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# Failed dental implants and their bone loss

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# Contents

# 1 Introduction

## 1.1 Motivation

With an increasing number of placed dental implants, the prevalence of implant failure rises. Despite high rates of implant survival, peri-implantitis is considered a major and growing problem in dentistry (Derks et al., 2016a). Even though peri-implantitis was defined by the European Workshops on Periodontology (Albrektsson, Isidor, Lang, & Karring, 1994; Lang, Berglundh, & Periodontology, 2011; Sanz, Chapple, & on behalf of Working Group 4 of the VIII European Workshop on Periodontology, 2012) and the World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions in 2017 (Berglundh et al., 2018), the clinical and diagnostic criteria have remained open to interpretation for a long time. Thus, this unsettled question continues to have an impact on treatment protocols.

The definition of implant failure becomes increasingly important. In particular, at which bone level should implants be removed or tried to be retained? Removing a treatable implant may cause new prosthetics, additional surgery, and implantation in a challenging bone environment. Trying to keep a failing implant may lead to additional operations that do not remove the infection and jeopardize available bone for future implantation. This calls for a scientific discussion.

There are few proposals at which bone level an implant should be removed (Lekholm et al., 1994; Misch et al., 2008). These seem to be arbitrary and explantation is still eminence and not evidence based, making it difficult for the clinician to decide whether an implant with peri-implantitis can be treated or should be removed. No study was found reporting on the actual bone level of explanted implants, hence this dissertation investigates implants explanted due to peri-implantitis by specialists for implantology.

## 1.2 Epidemiology

Two decades ago, it was estimated that more than 120,000 implants were placed annually in France, 185,000 in Spain, 400,000 in the United States, 410,000 in Italy, and 420,000 in Germany (Nogueira-Filho, Iacopino, & Tenenbaum, 2011; Tenenbaum, Glogauer, Lanzberg, & Goldberg, 2008). These numbers increased to about 700,000 implants in France, 1,100,000 in Spain, 3,000,000 in the United States, 1,300,000 in Italy, and 1,200,000 in Germany in 2019 with healthy growth rates (iData Research Inc, 2021). Implants show survival rates of about 95% after ten years (Buser, Sennerby, & Albrektsson, 2012; Moraschini, Poubel, Ferreira, & Barboza, 2015) and about 90% after 20 years (Lekholm, Gröndahl, & Jemt, 2006). For single tooth replacements, survival rates of 91.5% over 16 to 22 years (Dierens, Vandeweghe, Kisch, Nilner, & De Bruyn, 2012), and 96.8% over 17 to 19 years (Bergenblock, Andersson, Fürst, &

Jemt, 2012) have been reported. In edentulous jaws, implant survival rates of 92.8% and treated arch survival rates of 83.8% over 25 to 30 years have been reported using Kaplan-Meier estimations (Jemt, 2018). Success rates are dependent on success criteria and were described at about 75% over 20 years with survival rates of 89.5% (Chappuis et al., 2013). These promising numbers accelerate the trend toward replacing compromised teeth rather than saving them.

## 1.3 Osseointegration

The concept of osseointegration is defined as “direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant” (Albrektsson, Brånemark, Hansson, & Lindström, 1981). The histologic appearance resembles a functional ankylosis and is based on the absence of an intervening fibrous tissue (Brånemark et al., 1977). A critical aspect of osseointegration is maintaining a clinically asymptomatic functional loading (Zarb & Albrektsson, 1991). This definition was recently extended by Albrektsson and colleagues describing Osseointegration as “a foreign body reaction where interfacial bone is formed as a defense reaction to shield off the implant from the tissues” (Albrektsson, Chrcanovic, Jacobsson, & Wennerberg, 2017). The classical overall healing period lasts six months for implants inserted into the maxilla and three months for mandible implants (Brånemark et al., 1977). Esposito and colleagues described the healing period as three to nine months (Esposito, Hirsch, Lekholm, & Thomsen, 1998a). However, osseointegration is dependent on the individual jaw bone and can be delayed to 12 months for example by bisphosphonate- and radiotherapy (Brånemark et al., 1977; Granström, 2005; Wang, Weber, & McCauley, 2007), and it can be accelerated by surface roughness and hydrophilicity (Smeets et al., 2016).

## 1.4 Rating of implants

The rating of success, survival and failure determines the fate of the implant and is therefore indispensable for the clinician to decide on the treatment.

### 1.4.1 Success

Implant success describes optimum conditions. Success criteria for implant systems are defined by Albrektsson and colleagues in 1986 (Albrektsson, Zarb, Worthington, & Eriksson, 1986). Although these criteria were not the first (Schnitman & Shulman, 1979), they have been proven practical and are still widely accepted. The criteria include:

1. no mobility of the individual implant,
2. no peri-implant radiolucency,
3. no more than 0.2 mm of bone loss following the first year in function,

4. no neurological symptoms such as pain or sensitivity, and
5. implant survival of >85% after a five-year period and >80% after a ten-year period.

Noteworthy, probing depth and gingival changes were deliberately omitted (Albrektsson et al., 1986). Smith and Zarb (Smith & Zarb, 1989) revised the criteria and added

6. implant design that allows an aesthetic restoration.

It was concluded that iatrogenic complications should be considered separately, and that these criteria should only apply to implants in function. Iatrogenic complications include among others patient discomfort due to nerve damage, damage to adjacent teeth, violation of the maxillary sinus, mandibular canal, or floor of the nasal cavity (Smith & Zarb, 1989), as well as cement-associated infection (Wilson Jr., 2009), and malpositioning (Solderer et al., 2019). Bone loss due to remodelling was reported to amount to 1.5 mm in the first year of function and <0.2 mm in the following years (Adell, Lekholm, Rockler, & Brånemark, 1981). A consensus report from the 3rd European Workshop on Periodontology simplified acceptable bone loss to a maximum of 2 mm over a 5-year period after loading (Wennström & Palmer, 1999). Success criteria have lately included the whole implant/prosthodontic complex and focus more on aesthetics and patient satisfaction (Papaspyridakos, Chen, Singh, Weber, & Gallucci, 2012). Absence of success criteria does not necessarily signify disease (Albrektsson & Zarb, 2018; Jemt, Sundén Pikner, & Gröndahl, 2015).

### 1.4.2 Survival

Implants that do not fulfil the criteria for either success or failure should be considered as surviving (Albrektsson et al., 1994; Albrektsson & Zarb, 1993). Surviving implants can be further categorized as satisfactory and compromised depending on the indication of treatment. Compared to satisfactory implants, compromised implants may have sensitivity, peri-implantitis with radiographic bone loss >4 mm but less than 50% of the implant length, probing depth of >7 mm and history of suppuration (Misch et al., 2008). Implants in the compromised group have a worse prognosis than those in the satisfactory group but may still be treatable.

### 1.4.3 Failure

Implant failure describes the loss of an implant or a condition that indicates the removal of the implant. Criteria for failure include:

1. mobility,
2. pain,
3. bone loss ≥50% of the implant length,
4. uncontrolled progressive bone loss,
5. uncontrolled exudate,
6. implants unable to be restored (sleepers) or
7. implant loss (Misch et al., 2008).

A maximum of 2/3 of bone loss was proposed (Lekholm et al., 1994) and some authors suggested ≥75% of bone loss or less than 3 mm of remaining bone contact (Misch et al., 2008; Solderer et al., 2019). The Pisa Consensus Conference in 2007 lastly set more than 50% bone loss as criterion for failure (Misch et al., 2008), which encompasses the definition of advanced peri-implantitis by Froum and colleagues (Froum & Rosen, 2012). Any mobility is the cardinal sign of implant failure (Esposito et al., 1998a). It describes observable movement of the implant under 5 N forces in any direction (Misch et al., 2008). As long as one aspect of the implant remains osseointegrated, there should be no sign of mobility (Mombelli & Lang, 1998). Since the severity of pain is subjective, sensitive implants may be treated, while pain places the implant in the failure category (Misch et al., 2008). Nerve disturbance occurs in 1-2% in most of the few studies that report on respective cases (Berglundh, Persson, & Klinge, 2002). Probing reveals bleeding, suppuration, and pocket depth, which on its own is not a sign for failure (Misch et al., 2008).

#### 1.4.3.1 Early failure

Early failure refers to the failure of an implant in the healing and osseointegration phase. It is most commonly reported as failure prior to loading (Esposito et al., 1998a; Manzano et al., 2016). Other authors define early failure as failure within 12 months post-surgery (Albrektsson, 1988). More recently, this definition has also been used by Jemt and colleagues (Jemt, 2018). It encompasses the maximum period of osseointegration and should generally be used to describe early implant failure for consistent statistical comparison. The differentiation between early and late implant failure is important because of the different underlying aetiologies. Early implant failure must not be confused with peri-implantitis. There are three major aetiologies including infection/site contamination, early overloading, and excessive surgical trauma, such as overheating of the bone, together with impaired healing ability (Esposito, Thomsen, Ericson, & Lekholm, 1999; Solderer et al., 2019). Immediately after surgery osseous wound healing may be impaired and a fibrous capsule may form around the implant, accompanied by scar tissue and/or epithelial downgrowth that may lead to mobility (Esposito et al., 1999). At one-stage, non-submerged implant placement, plaque can directly attach to the implant early on. At the two-stage, submerged approach, the same can occur after perforation of the flap. Complications include swelling, fistulas, suppuration, dehiscences and osteomyelitis. These complications worsen the prognosis of the implant in early stages far more than if the same complication occurs later. Still, they are treatable and most of these implants survive. Signs of infection should only be used together with mobility or peri-implant radiolucency (”marsupialisation” or “saucerization”) to determine early failure (Esposito et al., 1998a; Esposito et al., 1999).

#### 1.4.3.2 Late failure

Late failure refers to failure of the functionalized implant after completed osseointegration and healing of hard and soft tissues (Esposito et al., 1998a). Late failures occur mainly due to peri-implantitis (Esposito et al., 1998a; Kourtis, Sotiriadou, Voliotis, & Challas, 2004; Solderer et al., 2019; Stajcic et al., 2016). After peri-implantitis, implant fracture may be the second most prevalent reason for late implant failure with a prevalence of around 0.5% after 9 years (Lee, Kim, Jeong, Kim, & Lee, 2018). Interestingly, older patients showed a significant correlation with implant fracture, and peri-implant bone loss and manufacturing-induced defects may likely be the major risk factors (Lee et al., 2018).

## 1.5 Overload

Occlusal overload has been described to lead to bone loss independently from bacterial influence. Once there is a deep pocket, the decrease in oxygen tension creates a niche for anaerobic bacteria, which may become the primary promoters for continued bone loss (Misch et al., 2008). In turn, progressed bone loss makes the implant more prone to occlusal trauma. This interplay between primary and secondary cause of disease can worsen the prognosis of the implant. Controversially, a recent literature review reported that occlusal overload does not lead to peri-implant bone loss and may even stimulate peri-implant bone formation (Duyck & Vandamme, 2017). Another systematic literature review found that in the presence of plaque, occlusal overload can stimulate bone loss (Chambrone, Chambrone, & Lima, 2010). Only when the forces exceed a certain limit, total loss of osseointegration can be observed (Chang, Chronopoulos, & Mattheos, 2013). Parafunctions, that certainly can create overloaded conditions, have been reported to be associated with implant failure (Sadowsky, 2019).

## 1.6 Peri-implantitis

### 1.6.1 Definition

Peri-implant mucositis is a reversible preliminary stage of peri-implantitis with inflammation only in supracrestal soft tissue (Albrektsson et al., 1994; Heitz-Mayfield & Salvi, 2018; Lindhe & Meyle, 2008). Peri-implantitis describes an inflammation of soft tissue around the functioning implant with progressive loss of supporting crestal bone beyond physiological bone remodeling (Sanz et al., 2012). The World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions in 2017 added that peri-implantitis is a plaque-associated pathologic condition around dental implants (Berglundh et al., 2018). Peri-implantitis is the main reason for late implant failure (Kourtis et al., 2004; Solderer et al., 2019). Currently, there is no single definition for clinical criteria of peri-implantitis universally accepted.

### 1.6.2 Diagnosis, case definition

Probing is the most reliable tool to diagnose inflammation (Lindhe & Meyle, 2008). Bleeding on probing is a sign for inflammation, which is in turn an indicator for an active disease.

In order to determine progressive bone loss, pocket probing depths compared to probing depth values collected at loading, and follow-up radiographs are compared to base-line radiographs (Renvert, Persson, Pirih, & Camargo, 2018). In the absence of radiographic records, a threshold vertical distance of ≥2 mm from the expected marginal bone level together with peri-implant inflammation was suggested by the 8th European Workshop on Periodontology (Sanz et al., 2012), which was changed by the World Workshop in 2017 to ≥3 mm apical of the most coronal portion of the intraosseous part of the implant, combined with probing depths ≥6 mm (Berglundh et al., 2018). Probing depth on its own without base-line values is insufficient for the diagnosis of peri-implantitis (Berglundh et al., 2018).

### 1.6.3 Aetiology

There is a debate about the initiating process for bone loss of which little is known about (Klinge, 2012). Some authors think of peri-implantitis primarily as a foreign body reaction and dispute the thesis that microbiota are the primary cause of the bone loss (Albrektsson, Canullo, Cochran, & De Bruyn, 2016). The “combined factor theory” on patient-, surgical-, implant-, and prosthetic-related level was developed (Albrektsson & Zarb, 2018; Ramanauskaite & Juodzbalys, 2016; Thilander, 2008). The majority of the profession follows the theory and definition by the 7th European Workshop on Periodontology (Lang et al., 2011) that peri-implantitis is an infectious disease, meaning that microorganisms are the primary cause (Heitz-Mayfield, 2008; Lindhe & Meyle, 2008; Mombelli & Lang, 1998; Quirynen, De Soete, & Van Steenberghe, 2002) and the World Workshop in 2017 agreed on the term “plaque-associated” (Berglundh et al., 2018). As in periodontitis, of course there would be risk factors for developing and amplifying the progress of the disease. It is consistent that the same bacterial strains may cause a similar disease around implants as around teeth, and the simplest explanation is usually adopted until proven otherwise (Occam’s razor) (Domingos, 1999).

Compared to periodontitis, the peri-implantitis infiltrate is not insulated by a pocket epithelium, nor by a 1 mm not inflamed soft tissue capsule and can reach the alveolar bone and possibly bone marrow. Fibrous tissue grows parallel to the implant surface instead of perpendicular to the tooth (Carcuac et al., 2013; Lindhe, Berglundh, Ericsson, Liljenberg, & Marinello, 1992; Schou et al., 2002). This is reflected by an increase in probe penetration with an increasing degree of inflammation (Etter, Håkanson, Lang, Trejo, & Caffesse, 2002; Schou et al., 2002), larger lesions (Lang et al., 2011) and faster bone loss (Cecchinato, Marino, & Lindhe, 2017). A more innate than adaptive immune response indicates a more acute form of disease (Carcuac & Berglundh, 2014).

Microbial communities can form a highly organised biofilm with increased metabolic efficiency, greater resistance to antimicrobial rinses and the immune system, and can pathogenically synergise enhancing the virulence (Marsh, 2005). Noticeably, it is not the bacteria that destroy the bone but most of the bone is resorbed by the body's own osteoclasts – probably as a defence mechanism of the immune system to retreat from the pathogens and repel the infected implant as described above (Albrektsson et al., 2019). The immune response is a two-edged sword (Schneider & Ayres, 2008). Of course, it is a complex interplay and bacteria can also actively trigger excessive immune reactions that injure the host. The peri-implant niche is distinct from any other and has its own ecosystem and microbial community (Belibasakis & Manoil, 2020). A systematic review identified *Porphyromonas gingivalis*, *Prevotella intermedia* and *Prevotella nigrescens* as the most common microorganisms in peri-implantitis. In comparison with periodontitis, peri-implantitis is a heterogenous infection of more complexity with predominantly non-cultivable gram-negative species (Lafaurie et al., 2017).

### 1.6.4 Apical inflammation

Apical inflammation (or retrograde peri-implantitis) has a different microflora than marginal peri-implantitis as it resembles the composition of endodontic pathogens (Ramanauskaite, Juodzbalys, & Tözüm, 2016). It results from the aetiology that describes in most cases an association with apically inflamed adjacent teeth or a residual infection of the alveolar socket pre-implantation (Ramanauskaite, Juodzbalys, et al., 2016). Other causes can be infection of bone substitutes, apical fenestration or overheating of the bone.

### 1.6.5 Treatment

The disease usually has a chronic course and leads to implant loss if left untreated. There has been no standard treatment procedure that offers effective, predictable results (Lindhe & Meyle, 2008; Madi, Htet, Zakaria, Alagl, & Kasugai, 2018; Renvert, Polyzois, & Maguire, 2009). All treatments aim for anti-infective measures and attempt to prevent the progression of the disease. Re-osseointegration, describing the formation of new bone onto previously biofilm contaminated implant surface, can be achieved (Koo et al., 2019; Renvert et al., 2009; A.-M. Roos-Jansåker, Renvert, & Egelberg, 2003). The treatment options vary from local mechanical therapy, use of antiseptics and local or systemic antibiotics, over resective surgery including debridement and decontamination with or without bone augmentation, to removal of the affected implant (Ramanauskaite, Daugela, Faria de Almeida, & Saulacic, 2016). In one study, implants with bone loss of more than 50%, suggested as failure by the Pisa Consensus Conference in 2007 (Misch et al., 2008), were treated with autogenous bone blocks and surface decontamination and showed promising results (Khoury & Buchmann, 2001). There is no final consensus on how to treat a compromised implant or if the unpredictable prognosis may indicate removal and new insertion.

## 1.7 Bone loss

The annual marginal bone loss (MBL) of periodontitis affected teeth is about 0.05 mm in the subjects with moderate progression, and about 0.1 mm up to 1.0 mm in subjects with severe progression (Löe, Anerud, Boysen, & Morrison, 1986; Norderyd, Hugoson, & Grusovin, 1999). Severe progression was recently classified as ≥2 mm over 5 years (Papapanou et al., 2018). Although peri-implantitis is a more aggressive disease than periodontitis (Carcuac & Berglundh, 2014), a suggested annual MBL of 0.2 mm as success criterion (Albrektsson et al., 1986) may be questionable since this value is as high as annual MBL of moderate to severe periodontitis (Fransson et al., 2010). Fixed values such as the suggested MBL <2 mm compared to bone level at surgery by the Pisa Consensus Conference in 2007 (Misch et al., 2008) or from the expected marginal bone level in absence of peri-implant inflammation suggested by the 8th European Workshop on Periodontology (Sanz et al., 2012) that correspond to remodeling and peri-implant health (Berglundh et al., 2018) as success criterion may be more appropriate. These resemble the radiographic criterion for periodontitis by the 5th European Workshop on Periodontology (Tonetti & Claffey, 2005) or periodontitis stage II by the World Workshop in 2017 (Papapanou et al., 2018). Peri-implant MBL without clinical signs of inflammation is considered a rare event (Schwarz, Derks, Monje, & Wang, 2018). With progressing peri-implant MBL, the microbial burden increases (Monje, Eick, Buser, & Salvi, 2020), hence the rate of bone loss increases over time in a non-linear pattern (Fransson et al., 2010). Accelerating bone loss was supported by another study and may represent the most frequent case (Derks et al., 2016b). The rate at which the bone is lost in patients with moderate to severe peri-implantitis was about 0.4 mm annually and can reach 1.5 mm annually (Derks et al., 2016b; Fransson et al., 2010). A literature review described four hypothetical patterns of peri-implant MBL after the first year:

1. linear low-rate MBL (Albrektsson's pattern),
2. low-rate MBL followed by rapid loss of bone as described above,
3. high-rate MBL stabilizing to almost no bone loss,
4. continuous high-rate MBL until complete loss of osseointegration (Schwartz-Arad, Herzberg, & Levin, 2005).

