stress: does the nucleus oscillate within the cytoplasm? *FASEB J*, 20, 854-864.
- Bakker, A.D., Klein Nulend, J., Tanck, E., Heyligers, I.C., Albers, G.H., Lips, P., & Burger, E.H. (2006). Different responsiveness to mechanical stress in bone cells from osteoporotic versus osteoarthritic donors. *OSTEOPOROSIS INT*, 17, 827-833.
- Berendsen, A.D., Bronckers, A.L.J.J., Smit, T.H., Walboomers, X.F., & Everts, V. (2006). Collagen type V enhances matrix contraction by human periodontal ligament fibroblasts seeded in three-dimensional collagen gels. *MATRIX BIOL*, 25, 515-522.
- Bronckers, A.L.J.J., Bervoets, T.J.M., Wolgtens, J.H.M., & Lyaruu, D.M. (2006). Effect of calcium, given before or after a fluoride insult, on hamster secretory amelogenesis in vitro. *EUR J ORAL SCI*, 114, 116-122.
- Everts, V., Korper, W., Hoeben, K.A., Jansen, I.D., Bromme, D., Cleutjens, K.B.J.M., Heeneman, S., Peters, C., Reinheckel, T., Saftig, P., & Beertsen, W. (2006). Osteoclastic bone degradation and the role of different cysteine proteinases and matrix metalloproteinases: differences between calvaria and long bone. *J BONE MINER RES*, 21, 1399-1408.
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- Haar, S.F. de, Tigchelaar-Gutter, W., Everts, V., & Beertsen, W. (2006). Structure of the periodontium in cathepsin C-deficient mice. *EUR J ORAL SCI*, 114, 171-173.
- Henriksen, K., Sorensen, M.G., Nielsen, R.H., Gram, J., Schaller, S., Dziegiel, M.H., Everts, V., Bollerslev, J., & Karsdal, M.A. (2006). Degradation of the organic phase of bone by osteoclasts: a secondary role for lysosomal acidification. *J BONE MINER RES*, 21, 58-66.
- Knippenberg, M., Helder, M.N., Zandieh Doulabi, B., Wuisman, P.I.J.M., & Klein Nulend, J. (2006). Osteogenesis versus chondrogenesis by BMP-2 and BMP-7 in adipose stem cells. *BIOCHEM BIOPH RES CO*, 342, 902-908.
- Krijnen, M.R., Mullender, M.G., Smit, T.H., Everts, V., & Wuisman, P.I.J.M. (2006). Radiographic, histologic, and chemical evaluation of bioresorbable 70/30 poly-L-lactide-CO-D, L-lactide interbody fusion cages in a goat model. *SPINE*, 31, 1559-1567.
- Loesberg, W.A., Walboomers, X.F., Loon, J.J.W.A. van, & Jansen, J.A. (2006). The effect of combined hypergravity and microgrooves surface topography on the behaviour of fibroblasts. *CELL MOTIL CYTOSKEL*, 63, 384-394.
- Lyaruu, D.M., Bervoets, T.J.M., & Bronckers, A.L.J.J. (2006). Short exposure to high levels of fluoride induces stage-dependent structural changes in ameloblasts and enamel mineralization. *EUR J ORAL SCI*, 114, 111-115.
- Mullender, M.G., Dijcks, S.J., Bacabac, R.G., Semeins, C.M., & Loon, J.J.W.A. van (2006). Release of nitric oxide, but not prostaglandin E2, by bone cells depends on fluid flow frequency. *J ORTHOPAED RES*, 24, 1170-1177.
- Oedayrajsingh-Varma, M.J., Ham, S.M. van, Knippenberg, M., Helder, M.N., Klein Nulend, J., Schouten, T.E., Ritt, M.J.P.F., & Milligen, F.J. van (2006). Adipose tissue-derived mesenchymal stem cell yield and growth characteristics are affected by the tissue-harvesting procedure. *CYTOTHERAPY*, 8, 166-177.
- Perez Amodio, S.G., Jansen, D.C., Schoenmaker, A.M., Vogels, I.M., Reinheckel, T., Hayman, A.R., Cox, T.M., Saftig, P., Beertsen, W., & Everts, V. (2006). Calvarial osteoclasts express a higher level of tartrate-resistant acid phosphatase than long bone osteoclasts and activation does not depend on cathepsin K or L activity. *CALCIFIED TISSUE INT*, 79, 245-254.
- Perez Amodio, S.G., Jansen, D.C., Tigchelaar-Gutter, W., Beertsen, W., & Everts, V. (2006). Endocytosis of tartrate-resistant acid phosphatase by osteoblast-like cells is followed by inactivation of the enzyme. *CALCIFIED TISSUE INT*, 78, 248-254.
- Silva, M.J., Brodt, M.D., Wopenka, B., Thomopoulos, S., Williams, D., Wassen, M.H., Ko, M., Kusano, N., & Bank, R.A. (2006). Decreased collagen organization and content are associated with reduced strength of demineralized and intact bone in the SAMP6 mouse. *J BONE MINER RES*, 21, 78-88.
- Stallmann, H.P., Faber, C., Bronckers, A.L.J.J., Nieuw Amerongen, A. van, & Wuisman, P.I.J.M. (2006). In vitro gentamicin release from commercially available calcium-phosphate bone substitutes influence of carrier type on duration of the release profile. *BMC MUSCULOSKEL DIS*, 26, 7-18.
- Steenvoorden, M.M., Huizinga, T.W., Verzijl, N., Bank, R.A., Runday, H.K., Luning, H.A., Lafeber, F.P., Toes, R.E., & DeGroot, J. (2006). Activation of receptor for advanced glycation end products in osteoarthritis leads to increased stimulation of chondrocytes and synoviocytes. *ARTH RHEUM/AR C RES*, 54, 253-263.
- Tan, S.D., Kuijpers-Jagtman, A.M., Semeins, C.M., Bronckers, A.L.J.J., Maltha, J.C., Von den Hoff, J.W., Everts, V., & Klein Nulend, J. (2006). Fluid shear stress inhibits TNF- $\alpha$ -induced osteocyte apoptosis. *J DENT RES*, 85, 905-909.

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- Tjabringa, G.S., Vezeridus, P.S., Zandieh Doulabi, B., Helder, M.N., Wuisman, P.I.J.M., & Klein Nulend, J. (2006). Polyamines modulate nitric oxide production and COX-2 gene expression in response to mechanical loading in human adipose tissue-derived mesenchymal stem cells. *STEM CELLS*, 24, 2262-2269.
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- Vatsa, A.V., Mizuno, D., Smit, T.H., Schmidt, C.F., MacKintosh, F.C., & Klein Nulend, J. (2006). Bio imaging of intracellular nitric oxide production in single bone cells after mechanical stimulation. *J BONE MINER RES*, 21, 1722-1728.
- Vezeridus, P.S., Semeins, C.M., Chen, Q., & Klein Nulend, J. (2006). Osteocytes subjected to pulsating fluid flow regulate osteoblast proliferation and differentiation. *BIOCHEM BIOPH RES CO*, 348, 1082-1088.
- Vries, T.J. de, Schoenmaker, A.M., Wattanaroonwong, N., Hoonard, M., Nieuwenhuijse, A., Beertsen, W., & Everts, V. (2006). Gingival fibroblasts are better at inhibiting osteoclast formation than periodontal ligament fibroblasts. *J CELL BIOCHEM*, 98, 370-382.

### Other scientific publications (international, refereed)

- Bacabac, R.G., Mizuno, D., Schmidt, C.F., MacKintosh, F.C., Smit, T.H., Loon, J.J.W.A. van, & Klein Nulend, J. (2006). Microrheology of mechanosensitive bone cells. *J GRAVITATIONAL PHYSIOL*, 13, 135-136.
- Bacabac, R.G., Smit, T.H., Loon, J.J.W.A. van, & Klein Nulend, J. (2005). Rapid Nitric Oxide production by bone cells in response to mechanical vibration. *J GRAVITATIONAL PHYSIOL*, 12, 153-155.
- Herranz, R., Benguria, A., Medina, J., Gasset, G., Loon, J.J.W.A. van, Zaballos, A., & Marco, R. (2005). Gene expression variations during *Drosophila* metamorphosis in space. The GENE experiment in the Spanish Cervantes mission to the ISS. *J GRAVITATIONAL PHYSIOL*, 12, 253-254.
- Klein Nulend, J., Bacabac, R.G., Vatsa, A.V., Tan, S.D., & Smit, T.H. (2006). Cell biology for mechano-adaptive bone remodeling. In Z. Davidovitch, J. Mah, & S. Suthanarak (Eds.), *Biological mechanisms of tooth eruption, resorption and movements* (pp. 159-168). Boston, MA, USA: Harvard Society for the Advancement of Orthodontics.
- Klein Nulend, J., Bacabac, R.G., Vatsa, A.V., Tan, S.D., Smit, T.H., & Loon, J.J.W.A. van (2005). Modulation of gene expression in bone cells during strain-adapted bone remodeling. *J GRAVITATIONAL PHYSIOL*, 12, 225-228.
- Loesberg, W.A., Loon, J.J.W.A. van, Walboomers, X.F., & Jansen, J.A. (2006). On gravity and grooves. *J GRAVITATIONAL PHYSIOL*, 13, 129-130.
- Loon, J.J.W.A. van, Tanck, E., Nieuwenhoven, F.A. van, Snoeckx, L.H.E.H., De Jong, H.A.A., & Wubbels, R.J. (2005). A brief overview of animal hypergravity studies. *J GRAVITATIONAL PHYSIOL*, 12, 5-10.
- Loon, J.J.W.A. van, Wamsteker, J., & Weterings, K.A.P. (2005). Seeds-in-Space education experiment during the Dutch Soyuz mission, DELTA. *J GRAVITATIONAL PHYSIOL*, 12, 213-214.
- Matia, I., Gonzalez-Camacho, F., Loon, J.J.W.A. van, & Medina, F.J. (2005). Effects of weightlessness on cell proliferation and ribosome biogenesis in *Arabidopsis* root meristems. *J GRAVITATIONAL PHYSIOL*, 12, 191-193.
- Perez-Amodio, S., & Everts, V. (2006). The bone lining cell and its role in bone remodeling. A Review. In Z. Davidovitch, J. Mah, & S. Suthanarak (Eds.), *Biological mechanisms of tooth eruption, resorption and movements* (pp. 99-108). Boston, MA, USA: Harvard Society for the Advancement of Orthodontics.
- Tan, S.D., Kuijpers-Jagtman, A.M., Semeins, C.M., Bronckers, A.L.J.J., Maltha, J.C., Von den Hoff, J.W., Bakker, A.D., Everts, V., & Klein Nulend, J. (2006). Mechanical loading by fluid shear stress inhibits osteocyte apoptosis. In Z. Davidovitch, J. Mah, & S. Suthanarak (Eds.), *Biological mechanisms of tooth eruption, resorption and movements* (pp. 169-178). Boston, MA, USA: Harvard Society for the Advancement of Orthodontics.
- Van Essen, G., Masseling, B.H.C.J., Jansen, M.B., & Loon, J.J.W.A. van (2005). Monitor activity, temperature and heart rate with a mouse telemeter to be used for animal research on board the international space station. *J GRAVITATIONAL PHYSIOL*, 12, 281-283.

### Professional publications

- Bronckers, A.L.J.J. (2006). Proefschriften 25 jaar na dato 11. Biomineralisatie van harde tandweefsels en bot; de rol van osteocalcine. *NED TIJDSCHR TANDHEELKD*, 113, 408-413.
- Grauwen, S.R., Jovanovic, A., Amir, L.R., & Becking, A.G. (2006). Verticale distractieosteogenese van de extreem geresorbeerde edentate onderkaak. Een retrospectieve beschrijving van 16 patiënten. *NED TIJDSCHR TANDHEELKD*, 113, 308-312.

- Knippenberg, M., Helder, M.N., Zandieh-Doulabi, B., Semeins, C.M., Wuisman, P.I.J.M., & Klein Nulend, J. (2006). Van stamcel tot botcel. NED TIJDSCHR CALC BOT, 4, 68-72.
- Tan, S.D., Mullender, M.G., Vico, L., Alexandre, C., & Klein Nulend, J. (2006). Botverschillen tussen mannen en vrouwen met en zonder osteoporose. NED TIJDSCHR CALC BOT, 4, 8-13.

## External reports

- Bacabac, R.G. (2006). 21st Century COE Program Report – Visiting Scientist Report. Kyoto, Japan: Kyoto University, Dept. Mechanical Engineering and Science. 16 pp.
- Bronckers, A.L.J.J. (2006). A tissue engineering approach to the regeneration of periodontal tissues. Progress Reports for: STW project NKG 6099. Amsterdam: ACTA. 11 pp.
- Bronckers, A.L.J.J. (2006). Enamel fluorosis: mechanisms of action. Progress report NIH grant DE13508. Amsterdam: ACTA. 2 pp.
- Bronckers, A.L.J.J. (2006). Evaluation report on PhD manuscript for the Faculty of Pharmacy University of Kuopio, Finland. Amsterdam: ACTA. 8 pp.
- Bronckers, A.L.J.J. (2006). Report on the scientific presentations COST ACTION B23. Orofacial development and regeneration. Working group 2 (stem cells and hard tissue formation, and clinical application). Report for: EU. Amsterdam: ACTA. 3 pp.
- Klein Nulend, J. (2006). 21st Century COE Program Report – Visiting Professor Report. Kyoto, Japan: Kyoto University, Dept. Mechanical Engineering and Science. 4 pp.
- Klein Nulend, J. (2006). Intercellular communication between cells involved in skeletal tissue (re)generation and homeostasis. Yearly report for: DPTE-NWO-STW. Amsterdam: ACTA. 7 pp.
- Klein Nulend, J. (2006). NWO-STW Progress report. Resorbable PLDLA (poly-L, D-lactic acid) cages filled with a stem cell loaded calcium phosphate carrier for spinal fusion, (STW Project No. VPG.5935). Report for: STW. Amsterdam: ACTA. 7 pp.
- Klein Nulend, J. (2006). Yearly Report 2005. Mechanosensing and chemical signalling in single osteocytes, (NWO-FOM project number FOM V 12). Report for: NWO-FOM. Amsterdam: ACTA. 7 pp.
- Klein Nulend, J. (2006). Yearly Report 2005. Microgravity and bone cell mechanosensitivity, (project number MG-055). Report for: SRON. Amsterdam: ACTA. 10 pp.

## Indicators of Esteem

### Grants: current projects with external funding

- Bacabac, R.G.: 21st Century COE Program Award – Visiting Scientist from Sept-Nov 2006. Host University: Kyoto University, Dept Mechanical Engineering and Science, Kyoto, Japan.
- Bacabac, R.G. One year post-doc for FLOW-2 experiment. ESA-ESTEC, Noordwijk, NL.
- Bacabac, R.G. & Klein-Nulend, J. Physics Development Project grant # PHL-146: Development of an optical tweezer setup (€ 63.000).
- Bank, R.A. "Improving the collagen network of tissue-engineered constructs by means of injectable scaffolds"; ICES/KIS-3 (=Bsik), €1.775.000,-. 2005-2009.
- Bronckers, A.L.J.J. & Jansen, J.. Project grant STW-NWO (#NK 6099) Tissue Engineering of the Periodontal Ligament 2004-2008: 1 OIO (ACTA) , 0.4 fte technician (ACTA) and 1 OIO (KUN)
- Bronckers, A.L.J.J. NIH (USA) RO1-project: "Enamel fluorosis; Mechanisms of Action" (September 2005-September 2010). Co-PI: Prof. P. DenBesten (University of California San Francisco). (total amount \$ 1.400.000; for ACTA: \$ 586.000).
- Everts, V. & Zentner, A. MOVE-ACTA project: The role of cell-cell interactions in the modulation of bone resorption during tooth movement (1 fte AIO). 2005-2009.
- Klein-Nulend, J. 21st Century COE Program Award – Visiting Professor from 14-30 Oct 2006. Host University: Kyoto University, Dept Mechanical Engineering and Science, Kyoto, Japan.
- Klein-Nulend, J. & Vries T.J. de. AstraZeneca project: Effects of C-Src inhibitors on (pre-) osteoclast-osteoblast interactions. (€ 80,450 1 fte postdoc, 0.5 fte technician for 4 mo). 2006-2007
- Klein-Nulend, J. & Loon, J.J.W.A. van. NWO – SRON Project "Microgravity and bone cell mechanosensitivity" (1 OIO and 0.4 postdoc; € 364.000). 2000-2006. Extension for spaceflight experiment FLOW for 1 postdoc 2007 (€ 55.000).
- Klein-Nulend, J., Smit, T.H., MacKintosh, F.C. & Schmidt, C.F. ALW – FOM - NWO Program Physical Biology II: Mechanosensing and chemical signalling in single osteocytes. (Participation Oral Cell Biology € 175.000). 2002-2007.
- Klein-Nulend, J. & Wuisman, P.I.J.M. MOVE-Vrije Universiteit Project: Adipose tissue-derived mesenchymal stem cells for bone and cartilage tissue engineering (1 fte postdoc for 4 yrs). 2004-2009.

- Klein-Nulend, J., Wuisman, P.I.J.M., Helder, M.N., Schuurhuis, G.J. & Ham, S.M. van. NWO-STW project: Resorbable PLDLA (poly-L,D-lactic acid) cages filled with a stem cell loaded calcium phosphate carrier for spinal fusion. (Participation Oral Cell Biology 1 PhD, 1 Postdoc, € 350.000). 2003-2006.
- Klein-Nulend, J., Wuisman, P.I.J.M., Helder M.N. & Smit, T.H. DPTE/NWO/STW Project: Intercellular communication between cells involved in skeletal tissue (re)generation and homeostasis. (Participation Oral Cell Biology 1 fte AIO for 4 yrs). 2005-2009.
- Klein-Nulend, J., Nolte, P.J. & Korstjens, C.M. Smith & Nephew project: Effect of low intensity pulsed ultrasound on established delayed union or nonunion of the fibula, after a high tibial osteotomy. (Participation Oral Cell Biology, 1 fte AIO for 2 yrs, 0.2 fte postdoc for 1 yr), 2005-2007.
- Klein-Nulend, J. Royal Friesland Foods project: Combined effect of physical activity and nutrition on bone metabolism, "NutriBone". (€ 422,880, 1 fte AIO for 4 yrs).
- Klein-Nulend, J., Wuisman, P.I.J.M., Helder M.N. & Smit, T.H. Universiteit van Amsterdam – Universitair Onderzoeksfonds 2006: Skeletal tissue engineering, in het kader van het BSIK programma Tissue Engineering. (€ 285,465 1 fte AIO for 4 yrs).
- Klein-Nulend, J. Personal grant to Vanessa Camila da Silva, DDS, and PhD student at State University of Sao Paulo School of Dentistry at Araraquara, Dept Periodontology, Araraquara, Brazil), obtained from the CAPES Foundation (Foundation for the Coordination of Higher Education and Graduate Training), a Brazilian Government Agency, for a 7-month research visit at Oral Cell Biology under supervision of J. Klein-Nulend, ACTA (Dec 2006 – June 2007).
- Loon, J.J.W.A. van, Hofmann, M. (project PI), Huyet, G., McInerney, J., Jones D., Meerholz, K., Eckhard, F., Voges H., Spahn, K., Hummelen, R., Thoma, B. & Corbett. Project: "Ballistic and 3-D holographic imaging of bone" (Participation DESC, €50.000) 2004-2007.
- Loon, J.J.W.A. van. Project title: "Dutch Experiment Support Center (DESC)" NWO-SRON project MG-057. (1fte post-doc for 5 yrs.) 2002-2007.

### **Membership of international editorial boards**

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

### **Scientific awards/honours**

- Bacabac, R.G., Mizuno, D., Vatsa, A.V., Schmidt, C.F., MacKintosh, F.C., Klein Nulend, J., & Smit, T.H. (2006). Perren Award (€ 6500). European Society for Biomechanics for the best publication: Round versus flat: bone cell morphology, elasticity, and mechanosensing. 5th World Congress of Biomechanics: Munich, Germany (2006, July 29).
- Knippenberg, M., Helder, M.N., Zandieh Doulabi, B., Wuisman, P.I.J.M., & Klein Nulend, J. (2006). Best poster award second prize. European Tissue Engineering Society: Comparison of the effect of BMP-2 and BMP-7 on osteogenesis and chondrogenesis in adipose tissue-derived mesenchymal stem cells. Annual Meeting of the European Chapter of Tissue Engineering and Regenerative Medicine International Society (TERMIS-EU): Rotterdam, the Netherlands (2006, November 08 - 2006, November 11).

### **Organisation of international congresses or symposia**

- Bank, R.A. (2006). TERMIS. 5th Annual Meeting European Tissue Engineering Society: Congress Center De Doelen, Rotterdam, the Netherlands (2006, October 08 - 2006, October 11).
- Klein Nulend, J. (2006). Organizer two minisymposia: Stem cells in regenerative medicine of the skeleton and Vitamin D; from basic research to bedside. Dutch Society for Calcium and Bone Metabolism: Woudschoten, the Netherlands (2006, November 09 - 2006, November 10).
- Loon, J.J.W.A. van (2006). Co-organizer. Science on European Soyuz Missions to the ISS (2001-2005): Toledo, Spain (2006, June 27 - 2006, June 30).
- Loon, J.J.W.A. van (2006). Organizer workshop Cell Mechanics. American Society for Gravitational and Space Biology, ASGSB: Arlington, Washington, USA (2006, November 02 - 2006, November 05).

