Predictors affecting implant treatment outcome:
short- and long-term clinical studies in daily practice

STIJN VERVAEKE

Thesis submitted in partial fulfillment of the requirements for the degree of Doctor in Health Sciences

Promoter: Prof. Dr. Hugo De Bruyn
Co-promoter: Dr. Bruno Collaert
The Clinical data collected for the research conducted in this PhD-thesis were obtained from:

1) Center for Periodontology and Implantology Leuven (CPIL)
   Head of Clinic: Dr. Bruno Collaert (Periodontist, Docent University of Malmö)
2) Besseler Tandheelkunde, Enschede
   Head of Clinic: Jos Besseler (Dentist, Implantologist)
3) Former Center for Periodontology and Implantology Brussels (CPIB)
   Dr. Bruno Collaert & Prof. Dr. Hugo De Bruyn

Independent data collection by Stijn Vervaeke

All projects were approved by the Ethics Committee of The Ghent University Hospital

The research project was supported by a grant from Dentsply Implants
Research overview and structure of the thesis

AIMS
1. TO EVALUATE THE CLINICAL OUTCOME OF DIFFERENT IMPLANT SURFACES.
2. TO EVALUATE SHORT-TERM IMPLANT TREATMENT OUTCOME IN TERMS OF SURVIVAL AND PERI-IMPLANT BONE LOSS, USING FLUORIDE-MODIFIED IMPLANTS IN DAILY PRACTICE
3. TO EVALUATE LONG-TERM IMPLANT TREATMENT OUTCOME IN TERMS OF SURVIVAL AND PERI-IMPLANT BONE LOSS IN DAILY PRACTICE
4. TO IDENTIFY PREDICTORS AFFECTING IMPLANT TREATMENT OUTCOME

STUDY 1: A prospective study on grit-blasted implants with a fluoride-modified surface
- Data from a private periodontal practice (CPIL, Leuven)
- 25 patients with 125 immediately loaded implants in the edentulous mandible (CPIL, Leuven)
- 2-year follow-up on survival and peri-implant bone loss

STUDY 2: A prospective study on grit-blasted implants
- Data from a private periodontal practice (CPIL, Leuven; former CPIB, Brussels)
- 50 patients with 320 immediately loaded implants in the maxilla or mandible
- 9-year follow-up on survival and peri-implant bone loss

STUDY 3: A retrospective study on grit-blasted implants with a fluoride-modified surface
- Data from a private periodontal practice (CPIL, Leuven)
- Total of 1106 implants in 300 patients

STUDY 4: A retrospective study on grit-blasted implants with a fluoride-modified surface
- Data from a private periodontal practice (CPIL, Leuven)
- Extension from study 3: 1320 implants in 376 patients

STUDY 5: A retrospective study on grit-blasted implants with a fluoride-modified surface
- Data from a private practice (Besseler Tandheelkunde, Enschede, The Netherlands)
- 1-year and 2-year clinical examination of 67 patients with 134 implants supporting mandibular overdentures

1. INTRODUCTION
2. RESEARCH PAPERS – RESULTS

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapter 1</td>
<td>Implant surface modifications.</td>
</tr>
<tr>
<td>Chapter 2</td>
<td>Smoking: a 2-year retrospective analysis in daily practice.</td>
</tr>
<tr>
<td>Chapter 3</td>
<td>Immediate loading in the maxilla.</td>
</tr>
<tr>
<td>Chapter 4</td>
<td>Short-term evaluation of predictors affecting implant treatment outcome.</td>
</tr>
<tr>
<td>Chapter 5</td>
<td>Soft tissue thickness.</td>
</tr>
<tr>
<td>Chapter 6</td>
<td>Long-term evaluation of predictors affecting implant treatment outcome.</td>
</tr>
</tbody>
</table>

3. GENERAL DISCUSSION
4. SUMMARY
5. CONCLUSIONS
Table of Contents

Glossary

List of Abbreviations

1. General Introduction & Aims

2. Research Chapters - Results

   Chapter 1: Implant surface modifications (Aim 1)

   Chapter 2: Smoking: a 2-year retrospective analysis in daily practice (Aim 1, 2, 4)

   Chapter 3: Immediate loading in the maxilla (Aim 1, 2, 4)

   Chapter 4: Short-term evaluation of predictors affecting implant treatment outcome (Aim 1, 2, 4)

   Chapter 5: Soft tissue thickness (Aim 1, 2, 4)

   Chapter 6: Long-term evaluation of predictors affecting implant treatment outcome (1, 3, 4)

3. General Discussion

4. Conclusions & Guidelines

5. Summary / Samenvatting

Acknowledgements

Curriculum Vitae
**Glossary**

**Osseointegration:**
A process whereby a clinically asymptomatic and rigid fixation of alloplastic materials, typically titanium, is achieved and maintained in bone, during functional loading.

**Dental implant:**
A titanium artificial ‘root’, installed directly into the jaw bone to replace one or more natural teeth, supporting a fixed or removable restoration.

**Abutment:**
A transmucosal piece that is connected on the implant (mostly screw-retained) and that supports and retains the prosthetic rehabilitation.

**Biologic width:**
The soft tissue component around teeth or implants including a barrier epithelium and a connective tissue portion.

**1-stage surgery:**
Implant procedure during which a transmucosal healing abutments is placed on the implant to secure the connection between the implant and the oral cavity, in order to allow non-submerged healing.

**2-stage surgery:**
Implant procedure during which a cover screw is placed and the soft tissues are closed covering the implant to allow undisturbed, submerged healing. A second surgical intervention is obligatory to assure the transmucosal connection between the oral cavity and the implant.

**Immediate loading:**
Internationally accepted definition for functional prosthetic loading of a dental implant within 72 hours after implant placement.

**Delayed loading:**
Functional, prosthetic loading of a dental implant at least 3 months after implant placement.

**Bone level:**
The distance measured from a reference point to the most marginal bone-to-implant contact point.

**Bone level change:**
Calculated as the difference between bone levels at two different time points.
Reference point:
The lower border of the smooth implant collar which corresponds with the uppermost point of the microthreaded part of the implant.

Bone loss:
Calculated as the amount of peri-implant bone that was lost between two time points.

Implant success:
Originally, implant success was described by Albrektsson et al. (1986), allowing 1.5 mm of bone loss during the first year and 0.2 mm annually thereafter. Collaert & De Bruyn (2008) described implant success arbitrarily, allowing 1 mm of bone loss. Recently, Klinge (2012) proposed 2 mm of bone loss as a long-term criterion for success.

Implant survival:
Defined as an implant that is still physically present in the mouth after implant installation at the time of examination.

Predictor:
Risk factor identified based on well-designed longitudinal studies and/or studies with appropriate multivariate analyses that correct for confounding.

Risk indicator:
A factor associated with the outcome variable based on cross-sectional studies. No cause-effect relation can be considered.

Outcome variable:
Independent variable.

Explanatory variable:
Dependent variable.

Surface roughness:
Based on surface roughness, implants are categorized as: smooth (Sa < 0.5 μm), minimally rough (Sa 0.5 – 1.0 μm), moderately rough (Sa: 1.1 – 2.0 μm), rough (Sa > 2.0 μm). Sa = arithmetic average height deviation.
List of abbreviations

**BIC**: bone-to-implant contact

**FDP**: fixed dental prosthesis (previous also called **FPD**: fixed partial denture)

**FFD**: fixed full denture

**SC**: solitary implant crown – single crown

**IIBL**: individual peri-implant bone loss

**PBL**: patient’s bone loss

**MBL**: mean bone loss

**1-DL**: 1-stage delayed loading

**2-DL**: 2-stage delayed loading

**IL**: immediate loading

**Sₚ**: arithmetic average height deviation

**NS**: not significant

**NR**: not reported

**mPI**: modified plaque index

**mGI**: modified gingiva index

**SPT**: supportive periodontal therapy

**CSR**: cumulative survival rate
INTRODUCTION AND AIMS
General Introduction

Implant treatment outcome

This thesis focusses on implant treatment outcome in daily practice. Therefore, implant treatment outcome is evaluated in terms of implant survival and peri-implant bone loss. Implant survival was defined as an implant that was still physically present in the oral cavity at the time of examination\(^1\). However, surviving implants may not always be successful, especially when peri-implant disease leads to unfavorable esthetic results causing patient discomfort and dissatisfaction. Therefore, peri-implant bone loss was evaluated and calculated as the difference in bone levels between two study time points. Marginal bone levels were determined both at the mesial and at the distal site of each implant by measuring the distance between a reference point (lower border of the smooth implant collar which coresponds with the uppermost point of the microthreaded part) and the marginal bone-to-implant contact. Mesial and distal values were averaged to obtain one single value for each implant. When statistics on patient level were appropriate, a mean value of all implants in the same patient was calculated to obtain a patient value.

Implant success was determined based on radiographic peri-implant bone loss. The oldest and generally accepted criteria by Albrektsson and co-workers\(^2\) can be considered excelled. Today, \(1.5\) mm of bone loss after one year and \(0.2\) mm annually thereafter, can no longer be considered successful. Implant designs have been altered and placement at the bone crest level is advocated. Bone loss will unavoidably lead to soft tissue recession, compromising the esthetic outcome. Moreover, exposure of the roughened implant surface may alter the bacterial environment in the peri-implant sulcus, compromising bone levels on the long run, and possibly initiating peri-implantitis. Hence, besides the criteria of Albrektsson et al.\(^2\), other criteria, dealing with bone loss from the day of surgery\(^3-5\) were adopted in the present thesis (Table 1).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Bone loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albrektsson et al.(^2)</td>
<td>Prosthesis insertion</td>
<td>(&lt; 1.5) mm the first year, (&lt; 0.2) mm annully thereafter</td>
</tr>
<tr>
<td>Misch et al(^3)</td>
<td>Implant surgery</td>
<td>(&lt; 2) mm</td>
</tr>
<tr>
<td>Collaert &amp; De Bruyn(^4)</td>
<td>Implant Surgery</td>
<td>(&lt; 1) mm after 1 year, (&lt; 1.5) mm after 3 years</td>
</tr>
<tr>
<td>Klinge(^5)</td>
<td>Implant surgery</td>
<td>(&lt; 2) mm</td>
</tr>
</tbody>
</table>

\(Table 1.\) Overview of success criteria adopted in this thesis.
Evolutions in implant treatment

Oral Implantology - implant treatment protocol

The first modern dental implants were introduced in the 1950’s. They consisted of subperiosteal frames, blade implants or transmandibular devices. At that time, there was no clinical or scientific evidence available to support these treatment protocols. The results of these treatments were poor and unpredictable, although individual successful cases were reported (Figure 1).

Figure 1 shows a radiographic image of a patient who recently visited the Departement of Periodontology at the Ghent University Hospital. The subperiosteal implant-supported rehabilitation was installed in the 1960’s and functioned well until tooth 4.6 was extracted, which induced an unfavorable occlusion. Persistent infection caused destruction of the alveolar bone with oro-antral fistulae.

In the 1950’s, Brånemark conducted an experimental study in rabbits to evaluate vascularization in living bone. During this vital microscopy study, titanium bone chambers were placed in rabbits. At the end of the follow-up, these bone chambers turned out to be extremely difficult to remove. Brånemark described this phenomenon as osseointegration⁶.
The term was first defined by Albrektsson and co-workers \(^7\) as direct contact between living bone and an implant at the light microscope level. Later, a more biomechanically definition was suggested and osseointegration was coined as “a process whereby clinically asymptomatic rigid fixation of alloplastic materials, typically titanium, is achieved and maintained in bone during functional loading” \(^8\).

Brånemark implemented his research findings in clinical dentistry for the treatment of edentulous patients with titanium, screw-shaped implants\(^6,9\). The first patient was treated in Sweden in 1965 and deceased in 2008 with all original implants still in function. The classic treatment protocol consisted of a two-stage delayed approach, were implants were kept unloaded for several months, allowing a stress-free healing period\(^9-12\). It was believed that premature loading, compromising direct bone healing, would result in disintegration of the implants. Hence, a second stage surgery was necessary to uncover the implants and to assure a transmucosal connection. Ever since this discovery, there has been a tendency towards optimisation and simplification of treatment protocols in order to shorten treatment time and increase patient comfort. In the 1970’s, a one-stage delayed treatment protocol was introduced by Schroeder\(^13\). In this treatment concept, a transmucosal healing abutment is placed immediately after implant installation to secure the connection between the implant and the oral cavity, avoiding a second surgery. Despite this one-stage approach, the protocol still advocated delayed loading.

Linkow and co-workers were among the first to describe immediate loading to shorten the timespan between implant placement and functional comfort for the patient \(^14\). However, fibrous encapsulation leading to disintegration of the implant was reported to be a common finding. Osseointegration can occur successfully under immediate loading conditions if excessive micromotions at the bone-to-implant interface are avoided. There is no consensus on the threshold that cannot be surpassed, but it is believed to range between 50 and 150 µm \(^15-17\). One can assume that micromotion is reduced when implants are splinted in multiple-unit restorations, but this cannot be accomplished when restoring solitary implants or small partial restorations.

Since the first description of this loading protocol and despite the unsuccessfull treatment outcome in the beginning, immediate loading of the fully edentulous jaw with a fixed
prosthesis has been extensively used. This holds true, especially since surface-roughened implants were introduced during the nineties. Despite, the extensive application of immediate loading in implant dentistry, long-term studies (> 5 years) are scarce. Table 2 summarizes prospective studies evaluating implant survival and peri-implant bone loss in fixed rehabilitations with immediate loading in healed ridges. Only studies with at least 10 patients and a minimum follow-up of 24 months were included. From this overview, one can conclude that different authors report implant failure rates ranging from 0 % to 6.3 % in the mandible and from 0 % to 6.1 % in the maxilla. Bone loss ranges from 0.11 mm to 1.78 mm in the mandible and from 0.70 mm to 1.60 mm in maxilla. Although long-term data on implant survival and peri-implant bone stability are scarce under immediate loading conditions, it is nowadays considered as a viable and predictable alternative for the treatment of full edentulism.

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Implants</th>
<th>Failures (%)</th>
<th>Follow-up</th>
<th>Bone loss (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MANDIBLE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ganeles et al. 19</td>
<td>27</td>
<td>161</td>
<td>0.6</td>
<td>25</td>
<td>NR</td>
</tr>
<tr>
<td>Henry et al. 20</td>
<td>51</td>
<td>153</td>
<td>9</td>
<td>25</td>
<td>0.4</td>
</tr>
<tr>
<td>Engstrand et al. 21</td>
<td>95</td>
<td>285</td>
<td>6.3</td>
<td>30</td>
<td>1.3</td>
</tr>
<tr>
<td>Nikellis et al. 22</td>
<td>10</td>
<td>51</td>
<td>0</td>
<td>24</td>
<td>NR</td>
</tr>
<tr>
<td>Testori et al. 23</td>
<td>19</td>
<td>116</td>
<td>2.6</td>
<td>38</td>
<td>NR</td>
</tr>
<tr>
<td>Testori et al. 24</td>
<td>62</td>
<td>325</td>
<td>0.6</td>
<td>25</td>
<td>NR</td>
</tr>
<tr>
<td>Aalam et al. 25</td>
<td>16</td>
<td>90</td>
<td>3.3</td>
<td>45</td>
<td>1.8</td>
</tr>
<tr>
<td>Capelli et al. 26</td>
<td>24</td>
<td>96</td>
<td>0</td>
<td>36</td>
<td>NR</td>
</tr>
<tr>
<td>Van de Velde et al. 27</td>
<td>18</td>
<td>91</td>
<td>3.3</td>
<td>45</td>
<td>1.8</td>
</tr>
<tr>
<td>De Bruyn et al. 28</td>
<td>25</td>
<td>125</td>
<td>0</td>
<td>36</td>
<td>1.2</td>
</tr>
<tr>
<td>Collaert et al. 29</td>
<td>25</td>
<td>125</td>
<td>0</td>
<td>24</td>
<td>0.11</td>
</tr>
<tr>
<td>Heschl et al. 30</td>
<td>30</td>
<td>120</td>
<td>5</td>
<td>up to 10 years</td>
<td>1.78</td>
</tr>
<tr>
<td><strong>MAXILLA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kinsel et al. 31</td>
<td>14</td>
<td>104</td>
<td>1.9</td>
<td>60</td>
<td>NR</td>
</tr>
<tr>
<td>Nikellis et al. 22</td>
<td>14</td>
<td>85</td>
<td>0</td>
<td>24</td>
<td>NR</td>
</tr>
<tr>
<td>Capelli et al. 26</td>
<td>41</td>
<td>246</td>
<td>2.1</td>
<td>36</td>
<td>NR</td>
</tr>
<tr>
<td>Collaert &amp; De Bruyn. 4</td>
<td>25</td>
<td>195</td>
<td>0</td>
<td>36</td>
<td>0.70</td>
</tr>
<tr>
<td>Bergkvist et al. 32</td>
<td>28</td>
<td>168</td>
<td>1.2</td>
<td>32</td>
<td>NR</td>
</tr>
<tr>
<td>Romanos &amp; Nentwig 33</td>
<td>15</td>
<td>90</td>
<td>3.3</td>
<td>42</td>
<td>NR</td>
</tr>
<tr>
<td>Degidi et al. 34</td>
<td>30</td>
<td>210</td>
<td>2.2</td>
<td>36</td>
<td>0.98</td>
</tr>
<tr>
<td>Tealdo et al. 35</td>
<td>34</td>
<td>163</td>
<td>6.1</td>
<td>36</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Table 2. Overview of prospective studies on immediate loading of implants supporting full-arch rehabilitations. Only studies with at least 10 patients and a minimum follow-up of 2 years were included.
The main reason for the popularity of immediate loading as treatment protocol is the significant reduction in treatment time and patient morbidity by avoiding a second stage surgery. This leads to a higher overall patient satisfaction and improved function, esthetics and phonetics. Dierens and co-workers described a major improvement within 1 week after implant installation and immediate provisionalisation and reported a further significant improvement of the different parameters after installation of the final restoration. The overall satisfaction increased from 40% before treatment to 98% after 1 year. Additionally, multiple sessions to reline a removable prosthesis during integration of submerged implants can be avoided, significantly reducing overall chair-side time for the patients and restorative dentists.

**Evolution of the Astra Tech™ implant system**

Astra Tech™ implants were introduced in the 1980’s as the first generation of implants with a conical connection. At that time, the first clinical studies with the system were initiated. In 1989, the implant surface was modified. The original smooth implant surface was grit-blasted with titanium dioxide particles resulting in a moderately rough surface topography (TiOblast™). During the nineties, the grit-blasted implant surface was chemically modified by an additional treatment with diluted hydrofluoric acid. This resulted in the development of the Osseospeed™ implant with a nanolevel surface roughness.

Surface characteristics are summarized in Table 3. Fluoride-modified implants have a slightly smoother surface (Sa: 0.91 +/- 0.14 μm) than the original TiOblast™ implants (Sa: 1.12 +/- 0.24 μm). Significantly higher removal torque values (85 +/- 16 Ncm vs 54 +/- 12 Ncm) and shear strength between bone and implants (23 +/- 9 N/mm2 vs 15 +/- 5 N/mm2) were measured for the fluoride-modified implants after 3 months and histomorphometric evaluations demonstrated higher bone-to-implant contact, 1 month (35% +/- 14% vs 26% +/- 8%) and 3 months (39% +/- 11% vs 31% +/- 6%) after implant placement.

<table>
<thead>
<tr>
<th></th>
<th>Sa</th>
<th>Scx</th>
<th>Sdr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osseospeed™</td>
<td>0.91 (0.14)</td>
<td>11.71 (0.83)</td>
<td>1.21 (0.04)</td>
</tr>
<tr>
<td>TiOblast™</td>
<td>1.12 (0.24)</td>
<td>11.33 (1.00)</td>
<td>1.34 (0.08)</td>
</tr>
</tbody>
</table>

Table 3. Surface characterization. Sa = average height deviation from the mean plane; Scx = average distance between surface irregularities; Sdr = surface developed area ratio.
These results showed that osseointegration is enhanced around fluoride-modified implant surfaces, especially during the first weeks of healing, with a faster bone formation and a stronger-bone-to-implant contact $^{40-43}$. Enhanced osteoblast differentiation $^{41,44-47}$, platelet activation and thrombogenic properties $^{46,48}$ of the fluoride-modified surface have been reported. Based on the aforementioned properties, it is believed that patients can benefit from these novel implant surfaces, especially in more demanding cases, such as immediate loading, immediate implant placement and implant installation in compromised bone (poor bone quality, limited bone volume, grafting procedures, medically compromised patients...).

TiOblast™ implants, without the additional fluoride modification, are well-documented. Long-term studies (> 5 years) are summarized in Table 5, showing good clinical results with high survival rates (87.7 % - 100 %) and limited peri-implant bone loss (0.01 – 2.60 mm). However, at the time this thesis was initiated, only a few studies were available on the clinical outcome of implants with fluoride-modified surfaces $^{49-55}$. 
<table>
<thead>
<tr>
<th>Author</th>
<th>Study-Design</th>
<th>Follow-up</th>
<th>Patients</th>
<th>Implants</th>
<th>Baseline</th>
<th>Survival (%)</th>
<th>Bone Loss (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gottfredsen &amp; Holm.</td>
<td>prospective</td>
<td>5 years</td>
<td>26</td>
<td>52</td>
<td>Prosthesis</td>
<td>100</td>
<td>0.20</td>
</tr>
<tr>
<td>Palmer et al.</td>
<td>prospective</td>
<td>5 years</td>
<td>15</td>
<td>15</td>
<td>Prosthesis</td>
<td>100</td>
<td>0.34</td>
</tr>
<tr>
<td>Gottfredsen &amp; Karlsson.</td>
<td>prospective</td>
<td>5 years</td>
<td>50</td>
<td>64</td>
<td>Prosthesis</td>
<td>100</td>
<td>1.11 (maxilla), 0.51 (mandible)</td>
</tr>
<tr>
<td>Steveling et al.</td>
<td>prospective</td>
<td>5 years</td>
<td>17</td>
<td>44</td>
<td>Prosthesis</td>
<td>100</td>
<td>0.90</td>
</tr>
<tr>
<td>van Wowern &amp; Gottfredsen.</td>
<td>prospective</td>
<td>5 years</td>
<td>22</td>
<td>44</td>
<td>Prosthesis</td>
<td>100</td>
<td>0.01</td>
</tr>
<tr>
<td>Astrand et al.</td>
<td>prospective</td>
<td>5 years</td>
<td>34</td>
<td>184</td>
<td>Surgery</td>
<td>98.4</td>
<td>1.74 (maxilla), 1.06 (mandible)</td>
</tr>
<tr>
<td>Gottfredsen et al.</td>
<td>prospective</td>
<td>5 years</td>
<td>20</td>
<td>20</td>
<td>Prosthesis</td>
<td>100</td>
<td>0.30</td>
</tr>
<tr>
<td>Wennström et al.</td>
<td>retrospective</td>
<td>5 years</td>
<td>51</td>
<td>-</td>
<td>Prosthesis</td>
<td>NR</td>
<td>0.40</td>
</tr>
<tr>
<td>Wennström et al.</td>
<td>prospective</td>
<td>5 years</td>
<td>51</td>
<td>70</td>
<td>Prosthesis</td>
<td>NR</td>
<td>0.48</td>
</tr>
<tr>
<td>Kahlberg &amp; Vannas-Löfqvist</td>
<td>prospective</td>
<td>5 years</td>
<td>11</td>
<td>78</td>
<td>Surgery</td>
<td>97.0</td>
<td>NR</td>
</tr>
<tr>
<td>Rasmusson et al.</td>
<td>prospective</td>
<td>7 years</td>
<td>36</td>
<td>199</td>
<td>Prosthesis</td>
<td>96.9</td>
<td>1.27</td>
</tr>
<tr>
<td>Wennström et al.</td>
<td>prospective</td>
<td>5 years</td>
<td>40</td>
<td>45</td>
<td>Prosthesis</td>
<td>97.7</td>
<td>0.11</td>
</tr>
<tr>
<td>Koutouzis &amp; Wennström.</td>
<td>retrospective</td>
<td>5 years</td>
<td>36</td>
<td>38</td>
<td>Prosthesis</td>
<td>NR</td>
<td>0.40</td>
</tr>
<tr>
<td>Cooper et al.</td>
<td>prospective</td>
<td>5 years</td>
<td>59</td>
<td>118</td>
<td>Prosthesis</td>
<td>95.9</td>
<td>0.09</td>
</tr>
<tr>
<td>Elasson et al.</td>
<td>retrospective</td>
<td>5 years</td>
<td>4</td>
<td>19</td>
<td>Prosthesis</td>
<td>94.7</td>
<td>0.18</td>
</tr>
<tr>
<td>Vroom et al.</td>
<td>prospective</td>
<td>12 years</td>
<td>20</td>
<td>40</td>
<td>Prosthesis</td>
<td>100</td>
<td>0.20</td>
</tr>
<tr>
<td>Chang &amp; Wennström.</td>
<td>prospective</td>
<td>5 years</td>
<td>43</td>
<td>130</td>
<td>Prosthesis</td>
<td>NR</td>
<td>0.38</td>
</tr>
<tr>
<td>García-Bellosta et al.</td>
<td>retrospective</td>
<td>5 years</td>
<td>323</td>
<td>980</td>
<td>Prosthesis</td>
<td>96.2</td>
<td>NR</td>
</tr>
<tr>
<td>Jacobs et al.</td>
<td>prospective</td>
<td>16 years</td>
<td>18</td>
<td>24</td>
<td>Prosthesis</td>
<td>100</td>
<td>0.02</td>
</tr>
<tr>
<td>Mertens &amp; Steveling</td>
<td>prospective</td>
<td>8 years</td>
<td>7</td>
<td>106</td>
<td>Prosthesis</td>
<td>99.0</td>
<td>0.30</td>
</tr>
<tr>
<td>Al-Nawas et al.</td>
<td>retrospective</td>
<td>10 years</td>
<td>75</td>
<td>381</td>
<td>Prosthesis</td>
<td>87.7</td>
<td>2.6</td>
</tr>
<tr>
<td>Chang &amp; Wennström.</td>
<td>retrospective</td>
<td>8 years</td>
<td>31</td>
<td>33</td>
<td>Prosthesis</td>
<td>100</td>
<td>0.10</td>
</tr>
<tr>
<td>Gottfredsen et al.</td>
<td>prospective</td>
<td>5 years</td>
<td>20</td>
<td>20</td>
<td>Prosthesis</td>
<td>100</td>
<td>0.75</td>
</tr>
<tr>
<td>Renvert et al.</td>
<td>prospective</td>
<td>13 years</td>
<td>19</td>
<td>80</td>
<td>1 year after surgery</td>
<td>100</td>
<td>0.80</td>
</tr>
<tr>
<td>Dasmah et al.</td>
<td>prospective</td>
<td>5 years</td>
<td>15</td>
<td>120</td>
<td>Prosthesis</td>
<td>NR</td>
<td>0.70</td>
</tr>
<tr>
<td>Ravald et al.</td>
<td>retrospective</td>
<td>12 years</td>
<td>46</td>
<td>183</td>
<td>Prosthesis</td>
<td>95.5</td>
<td>0.70</td>
</tr>
</tbody>
</table>
Risk evaluation in implant dentistry

Despite dental implants having demonstrated favorable long-term results\textsuperscript{10,82-84}, the outcome is still subjected to several factors. Early implant failures have been related to excessive surgical trauma, an impaired healing ability, premature loading and infection. In addition, late failures are mostly attributed to occlusal overload and/or progressive peri-implant bone loss \textsuperscript{85}. Likewise periodontitis, peri-implantitis is a multifactorial disease caused by an imbalance between causative pathogens, colonizing the subgingival biofilm, and the host response \textsuperscript{86}. Peri-implant mucositis has been described as a reversible inflammation of the peri-implant soft tissue without signs of loss of the supporting bone. Peri-implantitis is defined as inflammation of the soft tissues in combination with loss of the supporting peri-implant bone \textsuperscript{87}. \textbf{Poor oral hygiene} is known as an important risk factor in the development and progression of periodontal disease \textsuperscript{88}. Poor oral hygiene initiates a persistent gingivitis, which results in a 46-times higher risk for tooth loss \textsuperscript{89}. Similarly, there is evidence that poor oral hygiene is associated with peri-implant disease. Ferreira and co-workers showed that very poor oral hygiene (OR = 14.3), defined as median plaque scores \( \geq 2 \), and bleeding on probing in over 30 \% of the sites (OR = 3) significantly increased the risk for peri-implantitis \textsuperscript{90}. Moreover, Roccuzzo and co-workers showed better results for compliant patients under strict supportive periodontal therapy (SPT). They reported a correlation between lack of adhesion to SPT and the incidence of peri-implant disease and implant failure \textsuperscript{91}. One can assume that patients with a \textit{history of periodontitis}, indicating susceptibility to this opportunistic infection, will be susceptible to develop peri-implant disease as well. Indeed, different systematic reviews showed that patients with existing or ongoing periodontitis are more likely to experience implant failure and biological complications \textsuperscript{92-99}. However, it is difficult to draw strong conclusions due to the high heterogeneity among the studies and methodological variability \textsuperscript{100}.

Tobacco smoke contains nearly 4000 chemicals such as carbon monoxide, hydrogen cyanide, reactive oxidizing radicals and some of those chemicals are known to be toxic. As a consequence, smoking harms nearly every organ in the body including the tissues within the oral cavity. The negative effect of \textbf{smoking} is attributed to the impaired vascularity of the periodontal tissues rather than a vasoconstrictive effect \textsuperscript{101}. By affecting the revascularization it may lead to an impaired healing after surgery. Different systematic
reviews identified smoking as a factor affecting implant survival and peri-implant bone loss\textsuperscript{94,102,103}. Lindquist and co-workers identified smoking as the predominant factor affecting peri-implant bone loss. However, good oral hygiene reduced the pernicious effects of smoking while poor oral hygiene aggravated bone resorption\textsuperscript{104}. The literature is inconclusive about other potential risk factors such as diabetes mellitus and osteoporosis. Studies comparing patients with and without the condition in a controlled setting are sparse. The available literature is limited to case reports and case series\textsuperscript{105}. More well-designed studies are necessary to evaluate the effect of these factors on implant treatment outcome.