Type 3 is described by Chrcanovic and colleagues who found that implants can remain stable at low bone level and MBL can be insignificant in long-term observations (Chrcanovic, Kisch, Albrektsson, & Wennerberg, 2018). A steady state after substantial bone loss can be achieved. This complicates the question of how to identify a failed implant. MBL should be measured at the deepest margin on 2D radiographs and should not include the polished neck portion (Ramanauskaite & Juodzbalys, 2016; Schwartz-Arad et al., 2005).

## 1.8 Bone defect

Schwarz and colleagues categorized peri-implantitis defects into vertical and horizontal bone loss (Schwarz et al., 2007). Defects were assessed in humans and dogs by open flap surgery and presented a distribution of predominantly 4-wall circumferential defects combined with horizontal bone loss, which supports observations by Mombelli and Lang (Mombelli & Lang, 1998). Monje and colleagues hypothesized that the implant type (bone level versus soft tissue level) may influence the defect morphology (Monje, Pons, et al., 2019). Morphologic patterns for peri-implantitis defects were not shown. Bone loss only vestibular without inflammation may occur due to thin buccal plates and physiological bone resorption. Peri-implantitis most likely affects more than one implant site (Froum & Rosen, 2012). Whether the buccal implant site is more prone to peri-implantitis caused bone loss is controversial and probably dependent on correct positioning and oral hygiene techniques (García-García, Mir-Mari, Benic, Figueiredo, & Valmaseda-Castellón, 2016; Monje, Chappuis, et al., 2019; Monje et al., 2018; Monje, Pons, et al., 2019; Ramanauskaite & Juodzbalys, 2016; Serino, Turri, & Lang, 2013).

## 1.9 Radiography

The radiographic image is the most important source of information to evaluate bone around dental implants (Esposito et al., 1998a; Fransson et al., 2010). Intraoral radiographs have superior resolution compared to panoramic (Bundesministerium für Umwelt Naturschutz und nukleare Sicherheit, 2009a, 2009b; Kühl et al., 2016), fewer artifacts, can be modified for different angulations, and are therefore to be preferred (Frederiksen, 1995; Vandenberghe, Jacobs, & Bosmans, 2010). Marginal bone level and implant prognosis may be worse than radiographically presented (García-García et al., 2016). All two-dimensional radiographs only show the mesial and distal side of the implant, vestibulo-oral defects are superimposed by the implant and hidden in the third dimension. Therefore, the morphology of the bone defect and the classification into one-, two-, three- and four-walled defects cannot be assessed by two-dimensional radiographic analysis only. Still, intraoral radiographs are considered sufficient to evaluate peri-implant bone level (Misch et al., 2008; Ramanauskaite & Juodzbalys, 2016).

Alongside quality of the radiograph, the skill of the observer influences the diagnostic accuracy (Sundén, Gröndahl, & Gröndahl, 1995). Valid bone loss measurements below 0.2 mm are extremely difficult to achieve and the random measurement error in radiographs is around 0.2 mm (Benn, 1992; Esposito et al., 1998a; Hollender & Rockler, 1980; Larheim, Wie, Tveito, & Eggen, 1979). In general, an average measurement error of 0.5 mm can be expected (Berglundh et al., 2018). In clinical cases serially identical radiographs are rarely achieved, therefore stereoscopic intraoral radiographs are to be preferred (Sewerin, 1990). Mobility can be present without a radiolucency or radiographically observable bone changes (Grondahl &

Lekholm, 1997), and successful implants can show a radiolucency (Esposito et al., 1998a), which may be due to the Mach Band effect (Ratliff, 1965). Radiographic analysis shows a positive predictive value for implant failure of 83% (Grondahl & Lekholm, 1997). A more recent study reported the sensitivity of intraoral radiographs at 87% and 75% for supracrestal and intrabony defects respectively (García-García et al., 2016). It was concluded that the evaluation of intraoral radiographs is appropriate to diagnose progressed but not initial bone loss.

## 1.10 Risk factors

### 1.10.1 Early implant failure

Iatrogenic factors are the most prevalent in early implant failure (Baqain, Moqbel, & Sawair, 2012; Esposito, Hirsch, Lekholm, & Thomsen, 1998b; Jemt, 2017a; Kourtis et al., 2004). Poor bone quality and quantity leads to demanding anatomical situations and is also considered one of the most important factors for early implant failure (Esposito et al., 1998a; Jemt, 2017a). Further, systemic factors can interfere with osseointegration (Alsaadi, Quirynen, Komárek, & Van Steenberghe, 2007; Chen, Liu, Xu, Qu, & Lu, 2013). Especially smoking is often reported as a major risk factor (Chen et al., 2013; Derks et al., 2015; Manzano et al., 2016; Palma-Carrió, Maestre-Ferrín, Peñarrocha-Oltra, Peñarrocha-Diago, & Peñarrocha-Diago, 2011; Sakka, Baroudi, & Nassani, 2012). Another risk factor for early implant failure is poorly controlled diabetes (Naujokat, Kunzendorf, & Wiltfang, 2016). Data on Crohn's disease are occasionally collected and reported to have a strong adverse impact (Alsaadi et al., 2007; Van Steenberghe, Jacobs, Desnyder, Maffei, & Quirynen, 2002). Radiotherapy of the concerned area is most likely an influencing factor, but the data is not clear (Alsaadi et al., 2007; Chen et al., 2013; Lange, Laaß, & Retemeyer, 1993). In addition, certain implant brands, and initial diagnosis of periodontitis may have an adverse influence on early implant failure (Derks et al., 2015).

### 1.10.2 Late implant failure and peri-implantitis

In comparison with early implant failure, patients with late implant failure may be of male gender, older, with more medical problems, and a higher number of failed implants per patient (Manor, Oubaid, Mardinger, Chaushu, & Nissan, 2009). Peri-implantitis seems to be at the core of late implant failure (Kourtis et al., 2004; Solderer et al., 2019). A consensus statement identified the most important risk factors for peri-implantitis as poor oral hygiene, a history of periodontitis, diabetes mellitus and current smoking (Lindhe & Meyle, 2008). These have been supported by a recent systematic review (Turri, Orlato Rossetti, Canullo, Grusovin, & Dahlin, 2016). Multiple risk factors stack, and peri-implantitis and late implant failure occur frequently in a small subset of individuals (Esposito et al., 1998b; A. M. Roos-Jansåker, Lindahl, Renvert,

& Renvert, 2006; Solderer et al., 2019; Weyant & Burt, 1993). This so-called cluster effect occurs because most risk factors affect all implants in one patient.

## 1.11 Aim of the dissertation

Only few studies report on the radiographic type of bone loss around dental implants, and it is often not clear at which level of bone loss the implants are removed. There was no publication found, which reported on the bone level or radiographic type of bone loss at explantation. In this dissertation the following questions shall be answered:

i) what is the distribution of radiographic types of bone loss at explantation,

ii) is there a universally accepted bone level beyond which implants are not preserved, and

iii) which factors influence bone loss, the type of bone loss, and survival time in failed dental implants?

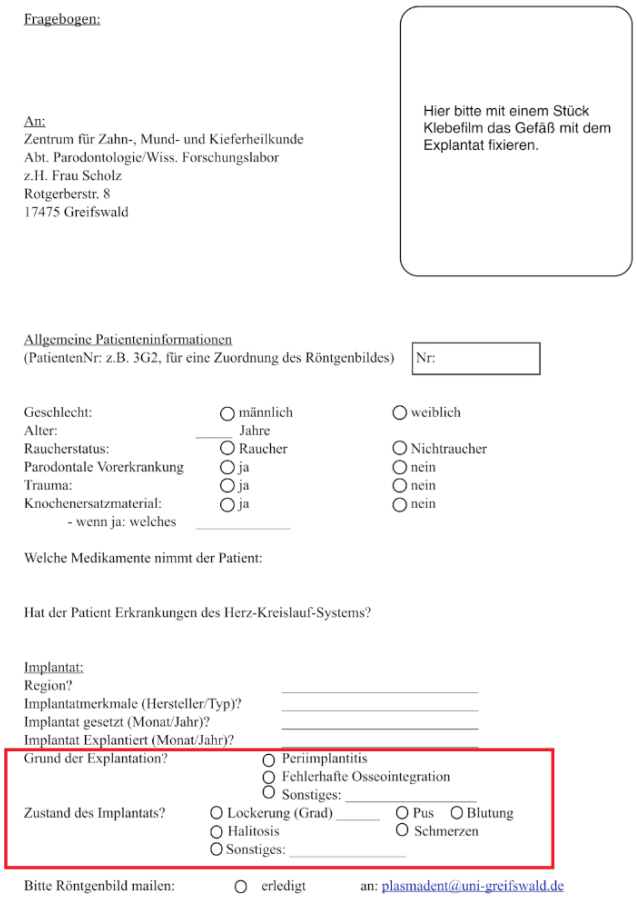
# 2 Material and methods

## 2.1 Data acquisition

Implantology specialists were recruited via the forum of the International Team for Implantology (ITI) and European Centers for Dental Implantology (ECDI), and some offices were contacted directly. Implants were received in vials either with saline or with glutaraldehyde, which arrived at the dental school in Greifswald between May 2012 and February 2015. All explants were stored in a 4°C fridge.

## 2.2 Questionnaire

The questionnaire was created in a way that clinicians can answer them easily at the time of implant removal. Questions were avoided if they included additional effort or imprecise outcome at different centres such as accessibility for oral hygiene (Figure 1). Radiographs were sent by email or added to the questionnaire. The latter were then scanned and sent back to the dental offices afterwards.



Fragebogen:

An:
Zentrum für Zahn-, Mund- und Kieferheilkunde
Abt. Parodontologie/Wiss. Forschungslabor
z.H. Frau Scholz
Rotgerberstr. 8
17475 Greifswald

Hier bitte mit einem Stück Klebefilm das Gefäß mit dem Explantat fixieren.

Allgemeine Patienteninformationen
(PatientenNr: z.B. 3G2, für eine Zuordnung des Röntgenbildes) Nr:

Geschlecht: ○ männlich ○ weiblich
Alter: _____ Jahre
Raucherstatus: ○ Raucher ○ Nichtraucher
Parodontale Vorerkrankung ○ ja ○ nein
Trauma: ○ ja ○ nein
Knochenersatzmaterial: ○ ja ○ nein
- wenn ja: welches _____

Welche Medikamente nimmt der Patient:

Hat der Patient Erkrankungen des Herz-Kreislauf-Systems?

Implantat:
Region? _____
Implantatmerkmale (Hersteller/Typ)? _____
Implantat gesetzt (Monat/Jahr)? _____
Implantat Explantiert (Monat/Jahr)? _____
Grund der Explantation? ○ Periimplantitis
○ Fehlerhafte Osseointegration
○ Sonstiges: _____
Zustand des Implantats? ○ Lockerung (Grad) _____ ○ Pus ○ Blutung
○ Halitosis ○ Schmerzen
○ Sonstiges: _____

Bitte Röntgenbild mailen: ○ erledigt an: plasmadent@uni-greifswald.de

**Figure 1.** Questionnaire. Later added questions are framed in red.

## 2.3 Adjustments of data

Answers for date of implantation varied, so the 15th was recorded as mean of the month and the 15th of July as the mean of the year. Answers giving an approximate survival time were recorded as fact. Two explants reported “over ten years”. Multilevel analysis worked with censored data. The survival time was calculated in months and rounded up from 15 days. For clarity of graphical display, dental offices with <5 patients and implant brands with ≤5 implants were pooled and IMZ, Xive, Ankylos and Astra Tech were combined to the group “Dentsply”. Further, location was grouped into anterior and posterior, jaw (maxilla and mandible), and crown type (incisor, canine, premolar, molar).

## 2.4 Eligibility criteria

Variables giving too many nominal options (implant brand for fully adjusted mixed-effects models, bone substitute brand), giving a very vague answer (medication and cardiovascular diseases), not affecting one single implant (trauma as leading cause for explantation) and being too inconsistent (reason for implant removal, symptoms) were excluded. Furthermore, pre-existing periodontitis was excluded (see below). Age at implantation was preferred to age at explantation as it reflects the risk factor and relative bone loss was preferred to absolute bone loss as it describes the most conclusive results and is more comparable with the literature. Implant design such as diameter, form (cylindric or tapered), or the difference of bone level or transgingival implants were not assessed. None of these are considered relevant risk factors (Lang et al., 2007).

## 2.5 Measurements

### 2.5.1 Explant

After removal from their container the explants were slightly dried with a napkin to avoid light reflections and were then positioned on the microscope slide. Pictures were taken with a video camera (Power HAD 3CCD. Sony, Köln, Germany) connected to an incidental light microscope (SZH-10 Research Stereo Microscope. Olympus Optical, Hamburg, Germany) with 5x magnification of the explant (objective of 0.5x, zoom ratio of 1x and an eyepiece of 10x) using an image analysis software (AnalySIS version 3.0 by Olympus Soft Imaging Solutions GmbH 48149 Münster, Germany). The length between a landmark point, locatable both on the explant and the radiograph, and explant apex was measured (*p*, Figure 2A) on the explant and then used to calibrate the radiograph. Surface of the explant that originally had bone contact was measured (*o*, Figure 2B) from implant shoulder or in case of transgingival implant design from the presumptive smooth-rough border to the apex.

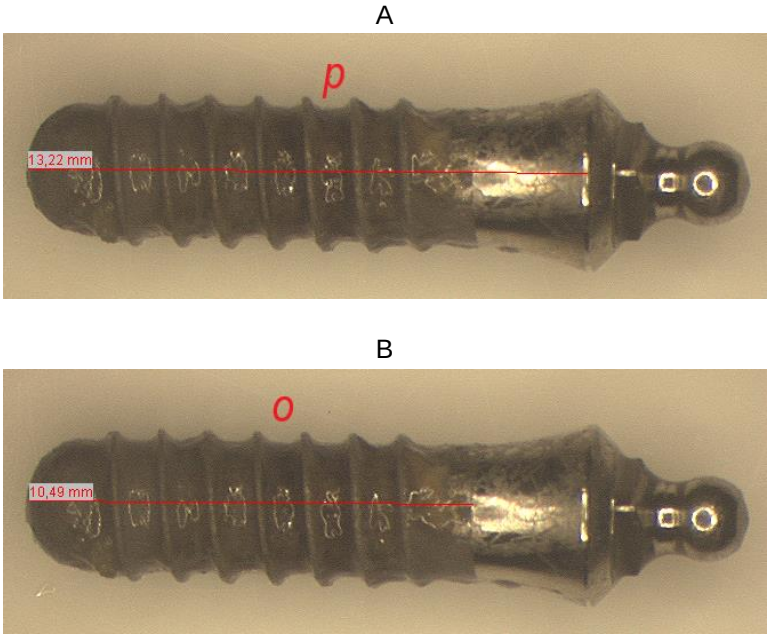



**Figure 2.** Distance between a landmark point and implant apex (A), and length of the implant surface that originally had bone contact (B).

One measurement error includes the implant design:

1. Cylindric implants (Figure 3A)

   $$x_1 = L$$

   Measured implant length $x_1$ equals real implant length $L$. There is no such measurement error in cylindric implants.

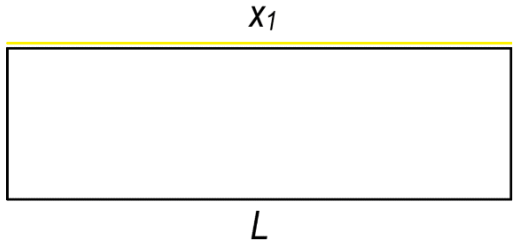



**Figure 3A**. Abstract representation of a cylindric implant. $x_1$ in yellow presents the measured implant length. L represents the real implant length.

2. Sharp tapered implants (Figure 3B)

   $$x_2 = L - \frac{{d_1}^2}{2 \times L}$$

   A sharp tapered implant with the real length $L$ of 10 mm and a diameter $d_1$ of 3 mm has a 4.50% shorter measured implant length $x_2$. Increasing the diameter to 4 mm leads to a measurement error of 8.00%. The shorter the implant and the wider the diameter, the higher the measurement error. None of the implants were sharp tapered, hence this represents the extreme for illustrative reasons.

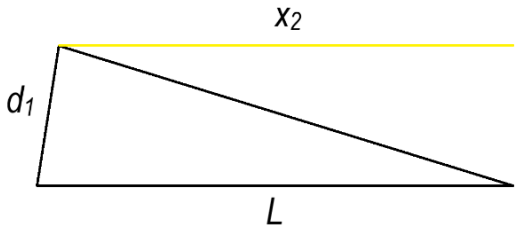



**Figure 3B**. Abstract representation of a sharp tapered implant. $x_2$ in yellow presents the measured implant length. L represents the real implant length.

3. Cut tapered implants (Figure 3C)

   $$x_3 = \cos(180° - 2 \times \propto) \times L$$

   A cut tapered implant with the real length $L$ of 10 mm, a diameter $d_1$ of 3 mm and a diameter at the apex $d_2$ of 2.5 mm ($\alpha$ = 88.57°) has a 0.12% shorter measured implant length $x_3$. Increasing the diameter $d_1$ to 4 mm and the diameter at the tip $d_2$ to 3 mm ($\alpha$ = 87.14°) leads to a measurement error of 0.50%. This is an approximation for all similar raises of the implant.

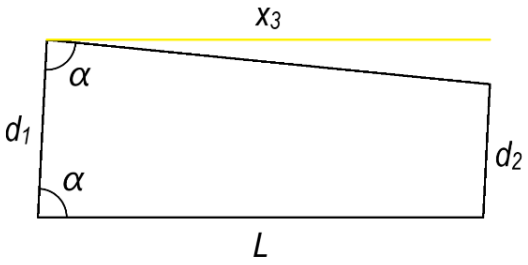



**Figure 3C**. Abstract representation of a cut tapered implant. $x_3$ in yellow presents the measured implant length. L represents the real implant length.

These measurement errors are small enough to be ignored but may become relevant when grouping implants such as <10 mm and ≥10 mm.

The pictures were labelled by x.a.1 and x.a.2 for original-bone-contact length and landmark-point length, respectively, with x being the patient number and a to c being different implants in one patient.