## Invited speakers at international congresses or symposia

- Bacabac, R.G. (2006, June 29). Rheology of mechanosensitive bone cells. Laxenburg, Austria, The Third Joint International Seminar, Applied Analysis and Synthesis of Complex Systems (ASCS).
- Bacabac, R.G. (2006, July). Noise-enhanced response of bone cells to fluid shear stress and bone cell morphology, elasticity, and mechanosensing (plenary lecture: S.M. Perren research award, most prestigious award of the European Society of Biomechanics. Munich, Germany, 5th World Congress of Biomechanics.
- Bacabac, R.G. (2006, October 21). Round versus flat: morphology, rheology, and mechanosensing by bone cells. Osaka, Japan, Osaka University, Dept. Mechanical Science and Bioengineering.
- Bacabac, R.G. (2006, October 21). Round versus flat: morphology, rheology, and mechanosensing by bone cells. Okayama, Japan, Okayama University Graduate School of Medicine, Dentistry, Pharmaceutical Sciences, Dept. Orthodontics and Dentofacial Orthopedics.
- Bacabac, R.G. (2006, September 06). Round versus flat: morphology, rheology, and mechanosensing by bone cells. Kyoto, Japan, COE lecture at Kyoto University, Dept. Mechanical Engineering and Science, Graduate School of Engineering.
- Bronckers, A.L.J.J. (2006, April 10). Enamel fluorosis and the anion exchanger Ae2 in ameloblasts. San Francisco, USA, Dept. Paediatric Dentistry, University of California.
- Everts, V. (2006, April 10). Intracellular remodeling of the matrix. Cambridge, UK, British Society of Matrix Biology.
- Everts, V. (2006, June 30). Cell biology of mechanoadaptive bone remodeling. Laxenburg, Austria, Third Joint International Seminar Applied Analysis and Synthesis of Complex Systems (ASCS).
- Everts, V. (2006, October 10). Proteolytic enzymes and bone degradation. Cambridge, UK, Medivir.
- Everts, V. (2006, September 13). The osteoclast and bone lining cell: their role in bone remodeling. Cleveland, Ohio, USA, Cleveland Clinic.
- Klein Nulend, J. (2006, July 03). 1) Cell biology of strain-adapted bone remodeling; 2) Bone stem cells from adipose tissue; 3) Evaluation of bone substitute materials in the reconstructed maxillary sinus; 4) Biological background of distraction osteogenesis; 5) Formation of new bone during vertical distraction osteogenesis of the human mandible. Doorn, the Netherlands, Edin Programm Current Concepts in American Dentistry.
- Klein Nulend, J. (2006, July 29). Tissue strain versus fluid shear stress: implications for osteocyte mediated bone adaptation. Charité – Universitätsmedizin, Berlin, Conference on current concepts in the interaction of mechanics and biology in knee joint restoration and regeneration – From cells to limbs – multiscale approaches for clinical implications.
- Klein Nulend, J. (2006, March 10). The role of the osteocyte and osteoblast in mechanotransduction. Cologne, Germany, Workshop Mechanotransduction Osteologie-Konferenz German Society of Osteology.
- Klein Nulend, J. (2006, October 23). Cell biology of mechanoadaptive bone remodeling. Kyoto, Japan, COE lecture, Kyoto University, Department of Mechanical Engineering and Science.
- Klein Nulend, J. (2006, October 23). Mechanoadaptive bone remodeling: role of the osteocyte network. Okayama, Japan, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Department of Orthodontics and Dentofacial Orthopedics.
- Loon, J.J.W.A. van (2006, July 19). The use of instruments for gravity related research. Beijing, COSPAR presentation, Gravitational Effects on Plants and Unicellular Systems.
- Loon, J.J.W.A. van (2006, June 28). Activities for Primary Schools: Seeds in Space. Toledo, Spain, Special education session, Science on European Soyuz Missions to the ISS (2001-2005) meeting.
- Loon, J.J.W.A. van (2006, November 03). Cell mechanosensing and gravity. Arlington, Washington, USA, Workshop Cell Mechanics, American Society for Gravitational and Space Biology, ASGSB annual meeting.

## Other international functions

- Bronckers, A.L.J.J.: Member of working committee, chair working group 2: Stem cells and dental hard tissues. COST-action B23, (European network on: Regeneration of orofacial tissues).
- Everts, V.: Member. Bone Quality Club, Procter and Gamble.
- Klein Nulend, J.: Founding member. Micro-mechanical Tissue Repair Society.
- Klein Nulend, J: Member Deutsche Forschungsgemeinschaft review panel of the Proposal for the Establishment and Funding 2007-2010 Functie bij : Collaborative Research Centre 760, coordinated by prof. dr.ing. G. Duda, Universitätsmedizin Berlin, Germany.
- Klein Nulend, J: Member review panel Functie bij : European Calcified Tissue Society Research Grants and Awards, ECTS-Career Establishment Awards.
- Loon, J.J.W.A. van: Management Board member. American Society for Gravitational and Space Biology, ASGSB.
- Loon, J.J.W.A. van: Member. Topical Team Low Back Pain, European Space Agency.
- Loon, J.J.W.A. van: Vice-President. European Low Gravity Research Association, ELGRA.

## Collaborations

- Alkmaar Medical Center. Dept Oral & Maxillofacial Surgery. Alkmaar NL: Dr. A. Jovanovic.
- Dept Oral & Maxillofacial Surgery, Gelderse Vallei Hospital, Ede, NL Drs. F. Perdijk.
- AMC, Dept Cell Biology and Histology (Prof.dr. C. van Noorden), Amsterdam, NL.
- AMC, Dept Experimental Hepatology (Prof.dr. R. Oude Elferink), Amsterdam, NL.
- City University of New York, Dept Mechanical Engineering (Prof.dr.ir. S.C. Cowin), New York, NY, USA.
- Erasmus University Rotterdam, Dept Orthopaedics (Prof.dr.ir. H. Weinans), Rotterdam, NL.
- Eindhoven University of Technology, Dept Biomedical Engineering (Prof.dr.ir. R. Huiskes), Eindhoven, NL.
- Hospital Hilversum, Dept Orthopaedics (Dr. G.H.R. Albers), Hilversum, NL.
- Keele University, Centre for Science and Technology in Medicine (Prof.dr A. El Haj), Stoke-on-Trent, UK.
- Brown Medical School/Rhode Island Hospital, Dept Orthopaedics, Providence, RI, USA (Dr. Q. Chen).
- Lund University, Dept. Molecular Medicine and Gene Therapy (M. Johansson, Dr. J. Richter), Lund, Sweden.
- Spaarne Hospital Heemstede, Dept Orthopaedics (Dr. P.A. Nolte), Heemstede, NL.
- University of Texas, Dept. Orthodontics (Dr. R.N.D'Souza, Dr. P.J. Duke), Houston, TX, USA.
- University of Helsinki, Dept Biosciences, Division Biochemistry (Dr H. Rauvala), Helsinki, Finland.
- University of Aberdeen Medical School, Dept Medicine and Therapeutics (Dr. M.H. Helfrich), Aberdeen, Schotland.
- Utrecht University Medical Center, Dept Orthopaedic Surgery (Dr. W.J.A. Dhert), Utrecht, NL.
- VUmc, Dept Endocrinology (Prof.dr. P. Lips), Amsterdam, NL.
- VUmc, Dept Orthopaedics (Prof.dr. P.I.J.M. Wuisman, Dr. M.N. Helder), Amsterdam, NL.
- VUmc, Dept Clinical Physics and Engineering (Prof.dr. R.M. Heethaar, Dr.ir. T.H. Smit), Amsterdam, NL.
- VUmc, Dept Molecular Cell Biology and Immunology (E. van Beek, Dr. T. van den Berg, B. Olivier) Amsterdam, NL.
- VUmc, Dept Pathology (Dr. F. van Milligen), Amsterdam, NL.
- VUmc, Dept Haematology (Dr. G.J. Schuurhuis), Amsterdam, NL.
- VUmc, Dept Plastic Surgery (Prof.dr. M. Ritt), Amsterdam, NL.
- VUA, Dept Biophysics and Complex Systems (Prof.dr. C.F. Schmidt), Amsterdam, NL.
- VUA, Dept Theoretical Physics (Prof.dr. F.C. MacKintosh), Amsterdam, NL.
- Radboud University Nijmegen, NL, Dept Orthodontics and Oral Biology, Prof.dr. A.M. Kuijpers-Jagtman, Dr. J.C. Maltha; Department of Biomaterials, Prof.dr. J. Jansen and Dr. X.F. Walboomers.
- University of Kiel. Dept. Biochemistry (Prof.dr P. Saftig), Kiel, Germany.
- NIDR (Prof.dr. H. Birkedal Hansen), Bethesda, Washington, USA.
- Nordic Bioscience (dr. M. Karsdal), Herlev, Denmark.
- TNO/VUmc (Prof.dr. R.A. Bank), Leiden/Amsterdam, NL.
- Kyoto University, Dept Mechanical Engineering and Science (Prof.dr.ir. T. Adachi, Dr. M. Tanaka), Kyoto, Japan.
- AMOLF (Dr. G. Koenderink), Amsterdam, NL.
- TNO Prevention and Health, Department Biosciences, Dr. R. Hanemaaijer, Leiden, The Netherlands.
- Technical University, Biomedical Engineering, Prof.dr.ir. F.P.T. Baaijens, Eindhoven, The Netherlands.

## Current PhD projects

- Amir, LR.** Histology of human jaw bone during distraction osteogenesis. Supervisors: prof.dr V. Everts & prof.dr. D.B. Tuinzing. Co-supervisors: dr. A.L.J.J. Bronckers & dr. A.G. Becking. Start: December 2001.
- Berendsen, AD.** Tissue engineering of the periodontium. Supervisor: prof.dr. V. Everts, Co-supervisors: dr. A.L.J.J. Bronckers & dr. T.H. Smit. Start: January 2004.
- Bloemen V.** The role of cell-cell interactions in the modulation of bone resorption during tooth movement. Supervisors: prof.dr. V. Everts & prof.dr. A. Zentner; co-supervisor: dr. T.J. de Vries. Start: October 2005.
- Faber, C.** Antimicrobial peptides (AMPs) linked to polymethyl-methacrylate (PMMA) beads for the prevention and treatment of osteomyelitis. Supervisors: prof.dr. A. van Nieuw Amerongen, prof.dr. P.I.J.M. Wuisman; Co-supervisor: dr. DM Lyaruu. Start: July 2000.
- Knippenberg, M.** Resorbable PLDLA (poly-L,D-lactic acid) cages filled with a stem cell loaded calcium phosphate carrier for spinal fusion. Supervisors: prof.dr. P.I.J.M. Wuisman & prof.dr. J. Klein Nulend; Co-supervisor: dr. M.N. Helder. Start: January 2003.
- Kroeze RJ.** Injectable biomaterials as stem cell carriers for intervertebral disc tissue engineering. Supervisors: prof.dr. R.A. Bank & prof.dr. P.I.J.M. Wuisman; Co-supervisor: dr. M.N. Helder, start 2005.
- Lu Z.** Differentiation of adipose-tissue derived stem cells towards chondrocytes by means of biomaterials and co-cultures. Supervisors: prof.dr. P.I.J.M. Wuisman & prof.dr. R.A. Bank; Co-supervisor: dr. M.N. Helder, Start: 2005.

- Rutten, S.** Effect of low intensity ultrasound on established delayed union or nonunion of the fibula, after a high tibial osteotomy. Supervisor: prof.dr. J. Klein Nulend. Co-supervisor: dr. P.J. Nolte. Start: 2005.
- Santos A.** Intercellular communication between cells involved in skeletal tissue (re)generation and homeostasis. Supervisors: prof.dr. J. Klein Nulend & prof.dr. P.I.J.M. Wuisman. Start: October 2005.
- Scheres CR.** Influence of human genetic variation on the host-parasite interaction in periodontitis. Supervisors: prof.dr. A.J. van Winkelhoff & prof.dr. V. Everts; Co-supervisors: dr. M. Laine & dr. T.J. de Vries. Start: September 2006.
- Stallmann H.** Use of lactoferrin-derived antibiotic peptide for prevention of deep infections. Supervisors: prof.dr. P.I.J.M. Wuisman & prof.dr. A. van Nieuw Amerongen; Co-supervisor: dr. A.L.J.J. Bronckers. Start: July 2001.
- Tan SD.** Osteocyte apoptosis and bone adaptation. Supervisors: prof.dr. J. Klein Nulend, prof.dr. V. Everts & prof.dr. A.M. Kuijpers-Jagtman. Co-supervisors: dr. A.L.J.J. Bronckers & dr. J. Maltha. Start: September 2002.
- Vatsa AV.** Mechanosensing and chemical signalling in single osteocytes. Supervisor: prof.dr. J. Klein Nulend, Co-supervisor: dr. T.H. Smit. Start: February 2003.
- Vonk LA.** The expression and role of collagen-modifying enzymes in (tissue engineering of) bone and cartilage. Supervisors: prof.dr. R.A. Bank & prof.dr. V. Everts; Co-supervisor: dr. B. Zandieh Doulabi. Start: 2005.

## Section: Oral Microbiology

### Microbiological Aspects of Oral Infections

#### Program leader

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#### IOT senior scientists and full professors



A.J. van Winkelhoff



J.J. de Soet



W. Crielaard

#### Research objectives

One research objective is to study the role of K antigens in the virulence of *Porphyromonas gingivalis*. The genetic basis of the different K antigens of this pathogen is currently under investigation. One aim of this study is to develop a molecular tool for serotyping of the species. Periodontal damage is caused by the interaction of the host and the bacterial biofilm. Therefore, host-parasite interactions have become a major part of our research aims. The interaction is studied by microbiological analysis of the subgingival plaque of well described periodontitis patients and by identification of gene polymorphisms in innate immunity genes. In this way, the relationship between genetic features of the host and the subgingival microflora in periodontitis is studied. In addition, new research has been initiated in which the interactions between the periodontal pathogen *P. gingivalis* and human fibroblasts are studied.

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

Research in Cariology involves the development of a molecular approach to determine the role of different streptococcal genes in microbial interactions and the pathogenesis of dental caries. Furthermore, the role of *Tannerella forsythensis* in microbial ecosystems will be investigated on a molecular level.

#### Results

In the development of molecular diagnosis of oral bacterial infections, the Real Time (RT) PCR Taqman technique has been further developed including the construction of an internal control. In collaboration with researchers of the Queen Mary London Hospital (prof.dr. M.A. Curtis) the locus responsible for the capsule production (K antigens) has been further explored. Emphasis has been put on the structure of the K1 locus using RFLP analysis. Results indicate a high level homogeneity of the locus, opening the possibility of a PCR-based K1 serotyping. In relation to the genetic background of periodontal diseases the candidate gene approach has been further developed. In collaboration with Dept. of Informatics, VU Medical Centre. A protected electronic patient database has been constructed that contains clinical, microbiological, genetic,

radiographic and demographic data. This project is supported by the EU. Bioinformatics is currently applied to identify risk markers and factors for onset and progression of periodontitis.

### Academic personnel in 2006 and 2007

Research staff ACTA - OM (in full time equivalents)				
position	name	fte 2006	plan 2007	funding
Full professors	Winkelhoff, prof.dr. A.J. van	0,60	0,50	1
	Crielaard, prof.dr. W.	0,30	0,40	1
Lecturers and other tenured research staff	Laine, dr. M.L.	0,40	0,40	1
	Reijden, dr. W.A. van der	0,30	0,30	1
	Soet, dr. J.J. de	0,50	0,50	1
<b>Total tenured staff</b>		<b>2,10</b>	<b>2,10</b>	
PhD students	Boutaga, ing. K.	0,20	--	1
	Brunner, drs. J.	0,70	0,70	1
	Scheres, drs. C.R.	0,20	0,70	1
<b>Total non tenured staff</b>		<b>1,10</b>	<b>1,40</b>	<b>1</b>
total 1st funding		3,20	3,50	1
<b>Total research staff</b>		<b>3,20</b>	<b>3,50</b>	

### Dissertations

Boutaga, K. (2006, September 19). Pathogens in periodontal disease. Vrije Universiteit Amsterdam (184 pag.). Prom./coprom.: prof.dr. A.J. van Winkelhoff, & prof.dr. P.H.M. Savelkoul.

### Publications in journals indexed in SCI

- Aduse-Opoku, J., Slaney, J.M., Hashim, A., Gallagher, A., Gallagher, R.P., Rangarajan, M., Boutaga, K., Laine, M.L., Winkelhoff, A.J. van, & Curtis, M.A. (2006). Identification and characterization of the capsular polysaccharide (K-antigen) locus of *Porphyromonas gingivalis*. *INFECT IMMUN*, 74, 449-460.
- Boutaga, K., Winkelhoff, A.J. van, Vandenbroucke-Grauls, C.M.J.E., & Savelkoul, P.H.M. (2006). The additional value of real-time PCR in the quantitative detection of periodontal pathogens. *J CLIN PERIODONTOL*, 33, 427-433.
- Enersen, M., Olson, I., Winkelhoff, A.J. van, & Caugant, D.A. (2006). Multilocus sequence typing of *Porphyromonas gingivalis* strains from different geographic origins. *J CLIN MICROBIOL*, 44, 35-41.
- Heijdenrijk, K., Raghoobar, G.M., Meijer, H.J., Stegenga, B., & Reijden, W.A. van der (2006). Feasibility and influence of the microgap of two implants placed in a non-submerged procedure: a five-year follow-up clinical trial. *J PERIODONTOL*, 77, 1051-1060.
- Laine, M.L., Leonardt, A., Roos-Jansaker, A.M., Pena, A.S., Winkelhoff, A.J. van, Winkel, E.G., & Renvert, S. (2006). IL-1RN gene polymorphism is associated with peri-implantitis. *CLIN ORAL IMPLAN RES*, 17, 380-385.
- Reijden, W.A. van der, Bosch-Tijhof, C.J., Strooker, H., & Winkelhoff, A.J. van (2006). prtH in *Tannerella forsythensis* is not associated with periodontitis. *J PERIODONTOL*, 77, 586-590.
- Rhemrev, G.E., Timmerman, M.F., Veldkamp, I., Winkelhoff, A.J. van, & Velden, U. van der (2006). Immediate effect of instrumentation on the subgingival microflora in deep inflamed pockets under strict plaque control. *J CLIN PERIODONTOL*, 33, 42-48.
- Szynol, A.T., Haard, J.J. de, Veerman, E.C.I., Soet, J.J. de, & Nieuw Amerongen, A. van (2006). Design of a peptibody consisting of the antimicrobial peptide dhvar5 and a llama variable heavy-chain antibody fragment. *CHEM BIOL*, 67, 425-431.
- Veen, M.H. van der, Thomas, R.Z., Huysmans, M.C.D.N.J.M., & Soet, J.J. de (2006). Red autofluorescence of dental plaque bacteria. *CARIES RES*, 40, 542-545.
- Velden, U. van der, Abbas, F., Armand, S., Loos, B.G., Timmerman, M.F., Weijden, G.A. van der, Winkelhoff, A.J. van, & Winkel, E.G. (2006). Java project on periodontal diseases. The natural

development of periodontitis: risk factors, risk predictors and risk determinants. J CLIN PERIODONTOL, 33, 540-548.

Winkelhoff, A.J. van (2006). Response. J CLIN PERIODONTOL, 33, 157-158.

Zynge, V., Winkelhoff, A.J. van, Welling, G., Abbas, F., Degener, J., & Harmsen, H. (2006). Denaturing gradient gel electrophoresis as a diagnostic tool in periodontal microbiology. J CLIN MICROBIOL, 44, 3628-3633.

### **Other scientific publications**

Loos, B.G., Laine, M.L., Palen, C. van der, Lessmann, F., Winkelhoff, A.J. van, Velden, U. van der, Crusius, J.B.A., Morree, S.A., Pena, A.S., Brooks, A.J., Pereira, A.S., Moor, G. de, Maoj, V., & Sanchez, F.M. (2006). Biomedical Informatics in chronic infectious and inflammatory disease research: periodontitis as a case study. In PROCEEDINGS MIE (pp. 77-83).

### **Professional publications**

Akveld, N., Rutten, R., & Reijden, W.A. van der (2006). Uitspoelen tandenborstel leidt tot reductie aantal anaërobe bacteriën. Een bron van besmetting? NED TANDARTSENBLAD, 61, 34-35.

Winkel, E.G., & Winkelhoff, A.J. van (2006). Wat zijn de voor- en nadelen van antibiotica in de tandheelkunde? MONDHYG VADEMECUM, 4.

Winkelhoff, A.J. van (2006). Antibiotica in de parodontologie: wat is de stand van zaken? NED TIJDSCHR TANDHEELKD, 113, 319-321.

Winkelhoff, A.J. van (2006). Multidisciplinair onderzoek naar cathepsine C. NED TIJDSCHR TANDHEELKD, 113, 298.

### **Indicators of Esteem**

#### **Grants: current projects with external funding**

INFOBIOMED, structuring European Biomedical Informatics to Support Individualized Healthcare. Sixth framework Programme. Contract number 507585, European Union, €15.000.-. Start: 2004, mid 2007.