Besides, the abovementioned patient-related factors, implant-related factors can possibly influence implant treatment outcome. Today, most marketed implant surfaces are moderately rough with $S_a$ values between 1.1 and 2. Increasing implant surface roughness, facilitates biofilm formation and plaque accumulation\textsuperscript{106}. Quirynen and co-workers suggested that implants with increased surface roughness may be more prone to peri-implant bone loss and consequently, late implant failure\textsuperscript{95}.

**Data Analysis**

The studies in the present thesis were conducted in private (periodontal) practices. Consequently, the results reflect daily reality, where all kind of patients are treated for different indications. No patients were excluded based on medical risk factors, history of periodontitis or smoking habits. Such study populations require adequate statistical analyses.

Identification of risk factors/predictors for disease demands preferably longitudinal studies in humans with a prospective design\textsuperscript{8}. Studies with the highest level of scientific evidence are randomized controlled clinical trials. In these studies, the effect of one variable can be evaluated in a controlled study population, were patients with well-known risk factors are excluded. Hence, care has to be taken to extrapolate these results to the daily practice were also ‘less than ideal’ patients are treated.

In this context, large prospective or even retrospective case series may become particularly important to evaluate the relative importance of one factor in relation to others. A thorough risk assessment requires multivariate analyses that correct for confounding factors.
Aims

The overall objective of this thesis was to scrutinize implants with and without additional fluoride modification, placed in daily practice, and to identify predictors affecting short- and long-term implant treatment outcome.

1. TO EVALUATE THE CLINICAL OUTCOME OF DIFFERENT IMPLANT SURFACES.
2. TO EVALUATE SHORT-TERM IMPLANT TREATMENT OUTCOME IN TERMS OF SURVIVAL AND PERI-IMPLANT BONE LOSS, USING FLUORIDE-MODIFIED IMPLANTS IN DAILY PRACTICE
3. TO EVALUATE LONG-TERM IMPLANT TREATMENT OUTCOME IN TERMS OF SURVIVAL AND PERI-IMPLANT BONE LOSS IN DAILY PRACTICE
4. TO IDENTIFY PREDICTORS AFFECTING IMPLANT TREATMENT OUTCOME
References

Introduction & Aims

2004; 19: 116-123.


Introduction & Aims


Introduction & Aims

CHAPTER I

IMPLANT SURFACE MODIFICATIONS

THIS CHAPTER HAS BEEN PUBLISHED AS:

THE EFFECT OF IMPLANT SURFACE MODIFICATIONS ON SURVIVAL AND BONE LOSS OF IMMEDIATELY LOADED IMPLANTS IN THE EDENTULOUS MANDIBLE

Vervaekte S, Collaert B & De Bruyn H

CHAPTER 1 : The effect of implant surface modifications on survival and bone loss of immediately loaded implants in the edentulous mandible

ABSTRACT

Purpose To compare the 2-year survival and peri-implant bone loss of implants with and without a fluoride modification under immediate loading conditions in completely edentulous mandibles.

Materials and Methods 125 Osseospeed implants (test group) were installed in 25 patients requiring a fixed rehabilitation. Implants were loaded immediately (baseline) with a provisional screw-retained bridge. Implant survival and bone level changes were analyzed at 3, 12, and 24 months. Results were compared with the outcome of 25 previously treated patients with immediately loaded TiOblast implants using the same treatment protocol (control group).

Results Implant survival was 100% for both groups. After 3, 12, and 24 months, the mean bone loss for the control group was 0.60, 0.81, and 0.84 mm on the patient level and 0.60, 0.80, and 0.86 mm on the implant level. For the test group, a mean bone loss of 0.14, 0.11, and 0.11 mm was for the patient; and 0.14, 0.11, and 0.11 mm with the implant as statistical unit after 3, 12, and 24 months, respectively. No statistically significant differences were observed comparing peri-implant bone loss at 3 months with 12 and 24 months in both groups, but the control group showed more peri-implant bone loss compared with the test-group (P < .001). Moreover, the control group showed an increasing interquartile range over time, suggesting that not every implant is reaching steady-state bone levels.

Conclusion Immediate loading of implants installed in the completely edentulous mandible is a successful treatment option with high survival rates and limited bone loss after 2 years. However, initial crestal bone preservation significantly benefits from fluoride modification.
1.1 Introduction

Immediate loading of dental implants has been defined as functional contact with the teeth of the opposing arch by means of the attachment of a provisional prosthesis to the implants within 72 hours after implant placement. Immediate loading does not necessarily lead to fibrous encapsulation of the implant as was thought previously. Osseointegration can occur successfully under immediate loading conditions when excessive micromotion at the bone-to-implant interface is avoided. The threshold of micromotion is believed to range between 50 and 150 μm. Several clinical studies have shown that immediate loading of full-arch mandibular rehabilitations is a successful treatment option with survival rates ranging from 91% to 100% (Table 1). Moreover, a recent consensus paper stated this treatment option was scientifically and clinically validated based on the available literature. Immediate rehabilitation on dental implants results in a significant reduction of treatment time and morbidity for patients by avoiding a second stage surgery and multiple relining procedures during the healing stage. Dierens and co-workers showed that immediate placement of a full-arch prosthesis resulted in an immediate improvement of esthetics, function, comfort, and overall patient satisfaction.

Experimental studies showed that surface modifications can influence osseointegration. Grit-blasted implants with an additional fluoridation of the surface showed a faster integration and a stronger bone-to-implant contact during the first weeks of healing. A faster healing reaction around the implant might be more important in demanding cases such as immediate loading or immediate implantation. This results in a rapid shift from primary to secondary implant stability, which may improve the clinical outcome and minimize the risk of early implant failures.

The aim of the present study is to compare the clinical outcome of immediately loaded full-arch mandibular prostheses on five implants with and without an additional surface modification (fluoridation) after 2 years in function.
### Table 1: Overview of clinical studies evaluating the clinical outcome of immediately loaded full-arch restorations in the edentulous mandible.

<table>
<thead>
<tr>
<th>Author</th>
<th>Implant System</th>
<th>Patient Nr</th>
<th>Implant Nr</th>
<th>Failures (%)</th>
<th>Follow-up</th>
<th>Bone loss (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ganeles et al.</td>
<td>Straumann TPS/SLA &amp; Friavit &amp; Astra Tech</td>
<td>27</td>
<td>161</td>
<td>0.6</td>
<td>25</td>
<td>NR</td>
</tr>
<tr>
<td>Henry et al.</td>
<td>Nobel Biocare Turned</td>
<td>51</td>
<td>153</td>
<td>9</td>
<td>25</td>
<td>0.4</td>
</tr>
<tr>
<td>Engstrand et al.</td>
<td>Nobel Biocare Turned</td>
<td>95</td>
<td>285</td>
<td>6.3</td>
<td>30</td>
<td>1.3</td>
</tr>
<tr>
<td>Nikkelis et al.</td>
<td>Southern Implants</td>
<td>10</td>
<td>51</td>
<td>0</td>
<td>24</td>
<td>NR</td>
</tr>
<tr>
<td>Testori et al.</td>
<td>Biomet 3i Osseotite</td>
<td>19</td>
<td>116</td>
<td>2.6</td>
<td>38</td>
<td>NR</td>
</tr>
<tr>
<td>Testori et al.</td>
<td>Biomet 3i Osseotite</td>
<td>62</td>
<td>325</td>
<td>0.6</td>
<td>25</td>
<td>NR</td>
</tr>
<tr>
<td>van Steenberghe et al.</td>
<td>Nobel Biocare Turned</td>
<td>50</td>
<td>150</td>
<td>7.3</td>
<td>12</td>
<td>1.1</td>
</tr>
<tr>
<td>Aalam et al.</td>
<td>Nobel Biocare Turned</td>
<td>16</td>
<td>90</td>
<td>3.3</td>
<td>45</td>
<td>1.8</td>
</tr>
<tr>
<td>Klee de Vasconcellos et al.</td>
<td>Conexao Connect AR</td>
<td>15</td>
<td>60</td>
<td>0</td>
<td>19</td>
<td>1.1</td>
</tr>
<tr>
<td>Fröberg et al.</td>
<td>Nobel Biocare TiUnite/Turned</td>
<td>15</td>
<td>89</td>
<td>0</td>
<td>18</td>
<td>0.8</td>
</tr>
<tr>
<td>Van de Velde et al.</td>
<td>Nobel Biocare TiUnite/Turned</td>
<td>18</td>
<td>91</td>
<td>3.3</td>
<td>45</td>
<td>1.8</td>
</tr>
<tr>
<td>De Bruyn et al.</td>
<td>Astra Tech TiOblast</td>
<td>25</td>
<td>125</td>
<td>0</td>
<td>36</td>
<td>1.2</td>
</tr>
<tr>
<td>Francetti et al.</td>
<td>Nobel Biocare TiUnite</td>
<td>44</td>
<td>172</td>
<td>0</td>
<td>12</td>
<td>0.7</td>
</tr>
<tr>
<td>Melo et al.</td>
<td>Neodent</td>
<td>11</td>
<td>44</td>
<td>0</td>
<td>12</td>
<td>NR</td>
</tr>
<tr>
<td>Agliardi et al.</td>
<td>Nobel Biocare TiUnite</td>
<td>24</td>
<td>96</td>
<td>0</td>
<td>19-47</td>
<td>NR</td>
</tr>
<tr>
<td>Agliardi et al.</td>
<td>Nobel Biocare TiUnite</td>
<td>93</td>
<td>388</td>
<td>0.3</td>
<td>12</td>
<td>0.85</td>
</tr>
<tr>
<td>Hinze et al.</td>
<td>Biomet 3i Nanotite</td>
<td>18</td>
<td>72</td>
<td>2.8</td>
<td>12</td>
<td>0.8</td>
</tr>
</tbody>
</table>
1.2 Materials & Methods

125 implants with a chemically modified surface (Osseospeed™, Astra Tech) were installed in 25 consecutively treated patients requiring a full-arch fixed prosthesis in the mandible (test group). No patients were excluded in this study. A crestal incision was made and the mucoperiosteal flap was reflected to visualize the bone crest. Implants were placed according to manufacturer guidelines in a prosthetically-driven way using the patient’s denture as a guide plate. Care was taken to avoid dehiscences and to have the implants completely surrounded by the crestal bone. After implant insertion, uni-abutments with a height ranging from 1 to 4 mm were placed, and an impression was made with the patient’s denture and conical impression copings using the repositioning technique. Implants were functionally loaded the day after surgery (baseline) with a provisional acrylic, glass fiber, or metal-reinforced screw-retained bridge. This treatment protocol was described previously by De Bruyn and co-workers and is illustrated in Figure 1.

Periapical radiographs were taken immediately after placement of the provisional restoration to determine the baseline bone level using digital software (Visi-Quick) with an accuracy of 0.1 mm. Care was taken to visualize the implant threads clearly using a guiding system (Rinn XCP, Dentsply) in order to obtain an x-ray direction perpendicular to the film. Whenever the implant threads were unclear, new radiographs were taken until the radiologic bone-to-implant contact level could be determined. The assessment of the radiographs was done by an external calibrated examiner (SV). Inter- and intraexaminer variability was very high and previously described by the same authors.

The bone level was defined as the most marginal bone-to-implant contact measured from a reference point (the lower border of the smooth implant collar or uppermost point of the microthreads). Mesial and distal values were averaged to obtain a single value per implant. After 3 to 4 months, the final 12-unit prosthetic was constructed by the referring dentist. All patients were scheduled for professional maintenance including radiographic follow-up. The frequency and content was adapted to the individual patient’s need. Radiographic bone loss was measured on periapical radiographs after 3, 12, and 24 months and compared with the baseline. The results were compared with the clinical outcome of 25 previously described patients with immediately loaded TiOblast™ implants using the same treatment protocol.
(control group). The Mann-Whitney U-test was adopted for the comparison of bone loss between the test and control groups for the different time points, both with the implant and patient as statistical units. The Friedman test was adopted to compare peri-implant bone loss after 3, 12, and 24 months for both groups, and the Bonferroni correction to correct for multiple testing. Tests were performed with both implants and patients as statistical units. The study was approved by the ethical committee of the Ghent University Hospital (Ghent, Belgium).
Chapter 1: Implant surface modifications

Figure 1. 

- **a** The patient’s denture was used as a guide for prosthetically-driven implant placement.
- **b** A crestal incision was made to visualize the bone. The guide pins indicate the implant angulation after preparation of the implant sites.
- **c** Care was taken so that the implants were completely surrounded by the alveolar bone.
- **d** Conical abutments with height ranging from 1 to 4 mm were placed on the implants.
- **e** Conical impression copings were placed on the uni-abutments.
- **f** An impression was made with the patient’s denture using the repositioning technique.
- **g** Suturing after the impression.
- **h** Placement of the provisional acrylic screw-retained bridge the day after surgery.
- **i** Periapical radiographs (baseline) after installation of the provisional restoration.
- **j** Provisional prosthesis 3 months after implant placement.
- **k** Radiographic control at the 1-year recall visit with the final restoration.
1.3 Results

A total of 250 implants were installed in 50 patients. The test group consisted of 10 men and 15 women with a mean age of 60.4 years (range, 39 to 78 years), and 3 patients were identified as smokers (> 10 cigarettes a day). The corresponding values for the control group were 10 men and 15 women with a mean age of 58 years (range, 35 to 76 years), and 6 patients were smokers. After 24 months, 3 out of 25 patients in the control group and 1 of 25 in the test group were lost to follow-up. During the 2-year observation period, no implants failed, resulting in a survival rate of 100% for both groups. After 3, 12, and 24 months the mean bone loss for the control group was 0.60 (SD, 0.68; range, −0.12 to 2.14), 0.81 (SD, 0.84; range, −0.30 to 2.34), and 0.84 mm (SD, 0.92; range, −0.21 to 2.57) on the patient level (Figure 2). When the implant was considered as the statistical unit, a mean bone loss of 0.60 (SD, 0.82; range, −0.6 to 3.95), 0.80 (SD, 1.02; range, −0.9 to 3.85), and 0.86 mm (SD, 1.14; range, −0.9 to 4.65) was found for the different time points, respectively (Figure 3). For the test group, a mean bone loss of 0.14 (SD, 0.18; range, −0.11 to 0.57), 0.11 (SD, 0.12; range, −0.11 to 0.30) and 0.11 mm (SD, 0.12; range, −0.11 to 0.43) was found with the patient as statistical unit (Figure 2). This corresponds with a mean bone loss of 0.14 (SD, 0.32; range, −0.55 to 1.75), 0.11 (SD, 0.22; range, −0.55 to 1.05), and 0.11 mm (SD, 0.21; range, −0.55 to 1.00) with the implant as statistical unit after 3, 12, and 24 months, respectively (Figure 3). No statistically significant differences were observed comparing peri-implant bone loss at 3 months with 12 and 24 months in both groups, suggesting steady-state bone levels after initial bone remodeling. At 3, 12, and 24 months, implants in the control group showed more peri-implant bone loss compared with the test group, both with the patient and the implant as statistical unit (P < .001). When taking 1 mm of bone loss as an arbitrarily set threshold, 66.4% of the individual implants in the control group and 99.2% in the test group were considered a success (Figure 4). According to the criteria of Albrektsson and co-workers, 84.5% of the control and 100% of the test implants are considered a success.
Figure 2. Boxplot presenting peri-implant bone loss (mm) for test and control implants with the patient as statistical unit after 3, 12 and 24 months. No statistically significant differences were found after initial bone remodeling in both groups. Patients in the control group showed more peri-implant bone loss compared with the test-group at 3, 12 and 24 months ($p < 0.001$)
Figure 3. Boxplot presenting peri-implant bone loss (mm) for test and control implants with the implant as statistical unit after 3, 12 and 24 months. No statistically significant differences were found after initial bone remodeling in both groups. Implants in the control group showed more peri-implant bone loss compared with the test-group at 3, 12 and 24 months ($p < 0.001$)
Figure 4. Presenting cumulative percentage of individual peri-implant bone loss after 24 months for test implants (green line) and control implants (blue dotted line). 66.4 % of the control and 99.2 % of the test implants showed less than 1 mm of bone loss. According to the criteria of Albrektsson and co-workers\textsuperscript{29}, allowing up to 1.7 mm of bone loss after 2 years, 84.5 % of the control and 100 % of the test implants were considered a success.
1.4 Discussion

Immediate loading of implants supporting a full-arch rehabilitation in the edentulous mandible has been reported as a successful treatment option with survival rates ranging from 91% to 100% (Table 1). When excluding studies where implants with a minimally rough and turned surface are used, survival rates increase to 97.2% to 100%. In the present study, a survival rate of 100% was reported for implants with and without a chemically modified surface, confirming the good clinical results in the aforementioned studies. Experimental studies showed a better and faster osseointegration during the first weeks of healing\(^{26,27}\) and the observed enhanced osteoblastic activity, platelet activation, and thrombogenic properties were attributed to the chemically modified surface\(^{30-35}\). However, the potential benefit of these novel implant surfaces in terms of survival could not be observed in the present study, as implants were splinted for 3 months in a provisional restoration and no failures were observed in the test or control group.

Bone loss values were analyzed both on patient and implant level as averaged values may hide important clinical information. One implant with extended bone loss, requiring an additional treatment can be masked when other implants in the same patient present no bone loss at all\(^{28}\). In the present study, an overall mean bone loss of 0.86 mm was found for the control group and 0.11 mm for the test group, with the implant as statistical unit from the day of provisional restoration to 2 years in function. The corresponding values with the patient as statistical unit were 0.84 mm and 0.11 mm. Although no statistically significant differences were observed after initial bone remodeling during the first three months, both the standard deviation and the range increased at 12 and 24 months for the control group but not for the test group. This suggests that not all control implants reached steady-state bone levels. This is also obvious from Figure 4, which shows the cumulative percentage of bone loss after 2 years for both groups. Whether this is indicative for future biological complications remains to be evaluated. This result suggests a decisive role for the implant surface on bone preservation. However, this decisive role is in contradiction with the findings of Fröberg and co-workers\(^ {16}\). They compared the clinical outcome of immediately loaded machined implants with oxidized implants in a split mouth study and found no statistically significant difference when comparing bone loss from baseline to 18 months in
function. They concluded that other factors, such as healing capacity of the bone and implant position, are as important as surface topography.\textsuperscript{16}

In the literature, only 5 clinical studies are available with bone loss data after 2 years for immediately loaded implants supporting full-arch restorations in the mandible (Table 1). Bone loss data range from 0.4 to 2.1 mm after 24 months up to 45 months.\textsuperscript{8,9,14,17,18} Due to the heterogeneity of the studies in terms of baseline values, follow-up time, and implant systems and designs, it is very difficult to make clear comparisons and to draw conclusions. It is important to reach steady-state bone levels after initial bone remodeling. No statistically significant values were found comparing mean bone loss values from 3 months up to 2 years, but the increasing standard deviation, outliers, and extreme values in the control group are indicative for some implants with continuous bone loss. Whether this bone loss is predictive for future biological complications, remains to be evaluated on the long term.

1.5 Conclusion

Immediate loading of implants installed in the completely edentulous mandible is a reliable and successful treatment option with high survival rates regardless of surface enhancement. However, crestal bone preservation is significantly better for implants with a fluoride modification surface, suggesting a decisive role for the implant surface.
1.6 References


Chapter 1: Implant surface modifications


CHAPTER 2

SMOKING: A 2-YEAR RETROSPECTIVE ANALYSIS IN DAILY PRACTICE

THIS CHAPTER HAS BEEN PUBLISHED AS:

THE EFFECT OF SMOKING ON SURVIVAL AND PERI-IMPLANT BONE LOSS OF IMPLANTS WITH A FLUORIDE MODIFIED SURFACE: A 2-YEAR RETROSPECTIVE ANALYSIS OF 1106 IMPLANTS PLACED IN DAILY PRACTICE.

Vervaeke S, Collaert B, Vandeweghe S, Cosyn S, Deschepper E & De Bruyn H

CHAPTER 2 : The effect of smoking on survival and bone loss of implants with a fluoride-modified surface: a 2-year retrospective analysis of 1106 implants placed in daily practice

ABSTRACT

AIM To compare the survival and peri-implant bone loss of implants with a fluoride-modified surface in smokers and nonsmokers.

MATERIALS AND METHODS Patient files of all patients referred for implant treatment from November 2004 to 2007 were scrutinized. All implants were placed by the same experienced surgeon (B. C.). The only inclusion criterion was a follow-up time of at least 2 years. Implant survival and bone loss were assessed by an external calibrated examiner (S. V.) comparing digital peri-apical radiographs taken during recall visits with the post-operative ones. Implant success was determined according to the international success criteria (Albrektsson et al. 1986). Survival of implants installed in smokers and nonsmokers was compared using the log-rank test. Both nonparametric tests and fixed model analysis were adopted to evaluate bone loss in smokers and nonsmokers.

RESULTS One-thousand one-hundred and six implants in 300 patients (186 females; 114 males) with a mean follow-up of 31 months (SD 7.15; range 24-58) were included. Nineteen implants in 17 patients failed, resulting in an overall survival rate of 98.3% at the implant level and 94.6% at the patient level. After a follow-up period of 2 years, the cumulative survival rates was 96.7% and 99.1% with the patient and implant as the statistical unit, respectively. Implant survival was significantly higher for nonsmokers compared with smokers (implant level P=0.025; patient level P=0.017). The overall mean bone loss was 0.34 mm (n=1076; SD 0.65; range 0-7.1). Smokers lost significantly more bone compared with nonsmokers in the maxilla (0.74 mm; SD 1.07 vs. 0.33 mm; SD 0.65; P<0.001), but not in the mandible (0.25 mm; SD 0.65 vs. 0.22 mm; SD 0.5; P=0.298).

CONCLUSION The present study is the first to compare peri-implant bone loss in smokers and nonsmokers from the time of implant insertion (baseline) to at least 2 years of follow-up. Implants with a fluoride-modified surface demonstrated a high survival rate and limited bone loss. However, smokers are at a higher risk of experiencing implant failure and more prone to show peri-implant bone loss in the maxilla. Whether this bone loss is predicting future biological complications remains to be evaluated.
Chapter 2: Smoking: a 2-year retrospective analysis

2.1 Introduction

Smoking is harmful for general health and has been associated with various diseases, such as cardiovascular diseases, cancer and respiratory diseases\(^1\text{-}^4\). Also, the usage of tobacco has an overwhelming impact on oral health and is associated with tooth loss, loss of attachment, vertical bone loss, dry socket and impaired wound healing after surgery\(^4\text{-}^{10}\). Although the mechanisms are not fully understood, wound healing is disturbed due to an impaired fibroblast function, less collagen production, an impaired vasculature affecting revascularization after surgery and an impaired polymorphonuclear neutrophilic and macrophagal function\(^11\text{-}^{15}\). Smoking is also known to affect the outcome of implant treatment. Several studies reported lower survival rates for implants installed in smokers\(^16\text{-}^{22}\). Some studies show that especially the maxilla is more prone to implant failure\(^23\). Most of these are early failures and occur before functional loading\(^23\text{-}^{25}\).

Only a limited number of studies, summarized in Table 1, have compared peri-implant bone loss in smokers and nonsmokers. Only one study failed to show a significant difference\(^26\). The other 15 reported significantly better peri-implant bone levels in nonsmokers compared with smokers\(^19,27\text{-}^{40}\).

In the last decade, most of the implant companies changed the implant surface to a moderately rough surface in order to enhance the osseointegration process. Fluoride-modified implants (Osseospeed™, Astra Tech®, Möldahl, Sweden) are grit-blasted with titanium dioxide particles, followed by an additional treatment with diluted hydrofluoric acid, which results in a nanoscale surface topography\(^41\). Results from experimental studies suggest that osseointegration is enhanced around fluoride-modified implant surfaces, especially during the first weeks of healing\(^41\text{-}^{43}\). Enhanced osteoblast differentiation\(^42,44\text{-}^{47}\), platelet activation and thrombogenic properties\(^46,48\) of the fluoride-modified surface have been reported. A recent comparative study shows that, despite smoking having an adverse effect on peri-implant bone healing, surface topography changes may affect bone-to-implant contact\(^49\). This might have an effect on peri-implant bone preservation and thus on the long-term success of dental implants.

The aim of this study was to evaluate implant survival and peri-implant bone loss of implants with a fluoride-modified surface with respect to self-reported smoking habits.
A statistically significant difference was found between smokers and nonsmokers when comparing peri-implant bone loss.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study Design</th>
<th>Observation period</th>
<th>Samples</th>
<th>Baseline/Reference Point</th>
<th>Bone Loss/Bone Level Changes</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haas et al. 27</td>
<td>Retrospective</td>
<td>22 months</td>
<td>366 implants in 107 smokers 1000 implants in 314 nonsmokers</td>
<td>Prosthetic loading</td>
<td>Smokers maxilla: 3.95 mm mandible: 1.47 mm Nonsmokers maxilla: 1.65 mm mandible: 1.53 mm</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>Lindquist et al. 28</td>
<td>Prospective</td>
<td>15 years</td>
<td>278 implants in 47 patients</td>
<td>Prosthetic loading</td>
<td>Not reported separately</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Lindquist et al. 29</td>
<td>Prospective</td>
<td>10 years</td>
<td>266 implants in 45 patients</td>
<td>Prosthetic loading</td>
<td>Smokers: 1.30 mm Nonsmokers: 0.65 mm</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Carlsson et al. 30</td>
<td>Prospective</td>
<td>15 years</td>
<td>273 implants in 44 patients</td>
<td>Prosthetic loading</td>
<td>Not reported separately</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Feloutsis et al. 31</td>
<td>Prospective</td>
<td>5.6 years</td>
<td>182 implants in 90 patients</td>
<td>Prosthetic loading</td>
<td>Nonsmokers: 1.85 mm Smokers (heavy): 1.98 mm</td>
<td>&lt; 0.02*</td>
</tr>
<tr>
<td>Karoussis et al. 32</td>
<td>Prospective</td>
<td>10 years</td>
<td>179 implants in 89 patients</td>
<td>Prosthetic loading</td>
<td>1 year</td>
<td>Not reported separately</td>
</tr>
<tr>
<td>Penarrocha et al. 33</td>
<td>Retrospective</td>
<td>1 year</td>
<td>47 implants in 16 smokers 61 implants in 26 nonsmokers</td>
<td>Prosthetic loading</td>
<td>Not reported separately</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>Wennström et al. 34</td>
<td>Prospective</td>
<td>5 years</td>
<td>149 implants in 51 patients (34 nonsmokers, 17 smokers)</td>
<td>Prosthetic loading</td>
<td>Smokers: 0.76 mm Nonsmokers: 0.22 mm</td>
<td>= 0.022*</td>
</tr>
<tr>
<td>Wennström et al. 35</td>
<td>Prospective</td>
<td>5 years</td>
<td>47 patients (15 smokers, 32 nonsmokers)</td>
<td>Prosthetic loading</td>
<td>Not reported separately</td>
<td>&lt; 0.05*</td>
</tr>
<tr>
<td>Galindo-Moreno et al. 36</td>
<td>Prospective</td>
<td>3 years</td>
<td>514 implants in 185 patients (63 smokers)</td>
<td>Prosthetic loading</td>
<td>Smokers: 1.36 mm Nonsmokers: 1.25 mm</td>
<td>&lt; 0.02*</td>
</tr>
<tr>
<td>Nitzan et al. 37</td>
<td>Retrospective</td>
<td>42.9 months 48.4 months</td>
<td>271 implants in 59 smokers 375 implants in 102 nonsmokers</td>
<td>Implant exposure</td>
<td>Smokers: 0.15 mm Nonsmokers: 0.05 mm</td>
<td>= 0.001*</td>
</tr>
<tr>
<td>Aalam &amp; Nowzari. 38</td>
<td>Retrospective</td>
<td>2 years</td>
<td>198 implants in 74 patients</td>
<td>Abutment-fixture interface</td>
<td>Not reported separately</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Schwartz-Arad et al. 39</td>
<td>Retrospective</td>
<td>37.9 months</td>
<td>50 implants in 8 smokers 227 implants in 53 nonsmokers</td>
<td>Implant exposure</td>
<td>Not reported separately</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Deluca &amp; Zarb. 40</td>
<td>Retrospective</td>
<td>1-20 years</td>
<td>767 implants in 235 patients</td>
<td>Prosthetic loading</td>
<td>Smokers: 0.073 mm / year Nonsmokers: 0.041 mm / year</td>
<td>= 0.010*</td>
</tr>
<tr>
<td>Levin et al. 41</td>
<td>Retrospective</td>
<td>1-14 years</td>
<td>64 implants in 64 patients</td>
<td>Implant exposure</td>
<td>Not reported separately</td>
<td>= 0.016*</td>
</tr>
<tr>
<td>Vandeweghe et al. 42</td>
<td>Retrospective</td>
<td>12 months</td>
<td>60 implants in 21 smokers 303 implants in 148 nonsmokers</td>
<td>Abutment-fixture interface</td>
<td>Smokers: 1.56 mm Nonsmokers: 1.32 mm</td>
<td>= 0.001*</td>
</tr>
</tbody>
</table>
2.2 MATERIALS & METHODS

2.2.1 PATIENT SELECTION AND CLINICAL PROCEDURES

All patients referred for implant treatment between November 2004 and 2007 were scrutinized. Patients were asked about smoking habits as part of the medical anamnesis during intake. The only inclusion criterion was a follow-up time of at least 2 years. All implants were placed by the same experienced surgeon (B. C.) in healed ridges. In case of previous tooth extraction, a healing time of at least 3 months was allowed before implant insertion. A crestal incision was made in order to raise the flap and implants were installed according to the manufacturer's guidelines. Digital peri-apical radiographs were taken by the surgeon immediately after implant insertion (baseline) with commercially available filmholders using the parallel long-cone technique in order to visualize the implant threads and marginal bone-to-implant contact level.