### 2.5.2 Radiographs

The radiographs were labelled by x_y_office, with x being the patient number to facilitate order and y being the original number given by the dental office in order to identify and associate it with the questionnaire. Radiographs used in this study with provided date (n=15) arrived at the dental school in Greifswald at mean ± SD 2.8 ± 5.4 months after recording. The type of bone loss was recorded on every radiograph with sufficient quality. For validation purposes, bone loss measurements were replicated. Two measurements including the final one for statistics used the app Preview (Apple inc. Cupertino CA 95014, USA) with an interval of over a year. Distance was measured by counting pixel from a starting point to an end point, using the Pythagorean theorem to calculate the diagonal.

$$\sqrt[2]{a^2 + b^2} = c$$

The results were recorded for length from i) apex of the implant to the landmark-point mentioned above ($c_1$, Figure 4A and B), and ii) the least distance between marginal bone level and the apex ($c_2$, Figure 4C). The absolute bone loss was then calculated:

$$o - \frac{c_2}{c_1} \times p = l$$

*o = original-bone-contact length [mm]*

*p = landmark-point length [mm]*

*$c_1$ = radiologic length from apex to landmark-point [pixel]*

*$c_2$ = least radiologic length from apex to marginal bone [pixel]*

*l = absolute bone loss [mm]*

*r = relative bone loss [%]*

To simplify in words: the residual alveolar bone subtracted from the length that originally had bone contact results in the absolute bone loss.

The relative bone loss was then calculated by dividing the absolute bone loss by the original-bone-contact length of the measured explant:

$$\frac{l}{o} = r$$

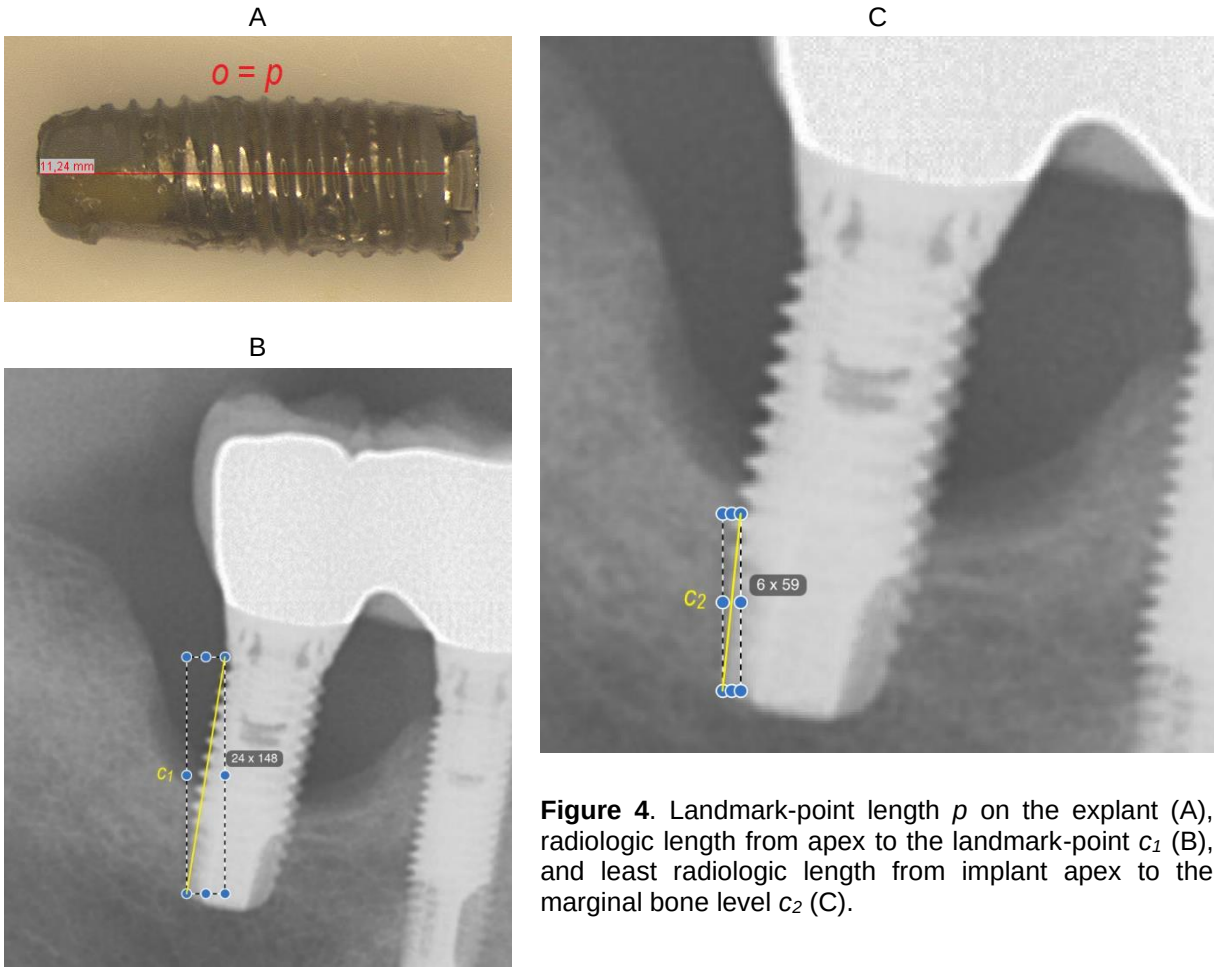



**Figure 4**. Landmark-point length *p* on the explant (A), radiologic length from apex to the landmark-point $c_1$ (B), and least radiologic length from implant apex to the marginal bone level $c_2$ (C).

An image analysis software was used for the second validation measurement (AnalySIS docu version 5.2 by Olympus Soft Imaging Solutions GmbH 48149 Münster, Germany). Radiographs were manually calibrated, and the software presented results in millimetres, which were then again divided by the original-bone-contact length for relative bone loss. Between the measurement with the different software and the final measurement, few original-bone-contact lengths were changed due to confusion of submerged bone level and non-submerged transgingival implant design. Hence, the comparison between those two includes i) the intra-examiner measurement error, ii) the measurement error of different software if present and iii) the error of different original-bone-contact-lengths. Still, those intraclass correlation coefficients (ICC) were 0.967 and 0.948, and mean intra-examiner differences were 1.8 ± 6.6% and 0.39 ± 0.82 mm for relative and absolute bone loss, respectively. Comparison between these two measurements had the largest deviations, and still agrees with the literature (Berglundh et al., 2018; De Smet, Jacobs, Gijbels, & Naert, 2002; Pikner, Gröndahl, Jemt, & Friberg, 2009). The examiner was blindfolded to the questionnaires to avoid bias. Despite evaluation of only one examiner, a high reliability may be assumed. The data validity depends on the quality and angulation of the radiograph and is higher for intraoral radiographs than for panoramic radiographs.

The radiographs were examined for the explantation causing bone defect and categorized into five groups: A horizontal bone loss, B vertical bone loss, A + B a combination of the previous, C apical inflammation and D peri-implant gap, defined as follows:

A) Horizontal bone loss as bone loss in an angle between intact crestal margin and deepest point of the defect to the implant surface of more than 60° and approaching perpendicular to the implant surface (Figure 5A),
B) Vertical bone loss in an angle of less than 60° or approaching parallel to the implant surface (Figure 5B), and a minimum defect width of >1mm,
C) Apical inflammation as radiolucency around the implant apex with largely intact crestal bone (Figure 5C),
D) Peri-implant gap in an angle of less than 10° and a maximum defect width of 1 mm (Figure 5D).

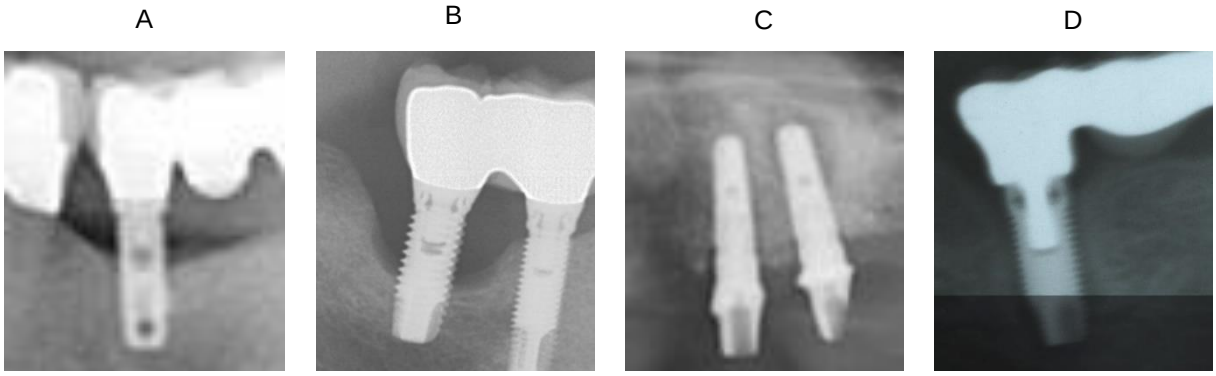



**Figure 5**. Horizontal (A), and vertical bone loss (B), apical inflammation (C), and peri-implant gap (D).

The larger angle of the mesial and distal implant site was decisive. For the group A + B, an estimated line was drawn connecting the crestal bone level outside the vertical bone invasion if necessary (Figure 6). Then, A and B were recorded separately, and total bone loss was used for further statistics.

The answers on the questionnaires concerning the pre-existing periodontitis did not completely match the related radiographs, thus the radiographs were measured for periodontitis as well. All teeth with deep bony pockets in an orthopantomogram (OPG) were measured from the cementoenamel junction. Here too, the deepest value of periodontitis associated bone

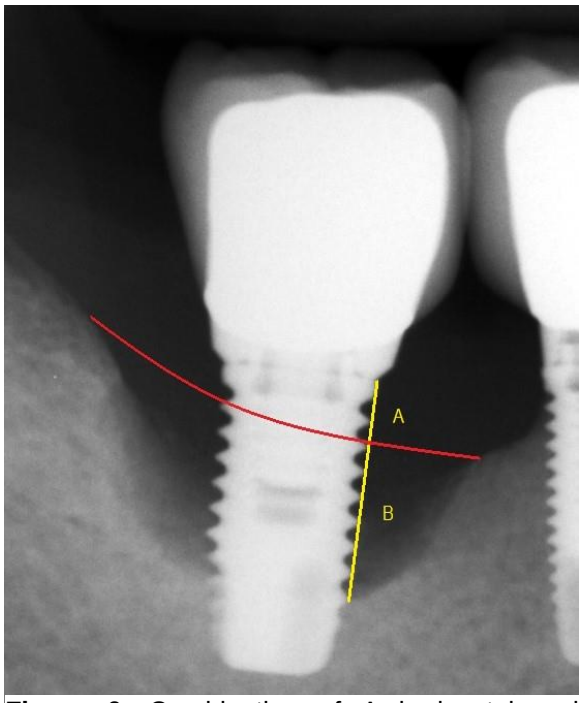



**Figure 6**. Combination of A horizontal and B vertical bone loss.

loss was recorded. Additionally to numeric maximum relative and absolute periodontal bone loss, these were grouped into

1. <33.33% relative and <3 mm absolute periodontal bone loss,
2. ≥3 mm absolute, but <33.33% relative periodontal bone loss,
3. ≥33.33%, but <50% relative periodontal bone loss, and
4. ≥50% relative periodontal bone loss.

For 52 patients, periodontal bone loss was measured on radiographs, and for 121 patients, data on periodontal history was provided on the questionnaires. There was no association between stated periodontitis on the questionnaire and numeric relative or absolute periodontal bone loss, or ordinal periodontal bone loss groups. Therefore, this data was declared unreliable and excluded from further statistics.

## 2.6 Statistics

Statistical analyses were performed using SPSS (IBM Corp., 2013). Normality of numerical variables was checked using Shapiro-Wilk tests (Supplement Table 1). Variance homogeneity (homoskedasticity) was checked with the Levene test. Although implants cluster in patients, independence of variables has been assumed. To examine pairwise interrelations, a two-sample t-test was used for normally distributed numeric and nominal variables with two categories, analysis of variance (ANOVA) was used for normally distributed numeric and nominal variables with three or more categories, Mann-Whitney-U test was used for non-normally distributed numeric and nominal variables with two categories, Kruskal-Wallis' test was used for non-normally distributed numeric and nominal variables with three or more categories, Fisher's exact test for two nominal variables with two categories, and Pearson's $Chi^2$ test for two nominal variables with three or more categories. Unknown values were not considered as separate test categories. Effect size was not explicitly mentioned but displayed graphically instead. Two-sided significance was chosen and p-values <0.05 were considered statistically significant.

# 3 Results

## 3.1 Overall data

Twelve German dental offices, specialised in implantology, provided 192 dental explants. For 94 implants the bone loss type was recorded of which 80 were considered late failures (Figure 7). For 75 implants bone loss was measured of which 66 were considered late failures.

In 10.6% implants were affected by horizontal bone loss (A), in 51.1% by vertical bone loss (B), in 22.3% by combined horizontal and vertical bone loss (A + B), in 4.3% by apical inflammation (C) and in 11.7% by peri-implant gap (D). Figure 8A describes the distribution of type of bone loss for early and late implant failures. In early implant failures peri-implant gap was the most prevalent (35.7%) and in late implant failures vertical bone loss (55.0%). Early implant failures made up for a large proportion of apical inflammations and peri-implant gap.

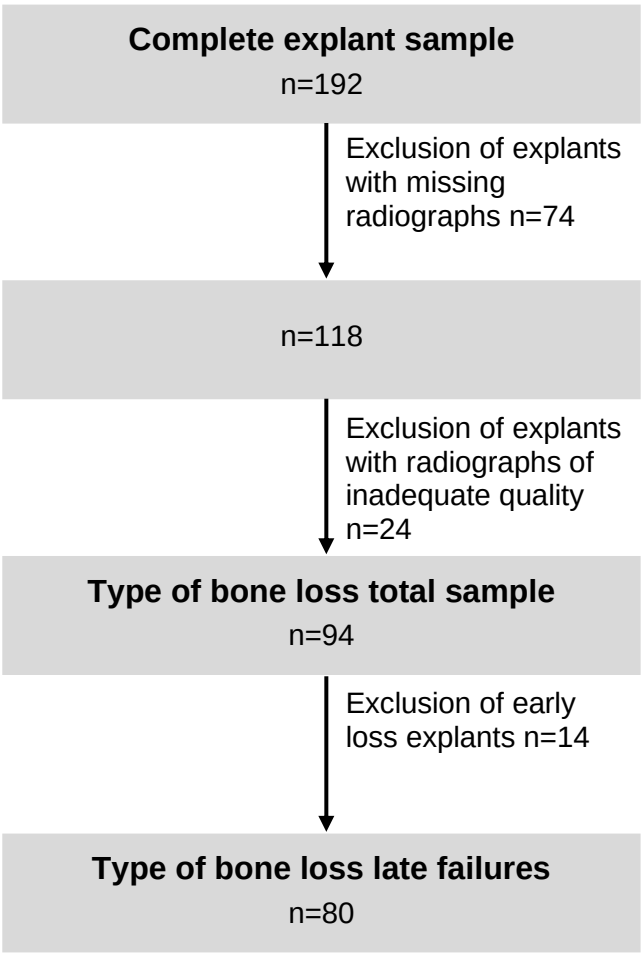
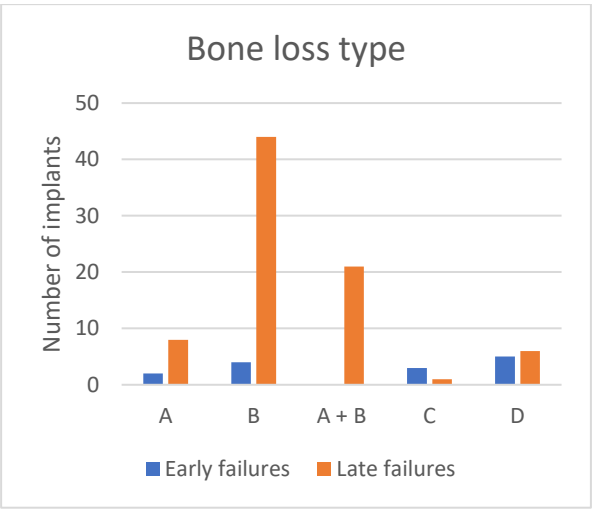



**Figure 7**. Flow-chart describing the final samples for type of bone loss.

Data on bone substitutes was given for 143 implants. Out of the group that used bone substitutes (n=42), *Geistlich Bio-Oss*® with 27 times (61.4%) was used the most, others were used eight times (18.2%), and nine manufacturers were unknown (20.5%). Excluding unknowns, 85.7% of the grafts were xenogenous, 5.7% alloplastic, 5.7% allogenous and 2.9% autogenous. Figure 8B describes the distribution of bone substitutes for early and late implant failures. Bone substitutes were more common in early implant failures (36.4%) than in late implant failures (18.9%).

A




B

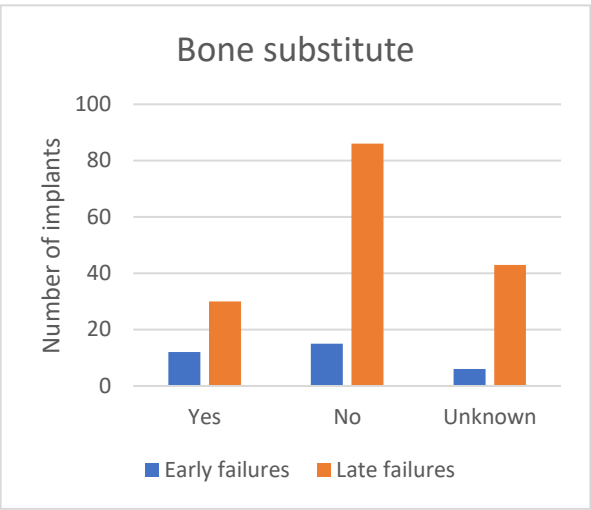
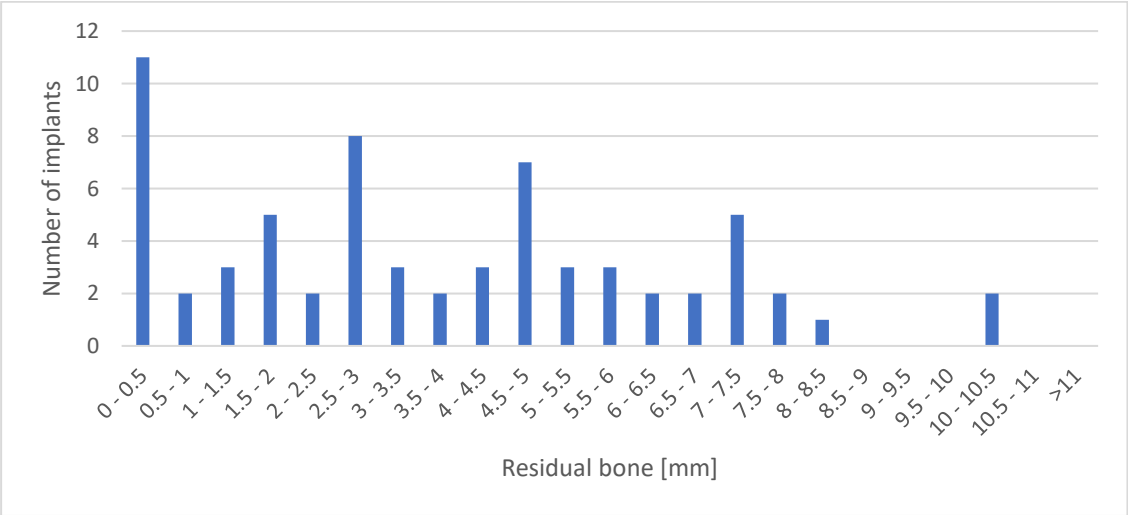



**Figure 8**. Associations between A) bone loss type (A horizontal, B vertical, C apical inflammation, D peri-implant gap) and time point of implant failure (n=143, p=0.056), and B) usage of bone substitute and time point of implant failure (n=143, p=0.056; unknown values were not considered as separate test category.)

