

# Impact of local and systemic factors on the incidence of oral implant failures, up to abutment connection

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#### Abstract

Aim: The aim of this retrospective study was to assess the influence of systemic and local bone and intra-oral factors on the occurrence of early implant failures, i.e. up to the abutment connection.

Material and Methods: The surgical records of 2004 consecutive patients from the total patient population who had been treated in the period 1982–2003 (with a total of 6946 Brånemark system<sup>®</sup> implants) at the Department of Periodontology of the Catholic University Leuven were evaluated. For each patient the medical history was carefully checked. Data collection and analysis mainly focused on endogenous factors such as hypertension, coagulation problems, osteoporosis, hypo-hyperthyroidy, chemotherapy, diabetes type I or II, Crohn's disease, some local factors [e.g. bone quality and quantity, implant (length, diameter, location), type of edentulism, Periotest<sup>®</sup> value at implant insertion, radiotherapy], smoking habits and breach of sterility during surgery.

**Results:** A global failure rate of 3.6% was recorded. Osteoporosis, Crohn's disease, smoking habits, implant (length, diameter and location) and vicinity with the natural dentition were all significantly associated with early implant failures (p < 0.05). **Conclusion:** The indication for the use of oral implants should sometimes be reconsidered when alternative prosthetic treatments are available in the presence of possibly interfering systemic or local factors.

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When a properly documented implant system with a long-term success rate has been selected, an implant-supported prosthesis is supposed to provide the patient a long-lasting rehabilitation (Lindquist et al. 1996). A failure of an implant can, on the other hand, compromise the achieved oral rehabilitation. Failures of the endosseous implants can be subdivided into early and late

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failures, depending on whether they occur before or at abutment connection (= early) or rather after occlusal loading took place by means of a prosthetic superstructure (= late). This subdivision is relevant as the failures in these two time periods are associated with different systemic and local factors. An early failure of an implant results from "an inability to establish an intimate boneto-implant contact" (Esposito et al. 1998, Quirynen et al. 2002). This means that bone healing after implant insertion is impaired or even jeopardized. Both systemic and local factors can interfere with these primarily cellular events. The

mechanisms that normally lead to wound healing by means of bone apposition do not take place, and rather a fibrous scar tissue is formed in between the implant surface and surrounding bone (Esposito et al. 1999). This can lead to epithelial downgrowth, a socalled saucerization or marsupialization of the implant, which results in mobility or even implant loss. Thus, the anchoring function of the endosseous implant cannot be assured. Late implant failures, on the other hand, are influenced by both the microbial environment and the prosthetic rehabilitation. These failures have been associated with both peri-implantitis resulting from plaque-induced gingivitis and peri-implantitis and/or occlusal overloading (van Steenberghe et al. 1990, Quirynen et al. 2002).

Systemic diseases may affect oral tissues by increasing their susceptibility to other diseases or by interfering with wound healing. Medications may also affect the outcome of implants. It remains a matter of debate as to which systemic factors compromise the achievement of an intimate bone-toimplant interface and/or its maintenance over time. It is especially during the healing time that systemic factors can be most easily identified as risk factors from many other (local) cofactors. After abutment surgery and especially after loading by prosthetic superstructures, many local factors also play a role (van Steenberghe et al. 2003). The influence of general health problems on the osseointegration process is poorly documented (van Steenberghe et al. 2002). Although many studies noted the role of systemic and local factors in the long-term maintenance of osseointegration, less is known concerning the factors affecting the initial bone apposition up to the abutment placement process (Kronström et al. 2000, 2001).

The aim of this large-scale retrospective study was to assess the influence of systemic and local bone and intra-oral factors on the occurrence of early implant failures up to abutment connection.

# Material and Methods Material

The surgical records of 2004 consecutive patients (1212 females, 792 males) treated by means of endosseous implants during the period 1982-2003 at the Department of Periodontology of the University Hospital of the Catholic University Leuven were evaluated. It is a general policy of the department to accept all patients who can benefit from implants for their oral rehabilitation even if systemic or local factors can compromise the outcome. These patients received a total of 6946 implants (all Brånemark system<sup>®</sup>, Nobel Biocare, Gothenburg, Sweden). These were inserted under strict aseptic conditions in the operating theatre of the department, according to the welldefined protocol described in the Surgical Manual for the Brånemark system®. For a total of 700 patients, patient's files were evaluated to check the reliability

of the surgical records. The surgical records are printed forms kept in the operation room, available for each patient provided with implants. They are divided into two parts; the first part – filled at implant surgery – concerns patient general health and habits – smoking, bone quality and quantity according to Lekholm & Zarb (1985) index, and information regarding the implant types used (location, type, length and diameter). The second part deals with the abutment surgery: abutment (type, length) and information regarding implant failure before or at this phase.

As a perfect coincidence with the patient files could be ascertained, checking in the patient files was abandoned afterwards and only the surgical files were further used.