Figure 1. Reference point (lower border of the smooth implant collar or the uppermost point of the microthreaded part) indicated by black arrow.
Hence, bone loss is reported from the time of surgery. After implant treatment, all patients were scheduled for professional maintenance including radiographic follow-up. The frequency and content of professional maintenance was based on the clinical situation and adapted to the individual needs of the patients. Basically, this implies a recall interval of 6 or 12 months during the first years. The final restorations were made by the referring dentist. All implants with at least 2 years of follow-up and thus part of the professional maintenance recall system were included to evaluate implant survival and peri-implant bone loss. An external examiner from the University of Ghent had access to the patient files. The study protocol was approved by the ethical committee of the Ghent University Hospital.

### 2.2.2 Examination criteria and statistical analysis

An implant was considered a failure when it was removed because of implant mobility, loss of integration, ongoing bone loss, infection and/or persistent pain or patient discomfort. An individual implant was dichotomized either as survival (value 0) or a failure (value 1) for Kaplan–Meier survival analysis. The log-rank test was used to compare implant survival in smokers and nonsmokers both with the patient and the implant as the statistical unit. Peri-implant bone loss was assessed by an external examiner (S. V.) comparing peri-apical radiographs, taken during recall visits, with the post-operative ones taken by the surgeon immediately after implant insertion using digital software (Visi-Quick®, Amsterdam, the Netherlands) with an accuracy of 0.1 mm. Care was taken to visualize the implant threads clearly. Marginal bone level was determined both at the mesial and at the distal site of each implant by measuring the distance between the reference point (lower border of the smooth implant collar or the uppermost point of the microthreaded part) and the marginal bone-to-implant contact (Figure 1). These values were averaged to obtain a single value per implant (individual implant bone loss [IIBL]). The reference point has been described by previous authors, using the same implant system. The patient’s bone loss (PBL) was calculated as the mean value of all IIBL’s. Differences between smokers and nonsmokers were evaluated using the Mann–Whitney U-test. Moreover, mixed model analysis was performed to analyze bone loss using PASW statistics because of clustering of implants in patients and jaws. Therefore, a logarithmic transformation of the data was performed to obtain linearity and homoskedasticity of the residuals. To evaluate the impact of time on bone loss, the Mann–Whitney U-test was adopted. Inter- and intra-examiner reliability was
assessed using percent agreement within a 0.2 mm deviation, Spearman correlation coefficient and the Wilcoxon signed ranks test. An individual implant was considered a success when bone loss was \( \leq 1.5 \) mm during the first year and \( \leq 0.2 \) mm additionally per year. Fisher’s exact test was used to compare the success rates between smokers and nonsmokers.

### 2.3 Results

#### 2.3.1 Implant survival

In total, 300 patients, 186 females and 114 males, with 1106 implants were evaluated (Table 2). The mean age was 56 years (SD 12.05; range 17–82). Hundred and fifty-seven patients received implants in the maxilla and 143 in the mandible. Twenty-six of them received implants in both the jaws.

<table>
<thead>
<tr>
<th>Implant Survival group</th>
<th>Implant bone loss group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Implants</strong></td>
<td><strong>Patients</strong></td>
</tr>
<tr>
<td>1106 (19)</td>
<td>300 (17)</td>
</tr>
<tr>
<td>244 (8)</td>
<td>60 (7)</td>
</tr>
<tr>
<td>849 (11)</td>
<td>235 (10)</td>
</tr>
<tr>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>648 (5)</td>
<td>170 (5)</td>
</tr>
<tr>
<td>458 (14)</td>
<td>156 (12)</td>
</tr>
</tbody>
</table>

Table 2. Implant and patient distribution with respect to smoking status and jaw. Failures are given between brackets.

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>8.00 (3)</th>
<th>9.00 (2)</th>
<th>10.00 (2)</th>
<th>11.00 (2)</th>
<th>12.00 (1)</th>
<th>13.00 (1)</th>
<th>14.00 (1)</th>
<th>15.00 (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.00</td>
<td>36 (2)</td>
<td>33 (1)</td>
<td>39 (1)</td>
<td>133 (1)</td>
<td>192 (1)</td>
<td>8 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.50</td>
<td>0</td>
<td>30 (1)</td>
<td>12</td>
<td>67</td>
<td>48</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.00</td>
<td>0</td>
<td>32</td>
<td>17 (2)</td>
<td>28 (1)</td>
<td>40</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Overview of implant length and diameter. Failures are given between brackets.
Out of 1106 implants, 121 implants supported single crowns, 318 supported fixed partial dentures, 631 supported fixed cross-arch bridges and 18 supported overdentures. An overview of implant length and diameter is shown in Table 3.

After a mean follow-up period of 31 months (SD 7.15; range 24–58), 19 implants failed (1.7%), resulting in an absolute survival rate of 98.3%. Nine failures occurred before prosthetic loading. In total, 17 patients out of 300 (5.6%) experienced implant failure. Table 4 shows the cumulative survival rates (CSR). After a follow-up period of 2 years, the CSR was 96.7% and 99.1%, with the patient and the implant as the statistical unit, respectively.

Of 244 implants installed in 60 smokers, eight implants (3.3%) failed; of 849 implants installed in 235 nonsmokers, 11 implants failed (1.3%); and of five patients with 13 implants, the smoking status was seemingly by mistake not registered into the patient record. In the smokers group, one out of 139 (0.7%) implant failed in the maxilla, whereas seven out of 105 (6.7%) implants failed in the mandible. In the nonsmoking group, four out of 502 (0.8%) implants failed in the maxilla and seven out of 347 (2%) in the mandible. In smokers, the mandible was significantly more prone to implant loss compared with the maxilla ($P=0.012$). This difference could not be found in nonsmokers ($P=0.085$). Seven out of 60 smokers (11.7%) and 10 out of 235 nonsmokers (4.3%) experienced implant failure. In-depth analysis showed a significant difference on comparing smokers and nonsmokers for the cumulative failure rates both at the patient ($P=0.017$) (Figure 2) and at the implant level ($P=0.025$) (Figure 3). Table 5 shows that individual cumulative implant failure rates in smokers affect only the maxilla. Patient cumulative failure rates were not affected by jaw location.
<table>
<thead>
<tr>
<th>IMPLANT</th>
<th>PATIENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smokers</td>
<td>Nonsmokers</td>
</tr>
<tr>
<td>Failures</td>
<td>CSR</td>
</tr>
<tr>
<td>0-5m</td>
<td>5(244)</td>
</tr>
<tr>
<td>6-11m</td>
<td>0(239)</td>
</tr>
<tr>
<td>12-17m</td>
<td>0(239)</td>
</tr>
<tr>
<td>18-23m</td>
<td>0(239)</td>
</tr>
<tr>
<td>24-29m</td>
<td>0(239)</td>
</tr>
<tr>
<td>30-35m</td>
<td>2(124)</td>
</tr>
<tr>
<td>36-41m</td>
<td>0(48)</td>
</tr>
<tr>
<td>42-47m</td>
<td>1(12)</td>
</tr>
<tr>
<td>48-53m</td>
<td>0(0)</td>
</tr>
<tr>
<td>54-58m</td>
<td>0(0)</td>
</tr>
</tbody>
</table>

Table 4. Overview of failures and cumulative survival rates in smokers and nonsmokers. The total number of patients/implants at the start of the follow-up period is given between brackets.
### Table 5. Overview of failures and cumulative survival rates in smokers and nonsmokers with respect to the jaw.

The total number of patients/implants at the start of the follow-up period is given between brackets.
Chapter 2: Smoking: a 2-year retrospective analysis

Figure 2. Kaplan-Meier Survival Curve showing estimated implant failures in function of time for smokers and nonsmokers with the patient as statistical unit.

Figure 3. Kaplan-Meier Survival Curve showing estimated implant failures in function of time for smokers and nonsmokers with the implant as statistical unit.
2.3.2 Peri-implant bone loss

Out of 1087 surviving implants, 1076 implants in 295 patients had readable radiographs and a follow-up of at least 2 years (Table 2). The intra-examiner repeatability on bone loss was high (95% agreement within 0.2 mm deviation; Spearman’s correlation coefficient 0.925, \( P<0.05 \); Wilcoxon’s signed ranks test \( P=0.673 \)) as was the inter-examiner variability (90% agreement within 0.2 mm of deviation; Spearman’s correlation coefficient 0.912, \( P<0.05 \); Wilcoxon’s signed ranks test \( P=0.532 \)). After a mean follow-up of 31 months, the overall mean bone loss was 0.34 mm (SD 0.65; range: 0–7.1) and 0.33 mm (SD 0.54; range: 0–4.9) with the implant and the patient as the statistical unit, respectively. The follow-up time of the individual implants did not influence peri-implant bone-level changes (\( P=0.084 \)). An overview of the bone loss values is given in Table 6. Individual implants installed in smokers are significantly more prone to experience peri-implant bone loss compared with nonsmokers (\( P<0.001 \)) (Figure 4), with a significant difference for the maxilla (\( P<0.001 \)), but not for the mandible (\( P=0.298 \)) (Figure 5).

Implants installed in the maxilla lost significantly more bone compared with those in the mandible both for smokers (\( P<0.001 \)) and for nonsmokers (\( P<0.001 \)). The same is valid when the PBL was considered as the statistical unit (Table 6). This was confirmed after a logarithmic transformation of the data and mixed model analysis to correct for clustering of implants in patients and jaws. The results are given in Table 7.

<table>
<thead>
<tr>
<th>Value</th>
<th>95 % CI</th>
<th>SE</th>
<th>p-value</th>
<th>Value</th>
<th>95 % CI</th>
<th>SE</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-1.90</td>
<td>0.15</td>
<td></td>
<td>-1.60</td>
<td>-1.74/-1.45</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Maxilla</td>
<td>0.83</td>
<td>0.19</td>
<td>0.000</td>
<td>0.80</td>
<td>0.20/0.85</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Mandible</td>
<td>0</td>
<td>0</td>
<td></td>
<td>-0.45</td>
<td>-0.65/-0.24</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>-0.15</td>
<td>0.17</td>
<td>0.378</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>0</td>
<td>0</td>
<td></td>
<td>0.52</td>
<td>0.20/0.85</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Maxilla * Nonsmoker</td>
<td>-0.37</td>
<td>-0.80/-0.05</td>
<td>0.22</td>
<td>0.084</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxilla * Smoker</td>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandible * Nonsmoker</td>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandible * Smoker</td>
<td>0</td>
<td>0</td>
<td></td>
<td>-0.37</td>
<td>-0.80/-0.05</td>
<td>0.22</td>
<td></td>
</tr>
</tbody>
</table>

Table 7. Linear mixed-effect model analysis after logarithmic transformation of the data evaluating bone loss in smokers and nonsmokers with respect to the jaw. Parameters set to zero as reference (a).
### Table 6. Overview of individual peri-implant bone loss values and patient’s bone loss values in smokers and nonsmokers with respect to the jaw. *Statistically significant at 0.05 level with Mann-Whitney U-test.*

<table>
<thead>
<tr>
<th>IMPLANT</th>
<th>non-smoker</th>
<th>smoker</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maxilla + Mandible</td>
<td>0.29 mm n=829 (SD 0.54) range: 0.00 - 7.10</td>
<td>0.53 mm n = 234 (SD 0.92) range: 0.00 - 5.90</td>
<td>p &lt; 0.001*</td>
</tr>
<tr>
<td>Maxilla</td>
<td>0.33 mm n=492 (SD 0.65) range: 0.00 - 7.10</td>
<td>0.74 mm n = 137 (SD 1.07) range: 0.00 - 5.90</td>
<td>p &lt; 0.001*</td>
</tr>
<tr>
<td>Mandible</td>
<td>0.22 mm n=337 (SD 0.50) range: 0.00 - 4.55</td>
<td>0.25 mm n = 97 (SD 0.56) range: 0.00 - 4.90</td>
<td>p = 0.298</td>
</tr>
<tr>
<td><strong>p value</strong></td>
<td>p &lt; 0.001*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| PATIENT                  |            |                |            |
| Maxilla + Mandible       | 0.30 mm n = 235 (SD 0.65) range: 0.00 - 4.90 | 0.46 mm n = 65 (SD 0.56) range: 0.00 - 2.80 | p = 0.009* |
| Maxilla                  | 0.33 mm n = 135 (SD 0.53) range: 0.00 - 4.90 | 0.61 mm n = 31 (SD 0.66) range: 0.00 - 2.80 | p = 0.008* |
| Mandible                 | 0.27 mm n = 117 (SD 0.58) range: 0.00 - 4.20 | 0.32 mm n = 34 (SD 0.43) range: 0.00 - 1.58 | p = 0.097 |
| **p value**              | p < 0.001* |                 | p = 0.020* |
Chapter 2: Smoking: a 2-year retrospective analysis

Figure 4. Cumulative percentage of individual peri-implant bone loss based on available radiographs (n=1076), smokers (n = 234) compared to nonsmokers (n = 829).

2.3.3 Implant success

Individual implant success was calculated with respect to the follow-up time. The overall success rate, based on radiographs taken between 24 and 58 months after implant insertion, was 95%. A significant difference was found between smokers (89.6%) and nonsmokers (96.5%) (P<0.001). Table 8 provides an overview of the success rates for smokers and nonsmokers with respect to the jaw. In the maxilla, the success rate was significantly higher for nonsmokers (96.8%) compared with smokers (87.8%) (P<0.001). This difference could not be found in the mandible (96.2% vs. 92.2%; P=0.083). If a threshold of <1 or <2 mm of bone loss was considered as the criterion for success, an overall success rate of 90.6% and 95.7% was found, respectively.
Chapter 2: Smoking: a 2-year retrospective analysis

Figure 5. Boxplot presenting individual peri-implant bone loss in smokers and nonsmokers after at least 2 years, comparing maxilla (n = 492 in nonsmokers; n = 137 in smokers) and mandible (n = 337 in nonsmokers; n = 97 in smokers).

Table 8. Overview of implant success rates in smokers and nonsmokers with respect to the jaw. *Statistically significant at 0.05 level with the Fisher’s Exact Test.
2.4 Discussion

This study scrutinized implant outcome in relation to smoking. Given the retrospective study design, it is based on patients' records. As such, it relies on the accuracy of the record and the self-reported smoking habits of the patients. It is known from clinical studies relating general health issues to smoking that patients cannot be considered truthful. Some patients considerably underreport their smoking behavior and biochemical techniques are necessary to objectively quantify tobacco usage. Therefore, a patient was considered a smoker when it was written down in the patient file, irrespective of the amount of cigarettes consumed on a daily basis. As such, the study makes no distinction between heavy and light smokers. Also, tobacco usage may change over time, but we consider smoking at the time of surgery as the decisive factor influencing peri-implant bone and soft tissue healing.

Only a few clinical studies or abstracts are available on implants with a fluoride-modified surface, showing an implant survival of 94.5–100%. Grit-blasted implants without the additional fluoride modification (TiOblast™, Astra Tech®, Mölndal, Sweden) are well documented and show good clinical results, with survival rates from 89.7% to 100%.

The present study reports an absolute survival rate of 98.3% after 24–58 months of follow-up, confirming the good results of the aforementioned studies. The cumulative survival calculation shows that the majority of the failures occur before prosthetic loading, although additional failures do occur after 2 years. Controlled long-term clinical trials to provide an insight into the stability and prognosis of these novel implant surfaces are still lacking. Additionally, this study reflects the everyday clinical practice where all implants, placed by one experienced clinician, are included.

The present study shows that smokers are 2.5 times more likely to experience implant failure, both at the implant and at the patient level when comparing absolute survival rates. This is in accordance with a previous meta-analysis showing a risk of implant failure for smokers of 2.4 considering all included studies on implant-related data and 2.6 considering all included studies on patient-related data. The CSR reveal a 4 and 3.3 times higher failure rate for smokers compared with nonsmokers at the patient level and the implant level, respectively. In our analysis, smokers showed significantly more implant failures in the mandible compared with the maxilla (P=0.012). All of the failures in the mandible occurred
in the posterior region. One could speculate that this may be caused by the high bone density and deficiency of vascularization known to occur in the posterior mandible, especially in elderly and edentulous patients. This, in combination with the negative effect of smoking on soft tissue healing due to an impaired revascularization, may compromise bone healing after implant insertion, possibly increasing the number of early implant failures. Additionally, negative effects of smoking on bone metabolism and delayed fracture healing are common in orthopedics. Smokers require a longer healing time after fractures and will have a higher incidence of nonunion of broken bones, infection and/or flap necrosis.

In the present study, an overall mean bone loss of 0.34 mm was found with implant insertion as the baseline value. Recent studies evaluating peri-implant bone-level changes around implants with a fluoride-modified surface reported mean bone-level changes of 0.25–0.5 mm. In a recent systematic review, a mean value of 0.25 mm was found for grit-blasted implants without fluoride modification. The included studies reported bone-level changes from the time of prosthetic loading or second-stage surgery, where the initial bone remodeling before prosthetic loading is not taken into account. As described by Åstrand et al. (2004), major changes in peri-implant bone level can take place between implant insertion and prosthetic loading. Additionally, Cooper et al. (2001) concluded that bone loss around early loaded implants amounted to 0.4 mm during the first 6 weeks of loading, while no further bone loss could be observed following the subsequent year. One could conclude that if the radiographic analysis is performed many months after implant insertion, the total bone loss may be underestimated. Hence, in the present study, a mean bone loss of 0.34 mm from the time of implant insertion can be considered very successful.

As smoking is a systemic factor, peri-implant bone loss was analyzed at the patient level. Moreover, the calculation of peri-implant bone loss was also performed with the individual implant as the statistical unit because a calculation at the patient level may conceal clinical complications when multiple implants are placed. In the present study, bone loss was 0.33 mm when calculated with the patient as the statistical unit but the range decreased considerably (0–7.1 vs. 0–4.9 mm). Indeed, one implant with extended bone loss can be masked when other implants in the same patient present no bone loss at all. Hence, calculating individual peri-implant bone loss is an appropriate way to evaluate biological complications.
The findings from the present study show that the mean peri-implant bone loss is higher in smokers compared with nonsmokers. This is in accordance with other studies summarized in Table 1, whereby 15 out of 16 studies reported a significant difference. In seven studies out of 16, separate values were not reported for smokers and nonsmokers but it was reported that a significant difference was observed. The difference in the present study was observed in the maxilla, but could not be found in the mandible. These results are in accordance with previous studies. This leads to the question regarding the different effects that cigarette smoking can exert on the maxilla and the mandible. A possible explanation is that the mandible is partially protected by the tongue, preventing a direct influence from tobacco smoke to the peri-implant tissues. This might explain the better results in the mandible, comparable to the results in nonsmokers. Moreover, it is reasonable to believe, as bone quality is in general more favorable in the mandible, that the maxilla is more prone to the pernicious effect of smoking over the years.

In the present paper, an overall success rate of 95% was found. Only 5% of the implants lost >1.5 mm during the first year of loading and additionally >0.2 mm per year. One should keep in mind that these criteria do not deal with bone remodeling before prosthetic loading, probably yielding an underestimation of the success rate in this study. If we lower the threshold for success to <1 mm of bone loss as proposed by De Bruyn and Collaert (2008), an overall success rate of 90.6% is found. Recently, implant success was defined as <2 mm of bone loss from the time of implant insertion. A success rate of 95.7% was found according to the latter. Taking into account that different baseline values and different success criteria are used in the literature, making a comparison between studies on implant success is extremely difficult.

Finally, surface modifications can influence bone preservation. Despite this enhanced outcome, smokers are more likely to experience implant failure and maxillary peri-implant bone loss. A recent comparative, controlled, prospective study by Shibli et al. (2010) comparing bone healing in smokers and nonsmokers around implants with an anodized surface showed more marginal bone loss and fibrous tissue in smokers. Also, bone-to-implant contact and bone density in the threaded area were significantly lower compared with nonsmokers. Randomized-controlled trials are warranted to investigate the effect of surface modifications on long-term bone preservation in smokers.
2.5 Conclusion

The present study is the first to compare peri-implant bone loss in smokers and nonsmokers from the time of implant insertion (baseline) to at least 2 years of follow-up. Implants with a fluoride-modified surface demonstrated a high survival rate and limited bone loss. However, smokers are more prone to experience implant failure and show more peri-implant bone loss in the maxilla. Whether this bone loss is predicting future biological complications remains to be evaluated. Prospective studies are required to assess the dose-dependent effect of smoking on implant outcomes. In the meantime, all patients should be informed about smoking cessation.
2.6 References


Chapter 2: Smoking: a 2-year retrospective analysis


CHAPTER 3

IMMEDIATE LOADING IN THE MAXILLA

THIS CHAPTER HAS BEEN PUBLISHED AS:

IMMEDIATE LOADING OF IMPLANTS IN THE MAXILLA: SURVIVAL AND BONE LOSS AFTER AT LEAST 2 YEARS IN FUNCTION

Vervaekte S, Collaert B, & De Bruyn H

CHAPTER 3: Immediate loading of implants with a fluoride-modified surface in the maxilla: survival and peri-implant bone loss after at least 2 years in function

ABSTRACT

Purpose: To compare survival and peri-implant bone loss around immediately loaded surface-enhanced implants in the maxilla supporting single crowns (SCs), fixed partial dentures (FPDs), and fixed full-arch dentures (FFDs).

Materials and Methods: The study included all subjects referred for implant treatment in the maxilla followed by immediate loading between November 2004 and 2007 with at least 2 years of follow-up. Smokers were excluded. Implant survival and bone loss were assessed by a calibrated external examiner who compared digital periapical radiographs taken during recall visits with baseline radiographs (day of loading = day after implant placement). An implant was considered successful when bone loss did not exceed 1 mm. Survival of implants supporting SCs, FPDs, and FFDs was compared using the log-rank test. A linear mixed-effect model analysis was used to evaluate bone loss because of clustering of implants in patients.

Results: Three hundred six implants were placed in 55 patients (31 women, 24 men; mean age, 57.5 ± 11.4 years; range, 19 to 77 years) and followed for a mean of 35 ± 10.2 months (range, 24 to 58 months). One implant failed, resulting in an overall survival rate of 99.7% on the implant level and 98.2% on the patient level. No statistically significant differences were observed in the survival rates for SCs (100%), FPDs (98%), and FFDs (100%). The overall mean bone loss was 0.27 ± 0.37 mm (range, 0.00 to 2.55 mm) and was not influenced by the prosthetic reconstruction.

Conclusion: Immediate loading of fluoride-modified implants in the maxilla is a predictable and reliable treatment option with high survival rates and limited peri-implant bone loss after 2 years. No statistically significant differences were found between implants supporting SCs, FPDs, and FFDs.
3.1 Introduction

Over the past few decades, implant treatment protocols have evolved. Because of new implant designs and surface configurations and better insights in surgical procedures, the time frame between implant placement and functional loading has been shortened. Immediate loading has been described as a successful treatment option for different dental applications, such as full-arch rehabilitations and single tooth replacement.

Osseointegration can occur successfully under immediate loading conditions if excessive micromotions at the bone-to-implant interface is avoided. There is no consensus on the threshold that cannot be surpassed, but it is believed to range between 50 and 150 µm. One can assume that micromotion is reduced when implants are splinted in multiple-unit restorations, but this can not be accomplished when restoring solitary implants or small partial restorations.

Immediate rehabilitation on dental implants results in a significant reduction of treatment time and morbidity for the patients by avoiding a second stage surgery to uncover the implants. A comparative clinical trial showed that this protocol results in a significantly higher patient satisfaction. Dierens and co-workers showed that immediate full-arch rehabilitation yields an instant significant improvement in general patient satisfaction and self-perceived factors related to comfort, function and esthetics. Eating comfort is the main concern for the patient and shows the highest improvement. Raes and coworkers (2011) showed that patients missing a single tooth in the anterior maxilla have limited problems with oral health related quality of life; nevertheless, statistically significant improvements in several domains were found after immediate provisionalisation with an implant.

In addition, adaptations and/or different relining procedures for removable prosthesis during preprosthetic healing of the implants are no longer required when immediate loading is applied. This further reduces post-operative care and chairside time for the clinician.

Recently, most companies have begun offering surface modifications of their implants to enhance osseointegration, providing possibilities to change both surgical and prosthetic loading protocols. The Osseospeed™ (Astra Tech Dental, Mölndal, Sweden) titanium implant surface is grit-blasted and then additionally treatment with diluted fluoride-acid. Fluoridation results in a nanoscale surface topography. The implant surface is slightly
Chapter 3: Immediate loading in the maxilla

A smoother (Sa: 0.91 +/- 0.14 micron) than the TiOblast\textsuperscript{TM} surface (Astra Tech Dental, Mölndal, Sweden), which does not have the additional surface modification (Sa: 1.12 +/- 0.24 micron)\textsuperscript{20}. The results of experimental studies showed faster and stronger establishment of bone-to-implant contact during the first weeks of healing after implant placement\textsuperscript{21,22}. This result suggests that patients can benefit from chemically modified implant surfaces, especially in more demanding cases such as immediate loading.

Limited data are available on survival and bone loss of immediately loaded implants with a fluoride-modified surface. A recent prospective study of Collaert and co-workers described immediate loading of these implants with a screw-retained fixed rehabilitation. They observed no implant failures and limited bone loss and concluded that this is an effective, predictable and reliable treatment option to restore the completely edentulous mandible\textsuperscript{23}. However little scientific evidence is available regarding immediate loading in the maxilla.

The purpose of the present study is to describe implant survival and peri-implant bone loss around immediately loaded implants with a fluoride-modified surface in the maxilla, and to determine whether the outcome is influenced by the type of prosthetic reconstruction.

3.2 Materials & Methods

3.2.1 Patient Selection and Clinical procedures

In this cross-sectional retrospective study, the files of all patients referred for implant treatment in the maxilla followed by immediate loading between November 2004 and 2007 were scrutinized. The study protocol was approved by the ethical committee of the Ghent University Hospital (EC 2008-357, UZGent).

All nonsmoking patients with at least 2 years of follow-up were included. Smokers were excluded because of the known effect of smoking on bone loss around implants placed in the maxilla\textsuperscript{24,25}. Subjects with inadequate bone volume, requiring guided bone regeneration or bone grafting were also excluded. All implants were placed by the same surgeon (BC) in healed ridges. In case of previous tooth extraction, a healing time of at least 3 months was allowed before implant placement. A crestal incision was made, a mucoperiosteal flap elevated and implants were placed according to the manufacturer’s guidelines in a
prosthetically driven way, using the patient’s denture as a surgical guide whenever applicable. Six to 8 implants were placed in edentulous patients. After implant placement, uni-abutments with a height ranging between 1 and 4 mm were placed when partial or full dentures were planned. In patients who required full dentures, the impression was made with the patient’s denture and conical copings using the repositioning technique\textsuperscript{7,8}. For single crowns and partial dentures, the impression was made with the pick-up technique using an open tray. A provisional acrylic resin screw-retained crown or metal-reinforced denture was placed the day after surgery. After implant treatment, all patients were scheduled for professional maintenance that included radiographic follow-up. The frequency and content of professional maintenance were based on the clinical situation and adapted to the individual need of the patient. The definitive restorations were made by the restorative dentists after at least three months of healing, allowing soft tissue adaptation. An external examiner from the University of Ghent (SV) had access to the anonymous patient files to evaluate implant survival and peri-implant bone loss.

Figure 1. The reference point, lower border of the smooth implant collar, indicated by the black arrow.
3.2.2 Examination Criteria and Statistical analysis

An implant was considered a failure when it was removed because of mobility, loss of integration, ongoing bone loss, infection and/or persistent pain or patient discomfort. An individual implant was considered as either surviving (value 0) or a failed (value 1) for Kaplan-Meier survival analysis. The log-rank test was used to compare the survival of individual with both patient and the implant as statistical unit. Peri-implant bone loss was assessed by an external examiner (SV), who compared periapical radiographs, obtained during recall visits; post-operative radiographs were obtained by the surgeon immediately after provisional loading (1 day after implant placement) using digital software (Visi-Quick®, Amsterdam, The Netherlands) with an accuracy of 0.1 mm. Care was taken to visualize the implant threads clearly. The marginal bone level was determined both at the mesial and distal of each implant by measuring the distance between a reference point (lower border of the smooth implant collar or the uppermost point of the microthreaded part) and the marginal bone-to-implant contact (Figure 1). The values were averaged to obtain a single value for each implant. The reference point was described by previous authors who used the same implant system protocol guide. The subject’s bone loss was calculated as the mean value for all individual implants to obtain a single value per patient. Differences in bone loss with respect to the type of prosthesis and location of the implants were scrutinized using the linear mixed-effect model analysis to correct for clustering implants in the same patient. This statistical analysis includes the patient as a factor. An individual implant was arbitrarily designated as successful when bone loss was ≤ 1.0.