Figure 9 describes the distribution of relative bone loss and residual alveolar bone in late implant failures. Mean residual alveolar bone was 3.70 ± 2.74 mm with median 3.43 mm, mean relative bone loss was 66.2 ± 23.7% with median 65.8%, and mean absolute bone loss was 7.07 ± 2.66 mm with median 6.78 mm. The relative bone loss and residual alveolar bone in late failures between the jaws and location are described in Figure 10.

A



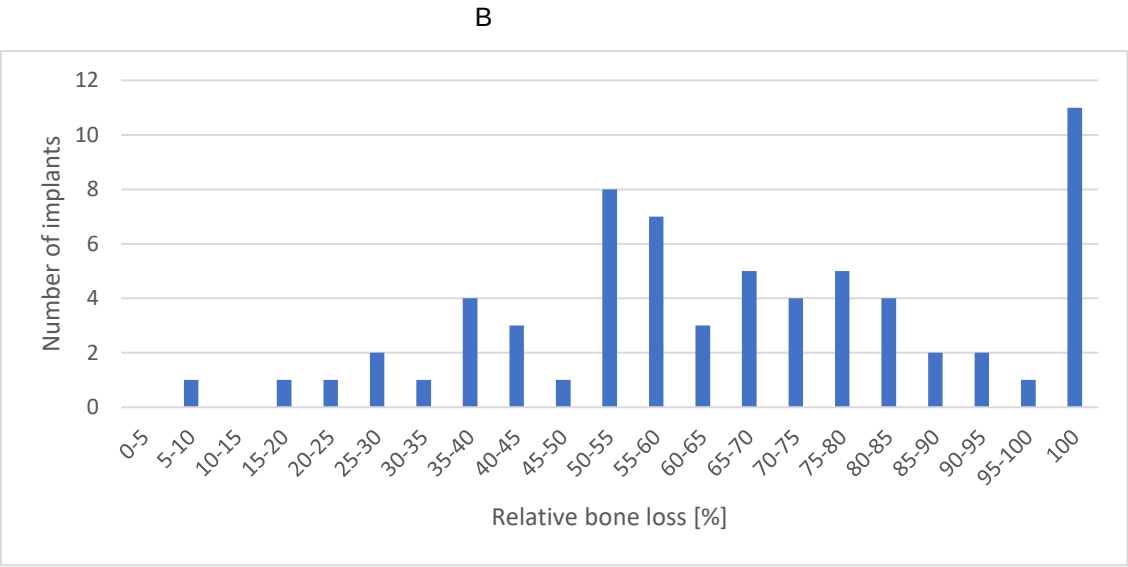



**Figure 9**. Distribution of A) residual alveolar bone and B) relative bone loss.

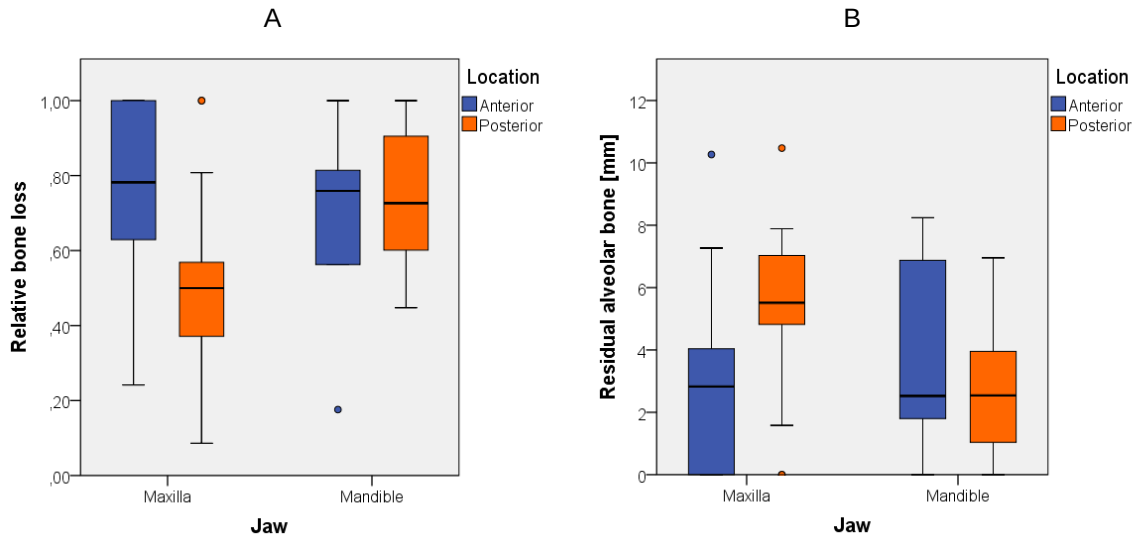



**Figure 10**. Associations of A) relative bone loss and B) residual alveolar bone with the jaw and anterior/posterior location (jaw and location: n=182, p=0.001; rel. bone loss and jaw: n=66, p=0.005; rel. bone loss and location: n=66, p=0.229; residual alv. bone and jaw: n=66, p=0.004; residual alv. bone and location: n=66, p=0.535)

## 3.2 Analysis

In the publication (Wentorp, Jablonowski, Pink, Holtfreter, & Kocher, 2021), bivariate associations between different variables and early or late implant failure are presented.

Additionally, the explanting dental office (*p=0.002*), implant brand (*p<0.001*), and type of bone loss (*p<0.001*) showed statistically significant correlations.

Table 1 and 2 describe bivariate associations between different variables and type of bone loss for total explant sample and only late implant failures, respectively. In late implant failures, mean horizontal bone loss was 40.6 ± 19.5% or 3.90 ± 1.80 mm with 5.98 ± 2.47 mm residual bone, mean vertical bone loss was 63.3 ± 30.9% or 6.93 ± 3.61 mm with 4.19 ± 2.68 mm residual bone, mean combined horizontal and vertical bone loss was 75.8 ± 39.0% or 7.46 ± 3.88 mm with 2.49 ± 1.88 mm residual bone, and peri-implant gap did not always radiologically cover the entire implant and demonstrated mean bone loss of 90.3 ± 15.8% or 9.91 ± 2.61 mm with 1.06 ± 1.73 mm residual bone (*p<0.003*). Respective values of bone loss in early failures largely matched; differences in bone loss between early and late failures mostly resulted from different distribution of type of bone loss. Survival time, as described above, was statistically significantly associated with type of bone loss in total explant sample (*p<0.001*) and also in late implant failures (*p=0.017*). Further, the implant brand demonstrated a strong correlation with types of bone loss in both total explant sample and late implant failures (*p<0.005*), while the explanting office did not. The implant position ungrouped for crown type was associated with bone loss type in late implant failures (*p=0.032*), while only a trend was seen in total explant sample (*p=0.055*). This was not reproduced when grouped to anterior and posterior location. Smoking may only have an influence on the type of bone loss in late implant failures (*p=0.044*). Relationships with type of bone loss in total explant sample are shown in Figure 11.

**Table 1**. Bivariate analysis of total explant sample variables with type of bone loss.

| Variable 1 | Variable 2 | Test | N | p-value |
|---|---|---|---|---|
| Survival time | Type of bone loss | Kruskal-Wallis | 87 | <0.001 |
| Age at implantation | Type of bone loss | ANOVA | 76 | 0.209 |
| Implant length | Type of bone loss | ANOVA | 79 | 0.383 |
| Rel. bone loss | Type of bone loss | Kruskal-Wallis | 74 | <0.001 |
| Abs. bone loss | Type of bone loss | ANOVA | 73 | <0.001 |
| Residual alv. bone | Type of bone loss | Kruskal-Wallis | 74 | <0.001 |
| Office | Type of bone loss | $Chi^2$ | 94 | 0.099 |
| Implant brand | Type of bone loss | $Chi^2$ | 71 | 0.004 |
| Sex | Type of bone loss | $Chi^2$ | 93 | 0.529 |
| Smoking | Type of bone loss | $Chi^2$ | 82 | 0.213 |
| Bone substitute | Type of bone loss | $Chi^2$ | 69 | 0.057 |
| Position crown type | Type of bone loss | $Chi^2$ | 94 | 0.055 |
| Ant./post. location | Type of bone loss | $Chi^2$ | 94 | 0.545 |
| Jaw | Type of bone loss | $Chi^2$ | 94 | 0.105 |
| X-ray type | Type of bone loss | $Chi^2$ | 94 | 0.287 |

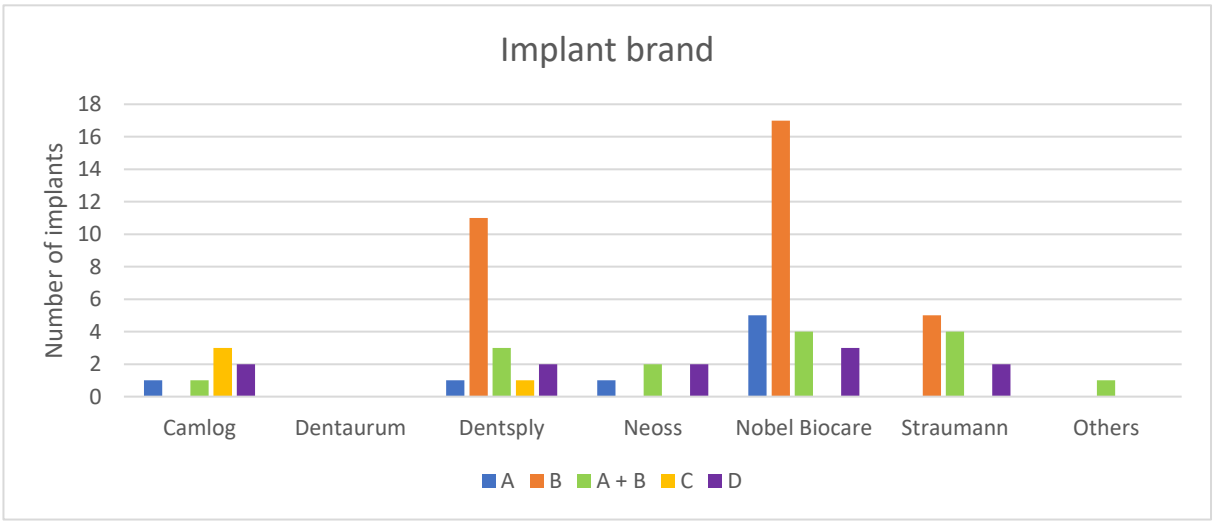
Varying implant numbers occurred due to missing information on different variables. P-values <0.05 are highlighted and describe significant associations. P-values <0.10 are marked in grey.

**Table 2**. Bivariate analysis of late implant failure variables with type of bone loss.

| Variable 1 | Variable 2 | Test | N | p-value |
|---|---|---|---|---|
| Survival time | Type of bone loss | Kruskal-Wallis | 73 | 0.017 |
| Age at implantation | Type of bone loss | ANOVA | 62 | 0.396 |
| Implant length | Type of bone loss | ANOVA | 67 | 0.247 |
| Rel. bone loss | Type of bone loss | Kruskal-Wallis | 65 | <0.001 |
| Abs. bone loss | Type of bone loss | ANOVA | 64 | <0.001 |
| Residual alv. bone | Type of bone loss | Kruskal-Wallis | 65 | 0.002 |
| Office | Type of bone loss | Chi² | 80 | 0.249 |
| Implant brand | Type of bone loss | Chi² | 58 | 0.001 |
| Sex | Type of bone loss | Chi² | 79 | 0.882 |
| Smoking | Type of bone loss | Chi² | 69 | 0.044 |
| Bone substitute | Type of bone loss | Chi² | 58 | 0.148 |
| Position crown type | Type of bone loss | Chi² | 80 | 0.032 |
| Ant./post. location | Type of bone loss | Chi² | 80 | 0.637 |
| Jaw | Type of bone loss | Chi² | 80 | 0.096 |
| X-ray type | Type of bone loss | Chi² | 80 | 0.757 |

Varying implant numbers occurred due to missing information on different variables. P-values <0.05 are highlighted and describe significant associations. P-values <0.10 are marked in grey.

A

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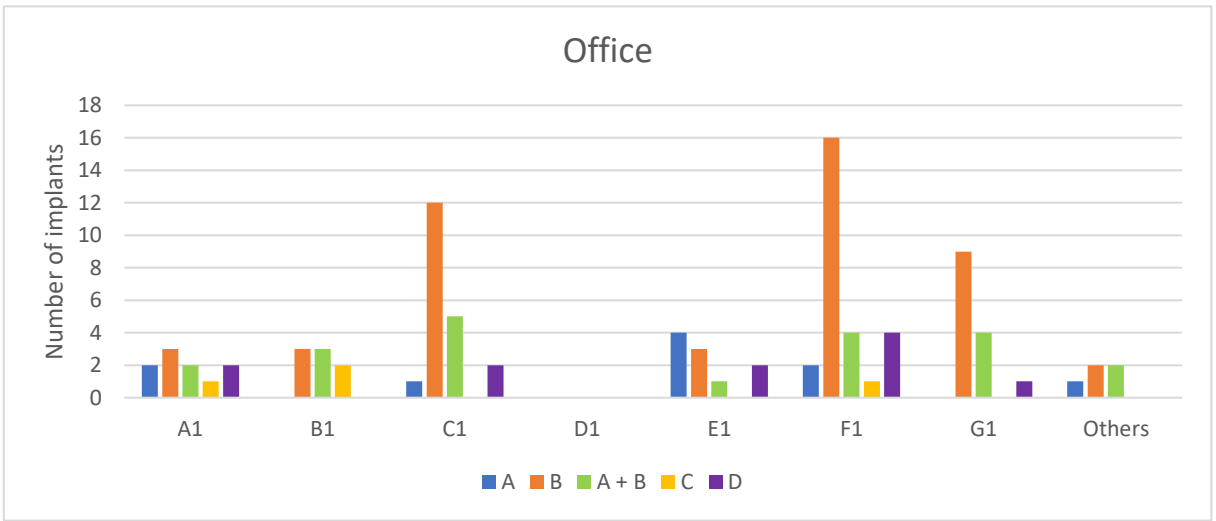

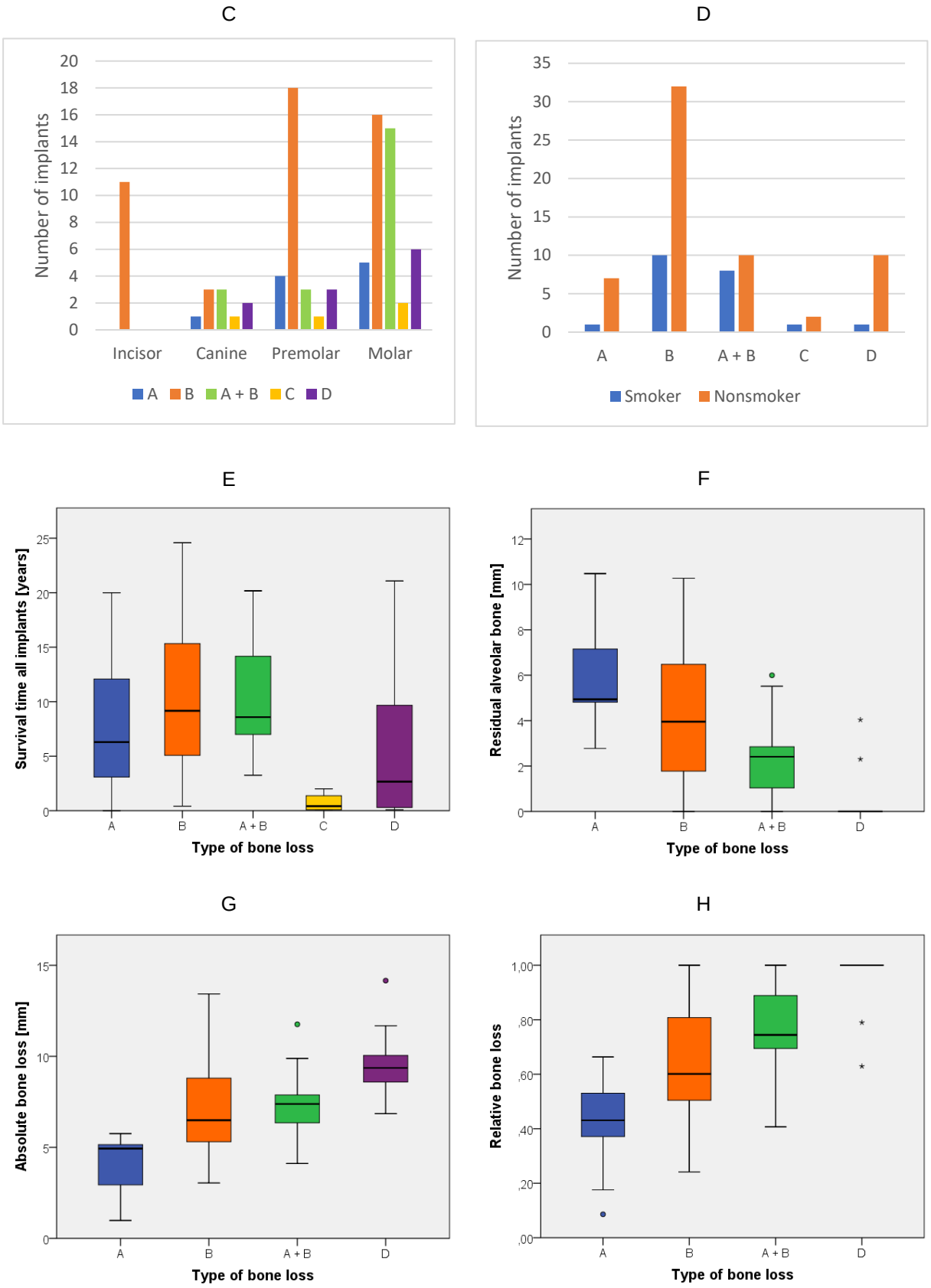


**Figure 11**. Bivariate associations of implant brand (A, n=71, p=0.004), explanting office (B, n=94, p=0.099), position crown type (C, n=94, p=0.055), smoking (D, n=82, p=0.213), survival time (E, n=87, p<0.001), residual alveolar bone (F, n=74, p<0.001), absolute bone loss (G, n=73, p<0.001), and relative bone loss (H, n=74, p<0.001) with type of bone loss (A horizontal, B vertical, C apical inflammation, D peri-implant gap) in total explant sample.