Early failure – i.e. before and up to abutment connection - was related to the presence of health or behavioural factors, implant length and diameter, bone quality and quantity, implant location, type of edentulism, prescription of antibiotics pre- or immediately after surgery, dehiscence or perforation of the jaw bone during surgery, Periotest® (Siemens A G, Bensheim, Germany) value (PTV) and placement torque measurement (OsseoCare™; Nobel Biocare, Gothenburg, Sweden), at the crestal third, the middle third and the apical third at implant insertion. The PTV measures the stability of the implant-bone continuum by tapping with an elctro-magnetically driven rod on the implant. The outcome is expressed in arbitrary units, ranging from -8 to +50 (Tricio et al. 1995). Implants should lead to values below +5; the more negative the values, the better the stability. Placement torque measurement was recorded during implant insertion, by means of an electronic torque force measurement device, which is a part of a controlled motor device. The latter measures the torque force (Ncm) while tapping or inserting the implant at the crestal third, the middle third and the apical third of each implant insertion trajectory.

If the surgical records were not fully complete the patient's file was examined. For a total of 232 patients because of purely administrative reasons, the files could not be retrieved.

### Data collection and analysis

Only screw-shaped Brånemark system<sup>®</sup> implants (Nobel Biocare, Gothenburg, Sweden) were used either with a

machined (n = 6316) or a Ti-Unite<sup>®</sup> surface (n = 630). As a statistical comparison showed no difference (p-value > 0.05), all implants could be grouped.

A minimal bone height of 7 mm was required for implant placement. The general health and the behavioural history of the patient were recorded on the surgery form after thorough questioning of the patients pre-operatively. Furthermore, two other forms, one dealing with all the information regarding the implants used and bone quality and quantity, and the other one dealing with all the information regarding abutment surgery were available. If the implant failed before or at abutment surgery, the failure was recorded. An implant was considered a failure if a peri-implant radiolucency could be detected on the intra-oral radiographs, if an individual implants showed the slightest sign of mobility corresponding to a PTV of  $\geqslant 5$  and if the patient showed subjective signs of pain or infection that required implant removal.

Jaw bone quality and the degree of jaw bone resorption were evaluated by the periodontologist at implant placement. Tactile evaluation during drilling and assessment of the alveolar crest both radiographically and clinically allowed classification according to the Lekholm & Zarb (1985) index.

The following health or behavioural factors were particularly (i.e. by questioning the patient and/or checking his medical records from other departments in the hospital) assessed: smoking habits, hypertension, ischaemic cardiac problems, coagulation anomalies, gastric problems such as ulcers, osteoporohypohyperthyroidism, or hypercholesterolaemia, asthma, diabetes type I or II, Crohn's disease, rheumatoid arthritis, chemotherapy and intake of medication (antidepressants, steroids). Patients who smoked were allocated to one of the following three categories: (<10 cigarettes/day, 10-20 cigarettes/ day or >20 cigarettes/day). Local bone factors, such as radiotherapy of the area concerned, were also recorded. Finally, a special note was made for patients with claustrophobia. These patients were treated with reduced coverage of the face, often without a nose cape and as such with a breach of asepsis (van Steenberghe et al. 1997). As the complication often occurred during surgery, the removal of some drapes often led to unavoidable microbial contamination.

The type of edentulism was classified according to the presence of the remaining teeth and their location towards the implants in the oral cavity: full edentulism, teeth present only in the antagonistic jaw, teeth present in the same jaw and in the vicinity or not of the implants.

In the department, a thorough sterility policy allows limiting the systemic use of antibiotics to well-defined indications such as endocarditis prophylaxis, a remaining infection at the site of surgery, coughing or sneezing by the patient during surgery. The use of antibiotics pre- or immediately after implant surgery was defined as yes or no.

As the type of edentulism was not mentioned on the surgical forms, the analysis was limited to 676 patients (2448 implants) for whom the entire patient file was scrutinized. PTV and torque force measurements were only performed on a fraction of the patient material because of irregular availability of the devices. Systemic diseases and behavioural factors were available for all patients.

#### Statistical methods

Logistic regression models were used to evaluate the effect of explanatory variables on the early failure of the implant. The generalized estimating equation (GEE) method (Liang & Zeger 1986, Zeger & Liang 1986) was used to account for the fact that repeated observations (several implants) were available for a single patient.

Firstly, a univariate effect of each implant-related, behavioural and local bone factor on the early failure was evaluated by fitting the univariate GEE logistic regression model. Odds ratios and their 95% confidence intervals (CIs) based on the robust standard errors from the GEE logistic regression model were computed. The Wald test based on robust standard errors was used to assess the significance of each factor. For categorical factors with more than two levels, robust Wald's *p*-values adjusted for the multiple comparison using the method of Holm (1979) were computed.

Secondly, we evaluated a multivariable effect of the health factors when controlled for the behavioural, implant-related and local bone factors that were univariately (at 5%) significant. Namely, the following factors were controlled for: smoking habits, bone quality and quantity, implant's site (posterior/anterior), length and diameter. Although

univariately significant, type of edentulism and PTV at implant insertion were not controlled for as the data were available for only a limited subgroup of patients. For the purpose of multivariable analysis, the implants with missing data on bone quality and quantity were removed (1100 implants). Consequently, it was not possible to evaluate statistically the effect of chemotherapy on early implant failures due to the fact that no early failures have been observed in the chemotherapy subgroup of the rest of the 5759 implants. Owing to the fact that no failures have been observed in the group of patients having a given disease, the effect of diabetes type I and rheumatoid arthritis could not be assessed statistically.

Statistical analyses were performed using the R 2.4.0 software (R Development Core Team 2005) and the R package gee (Carey 2002).