DNA Microarrays of *Porphyromonas gingivalis* for the project "Molecular and Genetic make-up of K-antigen and capsule regulation in *Porphyromonas gingivalis*". Pathogen Functional Genomics Resource Center (PFGR) at the Institute of Genomics (TIGR). 150 high quality arrays.

#### **Membership of international editorial boards**

Winkelhoff, A.J. van: CLIN ORAL IMPLAN RES

Winkelhoff, A.J. van: EVID DENT PRACT

Winkelhoff, A.J. van: J CLIN PERIODONTOL

Winkelhoff, A.J. van: J PERIODONTAL RES

Winkelhoff, A.J. van: J PERIODONTOL

#### **Invited speakers at international congresses or symposia**

Laine, M.L. (2006, June 01). Genetic mapping of the periodontal patient. Madrid, Spain, EuroPerio5.

Winkelhoff, A.J. van (2006, June 01). Antibiotics in peri-implantitis. Madrid, Spain, Eurperio5.

Winkelhoff, A.J. van (2006, June 16). Clinical microbiology and antibiotics in periodontics. Symposium, Italian Society Periodontology.

Winkelhoff, A.J. van (2006, November 12). Microbiology and treatment of peri-implantitis. Sevilla, Spain.

Winkelhoff, A.J. van (2006, November 02). Models of infection and transmission in periodontitis. Barcelona, Spain.

#### **Scientific awards/honours**

Akveld, N. (2006). NT Scriptieprijs 2006. Supervisor: W.A. van der Reijden: (2006, October 13).

## Other international functions

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

## Collaborations

- University Complutense Madrid, Dept. of Periodontology, prof.dr. M. Sanz, Madrid, Spain.
- University of Oslo, Dept. of Microbiology, prof.dr. I. Olson, Oslo, Norway.
- University of Gothenburg, Dept. of Oral Microbiology, prof.dr. G. Dahlén, Gothenburg, Sweden.
- University College of London, Queen Mary's School of Medicine and Dentistry, prof.dr. M. Curtis, London, UK.
- Department of Medical Microbiology and Infection prevention, VU University Medical Center, prof.dr. C.M.J.E. Vandenbroucke-Grauls, Amsterdam, the Netherlands.
- Laboratory of Immunogenetics, VU University Medical Center, prof.dr. A.S. Peña, Amsterdam, the Netherlands.
- Department of Oral and Maxillofacial Surgery and Maxillofacial Prosthetics, University of Groningen, prof.dr. B. Stegenga, Groningen, the Netherlands.
- Department of Health Sciences, Kristianstad University, prof.dr. S. Renvert, Kristianstad, Sweden.
- Department of Informatics, VU University Medical Center, dr. C.J.N.M. van der Palen, Amsterdam, the Netherlands.
- Department of Dentistry and Oral Hygiene and Department of Biomedical Engineering. Faculty of Medical sciences, University of Groningen, Groningen, the Netherlands. prof.dr. M.C.D.N.J.M. Huysmans.
- Ablynx, Gent, Belgium. prof.dr. H. de Haard.

## Current PhD projects

**Boutaga, K.** Molecular microbial diagnosis in periodontitis. Supervisors: prof.dr. C.M.J.E. Vandenbroucke-Grauls, prof.dr. A.J. van Winkelhoff; co-supervisor: dr. P.H.M. Savelkoul. Start: October 2001.

**Brunner, J.** Genetic background of K antigen and capsule production in *Porphyromonas gingivalis*. Supervisors: prof.dr. A.J. van Winkelhoff & prof.dr. W. Crielaard.

**Scheres CR.** Influence of human genetic variation on the host-parasite interaction in periodontitis. Supervisors: prof.dr. A.J. van Winkelhoff & prof.dr. V. Everts; Co-supervisors: dr. M. Laine & dr. T.J. de Vries. Start: September 2006.

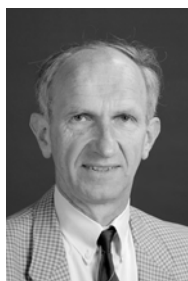
## Department of Oral and Maxillofacial Surgery / Oral Pathology

### Oral and maxillofacial disorders: diagnosis and treatment

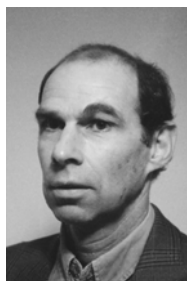
#### Program leader

Prof.dr. I. van der Waal  
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#### IOT senior scientists and full professors



I. van der Waal



D.B. Tuinzing



E. Bloemena



H.P. van den Akker

#### Research objectives

The research of the Department of Oral and Maxillofacial Surgery/Oral Pathology consists of six main areas of interest, being:

1. Early diagnosis of oral cancer and precancer, including cancer of the salivary glands.
2. Surgical orthopedics of the maxillofacial skeleton.
3. Maxillofacial implantology and reconstructive preprosthetic surgery.
4. Inflammatory and inflammatory-like diseases of the oral and perioral structures, including the jaw bones and the lymph nodes of the neck.
5. The effects of chemotherapy and bisphosphonates on the oral microcirculation and the possible role in the development of osteonecrosis of the jaw.
6. Evaluation of the effect of anticoagulant medication on blood loss during and after dentoalveolar surgery (the BLACK study)

A substantial percentage of oral cancer is preceded by so-called precursor lesions, particularly leukoplakia. Intervention in the precursor stage may prevent the development of frank malignancy. The ongoing intervention study of oral leukoplakia is being continued both in a retrospective and prospective manner. Amongst others, the prognostic value of the DNA content is examined with regard to the predictive value of malignant transformation. There is a close collaboration with both the General Pathology Department and the ENT - Department of the VU University Medical Center (VUmc) in Amsterdam, both being related to the VUmc-Institute for Cancer and Immunology (V-ICI).

The research on surgical orthopedics is focused on maxillofacial function and healing capacity after treatment of acquired and congenital jaw deformities. Attention is focused on the indications/contra-indications and preventive measures in surgical-orthodontic treatment of dentofacial deformities. In addition, the dynamics of the surrounding tissues after corrective surgery of maxillofacial bones is studied, e.g. the musculature and the temporal mandibular joint. In these studies there is a close collaboration with the Department of Orthodontics.

The research on maxillofacial implantology and reconstructive preprosthetic surgery deals primarily with bone and bone-substitutes in maxillofacial implantology. Research includes a

number of investigations on the maxillary sinus floor elevation model, where bone grafts and bone substitutes are investigated. Apart from that, the patient material in general and of post-oncological patients in particular form a valuable source for research. In the studies mentioned before there is a close collaboration with the section Oral Cell Biology of ACTA, the department of Endocrinology of the VUmc and the departments of Oral and Maxillofacial Surgery at the Rijnland Hospital, Leiderdorp and the St Antonius Hospital, Nieuwegein. The research on surgical orthodontics and on maxillofacial implantology is included in the recently established Onderzoeksinstituut MOVE of the VUmc.

Giant cell granuloma of the jaw bone is a rare, but sometimes aggressive disease. The research is focused on the possible value of the use of calcitonin, particularly in aggressive or recurrent giant cell granulomas. Furthermore, a study is undertaken on the treatment of non-tuberculous mycobacterial lymphadenitis in children, comparing surgical versus medical treatment.

Bisphosphonates are commonly prescribed for treatment and prevention of osteoporosis, and they are also used in combination with chemotherapy and radiotherapy to treat cancers that are metastatic to bone. Recent publications describe a condition, known as osteonecrosis of the jaw, in which patients receiving bisphosphonates while undergoing chemotherapy develop avascular necrosis of the jaw either spontaneously, due to oral trauma or following dental extraction. The aim of this study is to elucidate the effects of chemotherapy and bisphosphonates on the oral microcirculation of breast cancer and multiple myeloma patients. Furthermore, the effects of cytotoxic chemotherapy on the microvasculature, morphology and capillary density of the oral mucosa are evaluated. This research program is conducted in collaboration with the Departments of Internal Medicine, Division of Hematology and Oncology, Experimental Physiology and Clinical Epidemiology and Biostatistics, Academic Medical Center, Amsterdam.

The aim of the study on anticoagulant medication is to evaluate the effect of low dose regimes of aspirin, as well as the effect of ticlopidine and clopidogrel, on bleeding in patients undergoing oral surgical procedures.

This research program is performed in close collaboration with the Department of Internal Medicine, Vascular Medicine, Academic Medical Center Amsterdam.

## **Results**

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

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

The group on surgical orthopedics of the maxillofacial skeleton has been making steadily progress, focusing on condylar hyperplasia and on the use of imaging techniques on soft tissue changes after orthognatic surgery.

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

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

The studies on inflammatory and inflammatory-like diseases of the oral and peri-oral structures, including the jaw bones and the lymph nodes of the neck, have been running well. Theses on both subjects have successfully been defended in 2006.

In the study on the effects of chemotherapy on the oral microcirculation the animal protocol has been approved by the DEC. The first experiments have been performed and the first article will be submitted by the summer of 2007. The project on the evaluation of anticoagulation in patients are included.

**Academic personnel in 2006 and 2007**

<b>Research staff ACTA - MZ (in full time equivalents)</b>				
<b>position</b>	<b>name</b>	<b>fte 2006</b>	<b>plan 2007</b>	<b>funding</b>
Full professors	Akker, prof.dr. H.P., van den	0,30	0,20	1
	Bloemena, prof.dr. E.	0,20	0,20	1
	Tuinzing, prof.dr. D.B.	0,10	0,10	1
	Waal, prof.dr. I., van der	0,30	0,30	1
Senior lecturer	Steenbergen, dr. T.J.M. van	0,20	0,20	1
Other lecturers and tenured staff	Allard, mr.dr. R.H.B.	0,10	0,10	1
	Baart, drs. J.A.	0,10	0,10	1
	Becking, dr. A.G.	0,10	0,10	1
	Bruggenkate, dr. C.M., ten	0,10	0,10	1
	Diermen, drs. D.E. van	--	0,30	1
	Keuning, drs. K.H.D.M.	0,10	0,10	3
	Kroon, dr. F.H.M.	0,10	--	1
	Lange, dr. J. de	0,20	0,10	3
	Lindeboom, dr. J.A.H.	0,30	0,30	3
Schulten, dr. E.A.J.M.	0,10	0,10	1	
<b>Total tenured staff</b>		<b>2,30</b>	<b>2,40</b>	
Non tenured staff	Bosgra, drs. J.F.L.	0,10	--	1
	Goené, drs. R.J.	0,20	0,20	1
	Verlinden, drs. C.R.A.	0,10	0,10	1
PhD students	Bremmer, drs. J.F.	0,30	0,20	1
	Meleti, dds. M.	0,70	0,10	3
	Milstein, drs. D.M.J.	0,70	0,70	1
	Saridin, drs. C.P.	0,10	0,10	3
	Vékony, drs. H.	0,70	0,70	1
<b>Total non tenured staff</b>		<b>2,90</b>	<b>2,10</b>	
total 1st funding		3,80	3,80	1
total 3rd funding		1,40	0,70	3
<b>Total research staff</b>		<b>5,20</b>	<b>4,50</b>	

**Dissertations**

Lange, J. de (2006, June 29). Central giant cell granuloma of the jaw: epidemiology, therapy and related disorders. UvA Universiteit van Amsterdam (132 pag.). Prom./coprom.: prof.dr. H.P. van den Akker, & dr. H. van den Berg.

Lindeboom, J.A.H. (2006, October 31). Diagnosis and treatment of nontuberculous mycobacterial cervicofacial lymphadenitis in children. UvA Universiteit van Amsterdam (151 pag.). Prom./coprom.: prof.dr. H.P. van den Akker, dr. J.M. Prins, & dr. E.J. Kuijper.

**Publications in journals indexed in SCI**

Amir, L.R., Becking, A.G., Jovanovic, A., Perdijk, F.B.T., Everts, V., & Bronckers, A.L.J.J. (2006). Formation of new bone during vertical distraction osteogenesis of the human mandible is related to the presence of blood vessels. CLIN ORAL IMPLAN RES, 17, 410-416.

Amir, L.R., Becking, A.G., Jovanovic, A., Perdijk, F.B.T., Everts, V., & Bronckers, A.L.J.J. (2006). Vertical distraction osteogenesis in the human mandible: a prospective morphometric study. CLIN ORAL IMPLAN RES, 17, 417-425.

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- Lange, J. de, & Akker, H.P. van den (2006). Management of giant cell lesions. *INT J ORAL MAX SURG*, 35, 1076.
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- Lindeboom, J.A.H., Kuijper, E.J., Bruijnestein van Coppenraet, E.S., & Prins, J.M. (2006). First case of an oculofacial lesion due to Mycobacterium haemophilum infection in an immunocompetent child. *ORAL SURG ORAL MED O*, 101, 774-776.
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- Wolvius, E.B., Lange, J. de, Smeets, E.E.J., Wal, K.G.H. van der, & Akker, H.P. van den (2006). Noonan-like/multiple giant cell lesion syndrome: Report of a case and review of the literature. *J ORAL MAXIL SURG*, 64, 1289-1292.

### Other scientific publications (international, refereed)

- Amaral Mendes, R., & Waal, I. van der (2006). An unusual clinicoradiographic presentation of a lateral periodontal cyst. Report of two cases. *MEDICINA ORAL*, 11, E185-187.
- Frenken, J.W.F.H., Bravenboer, N., Zijderfeld, S.A., Schulten, E.A.J.M., & Bruggenkate, C.M. ten (2006). Straumann Bone Ceramic as a bone substitute in maxillary sinus floor augmentation: A case report. *STARGET*, 3, 6-7.
- Lange, J. de, & Akker, H.P. van den (2006). Noonan syndrome with giant cell lesions. *INT J PAEDIATR DENT*, 16, 69.
- Brand, H.S., & Vissink, A. (2006). General pathology. In R. Ireland (Ed.), *Clinical Textbook of Dental Hygiene and Therapy* (pp. 29-50). Oxford: Blackwell Munksgaard.

## Professional publications

- Akker, H.P. van den (2006). Lokale complicaties. In J.A. Baart & H.S. Brand (Eds.), Lokale anesthesie in de tandheelkunde (pp. 119-127). Houten: Bohn Stafleu Van Loghum.
- Allard, R.H.B. (2006). Aansprakelijkheid van het mondzorgteam. In C. de Baat, J.K.M. Aps, W.G. Brands, & C.E.L. Carels (Eds.), Het tandheelkundig jaar 2007 (pp. 40-49). Houten: Bohn Stafleu Van Loghum.
- Allard, R.H.B. (2006). Non-odontogenic cysts of the oral regions; 25 jaar na dato. NED TIJDSCHR TANDHEELKD, 113, 278-281.
- Amaral Mendes, R., & Waal, I. van der (2006). Een radiolucentie tussen de radices van 2 vitale gebitselementen. NED TIJDSCHR TANDHEELKD, 113, 326-327.
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- Baart, J.A., & Bosgra, J.F.L. (2006). Parodontitis apicalis uitgaande van een "gave" premolaar in de onderkaak. NED TIJDSCHR TANDHEELKD, 113, 239-240.
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- Bosgra, J.F.L. (2006). Welke schade kan het gebit oplopen door de aanwezigheid van een piercing? MONDHYG VADEMECUM, 4, 12.
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- Bosgra, J.F.L., Becking, A.G., & Baart, J.A. (2006). Kaakgewrichtsklachten. Een raakvlak tussen KNO en kaakchirurgie. NED TIJDSCHR KNO-HEELKD, 1, 7-14.
- Brand, H.S. (2006). De implanteerbare cardiale defibrillator in de tandartspraktijk. ACTA QP, 2, 172-175.
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- Hilbrands, L.B., Huysmans, F.T.M., & Brand, H.S. (2006). Aandoeningen van nieren en urinewegen. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene ziekteleer voor tandartsen* (pp. 10:131-144). Houten/Diegem: Bohn Stafleu Van Loghum.
- Laar, J.M. van, Breedveld, F.C., & Brand, H.S. (2006). Reumatische ziekten. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene ziekteleer voor tandartsen* (pp. 19:249-264). Houten/Diegem: Bohn Stafleu Van Loghum.
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- Saridin, C.P., & Becking, A.G. (2006). Unilaterale condylaire hyperactiviteit. *NED TANDARTSENBLAD*, 5, 30-31.
- Schulten, E.A.J.M. (2006). Dentale rehabilitatie met implantaten na oncologische chirurgie en reconstructie: bespreking van een casus. *NVOI BULLETIN*, 11, 28-29.
- Steenbergen, T.J.M. van (2006). Proefschriften 25 jaar na dato 12. Classificatie en virulentie van zwartgepigmenteerde bacteriën in relatie tot parodontitis. *NED TIJDSCHR TANDHEELKD*, 113, 513-515.
- Suikerbuijk, E., Brand, H.S., & Nieuw Amerongen, A. van (2006). Het speekselspreekuur – kenmerken van patiënten met het burning mouth syndroom en smaakstoornissen. *NED TANDARTSENBLAD*, 61, 18-19.
- Suttorp, C.M., Dijk, P.G.J.C. van, Cleen, M.J.H. de, Koch, A.E., & Waal, I. van der (2006). Resorptie van 2 bovenincisieven bij een 14-jarige jongen. *NED TIJDSCHR TANDHEELKD*, 113, 241-242.
- Teeseling, R.A. (2006). Tijdelijke verankering in de orthodontie. *NVOI BULLETIN*, 3, 32-33.
- Teeseling, R.A. van, & Goené, R.J. (2006). Implantologie en orthodontie bij oligodontie. In *Praktijkboek voor Tandheelkunde 2006*. Houten/Diegem: Bohn Stafleu Van Loghum.
- Vissink, A., & Brand, H.S. (2006). Medisch-tandheelkundige interactie. *NED TIJDSCHR TANDHEELKD*, 113, 170-171.
- Vries, J. de, Roodenburg, J.L.N., Waal, I. van der, & Bender, W. (2006). *Oncologie voor de tandheelkundige praktijk*. Assen: Van Gorcum. 301 pp.
- Waal, I. van der (2006). Een 60-jarige man met een blauwe verkleuring van het mondslijmvlies. In *Tandheelkundige Casuïstiek* (pp. 1-7). Houten: Bohn Stafleu Van Loghum.
- Waal, I. van der (2006). Premaligne afwijkingen van de mondholte en hun behandeling. *NED TIJDSCHR ONCOL*, 3, 137-143.
- Wierink, C., & Diermen, D.E. van (2006). Glazuurafwijkingen bij kinderen met coeliakie. In C. de Baat, J.K.M. Aps, W.G. Brands, & C.E.L. Carels (Eds.), *Het tandheelkundig jaar 2007* (pp. 40-49). Houten: Bohn Stafleu Van Loghum.

## Indicators of Esteem

### Grants: current projects with external funding

- Bruggenkate, C.M. ten: SBC (Straumann Bone Ceramic) bone substitute for sinus floor elevation (2005-2006) Straumann; € 52.000,-
- Lange, J. de, Akker & H.P. van den. Treatment of central giant cell granuloma of the jaw with calcitonin. Novartis Pharma B.V.; Duration of project: 2000-2005. €50.000.
- Lindeboom, J.A.H. Treatment of non-tuberculous mycobacterial lymphadenitis in children - surgery versus medical treatment. ZON - MW; Duration of project: 2001-2005. €300.000.
- Ince, C. & Lindeboom, J.A.H. Systemic chemotherapy modelling in lagomorphs with cyclophosphamide, methotrexate, and fluorouracil: a pilot study; and: Assessing the effects of bisphosphonates during chemotherapy in soft tissue microcirculation of the oral mucosa. Novartis Pharma; Duration of project: 2006-2010.

### Membership of international editorial boards

Brand, H.S.;	J DENT RES
Bruggenkate, C.M. ten;	CLIN ORAL IMPLAN RES
Waal, I. van der:	ACTA STOMATOLOGICA CROATICA
Waal, I. van der:	EUR J CANCER
Waal, I. van der	J DENT UNIV SAO PAOLO
Waal, I. van der:	MEDICINA ORAL

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

### **Scientific awards/honours**

Milstein, D.M.J. (2006). Eervolle vermeldingsprijs BOOA Research Grant. Najaarsvergadering Ned. Ver. voor Mondziekten, Kaak- en Aangezichtschiurgie: Groningen (2006, November 03).  
Saridin, C.P. (2006). BOOA Research Grant. Najaarsvergadering Ned. Ver. voor Mondziekten, Kaak- en Aangezichtschiurgie: Groningen, the Netherlands (2006, November 03).  
Suikerbuijk, E. (2006). NT Scriptieprijs. Het speekselspreekuur – karakteristieken van patiënten met het burning mouth syndrome. Begeleiders: dr. H.S. Brand and prof.dr. A. van Nieuw Amerongen.  
Vékony, H. (2006). 1e prijs Vrije Voordrachten. Pathologendagen: Ede, the Netherlands (2006, April 21).  
Vékony, H. (2006). 2e prijs Klinische voordrachten. OOA PhD student retreat: Texel, the Netherlands (2006, October 11 - 2006, October 13).  
Waal, I. van der (2006). Honorary Membership. International Association of Oral Pathologists: (2006, June 22).  
Waal, I. van der (2006). Koninklijke onderscheiding. Ridder in de Orde van de Nederlandse Leeuw: Amsterdam, the Netherlands (2006, December 08).