Usage of bone substitutes is highly interlinked with explanting office (*p<0.001*) and implant brand (*p=0.001*). In turn, bone substitutes show a trend for type of bone loss (*p=0.057*) with a large percentage in horizontal bone loss, apical inflammation and peri-implant gap. Bone substitutes were only used in a small percentage in vertical bone loss and even fewer in combined horizontal and vertical bone loss. Further, bone substitutes are associated with the maxilla (*p=0.002*). There seems to be a correlation between implant length and bone substitutes used (*p=0.048*), with more usage at shorter implant lengths (mean 9.80 ± 1.64 mm vs. 10.63 ± 2.04 mm). Relationships with bone substitutes in total explant sample are shown in Figures 12 and 13**.**

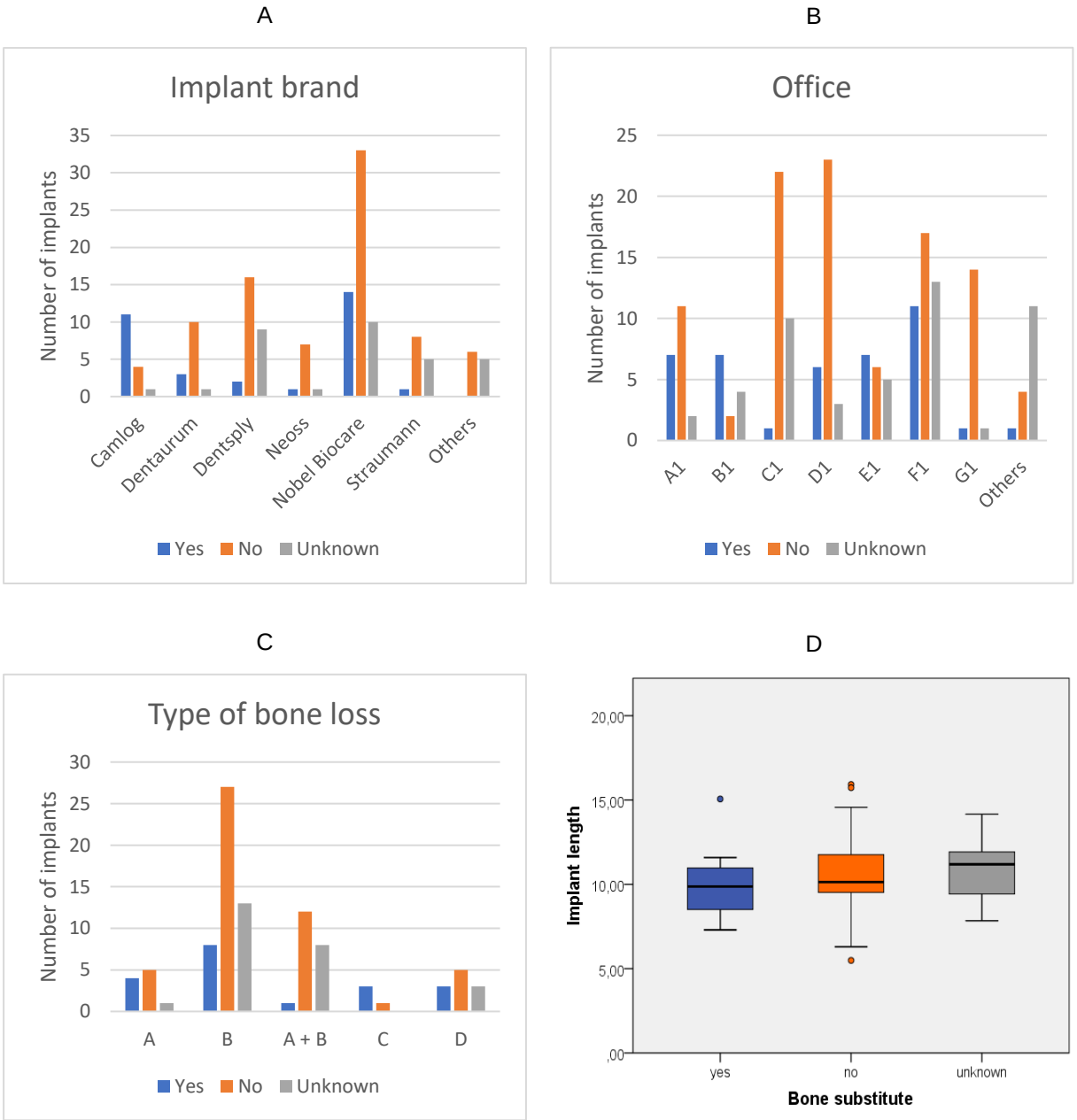


**Figure 12**. Bivariate associations of implant brand (A, n=116, p=0.001), explanting office (B, n=140, p<0.001), type of bone loss (C, n=69, p=0.057, A horizontal, B vertical, C apical inflammation, D peri-implant gap), and implant length (D, n=101, p=0.048) with usage of bone substitutes in total explant sample.

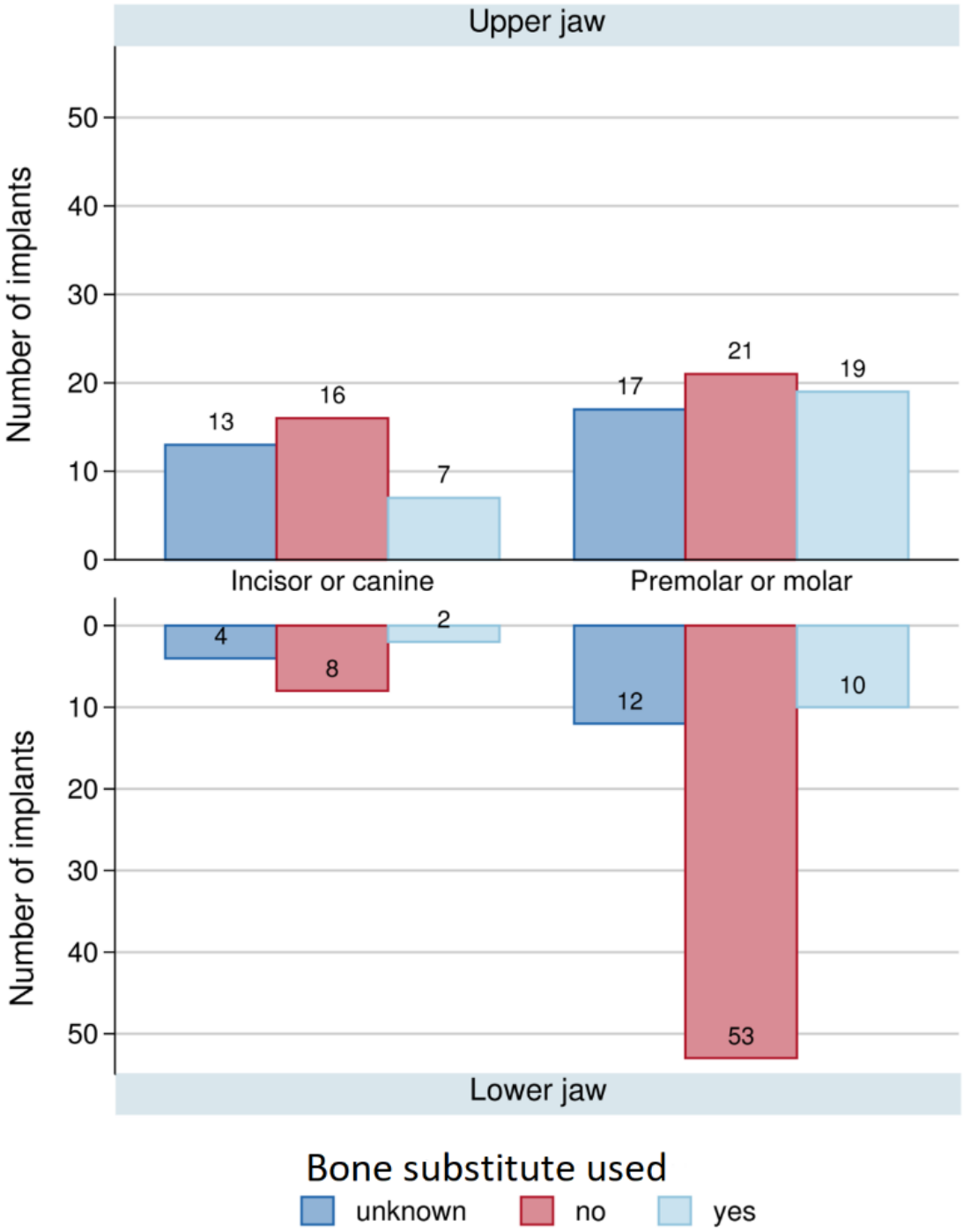


**Figure 13**. Association between jaw, location, and usage of bone substitute (jaw and location: n=182, p=0.001; jaw and bone substitute: n=136, p=0.002; location and bone substitute: n=136, p=1.000; unknown values were not considered as separate test category.)

# 4 Discussion

## 4.1 Summary of the study

In the results of this study, most bone loss types were vertical and only few were apical inflammations. 17.2% of all implant failures were early failures. Late failures were explanted at mean bone loss of 66.2% ± 23.7% or 7.0 ± 2.66 mm and residual alveolar bone of 3.70 ± 2.74 mm. The wide variation in bone levels suggests that the profession has no universally accepted threshold beyond which an implant cannot be preserved. The type of bone loss differed between early and late failures. Apical inflammation (21.4% vs. 1.3%) and peri-implant gap (35.7% vs. 7.5%) were associated with early failures, and vertical bone loss (28.6% vs. 55%) and combined vertical and horizontal bone loss (0% vs. 26.3%) with late failures. Survival time and implant brand were associated with type of bone loss. In late failures, combined vertical and horizontal bone loss (42.1% vs. 20.0%) was significantly associated with a current smoking habit, while horizontal bone loss (0.0% vs. 12.0%) and peri-implant gap (0.0% vs. 12.0%) were more common in non-smokers. There was a strong association between early and late failures for office and implant brand. Further, in early failures shorter implant length were more common and there was a trend for bone substitutes, leading to the assumption that early failures happen more often in challenging surgical situations. Smoking on the other hand was associated with late failures. In late failures, a higher age at implantation was associated with less survival time until explantation, probably due to bone and immunological changes. Implants placed in the mandible (73.7 ± 39.3% bone loss and 2.78 ± 2.21 mm residual alveolar bone in the mandible vs. 57.7 ± 32.7% bone loss and 4.73 ± 2.94 mm residual alveolar bone in the maxilla), probably due to bone quality, sinus floor elevations, and shorter implants were explanted at more relative bone loss (71.9 ± 38.8% bone loss and 2.56 ± 1.80 mm residual alveolar bone in implant lengths <10 mm vs. 61.6 ± 33.4% bone loss and 4.55 ± 3.01 mm residual alveolar bone in implant lengths ≥10 mm).

## 4.2 Type of bone loss

Bone defects can be grouped into marginal bone loss (horizontal, vertical and the combination) with an aetiology probably similar to periodontitis, peri-implant gap with a probably primary aseptic aetiology, similar to a foreign body reaction, and apical inflammation with an aetiology of local infection pre-implantation or from neighbouring structures.

In this study, failing implants were affected by horizontal bone loss in 10.6%, by vertical bone loss in 51.1%, by combined horizontal and vertical bone loss in 22.3%, by apical inflammation in 4.3%, and by peri-implant gap in 11.7%. Schwarz and colleagues reported on **marginal peri-implant defects** in open flap surgery and observed circumferential vertical bone loss in

most implants, generally associated with horizontal bone loss (Schwarz et al., 2007). Crater-like, circumferential peri-implant bone loss is often described in the literature (Mombelli & Lang, 1998; Schwarz et al., 2018). Still, the most severe bone loss occurs frequently at the buccal wall (Monje, Pons, et al., 2019). Zhang and colleagues differentiated flat (or horizontal) and vertical bone loss at an arbitrary angle of 90° to the implant surface (Zhang, Geraets, Zhou, Wu, & Wismeijer, 2014). An angle of 60° and approaching perpendicular to the implant surface may be more appropriate, considering the implants in this study failed due to bone loss. Zhang and colleagues categorized peri-implant defects on the radiograph into flat, slit-like, saucer-shaped, wedge-shaped, and undercut defects. Saucer-shaped, wedge-shaped, and undercut defects can be grouped into vertical and combined horizontal and vertical bone loss. In hindsight, it was reported on 77.6 to 83.9% for vertical and combined bone loss, 10.7 to 17.7% for horizontal/flat bone loss, and 4.7 to 5.4% for peri-implant gap/slit-like defects. Monje and colleagues (Monje, Pons, et al., 2019) did a recent cone-beam computed tomography study based on the defect categorization of Schwarz and colleagues (Schwarz et al., 2007). Vertical bone loss was reported in 74.7% of the implants, horizontal bone loss in 1.9%, and combined bone loss in 23.4%. The data of the present study goes in line with these reports: excluding all early failures and apical inflammations, implants were affected by horizontal bone loss in 10.1%, by vertical bone loss in 55.7%, by combined horizontal and vertical bone loss in 26.6%, and by peri-implant gap in 7.6%. Noteworthy, the studies reported strict eligibility criteria, so data are only comparable to a limited extend. Further, peri-implant gap may be added to vertical bone loss. A key difference is that peri-implantitis was observed instead of implant failure, and advanced bone loss (>50%) was only reported in 36.7% of the implants (Monje, Pons, et al., 2019) compared to 77.3% of late failures in this study. One study on failed implants, and therefore more comparable implant sample, reported mostly combined defects with advanced horizontal bone loss and broad circumferential vertical bone defects (Anitua, Murias-Freijo, & Alkhraisat, 2016).

**Apical inflammation** (or retrograde peri-implantitis) of an implant is an exceedingly rare event, and one study reported prevalence at 1.6% of implants in the maxilla and 2.7% of implants in the mandible (Quirynen et al., 2005). In that study 6 implants were diagnosed with retrograde peri-implantitis in <12 months, while 24 implants failed before, at or soon after loading, hence 25.0% of early failures occurred due to retrograde peri-implantitis. Interestingly, the proportion of retrograde peri-implantitis in early failures was higher in the mandible (42.9%) than in the maxilla (17.6%). The mean time of diagnosis was reported at 26.07 ± 39.7 weeks, median 16 weeks (Quirynen et al., 2005), which goes hand in hand with results for explantation of the present study with a mean of 8.75 ± 10.8 months (35.0 ± 43.4 weeks), median 5 months (20 weeks). The results match but must be considered with caution since only 4 implants failed due to apical inflammation. In the present study, 21.4% of early failures occurred due to apical

inflammation. The proportion of apical inflammation in the mandible was 42.9% and no early failures occurred in the maxilla due to apical inflammation. It was noted that most apical inflammations occurred together with the usage of bone substitutes (Figure 12C) and only in few offices with few implant brands (Figure 11A and B). This leads to the assumption that apical inflammation is highly dependent on the operator. On the contrary, the combination of vertical and horizontal bone loss was distributed evenly between the offices and implant brands and was associated with longer survival time. This observation leads to the assumption that combined vertical and horizontal bone loss is more dependent on patient characteristics such as smoking.

**A peri-implant gap** probably corresponds to a fibrous capsule around the implant, accompanied by scar tissue and/or epithelial downgrowth which may lead to mobility and is a sign of failed osseointegration (Esposito et al., 1999). Since it also happened in late failures, it may be a sign of abrupt loss of osseointegration, for example due to extreme overload (Chang et al., 2013).

In **statistical analysis**, Zhang and colleagues (Zhang et al., 2014) found that sex, smoking, treatment strategy and early/late failure influenced the type of bone loss on a significance level of $p<0.10$. Monje and colleagues reported on a significant correlation ($p<0.05$) between type of bone loss and age, and a tendency towards significance for smoking (Monje, Pons, et al., 2019). It was reported that heavy smokers were associated with 2 to 3 wall vertical bone loss (80.8%), and combined horizontal and vertical bone loss in heavy smokers was nearly non-existent (3.8%). In the present study, an association with smoking in late failures can be confirmed, but in the opposite direction; 42.1% of late failures in smokers occurred due to combined horizontal and vertical bone loss (Figure 11D). Moreover, neither age nor sex were significantly associated with type of bone loss. While early/late failure showed a strong correlation with type of bone loss, survival time did also in late failures in present results. Regarding implant brand, one canine study reported differences in defect width and concluded that the shape and size of peri-implant bone defects were influenced by different implant surfaces (Madi, Zakaria, & Kasugai, 2014). Another canine study reported no significant correlation and comparable tissue behaviour between implant surfaces (Madi, Zakaria, Noritake, Fuji, & Kasugai, 2013). The association between implant brand and type of bone loss could not be elucidated in this study.

## 4.3 Bone loss

Implant failure can occur at different levels of bone loss. In one study about implant fracture, 15% of bone loss lead to fracture due to the revelation of the embedded implant (Michailidis et al., 2013). Hence, it was asked for implant failure due to peri-implantitis, and mechanically

damaged implants were excluded. In the literature, there are opinion based proposals: a maximum of 50%, 66%, 75% bone loss or less than 3 mm remaining bone were regarded as criteria for implant failure (Lekholm et al., 1994; Misch et al., 2008). Considering the time between reaching 50% bone loss and diagnosis, a mean of 66.2% of bone loss in late implant failures in this study was to be expected. One reason for high MBL at explantation may be missing compliance to recall or generally low frequency of follow up radiographs.

Smoking as one of the main risk factors for implant failure may influence MBL (Monje, Pons, et al., 2019). In this study on implant failure, there was no statistically significant difference for late failures between smokers and non-smokers with a mean of 68.6% bone loss with 3.42 mm residual alveolar bone and 66.2% bone loss with 3.83 mm residual alveolar bone, respectively.