# Results

From the treated patient's population, a total of 252 implants – of different lengths and diameters – out of the 6946 implants installed, appear to have failed 1–6 months after placement. This corresponds to an early failure rate of 3.6%.

These failures occurred in 178 patients. The distributions of the numbers of failed implants per patient are described in Fig. 1.

Early implant failures related significantly to the following implant characteristics: implant diameter length and location.

Early failure rates related significantly to smoking habits and increased with cigarette consumption.

Early implant failure related significantly to the type of edentulism.

No significant correlation was found between early failure and the torque measurements at placement, either in the crestal, middle or apical third.

The PTVs, when recorded at implant placement, were related to early implant failure. Significantly more early failures occurred with increasing PTV values, which are indicative of a lower rigidity.

There was no significant effect of the presence of bony dehiscences or fenestrations at the implant site.

Bone volume (bone quantity) and bone quality as assessed by the use of Lekholm & Zarb (1985) index affected early implant failure significantly. A summary of the Univariate GEE logistic regression for all the above-mentioned factors can be found in Table 1a and b.

When a multiple comparison was performed; significantly more failures were detected in implants with a wide platform (5 mm) when compared with implant with regular platform (3.75 and 4 mm), [p-value = 0.004, 0.02, Odds ratio (95% CI) = 2.70 (1.53–4.79), 2.73 (1.37–5.44), respectively]. Significantly more early failures were detected with short implants (<10 mm) when

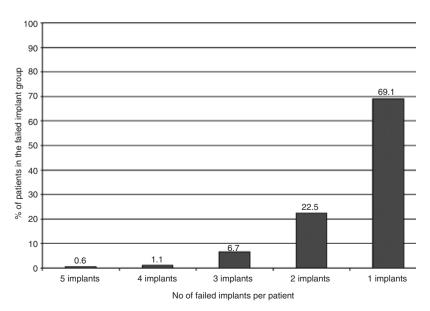


Fig. 1. Percentile distribution of failed implants per patient (178 patients provided with 252 implants experienced one/more failures).

*Table 1.* Univariate GEE logistic regression: implant-related, behavioural and local bone factors, the total number of patients in whom the factors were evaluated and the distribution of the failed and successful implants

factor (patient/implant)	success	failed	Odds	95% confidence
			ratio	interval
(a)		1 0.000*		
Diameter (2004/6936)	5700 (06 470)	<i>p</i> -value: 0.008*	1	
3.75	5709 (96.47%)	209 (3.53%)	1	(0.06, 4.40)
3.3 4	69 (94.52%)	4 (5.48%)	1.08 0.99	(0.26, 4.43)
5	776 (96.64%) 130 (91.55%)	27 (3.36%) 12 (8.45%)	2.70	(0.63, 1.55) (1.53, 4.79)
Length (2004/6946)	130 (91.33%)	<i>p</i> -value: 0.049*	2.70	(1.55, 4.79)
10–15	6086 (96.57%)	216 (3.43%)	1	
<10	427 (93.64%)	29 (6.36%)	1.71	(1.11, 2.64)
>15	181 (96.28%)	7 (3.72%)	1.21	(0.51, 2.89)
Location (2000/6931)	101 (70.20%)	p-value: 0.008*	1.21	(0.51, 2.07)
Mandible, anterior	1920 (97.66%)	46 (2.34%)	1	
Mandible, posterior	1277 (95.30%)	63 (4.70%)	1.99	(1.29, 3.07)
Maxilla, anterior	1953 (96.59%)	69 (3.41%)	1.48	(0.95, 2.18)
Maxilla, posterior	1529 (95.38%)	74 (4.62%)	1.88	(1.20, 2.94)
Smoking (2004/6946)	132) (33.30%)	p-value: $< 0.001*$	1.00	(1.20, 2.71)
0	5832 (96.72%)	198 (3.28%)	1	
<10	216 (95.15%)	11 (4.85%)	1.42	(0.48, 4.23)
10–20	303 (94.69%)	17 (5.31%)	1.87	(1.07, 3.26)
> 20	343 (92.95%)	26 (7.05%)	2.72	(1.63, 4.54)
Type edentulism (676/2448)	( , , , ,	p-value: $< 0.001*$		(, )
No teeth	697 (97.08%)	21 (2.92%)	1	
In the anterior jaw only	360 (97.83%)	8 (2.17%)	0.57	(0.17, 1.93)
In the same jaw	520 (94.55%)	30 (5.45%)	1.97	(0.94, 4.11)
Neighbouring implant	749 (92.24%)	63 (7.76%)	2.77	(1.45, 5.28)
(b)				
Crestal third Ncm (138/320)		<i>p</i> -value: 0.841		
Increase by 1	307 (95.94%)	13 (4.06%)	1.04	(0.70, 1.55)
Middle third Ncm (138/320)		<i>p</i> -value: 0.242		
Increase by 1	307 (95.94%)	13 (4.06%)	1.07	(0.96, 1.20)
Apical third Ncm (138/320)		<i>p</i> -value: 0.180		
Increase by 1	307 (95.94%)	13 (4.06%)	1.07	(0.97, 1.18)
PTV (71/189)		<i>p</i> -value: 0.05*		
Increase by 1	168 (88.89%)	21 (11.11%)	1.13	(1.000, 1.28)
Dehiscence (430/1380)		<i>p</i> -value: 0.362		
No	1238 (96.79%)	41 (3.21%)	1	
Yes	96 (95.05%)	5 (4.95%)	1.627	(0.571, 4.632)
Fenestration (418/1345)		<i>p</i> -value: 0.989		
No	1267 (96.79%)	42 (3.21%)	1	
Yes	35 (97.22%)	1 (2.78%)	0.986	(0.14, 6.86)
Bone quantity (1759/5800)		<i>p</i> -value: 0.002*		
A	998 (96.33%)	38 (3.67%)	1	
В	2362 (97.36%)	64 (2.64%)	0.66	(0.41, 1.05)
C	1700 (96.48%)	62 (3.52%)	0.88	(0.53, 1.46)
D	375 (95.42%)	18 (4.58%)	1.07	(0.51, 2.25)
E (1750/5702)	159 (86.89%)	24 (13.11%)	3.43	(1.49, 7.89)
Bone quality (1759/5782)	400 (04.06%)	<i>p</i> -value: < 0.001*	4	
1	480 (94.86%)	26 (5.14%)	1	(0.00, 0.77)
2	2390 (97.87%)	52 (2.13%)	0.42	(0.23, 0.77)
3	2074 (96.38%)	78 (3.62%)	0.70	(0.40, 1.22)
4 Sourface (2004/6046)	632 (92.67%)	50 (7.33%)	1.28	(0.67, 2.45)
Surface (2004/6946)	(000 (0( 200)	<i>p</i> -value: 0.999	1	
Machined	6088 (96.39%)	228 (3.61%)	1	(0.521 1.00)
Ti-Unite <sup>®</sup>	606 (96.19%)	24 (3.81%)	1.00	(0.531, 1.88)