3.3 RESULTS

3.3.1 Survival

Fifty-five patients (24 males, 31 females) with a mean age of 57.5 years (SD 11.4, range 19-77) with 306 implants met the inclusion criteria. The implant dimensions are given in table 1. Nine implants in nine subjects supported single crowns (SC), 53 implants (15 subjects) supported fixed partial dentures (FPD) and 244 implants (31 subjects) supported fixed full dentures (FFD). After a mean follow-up of 35 months (SD 10.2, range 24 – 58), one implant
failed resulting in overall cumulative survival rates of 99.7 % and 98.2 % with the implant and the patient as statistical unit, respectively. The failure occurred in the FPD group after 24 months, resulting in a prosthetic survival rate of 98.1 %. No statistically significant differences were found in survival rates in the different prosthetic groups (p = 0.734).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>SE</th>
<th>p - value</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>intercept</td>
<td>0.14</td>
<td>0.10</td>
<td>0.169</td>
<td>-0.06 – 0.34</td>
</tr>
<tr>
<td>SC</td>
<td>0.17</td>
<td>0.13</td>
<td>0.212</td>
<td>-0.10 – 0.43</td>
</tr>
<tr>
<td>FPD</td>
<td>0.13</td>
<td>0.09</td>
<td>0.169</td>
<td>-0.06 – 0.31</td>
</tr>
<tr>
<td>FFD</td>
<td>0(^a)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incisors - Canines</td>
<td>0.10</td>
<td>0.09</td>
<td>0.257</td>
<td>-0.08 – 0.29</td>
</tr>
<tr>
<td>Premolars</td>
<td>0.11</td>
<td>0.09</td>
<td>0.240</td>
<td>-0.07 – 0.029</td>
</tr>
<tr>
<td>Molars</td>
<td>0(^a)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Mixed model analysis estimating bone loss of implants supporting single crowns (SC), fixed partial dentures (FPD) and fixed full dentures with respect to implant location. 

\(^a\) Parameter set to zero as a reference value. No significant differences were found.

3.3.2 Peri-implant bone loss

Overall mean bone loss values of 0.27 mm (SD 0.37, range 0.00 – 2.55) and 0.30 (SD 0.30, range 0.00 – 1.53) were observed from the day of implant placement with the implant and the patient as statistical unit, respectively. Figure 2 shows peri-implant bone loss of all individual implants with their maximum follow-up time. Implants supporting SCs lost on average 0.39 mm (SD 0.26, range 0.10 – 0.85), those supporting FPDs lost 0.38 mm (SD 0.51,
range 0.00 – 2.55) and those supporting FFDs lost 0.24 mm (SD 0.34, range 0.00 – 1.95) (Figure 3). Results of the mixed model analysis are given in Table 2. No statistically significant differences in peri-implant bone loss were observed. The interaction between the prosthetic reconstruction and implant location was not statistically significant (p = 0.383).

![Figure 2](image)

*Figure 2. Scatter plot presenting individual peri-implant bone loss for implants supporting single crown’s (SC), fixed partial dentures (FPD) and fixed full dentures (FFD) with their respective maximum follow-up time.*

Fourteen implants lost more than 1.00 mm of bone after at least 2 years in function, resulting in an overall success rate of 95.4 %. Success rates for implants supporting SCs, FPDs and FFDs were 100 %, 90.6 % and 96.3 %, respectively (Figure 4). No statistically significant differences were found (p = 0.159).
Figure 3. Boxplot presenting peri-implant bone loss of implants supporting SC’s (n = 9), FPDs (n = 53) and FFDs (n = 244). The mean follow-up time for the three groups was respectively 43.2 (SD 13.1, range 25 – 58), 39.0 (SD 9.9, range 24 – 51) and 32.0 (SD 7.8, range 24 – 56) months.
Figure 4. Cumulative percentage of all implants related to their individual peri-implant bone loss for single crowns (SC, n = 9), fixed partial (FPD, n = 53) and fixed full dentures (FPD, n = 244). The black line indicates the threshold, set at 1mm, as an arbitrarily chosen criterion for success. All individual at the left side of the black line are considered a success. This respectively corresponds to 100 % for implants supporting SCs, 90.6 % for FPDs and 96.3 % for FFDs.
3.4 Discussion

The present retrospective, cross-sectional study observed an overall survival rate of 99.7 % for immediately loaded maxillary implants with a fluoride-modified surface. The result is in agreement with other studies using the same implant, which have reported survival rates from 94.5 % to 100 %. However, controlled clinical trials that might give insight in stability and prognosis of these novel implant surfaces in the long-term are still lacking. In the current study, one implant failed in the FPD group. No statistically significant differences were found between splinted and nonsplinted implants. These results suggest that immediate nonocclusal loading of single-tooth implants is a reliable treatment option if care is taken to avoid excessive micromotion. The result in the present study corresponds with the high survival rates for single implants with a fluoride-modified surface reported previously.

The reported mean bone loss of 0.27 mm and 0.30 mm with the implant and patient as statistical unit, respectively, from the day of loading to at least 2 years in function, are also in agreement with previous studies. A recent systematic review reported a mean bone loss of 0.24 mm after 5 years for the Astra Tech system. However, in most of the included studies, bone loss was reported beginning at the second stage surgery or the day of prosthetic loading, 3 to 6 months after implant placement. Åstrand and coworkers (2004) reported that important bone remodeling occurs between implant placement and prosthetic loading even when a 2-stage procedure is applied. This should be taken into account when considering the total amount of bone loss after a delay. Hence, a mean bone loss of 0.27 mm from the day of immediate loading to at least 2 years can be considered even more successful.

Collaert and coworkers (2011) observed a mean bone loss of 0.11 mm using the same implant system and the same baseline after up to two years in function for immediately loaded FFDs in the mandible. Compared to a mean bone loss of 0.24 mm for the FFDs in the maxilla, this suggests that the maxilla may be more prone to peri-implant bone loss compared with the mandible, as has been suggested by other studies.

Only 14 implants lost > 1mm of bone after at least 2 years in function, resulting in a 95.4 % success rate. Collaert & De Bruyn defined success as ≤ 1 mm of bone loss after 1 year and ≤...
1.5 mm after 3 years for immediately loaded maxillary implants and reported corresponding success rates of 82 % and 86 % \(^7\,^8\).

The 1986 success criteria according to Albrektsson and co-workers would allow 1.7 mm of bone loss after 2 years \(^34\). If these criteria are applied to the present study, a success rate of 99 % is achieved. However, their criteria do not deal with immediate loading and do not take initial bone remodeling between placement and loading into account, since in the 1980s and 1990s baseline values were frequently set at the day of prosthetic loading.

Today, 1.7 mm of bone loss should no longer be considered successful for several reasons. First, implant designs have been altered and placement at the bone crest level is advocated. Second, the esthetical demands of patients have increased, especially in the maxilla. Bone loss will unavoidably lead to soft tissue recession, compromising the esthetic outcome. An unesthetic result will often lead to patient dissatisfaction. Furthermore, bone loss leading to exposure of the roughened implant surface may alter the bacterial environment in the peri-implant sulcus, compromise the steady-state bone levels on the long run, and possibly initiate peri-implantitis. The success criteria, as revised here, that include bone loss from the day of implant placement or the day of loading may be more applicable to scrutinize currently used implant systems and different treatment protocols.

### 3.5 Conclusion

Immediate loading in the maxilla is a predictable and reliable treatment option, with high survival rates and limited peri-implant bone loss after 2 years. No statistically significant differences were found between implants that supported single crowns, fixed partial dentures and fixed full dentures.
3.6 References


Chapter 3: Immediate loading in the maxilla


CHAPTER 4

SHORT-TERM EVALUATION OF PREDICTORS AFFECTING IMPLANT TREATMENT OUTCOME

THIS CHAPTER HAS BEEN PUBLISHED AS:

A MULTIFACTORIAL ANALYSIS TO IDENTIFY PREDICTORS OF IMPLANT FAILURE AND PERI-IMPLANT BONE LOSS IN A LARGE PRIVATE PRACTICE COHORT

Vervaeke S, Collaert B, Cosyn J, Deschepper E & De Bruyn H

CHAPTER 4: A multifactorial analysis to identify predictors of implant failure and peri-implant bone loss in a large private practice cohort

ABSTRACT

Objective To identify risk factors for failure and bone loss of implants in a large study sample on the basis of multivariate analyses.

Materials and Methods Patient files of all patients referred for implant treatment from November 2004 to December 2007 were scrutinized, and information on implant- and patient-related factors was collected. The study sample in this retrospective cohort study consisted of both partially dentate and fully edentulous patients referred for various indications. The only inclusion criterion was a follow-up of at least 2 years. Implant survival and bone loss were assessed by an external investigator (SV) comparing digital periapical radiographs taken during recall visits with the postoperative ones. Univariate and multivariate tests were adopted to identify possible risk indicators for implant failure and peri-implant bone loss.

Results Twenty-one of 1,320 (1.6%) implants were lost in 19 of 376 (5.1%) patients (210 female, 166 male; mean age 56, range 17–82) after a mean follow-up of 32 months (range 24–62). Based on multivariate analysis, only smoking \((p = .001)\) and recall compliance \((p = .010)\) had a significant influence on implant failure, with smokers more prone to failure. The overall mean bone loss was 0.36 mm (SD 0.68, range 0.00–7.10). Smoking \((p = .001)\) and jaw of treatment \((p = .001)\) affected peri-implant bone loss. More peri-implant bone loss was observed in smokers and in the maxilla. A clear discrepancy was found between univariate and multivariate analysis with regard to identification of risk factors.

Conclusion Multivariate analysis demonstrated that implant-related factors did not affect the clinical outcome, but smoking was identified as a predictor for implant failure. Predictors for peri-implant bone loss were smoking and jaw of treatment.
Chapter 4: Short-term evaluation of predictors affecting implant treatment outcome

4.1 Introduction

A systematic review and meta-analysis based on multiple randomized controlled trials obtains the highest level of scientific evidence. In implant dentistry, such a level of evidence is available on the outcome of different implant treatment protocols \(^1,^2\) and different risk factors \(^3-^5\). A risk factor for treatment failure can be identified in a randomized controlled trial; however, the relative importance of one factor in relation to others cannot be assessed in such a study. A thorough risk assessment requires multivariate analyses correcting for confounding factors. In this context, large prospective or even retrospective case series may become particularly important.

A recent retrospective study evaluated the influence of different factors on long-term bone stability around immediately placed implants in a large retrospective cohort. \(^6\) Based on a univariate analysis, different factors such as age at time of implant placement, gender, implant surface, implant width, and implant location affected crestal bone loss. The authors described these factors as statistically significant but clinically irrelevant. Indeed, small differences can show statistical significance given the large number of implants but may not be clinically relevant. Another possible explanation is the adopted statistical analysis. Univariate tests do not correct for confounding factors. Given the large number of implants and explanatory variables, interaction between different variables may be conceivable. For this purpose a multivariate analysis was already suggested by Cosyn. \(^7\) They evaluated the influence of different factors on implant failure and found a clear discrepancy between results of univariate and multivariate statistical analyses.

The primary aim of the study was to evaluate implant survival and peri-implant bone loss of surface-modified implants with a minimum follow-up of 2 years.

The secondary aim was to identify predictors affecting implant treatment outcome using multivariate tests that correct for confounding.
4.2 Materials & Methods

4.2.1 Study Sample

All consecutively treated patients between November 2004 and December 2007 and with a minimum follow-up of 2 years were included in this retrospective cohort study. Patients were referred by their restorative dentist to a private periodontal practice for implant placement. No patients were excluded based on medical risk factors, history of periodontitis, or smoking habits. They comprised partially dentate and fully edentulous patients with various indications for implant rehabilitations. All patients were treated by the same surgeon using the same implant system (Osseospeed™, Astra Tech, Molndahl, Sweden). All implants were installed according to the manufacturer's guidelines based on proper presurgical radiographic planning. Patients with periodontitis or endodontic pathology were treated prior to implant placement to minimize the risk for biological complications. Implants were placed using different surgical techniques (one-stage and two-stage surgery) and different loading protocols (immediate loading and delayed loading). Hence, three different treatment protocols were analyzed, being immediate loading, one-stage delayed loading, and two-stage delayed loading. In the case of immediate loading, an impression was made directly after implant installation and a provisional acrylic, metal-reinforced, screw-retained restoration was placed the day after surgery. Immediate full-occlusal loading with balanced occlusion and articulation was applied for all cases, except for single tooth replacement, where nonocclusal loading was applied. The final restorations were made by the restorative dentists after a healing time of at least 3 months. The restorative dentists were both general practitioners and prosthodontists with different levels of experience. After implant treatment, all patients were invited by the surgeon for recall. Recall visits were adapted to individual patient needs and consisted of both clinical and radiological evaluation of the implants, including occlusion/articulation.
4.2.2 Dependent Variables and Covariates

All patient files were scrutinized by an external investigator from the Ghent University. Implant failure and interproximal peri-implant bone loss were considered the dependent variables. Information on different predictors was collected from the patient files, including surgical protocol, loading protocol, smoking habit, jaw location, patient's recall status, implant length, implant width, implant design, prosthetic reconstruction, and the antagonistic jaw. Peri-implant bone loss was assessed by an external examiner comparing digital radiographs taken during recall visits with the postoperative ones taken by the surgeon immediately after implant installation (baseline). Digital software with an accuracy of 0.1 mm (Visi-quick®, Amsterdam, the Netherlands) was used for radiological evaluation. Marginal bone level was determined at both the mesial and distal sites of each implant by measuring the distance between a reference point (lower border of the smooth implant collar or the uppermost point of the microthreaded part) and the marginal bone-to-implant contact point. Values were averaged to obtain a single value per implant. The study protocol was approved by the ethical committee of the Ghent University Hospital.

4.2.3 Statistical Analysis

Inter- and intraexaminer reliability were assessed using the intraclass correlation coefficient (ICC) based on a two-way random model with absolute agreement. The possible predictors and dependent variables were cross-classified using contingency tables. The impact of the explanatory variables on implant survival was analyzed using the Mantel-Cox log-rank test. For this reason, the continuous predictors or so-called covariates were categorized. Because of possible interaction between the explanatory variables, the univariate analysis can be considered exploratory. For this purpose, a multivariate analysis was adopted. This analysis consisted of the Cox proportional hazards regression. A model was fitted including as many variables as possible. The level of significance was set at .05.

The impact of the different explanatory variables on peri-implant bone loss was analyzed using both univariate and multivariate tests for the aforementioned reason. The Mann-
Whitney U-test was adopted to explore the impact of each variable. Multivariate analysis consisted of the linear mixed-effect model analysis after a logarithmic transformation of the data. This transformation was mandatory after validation of the statistical model in terms of linearity and homoskedasticity. The level of significance was set at .05. The statistical analyses were performed using IBM® SPSS® 19.0 for Windows.

4.3 RESULTS

4.3.1 Overall Clinical Outcome

Three hundred seventy-six patients (166 men, 210 women; mean age 56, range 18–82) with 1,320 implants met the inclusion criterion of 2 years of follow-up. The average time between implant installation (baseline) and evaluation in this cross-sectional study was 32 months. Twenty-one implants failed in 19 patients, resulting in an absolute survival rate of 98.4%. Implant failure was experienced by 5.1% of the patients (Table 1). Seventeen patients lost 1 implant and 2 patients lost 2 implants. Eleven failures occurred during the first 6 months and 10 implants failed during follow-up, 24 to 59 months after implant placement. Table 2 shows cumulative survival rates (CSR). After 24 to 29 months, the CSR was 98.7% and 96.8% with the implant and the patient as statistical unit, respectively.

Out of 1,299 surviving implants, 1,288 had readable radiographs. Intraexaminer repeatability on bone loss was high (ICC 0.969, 95% confidence interval (CI) 0.924–0.988), as was the interexaminer repeatability (ICC 0.964, 95% CI 0.910–0.985). A mean bone loss of 0.36 mm (SD 0.68, range 0.00–7.10) was observed after a mean follow-up of 32 months (Table 1). Individual peri-implant bone loss in relation to the follow-up time is given in Figure 1.
Chapter 4: Short-term evaluation of predictors affecting implant treatment outcome

<table>
<thead>
<tr>
<th>Survival Group</th>
<th></th>
<th>Bone Loss Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>n</td>
<td>Failures (%)</td>
</tr>
<tr>
<td>Total Group</td>
<td>1320</td>
<td>21(1.6)</td>
</tr>
<tr>
<td>Treatment Protocol</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1-stage delayed loading</td>
<td>460</td>
</tr>
<tr>
<td></td>
<td>2-stage delayed loading</td>
<td>211</td>
</tr>
<tr>
<td>Smoking Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-Smokers</td>
<td>1017</td>
</tr>
<tr>
<td>Jaw</td>
<td>Maxilla</td>
<td>757</td>
</tr>
<tr>
<td></td>
<td>Mandible</td>
<td>563</td>
</tr>
<tr>
<td></td>
<td>&lt; 10 mm</td>
<td>255</td>
</tr>
<tr>
<td></td>
<td>&gt; 10 mm</td>
<td>1065</td>
</tr>
<tr>
<td></td>
<td>Narrow (≤ 3.5 mm)</td>
<td>348</td>
</tr>
<tr>
<td></td>
<td>Regular (4.0 mm)</td>
<td>576</td>
</tr>
<tr>
<td></td>
<td>Wide (≥4.5 mm)</td>
<td>396</td>
</tr>
<tr>
<td></td>
<td>Cylindrical</td>
<td>866</td>
</tr>
<tr>
<td></td>
<td>Conical</td>
<td>454</td>
</tr>
<tr>
<td></td>
<td>Responder</td>
<td>1084</td>
</tr>
<tr>
<td></td>
<td>Non-Responder</td>
<td>236</td>
</tr>
<tr>
<td></td>
<td>Prosthetics</td>
<td>Fixed Full-arch</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fixed Partial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Single Tooth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Overdenture</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antagonist</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Removable denture</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Implants</td>
</tr>
</tbody>
</table>

Table 1. Implant Failure Rates and Peri-Implant Bone Loss with Respect to the Explanatory Variables

<table>
<thead>
<tr>
<th>N (implant)</th>
<th>Failures</th>
<th>Cum Surv</th>
<th>N (patient)</th>
<th>Failures</th>
<th>Cum Surv</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5m</td>
<td>1320</td>
<td>11</td>
<td>376</td>
<td>11</td>
<td>97,1</td>
</tr>
<tr>
<td>6-11m</td>
<td>1309</td>
<td>19,1</td>
<td>365</td>
<td>11</td>
<td>97,1</td>
</tr>
<tr>
<td>12-17m</td>
<td>1309</td>
<td>99,1</td>
<td>365</td>
<td>11</td>
<td>97,1</td>
</tr>
<tr>
<td>18-23m</td>
<td>1309</td>
<td>99,1</td>
<td>365</td>
<td>11</td>
<td>97,1</td>
</tr>
<tr>
<td>24-29m</td>
<td>1309</td>
<td>1</td>
<td>365</td>
<td>11</td>
<td>97,1</td>
</tr>
<tr>
<td>30-35m</td>
<td>708</td>
<td>7</td>
<td>216</td>
<td>11</td>
<td>94,3</td>
</tr>
<tr>
<td>36-41m</td>
<td>389</td>
<td>97,9</td>
<td>135</td>
<td>11</td>
<td>94,3</td>
</tr>
<tr>
<td>42-47m</td>
<td>234</td>
<td>1</td>
<td>86</td>
<td>11</td>
<td>93,2</td>
</tr>
<tr>
<td>48-53m</td>
<td>120</td>
<td>97,5</td>
<td>45</td>
<td>11</td>
<td>93,2</td>
</tr>
<tr>
<td>54-59m</td>
<td>48</td>
<td>1</td>
<td>78</td>
<td>11</td>
<td>62,1</td>
</tr>
<tr>
<td>60-66m</td>
<td>2</td>
<td>78</td>
<td>1</td>
<td>11</td>
<td>62,1</td>
</tr>
</tbody>
</table>

Table 2. Overview of Overall Cumulative Survival Rates and Failures
Chapter 4: Short-term evaluation of predictors affecting implant treatment outcome

Figure 1. Scatter plot presenting individual peri-implant bone loss in relation to the follow-up time. Trendline (Loess curve fitted at 50% of the data) is given in red suggesting that bone loss and follow-up are not related.

4.3.2 Predictors of Implant Failure and Peri-Implant Bone Loss

- **Treatment Protocol (Surgical and Loading Protocols)**

Implants were grouped according to surgical (one-stage vs two-stage surgery) and loading protocol (immediate vs delayed loading). Three different treatment protocols were defined: immediate loading (IL), one-stage delayed loading (1-DL), and two-stage delayed loading (2-DL). Six hundred forty-nine implants were loaded immediately and 671 implants were placed in a delayed loading protocol. Of the latter group, 211 implants were placed in a two-stage surgical protocol, allowing submerged healing. Primary reasons for a two-stage procedure were lack of primary stability or prosthesis wear, possibly interfering with implant
integration. In the IL group, 0.5% of the implants failed, whereas 3.9% failed in the 1-DL group and no failures occurred in the 2-DL group. The corresponding bone loss values were 0.33 mm (SD 0.63, range 0.00–5.05), 0.33 mm (SD 0.70, range 0.00–7.10), and 0.51 mm (SD 0.72, range 0.00–4.60) (Table 1). Univariate analysis showed a significant influence of the treatment protocol on implant survival ($p < 0.001$) and peri-implant bone loss ($p < 0.001$), with more failures in the 1-DL group and more peri-implant bone loss for the 2-DL group. However multivariate analysis failed to show significant differences between the defined groups ($p = 0.497$, $p = 0.346$) (Table 3).

<table>
<thead>
<tr>
<th></th>
<th>SURVIVAL</th>
<th>BONE LOSS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UNI</td>
<td>MULTI</td>
</tr>
<tr>
<td>Treatment Protocol</td>
<td>&lt; 0.001</td>
<td>0.497</td>
</tr>
<tr>
<td>IL vs 1-DL</td>
<td>&lt; 0.001</td>
<td>0.280</td>
</tr>
<tr>
<td>IL vs 2-DL</td>
<td>0.212</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>1-DL vs 2-DL</td>
<td>0.004</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Smoking Status</td>
<td>0.009</td>
<td>0.001*</td>
</tr>
<tr>
<td>Jaw</td>
<td>0.003</td>
<td>0.465</td>
</tr>
<tr>
<td>Implant Length</td>
<td>0.003</td>
<td>0.133</td>
</tr>
<tr>
<td>Implant Width</td>
<td>0.556</td>
<td>0.797</td>
</tr>
<tr>
<td>Implant Design</td>
<td>0.248</td>
<td>0.633</td>
</tr>
<tr>
<td>Recall Status</td>
<td>0.019</td>
<td>0.010*</td>
</tr>
<tr>
<td>Prosthetics</td>
<td>0.002</td>
<td>0.233</td>
</tr>
<tr>
<td>Single Tooth vs Full-arch</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Single Tooth vs Partial</td>
<td>0.289</td>
<td></td>
</tr>
<tr>
<td>Single Tooth vs overdenture</td>
<td>0.178</td>
<td></td>
</tr>
<tr>
<td>Partial vs Overdenture</td>
<td>0.275</td>
<td></td>
</tr>
<tr>
<td>Partial vs Full-arch</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Full-arch vs Overdenture</td>
<td>0.632</td>
<td></td>
</tr>
<tr>
<td>Antagonist</td>
<td>0.531</td>
<td>0.830</td>
</tr>
<tr>
<td>Natural teeth vs Implants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natural teeth vs removable denture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implants vs removable denture</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Results of the univariate and multivariate analyses on implant survival and peri-implant bone loss. The univariate analysis can be considered exploratory. Level of significance was set at 0.05. *Significant predictor. IL, immediate loading; 1-DL, one-stage delayed loading; 2-DL, two-stage delayed loading.
One thousand seventeen implants were installed in 297 nonsmokers and 290 in 74 smokers. Twelve failures occurred in 11 nonsmokers and 9 in 8 smokers. This corresponds with absolute survival rates of 98.8% and 96.9% with the implant as statistical unit. 10.8% of the smokers experienced implant failure compared with 3.7% of the nonsmokers. Cumulative survival rates are given in Table 4. After 24 to 29 months, the CSRs were 99.4% and 98.0% for nonsmokers at implant and patient level, respectively. The corresponding figures for smokers were 97.9% and 91.9%. Mean bone loss for implants installed in smokers was 0.57 mm (SD 0.93, range 0.00–5.90) compared with 0.30 mm (SD 0.58, range 0.00–7.10) for implants installed in nonsmokers (Table 1). Smoking was identified as a significant factor affecting implant treatment outcome ($p = 0.009, p < 0.001$) based on univariate analysis. Multivariate analysis confirmed the impact of smoking on implant survival with a hazard ratio of 0.228 (95% CI 0.089–0.559; $p = 0.001$) and peri-implant bone loss ($p < 0.001$) (Table 3).

Jaw of Treatment

Five out of 757 implants failed in the maxilla and 16 of 563 in the mandible. This corresponds with absolute survival rates of 99.3% and 97.2% (Table 1). After 24 to 29 months, the CSR was 99.3% for implants in the maxilla compared with 98.8% for implants installed in the mandible. The mean bone loss for maxillary implants was 0.42 mm (SD 0.70, range 0.00–7.10) compared with 0.28 mm for implants installed in the mandible (SD 0.63, range 0.00–4.95) (Table 1). Univariate analysis identified the jaw as a significant factor affecting implant survival ($p = 0.003$) and peri-implant bone loss ($p < 0.001$). However, multivariate analysis only confirmed the impact of this factor on peri-implant bone loss ($p < 0.001$) (Table 3).

Implant Features (Length, Width, Design)

Implants were cross-classified in Table 5 for implant length and implant width with the corresponding failures for each group. Implants were grouped according to implant length ($<10 \text{ mm} = \text{short}, >10 \text{ mm} = \text{long}$), width ($\leq 3.5 \text{ mm} = \text{small}, 4.0 \text{ mm} = \text{regular}, \geq 4.5 \text{ mm} = \text{wide}$), and design (conical and cylindrical). Survival rates and peri-implant bone loss values are given in Table 1. Implant length was the only factor with a significant influence on implant survival based on univariate analysis ($p = .003$). However, neither
<table>
<thead>
<tr>
<th>Implant level</th>
<th>Patient level</th>
<th>Nonsmoker</th>
<th>Smoker</th>
<th>Total</th>
<th>Failures</th>
<th>CSR</th>
<th>Failures</th>
<th>CSR</th>
<th>Failures</th>
<th>CSR</th>
<th>Failures</th>
<th>CSR</th>
<th>Failures</th>
<th>CSR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5-1 m</td>
<td>Nonsmoker</td>
<td>1017</td>
<td>5</td>
<td>99,5</td>
<td>284</td>
<td>1</td>
<td>97,9</td>
<td>297</td>
<td>98,3</td>
<td>6</td>
<td>91,9</td>
<td>1</td>
<td>89,8</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Smoker</td>
<td>1012</td>
<td>5</td>
<td>99,5</td>
<td>284</td>
<td>1</td>
<td>97,9</td>
<td>297</td>
<td>98,3</td>
<td>6</td>
<td>91,9</td>
<td>1</td>
<td>89,8</td>
<td>1</td>
</tr>
<tr>
<td>6.1-17 m</td>
<td>Nonsmoker</td>
<td>1012</td>
<td>6</td>
<td>97,9</td>
<td>292</td>
<td>1</td>
<td>97,9</td>
<td>293</td>
<td>98,3</td>
<td>6</td>
<td>91,9</td>
<td>1</td>
<td>89,8</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Smoker</td>
<td>1012</td>
<td>6</td>
<td>97,9</td>
<td>292</td>
<td>1</td>
<td>97,9</td>
<td>293</td>
<td>98,3</td>
<td>6</td>
<td>91,9</td>
<td>1</td>
<td>89,8</td>
<td>1</td>
</tr>
<tr>
<td>18.23 m</td>
<td>Nonsmoker</td>
<td>1012</td>
<td>2</td>
<td>99,4</td>
<td>284</td>
<td>2</td>
<td>97,9</td>
<td>296</td>
<td>98,3</td>
<td>6</td>
<td>91,9</td>
<td>1</td>
<td>89,8</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Smoker</td>
<td>1012</td>
<td>2</td>
<td>99,4</td>
<td>284</td>
<td>2</td>
<td>97,9</td>
<td>296</td>
<td>98,3</td>
<td>6</td>
<td>91,9</td>
<td>1</td>
<td>89,8</td>
<td>1</td>
</tr>
<tr>
<td>24.29 m</td>
<td>Nonsmoker</td>
<td>1012</td>
<td>6</td>
<td>98,2</td>
<td>169</td>
<td>2</td>
<td>96,8</td>
<td>171</td>
<td>95,3</td>
<td>4</td>
<td>95,3</td>
<td>4</td>
<td>95,3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Smoker</td>
<td>1012</td>
<td>6</td>
<td>98,2</td>
<td>169</td>
<td>2</td>
<td>96,8</td>
<td>171</td>
<td>95,3</td>
<td>4</td>
<td>95,3</td>
<td>4</td>
<td>95,3</td>
<td>4</td>
</tr>
<tr>
<td>30-35 m</td>
<td>Nonsmoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Smoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
<tr>
<td>36-41 m</td>
<td>Nonsmoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Smoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
<tr>
<td>42-47 m</td>
<td>Nonsmoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Smoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
<tr>
<td>48-53 m</td>
<td>Nonsmoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Smoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
<tr>
<td>54-59 m</td>
<td>Nonsmoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Smoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
<tr>
<td>60-66 m</td>
<td>Nonsmoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Smoker</td>
<td>1012</td>
<td>1</td>
<td>94,2</td>
<td>37</td>
<td>1</td>
<td>94,2</td>
<td>38</td>
<td>95,3</td>
<td>3</td>
<td>94,2</td>
<td>3</td>
<td>95,3</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 4. Overview of cumulative survival rates and failures in smokers and nonsmokers. CSR: cumulative survival rate.
implant length ($p = 0.133$) nor implant diameter ($p = 0.797$) nor implant design ($p = 0.633$) had a significant impact on implant survival based on a multifactorial analysis. Multifactorial analysis also failed to show a significant impact of the aforementioned parameters on peri-implant bone loss ($p = 0.212$, $p = 0.716$, $p = 0.263$).