The association with the jaw may be explained by different bone qualities. Bone quality is most often assessed by a scale of 1 to 4 ascending from hard to soft and mainly compact to mainly trabecular bone (Lekholm & Zarb, 1985). The mandible, predominantly with bone quality 1 and 2, provides higher implant stability with fewer bone than the maxilla. Therefore, symptoms like mobility may appear at a further progressed stage. Furthermore, the dentist may therefore assess the implant differently in the lower jaw. Bone qualities of type 4 followed by type 1, meaning too low and high bone densities, are associated with slightly higher total implant failure rates (Chrcanovic, Albrektsson, & Wennerberg, 2017). Even with no difference in implant failure rates between the jaws, bone may be lost more progressively in the mandible. Similar to risk of implant failure, the amount of MBL between the jaws in peri-implantitis cases is controversial. No study was found that looked for differential bone level at explantation or failure in relation to jaw. Some studies support the present data and report more peri-implantitis associated bone loss around stable implants in the mandible (Cecchinato et al., 2017; Derks et al., 2016a), and one study in the anterior mandible compared to any other region (Fransson et al., 2010), while other studies report more progressive bone loss in the maxilla (Pikner & Gröndahl, 2009). One study reported the highest number of implants involving >2/3 bone loss in the incisor area of the maxilla but had only limited data on the molar area (Serino & Turri, 2011). Most authors concluded that anatomical differences may attribute to the effect, such as thin buccal plate in anterior maxilla. The MBL in the posterior mandible leading to implant failure, which was most severe in this study is especially difficult for future bone augmentation procedures. The vertical dimension cannot be bypassed such as in the upper jaw with sinus floor elevations and poses a challenging surgical situation. Sinus floor elevations are reflected in that the posterior maxilla is strongly associated to usage of bone substitutes, while bone substitutes were less frequently used in the mandible (Figure 13). The maxillary sinus and sinus floor elevations may also be the reason why 50.0 ± 29.4% bone loss with 5.44 ± 2.52 mm residual alveolar bone in the posterior maxilla (n=21) was far below average in this study,

while the anterior maxilla (n=10) with 73.9 ± 37.0% bone loss with 3.25 ± 3.34 mm residual alveolar bone perfectly fit in the rest of the data of late implant failures (Figure 10). Perhaps implants in augmented sinus may suffer from mobility at less MBL.

Some authors agree that there is no level of relative bone loss (except 100%) that indicates an implant has failed (Greenstein & Cavallaro, 2014). Increased MBL leads to higher concentration of occlusal forces (Serino & Turri, 2011), and concomitantly to deeper pockets with higher pathogen load (Belibasakis & Manoil, 2020; Monje et al., 2020); hence, bone loss accelerates. On the other hand, implants can remain stable at low bone level, a steady state may be reached (Buser et al., 2012; Chrcanovic et al., 2018), and peri-implantitis treatment may be successful at high MBL (Khoury & Buchmann, 2001). Therefore, implants affected with a high MBL should not be condemned prematurely (Greenstein & Cavallaro, 2014). The defect type critically influences prognosis of peri-implantitis surgery (Schwarz, Sahm, Schwarz, & Becker, 2010).

## 4.4 Early vs. late implant failure

Early implant failure occurs primarily because of failure to establish osseointegration (Esposito et al., 1998a). This goes in line with the association of peri-implant gap with early implant failure. Definitions of early implant failure vary, and most studies differentiate between pre- and post-loading. In this sample 17.2% of implants were removed within one year after implant placement, which is largely in accordance with the literature (Antalainen, Helminen, Forss, Sandor, & Wolff, 2013; Moraschini et al., 2015) despite that it was asked for peri-implantitis affected implants. One study reported better health and younger age as an indicator for early implant failure in comparison to late implant failure (Manor et al., 2009). Although there was no association for age in the present study, the results follow the trend that patient associated risk factors such as smoking were more common in late implant failures and site specific risk factors such as implant length and bone substitutes were more common in early failures which mandate a higher surgical skill. The theory that surgical mismanagement is the main cause for early implant failure has been articulated by some publications. Some centres report most implants fail early (A. M. Roos-Jansåker et al., 2006) and in a 10 year-study 88.2% of all implant failures are accounted as early failures (Montes et al., 2007). The latter study is especially interesting as all implants were installed by postgraduate students and in 75% of the cases implants failed without apparent clinical cause. In the present study there is a strong association for early vs. late implant failure with office. Whether these results are due to challenging surgical situations, office philosophy, implant brand or unknown confounders remains unclear.

## 4.5 Survival time

The dental office and implant brand also showed a strong association to survival time in late implant failures. Significant correlations other than increasing age disappear in multilevel analysis clustered for patient, office, and implant brand. Reasons that in some dental offices the survival time of implant failures was longer than in others may include the patient selection, prosthetic rehabilitation, or education about implant maintenance therapy since surgical skill can be excluded in this highly selective sample of specialists. Albrektsson and Zarb stated that "peri-implantitis is an operator-facilitated treatment outcome" (Albrektsson & Zarb, 2018). The surgeon and implant brand may influence early and late implant failure (Derks et al., 2015; Jemt, 2018), but for late implant failure both are controversial (Jemt, 2017b; Manor et al., 2009). The present data cannot contribute to this discussion because choice of implant brand and dental office are highly interlinked, and the explant sample does not allow to draw conclusions about risk factors.

The strongest association with survival time showed age at implantation. The mean survival time of explants with late failure was 9.5 ± 5.8 years and in the analyses, a 10-year higher age at implantation was associated with a 2-year smaller survival time. A correlation between implant failure and age has been confirmed by a variety of studies (Jemt, 2018; Moraschini et al., 2015; Moy, Medina, Shetty, & Aghaloo, 2005; Porter & von Fraunhofer, 2005). Being of older age decreases trabecular number and thickness and therefore the trabecular bone volume fraction (Majumdar et al., 1997). This is reflected in higher parathyroid hormone secretion with age, both in men and women (Chapuy, Durr, & Chapuy, 1983). Advanced age has also been described to change mineral composition, collagen, bone morphogenetic proteins and fracture healing (Esposito et al., 1998b). Osteocytes have a life span of about 35 years and lacunae mineralize after cell death, leading to sclerotic brittle bone (Van Steenberghe, Quirynen, Molly, & Jacobs, 2003). Further, vascular supply of the bone constrains (Van Steenberghe et al., 2003). Hence, bone quality and ability of apposition is reduced, which may diminish osseointegration. Still, the data indicates that the osseointegration process is not as much adversely influenced by aging as the ability to maintain osseointegration. There seems to be no correlation for survival time in implant failure for sex despite the risk for osteoporosis in postmenopausal women (Antalainen et al., 2013). Osteoporosis also has only little effect on implant failure (Alsaadi et al., 2007; Tsolaki, Madianos, & Vrotsos, 2009), and once primary stability has been achieved, it seems that bone quality plays a minor role for implant failure in comparison with immunological changes due to aging. There are strong correlations between age and the immunologic landscape. Especially the proinflammatory cytokine interleukin (IL) 6, the main cytokine mediator of the immune response (Pickup & Crook, 1998), is increased in older people, which is also known to be

increased in peri-implantitis (Carr et al., 2016; Konttinen et al., 2006; Ooms, 2017). The reduction to cope with stressors and functional restriction of the innate and adaptive immune response is called “inflamm-aging” and described as a major characteristic of the aging process (Franceschi et al., 2000). Concluding, the immune system, which is significantly influenced by age and other important risk factors (Lindhe & Meyle, 2008), plays a major role in peri-implant bone loss and the immune response is a two-edged sword. Surgical skill and protocol and the individual immune response may be the major factors for implant failure.

## 4.6 Strengths and limitations

This is the first study combining data for explanted implants with corresponding radiographs, thereby providing accurate calculations for bone loss and evaluation of type of bone loss.

In this study, there were no radiographs at implant placement, loading or follow up available, so the progression of the bone defect could not be assessed. Two-dimensional radiographs only show the mesial and distal implant site, vestibulo-oral defects are superimposed by the implant and hidden in the third dimension. This leads to regions escaping detection for evaluation, which may likely have the deepest defect depth since MBL was reported to occur predominantly on the buccal site (Monje, Pons, et al., 2019). Further, a buccal dehiscence may be mistaken for horizontal bone loss. Still, radiographic examination is the most reliable method to assess peri-implant bone loss (Misch et al., 2008). Not all radiographs were periapical, some were panoramic and there were differences in the quality. However, radiograph type had no statistically significant influence on relative bone loss or residual alveolar bone, nor the decision which type of bone loss was present (Table 2). Measuring lengths by counting pixel performed the best possible evaluation. Additionally, the radiographs were well calibrated by measuring implants on length that originally had bone contact, and strict eligibility criteria. Intra-examiner differences showed acceptable results despite the possibility of many errors. In the literature, radiographic analysis shows a positive predictive value for implant failure of 83%, and there are also cases of clinically confirmed failed implants that could not be detected radiographically (Grondahl & Lekholm, 1997). These might partially explain implant removal with bone loss <30%. In this study, the amount and types of bone loss were evaluated only by radiographs. To the author’s knowledge, this is the first study comparing marginal bone loss, peri-implant gap, and apical inflammation.

Questionnaires open a full spectrum of limitations. Only a few questionnaires were completely answered. The MICE and the MID procedure, as well as mixed-effects models handled the multilevel structure of the data appropriately via inclusion of random effects for office and patient. However, the sample size was small and not large enough for complex statistical modelling like multinomial logistic regression of type of bone loss. Five explants for bone loss

and seven explants for type of bone loss with missing survival time were considered late failures after evaluation of respective radiographs.

This is a retrospective study, which might be biased. Some survival times were given in vague answers and periodontitis history did not consistently match the measurements. Periodontitis history might have an influence on survival time, bone loss, and type of bone loss since it is described as one of the main risk factors for peri-implantitis (Lindhe & Meyle, 2008).

## 4.7 Outlook

Treatment of peri-implant mucositis probably prevents the development of peri-implantitis (Heitz-Mayfield & Salvi, 2018; Lang, Salvi, & Sculean, 2019). Hence, different treatment strategies for peri-implant mucositis and early, moderate, and advanced peri-implantitis (Froum & Rosen, 2012) should be developed and investigated. Further, risk factors should be categorized as slight, moderate, and severe to simplify individual risk profiles for recall, follow up radiograph, and maintenance frequency, as well as prognosis of treatment modalities.

Concerning the treatment prognosis, patient related risk factors (especially current smoking, poorly controlled diabetes, history of periodontitis, poor oral hygiene, and immune response correlating diseases such as Crohn's disease), general state of health and office specific surgical skill and protocol should realistically be considered. Further, the hard and soft tissue situation (quality, quantity, inside/outside the contour, keratinized mucosa) and possibilities of the prosthetic rehabilitations should be evaluated regarding expenses and the financial situation of the patient, and the value to effort ratio based among others on the age of the patient.

The primary cause for peri-implant bone loss is not conclusively clarified and for many possibly influencing factors only limited data is available. Surgeons working with implants should know about sufficiently proven risk factors, therapy options and prognosis. "A deep understanding is needed for differentiation between long-term behavior of marginal bone around implants and that which occurs in periodontal disease" (Zarb & Albrektsson, 1991). In challenging situations, less trained dentists should refer to specialists. When subjected to peri-implantitis, the value to effort ratio of treatment options should be calculated for the individual patient and office (Kim et al., 2014) and be discussed with the patient regarding oral health-related quality of life (Kern, Kern, Wolfart, & Heussen, 2016; Mack et al., 2005). The patient needs to be informed on the the negative consequences of poor adherence to oral hygiene and positive effects of maintenance therapy as well as effects on the general state of health and vice versa.

# 5 Abstract

**Objectives**: Clear guidelines on when to remove an implant are missing. This study aimed to evaluate the amount of peri-implant bone loss at explantation by specialists.

**Material and Methods**: Implantology specialists were asked to provide implants explanted due to peri-implantitis with related clinical information. Questionnaires inquired age, sex, smoking habit, implant location, usage of bone substitutes, and implant brand. Early failures (survival time <12 months) were analysed separately. Explants were measured and bone loss and type of bone loss were assessed using radiographs. Bivariate analysis was used for the type of bone loss, and covariate-adjusted mixed-effects models were evaluated for the amount of bone loss and survival time.

**Results**: Twelve dental offices provided 192 explants from 161 patients with 99 related radiographs. Most implants were affected by vertical bone loss (51.1%), followed by combined horizontal and vertical bone loss (22.3%), peri-implant gap (11.7%), horizontal bone loss (10.6%), and only a few by apical inflammation (4.3%). Thirty-three (17.2%) explants were early failures. Type of bone loss was significantly associated with survival time and implant brand. Implant brand also showed a significant correlation with early/late implant failure. Excluding early failures, combined horizontal and vertical bone loss was additionally significantly associated with smoking, and the location when grouped to incisor, canine, premolar, and molar showed a significant association with the type of bone loss. Further, the average survival time was 9.5 ± 5.8 years with absolute and relative bone loss of 7.0 ± 2.7 mm and 66.2 ± 23.7%, respectively. Late failures were removed at a mean bone loss of 50.0% with 5.44 mm residual alveolar bone in the posterior maxilla and 73.8% with 2.89 mm residual alveolar bone in other locations. In fully adjusted mixed-effects models, only the age at implantation (B=-0.19; 95% CI: -0.27 to -0.10) remained a significant factor for survival time. Implants exhibited significantly more relative bone loss if they were positioned in the mandible (B=17.3; 95% CI: 3.91 to 30.72) or if they were shorter (B=-2.79; 95% CI: -5.50 to -0.08).

**Conclusions**:
Though the mean bone loss (66.2%) at which implants were explanted was in accordance with the literature, its wide variation and differentiation between the posterior maxilla and other locations showed that the profession has no universally accepted threshold beyond which an implant cannot be preserved.

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# 7 Supplemental Appendix

**Supplement Table 1.** Overview of normality distributions of numeric variables

| Variable | Sample | Test | p-value |
|---|---|---|---|
| Survival time | All implants | Shapiro-Wilk | <0.001 |
| Age at implantation | All implants | Shapiro-Wilk | 0.281 |
| Age at explantation | All implants | Shapiro-Wilk | 0.042 |
| Implant length | All implants | Shapiro-Wilk | 0.241 |
| Rel. bone loss | All implants | Shapiro-Wilk | 0.001 |
| Abs. bone loss | All implants | Shapiro-Wilk | 0.668 |
| Residual alv. bone | All implants | Shapiro-Wilk | 0.001 |
| | | | |
| Survival time | Only late implant failure | Shapiro-Wilk | <0.001 |
| Age at implantation | Only late implant failure | Shapiro-Wilk | 0.051 |
| Age at explantation | Only late implant failure | Shapiro-Wilk | 0.035 |
| Implant length | Only late implant failure | Shapiro-Wilk | 0.219 |
| Rel. bone loss | Only late implant failure | Shapiro-Wilk | 0.025 |
| Abs. bone loss | Only late implant failure | Shapiro-Wilk | 0.349 |
| Residual alv. bone | Only late implant failure | Shapiro-Wilk | 0.010 |

Testing numeric variables of total implant sample and late implant failures for normality distribution using the Shapiro-Wilk test. P-values <0.05 are highlighted and describe non-normally distributed data.

## 7.1 List of abbreviations

ANOVA……...analysis of variance
Abs……..absolute
Alv……..…..alveolar
Ant……anterior
IL……...interleukin
MBL……..marginal bone loss
OPG……..orthopantomogramm
Post……posterior
Rel……relative
SD……..……standard deviation
vs……versus
2D……..two dimensional

p-value (p): the probability of obtaining the observed results under the assumption that the null hypothesis is correct.

95% confidence interval (CI): range which contains the true parameter with a probability of 95%.

Beta coefficient (B): estimate for magnitude of the effect resulting from linear regression analysis with standardized data.

## 7.2 Publication

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ORIGINAL ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

# At which bone level are implants explanted?

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## Abstract

**Objectives:** Clear guidelines when to remove an implant are missing. The aim of this study was to evaluate the amount of peri-implant bone loss at explantation by specialists.

**Material and Methods:** Implantology specialists were asked to provide implants explanted due to peri-implantitis with related clinical information. Early failures (survival time <12 months) were analyzed separately. Questionnaires inquired age, sex, smoking, implant location, usage of bone substitutes, and implant brand. Explants were measured and bone loss was assessed using radiographs. Covariate-adjusted mixed-effects models were evaluated for bone loss and survival time.

**Results:** Twelve dental offices provided 192 explants from 161 patients with 99 related radiographs. Thirty-three (17.2%) explants were early failures. Excluding early failures, average survival time was 9.5 ± 5.8 years with absolute and relative bone loss of 7.0 ± 2.7 mm and 66.2 ± 23.7%, respectively. Late failures were removed at mean bone loss of 57.7% in the maxilla and 73.7% in the mandible irrespective of survival time. In fully adjusted mixed-effects models, only age at implantation ($B = -0.19$; 95% CI: −0.27, −0.10) remained a significant factor for survival time. Implants exhibited significantly more relative bone loss if they were positioned in the mandible ($B = 17.3$; 95% CI: 3.91, 30.72) or if they were shorter ($B = -2.79$; 95% CI: −5.50, −0.08).

**Conclusions:** Though the mean bone loss (66.2%) at which implants were explanted was in accordance with the literature, its wide variation and differentiation between jaws showed that the profession has no universally accepted threshold beyond which an implant cannot be preserved.

KEYWORDS

alveolar bone loss, dental implant, jaw, multilevel analysis, peri-implantitis, radiography, treatment failure

## 1 | INTRODUCTION

Frequency of dental implant failure is <5% within ten years (Moraschini et al., 2015) and <10% within 20 years (Lekholm et al., 2006). Since implantation becomes globally more common, the actual number of implant failure increases.

Implant failure describes implant loss or a condition that requires removal of the implant (Misch et al., 2008). Reasons for implant failure can be divided into biological, mechanical, and iatrogenic failure as well as inadequate patient adaption. Clinical criteria for removal are "(a) pain on palpation, percussion or function, (b) horizontal and/or vertical mobility, (c) uncontrolled progressive bone loss, (d) uncontrolled exudate, or (e) more than 50% bone loss around the implant" (Misch et al., 2008).

Implant removal within 12 months after implantation is regarded as early implant failure (Albrektsson, 1988; Jemt, 2018a). Early implant failure occurs primarily because of failure to establish osseointegration (Esposito et al., 1998a). Immediately after surgery, osseous wound healing is disturbed and a fibrous capsule is formed around the implant, accompanied by scar tissue and/or epithelial downgrowth, which may lead to mobility (Esposito et al., 1999). Local as well as systemic factors such as radiotherapy, poorly controlled diabetes mellitus or smoking can interfere with osseointegration (Alsaadi et al., 2007; Chen et al., 2013; Lange et al., 1993; Naujokat et al., 2016). Peri-operative contamination, unskillful surgical management of hard and soft tissue, lack of primary stability, and surgical trauma such as bone overheating seem to be the most important causes of early implant failure (Baqain et al., 2012; Esposito et al., 1998b; Jemt, 2017a; Kourtis et al., 2004).