<sup>\*</sup>Significant *p*-value < 0.05. PTV, Periotest<sup>®</sup> value.

compared with implants with a length raging from 10 to 15 mm [p-value = 0.04, Odds ratio (95% CI) = 1.710 (1.11–2.64)].

Significantly more early failures were detected in the mandibular and maxillary posterior regions when compared with the mandibular anterior region

[p-value = 0.01, 0.03, Odds ratio (95% CI) = 1.99 (1.29–3.07), 1.88 (1.196–2.940), respectively].

A significant difference was detected between the heavy smoking (>20 cigarettes/day) and no smoking groups [p-value <0.001, Odds ratio (95% CI): 2.72 (1.63–4.54)].

A significantly higher failure rate was noticed when the implants neighbouring a teeth were compared with implants in full edentulism, or to the presence of teeth in the antagonistic jaw only [*p*-values: 0.01, 0.03, Odds ratio (95% CI): 2.77 (1.45–5.279), 4.879 (1.59–15.11), respectively].

Significantly more failures were observed for implants placed in jaws with a quantity grade E (extreme) resorption when compared with grade A, B or C. [p-values: 0.03, <0.001, 0.009, Odds ratio (95% CI): 3.43 (1.49–7.89), 5.21(2.34–11.61), 3.90 (1.73–8.79), respectively].

Significantly more failures in bone quality grade 4 (soft bone with little cortical bone) were detected when compared with grade 2 [p-value <0.001, Odds ratio (95% CI): 3.05 (1.73–5.38), and more failures in grade 1 compared with grade 2 [p-value = 0.02, Odds ratio (95% CI): 0.42 (0.23–0.77)].

Systemic diseases and medical therapies were analysed when controlled for the other diseases and for factors significantly (at the 5% level) related to the early failure (smoking habits, bone quality and quantity, site, length and diameter).

Certain factors, such as cardiac and gastric diseases, controlled diabetes type II, coagulation problems, hypertension, hypo- or hyperthyroidism, hypercholestrolaemia, asthma, radiotherapy of the area concerned, claustrophobia and antidepressant and steroid medication, did not lead to an increased incidence of the early failures.

Crohn's disease and osteoporosis, in contrast, were significantly related to implant failures. Again, a significant correlation became evident between early failures and, implant diameter, implant location (anterior/posterior) and smoking habits (Table 2).

When a multiple comparison was performed; Significantly more failures were observed with wide platform implants when compared with regular implant diameters (4 mm) [p-value = 0.02, Odds ratio (95% CI): 3.02 (1.399–6.52)], and significantly more failures were detected in the posterior

Table 2. Multivariable GEE logistic regression: implant-related, behavioural and local bone factors and health factors