<table>
<thead>
<tr>
<th></th>
<th>3.5 mm</th>
<th>4.0 mm</th>
<th>4.5 mm</th>
<th>5 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 mm</td>
<td>49 (3)</td>
<td>47 (2)</td>
<td></td>
<td>96 (5)</td>
</tr>
<tr>
<td>9 mm</td>
<td>26 (2)</td>
<td>39 (1)</td>
<td>41 (2)</td>
<td>54</td>
</tr>
<tr>
<td>11 mm</td>
<td>52 (2)</td>
<td>87 (2)</td>
<td>28</td>
<td>50 (2)</td>
</tr>
<tr>
<td>13 mm</td>
<td>114</td>
<td>154 (1)</td>
<td>81</td>
<td>44 (1)</td>
</tr>
<tr>
<td>15 mm</td>
<td>107</td>
<td>240 (2)</td>
<td>57</td>
<td>42</td>
</tr>
<tr>
<td>17 mm</td>
<td>348 (7)</td>
<td>576 (9)</td>
<td>206 (2)</td>
<td>190 (3)</td>
</tr>
</tbody>
</table>

*Table 5. Implant Distribution according to Implant Length and Diameter. Number of failed implants is given in brackets.*

**Prosthetic Reconstruction**

Implants were grouped according to the type of prosthetic reconstruction. A distinction was made between implants supporting removable dentures, single crowns, fixed partial restorations, and fixed full-arch restorations. Results regarding implant survival and peri-implant bone loss are given in Table 1. Although a significant difference was found based on univariate tests, multivariate analysis failed to show a significant difference regarding either implant survival ($p = 0.233$) or peri-implant bone loss ($p = 0.388$) (Table 2).

**Antagonistic Structure in the Opposing Jaw**

Implants were grouped according to the antagonistic structure in the opposing jaw. Nine hundred twenty implants were placed opposing natural teeth, 172 opposing removable dentures, and 228 opposing dental implants. Results are given in Tables 1 and 2. No significant differences were found regarding implant survival with either univariate ($p = 0.531$) or multivariate tests ($p = 0.830$). Univariate analysis showed a significant influence of the antagonistic structure on peri-implant bone loss ($p < 0.001$), mainly because of increased bone loss around implants opposing natural teeth. However, multivariate analysis failed to confirm this impact ($p = 0.421$).
Recall Compliance

Two hundred ninety-three patients with 1,084 implants responded to the recall invitation after implant placement. All nonresponding patients were contacted by phone and invited for a free examination. Eighty-three patients with 236 implants were willing to attend this examination. Both groups were compared for implant survival and peri-implant bone loss. Results are given in Tables 1 and 2. Responding patients experienced more implant failures based on univariate \( p = 0.019 \) and multivariate tests \( p = 0.010 \). However, as most failures occurred before prosthetic loading, one can conclude that patients who experience implant failure are more compliant compared with patients with successfully integrated implants. After a mean follow-up of 32 months, a mean bone loss of 0.34 mm (SD 0.63, range 0.00–7.10) was observed for the responding group compared with 0.46 (SD 0.83, range 0.00–4.95) for the nonresponding group. The patient’s compliance had a significant impact on peri-implant bone loss based on univariate analysis \( p = 0.036 \), but this result was not confirmed based on multivariate analysis \( p = 0.387 \).

4.4 Discussion

The present study reports the outcome of all patients treated with fluoride-modified implants over a 3-year period in a private periodontal practice and with at least 2 years of follow-up. All patients were consecutively treated and included in the analysis regardless of their risk profile based on medical anamnesis, history of periodontitis, and smoking habits. Prospective studies are often based on small samples of selected patients to evaluate a novel technique or material. However, care has to be taken in extrapolating the results to daily practice, where less than ideal patients are treated. Hence, a survival rate of 98.4% after a mean follow-up of 32 months can be considered very successful, given the fact that this study represents “real-life” daily practice. The survival rate is in accordance with other studies using the same implant system and dealing with different indications and treatment protocols.\(^8\)\(^{-12}\) Out of 21 failures, 11 were categorized as early failures and occurred before prosthetic loading. Different factors such as excessive surgical trauma, smoking, and bone quality have been associated with biological complications due to impaired bone healing after implant placement, possibly leading to fibrous encapsulation and nonintegration.\(^13\) Peri-implantitis and/or occlusal overload are described as the main reasons for late failures.
Chapter 4: Short-term evaluation of predictors affecting implant treatment outcome

occurring after integration of the implant. In the present study, all late failures occurred after at least 2 years of functional loading. The final restorations were made by the referring dentists. They comprised both general practitioners and prosthodontists with different levels of experience. This may be an important factor concerning the late failures. However, the referring dentists and their dental technicians attended multiple training sessions in implant rehabilitation, including individual peer-reviewed sessions organized by the surgeon to enhance the quality of the team approach. Moreover, the recall by the surgeon always consisted of a clinical and radiological examination, including occlusion and articulation. The small number of late failures is a clear proof of a successful team approach.

Recent studies evaluating peri-implant bone level changes around surface-modified implants reported mean bone level changes of 0.25 to 0.50 mm. The current study reported a mean bone loss of 0.36 mm from the time of implant placement. Most studies reported bone loss from the time of prosthetic loading or second-stage surgery, often many months after implant placement. One has to take into account that an important amount of bone loss can already occur during the first months of healing. This bone remodeling occurs after implant placement in order to re-establish enough biological space to sustain the bacterial load in the oral cavity, especially in patients or at sites with thin soft tissues at the time of implant placement. In a recent study, the initial soft tissue thickness was associated with early bone remodeling. However, thereafter, stable bone conditions were described even for implants with early bone loss up to 2 years of function. In the present study most late failures occurred after 2 years and were associated with ongoing bone loss from the day of implant placement. Hence, it is suggested to monitor patients with initial peri-implant bone loss more strictly to prevent future biological complications.

In the current study, implant survival and peri-implant bone loss were comparable for immediate loading, one-stage delayed loading, and two-stage delayed loading. This is in accordance with the existing literature on submerged versus nonsubmerged healing and immediate loading versus delayed loading. In a retrospective analysis of 1,180 surface-modified implants placed in a university postgraduate training center, Cosyn and colleagues described early loading as the only factor with significant impact on implant failure, whereas immediate loading was found to be a viable alternative for delayed loading.
In the present study, the effect of smoking on implant survival and peri-implant bone loss was analyzed at both implant and patient level, as smoking is a systemic factor. Significantly more failures were observed in smokers, and one smoker out of 10 experienced implant failure. Moreover, implants installed in smokers showed significantly more peri-implant bone loss compared with nonsmokers. These results are in accordance with systematic reviews highlighting the effect of smoking on implant survival and peri-implant bone loss.\(^4\),\(^5\) This might explain both the early failures related to impaired wound healing and late implant failures due to ongoing bone loss in the present study.

Both univariate and multivariate analyses revealed significantly more peri-implant bone loss around implants in the maxilla compared with the mandible. This finding is in agreement with previous clinical studies.\(^35\)-\(^40\)

The present study showed more failures in the group with patients responding to the recall invitation after implant placement. As most failures were early failures, this could be interpreted as meaning that patients who experienced implant failure were more compliant compared with patients with successfully integrated implants.

The present study showed a clear discrepancy between univariate and multivariate tests. Univariate analysis consisted of the log-rank test to evaluate implant survival and the Mann-Whitney U-test to evaluate peri-implant bone loss. The Cox proportional hazards regression and the mixed-effect model analysis were the respective multivariate tests. Treatment protocol \((p = 0.001)\), smoking \((p = 0.001)\), jaw of treatment \((p = 0.003)\), patient’s compliance \((p = 0.019)\), implant length \((p = 0.003)\), and prosthetic reconstruction \((p = .002)\) were factors showing significant impact on implant survival on the basis of univariate analysis. However, when controlling for confounding factors, only smoking had a significant influence \((p = 0.001)\), with smokers more prone to failure. Univariate analysis identified treatment protocol \((p = 0.001)\), jaw of treatment \((p = 0.001)\), smoking \((p = 0.001)\), patient’s compliance \((p = 0.036)\), and prosthetic reconstruction \((p = 0.011)\) as risk indicators for peri-implant bone loss. Only smoking \((p = 0.001)\) and jaw of treatment \((p = 0.001)\) affected peri-implant bone loss when a multivariate analysis was adopted. The present study is a retrospective cohort study, which is a noncontrolled study design. Hence, controlling for confounding factors is necessary to identify true risk factors. This multivariate statistical approach was already
suggested by Cosyn and colleagues. They evaluated different factors associated with failure of surface-modified implants and considered the univariate analysis as exploratory because interaction between different predictors was conceivable.

4.5 Conclusion

The present study evaluated the clinical outcome of fluoride-modified implants in a well-organized surgical/prosthodontic team approach. Fluoride-modified implants are a reliable and highly successful treatment option with high survival rates and limited peri-implant bone loss after at least 2 years of function. Multivariate analysis demonstrated that implant-related factors did not affect the clinical outcome, but smoking was identified as a predictor for implant failure. Predictors for peri-implant bone loss were smoking and jaw of treatment.
4.6 References

CHAPTER 5

SOFT TISSUE THICKNESS

THIS CHAPTER HAS BEEN PUBLISHED AS:

THE INFLUENCE OF INITIAL SOFT TISSUE THICKNESS ON PERI-IMPLANT BONE REMODELING

Vervaeke S, Dierens M, Besseler J & De Bruyn H

Clin Implant Dent Relat Res, 2013 (Epub ahead of print)
CHAPTER 5 : The influence of initial soft tissue thickness on peri-implant bone remodeling

ABSTRACT

AIM To elucidate the influence of initial soft tissue thickness on peri-implant bone remodeling. The research hypothesis was that implants installed in patients or at sites with thin mucosal tissues would show increased peri-implant bone loss.

MATERIALS & METHODS 79 edentulous patients were consecutively treated with two non-splinted implants supporting an overdenture in the mandible. During recall-visits, peri-implant health was determined by means of probing pocket depth and the modified plaque/bleeding index. Digital peri-apical radiographs were taken from individual implants. Bone level changes were measured from a reference point (lower border of the smooth implant collar) to the marginal bone-to-implant contact level. The linear mixed-effect model analysis was adopted to analyze the influence of clinical parameters and transmucosal abutment height on peri-implant bone loss. RESULTS 67 patients attended the 1-year and 66 the 2-year recall-visit. Mean bone level changes were 0.89 mm (SD 0.62) and 0.90 mm (SD 0.66), plaque scores 0.82 (SD 0.94) and 0.87 (SD 0.92), bleeding scores 0.46 (SD 0.68) and 0.56 (SD 0.72) and PPD 1.65 mm (SD 0.60) and 1.78 mm (SD 0.59) after 1 year and 2 years respectively. The linear mixed-effect model revealed increasing bone level changes with decreasing abutment heights. Peri-implant bone level changes were significantly higher for implants with abutments of < 2 mm (1.17 mm, p < 0.01; 1.23 mm, p < 0.01), 2 mm (0.86 mm, p < 0.01; 1.03 mm, p < 0.01) or 3 mm (0.38 mm, p = 0.046; 0.41 mm, p = 0.044) compared to ≥ 4 mm-abutments (bone level changes set to zero as reference value) both after 1 year and 2 years and bone level changes were significantly influenced by probing pocket depth (p < 0.01, p < 0.01), but not by plaque (p = 0.31, p = 0.09) and bleeding scores (p = 0.30, p = 0.40).

CONCLUSION The present study suggests that implants with lower abutments, reflecting the initial gingival thickness, lose more peri-implant bone, possibly by a re-establishment of the biological width.
5.1 Introduction

The dentogingival junction defines the soft tissue dimensions around teeth including the gingival sulcus, the junctional epithelium and supracrestal connective tissue. Gargiulo and co-workers found an average biologic width, referring to the epithelial and connective tissue attachment of 2.04 mm around natural teeth in human skulls with corresponding average measures of 0.69 mm for the sulcus depth, 0.97 mm for the junctional epithelium and 1.07 mm for the connective tissue attachment. They further described a stable dimension in relation to the alveolar crest but an individual variation was observed within patients and within sites of the same patient, especially in the epithelial component. These findings were confirmed by Vacek and collaborators with the description of an average biological width of 1.91 mm in human cadaver jaws.

The term periodontal biotype was described by Seibert and Lindhe. They described a thick-flat biotype with quadratic looking teeth and a wide and voluminous zone of keratinized tissue and a thin-scalloped biotype with slender teeth and very narrow zones of keratinized tissue. De Rouck and co-workers found 1/3 of their sample corresponding to previously described thin-scalloped biotype and 2/3 to a clear thick biotype. But only half of the subjects in the latter group corresponded to the classical thick-flat biotype. The other half showed a clear thick biotype but with slender teeth and narrow zones of keratinized tissue and a high gingival scallop. From periodontal research the importance of the biotype is recognized especially in relation to the esthetic appearance. Subjects with a thin-scalloped biotype are more prone to gingival recessions, whereas thick-flat biotypes seem more resistant to trauma and hence protected against gingival recessions.

The outcome of dental implants is overall related to implant survival and bone preservation. These factors are included in success criteria and often used to scrutinize implant systems, surgical or prosthetic treatment protocols. Beside the implant as an important factor for peri-implant bone healing, multiple other factors, such as smoking habits, occlusal overload and surgical trauma are playing a role in peri-implant bone preservation, and consequently implant success. Over the last two decades the understanding of biology has improved and osseointegration of dental implants has become more predictable. Simultaneous to this
evolution, more attention was paid to the esthetic outcome in terms of soft tissue preservation. The crestal bone supports the gingival architecture. Therefore the stability of the crestal bone is believed to be the key factor for maintaining stable soft tissue dimensions over time. Likewise natural teeth, the same soft tissue barrier consisting of an epithelial part and a connective tissue part is found around dental implants. However, important quantitative and qualitative differences exist. An average biologic width of 3.08 mm was described around non-submerged implants installed in a one-stage surgical procedure\(^9\) and 3.42 - 3.80 mm around submerged implants installed in a two-stage surgical procedure\(^9,10\).

Besides the dimensional differences with teeth, a different collagen fiber orientation was observed in the peri-implant connective tissue component. Collagen fibers were primarily parallel to the implant surface whereas the inserting fibers were predominantly perpendicular in natural teeth\(^11\).

This biologic dimension and composition of the tissue is hardly influenced by the implant system\(^9\). Hermann and co-workers showed that the presence of a microgap, especially in close contact to the alveolar crest, influences significantly peri-implant bone loss and loss of soft tissue dimensions. In the absence of a microgap (in one-piece implants) the soft tissue dimensions are more similar to natural teeth compared to two-piece implants\(^12\). Linkevicius and co-workers showed significantly more peri-implant bone loss when tissues were thinner than 2 mm irrespective of the position of the micro-gap. On the contrary, implants at sites with thick mucosal tissues showed statistically significantly less crestal bone loss. The latter study suggests that the influence of the initial thickness at the time of implant installation might be more important on early bone remodeling than the position of the microgap\(^13\). A recent pilot study by the same author showed that platform-switching does not preserve the crestal bone better compared with a traditional flat-to-flat connection when thin mucosal tissues are present at the time of implant placement\(^14\). Collaert & De Bruyn (2002) suggested a relation between the height of the transmucosal abutment and peri-implant bone loss, although this was not statistically analyzed\(^15\). To our knowledge the impact of the soft tissue thickness on bone remodeling has received too few attention and may be a clinical factor that is largely overlooked during clinical research. Hence, the aim of the present study was to elucidate this aspect more in detail.
Chapter 5: Soft tissue thickness

The research hypothesis was that implants installed in patients or at sites with thin mucosal tissues would show increased peri-implant bone loss because of the biologic necessity to create enough space for re-establishment of a protective soft tissue seal acting as a barrier against bacterial contamination.

5.2 Materials & Methods

5.2.1 Patient population and surgical/prosthetic procedures

79 completely edentulous patients were consecutively treated with two non-splinted implants supporting an overdenture in the mandible. Both surgery and prosthetics were performed by the same clinician (JB). Dental implants (Astra Tech™, Mölndal, Sweden) measuring 4 mm in width and ranging between 8 and 17 mm in length were installed according to the manufacturer’s guidelines. In most cases, the existing removable denture was converted to a guide plate by drilling two access holes at the planned surgical sites being incisor or canine location. A full-thickness mucoperiosteal flap was prepared to expose the interforaminal bone, and implant recipient sites were prepared using the removable denture as direction guide plate. Care was taken to have the implant completely surrounded by bone after implant placement. In case of a knife edge or in case a dehiscence could be expected because of a tiny crest, the bone was reduced in height prior to implant installation. The height of the transmucosal healing abutment was chosen by the surgeon in function of the soft tissue thickness. The abutment was more or less flush with the soft tissue level after suturing and when necessary another healing abutment was placed after suturing. The aim was to avoid the healing abutment to be interfering with the denture base and to avoid weakening of the prosthesis by too extensive grinding. The abutment was not allowed to stick out more than 1 mm because uncontrolled premature contacts with the denture base could possibly result in higher failure risks. As a consequence of this standardized approach the height of the healing abutment reflected the initial soft tissue thickness. The clinical procedure has previously been described in detail and is basically a one-stage early loading procedure. The denture was relined with a soft relining material (Ufi-gel, Voco, Cuxhaven, Germany) either immediately or at the time of suture removal, 7 days after surgery. Antibiotics were given routinely starting 1 hour before surgery.
(clindamycin 300 mg three times daily for 5 days). A plaque control regimen was instructed from day 0 by means of 0.05% chlorhexidine rinsing (Perio-aid, Dentaid, Houten, the Netherlands) and patients were advised to brush the healing abutments with a very soft toothbrush (Surgical Care, TePe, Malmö, Sweden).

![Figure 1. Clinical images showing 2 transmucosal locator abutments (a) or ball abutments (b) to support a mandibular overdenture with the respective retention connectors (c,d). Treatment always included a metal- or glass fiber-reinforced mandibular overdure (e) and a new complete denture in the maxilla (f) to idealize function and esthetics.](image)

The patients were regularly checked until the healing abutments were changed by ball or locator abutments after soft tissue healing (Figure 1a,b). This was prior to the final impression for the new overdenture and varied from patient to patient from 2 weeks to 3 months after surgery. The retentive element of the abutments was located to the nearest distance to the soft tissue (Figure 1a,b) and the acrylic denture was in close contact with the
soft tissue in order to prevent soft tissue overgrowth and minimize the lever effect (Figure 1c,d). The final prosthesis was metal- or glassfiber-reinforced at the lingual side (Figure 1e) and was installed within 4 months after implant installation. The treatment always included a new complete denture in the maxilla to idealize function and esthetics using the lingualized occlusion concept (Figure 1f). After finalizing the prosthetic treatment, the patients were given oral hygiene instruction and scheduled for professional maintenance by an oral hygienist at least once a year. The recall interval was individually determined, depending on the patient's ability to perform oral hygiene measures.

5.2.2 Clinical and Radiographic Examination

Once a year all patients were invited to attend a recall visit organized by an independent research team from the University of Ghent. In brief during this visit, peri-implant health was determined by means of the peri-implant probing depth and the modified plaque and bleeding index17. The clinical examination parameters were assessed on four implant sites (midmesial, middistal, midbuccal, and midlingual) and averaged to obtain a single value per implant. Digital peri-apical radiographs were taken from each individual implant using a guiding system (Rinn XCP®, Dentsply, USA) in order to obtain the x-ray direction perpendicular to the film. Whenever the implant threads were unclear, new radiographs were taken until the radiologic bone-to-implant contact level could be determined. The computer calliper available in the data program (Visiquick, Amsterdam, the Netherlands) was used for the assessment of the marginal bone level under appropriate magnification. We used magnifications in the computer software program up to 200 % whenever necessary to evaluate the bone level. Possible distortions were adjusted by callibrating the measurements with the known implant width and abutment height. The lower edge of the smooth bevel of the coronal part of the implant was the baseline reference point as shown in Figure 2. Bone level changes were measured from this reference point to the most marginal bone-to-implant contact point. Mesial and distal values were averaged to obtain one single value per implant. This was statistically sustained because paired analysis did not show a statistically significant difference between mesial and distal values (p > 0.05).
research analysis of the current study are using the data of all consecutively treated patients from the start of the project in 2005 until the last research visit (January 2011).

Figure 2. Bone level changes were assessed from the reference point, being the lower border of the smooth implant collar (yellow dotted arrow) to the most marginal bone-to implant contact level (red arrow). The radiograph shows more bone loss on the short locator abutment (right) compared to the long locator abutment (left).
5.2.3 Statistical Analysis

Statistical analysis was performed using SPSS 19 for windows. The linear mixed-effect model analysis was adopted to analyze the influence of bleeding on probing, plaque and abutment height on peri-implant bone loss in order to correct for clustering implants in the same patient. Data were analyzed first in terms of linearity and homoskedasticity as requirements for mixed model analysis. The study protocol was approved by the Ethics committee of the University Hospital of Ghent University and all patients were examined only after written consent was obtained.

5.3 Results

79 patients were consecutively treated with 158 implants to support a mandibular overdenture. 67 patients were attending the 1 year recall and 66 the 2-year recall. The mean bone level changes after 1 year and 2 years of follow-up were 0.89 (n = 134, SD 0.62, range 0 – 3.35) mm and 0.90 mm (n = 132, SD 0.66, range 0 – 3.15) respectively. 61.9 % and 60.6% of the implants showed ≤ 1 mm of bone level changes after 1 year and 2 years respectively (Figure 3A). Mean bleeding scores, plaque scores and probing pocket depth after 1 year and 2 years are given in table 1.

<table>
<thead>
<tr>
<th></th>
<th>1 year</th>
<th></th>
<th></th>
<th>2 years</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Range</td>
<td>SD</td>
<td>Mean</td>
<td>Range</td>
<td>SD</td>
</tr>
<tr>
<td>Bone level changes (mm)</td>
<td>0.89</td>
<td>0 - 3.35</td>
<td>0.62</td>
<td>0.90</td>
<td>0 - 3.15</td>
<td>0.66</td>
</tr>
<tr>
<td>Plaque Scores</td>
<td>0.82</td>
<td>0 - 3</td>
<td>0.94</td>
<td>0.87</td>
<td>0 - 3</td>
<td>0.92</td>
</tr>
<tr>
<td>Bleeding Scores</td>
<td>0.46</td>
<td>0 - 3</td>
<td>0.68</td>
<td>0.56</td>
<td>0 - 3</td>
<td>0.72</td>
</tr>
<tr>
<td>Probing pocket depth</td>
<td>1.65</td>
<td>1 - 4.25</td>
<td>0.60</td>
<td>1.78</td>
<td>1 - 3.35</td>
<td>0.59</td>
</tr>
</tbody>
</table>

Table 1. Mean (SD) bone level changes after 1 and 2 years and respective plaque/bleeding scores and probing pocket depth.
### Table 2. Results of mixed-effect model analysis on the influence of abutment height, plaque/bleeding scores and probing pocket depth on bone level changes after 1 year and 2 years of follow-up. *Statistically significant at the 0.05 level.

<table>
<thead>
<tr>
<th></th>
<th>1 year</th>
<th>2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main Effects</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abutment height</td>
<td>&lt; 0.01*</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>Plaque Scores</td>
<td>0.31</td>
<td>0.09</td>
</tr>
<tr>
<td>Bleeding Scores</td>
<td>0.30</td>
<td>0.40</td>
</tr>
<tr>
<td>Probing pocket depth</td>
<td>&lt; 0.01*</td>
<td>&lt; 0.01*</td>
</tr>
</tbody>
</table>

> Figure 3a. Showing cumulative peri-implant bone level changes for all individual implants ($n = 134$ after 1 year and $n = 132$ after 2 years of follow-up). When taking 1 mm as a threshold, 61.9 % and 60.6 % of all implants were considered a success after 1 year and 2 years respectively.
A linear mixed-effect model analysis was performed to scrutinize the influence of abutment height, bleeding scores, plaque scores and probing pocket depth on bone level changes after 1 year and 2 years of follow-up. This statistical analysis corrects for clustering implants in the same patient. Results are given in table 2. The abutment height and probing pocket depth were found to be statistically significant factors both after 1 year and 2 years of follow-up. Bleeding scores and plaque scores did not influence peri-implant bone level changes.

In depth analysis is given in table 3. Peri-implant bone loss was significantly higher for implants with an abutment of < 2 mm, 2 mm or 3 mm compared to implants with an abutment of ≥ 4 mm. Significant additional bone level changes are observed for implants with an abutment of < 2 mm (1.17 mm, p < 0.001; 1.23 mm, p < 0.001), 2 mm (0.86 mm, p < 0.001; 1.03 mm, p < 0.001) or 3 mm (0.38 mm, p = 0.046; 0.41 mm, p = 0.044) compared to implants with ≥ 4 mm abutments (parameter set to zero as a reference value) after 1 year and 2 years respectively. Implants with deeper pockets, show more peri-implant bone loss. When the pocket depth increased with 1 mm, bone level changes increased with 0.34 mm after 1 year or 0.28 mm after 2 years. This is illustrated in figure 3B showing the cumulative percentage of bone level changes in relation to the abutment height and suggests that implants with smaller abutments, reflecting less initial gingival thickness, lose more peri-implant bone, possibly by a re-establishment of the biological width (Figure 4). When taking 1 mm bone level change as a threshold for success, all implants with an abutment of ≥ 4 mm were successful. The corresponding values for implants with abutments of 3 mm, 2 mm and < 2 mm were 79.4 %, 44.8 % and 31.3 %.
Table 3. Linear mixed-effect model analysis showing the effect of abutment height, plaque/bleeding scores, and probing pocket depth on peri-implant bone level changes.

A parameter set to zero as a reference value. *Statistically significant difference at the 0.05 level. This table shows that an implant with an abutment height of <2 mm lost an average 1.17 mm implant bone after 1 and 2 years respectively, compared to an implant with an abutment of 4 mm or more.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1 year</th>
<th></th>
<th></th>
<th>2 years</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>SE</td>
<td>p-value</td>
<td>95% CI</td>
<td>Estimate</td>
<td>SE</td>
</tr>
<tr>
<td>Intercept</td>
<td>-0.29</td>
<td>0.37</td>
<td>0.46</td>
<td>-1.05 - 0.48</td>
<td>-0.16</td>
<td>0.42</td>
</tr>
<tr>
<td>Abutment Height</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 mm</td>
<td>1.17</td>
<td>0.20</td>
<td>&lt;0.01*</td>
<td>0.76 - 1.57</td>
<td>1.23</td>
<td>0.22</td>
</tr>
<tr>
<td>2 mm</td>
<td>0.86</td>
<td>0.20</td>
<td>&lt;0.01*</td>
<td>0.46 - 1.26</td>
<td>1.03</td>
<td>0.23</td>
</tr>
<tr>
<td>3 mm</td>
<td>0.38</td>
<td>0.19</td>
<td>0.046*</td>
<td>0.01 - 0.74</td>
<td>0.41</td>
<td>0.20</td>
</tr>
<tr>
<td>≥4 mm</td>
<td>0°</td>
<td></td>
<td></td>
<td></td>
<td>0°</td>
<td></td>
</tr>
<tr>
<td>Plaque Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>-0.19</td>
<td>0.23</td>
<td>0.40</td>
<td>-0.65 - 0.26</td>
<td>-0.22</td>
<td>0.20</td>
</tr>
<tr>
<td>1</td>
<td>-0.33</td>
<td>0.23</td>
<td>0.15</td>
<td>-0.79 - 0.12</td>
<td>-0.24</td>
<td>0.19</td>
</tr>
<tr>
<td>2</td>
<td>-0.34</td>
<td>0.22</td>
<td>0.14</td>
<td>-0.78 - 0.11</td>
<td>0.10</td>
<td>0.20</td>
</tr>
<tr>
<td>3</td>
<td>0°</td>
<td></td>
<td></td>
<td></td>
<td>0°</td>
<td></td>
</tr>
<tr>
<td>Bleeding Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.17</td>
<td>0.34</td>
<td>0.62</td>
<td>-0.50 - 0.84</td>
<td>-0.04</td>
<td>0.30</td>
</tr>
<tr>
<td>1</td>
<td>0.33</td>
<td>0.34</td>
<td>0.33</td>
<td>-0.34 - 1.00</td>
<td>-0.11</td>
<td>0.30</td>
</tr>
<tr>
<td>2</td>
<td>0.22</td>
<td>0.32</td>
<td>0.48</td>
<td>-0.40 - 0.86</td>
<td>0.17</td>
<td>0.32</td>
</tr>
<tr>
<td>3</td>
<td>0°</td>
<td></td>
<td></td>
<td></td>
<td>0°</td>
<td></td>
</tr>
<tr>
<td>Probing pocket depth</td>
<td>0.34</td>
<td>0.09</td>
<td>&lt;0.01*</td>
<td>0.16 - 0.51</td>
<td>0.28</td>
<td>0.09</td>
</tr>
</tbody>
</table>
Figure 3b. Showing cumulative peri-implant bone level changes for all individual implants after 1 year in relation to the abutment height. When taking 1 mm bone level change as a threshold, all implants with a ≥ 4 mm abutment were considered a success. The corresponding values for abutments of 3 mm, 2 mm or < 2 mm were 79.4 %, 44.8 % and 31.3 %.
Figure 4. Illustration of the biologic width on peri-apical radiographs of an implant with a ball abutment of 3.0 mm (left) and 1.5 mm (right) in the same patient. The blue arrows are indicating the sum of the abutment height (red line) and bone level changes (yellow line). The implant with the abutment of 1.5 mm lost more peri-implant bone compared to the other implant (yellow lines) with the abutment of 3.0 mm.
5.4 Discussion

The present study reports mean bone level changes around early loaded non-splinted implants installed to provide retention to a mandibular overdenture of 0.89 mm and 0.90 mm after 1 year and 2 years respectively. This outcome is in accordance with other clinical reports evaluating the same implant system and reporting peri-implant bone loss ranging from 0.24 mm to 1.3 mm with overall steady-state bone levels after initial bone remodeling. In the present study, bone levels were measured from a reference point, the lower border of the smooth implant collar, up to the most marginal bone-to-implant contact level. This reference point is generally accepted and was described by previous authors using the same implant system. As mean values may hide important information, it is important to present additional information such as the range of values. Bone level changes ranged from 0 mm to 3.35 mm after 1 year and from 0 mm to 3.15 mm after 2 years of follow-up. No increase was found in the range from 1 year to two years of follow-up as reflected by the cumulative percent of bone level changes after 1 year (61.9 % ≤ 1mm) and 2 years (60.6 % ≤ 1mm) (Figure 3A).