### **Invited speakers at international congresses or symposia**

Becking, A.G. (2006, November 14). Combined orthodontic and surgical diagnosis and treatment. Shanghai, China, Course dept. of orthodontics and dept. of oral and maxillofacial surgery, 9th People Hospital, 2nd Medical School.  
Becking, A.G. (2006, November 11). Combined orthodontic and surgical diagnosis and treatment. Wuhan, China, Course department of orthodontics, University of Wuhan.  
Becking, A.G. (2006, June 09). Combined orthodontic en surgical treatment planning. Marburg, Germany, One day course.  
Becking, A.G. (2006, May 19). Orthognathic mandibular surgery in Class III deformity. Distraction osteogenesis in orthognathic surgery; hands-on workshop on treatment planning in condylar hyperactivity. Belek, Turkey, Strasbourg Osteosynthesis Research Group Modular Course.  
Bruggenkate, C.M. ten (2006, May 06). Sinus floor elevation. Bern, Switzerland, André Schroeder memorial symposium.  
Bruggenkate, C.M. ten (2006, August 26). Straumann Bone Ceramic. Basel, Switzerland, Biologics ITI group.  
Goené, R.J. (2006, April 02). Immediate versus delayed implant placement: soft and hard tissue management. Warsaw, Poland, Osteology symposium.  
Goené, R.J. (2006, February 17). Immediate versus delayed implant placement: soft and hard tissue management. Nice, France, 3i Research and Technology Forum.  
Goené, R.J. (2006, October 07). New opportunities for immediate placement in the anterior maxilla: importance of hard and soft tissue preservation. Zurich, Switzerland, European Association of Osseointegration.  
Goené, R.J. (2006, April 22). Yearly update in Dentistry. Paramaribo, Surinam, Intercongress.  
Spronsen, P.H. van (2006, January 30). Weak jaw muscles cause long-face growth patterns: how strong is the evidence? Going, Austria, Angle Society Europe.  
Waal, I. van der (2006, November 02). Oral non-squamous malignant tumors. Diagnosis and management and two cases for clinicopathological session. Bilbao, Spain, Oral and Maxillofacial Pathology unit of the Basque country in collaboration with the Spanish Society of Oral Medicine.  
Waal, I. van der (2006, October 24). Pathology and staging: problems and future directions. Cleveland, USA, Crile Centennial Symposium. Panelist on the panel discussion.

### **Other international functions**

Becking, A.G.: Member. Strasbourg Osteosynthesis Research Group.  
Bruggenkate, C.M. ten: Regular teacher. Basel University, Switzerland.  
Bruggenkate, C.M. ten: Delegate for Belgium. ITI.  
Bruggenkate, C.M. ten: Delegate for Finland. ITI.  
Bruggenkate, C.M. ten: Board member. ITI (International Team for Implantology).  
Bruggenkate, C.M. ten: Chairman. ITI Development Committee.  
Bruggenkate, C.M. ten: Member. ITI Expert Pool.  
Bruggenkate, C.M. ten: Regular ITI teacher. ITI Germany.

Waal, I. van der:	Councilor. International Association of Oral and Maxillofacial Surgeons.
Waal, I. van der:	Member. Scientific Committee STOMA.
Waal, I. van der:	Expert for the UICC. Telepathology Consultation Center for odontogenic tissue. International Union Against Cancer (UICC).
Waal, I. van der:	External examiner. Thesis "A detailed investigation of oral cancer in Southern Ireland", E. O'Sullivan.
Waal, I. van der:	External examiner Functie bij : Thesis "Squamous cell carcinoma an epithelial dysplasia of the oral cavity. Etiological, clinical biological and prognostic considerations", J. Rautava.

## Collaborations

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

## Current PhD projects

- Amir, LR.** Histology of human jaw bone during distraction osteogenesis. Supervisors: prof.dr. V. Everts & prof.dr. D.B. Tuizing; co-supervisors dr. A.L.J.J. Bronckers, & dr. A.G. Becking. Start: December 2001.
- Bremmer, JF.** Prognostic value of genetic markers in patients with preneoplastic oral lesions. Supervisors: prof.dr. I. van der Waal & prof.dr. R.H. Brakenhoff. Start: 2002.
- Dicker, GJ.** Muscular changes in orthognathic surgery. Supervisors: dr. P. van Spronsen, prof.dr. D.B. Tuizing, prof.dr. R.A. Manoliu. Start: 2002.
- Frank, MH.** The effect of anticoagulant therapy on blood loss during dentoalveolar surgery (BLACK-study). Supervisors: prof.dr. H.P. van den Akker, prof.dr. M.M. Levi & dr. J.A.H. Lindeboom. Start: September 2006.
- Frenken, J.** Sinus floor elevation with bone and bone substitutes. Supervisor: prof.dr. C.M. ten Bruggenkate; co-supervisors: dr. E.A.J.M. Schulten & dr. J.P.A. van den Bergh. Start: 2005.
- Lange, J de.** Treatment of central giant cell granuloma of the jaw with calcitonin. Supervisor: prof.dr. H.P. van den Akker. Start: 2000.
- Lindeboom, JAH.** Treatment of non-tuberculous mycobacterial lymphadenitis in children - surgery versus medical treatment. Supervisors: prof.dr. H.P. van den Akker & dr. E.J. Kuyper, co-supervisor: prof.dr. P.S. Speelman. Start: 2001.

- Meleti, M.** Malignant melanoma and melanoma-like lesions of the oral mucosa. Supervisor: prof.dr. I. van der Waal. Start: 2004.
- Milstein, DMJ.** The oral microcirculation and wound healing in maxillofacial surgery. Supervisors: prof.dr. H.P. van den Akker, prof.dr. C. Ince & dr. J.A.H. Lindeboom. Start: September 2005.
- Vékony, H.** Characterization and prognostication of salivary gland tumours. Supervisor: prof.dr. E. Bloemena. Co-supervisor: prof.dr. I. van der Waal. Start: 2004.
- Weijers, M.** The prognostic value of different parameters in surgically removed oral squamous cell carcinomas from the tongue and floor of the mouth. Supervisor: prof.dr. I. van der Waal. Start: October 1998.
- Saridin, CP.** Condylar hyperactivity. Supervisors: prof.dr. D.B. Tuinzing & prof.dr. I. van der Waal; co-supervisors; dr. Raaymakers & dr. A.G. Becking. Start: 2006.
- Zijderveld, SA.** Bone regeneration in maxillofacial surgery. Supervisor: prof.dr. C.M. ten Bruggenkate; co-supervisors: dr. E.A.J.M. Schulten & dr. J.P.A. van den Bergh. Start: 2000.

## Section: Oral and Maxillofacial Radiology

### Diagnostic Imaging of the Tissues in the Maxillo-facial Complex

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

#### Program leader

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

#### IOT senior scientist and full professor



P.F. van der Stelt

#### Research objectives

The research of the Department of Oral and Maxillofacial Radiology is focused on the development and improvement of diagnostic methods for the visualization of normal and abnormal structures in the maxillofacial complex. This is realized from different perspectives including fundamental as well as applied (clinical) components:

*1. Computer aided analysis of digital radiographic images*

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

*2. Three dimensional visualization of radiographic information*

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

*3. Diagnostic performance of radiographic systems*

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

Consequently, this part of the research is aiming at evaluation and improvement of image analysis procedures from the system perspective.

## **Results**

### *Computer aided analysis of digital radiographic images*

Digital subtraction radiography is a sensitive method for the detection of small changes in mineralized tissues. Two images of the same region of interest taken with identical projection geometry are required for this technique. We further developed software programs to match non-identical image projections. A new module is under investigation which applies statistical models to the images to predict the best match. This approach seems to be very promising because of its robustness. Testing is undertaken at this moment.

This technique has also been applied in a study as part of the I-Imas project (EU Framework 6). We were able to predict an optimised image based on a low dose scout image. A complete system including the image optimisation software is currently under construction by other partners in the project. The first images have been taken with the new sensor. Two publications have been completed and are submitted.

The Osteodent project (EU Framework 5), aiming at the early diagnosis of osteoporosis using dental radiography techniques, finished by the end of 2005. This project was done in collaboration with groups in Manchester (coordinator), Malmö, Athens and Leuven. It involved 600 osteoporotic patients and controls. Our contribution was focused on the quantitative analysis of the radiographic trabecular pattern on intra-oral radiographs and panoramic radiographs. We were able to demonstrate that quantitative analysis of the radiographic trabecular pattern is able to predict between 70 and 80% of the osteoporotic subjects. Several publications are in different stages at this moment.

### *Three dimensional visualization of radiographic information*

Two projects related to Local CT have been undertaken. These projects were set up to study the clinical application of Local CT and 3D visualisation. The results indicate that Local CT provides more information that can not be produced by conventional projection techniques. The results will be published.

In summer a Cone Beam CT device was installed. Several studies, both clinical and fundamental, have been started since then. The CBCT facilitates many opportunities for collaboration with other dental disciplines, such as orthodontics, CMD-treatment, implantology, oral surgery and endodontology. Several projects have been initiated or are being developed.

### *Diagnostic performance of radiographic systems*

The PhD-project on the implementation of digital radiography in general dental practice is making good progress and has resulted in some more papers. Erwin Berkhout will present his thesis about this subject in the beginning of 2007.

**Academic personnel in 2006 and 2007**

<b>Research staff ACTA - TR (in full time equivalents)</b>				
<b>position</b>	<b>name</b>	<b>fte 2006</b>	<b>plan 2007</b>	<b>funding</b>
Full professor	Stelt, prof.dr. P.F. van der	0,30	0,30	1
Senior lecturer	Sanderink, dr. G.C.H.	0,20	0,20	1
Lecturers and other tenured research staff	Geraets, dr. W.G.M.	0,60	0,60	1
	Mileman, dr. P.A.	0,30	0,30	1
	Verheij, dr. H.	0,80	0,80	3
<b>Total tenured staff</b>		<b>2,20</b>	<b>2,20</b>	
Non tenured staff	Li, dr. G.	0,80	0,20	3
PhD students	Berkhout, drs. W.E.R.	0,50	0,50	1
	Hassan, dds. B.A.	0,10	0,70	
<b>Total non tenured staff</b>		<b>1,40</b>	<b>1,40</b>	
total 1st funding		2,00	2,60	1
total 3rd funding		1,60	1,00	3
<b>Total research staff</b>		<b>3,60</b>	<b>3,60</b>	

**Publications in journals indexed in SCI**

- Geraets, W.G.M., Ruijven, L.J. van, Verheij, J.G.C., Eijden, T.M.G.J. van, & Stelt, P.F. van der (2006). A sensitive method for measuring spatial orientation in bone structures. *DENTOMAXILLOFAC RAD*, 35, 319-325.
- Li, G., Stelt, P.F. van der, Verheij, H., Speller, R.D., Galbiati, A., Psomadellis, F., Turchetta, R., Theodoridis, S., Hall, G., Avset, B.S., Triantis, F.A., & Longo, R. (2006). End-user survey for digital sensor characteristics: a pilot questionnaire study. *DENTOMAXILLOFAC RAD*, 35, 147-151.
- Nackaerts, O., Jacobs, R., Pillen, M., Engelen, L., Gijbels, F., Devlin, H., Lindh, C., Nicopoulou-Karayianni, K., Stelt, P.F. van der, Pavitt, S., & Horner, K. (2006). Accuracy and precision of a densitometric tool for jaw bone. *DENTOMAXILLOFAC RAD*, 35, 244-248.

**Other scientific publications**

- Geraets, W.G.M., Ruijven, L.J. van, Verheij, H., Eijden, T.M.G.J. van, & Stelt, P.F. van der (2006). A sensitive method for measuring spatial orientation in bone structures. *Fifth Quinquennial Review 2001-2006 CDROM publication of the Dutch Society of Pattern Recognition and Image Processing (Paper 12): (2006, november 05)*.
- Griffiths, J.A., Metaxas, M.G., Royle, G.J., Venanzi, C., Esbrand, C., Stelt, P.F. van der, Verheij, H., Li, G., Turchetta, R., Fant, A., Gasiorek, P., Theodoridis, S., Georgiou, H., Cavouras, D., Hall, G., Noy, M., Jones, J., Leaver, J., Machin, D., Greenwood, S., Khaleeq, M., Schulerud, H., Ostby, J., Triantis, F.A., Asimakis, A., Bolanakis, D., Manthos, N., Longo, R., Bergamaschi, A., & Speller, R.D. (2006). A multi-element detector system for intelligent imaging: I-ImaS. In *IEEE 2006 Nuclear Science Symposium, Medical Imaging Conference (NSS/MIC) Proceedings*. San Diego, California, USA.
- Speller, R.D., Royle, G.J., Griffiths, J.A., Metaxas, M.G., Li, G., Stelt, P.F. van der, Psomadellis, F., Turchetta, R., Fant, A., Georgiou, H., Theodoridis, S., Hall, G., Noy, M., Jones, J., Leaver, J., Machin, D., Ostby, J., Triantis, F.A., Asimidis, A., Bolanakis, D., Longo, R., Venanzi, C., & Bergamaschi, A. (2006). Intelligent imaging sensors: system development and preliminary results. In *International Workshop Digital Mammography 2006 Proceedings*. Manchester, UK: University of Manchester.
- Turchetta, R., Fant, A., Gasiorek, P., Esbrand, C., Griffiths, J.A., Metaxas, M.G., Royle, G.J., Speller, R.D., Venanzi, C., Stelt, P.F. van der, Verheij, H., Li, G., Theodoridis, S., Georgiou, H., Cavouras, D., Hall, G., Noy, M., Jones, J., Leaver, J., Machin, D., Greenwood, S., Khaleeq, M., Schulerud, H., Ostby, J., Triantis, F.A., Asimidis, A., Bolanakis, D., Manthos, N., Longo, R., & Bergamaschi, A. (2006). CMOS Monolithic Active Pixel Sensors (MAPS): developments and future outlook. In *15th International Workshop on Vertex detectors Proceedings*. Perugia, Italy.

## External reports

- Stelt, P.F. van der, Geraets, W.G.M., & Verheij, H. (2006). Image segmentation and quantitative analysis of the radiographic trabecular pattern. Report for Osteodent Workpackage 7. 8 pp. Amsterdam: ACTA.
- Stelt, P.F. van der, Horner, K., Lindh, C., Nicopoulou-Karayianni, K., Jacobs, R., & Devlin, H. (2006). Osteodent consortium. Final Report of the Osteodent project. 94 pp. Amsterdam: ACTA.
- Stelt, P.F. van der, & Li, G. (2006). Top level design of the I-Imas sensor. Final report of I-Imas Workpackage 5. 13 pp. Amsterdam: ACTA.

## Indicators of Esteem

### Grants: current projects with external funding

- The Diagnostic Validity of Dental Radiography Techniques for Identifying Osteoporotic Patients (OSTEODENT). Consortium by Horner, K. (Manchester), Lindh, C. (Malmö), Nicopoulou-Karayianni, K. (Athens), Jacobs, R. (Leuven), van der Stelt, P.F. (Amsterdam). EU-project Framework Programme 5, Contract QLRT-2001-02243. €1.427 million. 36 months. Finished January 31, 2006.
- Intelligent Imaging Sensors for Industry, Health & Security (I-Imas). Consortium by R. Speller (London), P.F. van der Stelt (Amsterdam), F. Psomadellis (Athens), R. Turchetta (Oxford), S. Theodoridis (Athens), G. Hall (London), F. Triantis (Ioannina), R. Longo (Trieste). Sixth Framework Programme, Priority 3 NMP "New generation of sensors, actuators and systems for health, safety and security of people and environment", contract no. NMP2-CT-2003-505593.
- Sigma Instrumentarium x-ray sensor and x-ray source, donated by Instrumentarium.

### Membership of international editorial boards

Mileman, P.A.;	DENTOMAXILLOFACIAL RAD
Sanderink, G.C.H.;	DENTOMAXILLOFACIAL RAD
Sanderink, G.C.H.;	ORAL RADIOL
Stelt, P.F. van der;	CLIN ORAL IMPLAN RES
Stelt, P.F. van der;	DENTOMAXILLOFACIAL RAD
Stelt, P.F. van der;	ODONTOLOGY
Stelt, P.F. van der;	ORAL SURG ORAL MED O
Stelt, P.F. van der;	EUR J DENT

### Invited speakers at international congresses or symposia

- Sanderink, G.C.H. (2006, May 31). From lectures to virtual class rooms. A faculty wide use of an electronic learning environment. Leuven, Belgium, 10th European Congress of DentoMaxilloFacial Radiology.
- Stelt, P.F. van der (2006, December 01). Diagnostic advantages of digital radiology in dentistry. Glasgow, Scotland, NHS Greater Glasgow and Clyde Board.

### Other international functions

Berkhout, W.E.R.:	Junior vice-president. International Association of DentoMaxillofacial Radiology.
Sanderink, G.C.H.:	Secretary General. International Association of DentoMaxilloFacial Radiology.
Stelt, P.F. van der:	Executive Secretary. European Academy of DentoMaxilloFacial Radiology.
Stelt, P.F. van der:	President. IADR-Diagnostic Systems Group.
Stelt, P.F. van der:	President Elect. International Association of DentoMaxillofacial Radiology.

## **Collaborations**

- Dr. W. van den Hout, Medical Decision Making Unit, Department of General Surgery, Leiden University Medical College, Leiden, the Netherlands.
- Prof. S.M. Dunn, Rutgers University Dept. of Biomedical Engineering, Piscataway NJ, USA.

## **Current PhD projects**

**Berkhout WER.** Impact of digital radiography on dental practice and diagnostic performance. Supervisor: prof.dr. P.F. van der Stelt. Start: April 2000.

**Hassan BA.** 3D Cone Beam CT. Supervisor: prof.dr. P.F. van der Stelt. Start: November 2006.

## Section: Orthodontics

### Craniofacial development, psychosocial aspects and biomaterials in orthodontics

#### Program leader

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

#### IOT full professors



H. van Beek



A. Zentner

#### Research objectives

The research activities at the Department of Orthodontics focus on basic and clinical research in orthodontics and related disciplines. Three main themes exist:

1. Basic and clinical description of environmentally and genetically induced aberrations of facial form.
2. To determine the impact of Orthodontics on the quality of life.
3. To optimize orthodontic material properties and procedures for clinical use.

#### Results

The research activities at the Department of Orthodontics focus on basic and clinical research in orthodontics and related disciplines, and the following directions were pursued in the year 2006.

1. Growth and growth regulation during normal and abnormal craniofacial development. A number of projects were carried out within this larger theme, which for a long time has been the department's major research field. Strong collaboration links have been established with Section of Functional Anatomy ACTA. Animal experimental set-ups with soft diet elucidate the function-morphology interrelation with regard to facial form and function.

The treatment of Cleft patients remains under scientific scrutiny and multicenter growth/development/treatment outcome is charted in collaboration with Nijmegen University.

2. Orthodontics and quality of life. This research theme has now been expanded and new projects have been started on the basis of previous work. In particular collaborative work with Section of Social Dentistry has been intensified.

3. Biomaterials. Studies were carried out in collaboration with the Section of Oral Biochemistry of the Department of Dental Basic Sciences, ACTA, and The University of Mainz, Germany, which were directed at the development of novel techniques of covalent immobilization on the surface of various biomaterials of biologically active molecules such as antimicrobial peptides, cell-attachment and mineralization promoting molecules. In addition, in collaboration with the Section

Dental Material Sciences of the Department of Dental Basic Sciences, ACTA, bond strength and setting characteristics of glass ionomer cements and fatigue fracture of orthodontic arch wires were investigated.

### Academic personnel in 2006 and 2007

Research staff ACTA - OR (in full time equivalents)				
position	name	fte 2006	plan 2007	funding
Full professors	Beek, prof.dr. H. van	0,20	0,20	1
	Zentner, prof.dr. A.	0,20	0,20	1
Senior lecturer	Habets, dr. L.L.H.M.	0,10	0,10	1
Lecturers and other tenured research staff	Etty, drs. E.	0,10	--	1
	Kuitert, dr. R.B.	0,20	0,20	1
	Grünheid, dr. T.	0,30	0,30	1
<b>Total tenured staff</b>		<b>1,10</b>	<b>1,00</b>	
non tenured staff	Beerens, drs. M.W.	--	0,05	3
	Bondt, drs. B., de	0,05	0,05	3
	Bos, dr. A.	--	0,20	1
	Calis, drs. E.M.	0,05	--	3
	Disse, drs. M.	0,05	--	3
	Dungen, drs. G.M., van den	0,05	0,05	3
	Gabriel, dr. M.O.	0,30	--	1
	Hiemstra, drs. R.	--	0,05	3
	Joosten, drs. M.W.	0,05	0,05	3
	Kooren, drs. O.	0,05	0,05	3
	Lie, drs. S.L.F.	0,05	--	3
	Mattousch, drs. T.J.H.	0,05	--	3
	Nijkamp, drs. P.G.	--	0,05	1
	Nijkamp, drs. P.G.	0,05	--	3
	Parys, drs. K. van	--	0,05	3
	Prahl, drs. C.	--	0,05	1
	Reitsma, drs. J.H.	--	0,05	3
	Sint Jago, drs. A.E.V.	0,05	0,05	3
	Tan, drs. S.P.K.	0,05	0,05	3
	Vreeke, drs. M.	--	0,05	3
Westing, drs. K. van	--	0,05	3	
PhD students	Algera, drs. T.J.	0,20	0,20	1
	Bos, drs. A.	0,10	--	1
	Geels, drs. L.M.	--	0,35	1
	Willems, drs. N.M.B.K.	0,30	0,30	1
<b>Total non tenured staff</b>		<b>1,45</b>	<b>1,75</b>	
total 1st funding		2,00	2,15	1
total 3rd funding		0,55	0,60	3
<b>Total research staff</b>		<b>2,55</b>	<b>2,75</b>	

### Dissertations

Bos, A. (2006, mei 30). Compliance in orthodontics. UvA Universiteit van Amsterdam (129 pag.). Prom./coprom.: prof.dr. B. Prahl-Andersen, & prof.dr. J. Hoogstraten.  
 Steenberg, E. van (2006, juni 22). Intrusion of the maxillary incisors. Vrije Universiteit Amsterdam (95 pag.). Prom./coprom.: prof.dr. B. Prahl-Andersen, & dr. C.J. Burstone.