Multivariable GEE logistic regression  number of patients = 1757, number of implants = 5759						
Hypertension (yes)	0.97	(0.56, 1.67)	0.91			
Cardiac problem (yes)	0.42	(0.15, 1.22)	0.11			
Gastric problem (yes)	1.81	(0.55, 5.97)	0.33			
Osteoporosis (yes)	2.88	(1.51, 5.48)	0.001*			
Hypothyroid (yes)	1.00	(0.32, 3.16)	0.998			
Hyperthyroid (yes)	1.40	(0.07, 26.51)	0.82			
Radiotherapy (yes)	0.36	(0.028, 4.65)	0.43			
Crohn's disease (yes)	7.95	(3.47, 18.24)	< 0.001*			
Diabetes II (yes)	0.25	(0.05, 1.20)	0.08			
Coagulation (yes)	2.00	(0.93, 4.28)	0.08			
Claustrophobia (yes)	2.45	(0.64, 9.39)	0.19			
Antidepressant medication (yes)	1.28	(0.64, 2.58)	0.49			
Steroid medication (yes)	1.25	(0.32, 4.98)	0.75			
Hypercholesterol (yes)	1.02	(0.31, 3.35)	0.98			
Asthma (yes)	1.92	(0.37, 9.97)	0.44			
Smoking (<10)	1.76	(0.60, 5.16)	0.02*			
Smoking (10–20)	1.90	(1.007, 3.60)				
Smoking $(>20)$	2.18	(1.20, 3.97)				
Bone quality (2)	0.56	(0.29, 1.05)	0.15			
Bone quality (3)	0.82	(0.46, 1.47)				
Bone quality (4)	1.04	(0.53, 2.07)				
Bone quantity (B)	0.64	(0.40, 1.02)	0.10			
Bone quantity (C)	0.86	(0.51, 1.46)				
Bone quantity (D)	0.95	(0.4437, 2.06)				
Bone quantity (E)	2.00	(0.77, 5.21)				
Site (posterior)	1.81	(1.30, 2.53)	< 0.001*			
Length (<10 mm)	1.04	(0.61, 1.77)	0.99			
Length (>15 mm)	1.01	(0.41, 2.48)				
Diameter (3.3 mm)	1.18	(0.35, 4.04)	0.04*			
Diameter (4 mm)	0.75	(0.45, 1.24)				
Diameter (5 mm)	2.26	(1.20, 4.27)				

<sup>\*</sup>Significant p-value < 0.05.

regions when compared with the anterior regions of both jaws [p-value >0.001, Odds ratio (95% CI): 1.18 (1.298–2.53)].

#### **Discussion**

Early implant failures occur because, instead of an intimate bone-to-implant contact, a fibrous scar tissue is formed between the bone and the implant surface. A large variety of causes can be imagined that interfere with the normal bone wound healing. The tissue reactions following the insertion of an implant in the bone can be compared with fracture healing. The healing of the tissue starts with a blood clot that forms between the remaining bone and the implant surface. Depending on the environment and the relative immobility of the bone-to-implant interface, pluripotent mesenchymal cells will differentiate either into fibroblasts or osteoblasts, leading to the formation of, respectively, a scar tissue or bone (Sennerby 1991). Conditions of poor vascularity or low oxygen tension may direct the mesenchymal cells to a chondrogenic differentiation. The mechanical stress to which the tissues are subjected may also influence cellular differentiation. Distortional stresses may deform cells, altering their genetic expression and synthetic activity, which explains why micromovements of the implants during the healing phase can affect a correct bone-to-implant bond, instead forming fibrous scar tissue (Ivanoff et al. 1996, Szmukler-Moncler et al. 2000). The role of endogenous factors in cellular turnover and differentiation is less documented.

Renouard & Nisand (2006) reported in a review paper that there is a trend towards an increased failure rate with short and wide-diameter machined-surface implants. The increased failure rate of wide-diameter implants reported in some studies was mainly associated with a learning curve, poor bone density, implant design and site preparation and the fact that this implant was usually used as a "rescue" implant.

In the present study, significant effects of implant length and diameter were detected, more failures occurring with short and wide-diameter implants. These implants were systematically installed in compromised sites, marked by poor bone quality and quantity. Thus, these confounding factors may explain the higher failure rate.

The Ti-Unite<sup>®</sup> surface in the present study did not influence the outcome as no statistical difference or even a tendency concerning the failure rate could be found. In a previous paper from our centre, a reduced failure rate for Ti-Unite<sup>®</sup>-surfaced implants was reported (Alsaadi et al. 2006). This concerned, however, failed implant replacement instead of insertions in pristine sites.

Too high and low bone densities, as assessed clinically or radiologically, have also been pointed out as two possible reasons for non-integration (Engquist et al, 1988, Friberg et al. 1991, Jaffin & Berman 1991). In our present findings, it also appears that bone quality types 1 and 4 according to the Lekholm and Zarb classification are associated with slightly higher failure rates.

The effects of the inhaled tobacco smoke can be divided into two phases: a volatile and a particulate phase. The volatile phase, accounting for 95% of the cigarette smoke, provides nearly 500 different components, including nitrogen, carbon monoxide and carbon dioxide. The roughly 3500 different chemicals released in the particulate phase include nicotine, nornicotine, anatabine and anabasine (Hoffmann & Hoffmann 1997). Stripped of water, the particulate matter that remains, or "tar", contains the majority of the carcinogens of cigarette smoke.

Nicotine has been shown to increase platelet aggregation, decrease microvascular prostacyclin levels and inhibit the function of fibroblasts, erythrocytes and macrophages (Jorgensen et al. 1998, Zevin et al. 1998). Carbon monoxide binds to haemoglobin considerably more easily than oxygen, thus displacing oxygen from the molecule and lowering the oxygen tension in the tissues (Leow & Maibach 1998). Smoking

has been determined to adversely affect bone mineral density, lumbar disc health, the relative risk of sustaining wrist and hip fractures, low back pain and the dynamics of bone and wound healing (Porter & Hanley 2001).

Several studies revealed the negative effect of smoking on osseointegration, and its dose-related effect (for a review, see Bain 1996). This is in accordance with the present findings.