Early bone remodeling was not influenced by plaque and bleeding scores in the present study. These results are in contradiction with previous papers. In the present study patients were well-maintained and had relatively low plaque and bleeding scores. Whenever necessary, the individual maintenance program was reinforced. This may explain why results were not influenced by plaque and bleeding scores. Moreover, Verhoeven and co-workers analyzed the reliability of different periodontal parameters to reflect the clinical condition of a dental implant. They found a rather poor specificity and sensitivity for the plaque and bleeding index and considered the aforementioned parameters as unreliable for clinical evaluation in implant dentistry. They suggest that radiographs are needed to assess critical peri-implant bone level changes. Likewise, it was shown that the absence of bleeding on probing is a parameter with a high negative predictive value (98.5%) indicating periodontal stability around natural teeth, rather than the presence of bleeding on probing as a positive indicator for disease.

The present study shows that early bone remodeling is influenced by the initial soft tissue thickness at the time of implant placement as reflected by the height of the abutment.
Greater bone level changes were observed in cases where small abutments were placed. We did not measure the thickness of the soft tissue at the time of implant placement because originally this was not the aim of our study. But after 1 year we noticed more crestal bone loss around implants with short abutments. However, due to the standardized protocol described in the materials and methods, the height of the abutment reflects the initial soft tissue thickness. This relationship was already described by Collaert & De Bruyn (2002), but not statistically analyzed. They treated a group of 25 edentulous patients with 4 to 5 mandibular implants each. Conical abutments were used as transmucosal components and restored with a fixed screw-retained cross arch restoration. They observed that short abutments, installed when thin mucosal tissue thickness was present, resulted in an increased peri-implant bone remodeling. They attributed this bone loss to biological width establishment requiring enough space for the biological dimensions\(^\text{15}\). When applying the same immediate loading protocol using implants with a grit-blasted surface (TiOblast\(^\text{TM}\), Astra Tech\(^\text{TM}\), Mölndal, Sweden) in both maxilla or mandible, they found more initial peri-implant bone remodeling in the mandible compared to the maxilla. The authors attributed this to different surgical flap preparation and slightly subcrestal implant placement in the maxilla aiming both for soft tissue thickness in the maxilla and more space for biologic width formation. In the mandible implants were often placed flush with the crest which in combination with thin tissues may provide too little space for the biologic attachment\(^\text{18,19}\). The results in the present study are also in accordance with the results of a randomized clinical trial reporting that up to 1.45 mm of bone loss can occur after 1 year in cases with thin mucosal tissues at the time of implant placement\(^\text{13}\). In the present study a mean bone loss of 0.89 mm is described after 1 year. This is slightly better compared with the aforementioned study. A possible explanation is that implants with a different connection were used in both. In the present study implants with an internal conical connection were installed. It is well-known that an internal conical connection minimizes microbiol leakage\(^\text{30}\) and micro-movements\(^\text{31}\) preventing crestal bone loss. On the contrary, a recent study evaluating implant leakage could not confirm the superiority of an internal conical connection\(^\text{32}\). An other study by the same authors reported a mean bone loss at sites with thin mucosal tissues of 1.81 mm on the mesial and 1.70 mm on the distal aspect for implants with platform-switching and 1.60 mm on the mesial and 1.76 mm on the distal aspect of implants without platform-switching\(^\text{14}\). They concluded that soft tissues of \(\leq 2\) mm are
insufficient for a stable peri-implant seal formation. This factor may be more important than the type of implant-abutment connection. In literature a biological width of 3.08 mm was described around non-submerged implants. After implant placement, it is believed this biologic width establishes. In case of soft tissues of 2mm, this precludes either 1 mm of bone loss or a soft tissue regrowth through hypertrophia. Since the base of the relined removable denture was made in direct contact with the gingiva, very limited gingival hypertrophia could occur. Nevertheless, the same phenomenon was observed in immediately loaded full-arch, mandibubary rehabilitations on 5 implants. Despite enough space, provided for oral hygiene measures, still peri-implant bone loss was observed. On the other hand, in a recent paper by the same authors, very limited bone loss was observed for the same treatment, but with a deeper implant placement protocol in cases of limited bone volume in order to avoid buccal dehiscences. In other indications, such as single-tooth replacement, a regrowth of the papilla is often observed after delivery of the final restoration. However, the level of the alveolar crest at the neighbouring teeth and a proper crown design allow the gingiva to fill the interproximal embrasures. This is not possible in overdenture cases. This might explain the greater bone level changes around implants with short abutments in the present study.

5.5 Conclusion

The results of the present study suggest an anticipation on the bone-remodeling that occurs after implant placement in healed sites by adapting the vertical position of the implant to the thickness of the gingiva. Especially patients or sites with inadequate gingival thickness may present more peri-implant bone loss after re-establishment of the biological width when implants are placed equally with the crest as described in the manufacturer’s guidelines. Although deeper placement is suggested to induce crestal bone loss due to the microgap between implant and abutment during the initial healing stage, this may be preferable to unforeseen exposure of the implant neck. The latter may lead to soft tissue recession and could hamper aesthetics as well as increase the risk for soft and hard tissue pathology due to exposure of the implant threads. Hence, it is suggested that the surgeon should proactively keep soft tissue thickness into account when installing implants especially in cases with a thin biotype. For future research it is suggested to include information on the
soft tissue thickness, especially when implant systems or treatment protocols are evaluated or compared. Whether the findings in the present study are valid for all implant systems/implant connections remains to be investigated.
5.6 References

CHAPTER 6

LONG-TERM EVALUATION OF PREDICTORS AFFECTING IMPLANT TREATMENT OUTCOME

THIS CHAPTER HAS BEEN PUBLISHED AS:

A 9-YEAR PROSPECTIVE CASE SERIES USING MULTIVARIATE ANALYSES TO IDENTIFY PREDICTORS OF EARLY AND LATE PERI-IMPLANT BONE LOSS

Vervaekte S, Collaert B, Cosyn J & De Bruyn H

Clin Implant Dent Relat Res.
CHAPTER 6 : A 9-year prospective case series using multivariate analyses to identify predictors of early and late peri-implant bone loss.

ABSTRACT

PURPOSE To identify predictors of early and late peri-implant bone loss following complete implant-supported rehabilitation using multivariate analyses.

MATERIALS & METHODS 50 patients (28 women, 22 men; mean age 58, range 35-76) in need for a complete implant-supported rehabilitation on 5 to 8 implants were consecutively treated. Patients were reinvited for a clinical and radiographic examination after on average 9 years of function. Implant survival and peri-implant bone loss were considered the dependent variables. Multivariate analyses were adopted to identify predictors of early and late peri-implant bone loss.

RESULTS In total, 39 patients were examined. Two implants failed after 4 years of function, resulting in an overall survival rate of 99.2 %. After a mean follow-up of 9 years, mean bone loss of 1.68 mm (SD 2.08, range -1.05 – 10.95) was found. The abutment height was a significant predictor of early peri-implant bone loss (1 year) (p = 0.024), whereas smoking (p = 0.046) and history of periodontitis (p = 0.046) affected late peri-implant bone loss.

CONCLUSION Within the limits of this study, it can be concluded that initial bone remodelling was affected by soft tissue thickness as reflected by the height of the abutment, whereas smoking and history of periodontitis affected long-term peri-implant bone stability.
6.1 Introduction

Although long-term data on implant survival and peri-implant bone stability are scarce, immediate loading is considered as a viable and predictable alternative for a two-stage delayed approach in the treatment of full edentulism. The main reason is a significant reduction in treatment time and patient morbidity by avoiding a second stage surgery. This leads to a high overall patient satisfaction and improved function, esthetics and phonetics. Regardless the adopted treatment protocol, different complications in implant treatment can occur. The prevalence of peri-implantitis has been evaluated in a recent systematic review by Mombelli et al. (2012) They reported peri-implantitis in approximately 10% of the implants and 20% of the patients. Hence, risk assessment is required to identify factors affecting peri-implant bone loss.

In a recent retrospective study 1320 implants in 376 patients were evaluated after on average 32 months of function. Multivariate analyses identified smoking as a predictor for implant failure and peri-implant bone loss. Additionally, more bone loss was described in the maxilla compared with the mandible.

Large retrospective studies can be usefull to evaluate the relative importance of one factor in relation to others when multivariate analyses are adopted that correct for confounding. However, identification of true risk factors for disease requires preferably longitudinal studies with a prospective design to be carried out in humans.

Hence, the aim of the present study was to identify predictors affecting early and late peri-implant bone loss in a longitudinal prospective case series, using multivariate analyses.

6.2 Materials & Methods

6.2.1 Study sample

In total, 50 patients (28 women, 22 men; mean age 58, range 35-76) in need for a complete implant-supported rehabilitation in either the maxilla or the mandible were consecutively treated between April 2002 and January 2004. Twenty-five patients received 195 implants in the maxilla and in 25 patients, 125 implants were placed in the mandible. The 3-year
results of this prospective follow-up study were described previously \textsuperscript{9,10}. After 3 years, 7 patients were lost to follow-up, 3 in the maxilla-group and 4 in the mandible-group. In the present study, all patients were re-invited for a clinical and radiographic examination.

6.2.2 Surgical and Prosthetic treatment

The surgical and prosthetic treatment protocol was extensively described previously \textsuperscript{9,10}. In brief, 5 to 8 implants (TiOblast, Astra Tech, Molndahl, Sweden) were installed in either the edentulous maxilla or mandible. In cases of remaining teeth in the opposing jaw with signs of periodontal breakdown, a periodontal treatment was performed prior to implant installation. Periodontal treatment comprised of both mechanical and surgical therapy, including tooth extractions, whenever it was indicated. In most cases, the existing complete denture was modified before surgery and used for implant positioning, impression taking and occlusal registration. When there was no denture available a surgical guide plate, made by the referring dentist, was used for these purposes. After implant insertion, conical abutments (uni-abutments, Astra Tech, Möldahl, Sweden) were inserted and an impression was made with conical copings using the repositioning technique. The height of the abutments was chosen in function of the site-specific soft tissue thickness and were not allowed to stick out of the gingiva for esthetical reasons. Implants were functionally loaded within 2 days after surgery (baseline) with a provisional, acrylic, glass-fibre or metal reinforced, screw-retained bridge. The final prosthetic reconstruction was made by the referring restorative dentist and consisted of a screw-retained metal–ceramic or metal–resin reconstruction with 10–12 teeth in function of the patient’s need and demand. Maintenance care was performed by the surgeon up to 3 years during the original study follow-up \textsuperscript{9,10}. Afterwards patients were referred to the restorative dentist for professional maintenance.

6.2.3 Dependent variables and covariates

Patients were re-examined 9 years after implant placement by an external investigator from the University of Ghent (SV). Implant survival and peri-implant bone loss were considered the dependent variables. Information on the following explanatory variables was collected from the patient files: healing time between tooth extraction and implant installation,
smoking habit, history of periodontitis, jaw location (maxilla or mandible) and abutment height (≤ 1.5 mm, = 3mm, ≥ 4.5mm). Smoking was related to self-reported smoking habits and was defined as ≥ 10. Patients were classified as patients with or without a history of periodontitis based on the following: 1) radiographic evidence of bone loss extending 1/3 of the root length of the remaining teeth at the time of referral; 2) patients actively treated before implant surgery with surgical and/or non-surgical therapy due to periodontal breakdown; 3) patients whereby hopeless teeth had to be extracted by the surgeon prior to implant placement due to periodontal disease; 4) edentulous patients at the time of referral with evidence of tooth loss due to periodontitis based on radiographs that were obtained in retrospect from the referring dentist.

Figure 1. Crestal bone levels were determined by measuring the distance between a reference (indicated by the yellow arrow) and the crestal bone-to-implant contact point (indicated by the red arrow).

The modified plaque index\textsuperscript{11} was adopted to evaluate oral hygiene around the implants at six sites (mesial, central, distal; buccally as well as orally). Afterwards, the bridge was removed prior to further clinical examination. Probing pocket depths were measured using a
Chapter 6: Long-term evaluation of predictors affecting implant treatment outcome

manual periodontal probe (CP 15 UNC, Hu-Friedy Mfg. Co. Inc., Chicago, IL, USA). At the same sites, bleeding on probing (BoP) was determined using the modified bleeding index\textsuperscript{11}. Peri-implant bone loss was assessed comparing peri-apical radiographs, taken during study visits, with the post-operative ones taken by the surgeon immediately after implant installation (baseline). Radiographs were taken using the long-cone parallel technique and analyzed using digital software with an accuracy of 0.1 mm (Visi-quick\textsuperscript{®}, Amsterdam, the Netherlands). Marginal bone level was determined radiographically both at the mesial and distal site of each implant by measuring the distance between a reference point\textsuperscript{12,13} (lower border of the smooth implant collar or the uppermost point of the microthreaded part) and the crestal bone-to-implant contact point (Figure 1). Values were averaged to obtain a single value per implant. All patients were thoroughly informed and signed a consent form. The study protocol was approved by the ethical committee of the Ghent University Hospital.

6.2.4 Statistical analysis

Implant survival was analyzed using the Cox proportional Hazards regression that corrects for confounding factors. The mixed-effect model analysis was adopted to evaluate peri-implant bone loss over time. P-values were adjusted for multiple testing using Bonferroni. The impact of the different explanatory variables on peri-implant bone loss was analyzed using multivariate tests to correct for clustering implants in the same patients and possible interaction between different variables. Multivariate analysis consisted of the linear mixed-effect model analysis. A model was fitted using as much variables as possible to identify predictors affecting peri-implant bone loss after 1 year (early bone loss) and after 9 years (late bone loss) of function. The statistical model was validated in terms of linearity and homoscedasticity. The level of significance was set at 0.05. The statistical analyses were performed using IBM\textsuperscript{®} SPSS\textsuperscript{®} 19.0 for windows.
6.3 Results

6.3.1 Overall

In total, 39/50 patients responded to the 9-year recall invitation, resulting in a drop-out range of 22%. Four additional patients were lost to follow-up compared with the 3-year examination. One patient died, 2 moved abroad, 4 refused to participate and 4 were untraceable. Out of 39 patients, 12 patients were identified as smokers. Eleven patients were considered periodontally healthy and 25 had a history of periodontitis. Of 3 fully edentulous patients without radiographic information from the past, the periodontal history remained unclear.

Eighteen patients received implants in the maxilla and 21 in the mandible. In 26 patients, implants were placed at least 3 months after tooth extraction. In 13 patients the healing time was less than 3 months.

The initial 3-year reports showed a 100 % survival rate. After a mean follow-up of 108 months (SD 7.28, range 96 – 123) two implants out of 245 failed in 1/39 patients, resulting in an overall survival rate of 99.2 % and 97.4 % on implant and patient level, respectively. Both failures occurred in the mandible of a non-smoking patient after 4 years of function. The corresponding survival rates on implant level for maxilla and mandible were 100 % and 98.1 %, respectively. Statistical risk assessment was impossible given the low number of failures (events). Hence, no predictors for implant survival could be identified.

After a follow-up of 3, 12, 24, 36 and 108 months, a mean bone loss of 0.62 mm (SD 0.79, range -0.60 – 5.50), 0.68 mm (SD 0.86, range -0.90 – 4.35), 0.72 mm (SD 0.94, range -0.65 – 5.65), 0.91 mm (SD 1.13, range -1.00 – 5.80) and 1.68 mm (SD 2.08, range -1.05 – 10.95) was found, respectively (Table 1).

Table 2 gives an overview of the estimated mean bone levels for the different study time points based on a linear mixed-effect model analysis. A statistically significant difference was found between every time point and baseline (p < 0.001) (Figure 2).
Table 1: Mean bone loss, standard deviation (SD) and range for the different explanatory variables during the study follow-up.

<table>
<thead>
<tr>
<th>Bone Loss</th>
<th>3m</th>
<th>12m</th>
<th>24m</th>
<th>36m</th>
<th>108m</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Range</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Overall</td>
<td>0.62</td>
<td>0.79</td>
<td>-0.60 / 5.50</td>
<td>0.68</td>
<td>0.86</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>0.50</td>
<td>0.54</td>
<td>-0.30 / 2.85</td>
<td>0.53</td>
<td>0.65</td>
</tr>
<tr>
<td>Smoker</td>
<td>0.90</td>
<td>1.15</td>
<td>-0.60 / 5.50</td>
<td>1.02</td>
<td>1.14</td>
</tr>
<tr>
<td>History of periodontitis</td>
<td>0.64</td>
<td>0.81</td>
<td>-0.20 / 5.50</td>
<td>0.77</td>
<td>0.88</td>
</tr>
<tr>
<td>No history of periodontitis</td>
<td>0.45</td>
<td>0.67</td>
<td>-0.60 / 2.85</td>
<td>0.32</td>
<td>0.69</td>
</tr>
<tr>
<td>Maxilla</td>
<td>0.63</td>
<td>0.83</td>
<td>-0.30 / 5.50</td>
<td>0.63</td>
<td>0.76</td>
</tr>
<tr>
<td>Mandible</td>
<td>0.60</td>
<td>0.73</td>
<td>-0.60 / 2.85</td>
<td>0.74</td>
<td>0.96</td>
</tr>
<tr>
<td>Abutment height ≤ 1.5mm</td>
<td>0.69</td>
<td>0.80</td>
<td>-0.30 / 5.50</td>
<td>0.76</td>
<td>0.87</td>
</tr>
<tr>
<td>Abutment height = 3.0mm</td>
<td>0.20</td>
<td>0.50</td>
<td>-0.40 / 2.15</td>
<td>0.19</td>
<td>0.41</td>
</tr>
<tr>
<td>Abutment height ≥ 4.5mm</td>
<td>0.08</td>
<td>0.38</td>
<td>-0.60 / 0.60</td>
<td>0.08</td>
<td>0.43</td>
</tr>
</tbody>
</table>
Chapter 6: Long-term evaluation of predictors affecting implant treatment outcome

<table>
<thead>
<tr>
<th>Bone Level</th>
<th>Mean</th>
<th>SE</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.14</td>
<td>0.05</td>
<td>0.05 - 0.24</td>
</tr>
<tr>
<td>3m</td>
<td>0.78</td>
<td>0.08</td>
<td>0.63 - 0.93</td>
</tr>
<tr>
<td>12m</td>
<td>0.82</td>
<td>0.08</td>
<td>0.67 - 0.98</td>
</tr>
<tr>
<td>24m</td>
<td>0.89</td>
<td>0.08</td>
<td>0.72 - 1.05</td>
</tr>
<tr>
<td>36m</td>
<td>1.00</td>
<td>0.09</td>
<td>0.82 - 1.18</td>
</tr>
<tr>
<td>9y</td>
<td>1.82</td>
<td>0.15</td>
<td>1.52 - 2.12</td>
</tr>
</tbody>
</table>

Table 2. Mean bone levels as estimated by mixed-effect model analysis. SE = standard error, CI = confidence interval.

Figure 2. Boxplot showing peri-implant bone levels at the different study time points indicative of unstable bone conditions during follow-up. Increasing interquartile ranges and outliers/extreme values are found after 9 years. NS = not significant.
Chapter 6: Long-term evaluation of predictors affecting implant treatment outcome

No significant bone level changes occurred between 3 months and 24 months. On the contrary, a significant difference was found between 3 months and 36 months ($p = 0.001$) and additionally between 36 months and 9 years ($p < 0.001$). These results suggest that no steady-state bone levels were obtained during the follow-up. When taking 2mm as a threshold for long-term success, suggested by Klinge (2012)$^{14}$, 93.6 %, 90.9 %, 91.2 %, 86.1 % and 69.8 % of the implants can be considered successful after 3, 12, 24, 36 months and 9 years, respectively (Figure 3).

### 6.3.2 Predictors for early bone peri-implant bone loss

The impact of the different explanatory variables on peri-implant bone loss is given in Table 1. After 1 year, only the abutment height ($p = 0.024$), reflecting initial soft tissue thickness, was identified as a predictor for peri-implant bone loss, whereas smoking ($p = 0.073$), history of periodontitis ($p = 0.228$), jaw ($p = 0.342$) and healing time after tooth extraction ($p = 0.671$) were not (Table 3). No information was available on plaque and bleeding scores at 1 year.

Results of multivariate analysis are given in Table 4. An additional bone loss of 0.79 mm is estimated for implants with an abutment height of $\leq 1.5$ mm compared with implants with an abutment height $\geq 4.5$ mm.

<table>
<thead>
<tr>
<th>Fixed effects</th>
<th>1 year</th>
<th>9 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.036</td>
<td>0.126</td>
</tr>
<tr>
<td>Smoking status</td>
<td>0.073</td>
<td>0.046</td>
</tr>
<tr>
<td>History of periodontitis</td>
<td>0.228</td>
<td>0.046</td>
</tr>
<tr>
<td>Jaw</td>
<td>0.342</td>
<td>0.251</td>
</tr>
<tr>
<td>Abutment height</td>
<td>0.024</td>
<td>0.099</td>
</tr>
<tr>
<td>Healing time after extraction</td>
<td>0.671</td>
<td>/</td>
</tr>
<tr>
<td>Plaque score</td>
<td>/</td>
<td>0.908</td>
</tr>
<tr>
<td>Bleeding score</td>
<td>/</td>
<td>0.040</td>
</tr>
</tbody>
</table>

*Table 3 Main effects of the linear mixed-effect model analysis. Level of significance set at $p < 0.05$.)*
Chapter 6: Long-term evaluation of predictors affecting implant treatment outcome

Figure 3. Cumulative percentage of individual peri-implant bone levels at different study timepoints. Success rates for the different timepoints were 93.6 %, 90.9 %, 91.2 %, 86.1 % and 69.8 % when taking 2 mm as a threshold (Klinge 2012).
### Table 4

**Linear mixed-effect model analysis estimating the effect of the explanatory variables on peri-implant bone loss.** Parameter set to zero as a reference value.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1 YEAR</th>
<th>9 YEARS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>SE</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.40</td>
<td>0.36</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>-0.45</td>
<td>0.24</td>
</tr>
<tr>
<td>Smoker</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>No history of periodontitis</td>
<td>-0.30</td>
<td>0.25</td>
</tr>
<tr>
<td>History of periodontitis</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Maxilla</td>
<td>-0.21</td>
<td>0.22</td>
</tr>
<tr>
<td>Mandible</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Abutment height ≤ 1.5mm</td>
<td>0.79</td>
<td>0.33</td>
</tr>
<tr>
<td>Abutment height = 3.0mm</td>
<td>0.42</td>
<td>0.31</td>
</tr>
<tr>
<td>Abutment height ≥ 4.5mm</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Healing time &lt; 3 months</td>
<td>0.10</td>
<td>0.23</td>
</tr>
<tr>
<td>Healed ridge</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Plaque</td>
<td>0.02</td>
<td>0.20</td>
</tr>
<tr>
<td>Bleeding</td>
<td>0.30</td>
<td>0.14</td>
</tr>
</tbody>
</table>
6.3.3 Predictors for long-term peri-implant bone loss

The impact of the different explanatory variables on peri-implant bone loss is given in Table 1. After 9 years, smoking (p = 0.046), history of periodontitis (p = 0.046) and bleeding on probing (0.040) were identified as predictors for peri-implant bone loss (Table 3). Table 4 shows the estimated bone loss for the different explanatory variables based on the linear mixed-effect model analysis. The estimated bone loss is 1.18 mm higher for smokers compared with nonsmokers (p = 0.046) and 1.19 mm higher for patients with a history of periodontitis compared with periodontally healthy patients (p = 0.046). These values express cumulative effects. Implants installed in smokers with a history of periodontitis were estimated to lose 2.37 mm more bone compared with implants in nonsmokers without a history of periodontitis. The corresponding success rates for both groups were 45.3 % vs 95.7% when taking 2mm as a threshold for success \(^{14}\) (Figure 4). Table 5 shows the worst implant for each patient. Each patient contributes the one implant with the most bone loss, related to smoking and history of periodontitis.

<table>
<thead>
<tr>
<th></th>
<th>&lt; 1 mm</th>
<th>1-2 mm</th>
<th>2-3 mm</th>
<th>3-4 mm</th>
<th>4-5 mm</th>
<th>&gt; 5 mm</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Smoker * No history of periodontitis</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td>8 (22.2 %)</td>
</tr>
<tr>
<td>Smoker * No history of periodontitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 (5.6 %)</td>
</tr>
<tr>
<td>Non Smoker * History of periodontitis</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td></td>
<td>17 (47.2 %)</td>
</tr>
<tr>
<td>Smoker * History of periodontitis</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td></td>
<td>4</td>
<td></td>
<td>9 (25.0 %)</td>
</tr>
<tr>
<td>Total</td>
<td>8 (22.2 %)</td>
<td>8 (22.2 %)</td>
<td>5 (13.9 %)</td>
<td>4 (11.1 %)</td>
<td>3 (8.3 %)</td>
<td>8 (22.2 %)</td>
<td>36 (100 %)</td>
</tr>
</tbody>
</table>

Table 5. Worst implant per patient in relation to smoking habits and history of periodontitis. History of periodontitis remained unclear in 3 patients. For this reason, these patients were not included in this table.
Figure 4. Cumulative percentage of individual peri-implant bone loss in function of smoking habits and history of periodontitis. When taking 2 mm as a threshold for success (Klinge 2012), success rates for the different groups were 95.7 % (non-smoker without a history of periodontitis), 100 % (non-smoker with a history of periodontitis), 74.3 % (smoker without history of periodontitis), 45.3 % (smoker with a history of periodontitis).
6.4 Discussion

In the present study, only 2 implants failed after a mean follow-up of 9 years, resulting in an overall survival rate of 99.2 % and 97.4 % on implant level and patient level, respectively. This result is in accordance with other studies on immediate loading of implants in the fully edentulous mandible\textsuperscript{15-21} and maxilla\textsuperscript{22-25}. No information was available on implant survival of 2 patients that moved abroad and 4 untraceable patients. Hence, one can not exclude that the survival rate is slightly overestimated.

After 9 years of function, mean overall bone loss was 1.68 mm (range -1.05 – 10.95) with implant installation as baseline. This is in accordance with a prospective study on the same implant system by Rasmusson and co-workers (2005) describing mean bone loss of 1.27 mm (range 0 – 5.21) after 7 years of function\textsuperscript{26}. A recent study by Ravald and co-workers (2013) evaluating the same implant system with 12-15-year follow-up, demonstrated mean bone loss of 0.67 mm, yet using bridge installation as baseline\textsuperscript{27}. In a previous paper from the same group with 5-year follow-up, bone loss from the moment of implant installation was reported and amounted to 1.74 mm in the maxilla and 1.06 mm in the mandible\textsuperscript{12}. These findings demonstrate that major changes in marginal bone level occur during the early phases of healing, during which the biologic width is established. A number of studies have indicated stable bone levels following such initial remodelling\textsuperscript{12,26-28}, however the present report may not support these findings demonstrating ongoing bone loss in the long term. In order to elucidate its causes, a multivariate analysis was performed.

In the present study mean full-mouth plaque and bleeding scores amounted to respectively 1.18 and 1.25, suggesting rather poor oral hygiene. This outcome may not be surprising knowing that the present sample included referred patients. Although they were invited by the surgeon for specific maintenance care, patients went back to the referring general dentist after 3 years. No information is available on the frequency and content of specific maintenance care. However, based on the plaque and bleeding scores after 9 years, one can conclude that patients were erratic or non-compliant regarding oral hygiene measures. Such a sample could be considered at risk for peri-implant disease\textsuperscript{29,30}. In line with this, multivariate analyses identified bleeding on probing as a predictor of long-term bone loss in
the present study. We believe this finding should be interpreted with caution because of the following. First, the prognostic value of peri-implant bleeding on probing remains a matter of debate. Very poor oral hygiene (OR = 14.3) and bleeding on probing in over 30% of the sites (OR = 3) significantly increased the risk for peri-implantitis as described by Ferreira and co-workers (2006) \(^{31}\). On the contrary, Lekholm and co-workers (1986) could not demonstrate a correlation between peri-implant bleeding on probing and bone loss \(^{32}\). Second, bleeding on probing was only registered after 9 years of function. As this registration did not actually precede the outcome evaluation, *stricto sensu* bleeding on probing cannot be considered a predictor.

The abutment height was identified as the only predictor for early peri-implant bone loss. Multivariate analysis showed significantly more bone loss around implants with a short abutment, compared with implants with longer abutments. In the present study, abutments were placed at the time of implant placement and the height was adapted to the site-specific soft-tissue thickness. Hence, the height of the abutment reflects the initial soft tissue thickness. Recently, the dimensions of the peri-implant soft tissues were described by Tomasi and co-workers (2013) based on the analysis of human biopsies \(^{33}\). They described soft tissue dimensions of 3.6 mm, including a barrier epithelium of 1.9 mm and a connective tissue portion of 1.7 mm. The re-establishment of these dimensions around dental implants can explain the greater amount of bone loss around implants installed at sites with thin soft tissues, as already suggested by Collaert & De Bruyn (2002) \(^{34}\). A recent study by Canullo & co-workers (2012) evaluated the effect of platform-switching on crestal bone preservation. They suggested that bone resorption is predominantly related to biologic factors (biologic width re-establishment) rather than biomechanical factors (platform-switching) \(^{35}\). Different authors suggested to anticipate this initial bone remodeling. Vervaeke & co-workers (2013) suggested to adapt the vertical position of the implant based on the soft tissue thickness, which is mostly feasible in edentulous zones \(^{36}\). For solitary tooth replacement, increasing soft tissue dimensions by means of membranes or connective tissue grafts was suggested to avoid early peri-implant bone loss \(^{37}\).