## Publications in journals indexed in SCI

- Algera, T.J., Kleverlaan, C.J., Prah-Andersen, B., & Feilzer, A.J. (2006). The influence of environmental conditions on the material properties of setting glass-ionomer cements. *DENT MATER*, 22, 852-856.
- Bongaarts, C.A., Hof, M.A. van 't, Prah-Andersen, B., Dirks, I.V., & Kuijpers-Jagtman, A.M. (2006). Infant orthopedics has no effect on maxillary arch dimensions in the deciduous dentition of children with complete unilateral cleft lip and palate (Dutchcleft). *CLEFT PALATE-CRAN J*, 43, 665-672.
- Gabriel, M.O., Nazmi, K., Veerman, E.C.I., Nieuw Amerongen, A. van, & Zentner, A. (2006). Preparation of LL-37-grafted titanium surfaces with bactericidal activity. *BIOCONJUGATE CHEM*, 17, 548-550.
- Gabriel, M.O., Nieuw Amerongen, G.P. van, Hinsbergh, V.W.M. van, Nieuw Amerongen, A. van, & Zentner, A. (2006). Direct grafting of RGD-motif containing peptide on the surface of polycaprolactone films. *J BIOMAT SCI-POLYM E*, 17, 567-577.
- Grünheid, T., Langenbach, G.E.J., Zentner, A., & Eijden, T.M.G.J. van (2006). Duty time of rabbit jaw muscles varies with the number of activity bursts. *J DENT RES*, 85, 1112-1117.
- Klages, U., Claus, N., Wehrbein, H., & Zentner, A. (2006). Development of a questionnaire for assessment of the psychosocial impact of dental aesthetics in young adults. *EUR J ORTHODONT*, 28, 103-111.
- Kuitert, R.B., Beckman, S., Loenen, M. van, Tuinzing, D.B., & Zentner, A. (2006). Dentoalveolar compensation in subjects with vertical skeletal dysplasia. *AM J ORTHOD DENTOFAC*, 129, 649-657.
- Lie, S.L.F., Kuitert, R.B., & Zentner, A. (2006). Post-treatment development of the curve of Spee. *EUR J ORTHODONT*, 28, 262-268.
- Louwerse, T.J., Aartman, I.H.A., Kramer, G.J.C., & Prah-Andersen, B. (2006). The reliability and validity of the index of complexity, outcome and need for determining treatment need in Dutch orthodontic practice. *EUR J ORTHODONT*, 28, 58-64.
- Prah, C., Prah-Andersen, B., Hof, M.A. van 't, & Kuijpers-Jagtman, A.M. (2006). Infant orthopedics and facial appearance: a randomized clinical trial (Dutchcleft). *CLEFT PALATE-CRAN J*, 43, 659-664.
- Prah-Andersen, B., & Ju, Q. (2006). Quality improvement of cleft lip and palate treatment. *ANGLE ORTHOD*, 76, 265-268.
- Steenbergen, E. van, Burstone, C.J., Prah-Andersen, B., & Aartman, I.H.A. (2006). Influence of buccal segment size on prevention of side effects from incisor intrusion. *AM J ORTHOD DENTOFAC*, 129, 658-665.
- Wijk, A.J. van, & Tan, S.P.K. (2006). A numeric code for identifying patterns of human tooth agenesis: a new approach. *EUR J ORAL SCI*, 114, 97-101.

## Other scientific publications (international, refereed)

- Schoonheim-Klein, M., Habets, L.L.M.H., Aartman, I.H.A., Vleuten, C.P.M. van der, Hoogstraten, J., & Velden, U. van der (2006). Implementing an objective structured clinical examination (OSCE) in dental education: effects on students' learning strategies. *EUR J DENT EDUC*, 10, 226-235.

## Professional publications

- Bos, A., Hoogstraten, J., & Prah-Andersen, B. (2006). Attituden ten aanzien van orthodontische behandeling. *NED TIJDSCHR TANDHEELKD*, 113, 230-233.
- Kuitert, R.B. (2006). M6 Orthodontische behandeling met tien jaar follow-up bij patiënten met gereduceerd parodontium. In N.H.J. Creugers, W.M.M. Fennis, & P.J.B. Leempoel (Eds.), *Tandheelkundige Casuïstiek*, supplement 9. Houten: Bohn Stafleu Van Loghum.
- Kuitert, R.B. (2006). Roken en Orthodontie. *NED TIJDSCHR TANDHEELKD*, 113, 506-512.

## Indicators of Esteem

### Membership of international editorial boards

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

### **Invited speakers at international congresses or symposia**

- Beek, H. van (2006, februari 02). Mandibular distraction osteogenesis. Going, Austria, Angle Society of Europe.
- Beek, H. van (2006, maart 07). Day course on facial orthopedics. Geneva, Switzerland, University of Geneva.
- Beek, H. van (2006, mei 16). Van Beek headgear-aktivator. Hannover, Germany, Deutsche Zahnärztekammer.
- Beek, H. van (2006, oktober 11). Vectors in mandibular distraction osteogenesis. Edinburgh, British Orthodontic Society conference.

### **Other international functions**

- Habets, L.L.M.H.;                      Honorary Treasurer. International Association of Dento-Maxillary-Facial Radiology.
- Zentner, A.:                              Honorary Treasurer. European Orthodontic Society.

### **Current PhD projects**

- Algera, TJ.** A material and clinical study of orthodontic cements for fastening brackets. Supervisors: prof.dr. A.J. Feilzer & prof.dr. B. Prah-Anderson. Start: July 2001.
- Bos, A.** Compliance in orthodontics. Supervisors: prof.dr. B. Prah-Andersen & prof.dr. J. Hoogstraten. Start January 2001.
- Geels, LM.** Quality of life in orthodontics. Supervisors: prof.dr. A. Zentner & prof.dr. J. Hoogstraten. Start January 2007.
- Grünheid T.** Adaptation of the masticatory system to varying functional demands. Supervisors: prof.dr. T.M.G.J. van Eijden & prof.dr. A. Zentner. Start: 2006.
- Steenbergen, E van.** Intrusion of maxillary incisors. Supervisors: prof.dr. B. Prah-Andersen & prof.dr. C. Burstone. Start 1998.
- Willems, NMBK.** Development of architecture and mineralization of cortical and trabecular bone of the mandible. Supervisors: prof.dr. T.M.G.J. van Eijden & prof.dr. A. Zentner. Start: April 2005.

## Section: Social Dentistry and Behavioural Sciences

### Dental Care and Dental Care Systems: Quality and Efficiency

#### Program leader

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#### IOT senior scientists and full professors



J. Hoogstraten



M.A.J. Eijkman



A. de Jongh

#### Research objectives

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

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

#### Results

The pain and anxiety research line within the section resulted in a completed PhD thesis and a series of international publications. A Fear of pain questionnaire was developed and analyzed. Factor analysis supported the three-factor structure found earlier by McNeil and also the results concerning divergent and convergent validity were satisfactory. Also, a short version of the Fear of Dental Pain was developed.

Five items of the original 18 item version were selected, based on psychometric characteristics and face validity, allowing rapid identification of patients who may require special attention and specific dental pain management. Furthermore it appeared that it is possible to reduce the fear of

pain associated with endodontic treatment by providing subjects with positive information about endodontic treatment.

It goes without saying that post-traumatic symptoms are possible accompaniments of severe forms of dental anxiety. It was shown that highly anxious individuals indeed reported a significant higher number of traumatic events, both within and outside the dental or medical setting, than individuals of a reference group (73% vs. 21%). As for very young children the Dental Discomfort Questionnaire, measuring pain-related behaviours, was introduced. This 8-item instrument proved reliable and valid, which could be helpful in identifying toothache in very young children.

The section's research on work stress and communication showed that gender of the dentist does influence dental nurses' perceptions of the communication styles used in the primary dental care setting. It was recommended to raise both dentist' and nurses' awareness of gender influences in professional communication by introducing these topics in their educational training program. Moreover, an instrument assessing job resources of dentists was introduced. It was shown that dentists see immediate results and aesthetics, and long term results of working with patients to be the most rewarding aspects. Stimulating a greater awareness of these aspects may serve a positive role in burnout prevention. Finally, in a study on the dental check-up frequency preferred by Dutch patients it was shown that patients prefer to attend their dentist regularly, at fixed intervals of about six months.

To conclude, our section gets more and more involved in collaborative research activities with other ACTA departments. We refer to the research results sections of the departments of Orthodontics, Oral Biochemistry, Periodontology and Oral and Maxillofacial Surgery.

**Academic personnel in 2006 and 2007**

<b>Research staff ACTA - ST (in full time equivalents)</b>				
<b>position</b>	<b>name</b>	<b>fte 2006</b>	<b>plan 2007</b>	<b>funding</b>
Full professors	Hoogstraten, prof.dr. J.	0,35	0,35	1
	Jongh, prof.dr. A., de	0,40	0,40	1
	Verrips prof.dr. G.H.W.	--	0,30	1
Senior lecturer	Gorter, dr. R.C.	0,40	0,40	1
Lecturers and other tenured research staff	Aartman, dr. I.H.A.	0,10	0,10	1
	Dekker, dr. J., den	0,05	0,05	1
	Duyx, drs. M.P.M.A.	0,05	0,05	1
	Gresnigt, dr. C.O.V.M.	0,10	0,05	1
	Poorterman, dr. J.H.G.	0,30	0,25	1
	Wijk, dr. A.J., van	--	0,40	
<b>Total tenured staff</b>		<b>1,75</b>	<b>2,35</b>	
non-tenured staff	Bos, dr. A.	--	0,20	1
	Eijkman, prof.dr. M.A.J.	0,05	--	guest
	Heuvel, drs. J. van den	0,05	--	guest
PhD students	Bos, drs. A.	0,10	--	1
	Edeler jr. MA., drs. H.A.	0,70	0,70	1
	Geels, drs. L.M.	--	0,35	1
	Kieffer, drs. J.M.	--	0,70	1
	Klaassen, drs. M.A.	0,20	0,20	1
	Oosterink-Wubbe, drs. F.M.D.	0,70	0,70	1
	Vermaire, drs, J.H.	0,40	0,40	3
	Versloot, drs. J.	0,35	--	1
	Wijk, drs. A.J., van	0,40	--	1
<b>Total non tenured staff</b>		<b>2,95</b>	<b>3,25</b>	
total 1st funding		4,20	5,20	1
total 3rd funding		0,40	0,40	3
total guests		0,10	--	guest
<b>Total research staff</b>		<b>4,70</b>	<b>5,60</b>	

**Dissertations**

- Bos, A. (2006, May 30). Compliance in orthodontics. UvA Universiteit van Amsterdam (129 pag.). Prom./coprom.: prof.dr. B. Prah-Andersen, & prof.dr. J. Hoogstraten.
- Wijk, A.J. van (2006, June 07). Acute pain in dentistry. UvA Universiteit van Amsterdam (184 pag.). Prom./coprom.: prof.dr. J. Hoogstraten.

**Publications in journals indexed in SCI**

- Bots, C.P., Poorterman, J.H.G., Brand, H.S., Kalsbeek, H., Amerongen, B.M. van, Veerman, E.C.I., & Nieuw Amerongen, A. van (2006). The oral health status of dentate patients with chronic renal failure undergoing dialysis therapy. *ORAL DIS*, 12, 176-180.
- Gorter, R.C., Bleeker, J.C., & Freeman, R. (2006). Dental nurses on perceived gender differences in their dentist's communication and interaction style. *BRIT DENT J*, 201, 159-164.
- Gorter, R.C., Brake te, J.H.M., Eijkman, M.A.J., & Hoogstraten, J. (2006). Job resources in Dutch dental practice. *INT DENT J*, 56, 22-28.
- Jongh, A. de, Fransen, J., Oosterink-Wubbe, F.M.D., & Aartman, I.H.A. (2006). Psychological trauma exposure and trauma symptoms among individuals with high and low levels of dental anxiety. *EUR J ORAL SCI*, 114, 286-292.

- Lindeboom, J.A.H., Mathura, K.R., Ramsoekh, D., Harkisoen, S., Aartman, I.H.A., Akker, H.P. van den, & Ince, C. (2006). The assessment of the gingival capillary density with orthogonal spectral polarization (OPS) imaging. *ARCH ORAL BIOL*, 51, 697-702.
- Louwerse, T.J., Aartman, I.H.A., Kramer, G.J.C., & Prah-Andersen, B. (2006). The reliability and validity of the index of complexity, outcome and need for determining treatment need in Dutch orthodontic practice. *EUR J ORTHODONT*, 28, 58-64.
- Meulen, M.J. van der, Lobbezoo, F., Aartman, I.H.A., & Naeije, M. (2006). Self-reported oral parafunctions and TMD pain intensity in temporomandibular disorder patients. *J OROFAC PAIN*, 20, 31-35.
- Steenbergen, E. van, Burstone, C.J., Prah-Andersen, B., & Aartman, I.H.A. (2006). Influence of buccal segment size on prevention of side effects from incisor intrusion. *AM J ORTHOD DENTOFAC*, 129, 658-665.
- Versloot, J., Veerkamp, J.S.J., & Hoogstraten, J. (2006). Dental Discomfort Questionnaire: assessment of dental discomfort and/ or pain in very young children. *COMMUNITY DENT ORAL*, 34, 47-52.
- Wijk, A.J. van, & Hoogstraten, J. (2006). Dutch translation of the Fear of pain Questionnaire: factor structure, reliability and validity. *EUR J PAIN*, 10, 479-486.
- Wijk, A.J. van, & Hoogstraten, J. (2006). Reducing fear of pain associated with endodontic therapy. *INT ENDOD J*, 39, 384-388.
- Wijk, A.J. van, & Tan, S.P.K. (2006). A numeric code for identifying patterns of human tooth agenesis: a new approach. *EUR J ORAL SCI*, 114, 97-101.
- Wijk, A.J. van, McNeil, D.W., Ho, C.J., Buchanan, H., & Hoogstraten, J. (2006). A short English version of the fear of dental pain questionnaire. *EUR J ORAL SCI*, 114, 204-208.

### Other scientific publications (international, refereed)

- Heuvel, J. van den, Bogers, A., Does, R.J.M.M., Dijk, A. van, & Berg, M. (2006). Quality management: Does it pay off? *QUAL MANAG HEALTH CARE*, 15, 137-149.
- Jongh, A. de, & Broeke, E. ten (2006). Die anwendung von EMDR bei der behandlung Spezifischer Phobien. In F. Lamprecht (Ed.), *Praxisbuch EMDR: modifizierungen für spezielle anwendungsgebiete* (pp. 68-96). Stuttgart: Klett-Cotta.
- Schoonheim-Klein, M., Habets, L.L.M.H., Aartman, I.H.A., Vleuten, C.P.M. van der, Hoogstraten, J., & Velden, U. van der (2006). Implementing an objective structured clinical examination (OSCE) in dental education: effects on students' learning strategies. *EUR J DENT EDUC*, 10, 226-235.
- Schouten, B.C., Mettes, T.G., Weeda, W.D., & Hoogstraten, J. (2006). Dental check-up frequency: preferences of Dutch patients. *COMMUNITY DENTAL HEALTH*, 23, 133-139.
- Versloot, J., Veerkamp, J.S.J., & Hoogstraten, J. (2006). Dental Discomfort Questionnaire for young children following full mouth rehabilitation under general anaesthesia. *EUR ARCH PAEDIATRIC DENT*, 7, 126-129.

### Professional publications

- Beek, J.H.D.A. van, & Hoogstraten, J. (2006). Tandartsen over hun opleiding van 1997 tot 2004. *NED TIJDSCHR TANDHEELKD*, 113, 397-400.
- Bos, A., Hoogstraten, J., & Prah-Andersen, B. (2006). Attituden ten aanzien van orthodontische behandeling. *NED TIJDSCHR TANDHEELKD*, 113, 230-233.
- Dinter, N. van, Maanen, E.J. van, Versloot, J., & Veerkamp, J.S.J. (2006). Ongemak van kinderen tijdens het geven van lokale anesthesie. Vergelijking van een geautomatiseerd systeem en de traditionele methode. *NED TIJDSCHR TANDHEELKD*, 113, 137-141.
- Eijkman, M.A.J., & Loon, L.A.J. van (2006). Claims: onaangename wensen. *ACTA QP*, 2, 102-109.
- Eijkman, M.A.J., Duyx, M.P.M.A., & Visser, A. (2006). Patiëntenvoorlichting en mondgezondheid. Houten: Bohn Stafleu Van Loghum. 346 pp.
- Eijsink, M., & Edeler jr. MA., H.A. (2006). Mijlpaal in de tandheekunde. Het jaar februari ' 47. *ACTA QP*, 2, 110-113.
- Gorter, R.C. (2006). Burnoutpreventie en bevlogenheid. In A.J. Feilzer, C.M. Kreulen, J.D. Scholtanus, & F. de Vries (Eds.), *Praktijkboek Tandheekunde*, hoofdstuk O8, afl. 9 (pp. 1-16). Houten: Bohn Stafleu Van Loghum.
- Gorter, R.C. (2006). Effectieve communicatie in de praktijk. *TANDARTSPRAKTIJK*, 27, 56-57.
- Gorter, R.C. (2006). Enige aandachtspunten bij gespreksvoering in de praktijk. *ACTA QP*, 2, 8-16.
- Gorter, R.C., & Kersten, H.W. (2006). Patiënten met wensen zijn moeilijke mensen. *ACTA QP*, 2, 1.
- Jongh, A. de (2006). Afwijkend gedrag. *ACTA QP*, 2, 82-89.
- Jongh, A. de (2006). Angst voor de tandarts. Assen: Van Gorcum. 251 pp.
- Jongh, A. de (2006). Het beoordelen van de psychische gesteldheid van een patiënt. In A.J. Feilzer, C.M. Kreulen, J.D. Scholtanus, & F. de Vries (Eds.), *Praktijkboek Tandheekunde*, hoofdstuk T5, afl. 9 (pp. 1-20). Houten: Bohn Stafleu Van Loghum.

- Jongh, A. de (2006). Wat is mooi ? Psychologische aspecten van de beoordeling van lichaam, gelaat en gebitselementen. ACTA QP, 5, 9-15.
- Jongh, A. de, & Latenstein, E. (2006). EMDR: kortdurende behandelmethodes voor de gevolgen van beschadigende ervaringen. In E. Lamers, F. Bosch, L. Hinderink, & C. Verschuren (Eds.), *Psychologie in de eerste lijn* (pp. 223-227). Harcourt Publishers.
- Jongh, A. de, Vo, G., Lie, S.L.S.D.F., Oosterink-Wubbe, F.M.D., & Rood, Y.R. van (2006). De populariteit van esthetische behandelingen. Resultaten van een landelijk onderzoek. NED TIJDSCHR TANDHEELKD, 113, 356-360.
- Poorterman, J.H.G., & Schuller, A.A. (2006). Tandheelkundige verzorging jeugdige ziekenfondsverzekerden; een onderzoek naar veranderingen in mondgezondheid en preventief gedrag. Eindmeting 2005, december 2006. Amsterdam: ACTA. 199 pp.
- Roos, C. de & Jongh, A. de. (2006). Stikken of slikken. KIND JEUGDPSYCHOTHER, 33, 83-102.
- Schuller, A.A., & Poorterman, J.H.G. (2006). Trends in mondgezondheid cariës prevalentie en frequentie van controlebezoeken aan de tandarts. NED TIJDSCHR TANDHEELKD, 123, 303-307.

## **External reports**

- Jongh, A. de, Kieffer, J.M., & Nelen, T.K. (2006). Tandheelkundige zorgverlening aan mensen met een verstandelijke beperking die thuis of semi-zelfstandig wonen. Report for College voor Zorgverzekeringen (CVZ). Amsterdam: ACTA. 83 pp.

## **Indicators of Esteem**

### **Invited speakers at international congresses or symposia**

- Edeler jr. MA., H.A. (2006, November 18). Water fluoridation in historical context. Geneva, Switzerland, (First) global consultation on oral health through fluoride. FDI, IADR, WHO.
- Versloot, J. (2006, June 09). Pain: its recognition and treatment in paediatric dentistry. Amsterdam, the Netherlands, 8th congress of the European Academy of Paediatric Dentistry.