Some studies have shown that systemic antibiotic used before implant surgery can reduce the occurrence of infections after surgery and increase the success rates of integration (Dent et al. 1997, Laskin et al. 2000). Another study found no such effect (Gynther et al. 1998), which is in accordance with the present study. The trouble with this kind of studies is that the asepsis cannot be taken for granted. Many people perform surgery in this field without a proper surgical background. Often, sterility measures do not even involve covering of the nose, the most infected site in this area (van Steenberghe et al. 1997). In the present study, a series of 120 patient files (516 implants) were analysed for the use of antibiotics in the peri-operative period. There was no statistical effect on the failure rate (p = 0.8). The prescription of antibiotics when sterility is truly respected proves to be unnecessary and, considering the possible sideeffects, it should even be discouraged. Indeed, systematic prescription of antibiotics leads to unnecessary side-effects and costs (Lawler et al. 2005)

The impact of breach of sterility that was constantly compensated by antibiotics in the present study did not seem to affect the outcome but the few observations do not allow a final conclusion.

Crohn's disease can affect the entire gastro-intestinal system as it is a generalized autoimmune disease, and can thus even lead to periodontal lesions (van Steenberghe et al. 1976). Crohn's disease is characterized by the presence of many antibody-antigen complexes, leading to an autoimmune inflammatory process in several parts of the body. Symptoms are enteritis, vasculitis, recurrent oral ulceration, arthritis or keratoconjuctivitis. The same can occur at the interface with biocompatible implants, normally considered by the host as a part of the body. In Crohn's patients, they could be recognized as non-self, thus affecting the outcome of implant osseointegration (van Steenberghe et al. 2002). Moreover, the

malnutrition encountered in Crohn's patients can also cause a deficient bone healing around the implant (Esposito et al. 1998).

Osteoporosis has been defined as a decrease in bone mass and bone density and an increased risk and/or incidence of bone fracture. However, it has been noted that patients without fractures may have lost a significant amount of bone, while many patients with fractures display levels of bone mass similar to those of control subjects (Cummings 1985, Melton & Wahner 1989, Jacobs et al. 1996)

In addition, the relationship between skeletal and mandibular or maxillary bone mass is limited (von Wowern & Melsen 1979, von Wowern et al. 1988). The Word Health Organization has established diagnostic criteria for osteoporosis based on bone density measurements determined by dual energy X-ray absorptiometry: a diagnosis of osteoporosis is made if the bone mineral density level is 2.5 SDs below that of a mean young population (Glaser & Kaplan 1997).

There are two types of osteoporosis; Type I – or high turnover – which mostly occurs in women aged 50–75 due to a sudden decrease in oestrogen as a result of (early) menopause. This causes rapid calcium loss from the bones, making the woman susceptible to hip, wrist, forearm and spinal compression fractures.

Type II – or low turnover, age-related or senile osteoporosis. It occurs when bone loss and formation are not equal and more bone is broken down than replaced. It affects both men and women. It is associated with leg and spinal fractures in both genders.

The disease may have an influence on periodontal attachment loss (Wactawski-Wende et al. 1996). Although no studies prove an association between implant failure and the state of osteoporosis, it has been suggested as a risk factor for implant failure especially for postmenopausal women (Becker et al. 2000). In the present study, a significant association was detected between early implant failures and osteoporosis.

When using implants in treating partial edentulism, one of the most important questions that does concern the clinician is: is the influence of the periodontal and endodontic status of the neighbouring arch of importance?

A significant plaque accumulation and gingival inflammation at the time

of implant placement seems to increase the risk of failure as revealed in a multicentre study (van Steenberghe et al. 1990). Some of the early failures may be linked to an endodontic pathology, either remaining after tooth extraction or around neighbouring teeth (van Steenberghe et al. 1999). The higher incidence of these pathologies for failed implants and/or implants with retrograde peri-implantitis versus successful implants is obvious (with  $3 \times$  or even higher incidence). Ouirvnen et al. (2005) reported pathology of the extracted tooth (scar tissue-impacted tooth) or possible endodontic pathology from the neighbouring tooth. These findings were in accordance with other studies (for a review, see Quirynen & Teughels 2003, Quirynen et al. 2003). In the present study, a significant association was detected between early implant failures and vicinity to natural teeth.

The use of the Periotest<sup>®</sup> at insertion seems to be relevant as more early failures occur, with implants demonstrating higher PTV values at implant insertion. Achieving good primary stability seems to increase the chances of achieving a proper osseointegration. The use of this biomechanical assessment can thus be recommended.

# Conclusions

This vast number of consecutive patients allows identification of – because of the homogeneity of the treatment hardware and software – a number of systemic and local factors that may interfere with the osseointegration process, although a causal relationship cannot be ascertained. As it limits the observation to the stage before the prosthetic treatment, confounding factors are eliminated.

Some identified factors for failure could be expected, such as smoking, while others like Crohn disease, osteoporosis and vicinity to the natural dentition are less known.

The indication for the use of oral implants should sometimes be reconsidered when alternative prosthetic treatments are available and when possibly interfering systemic or local factors are identified.