Late implant failure occurs because osseointegration breaks down over the years (Esposito et al., 1998a). The main reason for late implant failure is peri-implantitis (Kourtis et al., 2004; Solderer et al., 2019). Peri-implantitis describes an inflammation around the functioning implant accompanied by loss of supporting crestal bone beyond physiological bone remodelling (Sanz et al., 2012). Though not undisputed, the majority of the profession thinks peri-implantitis is a microbiological driven disease and that microbiota play a decisive role in the inflammatory process and the ensuing bone loss (Albrektsson et al., 2016). The microbiota of peri-implantitis and periodontitis are comparable although peri-implantitis is a more complex and heterogeneous infection (Eick et al., 2016; Lafaurie et al., 2017). The shift from a healthy peri-implant situation to peri-implantitis goes along with a gradual decrease of commensal bacteria and an increase in putative typically periodontitis associated pathogens (Belibasakis & Manoil, 2020). Also, the number of bacteria increases with progressing marginal bone loss (Monje et al., 2020). Microbial plaque accumulation boosted by insufficient rehabilitation causes peri-implantitis. Major contributing factors are poor oral hygiene and lack of peri-implant maintenance therapy (Lindquist et al., 1996; Monje et al., 2016). Also, poor prosthetics (misfit of the supraconstruction, excess cement, and accessibility for hygiene measures) impact on implant failure (Jemt, 2017b; Serino & Ström, 2009). Furthermore, there seems to be a higher risk to develop peri-implantitis for smokers, for patients with periodontitis, or for those having systemic diseases such as poorly controlled diabetes mellitus (Naujokat et al., 2016; Safii et al., 2010; Strietzel et al., 2007). A correlation between bone augmentation and implant failure is controversial (Khoury & Hanser, 2015; Tonetti & Hämmerle, 2008; Tran et al., 2016). Peri-implantitis and late implant failure occurred frequently in a small subset of individuals (Derks et al., 2016; Jemt, 2017b). Clustering of implant failure within patients occurs because risk factors cluster and amplify susceptibilities.

In contrast to teeth, implants remain stable until osseointegration is lost at the last apical aspect (Solderer et al., 2019). In many studies, survival time and number or percentage of lost implants are reported, but it is often not clear at which level of bone loss the implants are explanted. We did not find publications, which have measured the actual bone loss concurrent with explantation; only suggestions, when implants are considered as a failure, were reported. Clear guidelines are still missing (Solderer et al., 2019). This multicentre study reports the bone level at explantation and survival time of explants from 12 in implantology specialized dental offices in Germany. We tried to answer the following questions: Is there a universally accepted bone level beyond which implants are not preserved? And which factors influence bone loss and survival time of explants?

## 2 | MATERIAL AND METHODS

### 2.1 | Study design and collection of extracted implants

In order to recruit dentists, the goals of this study were presented online on the forum of the International Team for Implantology (ITI) and European Centers for Dental Implantology (ECDI). In addition, some offices were contacted directly, resulting in a sample of highly specialized implantologists. Questionnaires were sent to accepting offices asking them for implants removed due to peri-implantitis as well as related clinical and demographic data and radiographs if available (Question for dentists: Wir bitten Sie, uns Periimplantitis betroffene, nicht erhaltungsfähige Implantate zuzusenden. Please send us peri-implantitis affected, non-preservable implants). As we noticed that explants were sent in with survival times <1 month, a question concerning the reason of explantation was added on the questionnaire. After integration of this question, 40 additional questionnaires returned including 34 late failures and six early failures with survival times between 3 and 7 months. Three of those early failures were reported with peri-implantitis and three with missing osseointegration. All participants gave informed written consent and the study was approved by the Ethics Committee of the University of Greifswald (registration: BB 16/12).

Using a questionnaire, we asked for the implant brand, region in the jaw, bone substitutes material (if used), date of implantation and explantation, sex, age (years), smoking habits (current non-smoker, current smoker), pre-existing periodontitis, cardiovascular

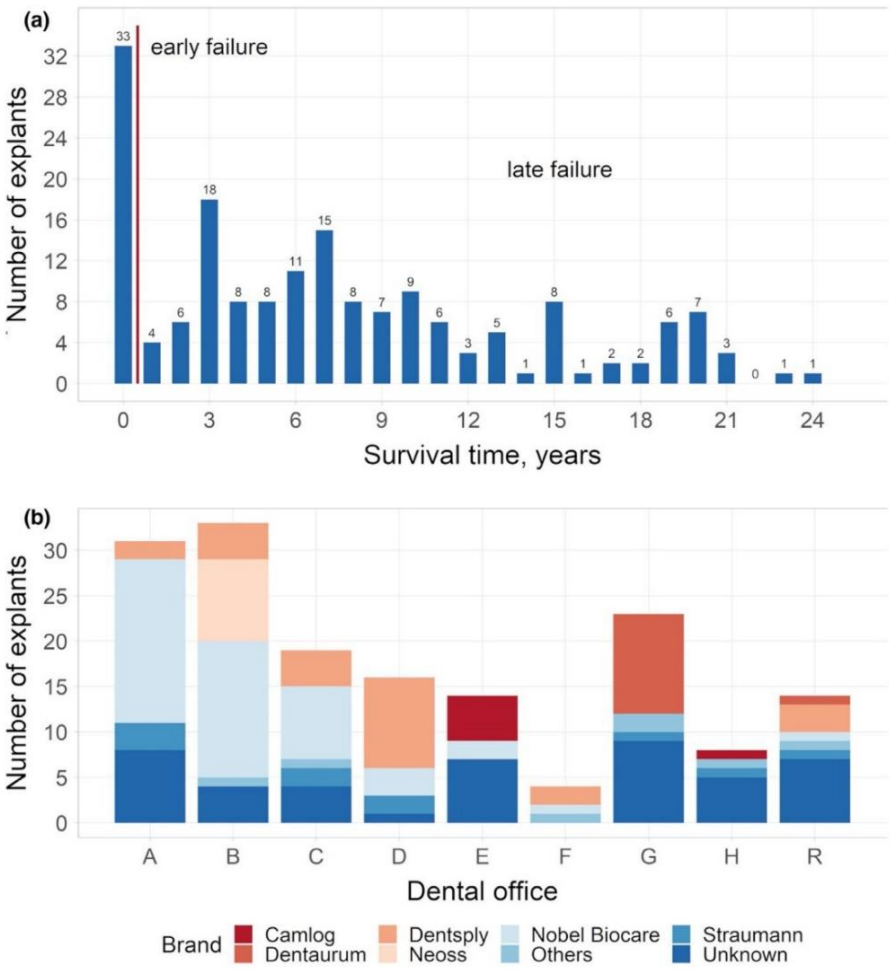


**FIGURE 1** Distribution of survival time (a) and implants brands (b). (a) Bar chart displaying the number of explants according to survival time. There were 33 early failures (left), 140 late failures with known survival time (right). (b) Stacked bar chart displaying the distribution of implant brands of late losses across implanting dental offices. For graphical display, all dental offices contributing <5 patients were combined to one group (R) ($n = 159$)

diseases, and medications of the patients. Answers for cardiovascular diseases and the corresponding medications had large variations and were therefore not considered in further analyses. Reported periodontitis was reassessed on panoramic radiographs (if available). Because vast inconsistencies with questionnaires were identified, information on pre-existing periodontitis was not considered any further. All dentists sent their explants in vials either with saline or with glutaraldehyde, which arrived at the dental school in Greifswald between May 2012 and February 2015. All explants were stored in a 4°C fridge.

## 2.2 | Implant and bone loss measurements

On the explants, two measurements were taken with a video camera (Power HAD 3CCD. Sony, Köln, Germany) connected to an incidental light microscope (SZH-10 Research Stereo Microscope. Olympus Optical, Hamburg, Germany) using an image analysis software (Olympus Soft Imaging Solutions GmbH, Münster, Germany). The first measurement of the explant served for the calibration of the radiograph, the second determined the implant length that originally had bone contact, measured from the implant shoulder or in case of transgingival implant design from the presumptive smooth-rough border to the apex. In order to calculate bone loss, the residual bone was measured on the calibrated radiograph as the least distance between marginal bone level and the apex.

Panoramic and intraoral radiographs were provided for 80 explants (65 patients) and 38 explants (34 patients), respectively. Bone loss on these radiographs was measured with the above-named image analysis method and recorded in millimeter (absolute) and as percentage (relative). For 74 explants (62 patients), no radiographs were obtained.

For validation, bone loss measurements were replicated. Intraclass correlation coefficients (ICC) for individual absolute agreement were calculated (relative bone loss ICC 0.948 and absolute bone loss ICC 0.967). Moreover, consistency was graphically checked using Bland–Altman plots (Figure S1).

## 2.3 | Statistical analysis

Descriptive statistics comprised calculation of means and standard deviations for continuous data or assessment of frequency distributions for categorical data. Normality of continuous variables was checked using Shapiro–Wilk tests. $p$-values for differences between early and late failures were obtained via $t$-tests for normally distributed continuous variables, Wilcoxon rank-sum tests for

non-normally distributed continuous variables and Chi-square tests for categorical variables. For clarity of graphical display, dental offices with <5 patients and implant brands with ≤5 implants were pooled and IMZ, Xive, Ankylos, and Astra Tech were combined to the group "Dentsply". Except for the graphical display of survival time (Figure 1a), early failures were excluded from subsequent analyses. Depending on the type of variables, bivariate linear regression analyses, *t*-tests, Chi-square tests, or Kruskal–Wallis tests were applied to examine pairwise interrelations.

For graphical display of associations between different variables, scatterplots and box plots were utilized. In scatterplots, spline-smoothers with 95% confidence bounds were provided. Circle sizes were proportional to the number of implants clustered in the same patient with identical dates of implantation and explantation (see Figure 3).

Covariate-adjusted mixed-effects linear regression models (including random intercepts for office and patient) were performed to evaluate associations of potential risk factors (age, sex, smoking, jaw, implant location, implant length, and usage of bone substitutes) with survival time and relative bone loss of implants. For fixed effects, linear regression coefficients (B), 95% confidence intervals (CI) and respective p-values were reported.

Since complete data were only available for 36 implants (30 late failures and 6 early failures), missing value imputation was performed on patient and implant level using the multiple imputation by chained equations (MICE) procedure. As suggested by Hippel (von Hippel, 2007) a multiple imputation followed by deletion (MID) approach was used. Detailed information on the imputation process is provided in Table S1. As a result, two samples, comprising 140 and 66 explants, were obtained for analyses on survival time and relative bone loss, respectively (amount of imputed information is given in Tables S2 and S3).

No a priori analysis was performed to determine the sample size required to test for specific differences to literature values for mean bone loss of explants or proportion of early failures. However, given a proportion of 30% early failures, a sample size of 62 would achieve about 90% power to detect a −20% difference to random assignment of early/late failure.

All statistical analyses were performed using Stata 14.2 (StataCorp., 2015) and R 3.5.1 (R Development Core Team, 2008). Two-sided P-values <0.05 were considered statistically significant.

Strengthening the reporting of observational studies in epidemiology (STROBE) guidelines were followed (von Elm et al., 2007).

## 3 | RESULTS

### 3.1 | Description of explants

Twelve German dental offices provided 192 explants from 161 patients with 99 related radiographs. Regarding all 192 explants, 133 patients lost one, 25 lost two, and three patients lost three implants and survival time ranged from <1 month to 25 years (Figure 1a). Mean age at implantation was 53.0 ± 12.1 years and mean age at explantation was 60.9 ± 12.1 years. Nobel Biocare was the most used implant brand (29.7%), followed by Dentsply (14.1%), Camlog (8.3%), Straumann (7.3%), Dentaurum (7.3%), Neoss (4.7%), and others (5.7%). In 22.9% of cases, the implant brand could not be specified. Regarding the distribution of implant brands, there was only small heterogeneity of brands within dental offices: three offices mainly sent Nobel Biocare explants, three others mainly sent either Dentsply, Camlog, or Dentaurum explants and only one office sent Neoss explants (Figure 1b).

Thirty-three explants (17.2%) were early failures. For survival time analysis of late failure explants, early failures and explants with missing survival time ($n = 19$) were excluded, leaving 140 explants (Table 1). Late failure explants exhibited 9.5 ± 5.8 years survival time and relative and absolute bone loss of 66.2 ± 23.7% and 7.0 ± 2.7 mm, respectively. Regarding radiographic analysis, early failures ($n = 33$), not radiographically matching and damaged explants ($n = 47$), explants with missing radiographs ($n = 33$) and radiographs of inadequate quality or with apical inflammation ($n = 13$) were excluded, resulting in 66 explants with measured bone loss (Figure 2). Statistically significant differences between early and late failures were observed for age at explantation ($p < .01$), smoking ($p = .03$), implant length ($p = .02$) and relative bone loss ($p = .05$). Interestingly, late failures were about 0.9 mm longer than early failures and respective patients were more often smokers (Table 1).

### 3.2 | Analysis of late failure explants

Figure 3 depicts associations of different factors with survival time for late failures. Younger age at implantation was significantly associated with longer survival ($p < .01$, Figure 3a). Moreover, longer implants also tended to stay longer in situ ($p = .04$, Figure 3b). However, neither absolute nor relative bone loss levels correlated with survival time (Figure 3c,d), whereas explants with initial usage of bone substitutes survived significantly shorter than those without ($p < .01$, Figure 3e). The median survival time of dental offices with at least 5 explants primarily ranged between 6.9 and 8.4 years with two divergent offices with mean explantation times of 3.4 and 19.1 years ($p < .01$, Figure 3f).

Figure 4 describes associations of different factors with measurements of absolute and relative bone loss. Late failures were explanted at a mean relative bone loss of 66.2%. Longer implants showed significantly higher values of absolute bone loss at extraction ($p < .01$, Figure 4a), whereas relative bone loss did not notably differ according to implant length (Figure 4b). The median bone loss of maxilla explants equalled 53.0% or 5.8 mm, while relative and absolute median bone loss of mandible explants were significantly higher at 72.8% or 7.0 mm ($p < .01$, Figure 4c). Different dental

**TABLE 1** Characteristics of examined explants

| | n | Total Sample (n = 192) | n | Late failures (n = 159) | n | Early failures (n = 33) | p-value |
|---|---|---|---|---|---|---|---|
| Sex | | | | | | | 0.13 |
| Male | | 85 (44.3) | | 66 (41.5) | | 19 (57.6) | |
| Female | | 101 (52.6) | | 87 (54.7) | | 14 (42.4) | |
| Unknown | | 6 (3.1) | | 6 (3.8) | | 0 (0.0) | |
| Age at implantation, years | 147 | 53.0 ± 12.1 | 116 | 53.0 ± 11.8 | 31 | 53.2 ± 13.3 | 0.93 |
| Age at explantation, years | 157 | 60.9 ± 12.1 | 126 | 62.7 ± 11.1 | 31 | 53.6 ± 13.3 | <0.001 |
| Survival time, years | 173 | 7.7 ± 6.4 | 140 | 9.5 ± 5.8 | 33 | 0.4 ± 0.3 | <0.001 |
| Smoking | | | | | | | 0.03 |
| No | | 119 (62.0) | | 92 (57.9) | | 27 (81.8) | |
| Yes | | 48 (25.0) | | 44 (27.7) | | 4 (12.1) | |
| Unknown | | 25 (13.0) | | 23 (14.5) | | 2 (6.1) | |
| Jaw | | | | | | | 0.79 |
| Maxilla | | 95 (48.4) | | 77 (48.4) | | 16 (48.5) | |
| Mandible | | 89 (46.4) | | 75 (47.2) | | 14 (42.4) | |
| Unknown | | 10 (5.2) | | 7 (4.4) | | 3 (9.1) | |
| Location | | | | | | | 0.32 |
| Incisor or canine | | 50 (26.0) | | 44 (27.7) | | 6 (18.2) | |
| Premolar or molar | | 132 (68.8) | | 108 (67.9) | | 24 (72.7) | |
| Unknown | | 10 (5.2) | | 7 (4.4) | | 3 (9.1) | |
| Implant length, mm | 138 | 10.5 ± 1.9 | 111 | 10.7 ± 1.9 | 27 | 9.8 ± 1.7 | 0.03 |
| Bone substitute material | | | | | | | 0.06 |
| No | | 101 (52.6) | | 86 (54.1) | | 15 (45.4) | |
| Yes | | 42 (21.9) | | 30 (18.9) | | 12 (36.4) | |
| Unknown | | 49 (25.5) | | 43 (27.0) | | 6 (18.2) | |
| Absolute bone loss, mm | 74 | 7.1 ± 2.7 | 65 | 7.0 ± 2.7 | 9 | 7.8 ± 2.1 | 0.26 |
| Relative bone loss, % | 75 | 68.3 ± 24.4 | 66 | 66.2 ± 23.7 | 9 | 83.4 ± 25.9 | 0.045 |

*Note:* Data are presented as mean ± *SD* or number (percentage). Varying numbers occurred as a consequence of missing information on different variables. *p*-values were obtained via *t*-tests for normally distributed continuous variables, Wilcoxon rank-sum tests for non-normally distributed continuous variables and Chi-square tests for categorical variables. Unknown values were not considered as separate variable categories.

offices removed implants at a median relative bone loss between 55% and 80%, with greater intra-office variability with increasing number of explants per office and no statistically significant difference between offices (Figure 4d).

We finally assessed effects of potential risk factors on survival times of late implant failures (Table 2) and relative bone loss (Table 3) employing mixed-effects linear regression models. For late implant failures, only age at implantation was significantly negatively associated with survival time (B = −0.19, 95% CI: −0.27, −0.10, Table 2). In example being 10 years older at implantation is associated with on average two years shorter survival time in case of implant failure. Relative bone loss at the time of explantation (Table 3), was significantly associated with jaw and implant length. Mandible implants exhibited about 17.3% more relative bone loss than those located in the maxilla ($p$ = .01). Also, each mm of a higher implant length was associated with 2.8% less relative bone loss at explantation ($p$ = .04, Table 3).

## 4 | DISCUSSION

12 German dental offices, specialized in implantology, provided 192 dental explants. 17.2% of the implant failures were early failures. Late failing implants (average implant length 10.7 ± 1.9 mm) were explanted at mean bone loss of 66.2% or 7.0 mm. The wide variation in bone levels suggests that the profession has no universally accepted threshold beyond which an implant cannot be preserved. Shorter implant length and non-smokers were more common in early failures. In late failures, a higher age at implantation was associated with less survival time until explantation. Implants placed in the mandible, probably due to bone quality, as well as shorter implants were explanted at more relative bone loss.

This study reports only on removed implants; we have no information on the total number of implants installed in the collaborating dental offices or on the risk profiles of those implants that are still in situ. Observations of this study are therefore valid for explants but do not allow conclusions toward potential risk factors for implant failure.