### **Current PhD projects**

- Geels, LM.** Quality of life in orthodontics. Supervisors: prof.dr. A. Zentner & prof.dr. J. Hoogstraten. Start January 2007.
- Edeler, jr. HA.** De ontwikkeling van de tandheelkundige beroepsuitoefening van 1940 - 2000. Supervisors: prof.dr. M.A.J. Eijkman & prof.dr. E.S. Houwaart. Co-supervisor: dr. J. den Dekker. Start September 2003.
- Kieffer, JM.** Oral health, general health and quality of life. Supervisors: prof.dr. J. Hoogstraten & dr. R.C. Gorter. Start October 2006.
- Klaassen, MA.** Dental anxiety in children. Supervisors: prof.dr. J.M. ten Cate & prof.dr. J. Hoogstraten. Co-supervisor: dr. J.S.J. Veerkamp. Start: January 2006.
- Oosterink-Wubbe FMD.** Tandartsangst: oorzaken, classificatie en symptomatologie. Supervisors: prof.dr. A. de Jongh & prof.dr. Joh. Hoogstraten. Start: September 2004.
- Schoonheim- Klein, ME.** Implementing an Objective Structured Clinical Examination (OSCE) in dental education: effects on students' learning strategies. Supervisors: prof.dr. U. van der Velden & prof.dr. J. Hoogstraten. Start 2005.
- Vermaire, JH.** Children's dental health. Supervisors: prof.dr. J. Hoogstraten, prof.dr. C. van Loveren & dr. J.H.G. Poorterman. Start: January 2005.
- Versloot, J.** Recognition, prevention and treatment of pain in child dental patients. Supervisors: prof.dr. J.M. ten Cate & prof.dr. J. Hoogstraten. Co-supervisor: dr. J.S.J. Veerkamp. Start: January 2003.

## Section: Dental Material Sciences

### Dental Restorations

#### Program leader

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#### IOT senior scientists and full professors



A.J. Feilzer



C.J. Kleverlaan



A.J. de Gee



J.M. van der Zel

#### Research objectives

The general objective of our research program is to predict and improve the clinical performance of dental restorative materials covering the complete range of materials involved in creating restorations with direct or indirect techniques. Composition, structure and fabrication of the materials as well as their handling and application techniques are studied in vitro as well as in vivo. Moreover, also their possible health side effects are subject of study. Historically, our main interest has concentrated on all materials applied in 'adhesive' dentistry.

The increasing trend to replace the difficult and costly manual procedures by automated procedures using information technology, is being studied on its merits. In particular the possible advantages of the automated production of indirect restorations by CAD/CAM technology are evaluated on the physical properties and quality of restorations, as well as the esthetic properties like digital color measurement and reproduction. CAD/CAM technology offers the possibility to use new strong ceramic materials as a base for all-ceramic restorations. Mainly the research into Y-TZP zirconia indicates that the excellent physical properties of this material, make it an alternative for metal alloys in stress-bearing substructures.

Apart from basic scientific research, a substantial part of our research involves the development of laboratory experiments and equipment that simulates the clinical conditions as closely as possible, ultimately to be used as standard quality control tests (so-called 'accelerated tests'). Examples of such equipment are the 'ACTA-wear machine', the 'ACTA-intense' and the 'ACTA-fatigue device'. A special place in this part of our research takes the finite element analysis as a tool to reveal internal stresses which cannot simply be measured with tensiometer equipment.

Since 2002 the research area of the section includes clinical research on dental materials. For instance a European granted project on the clinical behavior of large class I and II glass-ionomer cement restorations and a clinical study into the performance of a new denture resin base material are finished, while a new 3-5 year clinical study into the performance of indirect resin composite posterior crowns has started in 2006. Besides these studies, experience was acquired with fiber reinforced resin composite adhesively fixed partial dentures. In 2003 in the department clinic a start was made with special consulting hours where patients, suspected of health effects of metals used in dental restorative materials, can be referred to. This project has developed both clinically and on basic science aspects quite well.

## **Results**

Substantial progress has been made in revealing the mechanisms that play a role in the stress distribution in specimens exposed to functional stresses. For this research FEA was used to demonstrate the stress distributions in test specimens in more detail.

A study into the applicability of this method in orthodontic bracket cementation is in progress.

In 2003 a start was made to develop a laboratory test to determine the composition of metal alloys used intra-orally for indirect restorations. This test is of main interest, as only traces of the metals need to be collected in situ to be analyzed on allergenic substances. The incidence of metal-ion release by the use of metallic restorative materials is a topic of main interest. However, in spite of an extensive amount of literature, there is a lack of overview on the dental consequences of these effects. Because of the medical aspects involved, cooperation has been sought with the departments of Immunology and of Dermatology of the VUmc, a project was developed which is to be submitted in January 2007 to the medical ethical committee of the VUmc. A specific diagnostic system was developed and applied to more than 500 patients with suspected side effects on dental materials. Cooperation with a few dermatology clinics resulted in a growing expertise and recognition.

Developments in the field of dental materials science made great strides forward. Experimental versions of low shrinking restorative monomer systems are recently introduced in dentistry and tested in our department. The development of 'smart' ceramics such as Y-TPZ-Zirconia is of main interest as a strong base for full ceramic restorations that might replace the use of metallic materials in restorative dentistry. In applied science nano-technology is an example of a field of increasing interest, which has been introduced in dentistry.

The CAD/CAM-technology in dentistry has reached a stage that can compete with all manual restorative methods. This fast-growing technique becomes a main area of interest in the field of quality assessment. A new technique in CAD/CAM is the rapid fabrication technique, which opens new opportunities for chairside indirect ceramic restorations and introduction of new ceramic materials. The department is closely involved in these developments.

## Academic personnel in 2006 and 2007

Research staff ACTA - MW (in full time equivalents)				
position	name	fte 2006	plan 2007	funding
Full professors	Feilzer, prof.dr. A.J.	0,40	0,40	1
	Zel, prof.dr.ir. J.M., van der	0,30	0,20	3
Senior lecturers	Kleverlaan, dr. C.J.	0,60	0,60	1
	Gee, dr. A.J., de	0,05	0,05	guest
Lecturers and other tenured research staff	Pallav, dr. P.	0,20	0,10	1
	Paridon, drs. M.W., van	0,05	0,05	1
	Bolhuis, dr. H.P.B.	0,10	--	1
	Dozic, dr. A.	0,60	0,40	1
<b>Total tenured staff</b>		<b>2,30</b>	<b>1,80</b>	
Non tenured staff	Jager, dr.ir. N., de	--	0,05	1
PhD students	Abou Shelib, dds. M.N.M.	0,80	0,80	3
	Algera, drs. T.J.	0,20	0,05	1
	Dalen, drs. A., van	0,10	0,10	1
	Kler, ing. M., de	0,05	0,05	guest
	Keulemans, drs. F.	0,40	0,40	1
	Meegdes, ing. M.	0,05	--	guest
	Mirmohammadi, dds. S.H.	0,50	0,80	guest
	Muris, drs. J.	0,50	0,50	1
	Wang, dds. H.	0,50	0,80	1
<b>Total non tenured staff</b>		<b>3,10</b>	<b>3,55</b>	
total 1st funding		3,65	3,40	1
total 3rd funding		1,10	1,05	3
total guests		0,65	0,90	guest
<b>Total research staff</b>		<b>5,40</b>	<b>5,35</b>	

## Dissertations

Dalen, A. van (2006, December 19). Two-unit adhesive cantilevers supported. UvA Universiteit van Amsterdam (124 pag.). Prom./coprom.: prof.dr. A.J. Feilzer, & dr. C.J. Kleverlaan.

## Publications in journals indexed in SCI

Abou Shelib, M.N.M., Kleverlaan, C.J., & Feilzer, A.J. (2006). Microtensile bond strength of different components of core veneered all-ceramic restorations part II: zirconia veneering ceramics. *DENT MATER*, 22, 857-863.

Algera, T.J., Kleverlaan, C.J., Prah-Andersen, B., & Feilzer, A.J. (2006). The influence of environmental conditions on the material properties of setting glass-ionomer cements. *DENT MATER*, 22, 852-856.

Bolhuis, H.P.B., Gee, A.J. de, Kleverlaan, C.J., El-Zohairy, A.A., & Feilzer, A.J. (2006). Contraction stress and bond strength to dentin for compatible and incompatible combinations of bonding systems and chemical and light-cured core build-up resin composites. *DENT MATER*, 22, 223-233.

Duinen, R.N.B. van (2006). Clinical effects at the glass-ionomer/tooth/saliva interfaces. *J DENT*, 618-619.

Erickson, R.L., Gee, A.J. de, & Feilzer, A.J. (2006). Fatigue testing of enamel bonds with self-etch and total-etch adhesive systems. *DENT MATER*, 22, 981-987.

Feilzer, A.J., Muris, J., & Valentine-Thon, E. (2006). Electrical shavers as possible risk factor for metal exposure. *ARCH DERMATOL*, 142, 1361-1362.

Hashimoto, M., Gee, A.J. de, Kaga, M., & Feilzer, A.J. (2006). Contraction stress in dentin adhesives bonded to dentin. *J DENT RES*, 85, 728-732.

- Hashimoto, M., Tay, F.R., Svizero, N.R., Gee, A.J. de, Feilzer, A.J., Sano, H., Kaga, M., & Pashley, D.H. (2006). The effects of common errors on sealing ability of total-etch adhesives. *DENT MATER*, 22, 560-568.
- Jager, N. de, Kler, M. de, & Zel, J.M. van der (2006). The influence of different core material on the FEA-determined stress distribution in dental crowns. *DENT MATER*, 22, 234-242.
- Muris, J., & Feilzer, A.J. (2006). Micro analysis of metals in dental restorations as part of a diagnostic approach in metal allergies. *NEUROENDOCRINOL LETT*, 1, 49-52.
- Vlaar, S.T., & Zel, J.M. van der (2006). Accuracy of dental digitizers. *INT DENT J*, 56, 301-309.

### **Other scientific publications (international, refereed)**

- Davidson, C.L. (2006). Advances in glass-ionomer cements. *J APPL ORAL SCI*, 14, 3-9.

### **Professional publications**

- Bolhuis, H.P.B., Gee, A.J. de, & Feilzer, A.J. (2006). De invloed van vermoeiing op het bevestigingscement rondom glasvezel/koolstofvezel wortelkanaalstiften bij composietopbouwen. *NED TIJDSCHR TANDHEELKD*, 113, 361-367.
- Denissen, H.W., & Dozic, A. (2006). Digitale proefopstelling met gingiva bij kroon- en brugwerk. *ACTA QP*, 2, 32-41.
- Feilzer, A.J., & El-Zohairy, A.A. (2006). Cementeren in de prothetische tandheelkunde. *ACTA QP*, 2, 8-13.
- Gee, A.J. de, Kleverlaan, C.J., & Degrange, M. (2006). Retrait et contraintes de polymérisation des composites. *L'INFORMATION DENTAIRE*, 34, 2049-2057.
- Zel, J.M. van der (2006). Keramiek in systemen. *ACTA QP*, 2, 20-29.

### **External reports**

- Gee, A.J. de (2006). Additional data for various products from previous experiments on Volumetric Polymerization Shrinkage, Shrinkage Stress and ACTA Wear. Report for Tokuyama. 3 pp. Amsterdam: ACTA.
- Gee, A.J. de (2006). Additional data for Volumetric Polymerization Shrinkage and Shrinkage Stress of various products from previous experiments. Report for Kuraray. 3 pp. Amsterdam: ACTA.
- Gee, A.J. de (2006). Shear bond strength of Gilb, Vitrebond and Ketac Bond to human enamel and dentin. Report for 3M Espe. 6 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Rezende, J.A. (2006). Setting Shrinkage of ELS and MHC FOC determined in the ACTA dilatometer. Report for Saremco. 5 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Rezende, J.A. (2006). Setting shrinkage of ELS Flow, Ice, Glacier, Premise Dentine, Ceram, X Mono and Charisma determined in the ACTA dilatometer. Report for Saremco. 5 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Rezende, J.A. (2006). Setting shrinkage of ELS Schmelz and ELS Schmelz Weiss determined in the ACTA dilatometer. Report for Saremco. 5 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Rezende, J.A. (2006). Setting shrinkage of PCR-100, Esthet.X and Filtek Supreme XT determined in the ACTA dilatometer. Report for Kuraray. 5 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Rezende, J.A. (2006). Setting Shrinkage Stress of ELS and MHC FOC. Report for Saremco. 6 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Rezende, J.A. (2006). Setting shrinkage stress of Estelite Flow Quick. Report for Tokuyama. 6 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Rezende, J.A. (2006). Setting shrinkage stress of FCR-300 and Filtek Supreme XT Flow. Report for Kuraray. 6 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Rezende, J.A. (2006). Setting shrinkage stress of Nanopaq and Els. Report for Gesellschaft für Dentale Forschung und Innovationen mbH. 6 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Rezende, J.A. (2006). Setting shrinkage stress of PCR-100, Esthet.X and Filtek Supreme XT. Report for Kuraray. 6 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Rezende, J.A. (2006). Volumetric polymerization shrinkage of Estelite Flow Quick, Grandio Flow and Venus Flow determined in the ACTA dilatometer. Report for Tokuyama. 5 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Rezende, J.A. (2006). Volumetric Polymerization Shrinkage of FCR-300 and Filtek Supreme XT Flow determined in the ACTA dilatometer. Report for Kuraray. 5 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Werner, A. (2006). SEM examination of surfaces of Estelite Flow Quick, Filtek Supreme XT Flow, Filtek Supreme XT and Venus after wear in the ACTA Wear Machine. Report for Tokuyama. 6 pp. Amsterdam: ACTA.

- Gee, A.J. de, & Werner, A. (2006). Vickers hardness of Estelite Flow Quick, Tetric Flow, Grandio Flow, Venus Flow, Tetric Evo Ceram and Z250. Report for Tokuyama. 6 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Werner, A. (2006). Wear determined in the ACTA wear machine of Signum-Neco, Artglass (status 05/08/01) and Z250. Report for Heraeus Kulzer. 5 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Werner, A. (2006). Wear of ELS Schmelz and ELS Schmelz Weiss determined in the ACTA wear machine. Report for Saremco. 5 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Werner, A. (2006). Wear of Estelite Flow Quick, Filtek Supreme XT Flow, Filtek Supreme XT, Venus and Filtek Z250 determined in the ACTA wear machine. Report for Tokuyama. 6 pp. Amsterdam: ACTA.
- Gee, A.J. de, & Werner, A. (2006). Wear of EX672A Nano-Ionomer, Fuji Fil LC, Fuji II LC, Fuji II and Fuji IX determined in the ACTA wear machine. Report for 3M Espe. 5 pp. Amsterdam: ACTA.
- Gee, A.J. de, Rezende, J.A., & Feilzer, A.J. (2006). Setting shrinkage stress of ELS Flow, Ice, Glacier, Premise Dentine Ceram, X Mono and Charisma. Report for Saremco. 6 pp. Amsterdam: ACTA.
- Gee, A.J. de, Rezende, J.A., & Feilzer, A.J. (2006). Setting shrinkage stress of ELS Schmelz and ELS Schmelz Weiss. Report for Saremco. 6 pp. Amsterdam: ACTA.

## **Patents**

- Feilzer, A.J. (2006). European Patent application P74438EP00: New surface treatment for zirconia based materials.

## **Indicators of Esteem**

### **Grants: current projects with external funding**

- Clinical study into the clinical performance of indirect resin composite posterior crowns (Signum-Neco study), ±€ 75.000.-
- Grant for the achievement of a Perkin Elmer ICP-MS € 20.000

### **Membership of international editorial boards**

- |                    |                |
|--------------------|----------------|
| Feilzer, A.J.:     | AM J DENT      |
| Feilzer, A.J.:     | ODONTOLOGY     |
| Zel, J.M. van der: | DIGITAL DENT J |

### **Organization of international congresses and symposia**

- Zel, J.M. van der (2006). Status of dental CAD/CAM – What's Next? IADR-CEF-PEF: Dublin, Ireland (2006, September 13 - 2006, September 16).

### **Invited speakers at international congresses or symposia**

- Feilzer, A.J. (2006, June 02). Allergie in de tandheekunde. Belgium, Belgian Dental Beauty Team.
- Feilzer, A.J. (2006, September 15). Careers in Dental Research. Dentist a magnificent profession. Dublin, Ireland, IADR-CED-PEF Workshop.
- Feilzer, A.J. (2006, November 15). Light polymerization, state of art and behavior of 2-Unit Cantilever resin bonded bridge. Alexandria, Egypt, Alexandria International Dental Congress.
- Feilzer, A.J. (2006, September 16). Present Status of Dental CAD/CAM- What's next? Standardization of CAD/CAM modalities. Dublin, Ireland, IADR-CED-PEF Symposium.
- Feilzer, A.J. (2006, September 14). Transition from amalgam to composite resin materials. Health side effects of dental restorative materials. Dublin, Ireland, IADR-CED-PEF Symposium.
- Gee, A.J. de (2006, June 02). Composietlampen. Belgium, Belgian Dental Beauty Team.
- Zel, J.M. van der (2006, May 19). Computer aided diagnosis and decision support for implant planning. Rome, Italy, 1st International Congress of the Computer Aided Implantology Academy.
- Zel, J.M. van der (2006, September 16). Status of dental CAD/CAM – What's Next? Dublin, Ireland, IADR-CED-PEF Symposium.

## Other international functions

Zel, J.M. van der.: Chairman. ISO/TC106 ad hoc committee for standardization of Dental CAD/CAM systems.

## Collaborations

- Degudent GmbH.
- Heraeus Kulzer GmbH.
- 3M-ESPE.
- Oratio BV.
- Elephant Industries, Hoorn, the Netherlands.
- Mauritsklinieken Den Haag, (dr. M.M.H.M. Meinardi), Amsterdam, the Netherlands.
- Melisa.org, (prof.dr. V. Stejskal), Stockholm, Sweden.
- Department of Immunology, Laboratory dr. M. Sandkamp, B. Köster, dr. R. Hiller, Bremen, Germany (dr. E. Valentine-Thon PhD).
- Albert Schweitzer Ziekenhuis Dordrecht, R. Laeijendekker
- VUmc Department of Immunology (prof. R. Scheper dr M. von Blomberg).
- VUmc Department of Dermatology (dr. Th. Rustemeyer).
- Universität Regensburg, prof.dr. M. Behr.
- University of Geneva, School of Dentistry, Division of Cariology and Endodontology, prof.dr. I. Krejci.
- Nova Southeastern University, Fort Lauderdale, Florida, College of Dental Medicine, dr. Franklin Garcia-Godoy.
- Department of Operative Dentistry, Faculty of Oral and Dental Medicine, Cairo University (dr. A. El Zohairy).
- University of Tanta, Tanta, Egypt, Faculty of Dentistry, Department of Restorative Dentistry (dr. A.I. Abdallah).

## Current PhD projects

**Aboushelib MNM.** Zirconia based all-ceramic restorations. Supervisor: prof.dr. A.J. Feilzer. Start: January 2004.

**Algera TJ.** A material and clinical study of orthodontic cements for fastening brackets. Supervisors: prof.dr. B. Prah-Anderson & prof.dr. A.J. Feilzer. Start: July 2001.

**Dalen A van.** Retention of cantilever resin-bonded bridges. Supervisor: prof.dr. A.J. Feilzer. Start: January 2002

**Kler M de.** Veneering ceramics for zirconia CAD-CAM restorations, Supervisor: prof.dr.ir. J.M. van der Zel. Start: January 2005.

**Keulemans F.** Bridges made of glass fiber enforced composites. Supervisors: prof.dr. A.J. Feilzer & prof.dr. M.A.J. van Waas. Start: January 2005

**Mirmohammadi S.H.** Resin composites for indirect applications. Supervisor: prof.dr. A.J. Feilzer. Start: April 2006.

**Muris J.** Diagnosis of orally related metal allergy. Supervisor: prof.dr. A.J. Feilzer. Start: September 2005.

**Wang H.** All ceramic restorations; material properties for the all ceramic framework. Supervisor: prof.dr. A.J. Feilzer. Start: April 2006.