# References

Alsaadi, G., Quirynen, M. & van Steenberghe, D. (2006) The importance of implant surface

- characteristics in the replacement of failed implants. *International Journal of Oral & Maxillofacial Implants* **2**, 270–274.
- Bain, C. A. (1996) Smoking and implant failure
  benefits of a smoking cessation protocol.
  International Journal of Oral & Maxillofacial Implants 11, 756–759.
- Becker, W., Hujoel, P. P., Becker, B. E. & Willingham, H. (2000) Osteoporosis and implant failure: an exploratory case-control study. *Journal of Periodontology* 4, 625–631.
- Carey, V. gee: Generalized Estimation Equation solver. R package version 4.13–10, ported to R by Thomas L. (version 3.13 and 4.4) and Brain R. (version 4.13).
- Cummings, S. R. (1985) Are patients with hip fractures more osteoporotic? Review of the evidence. *The American Journal of Medicine* 78, 487–494.
- Dent, C. D., Olson, J. W., Farish, S. E., Bellome, J., Casino, A. J., Morris, H. F. & Ochi, S. (1997) The influence of preoperative antibiotics on success of endosseous implants up to and including stage II surgery: a study of 2641 implants. *Journal of Oral and Maxillofacial Surgery* 55, 19–24.
- Engquist, B., Bergendal, T., Kallus, T. & Linden, U. (1988) A retrospective multicenter evaluation of osseointegrated implants supporting overdentures. *International Journal of Oral & Maxillofacial Implants* 3, 129–134.
- Esposito, M., Hirsch, J. M., Lekholm, U. & Thomsen, P. (1998) Biological factors contributing to failures of osseointegrated oral implants. (II). Etiopathogenesis. *European Journal of Oral Sciences* 3, 721–764.
- Esposito, M., Thomsen, P., Ericson, L. E. & Lekholm, U. (1999) Histopathologic observations on early oral implant failures. *Interna*tional Journal of Oral & Maxillofacial Implants 6, 798–810.
- Friberg, B., Jemt, T. & Lekholm, U. (1991) Early failures in 4641 consecutively placed Brånemark dental implants, a study from stage 1 surgery to the connection of completed prostheses. *International Journal of Oral & Maxillofacial Implants* 6, 142–146.
- Glaser, D. L. & Kaplan, F. S. (1997) Osteoporosis. Definition and clinical presentation. *Spine* 22, 12–16.
- Gynther, G. W., Kondell, P. A., Moberg, L. E. & Heimdahl, A. (1998) Dental implant installation without antibiotic prophylaxis. Oral Surgery, Oral Medicine, Oral Pathology, Oral Pathology, Oral Radiology and endodontics 85, 509–511.
- Hoffmann, D. & Hoffmann, I. (1997) The changing cigarette, 1950–1995. Journal of Toxicology and Environmental Health 50, 307–364.
- Holm, S. (1979) A simple sequentially rejective multiple test procedure. Scandinavian Journal of Statistics 6, 65–70.
- Ivanoff, C. J., Sennerby, L. & Lekholm, U. (1996) Influence of initial implant mobility on the integration of titanium implants. An experimental study in rabbits. Clinical Oral Implants Research 7, 120–127.
- Jacobs, R., Ghyselen, J., Koninckx, P. & van Steenberghe, D. (1996) Long-term bone mass

- evaluation of mandible and lumbar spine in a group of women receiving hormone replacement therapy. *European Journal of Oral Sciences* **104**, 10–16.
- Jaffin, R. A. & Berman, C. L. (1991) The excessive loss of Brånemark fixtures in type IV bone, a 5-year analysis. *Journal of Periodontology* 62, 2–4.
- Jorgensen, L. N., Kallehave, F., Christensen, E., Siana, J. E. & Gottrup, F. (1998) Less collagen production in smokers. Surgery 123, 450–455.
- Kronström, M., Svenson, B., Hellman, M. & Persson, G. R. (2001) Early implant failures in patients treated with Brånemark System titanium dental implants: a retrospective study. *International Journal of Oral & Max*illofacial Implants 16, 201–207.
- Kronström, M., Svensson, B., Erickson, E., Houston, L., Braham, P. & Persson, G. R. (2000) Humoral immunity host factors in subjects with failing or successful titanium dental implants. *Journal of Clinical Periodontology* 27, 875–882.
- Laskin, D. M., Dent, C. D., Morris, H. F., Ochi, S. & Olson, J. W. (2000) The influence of preoperative antibiotics on success of endosseous implants at 36 months. *Annals of Periodontology* 5, 166–174.
- Lawler, B., Sambrook, P. J. & Goss, A. N. (2005) Antibiotic prophylaxis for dentoalveolar surgery, is it indicated? *Australian Dental Journal* 50, 54–59.
- Lekholm, U. & Zarb, G. A. (1985) Patient selection and preparation. In: Brånemark, P.-I., Zarb, G. & Albrektsson, T. (eds). Tissue integrated prosthesis: Osseointegration in clinical dentistry, p. 199. Chicago: Ouintessence.
- Leow, Y. H. & Maibach, H. I. (1998) Cigarette smoking, cutaneous vasculature, and tissue oxygen. Clinics in Dermatology 16, 579–584.
- Liang, K. Y. & Zeger, S. L. (1986) Longitudinal data analysis using generalized linear models. *Biometrika* **73**, 13–22.
- Lindquist, L. W., Carlsson, G. E. & Jemt, T. (1996) A prospective 15-year follow-up study of mandibular fixed prostheses supported by osseointegrated implants. Clinical results and marginal bone loss. Clinical Oral Implant Research 7, 329–336.
- Melton, L. J. IIIrd & Wahner, H. W. (1989) Defining osteoporosis. Calcified Tissue International 45, 263–264.
- Porter, S. E. & Hanley, E. N. Jr. (2001) The musculoskeletal effects of smoking. The Journal of the American Academy of Orthopaedic Surgeons 9, 9–17.
- Quirynen, M., De Soete, M. & van Steenberghe, D. (2002) Infectious risks for oral implants: a review of the literature. *Clinical Oral Implants Research* 13, 1–19.
- Quirynen, M., Gijbels, F. & Jacobs, R. (2003) An infected jawbone site compromising successful osseointegration. *Periodontology* 2000 33, 129–144.
- Quirynen, M. & Teughels, W. (2003) Microbiologically compromised patients and impact on oral implants. *Periodontology* 2000 33, 119–128.