Smoking is a well-known risk factor affecting implant treatment outcome \(^{13,38-43}\). A systematic review by Strietzel and co-workers (2007) showed an increased risk for implant
failure among smokers with an implant-related odds ratio of 2.25 and a patient-related odds ratio of 2.64.

In the present study smoking did not affect implant survival. However, the effect of smoking was estimated to induce 1.18 mm additional bone loss for implants installed in smokers compared with non-smokers. In 2008, Collaert & De Bruyn described stable bone levels in nonsmokers and a time-dependent effect of smoking on peri-implant bone loss. This was confirmed in the present study after a mean follow-up of 9 years.

In the present study implants in patients with a history of periodontitis were more prone to show peri-implant bone loss. After 9 years, periodontal disease was estimated to induce 1.19 mm additional bone loss for implants installed in periodontally affected patients compared with periodontally healthy patients. There is evidence that patients with existing or ongoing periodontitis are more likely to experience implant failure and biological complications. However, due to the high heterogeneity among the studies and methodological variability, it is difficult to draw strong conclusions. Papers on chronic periodontitis showed an increased risk of implant failure with odds ratios between 3.1 and 4.7 for affected patients. Patients with a history of aggressive periodontitis may be worse off having an increased risk for implant failure (OR = 4.80), mucositis (OR = 3.61) and peri-implantitis (OR = 14.09). These results suggest that periodontal disease jeopardizes long-term peri-implant bone stability, possibly leading to future implant failures. This is in accordance with the findings in the present study.

In a review on the effect of smoking and history of periodontitis on implant treatment, Heitz-Mayfield and Huynh-Ba (2009) suggest a combined effect of these factors. However, they conclude that multivariate analyses are necessary for proper risk assessment and quantification of the effects. Indeed, in the present study, the patients with the worst peri-implant conditions were smokers with a history of periodontitis. The combined impact of smoking and a history of periodontitis was estimated to induce 2.37 mm additional bone loss, compared with implants installed in non-smokers without a history of periodontitis (Table 4). To our knowledge, the present study is the first to quantify these combined effects based on a multivariate statistical analysis in a prospective case series.
6.5 Conclusion

Immediate loading of implants supporting full-arch rehabilitations is a predictable and successful treatment option with high survival rates after 9 years of function. However, within the limits of this study, it can be concluded that initial bone remodeling was affected by soft tissue thickness as reflected by the height of the abutment, whereas smoking, history of periodontitis and bleeding on probing affected long-term peri-implant bone stability. Whether this bone loss is predicting future implant failures remains to be evaluated. More well-designed prospective studies are required to evaluate the different factors on implant treatment outcome.
6.6 References


Chapter 6: Long-term evaluation of predictors affecting implant treatment outcome


GENERAL DISCUSSION
DISCUSSION

Today, osseointegration is no longer the key issue in research related to oral implantology. Predictability in treatment outcome is rather established due to the improvement of biomaterials and better insights in surgical procedures. Multiple long-term studies show successful treatment outcomes in terms of functional rehabilitations with survival rates ranging from 89.5 to 99.2 % 1-7. However, nowadays patients do not always prioritize functional restoration but also demand an esthetic solution. Consequently, peri-implant bone stability is the key factor to fulfill these demands since they determine long-term success 8,9. Peri-implant bone maintenance is a prerequisite for soft tissue preservation and hence, bone loss will inevitably lead to soft tissue recession which may yield a non-esthetic outcome. Moreover, exposure of the implant threads may increase the risk for peri-implantitis due to bacterial colonization of the implant surface 10-12, possibly initiating bone loss and increasing the risk for implant failure.

The present PhD-thesis evaluated to outcome of implants with and without additional surface modification in terms of survival and peri-implant bone loss. Results of the different research chapters are summarized in Table 1, and present implant survival and bone loss from the time of surgery to 2-9 years of function for implants with (Osseospeed™) and without (TiOblast™) additional surface modification (fluoridation).

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Surface</th>
<th>Follow-up</th>
<th>Patients</th>
<th>Implants</th>
<th>Survival</th>
<th>Bone Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapter 1</td>
<td>TiOblast™</td>
<td>2 years</td>
<td>25</td>
<td>125</td>
<td>100.0%</td>
<td>0.86mm</td>
</tr>
<tr>
<td></td>
<td>Osseospeed™</td>
<td>2 years</td>
<td>25</td>
<td>125</td>
<td>100.0%</td>
<td>0.11mm</td>
</tr>
<tr>
<td>Chapter 2</td>
<td>Osseospeed™</td>
<td>31 months</td>
<td>300</td>
<td>1106</td>
<td>98.3%</td>
<td>0.36mm</td>
</tr>
<tr>
<td>Chapter 3</td>
<td>Osseospeed™</td>
<td>35 months</td>
<td>55</td>
<td>306</td>
<td>99.7%</td>
<td>0.27mm</td>
</tr>
<tr>
<td>Chapter 4</td>
<td>Osseospeed™</td>
<td>32 months</td>
<td>376</td>
<td>1320</td>
<td>98.4%</td>
<td>0.36mm</td>
</tr>
<tr>
<td>Chapter 5</td>
<td>Osseospeed™</td>
<td>2 years</td>
<td>66</td>
<td>132</td>
<td>100.0%</td>
<td>0.90mm</td>
</tr>
<tr>
<td>Chapter 6</td>
<td>TiOblast™</td>
<td>9 years</td>
<td>39</td>
<td>245</td>
<td>99.2%</td>
<td>1.68mm</td>
</tr>
</tbody>
</table>

Table 1. Overview of survival and peri-implant bone loss as presented in the different research chapters.
**IMPLANT SURFACE**

CHAPTER 1 compared the 2-year outcome of implants with and without fluoride modification and reported 100 % survival for both implant surfaces. Although experimental studies showed a better and faster osseointegration during the first weeks of healing\textsuperscript{13,14}, the potential benefit of fluoride modification in terms of survival could not be observed in this thesis, as implants were splinted for 3 months in a provisional restoration. However, implants with fluoride modification showed significantly less peri-implant bone loss after 2 years in function, suggesting that implant surface topography plays a decisive role in bone preservation. A possible explanation may be found in the difference of surface roughness. Osseospeed\textsuperscript{TM} implants are slightly smoother compared to TiOblast\textsuperscript{TM} implants\textsuperscript{13}. It is tempting to suggest that the latter may yield increased bone loss due to a facilitated biofilm formation and maturation, as described by Teugels and co-workers\textsuperscript{15}. Different authors described more bone loss for rough implant surfaces\textsuperscript{16-18} and suggested a higher incidence of late implant losses due to ongoing peri-implant bone loss\textsuperscript{18}. On the other hand, Chappuis and co-workers showed in a prospective study satisfactory long-term results (20 years follow-up) for rough implant surfaces in partially edentulous patients\textsuperscript{7}. Only 8 % of the implants yielded > 1 mm bone loss with a maximum value of 1.8 mm after 20 years. One can conclude that the literature is inconclusive regarding the effect of implant surface roughness on peri-implant bone loss. The contradictory results of different studies on peri-implant bone stability suggest other predominant factors, rather than implant surface roughness alone.

**SHORT-TERM RESULTS**

At the time this thesis was initiated, only a few studies were available on the clinical outcome of implants with fluoride-modified surfaces\textsuperscript{19-25} whereas implants without the additional fluoride modification, were well-documented and reported high survival rates (87.7 % - 100 %) and limited peri-implant bone loss (0.01 – 2.60 mm)\textsuperscript{26-51} up to 16 years of function. Recently, more studies (table 2) became available describing the clinical outcome of Osseospeed\textsuperscript{TM} implants\textsuperscript{52-64}. In the present thesis, both implants with and without fluoride modification yielded very high survival rates, ranging from 98.3 % to 100 % and limited short-term peri-implant bone loss (0.11 mm – 0.90 mm). This is in accordance with the literature as summarized in Table 2.
Table 2. Overview of recent studies considered key references on implants with a fluoride-modified surface.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Follow-up</th>
<th>Patients</th>
<th>Implants</th>
<th>Baseline</th>
<th>Survival</th>
<th>Bone Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al.</td>
<td>Prospective</td>
<td>1 year</td>
<td>12</td>
<td>24</td>
<td>Prosthesis</td>
<td>100.0 %</td>
<td>0.06 mm</td>
</tr>
<tr>
<td>Collaert et al.</td>
<td>Prospective</td>
<td>2 years</td>
<td>25</td>
<td>125</td>
<td>Surgery</td>
<td>100.0 %</td>
<td>0.11 mm</td>
</tr>
<tr>
<td>Guljé et al.</td>
<td>Prospective</td>
<td>1 year</td>
<td>12</td>
<td>48</td>
<td>Surgery</td>
<td>96.0 %</td>
<td>0.10 mm</td>
</tr>
<tr>
<td>Koutouzis et al.</td>
<td>Prospective</td>
<td>1 year</td>
<td>18</td>
<td>20</td>
<td>Surgery</td>
<td>95.0 %</td>
<td>0.19 mm</td>
</tr>
<tr>
<td>Tsuda et al.</td>
<td>Prospective</td>
<td>1 year</td>
<td>10</td>
<td>10</td>
<td>Surgery</td>
<td>100.0 %</td>
<td>-0.10 mm</td>
</tr>
<tr>
<td>Galindo-Moreno et al.</td>
<td>Prospective</td>
<td>1 year</td>
<td>69</td>
<td>97</td>
<td>Surgery</td>
<td>95.9 %</td>
<td>0.07 mm</td>
</tr>
<tr>
<td>Raes et al.</td>
<td>Prospective</td>
<td>1 year</td>
<td>48</td>
<td>48</td>
<td>Surgery</td>
<td>98.0 %</td>
<td>-0.31 mm</td>
</tr>
<tr>
<td>Schliephake et al.</td>
<td>Prospective</td>
<td>5 years</td>
<td>44</td>
<td>134</td>
<td>Prosthesis</td>
<td>100.0 %</td>
<td>0.16 mm</td>
</tr>
<tr>
<td>Aguirre-Zorzano et al.</td>
<td>Retrospective</td>
<td>1 year</td>
<td>94</td>
<td>246</td>
<td>Prosthesis</td>
<td>99.6 %</td>
<td>0.39 mm</td>
</tr>
<tr>
<td>De Bruyn et al.</td>
<td>Prospective</td>
<td>3 years</td>
<td>113</td>
<td>113</td>
<td>Surgery</td>
<td>96.5 %</td>
<td>-0.57 mm</td>
</tr>
<tr>
<td>Ghoveizi et al.</td>
<td>Prospective</td>
<td>1 year</td>
<td>10</td>
<td>20</td>
<td>Prosthesis</td>
<td>100.0 %</td>
<td>0.24 mm</td>
</tr>
<tr>
<td>Sanz et al.</td>
<td>Prospective</td>
<td>3 years</td>
<td>84</td>
<td>84</td>
<td>Prosthesis</td>
<td>98.9 %</td>
<td>-0.17 mm</td>
</tr>
<tr>
<td>Slot et al.</td>
<td>Prospective</td>
<td>1 year</td>
<td>24</td>
<td>96</td>
<td>Prosthesis</td>
<td>100.0 %</td>
<td>0.24 mm</td>
</tr>
</tbody>
</table>
**LONG-TERM RESULTS**

CHAPTER 6 presents the long-term clinical outcome of immediately loaded TiOblast™ implants supporting full-arch rehabilitations in edentulous jaw. During the study follow-up, two implants failed, resulting in an overall survival rate of 99.2 % and 97.4 % on implant level and patient level, respectively. This result is in accordance with other studies on immediate loading of implants in the fully edentulous mandible\(^{65-71}\) and maxilla\(^{72-75}\), suggesting favorable long-term results in terms of implant survival.

In this thesis, an overall mean bone loss of 1.68 mm (range -1.05 – 10.95) was found after a mean follow-up of 108 months with implant installation as baseline. A recent study by Ravalde and co-workers, evaluating the same implant system with a follow-up of 12-15 years demonstrated a patient mean bone loss of 0.67 mm with the time of bridge connection as baseline. A mean patient bone loss of 0.30 mm was reported from 5 years to 12 years follow-up\(^{51}\). The latter does not report the bone loss that occurred between implant installation and baseline (bridge connection). However, this has been described in an earlier paper by the same group\(^{76}\) reporting 1.74 mm bone loss in the maxilla and 1.06 mm in the mandible from implant installation to 5 years follow-up. The major changes in peri-implant bone levels, however, occurred between implant installation and prosthetic loading.

Bringing this information together, one can conclude that the patient mean bone loss in the study of Ravalde and co-workers amounted to approximately 2 mm in the maxilla and 1.30 mm in the mandible.

In a prospective follow-up study, Rasmusson and co-workers evaluated peri-implant bone levels around 68 TiOblast implants after 7 years of prosthetic loading and reported a mean bone loss of 1.27 mm (range 0 – 5.21\(^{36}\). The reported bone loss of 1.68 mm after 9 years in our work is in accordance with the aforementioned studies. However, different studies reported stable marginal bone conditions after initial bone remodeling\(^{36,44,51,77}\) which is in contradiction with the findings in the present thesis. Hence, taking this into consideration, appropriate statistical analyses to identify predictors for early and late bone loss were performed.
**PREDICTORS**

- **SMOKING**

Smoking is considered a well-known risk factor in implant dentistry. Results related to smoking are summarized in Table 3. The effect of smoking on implant treatment outcome was analyzed both on implant and patient level, as smoking is considered a systemic factor. CHAPTER 2 and 4 showed significantly more failures in smokers. Approximately one smoker out of 10 experienced implant failure. Different systematic reviews and meta-analyses, identified smoking as a detrimental factor in implant dentistry. In the systematic review of Strietzel and coworkers the meta-analysis showed increased risk for implant failure in smokers both when the implant (odds ratio 2.25, 95% CI; 1.96 to 2.59) and the patient (odds ratio 2.64, 95% CI; 1.70 to 4.09) were considered the statistical unit. In another meta-analysis, Hinode and coworkers reported a 2.2 higher odds ratio for implant failure in smokers. The findings in the present thesis confirmed the aforementioned results. However, in CHAPTER 6 smoking did not affect implant survival. Only 2 failures were observed in a non-smoking patient.

The different studies related to smoking showed significantly more bone loss around implants installed in smokers. In CHAPTER 2, smoking was found to affect peri-implant bone loss in the maxilla, but this was not observed in the mandible. These findings are in accordance with other studies. A possible explanation for this observation could be the inferior bone quality in the maxilla (more spongiosa) compared with the mandible, which is also observed in non-smoking patients. A second explanation is related to the local influence of tobacco smoke on the peri-implant tissues. As a consequence of smoking, an impaired vascularization has been described in smokers. However, the mandible is partially protected by the tongue, possibly preventing the direct influence of the toxic chemicals. Taking this into account, it is reasonable to believe, that the maxilla is more prone to the pernicious effect of smoking over the years.

In CHAPTER 6, smoking was identified as a predictor for late peri-implant bone loss. The effect of smoking was estimated to yield an additional 1.18 mm of bone loss compared to...
non-smokers. Collaert & De Bruyn already suggested after 3 years of follow-up that the stable bone levels in non-smokers were indicative of a good long-term prognosis. On the contrary, smokers showed already deteriorating results at the end of the 3-year follow-up when the patient was considered as statistical unit. They suggested a time-dependent effect of smoking on the oral tissues, i.e. the longer the exposure, the worse the clinical outcome. This finding was confirmed in CHAPTER 6 after a mean follow-up of 9 years.

In the present thesis, no distinction was made between light and heavy smokers although a dose-dependent affect was described on bone loss around natural teeth. This may be a shortcoming. On the other hand, studies on the effect of smoking are based on self-reported smoking habits. Hence, they rely on the accuracy of the reported behavior. It is known that patients cannot be considered truthful about their smoking habits and significantly underreport their daily cigarette consumption. Hence, biochemical techniques are necessary to objectively quantify tobacco consumption. Therefore, a patient was considered a smoker irrespective of the amount of cigarettes consumed on a daily basis.

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Smokers</th>
<th>Non-smokers</th>
<th>Implants</th>
<th>Patients</th>
<th>Survival</th>
<th>Bone Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapter 2</td>
<td>244</td>
<td>849</td>
<td>60</td>
<td>300</td>
<td>96.7 %</td>
<td>0.53 mm</td>
</tr>
<tr>
<td></td>
<td>290</td>
<td>1017</td>
<td>74</td>
<td>297</td>
<td>96.9 %</td>
<td>0.57 mm</td>
</tr>
<tr>
<td>Chapter 6</td>
<td>12</td>
<td>27</td>
<td>75</td>
<td>170</td>
<td>100.0 %</td>
<td>2.81 mm</td>
</tr>
<tr>
<td></td>
<td>27</td>
<td>170</td>
<td>98.8 %</td>
<td></td>
<td>1.20 mm</td>
<td></td>
</tr>
</tbody>
</table>

*Table 3. Overview of studies in the present thesis comparing implant treatment outcome in smokers and non-smokers.*

**ORAL HYGIENE**

In the present thesis, plaque and bleeding scores, evaluating oral hygiene, were measured and reported in CHAPTER 5 & CHAPTER 6. The other studies (except for CHAPTER 1) were retrospective studies based on patient files. Hence, information on oral hygiene was not reliable because no standardized plaque and bleeding scores were available.

In CHAPTER 5 relatively low plaque and bleeding scores are described. Plaque scores were 0.82 and 0.84 and bleeding scores were 0.46 and 0.56 after 1 year and 2 years, respectively.
This may explain why early bone remodeling was not influenced by plaque and bleeding scores, although is reported in literature \(^{90-92}\). This study was conducted in the Netherlands were auxillary personal, such as oral hygienists are present. Consequently, these patients were well-maintained and and received an individually based professional maintenance program. This may explain why results were not influenced by plaque and bleeding scores.

In CHAPTER 6 mean full-mouth plaque and bleeding scores of 1.18 and 1.25 are reported, suggesting a rather poor oral hygiene. These findings are in contrast with the outcome reported in the well-maintained population of CHAPTER 5. However, in CHAPTER 6 the study sample consisted of referred patients. Most of these patients neglected the recall invitation by the surgeon after the end of the original study follow-up (3 years) and can be classified as non-compliant. Moreover, based on the reported plaque and bleeding scores after 9 years, it is tempting to conclude that patients were erratic or non-compliant regarding oral hygiene measures. Is these cases an increased risk for peri-implant disease can be highly expected \(^{18,93}\). In line with this, multivariate analyses identified bleeding on probing as a predictor of long-term bone loss. However, this finding should be interpreted with caution for two reasons, being the limited prognostic value of bleeding on probing and the timing of registration. Firstly, the prognostic value of peri-implant bleeding on probing remains a matter of debate. Ferreira and co-workers evaluated the effect of different risk variables for peri-implant disease \(^{96}\). They showed a statistically significant association between the periodontal status and a worse peri-implant condition with odds ratios for very poor oral hygiene and BOP (> 30 % of the sites) of 14.3 and 3.4, respectively. On the contrary Lekholm and co-workers (1986) could not demonstrate a correlation between radiographic changes and bleeding on probing around dental implants \(^{95}\). Moreover, it was shown that even the majority of healthy implants can demonstrate bleeding on probing \(^{96}\), especially in combination with a high probing force or inappropriate transmission of the probing force to the tissues \(^{97}\). Secondly, bleeding on probing was only registered after 9 years of function. As this registration did not precede the outcome evaluation, *stricto sensu* bleeding on probing cannot be considered a predictor.

One can conclude that the literature is inconclusive about the reliability of periodontal parameters for the assessment of peri-implant health. For this reason radiographic analysis was suggested to evaluate critical bone level changes \(^{98}\).
• **HISTORY OF PERIODONTITIS**

In the CHAPTER 6 the long-term effect of a history of periodontitis on implant treatment outcome was evaluated. Implants in patients with a history of periodontitis were more prone the show peri-implant bone loss. After 9 years, the effect was estimated at 1.19 mm additional bone loss compared with implants installed in periodontally healthy patients. In the literature, there exists evidence that patients with existing or ongoing periodontitis are more likely to experience implant failure and biological complications\(^94,99-103\). From these papers, the evidence is mainly related to chronic periodontitis and aggressive periodontitis. However, due to the high heterogeneity of data, it is difficult to draw strong conclusions. Different studies reported odds ratios ranging from 3.1 to 4.7 showing a statistically significant greater risk for peri-implantitis in patients with a history of periodontitis\(^101-103\). A recent long-term prospective study by Swierkot and co-workers compared the outcome of dental implant treatment in patients with treated aggressive periodontitis and periodontally healthy patients. They concluded that patients with treated aggressive periodontitis have a 5 times greater risk of implant failure, a 3 times greater risk of mucositis and a 14 times greater risk of peri-implantitis\(^104\). These results suggest that periodontal disease, despite treatment, jeopardizes long-term peri-implant bone stability, possibly leading to future implant failures. This is in accordance with the findings of the study presented in CHAPTER 7. In a review on the effect of smoking and history of periodontitis on implant treatment, Heitz-Mayfield and Huynh-Ba suggest a combined effect of these factors\(^105\). However, they conclude that multivariate analyses are necessary for proper risk assessment and quantification of the effects. Indeed, in the present study, the patients with the worst peri-implant conditions were smokers with a history of periodontitis. This effect was estimated at 2.37 mm additional bone loss, compared with implants installed in nonsmokers without a history of periodontitis. To our knowledge, the present study is the first to quantify these combined effects based on a multivariate statistical analysis in a prospective case series.

• **SOFT TISSUE THICKNESS**

In literature, an average biologic width of 3.08 mm was described around non-submerged implants installed in a one-stage surgical procedure\(^106\) and 3.42 - 3.80 mm around submerged implants installed in a two-stage surgical procedure\(^107,18\). More recently, the
dimensions of the peri-implant soft tissues were described by Tomasi and co-workers based on the analysis of human biopsies. They described soft tissue dimensions of 3.6 mm, including a barrier epithelium of 1.9 mm and a connective tissue portion of 1.7 mm. It is believed that the biologic width establishes after implant placement in order to create enough space acting as barrier against bacterial contamination. One can assume that in case of soft tissues of 2 mm, this precludes either 1 - 1.5 mm of bone loss or a soft tissue regrowth through hypertrophia to create this protective seal, based on the quantitative descriptions in the afore-mentioned studies.

Both CHAPTER 5 & CHAPTER 6 showed that early bone remodeling was influenced by the initial soft tissue thickness at the time of implant placement as reflected by the height of the abutments. Results are summarized in Table 4. This outcome was not the primary aim of the studies and can be considered a coincidental finding.

<table>
<thead>
<tr>
<th>CHAPTER 5</th>
<th>Abutment height</th>
<th>Bone Loss</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 mm</td>
<td>3 mm</td>
<td>≥ 4 mm</td>
</tr>
<tr>
<td></td>
<td>&lt; 2 mm</td>
<td>0.86 mm</td>
<td>0.38 mm</td>
</tr>
<tr>
<td></td>
<td>3 mm</td>
<td>1.17 mm</td>
<td></td>
</tr>
<tr>
<td>≥ 4 mm</td>
<td>0.41 mm</td>
<td>0a</td>
<td></td>
</tr>
<tr>
<td>CHAPTER 6</td>
<td>≤ 1.5 mm</td>
<td>0.79 mm</td>
<td>0a</td>
</tr>
<tr>
<td></td>
<td>3 mm</td>
<td>0.42 mm</td>
<td>0a</td>
</tr>
<tr>
<td></td>
<td>≥ 4.5 mm</td>
<td>1.23 mm</td>
<td>1.03 mm</td>
</tr>
</tbody>
</table>

*Table 4. Overview of studies reporting on the influence of soft tissue thickness on peri-implant bone loss. a Parameter set to zero as a reference value.*

In CHAPTER 5 and CHAPTER 6, abutments were placed at the time of implant placement and the height was adapted to the site-specific soft tissue thickness. As a consequence of this standardized approach in both studies, the height of the abutments reflected the initial soft tissue thickness.

The re-establishment of these dimensions around dental implants can explain the greater amount of bone loss around implants installed at sites with thin soft tissues, as already
suggested by different authors \textsuperscript{110,111}. Canullo & co-workers suggested that bone resorption is predominantly related to biologic factors (biologic width re-establishment) rather than biomechanical factors (platform-switching)\textsuperscript{112}. This was in accordance with Linkevicius and co-workers who described that implants with platform-switching did not prevent peri-implant bone loss when thin soft tissues were present \textsuperscript{113}.

It is important, however, to anticipate on this initial bone remodeling in order to prevent unforseen exposure of the implant threads. Bacterial colonization of the implant surface \textsuperscript{10-12} may increase the risk for peri-implantitis, especially in patients with other risk factors such as, smoking, history of periodontitis and poor oral hygiene. This was shown in CHAPTER 6 were ongoing bone loss in different patients with initial bone loss occurred. Hence, it was suggested to adapt the vertical position of the implant based on the soft tissue thickness, which is mostly feasible in edentulous zones (CHAPTER 5). For solitary tooth replacement, increasing soft tissue dimensions by means of membranes or connective tissue grafts was suggested to avoid early peri-implant bone loss \textsuperscript{111}.

**JAW OF TREATMENT**

We already discussed the effect of smoking on implant treatment outcome in the maxilla and the mandible previously. In CHAPTER 4 and CHAPTER 6, implant treatment outcome was evaluated in relation to the jaw of treatment. Results are summarized in Table 5.

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Implants</th>
<th>Survival</th>
<th>Bone Loss (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHAPTER 2</strong></td>
<td>Maxilla</td>
<td>648</td>
<td>99.2%</td>
</tr>
<tr>
<td></td>
<td>Mandible</td>
<td>485</td>
<td>97.1%</td>
</tr>
<tr>
<td><strong>CHAPTER 4</strong></td>
<td>Maxilla</td>
<td>757</td>
<td>99.3%</td>
</tr>
<tr>
<td></td>
<td>Mandible</td>
<td>563</td>
<td>97.2%</td>
</tr>
<tr>
<td><strong>CHAPTER 6</strong></td>
<td>Maxilla</td>
<td>140</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>Mandible</td>
<td>105</td>
<td>98.4%</td>
</tr>
</tbody>
</table>

*Table 5. Overview of studies reporting on implant treatment outcome of implants in mandible vs maxilla. S = smoker, NS = non-smoker.*
In CHAPTER 4 univariate analysis identified the jaw as a significant factor affecting implant survival and peri-implant bone loss with more implant failures occurring in the mandible and more peri-implant bone loss in the maxilla. However, univariate analyses do not correct for confounding factors and can be considered exploratory for this reason. Multivariate analyses only confirmed the impact of this factor on peri-implant bone loss.

This finding is in agreement with previous clinical studies\textsuperscript{33,80,81,114-116}. However, this could not be observed in CHAPTER 6 were multivariate analyses failed to show a long-term effect of the jaw of treatment on survival and peri-implant bone loss. Other studies could not observe this difference between mandible and maxilla as well\textsuperscript{117-118}. Hence, the results in the present thesis and the literature are inconclusive about the effect of the jaw of treatment on implant treatment outcome. More well-designed studies are necessary to elucidate this topic of debate.

Although not statistically significant after multivariate analysis, the higher failure rate observed in the mandible can be of clinical relevance. In CHAPTER 2 and CHAPTER 4, all failures in the mandible occurred in the posterior region. Most implants were short and small diameter implants because of limited bone volume. These factors in combination with the high bone density and deficiency of vascularization known to occur in the posterior mandible, especially in elderly and edentulous patients\textsuperscript{119}, may explain the higher failure rate for this particular indication.
REFERENCES

45. Mertens C, Steveling HG. Implant-supported fixed prostheses in the edentulous maxilla: 8-year


66. Engstrand P, Grondahl K, Ohrnell LO, Nilsson P, Nannmark U, Branemark PI. Prospective follow-up study
of 95 patients with edentulous mandibles treated according to the Branemark Novum concept. Clin Implant Dent Relat Res. 2003; 5: 3-10.


CONCLUSIONS

& CLINICAL GUIDELINES
GENERAL CONCLUSIONS

Fluoride-modified implants are a reliable and highly successful treatment option when used for different indications and treatment protocols in daily practice. High survival rates and limited peri-implant bone loss after at least 2 years and up to 5 years of function were reported in the present thesis.

Both immediately loaded implants with and without additional fluoride modification in the edentulous mandible yielded excellent short-term results with 100% survival and very limited peri-implant bone loss after 2 years of function.

However, implants without additional fluoride-modification were more prone to peri-implant bone loss, suggesting a decisive role for implant surface modifications regarding bone preservation. Long-term results still showed very high survival rates. However, continuing bone loss was observed after 9 years of function.

Within the limits of this thesis, it can be concluded that initial bone remodeling around implants with and without fluoride modification was affected by soft tissue thickness as reflected by the height of the abutment.

Multivariate analysis demonstrated that implant-related factors did not affect the clinical outcome of implants with fluoride-modification, but smoking was identified as a predictor for implant failure. Predictors for peri-implant bone loss were smoking and jaw of treatment, with more bone loss for implants installed in smokers and in the maxilla.