**Rosentritt M.** Supervisors: prof.dr A.J. Feilzer & prof.dr.ir. J.M. van der Zel. Start: October 2006.

**Ardu S.** Supervisors: prof.dr A.J. Feilzer & prof.dr. I. Krejci. Start: September 2006.

**Garcia Godoy F.** Supervisor: prof.dr. A.J. Feilzer.

**Wendt S.** Approximal wear of resin composite restorations. Supervisor: prof.dr. A.J. Feilzer. Start: January, 2007.

**Vlaar S.** Supervisor: prof.dr ir J.M. van der Zel. Start: January 2007.

**Jongsma LA.** Supervisor: prof.dr. A.J. Feilzer. Start: January 2007.

## Section: Functional Anatomy

### Oral Function and Oral Rehabilitation: Functional Anatomy

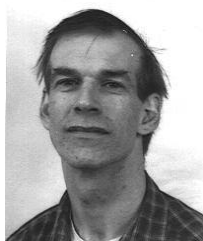
#### Program leader

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#### IOT senior scientists



T.M.G.J. van Eijden



J.H. Koolstra

#### Research objectives

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

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

## Results

Since both the number and the length of activity bursts contribute to the duty time, it was hypothesized that these variables would show intra-day variations similar to those of the duty time. To test this, we determined duty times, burst numbers, and burst lengths per hour, in relation to multiple activity levels, in a 24-hour period of concurrent radiotelemetric long-term electromyograms of various rabbit jaw muscles. The duty times were more highly correlated with the number than with the length of bursts at all activity levels. Thus, the variation of the duty time in rabbit jaw muscles is caused mainly by changes in burst numbers. In a separate study it was hypothesized that changes in fiber-type composition during postnatal development are accompanied by changes in daily activity, and that individuals with muscles showing predominantly slow-type fibers present higher amounts of daily activity than individuals with lower numbers of slow-type fibers. To test these hypotheses, the masseter and digastric muscles of 3 groups of rabbits (young, juvenile and adult) were examined for their phenotype and their daily activity. Fiber-type composition of the muscles was classified by the MyHC content of their fibers, whereas daily activity was characterized by the total daily number of activity bursts. During development, the masseter showed a strong increase in the number of fast-type fibers compared to the number of slow-type fibers. During development, also the number of powerful bursts in the masseter increased. The digastric showed no significant changes in fiber types or burst numbers. These results suggest that activity related influences are of relatively minor importance during development and that other factors are dominant in determining fiber-type composition. In another study, we investigated the postnatal development of the fibre type composition in the jaw muscles of male rabbits. The MyHC content of fibres was determined to classify the muscle fibres. At 20 weeks after birth, the fibre type composition was not different between the muscles. During development the deep temporalis, medial pterygoid, and superficial masseter displayed a similar pattern, i.e. an increase of alpha fibres during early, followed by a decrease during late postnatal development. The deep masseter and superficial temporalis, however, displayed a developmental pattern similar to the jaw openers (digastric and lateral pterygoid), i.e. a fair increase of alpha fibres during early development which levelled during late development. The superficial temporalis and the deep masseter deviated from the developmental pattern found in other jaw-closing muscles.

Using microCT we have been able to determine the porosity and three-dimensional orientation of the cortical canalicular network in the human mandibular condyle. We hypothesized differences in porosity and orientation of cortical canals between various cortical regions. In addition, as a larger cortical and trabecular porosity are likely to coincide with a greater surface area of cortical canals and trabeculae available for osteoblastic and osteoclastic activity, we hypothesized that this surface area is inversely proportional to the degree of mineralization of cortical and trabecular bone, respectively. The orientation of cortical canals differed significantly between the cortical regions; in contrast, cortical porosity (average 3.5%) did not differ significantly. The results suggest that adaptive remodeling is independent and different between trabecular and cortical bone. We concluded that the principal directions of stresses and strains are presumably directed mediolaterally in the subchondral cortex and superoinferiorly in the anterior and posterior cortex, that the amount of remodeling is larger in the trabecular than in the cortical bone of the mandibular condyle, and that in trabecular bone variation in the amount of remodeling is related to the available surface area of the trabeculae.

We also used microCT to analyze in pigs the postnatal simultaneous changes in microarchitecture and mineralization of the mandibular cancellous bone. Both the mean degree of mineralization and intratrabecular differences in mineralization between the surfaces and cores of trabecular elements increased during development. The trabecular surfaces were more highly mineralized in the older condyles compared to the younger ones. Together with the observed decrease of the relative size of trabecular surface, this finding suggests a decrease in (re)modeling activity during development. It was concluded that most developmental changes in cancellous bone occur until the age of 40 weeks postpartum.

By combining nanoindentation and microCT, we investigated the relation between bone tissue stiffness and degree of mineralization distribution and to examine possible changes during prenatal development of pig mandibular condyles. Intratrabecular variations in bone tissue stiffness and degree of mineralization showed a similar pattern; low at trabecular surfaces and higher in the cores. It was concluded that bone tissue in fetal and newborn trabecular cores resembles adult trabecular bone tissue properties and is distributed in a regular radial pattern in trabeculae.

Using finite element modelling and viscoelastic material models for the temporomandibular joint disc, the applicability of a material model that takes the viscous behavior at a wide range of frequencies into account was assessed. To that purpose a non-linear multi-mode Maxwell model was tested in cyclic large-strain compression tests. Its material constants were approximated from dynamic small-strain shear deformation tests. The storage and loss moduli as obtained from a disc sample could be approximated with a four-mode Maxwell model. In simulated large-strain compression tests it behaved similarly as observed from the experimental tests. The underestimation of energy dissipation, as obtained from a single-mode Maxwell model was considerably reduced, especially for deformations with a higher strain rate. Furthermore, in contrast to the latter it was able to predict the increase of the stress amplitude with the compression frequency much better.

### Academic personnel in 2006 and 2007

<b>Research staff ACTA - AN (in full time equivalents)</b>				
<b>position</b>	<b>name</b>	<b>fte 2006</b>	<b>plan 2007</b>	<b>funding</b>
Full professors	Eijden, prof.dr. T.M.G.J. van*	0,50	0,10	1
	Weijs, prof.dr. W.A.	--	0,10	1
Senior lecturer	Koolstra, dr.ir. J.H.	0,70	0,70	1
Lecturer	Langenbach, dr. G.E.J.	0,60	0,60	1
<b>Total tenured staff</b>		<b>1,80</b>	<b>1,50</b>	
Non tenured staff	Chen, prof.dr. Y.	--	0,10	guest
	Cioffi, drs. I.	0,05	0,05	guest
	Kawai, dr. N.	0,05	0,05	guest
	Mulder, ir. L.	--	0,70	1
	Sano, dds. R.	0,10	--	guest
	Tanaka, dr. E.	0,05	0,05	guest
PhD students	Jong, drs. W.C. de	0,25	0,70	1
	Mulder, ir. L.	0,70	0,05	1
	Tuyt, drs. M.	--	0,25	1
	Wessel, drs. T. van	0,25	--	1
	Willems, drs. N.M.B.K.	0,20	0,30	1
<b>Total non tenured staff</b>		<b>1,65</b>	<b>2,25</b>	
total 1st funding		3,20	3,50	1
total guests		0,25	0,25	guest
<b>Total research staff</b>		<b>3,45</b>	<b>3,75</b>	

\* We regret to mention that prof. Van Eijden has past away early 2007.

### Dissertations

Wessel, T. van (2006, January 26). Daily activity of developing jaw muscles. UvA Universiteit van Amsterdam (141 pag.). Prom./coprom.: prof.dr. T.M.G.J. van Eijden, & dr. G.E.J. Langenbach.

### Publications in journals indexed in SCI

Eijden, T.M.G.J. van, Helm, P.N. van der, Ruijven, L.J. van, & Mulder, L. (2006). Structural and mechanical properties of mandibular condylar bone. J DENT RES, 85, 33-37.

Geraets, W.G.M., Ruijven, L.J. van, Verheij, J.G.C., Eijden, T.M.G.J. van, & Stelt, P.F. van der (2006). A sensitive method for measuring spatial orientation in bone structures. DENTOMAXILLOFAC RAD, 35, 319-325.

- Goto, T.K., Nishida, S., Yahagi, M., Langenbach, G.E.J., Nakamura, Y., Tokumori, K., Sakai, S., Yabuuchi, H., & Yoshiura, K. (2006). Size and orientation of masticatory muscles in patients with mandibular laterognathism. *J DENT RES*, 85, 552-556.
- Grünheid, T., Langenbach, G.E.J., Zentner, A., & Eijden, T.M.G.J. van (2006). Duty time of rabbit jaw muscles varies with the number of activity bursts. *J DENT RES*, 85, 1112-1117.
- Hansma, H.J., Langenbach, G.E.J., Koolstra, J.H., & Eijden, T.M.G.J. van (2006). Passive resistance increases differentially in various jaw displacement directions. *J DENT*, 34, 491-497.
- Hirose, M., Tanaka, E., Tanaka, M., Fujita, R., Kuroda, Y., Yamano, E., Eijden, T.M.G.J. van, & Tanne, K. (2006). Three-dimensional finite element model of the human temporomandibular joint disc during prolonged clenching. *EUR J ORAL SCI*, 114, 441-448.
- Koolstra, J.H., & Eijden, T.M.G.J. van (2006). Prediction of volumetric strain in the temporomandibular joint cartilage during jaw movement. *J ANAT*, 209, 369-380.
- Korfage, J.A.M., Wessel, T. van, Langenbach, G.E.J., & Eijden, T.M.G.J. van (2006). Heterogeneous postnatal transitions in myosin heavy chain isoforms within the rabbit temporalis muscle. *ANAT REC PART A*, 288A, 1095-1104.
- Korfage, J.A.M., Wessel, T. van, Langenbach, G.E.J., Ay, F., & Eijden, T.M.G.J. van (2006). Postnatal transitions in myosin heavy chain isoforms of the rabbit masseter and digastric muscle. *J ANAT*, 208, 743-751.
- Langenbach, G.E.J., Zhang, F., Herring, S.W., Eijden, T.M.G.J. van, & Hannam, A.G. (2006). Dynamic mechanics in the pig mandibular symphysis. *J ANAT*, 209, 69-78.
- Mulder, L., Koolstra, J.H., & Eijden, T.M.G.J. van (2006). Accuracy of MicroCT in the quantitative determination of the degree and distribution of mineralization in developing bone. *ACTA RADIOL*, 47, 882-883.
- Mulder, L., Koolstra, J.H., Jonge, H.W., & Eijden, T.M.G.J. van (2006). Architecture and mineralization of developing cortical and trabecular bone of the mandible. *ANAT EMBRYOL*, 211, 71-78.
- Mulder, L., Groningen, L.B. van, Potgieser, Y.A., Koolstra, J.H., & Eijden, T.M.G.J. van (2006). Regional differences in mineralization of developing mandibular bone. *ANAT REC*, 288A, 954-961.
- Renders, G.A.P., Mulder, L., Ruijven, L.J. van, & Eijden, T.M.G.J. van (2006). Degree and distribution of mineralization in the human mandibular condyle. *CALCIFIED TISSUE INT*, 79, 190-196.
- Tanaka, E., Hirose, M., Yamano, E., Dalla-Bona, D.A., Fujita, R., Tanaka, M., Eijden, T.M.G.J. van, & Tanne, K. (2006). Age-associated changes in viscoelastic properties of the bovine temporomandibular joint disc. *EUR J ORAL SCI*, 114, 70-73.
- Tanaka, E., Inubushi, T., Koolstra, J.H., Eijden, T.M.G.J. van, Sano, R., Takahashi, K., Kawai, N., Rego, E.B., & Tanne, K. (2006). Comparison of dynamic shear properties of the porcine molar and incisor periodontal ligament. *ANN BIOMED ENG*, 34, 1917-1923.
- Tanaka, E., Yamano, E., Dalla-Bona, D.A., Watanabe, M., Inubushi, T., Shirakura, M., Sano, R., Takahashi, K., Eijden, T.M.G.J. van, & Tanne, K. (2006). Dynamic compressive properties of the mandibular condylar cartilage. *J DENT RES*, 85, 571-575.
- Tanaka, E., Ishino, Y., Sasaki, A., Hasegawa, T., Watanabe, M., Dalla-Bona, D.A., Yamano, E., Eijden, T.M.G.J. van, & Tanne, K. (2006). Fibroblast growth factor-2 augments recombinant human bone morphogenetic protein-2-induced osteoinductive activity. *ANN BIOMED ENG*, 34, 717-725.
- Tanaka, E., Dalla-Bona, D.A., Iwabe, T., Kawai, N., Yamano, E., Eijden, T.M.G.J. van, Tanaka, M., Miyauchi, M., Takata, T., & Tanne, K. (2006). The effect of removal of the disc on the friction in the temporomandibular joint. *J ORAL MAXILLOFAC SURG*, 64, 1221-1224.
- Wessel, T. van, Langenbach, G.E.J., Brugman, P., Korfage, J.A.M., & Eijden, T.M.G.J. van (2006). Daily activity of the rabbit jaw muscles during early postnatal development. *NEUROSCIENCE*, 140, 137-146.

### **Other scientific publications**

- Geraets, W.G.M., Ruijven, L.J. van, Verheij, H., Eijden, T.M.G.J. van, & Stelt, P.F. van der (2006). A sensitive method for measuring spatial orientation in bone structures. Fifth Quinquennial Review 2001-2006 CD-ROM publication of the Dutch Society of Pattern Recognition and Image Processing (Paper 12): (2006, November 05).

### **Professional publications**

- Baart, J.A., Diermen, D.E. van, & Eijden, T.M.G.J. van (2006). Parese na mandibulaire blok anesthesie. *NED TIJDSCHR TANDHEELKD*, 113, 418-420.

## External reports

Koolstra, J.H. (2006). Kaakbewegingsmogelijkheden voor en tandprothese stabilisator. Amsterdam: ACTA. Contractonderzoek voor A. van der Kerken. 9 pp.

## Indicators of Esteem

### Grants: current projects with external funding

Koolstra J.H., Eijden T.M.G.J. van, Ruijven, L.J. van (2006). Influence of mineral density on the stresses and strains in trabecular bone of the mandibular bone. NWO-National Computer Facilities project SG-06-253; 150,000 pnu (€ 18,000).

### Scientific awards/honours

Wessel, T. van, Langenbach, G.E.J., Korfage, J.A.M., Brugman, P., Kawai, N., Tanaka, E., & Eijden, T.M.G.J. van (2006). Fiber-type composition of rabbit jaw muscles is related to their daily activity. Bohn Stafleu van Loghum/Thoden van Velzen Research Prize 2006: Lunteren (February 02 - 03).

### Organisation of international congresses or symposia

Eijden, T.M.G.J. van (2006). TMJ replacement and tissue engineering. International Symposium: Hiroshima (March 20 - 21).

### Invited speaker at international symposia

Koolstra, J.H., & Eijden, T.M.G.J. van (2006, March 20). Contribution of Finite Element modeling to assessment of TMJ loading patterns. Hiroshima, International Symposium.

Ruijven, L.J. van (2006, October 16). Mechanical significance of the trabecular microstructure of the human mandibular condyle. University of Naples, Italy, Symposium Dept. of Orthodontics.

### Other international functions

Koolstra, J.H.: Member International Scientific Committee. 5th World Congress of Biomechanics: Munich, Germany. 2006, June 29 & August 4.

## Collaborations

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

## Current PhD projects

**Grünheid T.** Supervisors: dr. G.E.J. Langenbach, prof.dr. A. Zentner & prof.dr. T.M.G.J. van Eijden. Title project: Influence of food hardness and consistency on jaw muscle and jaw bone adaptation. Start project: 2006.

**Jong WC de.** Supervisors: dr. G.E.J. Langenbach, prof.dr. T.M.G.J. van Eijden. Title project: Influence of muscle use on bone adaptation. Start project: 2006.

**Mulder L.** Supervisors: dr. J.H. Koolstra & prof.dr. T.M.G.J. van Eijden. Title project: Structure and mechanical properties of developing mandibular bone. Start project: 2003.

**Wessel T van.** Supervisors: dr. G.E.J. Langenbach & prof.dr. T.M.G.J. van Eijden. Title project: Daily activity of the masticatory muscles during development. Start project: 2002.

**Willems NMBK.** Supervisors: dr. G.E.J. Langenbach, dr. T. Grünheid, prof.dr. A. Zentner & prof.dr. T.M.G.J. van Eijden. Title project: Development of architecture and mineralization of cortical and trabecular bone of the mandible. Start project: 2006.

## Section: Oral Biochemistry

### Protective Functions of Saliva for the Oral Cavity

#### Program leader

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#### IOT senior scientists and full professors



A. van NieuwAmerongen



E.C.I. Veerman

#### Research objectives

Without saliva all oral tissues will be affected by exogenous factors as microorganisms and aggressive nutritional components. Saliva apparently protects oral surface tissues against harmful attacks. The primary aim of the research of the Department of Oral Biochemistry is to analyse the contribution of the individual salivary components, particularly of the (glyco) proteins to maintain oral tissues healthy, also in relation to microbiological aspects of oral infections. The research is focussed on answering the following questions:

1. What are the biological functions of the salivary (glyco) proteins and subsequently what is the biological significance of the variation in glandular (glyco) proteins from the submandibular, sublingual and parotid glands?
2. What is the biological significance of the whole set of salivary proteinase inhibitors, particularly the specific salivary cystatins? Are they involved in the regulation of oral inflammatory processes? What is the relation between immuno-neuro-regulatory processes in the periodontium and mucosa and the expression of inhibitory proteins in the salivary glands?
3. Can synthetic peptide analogues of histatins be applied as broad spectrum antibiotics, particularly to *Candida albicans* and other oral pathogens? In future such peptides might be useful in newly developed saliva substitutes.
4. The effect of conditions known for their potential to impair oral health (such as the use of medical drugs, systemic diseases and psychological stress) on the quality of saliva.
5. Influence of saliva on the interaction of oral microorganisms with oral epithelial cells.

#### Results

##### **Energy metabolism and sensitivity to salivary antimicrobial peptides**

The effect of the target cells metabolism on the microbicidal activity of antimicrobial peptides has been investigated. Lowering the energy charge of *C. albicans* renders the yeast insensitive to antimicrobial peptides such as Histatin 5. Evidence has been obtained suggesting a role of the membrane fluidity in this process. Future research to the molecular basis underlying the desensitizing effects will provide insight in factors controlling the sensitivity of target cells under more physiological conditions, and provides clues for development of more potent antimicrobial peptides.

The structure-function relation has been investigated of Lfampin, an antimicrobial domain in bovine lactoferrin that was recently discovered by us. The N-terminal part of Lfampin induces the formation of a helical peptide structure, resulting in enhanced killing activity against *C. albicans* and a series of Gram-positive and Gram-negative bacteria. Moreover this peptide possessed out of a large series of membrane active peptides the highest HIV-1 neutralizing activities, measured in collaboration with dr. F. Groote and prof.dr. B. Berkhout of the Department of Human Retrovirology, AMC. We have succeeded in liberating this active domain from the native lactoferrin by a one-enzyme protocol. In lactoferrin the LFampin domain is situated in close vicinity to the previously described antimicrobial domain LFCin. To mimic this active site we have constructed a chimerical peptide in which LFampin and LFCin are linked. This chimerical peptide possessed enhanced activity against a.o. *C. albicans*. Strikingly, whereas the separated peptides are inactive against *Helicobacter pylori*, a low concentration of the chimerical peptide kills this pathogen. In the next year the effects of Lfampin on morphological and biophysical aspects of membranes will be studied in collaboration with dr. J. van Marle and dr. M. Bastos, University of Porto.

### **Antimicrobial peptides against the stomach pathogen *Helicobacter pylori***

In a project funded by the MLDS we have investigated the applicability of antimicrobial peptides against *Helicobacter pylori*. The unique conditions of the niche of *H. pylori* present in the stomach, e.g., low pH, proteolytic activity, and a mucous environment, hamper the bactericidal activity of defence systems. Screening of *H. pylori* with previously developed antimicrobial peptides indicated the human cathelicidin peptide LL-37 as the most promising candidate for fighting *H. pylori*. Truncated derivatives of LL37 as well as its all-D isomer possessed a higher bactericidal activity than the parent molecule. Sub-lethal doses of these variant peptides sharply increased the sensitivity to amoxicillin of an amoxicillin-resistant strain of *H. pylori*. LL-37 interfered in the pH-dependent adherence of *H. pylori* to the salivary mucin MUC5b and in the pH-undependable binding to MUC7.

### **Saliva as intermediate between epithelium and micro-organisms**

A new PhD project has started, which focusses on the role of saliva in the homeostasis of the epithelium-saliva-microorganism milieu. An epithelial cells test systems has been set up using Transwell® plates which enables the culture of cells at the air-medium interface and intervention at both sites. Currently this system is used for investigating the overall effects of glandular salivas on the maintenance and proliferation of epithelial cells, in the presence and absence of the yeast *C. albicans*. In the following stage the effects of specific salivary components such as LL-37, defensins, lactoferrin and lactoferrin derived peptides will be examined.

### **Binding characteristics of salivary agglutinin**

A large number of bacteria were tested for binding of salivary agglutinin (SAG) and a peptide representing the binding site of SAG. There was a good correlation between binding to the parent SAG molecule and the peptide for a number of different bacterial species, suggesting that this peptide domain is responsible for the broad-binding properties of SAG. By an alanine scan was demonstrated that all bacteria shared a common binding motif within this peptide, although small differences in critical residues were found. In collaboration with dr T. van de Berg (Molecular Cell Biology, VUmc) it was shown that a homologous fragment of the SRCR 3 domain of SAG in the immune protein CD163 plays a role in phagocytosis of haptoglobin-hemoglobin complexes. In collaboration with dr. K. Hartshorn (New York) it was shown that salivary agglutinin could bind and neutralize influenza A viruses. This virus inhibiting activity depended on the presence of 2,3 bound sialic acid and varied with the tissue source (lung vs. saliva) and donor source of the proteins.

Future research will be aimed at identification of the bacterial receptor for SAG. Another part of the research will focus on the mutual effects that SAG binding to salivary proteins, including salivary gA and lactoferrin, will have on the activity.