- Quirynen, M., Vogels, R., Alsaadi, G, Naert, I., Jacobs, R. & van Steenberghe, D. (2005) Predisposing conditions for retrograde periimplantitis, and treatment suggestions. Clinical Oral Implants Research 16, 599–608.
- R Development Core Team. (2005). R: A language and environment for statistical computing, ISBN 3-900,051-07-0, R Foundation for Statistical Computing, Vienna, Austria
- Renouard, F. & Nisand, D. (2006) Impact of implant length and diameter on survival rates. Clinical Oral Implants Research 2 (Suppl.), 35–51
- Sennerby, L. (1991) On the bone tissue response to titanium implants, Thesis, Gothenburg University, Gothenburg, Sweden.
- van Steenberghe, D., Jacobs, R., Desnyder, M., Maffei, G. & Quirynen, M. (2002) The relative impact of local and endogenous patient-related factors on implant failure up to the abutment stage. *Clinical Oral Implants Research* 13, 617–622.
- van Steenberghe, D., Lekholm, U., Bolender, C., Folmer, T., Henry, P., Herrmann, I., Higuchi, K., Laney, W., Linden, U. & Astrand, P. (1990) Applicability of osseointegrated oral implants in the rehabilitation of partial edentulism: a prospective multicenter study on 558 fixtures. *International Journal of Oral & Maxillofacial Implants* 53, 272–281.
- van Steenberghe, D., Quirynen, M., Molly, L. & Jacobs, R. (2003) Impact of systemic diseases and medication on osseointegration. *Perio-dontology* 2000 33, 163–171.
- van Steenberghe, D., Quirynen, M. & Naert, I. (1999) Survival and success rates with oral endosseous implants. In: Lang, N. P., Attstrom, R. & Lindhe, J. (eds). Proceedings of the 3de European Workshop on Periodontology. 242–254. Berlin: Quintessence.
- van Steenberghe, D., Vanherle, G. V., Fossion, E. & Roelens, J. (1976) Crohn's disease of the mouth, report of case. *Journal of Oral* Surgery 34, 635–638.
- van Steenberghe, D., Yoshida, K., Papaioannou, W., Bollen, C., Reybroeck, G. I. & Quirynen, M. (1997) Complete nose coverage to prevent airborne contamination via nostrils is unnecessary. Clinical Oral Implants Research 8, 512–516.
- Szmukler-Moncler, S., Piattelli, A., Favero, G. A. & Dubruille, J. H. (2000) Considerations preliminary to the application of early and immediate loading protocols in dental implantology. *Clinical Oral Implants Research* 11, 12–25.
- Tricio, J., Laohapand, P., van Steenberghe, D., Quirynen, M. & Naert, I. (1995) Mechanical state assessment of the implant–bone continuum, a better understanding of the Periotest method. *International Journal of Oral & Maxillofacial Implants* 101, 43–49.
- Wactawski-Wende, J., Grossi, S. G., Trevisan, M., Genco, R. J., Tezal, M., Dunford, R. G., Ho, A. W., Hausmann, E. & Hreshchyshyn, M. M. (1996) The role of osteopenia in oral bone loss and periodontal disease. *Journal of Periodontology* 67, 1076–1084.

von Wowern, N. & Melsen, F. (1979) Comparative bone morphometric analysis of mandibles and iliac crests. *Scandinavian Journal of Dental Research* **87**, 351–357.

von Wowern, N., Storm, T. L. & Olgaard, K. (1988) Bone mineral content by photon absorptiometry of the mandible compared with that of the forearm and the lumbar spine. Calcified Tissue International 42, 157–161.

Zeger, S. L. & Liang, K. Y. (1986) Longitudinal data analysis for discrete and continuous outcomes. *Biometrics* **42**, 121–130.

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#### **Clinical Relevance**

Scientific rational for the study: Some identified factors for implant failure could be expected, such as smoking while others like Crohn, osteoporosis and vicinity to the natural dentition are less known. Principal findings: The vast number of consecutive patients allows identification of a number of systemic and local factors that interfere with the osseointegration process. As it limits the observation to the stage before the prosthetic treatment, confounding factors are eliminated.

Practical implications: The indication for the use of oral implants should sometimes be reconsidered when alternative prosthetic treatments are available and when possibly interfering systemic or local factors are identified.