Smoking, history of periodontitis and bleeding on probing affected long-term peri-implant bone stability. Whether this bone loss is predicting future implant failures remains to be evaluated. More well-designed prospective studies are required to evaluate the different factors on implant treatment outcome.
CLINICAL GUIDELINES & CONSIDERATIONS

TREATMENT PROTOCOL
Immediate loading, 1-stage delayed and 2-stage delayed loading are effective treatment options. It is suggested to adopt a 2-stage delayed procedure in cases of lack of primary stability or prosthesis wear, possibly interfering with implant integration. If primary stability is achieved, implants can be functionally loaded immediately using a temporary provisional restoration. In cases of single implants, a non-occlusal immediate provisionalisation is suggested to avoid too excessive micromotions at the bone-to-implant interface.

SOFT TISSUE THICKNESS
The re-establishment of the biological width around dental implants can explain the greater amount of bone loss around implants installed at sites with thin soft tissues. To anticipate this initial bone remodeling, it is suggested to adapt the vertical position of the implant based on the soft tissue thickness, which is mostly feasible in edentulous zones. For solitary tooth replacement, increasing soft tissue dimensions by means of membranes or connective tissue grafts is suggested to avoid early peri-implant bone loss.

SMOKING
Smoking is not an absolute contra-indication in implant therapy. However, smokers should be informed about the adverse effects on implant treatment outcome. Smokers are at higher risk to experience implant failure. Moreover, increased bone loss in smokers can lead to peri-implantitis and unesthetic results. Therefore, smoking cessation should be advised at the start of all periodontal and implant treatments.

HISTORY OF PERIODONTITIS
Patients should be informed that implants can only be installed in a periodontally stable environment. This may not prevent biological complications, but could reduce the risks for peri-implantitis. Patient compliance, including supportive therapy and good oral hygiene, is a prerequisite to maintain this stability. The frequency and content of supportive therapy should be adapted based on the oral hygiene and risk profile of the patient to prevent future complications.
SUMMARY

Dental implants became commercially available in the seventies and ever since, millions of people worldwide were treated to restore oral function and facial esthetics. During the last two decades implant dentistry has evolved to a faster and more predictable treatment due to better insights in surgical procedures and biomaterials and coincides better with the increased expectations of the patients. Most implant surfaces today, are moderately rough. Astra Tech Dental (Möldahl, Sweden) introduced an additional fluoridation of their existing grit-blasted surface. Experimental studies showed a faster and stronger bone-to-implant contact after implant installation. Based on these findings, it is believed that patients can benefit from these novel implant surfaces, especially in more demanding cases. At the time this thesis was initiated, only a few studies were available on the clinical outcome of implants with this fluoride-modified surface.

Despite the enhancement of implant design and surface, different factors are described that affect implant treatment outcome, resulting in early or late implant failures. Early implant failures have been related to excessive surgical trauma, an impaired healing ability, premature loading and infection. Late failures are mostly attributed to occlusal overload and/or progressive peri-implant bone loss. Identification of risk factors/predictors for disease occurrence requires preferably longitudinal studies in humans with a prospective design. Randomized controlled studies can evaluate the effect of one variable in a controlled and selected study population, were confounding factors are excluded. Care has to be taken to extrapolate these results to the daily practice were also ‘less than ideal’ patients are treated.

In this context, large prospective or even retrospective case series may become particularly important to evaluate the relative importance of one factor in relation to others. A thorough risk assessment requires multivariate analyses correcting for confounding factors. The overall objective of this thesis was to scrutinize implant treatment outcome of implants with and without fluoride modification, placed in daily practice, and to identify predictors affecting short- and long-term implant treatment outcome.

CHAPTER 1 described a prospective 2-year evaluation of implants with a fluoride-modified surface under immediate loading conditions in the edentulous mandible. Implant treatment
outcome was compared with a historic control-group, using implants with the same design without the additional surface modification. Implants were functionally loaded the day after surgery with a provisional screw-retained prosthesis. Both groups showed excellent short-term results with 100 % survival after 2 years and steady-state bone levels after initial bone remodeling. However, at every study time point, implants without fluoride modification, showed significantly more peri-implant bone loss, suggesting a decisive role for the implant surface regarding bone preservation.

CHAPTER 2 further documents the clinical outcome of implants with a fluoride-modified surface. In this retrospective cohort study, evaluating 1106 implants in 300 patients with a minimum follow-up of 2 years, the impact of smoking on implant treatment outcome was evaluated. Survival rates of 98.3% and 94.6% at implant and patient level were described after a mean follow-up of 32 months, respectively. Implant survival was significantly higher for nonsmokers compared with smokers both with the implant and the patient as statistical unit. Implants with a fluoride modified surface showed a mean peri-implant bone loss of 0.34 mm. Smoking significantly affected the outcome in the maxilla (0.74 mm vs. 0.33 mm, p <0.001), but this difference could not be observed in the mandible (0.25 mm vs. 0.22 mm p=0.298).

To our knowledge, this study was at the time of submission the first to compare peri-implant bone loss in smokers and nonsmokers from the time of implant insertion to at least 2 years of follow-up. Implants with a fluoride-modified surface demonstrated a high survival rate and limited bone loss. However, smokers were at higher risk of experiencing implant failure and more prone to show peri-implant bone loss in the maxilla. Whether this bone loss is predicting future biological complications remains to be evaluated.

CHAPTER 3 described the outcome of immediately loaded implants with a fluoride-modified surface in the maxilla. In this retrospective cohort study based on patient files, information on 306 implants in 55 patients was available for statistical analysis. Implant treatment outcome was scrutinized in terms of implant survival and peri-implant bone loss for different prosthetic reconstructions. Immediate loading was described as a predictable and reliable treatment option with high survival rates (99.7 %) and limited peri-implant bone loss (0.27
mm) after a mean follow-up of 35 months. No statistically significant differences were found between implants supporting single crowns, fixed partial dentures and fixed full dentures.

**CHAPTER 4** is an extension of the study described in chapter 2. In this retrospective cohort study, conducted in a private periodontal clinic, multivariate analysis based on 1320 implants in 376 patients demonstrated that implant-related factors did not affect the clinical outcome, but smoking was identified as a predictor for implant failure. Predictors for peri-implant bone loss were smoking and jaw of treatment, with more peri-implant bone loss for implants installed in smokers (0.57 mm vs 0.30 mm) and in the maxilla (0.42 mm vs 0.28 mm). The study also revealed a clear discrepancy between univariate and multivariate analysis. Given the large number of implants and explanatory variables, interaction between different variables may be conceivable. For this purpose a multivariate analysis was adopted, corrected for confounding. Hence, the univariate analysis can be considered exploratory.

**CHAPTER 5** described the influence of the soft-tissue thickness at the time of implant placement on early bone remodeling. 79 patients were consecutively treated with 2 interforaminal implants to support an overdenture in the mandible. After implant installation, the height of the abutment was adapted to the site-specific soft-tissue thickness. An independent research team of the Ghent University organized a 1-year and 2-year recall examination. The linear mixed-effect model analysis revealed increasing bone level changes with decreasing abutment heights. Peri-implant bone level changes were significantly higher for implants with abutments of < 2 mm (1.17 mm, p < 0.01; 1.23 mm, p < 0.01), 2 mm (0.86 mm, p < 0.01; 1.03 mm, p < 0.01) or 3 mm (0.38 mm, p = 0.046; 0.41 mm, p = 0.044) compared to ≥ 4 mm abutments (bone level changes set to zero as reference value) both after 1 year and 2 years. Hence, it was suggested that the surgeon should proactively keep soft tissue thickness into account when installing implants especially in cases with a thin biotype.

**CHAPTER 6** described the long-term treatment outcome of immediately loaded implants supporting full-arch rehabilitations in the edentulous jaw. 50 patients in need for a complete implant-supported rehabilitation on 5 to 8 implants were consecutively treated. Patients were reinvited for a clinical and radiographic examination after on average 9 years of function and multivariate analyses were adopted to identify predictors of early and late peri-
implant bone loss. During the study follow-up, two implants failed, resulting in an overall survival rate of 99.2 % and 97.4 % on implant level and patient level, respectively. After 9 years, a mean bone loss of 1.68 mm was found. Bone level changes were statistically significant between 3 months and 36 months and additionally between 36 months and 9 years, suggesting that no steady-state bone levels were obtained. Multivariate analyses showed that initial bone remodeling was affected by soft-tissue thickness as reflected by the height of the abutment, whereas smoking, history of periodontitis and bleeding on probing were identified as predictors affecting long-term peri-implant bone loss.

In the discussion, the outcome of the various clinical studies was scrutinized in relation to the aims of this thesis. By and large the following research conclusions and clinical guidelines were adopted as an overall result:

**Conclusions**

- *Fluoride-modified implants are a reliable and highly successful treatment option with high survival rates and limited peri-implant bone loss.*
- *Implants without additional fluoride modification were more prone to peri-implant bone loss.*
- *Initial bone remodeling is affected by soft-tissue thickness.*
- *Smoking affects short-term implant survival and peri-implant bone loss.*
- *Implants installed in the maxilla are more prone to peri-implant bone loss.*
- *Smoking and history of periodontitis affected long-term peri-implant bone stability.*

**Guidelines**

- *When primary stability is achieved, Implants can be functionally loaded immediately using a temporary provisional restoration.*
- *To anticipate initial bone remodeling, it is suggested to adapt the vertical position of the implant based on the soft-tissue thickness or to increase soft tissue dimensions to avoid early peri-implant bone loss.*
- *Smokers should be informed about the adverse effects on implant treatment outcome. Smoking cessation should be advised at the start of every treatment.*
• *Patients should be informed that implants can only be installed in a periodontally stable environment. Patient compliance, including supportive therapy and good oral hygiene, is a prerequisite to maintain this stability. The frequency and content of supportive therapy should be adapted based on the oral hygiene and risk profile of the patient.*
SAMENVATTING

Sinds de commercialisering tijdens de jaren ’70, werden bij miljoenen mensen wereldwijd functie en esthetiek hersteld met behulp van implantaat gedragen reconstructies. De laatste 20 jaren zijn behandelingen versneld en vereenvoudigd door nieuwe inzichten in chirurgische procedures en verbeteringen van de gebruikte biomaterialen. Dit alles om tegemoet te komen aan de steeds hogere verwachtingen van patiënten. De meeste commercieel beschikbare implantaten hebben vandaag een gematigd ruw oppervlak. Astra Tech Dental introduceerde een aangepast oppervlak door het bestaande gezandstraalde oppervlak te fluorideren. Experimentele studies toonden aan dat deze implantaten sneller en beter integreren. Men kan op basis van deze bevindingen besluiten dat deze nieuwe generatie implantaten meer geschikt is voor veeleisende situaties. Toen deze thesis opgestart werd, waren slechts enkele klinische studies beschikbaar die de uitkomst van deze nieuwe implantaten rapporteerden. Ondanks de verbeteringen aan de implantaten en behandelingen, zien we nog steeds falingen die veroorzaakt worden door verschillende factoren. Vroegtijdige falingen werden reeds gerelateerd aan chirurgisch trauma, een verstoorde genezing, ongecontroleerde belasting en infectie. Laattijdige falingen zijn meestal toe te schrijven aan overbelasting of progressief botverlies. Longitudinale studies op mensen, bij voorkeur met een prospectief design, zijn noodzakelijk om risicofactoren/predictoren van ziekte te identificeren. Gerandomizeerde, gecontroleerde studies kunnen het effect van één factor evalueren waarbij andere factoren die het resultaat kunnen beïnvloeden, geëxcludeerd worden. Het is dan ook aan te raden voorzichtig te zijn om deze resultaten te extrapoleren naar de dagelijkse realiteit, waar ook minder ‘ideale’ patiënten behandeld worden. Hiervoor zijn grote, niet-gecontroleerde, prospectieve, of zelfs retrospectieve studies belangrijk. In deze studiepopulaties kan het relatieve effect van een factor ten opzichte van andere factoren geëvalueerd worden. Bij dergelijke risicoanalyses zijn multivariate statistische analyses noodzakelijk om het gewicht van de verschillende factoren in rekening te brengen. Het doel van deze thesis was om de uitkomst van dentale implantaten met en zonder fluoridering van het oppervlak te evalueren in de dagelijkse praktijk en om predictoren te identificeren die de korte- en lange-termijn resultaten van deze implantaten beïnvloeden.
HOOFDSTUK 1 beschrijft in een prospectieve studie de 2 jaar uitkomst van onmiddellijk belaste implantaten met gefluorideerd oppervlak in de edentate onderkaak. Deze resultaten werden vergeleken met een historische controle groep die behandeld werd met dezelfde implantaten, maar zonder additionele fluoridering. De implantaten werden functioneel belast met een tijdelijke, verschroefde brug, 1 dag na de chirurgische ingreep. Beide groepen vertoonden goede korte- termijn resultaten met 100 % implantaatoverleving en stabiele botwaarden na initiële botremodellage. Desalniettemin, vertoonden implantaten zonder gefluorideerd oppervlak op elk tijdstip meer botverlies in vergelijking met de gefluorideerde implantaten. Deze resultaten suggereren dat het implantaatoppervlak een belangrijke rol speelt bij crestaal botbehoud rondom implantaten.

HOOFDSTUK 2 beschrijft de klinische uitkomst van gefluorideerde implantaten in de dagelijkse praktijk. In een retrospectieve cohort-studie werden 1106 implantaten bij 300 patiënten met een minimale opvolging van 2 jaren, geëvalueerd. Na een gemiddelde opvolging van 32 maanden werd een implantaatoverleving gerapporteerd van 98.3 % op implantaatniveau en 94.6 % op patiëntniveau. De implantaatoverleving was significant hoger bij niet-rokers. Het gemiddelde botverlies rond de implantaten was 0.34 mm. Roken had een invloed op botverlies rond de implantaten in de bovenkaak (0.74 mm vs 0.33 mm), maar dit verschil werd niet waargenomen in de onderkaak (0.25 mm vs 0.22 mm). Deze studie was de eerste om botverlies te vergelijken bij rokers en niet-rokers vanaf de implantaatplaatsing tot 2-jaar opvolging. Gefluorideerde implantaten bleken zeer succesvol, met een hoge implantaatoverleving en zeer gelimiteerd botverlies. Rokers bleken een hoger risico te hebben op implantaatfalen en vertoonden meer botverlies rondom de implantaten. Of dit botverlies ook daadwerkelijk een aanleiding vormt voor toekomstige complicaties, moet verder onderzocht worden.

HOOFDSTUK 3 beschrijft de uitkomst van onmiddellijk belaste, gefluorideerde implantaten in de bovenkaak. 306 implantaten bij 55 werden in deze retrospectieve cohort-studie geïncludeerd voor statistische analyse, op basis van een minimale opvolging van 2 jaar. De uitkomst van implantaten die solitaire kronen, partiële bruggen en volledige bruggen ondersteunen, werden vergeleken. Onmiddellijke belasting in de bovenkaak bleek een voorspelbaar en betrouwbaar protocol met hoge implantaatoverleving (99.7 %) en minimaal
Summary/Samenvatting

botverlies (0.27 mm) na gemiddeld 35 maanden opvolging. Er werden geen verschillen gevonden tussen implantaten die solitaire kronen, partiële bruggen of volledige bruggen ondersteunen.

HOOFDSTUK 4 beschrijft een uitbreiding van de studie in hoofdstuk 2. In deze retrospectieve cohort-studie, uitgevoerd in een private praktijk voor parodontologie en implantologie, faalden 21/1320 (1.6 %) implantaten bij 19/376 (5.1 %) na een gemiddelde opvolging van 32 maanden. Multivariate statistische tests toonden aan dat implantaat-gerelateerde factoren geen invloed hadden op de uitkomst, maar roken bleek een predictor voor implantaatfalen. Roken en de behandelde kaak werden geïdentificeerd als predictoren voor botverlies. Implantaten bij rokers en in de bovenkaak vertoonden significant meer botverlies. De studie toonde eveneens een discrepantie tussen resultaten op basis van univariate en multivariate analyses. De univariate analyse kan echter als exploratief beschouwd worden, omdat deze geen rekening houdt met het relatieve effect van de factoren te opzichte van elkaar.

HOOFDSTUK 5 beschrijft de invloed van de dikte van de gingiva op botremodellage. In deze studie werden 79 patiënten consecutief behandeld met 2 implantaten ter ondersteuning van een overkappingsprothese in de onderkaak. Na het plaatsen van de implantaten, werd de hoogte van de abutments aangepast aan de dikte van de gingiva. Door deze gestandaardiseerde procedure reflecteert de abutmenthoogte de dikte van de gingiva. Implantaten met een abutment kleiner dan 2mm, 2mm of 3 mm vertoonden na 1 jaar respectievelijk 1.17 mm, 0.86 mm en 0.38 mm meer botverlies in vergelijking met abutments van 4 mm of meer. De corresponderende waardes na 2 jaar waren 1.23 mm, 1.03 mm and 0.41 mm. Er werd dan ook gesuggereerd dat de chirurg rekening dient te houden met de dimensies van de zachte weefsels bij patiënten met een dun biotype en dit om initiële crestaal botverlies te vermijden.

HOOFDSTUK 6 beschrijft de lange-termijn resultaten van onmiddellijk belaste implantaten ter ondersteuning van een volledige brug. 50 patiënten werden consecutief behandeld met 5 tot 8 implantaten in de edentate onder- of bovenkaak. Patiënten werden uitgenodigd voor een klinisch en radiologisch onderzoek na gemiddeld 9 jaar opvolging. Multivariate analyses
werden toegepast om het effect van verschillende factoren op vroegtijdig en laattijdig botverlies te evalueren.

De studie rapporteert een implantaatoverleving van 99.2 % op implantaatniveau en 97.4 % op patiëntniveau. Na 9 jaar opvolging vertoonden de implantaten gemiddeld 1.68 mm botverlies. Er werden statistisch significante botveranderingen beschreven tussen 3 maanden en 36 maanden en tussen 36 maanden en 9 jaar, suggestief voor progressief botverlies. Multivariate analyses toonden aan dat de initiële dikte van de gingiva een negatief effect had op vroegtijdig botverlies en roken, voorgeschiedenis van parodontitis en bloeding na sonderen op laattijdig botverlies.

In de algemene discussie wordt de uitkomst van de verschillende klinische studies bediscussieerd ten opzichte van de doelstellingen van deze thesis. Dit leidde tot de volgende conclusies en klinische richtlijnen:

**Conclusies**

- **Fluoride-gemodificeerde implantaten zijn betrouwbaar en succesvol met een hoge implantaatoverleving en zeer beperkt botverlies.**
- **Implantaten zonder deze modificatie vertonen meer crestaal botverlies.**
- **De initiële botremodellage wordt beïnvloed door de dikte van de gingiva.**
- **Rokers hebben meer kans op een implantaatfaling en vertonen meer crestaal botverlies op korte termijn.**
- **Implantaten in de bovenkaak vertonen meer crestaal botverlies.**
- **Roken en een voorgeschiedenis van parodontitis zijn predictoren voor crestaal botverlies op lange termijn.**

**Richtlijnen**

- **Bij voldoende primaire stabiliteit kunnen implantaten onmiddellijk belast worden.**
- **Om initiëel crestaal botverlies te beperken, dient de verticale positie van het implantaat aangepast te worden aan de dikte van de gingiva, of worden de zachte weefsels best geaugmenteerd.**
- **Rokers moeten geïnformeerd worden over de nadelige effecten op de**
behandeluitkomst. Een rookstop moet geadviseerd worden bij de start van elke behandeling.

• **Implantaten kunnen enkel geplaatst worden in een parodontaal stabiele, infectievrije mond.** Therapietrouw is onontbeerlijk om een stabiel resultaat te behouden. De nazorg dient aangepast te worden aan de mondhygiëne en het risicoprofiel van de patient.
DANKWOORD / Acknowledgement

Een thesis maak je niet alleen, maar is het werk van een team. Graag wil ik iedereen bedanken die rechtstreeks of onrechtstreeks bijgedragen heeft aan het tot stand komen van dit werk.

In de zomer van 2008 kwam de vraag van Prof. De Bruyn of ik in het kader van mijn masterthesis ‘wat implantaatjes’ wou analyseren bij Dr. Collaert in Leuven. Voor ik het goed en wel besefte, evolueerde ‘wat implantaatjes’ onder zijn impuls naar een welafgelijnd project. Beste Hugo, je bent een meester-motivator. Je enthousiasme voor onderzoek werkte bij mij aanstekelijk en hielp me doorheen het ganse traject. Ik dank je voor de kans die je mij gaf om te doctoreren en je steun gedurende mijn opleiding en doctoraat. Vele uren hebben we samen gediscussieerd, liters koffie verzet. Af en toe eens stevig doorzakken op congress of teambuilding hoorde er ook stevat bij. Hugo, bedankt voor alles. Zonder jou was dit zoveel moeilijker geweest!

Graag wil ik ook mijn co-promotor, Dr. Bruno Collaert, bedanken. Beste Bruno, jij bent (samen met Filiep) de persoon die het meeste invloed gehad heeft op wie ik als clinicus geworden ben. Ik had het geluk om naast de wetenschappelijke activiteiten bij jou stage te mogen lopen. Je klinische vaardigheden staan buiten kijf (cfr chapter 1, 2, 3, 4 en 6), maar wat me vooral bijblijft, is je communicatie met patiënten en zorgzaamheid. Met spijt in het hart gingen onze (klinische) wegen uiteen in de zomer van 2012, maar ik denk met veel plezier en een tikkeltje weemoed terug aan onze toffe samenwerking. Bruno, bedankt!

Prof Dr. Jan Cosyn, beste Jan, de Prof stelde jou voor als derde lid van de begeleidingscommissie: ‘Als mijn vliegtuig zou neerstorten, dan is er niemand meer geschikt om je te helpen bij je doctoraat’. Gelukkig is het eerste niet gebeurd maar heb ik toch beroep kunnen doen op je inzichten en kennis bij het finaliseren van enkele papers. Jan, bedankt voor alle hulp en steun.

Dr. Filiep Raes, beste Filiep, je hebt een vooraanstaande rol gespeeld tijdens mijn opleiding en erna. We delen dezelfde passie en interesse voor esthetische cases. Het is dan ook steeds een geruststelling om de complexe gevallen met je te kunnen doornemen. Daarnaast hebben we al vele uren samen doorgebracht aan de unief, op congres en in de praktijk.
Gelukkig hoeft het niet steeds over tanden en implantaten te gaan. Er zijn nog belangrijke(re) zaken in het leven. Filiep, bedankt dat je je kennis en kunde wil delen, bedankt voor alle steun en de toffe samenwerking.

Verder wil ik alle mensen bedanken die aan de onderzoeksprojecten hebben meegewerkt: Dr. Ellen Deschepper & Roos Colman voor de statistische ondersteuning, Jos & Marianne Besseler en hun team in Enschede, Drs. Carine Matthijs, Drs. Melissa Dierens, Maarten Glibert & Rima Nassar.

I would like to express my sincere gratitude to the members of the jury, Prof. Dr. Luc Martens, Prof. Dr. Reinhilde Jacobs, Prof. Dr. Lars Rasmusson, Prof. Dr. Ryō Jimbo, Prof. Dr. Linda Vandenberghhe, Dr. Jan D’Haese en Dr. Stefan Vandeweghe, for their critical and constructive review of the thesis. Tevens wens ik de leden van de jury te bedanken voor hun constructieve en kritische bijdrage bij het tot stand komen van deze thesis.

Graag wil ik ook alle medewerkers en collega’s van de P8 tandheelkunde bedanken, in het bijzonder onze verpleegkundigen, Patsy, Patricia & Ingeborg. Zonder jullie zou den boel in het honderd lopen! Daarnaast wens ik ook Nadja en Marleen te bedanken voor alle hulp bij de praktische organisatie van het symposium en de doctoraatsverdediging. Ook de collega’s en medewerkers van de afdeling parodontologie & orale implantologie verdienen een special vermelding. Bedankt allemaal voor de (onder)steun(ing) en de hulp!

I also want to express my gratitude to the company Dentsply Implants (Astra Tech) for their support throughout this thesis. Special thanks go to Charlotte Almgren. Lotta, thank you for the support and monitoring of the research projects during the last four years.

Graag wil ik ook de andere commerciële partners bedanken. Mede dankzij hen konden we deze dag organiseren. Dank aan Ekip Dental, Elysee Dental, Oral-B, Mediplus, Dent-Aid & Corilus.

Bovenal wil ik heel graag mijn ouders bedanken voor hun jarenlange, onvoorwaardelijke steun. Moeke & Vake, ik heb van jullie alle kansen gekregen om mij te ontplooien, zowel op school als daarbuiten. Jullie leerden me dat niets vanzelf komt. Toen ik het wat lighter opnam, sprak moeke ooit de gevleugelde woorden dat ik ooit wel eens tegen de lamp zou
lopen... Na vandaag denk ik dat het er niet meer van komt ;-) ! Dank je wel voor alles!

Hanne & Anneleen, mijn zusjes, we hebben vroeger het bloed van onder elkaars nagels gehaald, zoals het elke goede broer of zus betaamt. Maar ik denk dat we kunnen terugkijken op een fantastische jeugd, waarbij we veel aan elkaar gehad hebben. Ik ben blij en trots als ik zie hoe jullie vandaag in het leven staan. Henri & Dries, jullie hebben het getroffen. Dank jullie wel!

Graag wil ik ook familie en vrienden bedanken. Jullie steun, telefoontjes, op tijd eens goed doorzakken, een etentje, een frisse pint of een goed glas wijn... ‘t Zit soms in de kleine dingen. Bedankt voor de vriendschap! Bedankt maten!

Mamie & Papie, bedankt dat jullie er altijd zijn om de kindjes op te vangen. We weten soms niet hoe we het zonder jullie zouden moeten oplossen als ze weer eens ziek zijn, of als we niet op tijd thuis kunnen zijn om ze van de crèche af te halen. Dank voor de goede zorgen.

Liefste Ralph en Léon, mijn sloebers, mijn schatten. Ik heb mijn best gedaan om de kerk in het midden te houden, maar twee kleine spruiten entertainen en een doctoraat afwerken is niet evident. Ondanks de vele slapeloze nachten, gaven jullie mij de energie om dit af te werken. Het is fantastisch om jullie te zien groeien en bloeien. Ik ben fier op mijn kroost!

Pomme, liefste, we zijn nu meer dan vijf jaar gelukkig samen en we hebben al een fantastische weg afgelegd. De laatste maanden zijn hectisch geweest, maar achter elke man staat een sterke vrouw... Gelukkig was jij er altijd om me op te vangen, te steunen, moed in te spreken en me door de zware momenten heel te loodsen. Dank je wel ook voor de hulp bij de lay-out van dit boekje en de fantastische grafische vormgeving! Dank je voor alles! Ik zie je graag!
CURRICULUM VITAE

PERSONALIA

Stijn Vervaeke
*26/01/1984 in Menen, Belgium

Private address: Wervikstraat 1
8940 Geluwe – Belgium

Working address: P8 De Pintelaan 185
9000 Ghent – Belgium

Email: stijn.vervaeke@ugent.be
stijn@vervaekeparodontologie.com

Mobile: +32 494367454

Married to Pomme Gouwy

Children Ralph (05/12/2011)
Léon (15/07/2013)

CURRENT POSITION

PhD-student University of Ghent. Promotores: Prof. Dr. Hugo De Bruyn & Prof. Dr. Bruno Collaert “Clinical outcome of dental implants: Predictors affecting implant survival and peri-implant bone loss”

Specialist in periodontics and oral implantology in Centrum voor Tandheelkunde Geluwe, Wervikstraat 1A, 8940 Geluwe

Specialist in periodontics and oral implantology in Centrum voor parodontologie en implantologie Brugge, Komvest 31, 8000 Brugge

EDUCATION

PRIMARY –SECONDARY SCHOOL

1990 – 1996 Vrije Basisschool Geluwe
1996 – 2002 Sint-Aloysiuscollege Menen with great honour

UNIVERSITY

2002 – 2005 Catholic University of Leuven
Candidate in dentistry, with great honour

2005 - 2007 Catholic University of Leuven
Master in dentistry, with honour

2007 – 2010 University of Ghent
**Master in Periodontology**, with greatest honour
Subject master thesis: “Implant survival and peri-implant bone loss around implants with a fluoride-modified surface: a retrospective analysis of 1106 implants placed in daily practice”

2007 – 2010 **Permanent education in Periodontology**, department of periodontology and oral implantology, University of Ghent

2008 – 2010 **Postgraduate course in Oral Implantology**, department of periodontology and oral implantology, University of Ghent

2009 **Postgraduate course in Statistics**, University of Ghent

**Professional experience**

2007 – 2010 Clinical training, department of periodontology and oral implantology, University of Ghent

2007 – 2008 Clinical training, periodontal clinic Dirk Verbist, Jan Van Rijswijklaan, Antwerpen

2008 – 2010 Clinical training, CPIL Dr. Bruno Collaert, Leuven

2010 – 2012 Specialist in periodontics and oral implantology, CPIL Dr bruno Collaert, Leuven

2010 - ........ Scientific co-worker, department of periodontology and oral implantology, University of Ghent

2010 - ........ Specialist in periodontics and oral implantology, Centrum voor tandheelkunde, Geluwe

2012 - ........ Specialist in periodontics and oral implantology, Centrum voor parodontologie en implantologie Dr. Filiep Raes, Brugge

**Scientific and Academic activities**

**Publications**


Poster Presentations

March 2010 Clinical analysis of 602 implants with a fluoride-modified surface after 2 years. Academy of Osseointegration. Orlando, Florida, USA


March 2013 Multifactorial analysis on factors affecting survival and peri-implant bone loss of implants with a fluoride-modified surface up to 5 years of function. Academy of Osseointegration. Tampa, Florida, USA

Oral Presentations
May 2012 Implant survival and marginal bone maintenance around Astra Tech Osseospeed implants. Astra Tech World Congres, Gothenburg, Sweden

June 2012 The influence of initial soft tissue thickness on peri-implant bone remodeling. Europerio, Vienna, Austria.