**Academic personnel in 2006 and 2007**

<b>Research staff ACTA - OB (in full time equivalents)</b>				
<b>position</b>	<b>name</b>	<b>fte 2006</b>	<b>plan 2007</b>	<b>funding</b>
Full professors	Nieuw Amerongen, prof.dr. A. van	0,50	0,40	1
	Veerman, prof.dr. E.C.I.	0,70	0,70	1
Lecturers and other tenured research staff	Bolscher, dr. J.G.M.	0,70	0,70	1
	Brand, dr. H.S.	0,40	0,40	1
	Ligtenberg, dr. A.J.M.	0,20	0,70	1
	Ligtenberg, dr. A.J.M.	0,50	--	3
<b>Total tenured staff</b>		<b>3,00</b>	<b>2,90</b>	
PhD students	Leito, ing. J.T.L.	0,70	0,70	1
	Oudhoff, drs. M.J.	0,50	0,70	1
<b>Total non tenured staff</b>		<b>1,20</b>	<b>1,40</b>	
total 1st funding		3,70	4,30	1
total 3rd funding		0,50	--	3
<b>Total research staff</b>		<b>4,20</b>	<b>4,30</b>	

**Dissertations**

Hertog, A.L. den (2006, January 27). Membrane effects of LL-37 and histatin 5 in relation to their antimicrobial activity. Vrije Universiteit Amsterdam (151 pag.). Prom./coprom.: prof.dr. A. van Nieuw Amerongen, prof.dr. E.C.I. Veerman, & dr. J.G.M. Bolscher.

**Publications in journals indexed in SCI**

- Bolscher, J.G.M., Kraan, M.I.A. van der, Nazmi, K., Kalay, H., Grün, C.H., Groenink, J., Hof, W. van 't, Veerman, E.C.I., & Nieuw Amerongen, A. van (2006). A one-enzyme strategy to release an antimicrobial peptide from the LFampin-domain of bovine lactoferrin. *PEPTIDES*, 27, 1-9.
- Bots, C.P., Poorterman, J.H.G., Brand, H.S., Kalsbeek, H., Amerongen, B.M. van, Veerman, E.C.I., & Nieuw Amerongen, A. van (2006). The oral health status of dentate patients with chronic renal failure undergoing dialysis therapy. *ORAL DIS*, 12, 176-180.
- Gabriel, M.O., Nieuw Amerongen, G.P. van, Hinsbergh, V.W.M. van, Nieuw Amerongen, A. van, & Zentner, A. (2006). Direct grafting of RGD-motif containing peptide on the surface of polycaprolactone films. *J BIOMAT SCI-POLYM E*, 17, 567-577.
- Gabriel, M.O., Nazmi, K., Veerman, E.C.I., Nieuw Amerongen, A. van, & Zentner, A. (2006). Preparation of LL-37-grafted titanium surfaces with bactericidal activity. *BIOCONJUGATE CHEM*, 17, 548-550.
- Groot, F. de, Sanders, R.W., Brake, O. ter, Nazmi, K., Veerman, E.C.I., Bolscher, J.G.M., & Berkhout, B. (2006). A histatin 5 derived peptide with improved fungicidal properties enhances HIV-1 replication by promoting viral entry. *J VIROL*, 80, 9236-9243.
- Hartskorn, K.L., Ligtenberg, A.J.M., White, M.R., Eijk, M. van, Hartshorn, M., Pemberton, L., Holmskov, U., & Crouch, E. (2006). Salivary agglutinin and lung scavenger receptor cysteine-rich glycoprotein 340 have broad anti-influenza activities and interactions with surfactant protein D that vary according to donor source and sialylation. *BIOCHEM J*, 393, 545-553.
- Hertog, A.L. den, Marle, J. van, Veerman, E.C.I., Valentijn-Benz, M., Nazmi, K., Kalay, H., Grün, C.H., Hof, W. van 't, Bolscher, J.G.M., & Nieuw Amerongen, A. van (2006). The human cathelicidin peptide LL-37 and truncated variants induce segregation of lipids and proteins in the plasma membrane of *Candida albicans*. *BIOL CHEM*, 387, 1495-1502.
- Kraan, M.I.A. van der, Nazmi, K., Hof, W. van 't, Nieuw Amerongen, A. van, Veerman, E.C.I., & Bolscher, J.G.M. (2006). Distinct bactericidal activities of bovine lactoferrin peptides LF-ampin 268-284 and LF-ampin 265-284: Asp-Leu-Ile sequence makes the difference. *BIOCHEM CELL BIOL*, 84, 358-362.

- Kämper, N., Day, P.M., Nowak, T., Selinka, H.C., Florin, L., Bolscher, J.G.M., Hilbig, L., Schiller, J.T., & Sapp, M. (2006). A membrane-stabilizing peptide in capsid protein L2 is required for egress of papillomavirus genomes from endosomes. *J VIROL*, 80, 759-768.
- Stallmann, H.P., Faber, C., Nieuw Amerongen, A. van, & Wuijsman, P.I.J.M. (2006). Antimicrobial peptides, their application in musculoskeletal infections: review. *INJURY*, 37, S34-S40.
- Stallmann, H.P., Faber, C., Bronckers, A.L.J.J., Nieuw Amerongen, A. van, & Wuisman, P.I.J.M. (2006). In vitro gentamicin release from commercially available calcium-phosphate bone substitutes influence of carrier type on duration of the release profile. *BMC MUSCULOSKEL DIS*, 26, 7-18.
- Szynol, A.T., Haard, J.J. de, Veerman, E.C.I., Soet, J.J. de, & Nieuw Amerongen, A. van (2006). Design of a peptibody consisting of the antimicrobial peptide dhvar5 and a llama variable heavy-chain antibody fragment. *CHEM BIOL*, 67, 425-431.

### Other scientific publications (international, refereed)

- Brand, H.S., Bruins, M.L., Veerman, E.C.I., & Nieuw Amerongen, A. van (2006). Secretion rate and amylase concentration of whole saliva after consumption of beer. *INT J DENT HYG*, 4, 160-161.
- Brand, H.S., & Vissink, A. (2006). General pathology. In R. Ireland (Ed.), *Clinical Textbook of Dental Hygiene and Therapy* (pp. 29-50). Oxford: Blackwell Munksgaard.
- Ligtenberg, A.J.M., Brand, H.S., Bots, C.P., & Nieuw Amerongen, A. van (2006). The effect of toothbrushing on secretion rate, pH and buffering capacity of saliva. *INT J DENT HYG*, 4, 104-105.

### Professional publications

- Baart, J.A., & Brand, H.S. (2006). *Lokale anesthesie in de tandheelkunde*. Houten: Bohn Stafleu Van Loghum.
- Bartelsman, J.F.W.M., Depla, A.C.T.M., & Brand, H.S. (2006). Ziekten van het maag-darmkanaal. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene ziekteleer voor tandartsen* (pp. 13:169-188). Houten/Diegem: Bohn Stafleu Van Loghum.
- Bots, C.P. (2006). Orale aspecten bij chronisch nierfalen. *ACTA QP*, 2, 156-159.
- Bots, C.P. (2006). Speekselonderzoek neemt grote vlucht. *ACTA QP*, 2, 124-127.
- Bots, C.P., Brand, H.S., Franse, R.L., & Nieuw Amerongen, A. van (2006). Nierfalen en mondgezondheid. *NED TIJDSCHR TANDHEELKD*, 113, 182-185.
- Brand, H.S. (2006). De implanteerbare cardiale defibrillator in de tandartspraktijk. *ACTA QP*, 2, 172-175.
- Brand, H.S. (2006). Nieuwe richtlijnen voor het verrichten van reanimatie bij volwassenen. *NED TIJDSCHR TANDHEELKD*, 113, 243-246.
- Brand, H.S., & Blanksma, C.J. (2006). Cocaïnegebruik een toenemend probleem. *NED TANDARTSENBLAD*, 61, 26-27.
- Brand, H.S., & Bots, C.P. (2006). Mondgezondheid van Crohnpatiënten. *ACTA QP*, 1, 28-33.
- Brand, H.S., & Fennis, J.F.M. (2006). Risicopatiënten. In J.A. Baart & H.S. Brand (Eds.), *Lokale anesthesie in de tandheelkunde* (pp. 139-150). Houten: Bohn Stafleu Van Loghum.
- Brand, H.S., Diermen, D.E. van, & Fennis, J.F.M. (2006). Acute situaties in de tandheelkundige praktijk. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene ziekteleer voor tandartsen. 2e herziene druk* (pp. 315-321). Houten/Diegem: Bohn Stafleu Van Loghum.
- Brand, H.S., Diermen, D.E. van, & Makkes, P.C. (2006). *Algemene ziekteleer voor tandartsen. 2e herziene druk*. Houten/Diegem: Bohn Stafleu Van Loghum.
- Brand, H.S., Frankhuijzen, A.L., & Fennis, J.F.M. (2006). Systemische complicaties. In J.A. Baart & H.S. Brand (Eds.), *Lokale anesthesie in de tandheelkunde* (pp. 129-138). Houten: Bohn Stafleu Van Loghum.
- Cornelissen, J.J., & Brand, H.S. (2006). Kwaadaardige aandoeningen van het immuunsysteem. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene ziekteleer voor tandartsen* (pp. 5:61-68). Houten/Diegem: Bohn Stafleu Van Loghum.
- Diermen, D.E. van, Brand, H.S., & Makkes, P.C. (2006). De medische anamnese in de tandheelkundige praktijk. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene ziekteleer voor tandartsen* (pp. 1:11-18). Houten/Diegem: Bohn Stafleu Van Loghum.
- Diermen, D.E. van, Brand, H.S., & Vissink, A. (2006). Het belang van een goede medische anamnese. *NED TIJDSCHR TANDHEELKD*, 113, 172-175.
- Gambon, D.L., Keijbus, P.A.M. van den, & Nieuw Amerongen, A. van (2006). Snoepsprays en gels: invloed op speekselsecretie en zuurgraad. *CONTACTPUNT*, 4, 19-23.
- Gambon, D.L., Keijbus, P.A.M. van den, & Nieuw Amerongen, A. van (2006). Snoepsprays en gels: invloed op speekselsecretie en zuurgraad. *NED TIJDSCHR TANDHEELKD*, 113, 27-32.
- Heine, R.J., Stehouwer, C.D.A., & Brand, H.S. (2006). Diabetes mellitus. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene ziekteleer voor tandartsen* (pp. 15:199-212). Houten/Diegem: Bohn Stafleu Van Loghum.

- Hilbrands, L.B., Huysmans, F.T.M., & Brand, H.S. (2006). Aandoeningen van nieren en urinewegen. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene ziekteleer voor tandartsen* (pp. 10:131-144). Houten/Diegem: Bohn Stafleu Van Loghum.
- Laar, J.M. van, Breedveld, F.C., & Brand, H.S. (2006). Reumatische ziekten. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene ziekteleer voor tandartsen* (pp. 19:249-264). Houten/Diegem: Bohn Stafleu Van Loghum.
- Montfrans, G.A. van, Lieshout, J.J. van, & Brand, H.S. (2006). Hypertensie en circulatiestoornissen. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene ziekteleer voor tandartsen* (pp. 8:99-108). Houten/Diegem: Bohn Stafleu Van Loghum.
- Nieuw Amerongen, A. van (2006). Droge mond: oorzaak en gevolg. *ACTA QP*, 2, 139-146.
- Nieuw Amerongen, A. van (2006). Speeksel als spiegel van ons lichaam. *ACTA QP*, 2, 128-132.
- Nieuw Amerongen, A. van, & Veerman, E.C.I. (2006). Speeksel: een spiegel van ons lichaam. *ACTA QP*, 1, 47-51.
- Nieuw Amerongen, A. van, Veerman, E.C.I., Brand, H.S., & Vissink, A. (2006). Speeksel: een mondoverstijgende gezondheidsfactor. *NED TIJDSCHR TANDHEELKD*, 113, 176-181.
- Suikerbuijk, E., Brand, H.S., & Nieuw Amerongen, A. van (2006). Het speekselspreekuur – kenmerken van patiënten met het burning mouth syndroom en smaakstoornissen. *NED TANDARTSENBLAD*, 61, 18-19.
- Veerman, E.C.I. (2006). Oorzaken en behandeling van sialorroe. *ACTA QP*, 2, 133-138.
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- Vissink, A., Nieuw Amerongen, A. van, & Spijkervet, F.K.L. (2006). Bijwerkingen van geneesmiddelen in het orofaciale gebied. In H.S. Brand, D.E. van Diermen, & P.C. Makkes (Eds.), *Algemene ziekteleer voor tandartsen* (pp. 23:301-314). Houten/Diegem: Bohn Stafleu Van Loghum.
- Vissink, A., Spijkervet, F.K.L., Burlage, F.R., Veerman, E.C.I., & Nieuw Amerongen, A. van (2006). Hyposialie als gevolg van radiotherapie en chemotherapie: preventie en behandeling. *ACTA QP*, 2, 148-155.

## **External reports**

- Bolscher, J.G.M. (2006). Lactoferrine: structure, function and application. Report for Campina-DMV International. Amsterdam: ACTA. 12 pp.
- Bolscher, J.G.M. (2006). Ontwikkeling van antimicrobiële peptiden voor de bestrijding van *Helicobacter pylori* (eindverslag medisch wetenschappelijk onderzoek, MLDS). Report for Maag-Lever-Darmstichting. Amsterdam: ACTA. 3 pp.

## **Indicators of Esteem**

### **Grants: current projects with external funding**

- Bolscher, J.G.M., Veerman, E.C.I. & Nieuw Amerongen A. van Ontwikkeling van antimicrobiële peptiden voor de bestrijding van *Helicobacter pylori* Maag-Lever-Darm Stichting (€1000512,- April 2004 April 2006).
- Grant from Thailand government, covering: PhD-student, visits to foreign research labs and visits of co-investigators to Khon Kaen university. Principal Investigator: prof.dr. Suwimol Taweekhaisupapong, Department of Oral Diagnosis, Faculty of Dentistry, and Melioidosis Research Center, Khon Kaen University, Thailand. Co-Investigators: dr. Surasakdi Wongratanacheewin, Melioidosis Research Center, and Department of Microbiology, Faculty of Medicine, Khon Kaen University, Thailand. Dr. J.G.M. Bolscher, prof.dr. A. van Nieuw Amerongen, Academic Centre for Dentistry Amsterdam (ACTA), the Netherlands.

### **Membership of international editorial boards**

- Brand, H.S.: J DENT RES  
Nieuw Amerongen, A. van: ODONTOLOGY

## Invited speakers at international congresses or symposia

- Ligtenberg, A.J.M. (2006, October 10). Oral samples/Oral diseases: from detection to diagnostics. Atlanta, USA, Oral-based diagnostics.
- Nieuw Amerongen, A. van (2006, October 10). Biochemistry/Physiology of saliva: implications for diagnostics. Atlanta, USA, Oral-based Diagnostics.
- Nieuw Amerongen, A. van (2006, January 06). Gastcolleges. Thailand, University of Khon Kaen, Bangkok and Chang Mai.
- Nieuw Amerongen, A. van (2006, May 23). Mucosal secretions like sweat, saliva etc. Port Sunlight, Brainstorm session Unilever.
- Veerman, E.C.I. (2006, June 01). The salivary film, aspects of its role and formation. Brisbane, Australia, International Association of Dental Research (IADR), 84th General Session and Exhibition.

## Scientific awards/honours

- Suikerbuijk, E. (2006). NT Scriptieprijs. Het speekselspreekuur - karakteristieken van patiënten met het burning mouth syndrome. Supervisors: dr. H.S. Brand and prof.dr. A. van Nieuw Amerongen.

## Other international functions

- Bolscher, J.G.M.: Co-investigator and co-promotor thesis: Antimicrobial peptides against Burkholderia pseudomalle. University of Khon Kaen.
- Ligtenberg, A.J.M.: Organizer committee. Oral Based Diagnostics.
- Nieuw Amerongen, A. van: Jury G. Bachrach: Identification of a human salivary factor that protects antimicrobial peptides from degradation by pathological pathogens. Israel Science Foundation.

## Collaborations

- VUmc, afdeling Medische Microbiologie (prof.dr. C.M.J.E Vandenbroucke-Grauls, dr. B. Appelmek).
- VUmc, afd. Orthopedie (prof.dr. P.I.J.M Wuijsman).
- VUmc, afdeling Moleculaire Celbiologie en Immunogenetica, sectie Immunomodulatie (dr. T. van den Berg, dr. T.B.H. Geijtenbeek).
- VUmc, afdeling Moleculaire Celbiologie en Immunogenetica, sectie Glycoimmunologie (dr. I van Die).
- VUmc, afdeling Toxicologie (dr. Micaela Damsten).
- Universiteit van Amsterdam, AMC, afdeling Celbiologie en Histologie (dr. J. van Marle).
- Universiteit van Amsterdam, AMC, afdeling Humane Retrovirologie (prof.dr. B. Berkhout).
- Rode Kruisziekenhuis Beverwijk, Skin regeneration and woundhealing (prof.dr. E. Middelkoop, dr. B. Ulrich).
- Rijksuniversiteit Groningen, afdeling Mondziekten en Kaakchirurgie (prof.dr. A. Vissink).
- Leiden Universitair Medisch Centrum (dr. M.M. Welling).
- DMV-Campina (dr. J. Steins en dr. R. de Waart).
- TNO Defence, Security and Safety (dr. F.J. Bikker).
- University of Chile, Santiago, Institute of Biomedical Sciences (prof.dr. M. González).
- University of Madrid, Centro de Investigaciones Biológicas (prof.dr. L. Rivas).
- University of Oporto, Portugal, Dept. of Chemistry (dr. M. Bastos).
- Khon Kaen University, Thailand. Dept. of Oral Diagnosis (dr. S. Taweekaisupapong).
- University of Aquila (Italy), Department of Biomedical Sciences and Technology (dr. A. Bozzi).
- Deutsche Krebsforschungszentrum Division of Molecular Genome Analysis, Heidelberg (prof.dr. A.-M. Poustka, dr. J. Mollenhauer).
- University of California at Los Angeles. Dept. of Oral Biology and Medicine (prof.dr. D.T. Wong).

## Current PhD projects

- Leito JTD.** The interaction of salivary agglutinin/DMBT1 with oral micro-organisms and its influence on biofilm formation. Supervisor: prof. dr. A. van Nieuw Amerongen & prof.dr. E.C.I. Veerman; co-supervisor: dr. A.J.M. Ligtenberg. Start: October 2005.
- Oudhoff MJ.** The role of saliva in the micro-environment: epithelium-saliva-microorganisms. Supervisors: prof.dr. E.C.I.Veerman & prof.dr. A. van Nieuw Amerongen; co-supervisor: dr. J.G.M. Bolscher. Start: April 2006.

## Appendix

List of SCI journals, their impact factors and the number of ACTA publications in 2006 in each journal

<u>Tijdschrift</u>	<u>IF</u>	<b>Number of publications</b>	<u>Tijdschrift</u>	<u>IF</u>	<b>Number of publications</b>
ACTA RADIOL	1.031	1	INT ENDOD J	1.606	4
AM J ORTHOD DENTOFAC	0.916	2	INT J ORAL MAX SURG	1.123	4
ANAT EMBRYOL	1.255	1	INT J RADIAT ONCOL	4.556	1
ANAT REC PART A	1.807	2	J ANAT	2.010	4
ANGLE ORTHOD	0.778	1	J BIOMAT SCI-POLYM E	1.409	1
ANN BIOMED ENG	1.997	2	J BONE MINER RES	6.527	4
APPL ENVIRON MICROB	3.818	1	J CELL BIOCHEM	3.591	1
ARCH DERMATOL	3.434	1	J CLIN MICROBIOL	3.537	2
ARCH ORAL BIOL	1.288	2	J CLIN PERIODONTOL	2.225	9
ARTH RHEUM/AR C RES	7.421	2	J CUTAN PATHOL	1.333	1
BIOCHEM BIOPHYS RES CO	3.000	2	J DENT	1.636	2
BIOCHEM CELL BIOL	2.870	1	J DENT RES	3.192	7
BIOCHEM J	4.224	1	J ORAL MAXIL SURG	0.180	3
BIOCONJUGATE CHEM	3.943	1	J ORAL REHABIL	0.717	4
BIOL CHEM	2.577	1	J OROFAC PAIN	1.932	1
BMC MUSCULOSKEL DIS	1.316	1	J ORTHOPAED RES	2.916	1
BRIT DENT J	0.658	1	J PERIODONTOL	1.784	3
CALCIFIED TISSUE INT	2.487	4	J VIROL	5.178	2
CARIES RES	1.721	10	KEY ENG MATER	0.224	1
CELL MOTIL CYTOSKEL	2.485	1	MATRIX BIOL	4.469	1
CHEM BIOL	6.138	1	NEUROENDOCRINOL LETT	1.005	1
CLEFT PALATE CRAN J	0.574	2	NEUROSCIENCE	3.410	1
CLIN INFECT DIS	6.510	1	ORAL DIS	1.445	2
CLIN ORAL IMPLAN RES	1.897	3	ORAL ONCOL	2.266	2
COMMUNITY DENT ORAL	1.631	1	ORAL SURG ORAL MED O	1.193	4
CYTOTHERAPY	1.795	1	ORG LETT	4.368	1
DENT MATER	2.056	6	OSTEOPOROSIS INT	4.216	1
DENTOMAXILLOFAC RAD	0.640	3	PEDIATR RADIOL	0.814	1
EUR J ORAL SCI	1.784	10	PEPTIDES	2.231	1
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