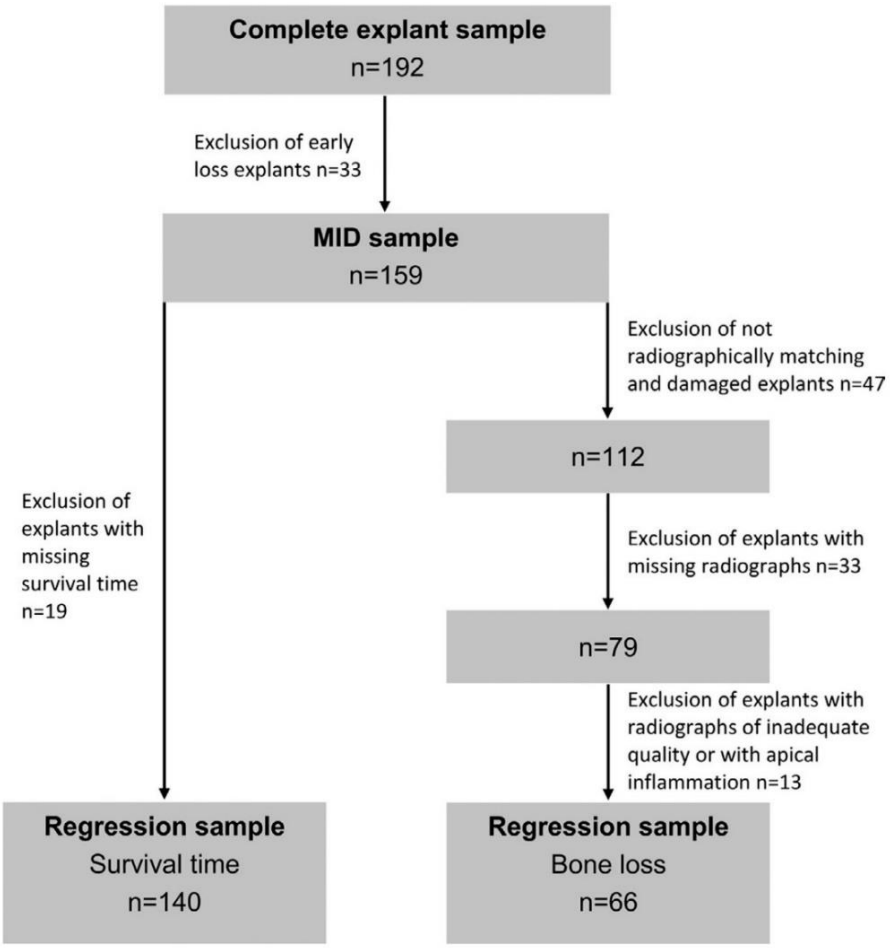


**FIGURE 2** Flow-chart describing the final samples for survival time and relative bone loss. MID method: multiple imputation followed by deletion of imputed outcomes

### 4.1 | Early versus late failure

In our sample, 17.2% of implants were removed within one year after surgery. In a population-based Swedish study which examined survival after 9 years, 36.1% of all implant failures were early failures (prior to connection of supraconstruction; Derks et al., 2015). A Greek study on private practice results reported 24% early failure (before placement of prosthetic restoration) at mean observation time of 4.6 years (Kourtis et al., 2004). A literature review reported approximately 30% early failure (after placement of the abutment and prosthetic loading) on 7,711 implants (Moraschini et al., 2015). A Finnish national registry study with an observation time of up to 18 years and with 198.538 implants reported that early failures (in the first 142 days) constituted a third of all failures (Antalainen et al., 2013). A systematic review, based on over 2,100 patients with approximately 5,200 implants calculated the prevalence of early failure (before loading) to 2.4% and total failure after 10 years to 6.9% (Pjetursson et al., 2012), which equals 35% of early failure after 10 years. A recent large study reported 642 failures out of 10.096 implants, whereby 49% were removed during the first 12 months after surgery (Chrcanovic et al., 2017). Though we asked for peri-implantitis affected implants, our data goes in line with these reports: If we restrict survival time to <10 years ($n = 118$), our early failures represent 28.0% of explants. Smoking is described as a risk factor for early as well as late implant failure (Strietzel et al., 2007). In the present study, a significant association of smoking with late implant failure was found compared to early failure (late: 27.7% smoker, 14.5% unknown versus early: 12.1% smoker, 6.1% unknown). Furthermore, implants with early failure were nearly 1 mm shorter (9.8 ± 1.7 mm) than implants with late failure (10.7 ± 1.9 mm), and these differences were even more intriguing, when looking at the relative bone loss (late: 66.2 ± 23.7% versus early: 83.4 ± 25.9%). Probably early failure happens more often in demanding anatomical situations with inadequate vertical and horizontal bone, which is reflected by use of shorter implants and more bone augmentation material (18.9% versus 36.4%) in our study. Including early failure, implants ≥10 mm had a considerably longer survival time compared to implants <10 mm (9.0 ± 6.5 years versus 5.5 ± 5.8 years). Our results indicate, that the failure rate is higher with shorter implants which is supported by two recent meta-analyses (Lemos et al., 2016; Papaspyridakos et al., 2018). Demanding anatomical situations still confer an increased risk despite the ease to use therapeutic options of shorter implants and of bone augmentation material. Even in the hand of experienced operators, early failure occurs in a considerable proportion, which has to be explained to patients before undergoing implant surgery.

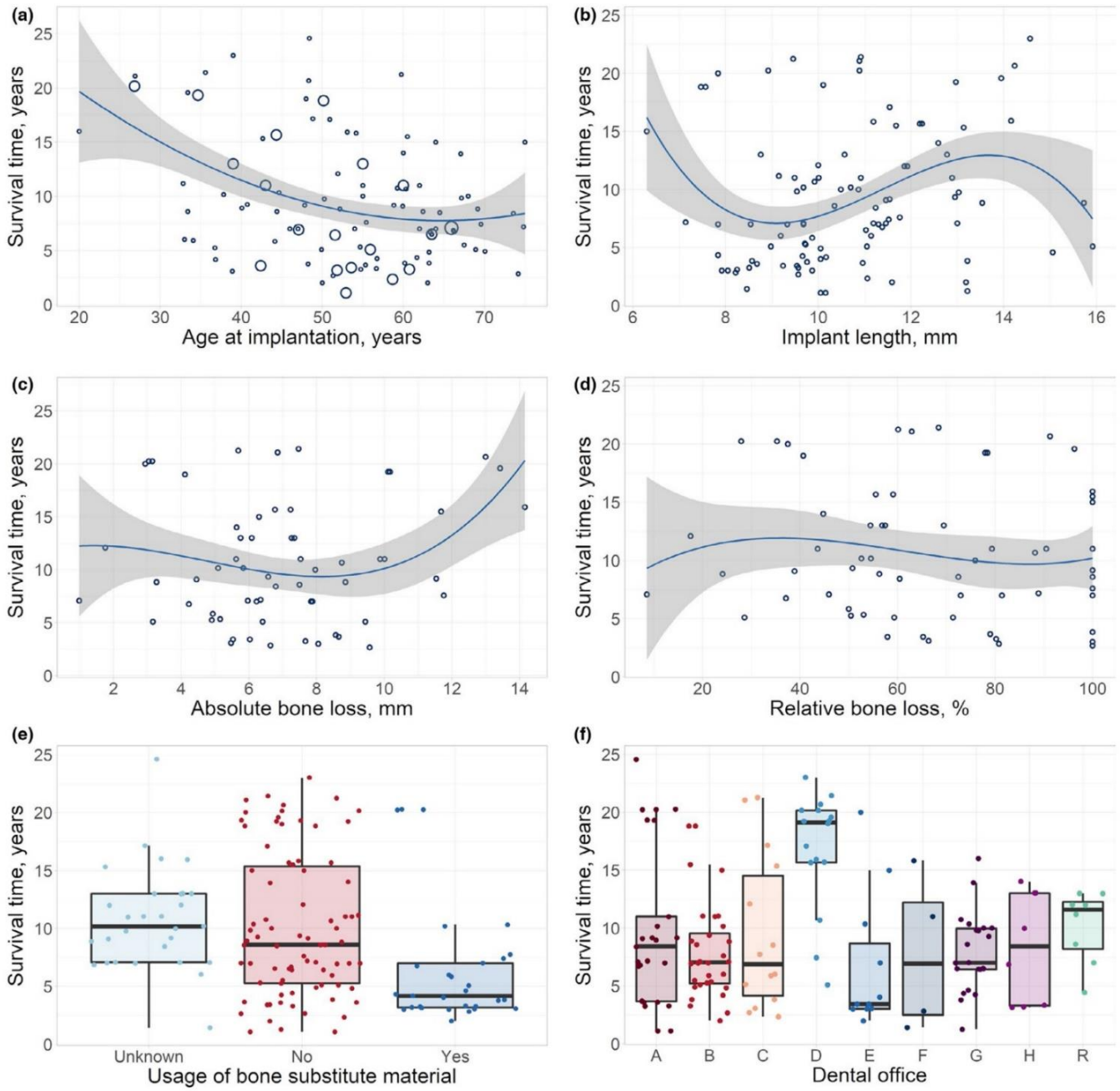


**FIGURE 3** Bivariate associations of age at implantation (a; $n = 116$, $p < .001$), implant length (b; $n = 99$, $p = .04$), absolute bone loss (c; $n = 60$, $p = .39$), relative bone loss (d; $n = 61$, $p = .47$), usage of bone substitute material (e; $n = 111$, $p < .001$; implants with unknown usage of bone substitute material were graphically displayed but not included in statistical testing) and dental office (f; $n = 140$, $p = .003$; all dental offices with <5 patients were combined to one group, R) with survival time of explants. In scatterplots, spline-smoothers with 95% confidence bounds are provided; circle sizes are proportional to the number of implants clustered in the same patient with identical dates of implantation and explanation

## 4.2 | Bone loss at late failure

To our knowledge, no study looked for the threshold of explantation in late failures. In the literature, there are opinion-based proposals: A maximum of 50%, 66%, and 75% bone loss or less than 3 mm remaining bone were regarded as criteria for implant failure (Lekholm et al., 1994; Misch et al., 2008). We found an average of ~60% of bone loss at an implant length between 9 and 14 mm or ~6 mm bone loss for an implant length 8 to 12 mm. Only for shorter or longer implants length impacted mean residual bone. Thus, our calculated mean data agree quite well with these proposals. However, if we look at the distribution, there is wide variation of bone loss; some implants were no longer anchored in bone whereas others had as little as 30% or 3 mm bone loss. Removal of implants with <3 mm or <30% ($n = 6$) may be due to malpositioning, no longer produced replacement parts for a new

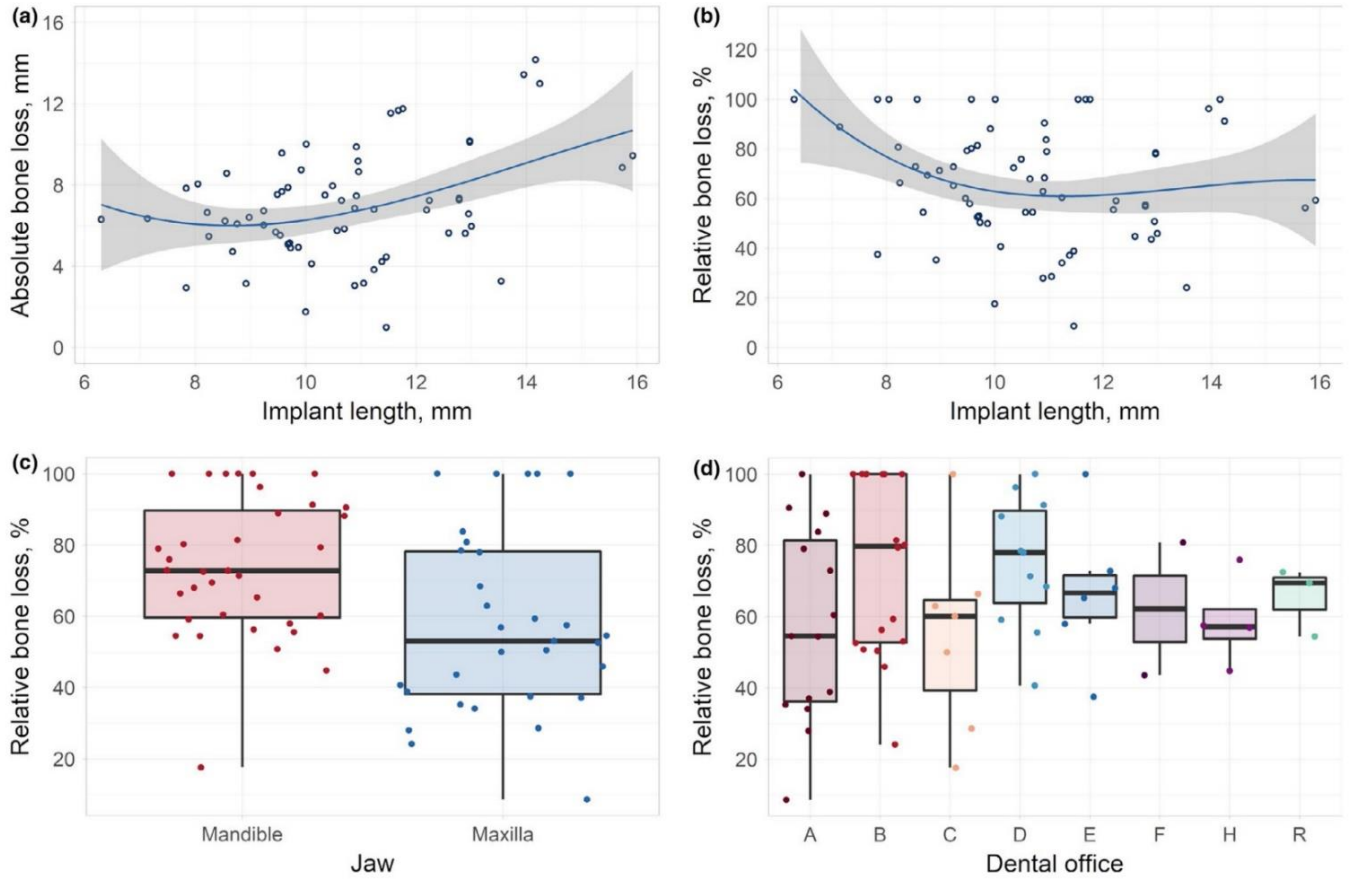


**FIGURE 4** Bivariate associations of implant length with absolute (a; $n = 65$, $p = .003$), and relative bone loss (b; $n = 65$, $p = .18$); bivariate associations of jaw (c; $n = 66$, $p = .004$) and dental office (d; $n = 66$, $p = .58$; all dental offices <5 patients were combined to one group, R; Office G did not sent any radiographs and was therefore not displayed.) with relative bone loss of explants. In scatterplots, spline-smoothers with 95% confidence bounds are provided

suprastructure, unexplicable pain, or inadequate patient adaptation. According to (Anitua et al., 2016) about 17% of nonmobile implants and according to (Kourtis et al., 2004) 49% of all implants are removed for reasons other than peri-implantitis. Why implants with a relative bone loss between 30% and 60% ($n = 26$) were removed and not tried to treat is unknown. This portion of removed implants calls for an intensive scientific discussion, at which level implants should be removed. Increased number of pathogens leads to increased inflammation and ensuing bone loss, which jeopardizes the implant site for future implantation (Fransson et al., 2010; Monje et al., 2020). The wide variation of bone loss shows that implant failure or the decision to remove an implant is a very unique situation. Thus, decision-making is not evidence but eminence based.

Late failure implants were explanted in the maxilla with less bone loss than in the mandible (57.7 ± 25.5% and 6.4 ± 3.1 mm in comparison to 73.7 ± 19.4% and 7.5 ± 2.3 mm). This association reached significance in bivariate and multilevel analysis (Table 3). The mandible has more compact bone, leading to loosening of the implant in a further progressed state (Lekholm & Zarb, 1985). Not undisputed (Antalainen et al., 2013; Jemt, 2017b) but most studies report a higher rate of implant failure in the maxilla than the mandible (Esposito et al., 1998a; Jemt, 2018b; Snauwaert et al., 2000). Moreover, a smaller implant length was significantly associated with enhanced relative bone loss at explantation. With decreasing implant length, less absolute bone loss reaches the same relative bone loss.

## 4.3 | Survival time

Other studies confirm that most implant failures occur in the first few years, and there is a correlation between survival rate and time in function with minor implant failure over time (Chrcanovic et al., 2018; Doornewaard et al., 2018).

The mean survival time of explants with late failure was 9.5 ± 5.8 years and in our analyses, a 10-year higher age at implantation was associated with a 2 years smaller survival time (Table 2). A correlation between implant failure and age has been confirmed by a variety of studies (Jemt, 2018a; Moraschini et al., 2015; Moy et al., 2005; Porter & von Fraunhofer, 2005). Increasing age decreases trabecular number and thickness and therefore the trabecular bone volume fraction (Majumdar et al., 1997) and relates to immunological changes (Carr et al., 2016; Konttinen et al., 2006).

**TABLE 2** Associations with survival time from mixed-effects (including random intercepts for office and patient) linear regression models ($n = 140$)

| Fixed effects | B (95% CI) | | *p*-value |
|---|---|---|---|
| Age at implantation, years | −0.19 (−0.27; −0.10) | | <0.001 |
| Sex | | | 0.70 |
| Female | 0 (reference) | | |
| Male | −0.40 (−2.39; 1.59) | | |
| Current smoking | | | 0.10 |
| No | 0 (reference) | | |
| Yes | −1.94 (−4.25; 0.38) | | |
| Jaw | | | 0.42 |
| Upper jaw | 0 (reference) | | |
| Lower jaw | −7.03 (−2.42; 1.01) | | |
| Location | | | 0.91 |
| Incisor or canine | 0 (reference) | | |
| Premolar or molar | −0.04 (−0.77; 0.68) | | |
| Implant length, mm | 0.06 (−0.18; 0.31) | | 0.61 |
| Usage of bone replacement material | | | 0.87 |
| No | 0 (reference) | | |
| Yes | −0.09 (−1.18; 1.00) | | |
| Relative bone loss, % | −0.004 (−0.03; 0.02) | | 0.75 |
| **Random effects** | | **Estimate** | **Standard error** |
| Office | | 1.90 | 1.08 |
| Patient | | 4.91 | 0.42 |
| Residual | | 0.50 | 0.23 |

*Note:* Missing value imputation was performed on patient and implant level using MICE and an MID approach. Detailed information and an overview of the imputed values for this regression model are given in Tables S1 and S2.

Abbreviations: B, linear regression coefficient; CI, confidence interval.

## 4.4 | Implant brand and surgeon

Our study is a highly selective sample, and we cannot associate surgeon and/or implant brand with implant failure. The surgeon has been reported to have the highest influence on implant failure (Jemt, 2017b, 2018a). Operator skill, protocol, and early overloading are most likely relevant causes for implant failure (Albrektsson & Zarb, 2018; Esposito et al., 2010). Since the implant providing offices were all specialized in implant dentistry, we assume that surgical misconduct can be excluded. Implant brand as a determinant factor is highly controversial (Derks et al., 2015; Manor et al., 2009). Our data cannot contribute to this discussion because choice of implant brand and dental office are highly interlinked (Figure 1b).

## 4.5 | Strengths and Limitations

This is the first study combining survival data for extracted implants with corresponding radiographs, thereby providing accurate bone loss data. The radiographically determined bone level could precisely be converted in millimeter, because the radiographically measured implant length was calibrated with the known explant length. This ratio could be used for correcting the radiographical bone loss. However, not all radiographs were periapical; some were panoramic and there were quality differences, but double measurements revealed an intra-examiner differences of 1.8 ± 6.6% and 0.39 ± 0.82 mm. This is in agreement with the literature (De Smet et al., 2002).

Only few questionnaires were completely answered and the given information may be questionable. Reported periodontitis, which might have an influence on both survival time and bone loss (Aglietta et al., 2011; Heitz-Mayfield, 2008), was compared with reassessed panoramic radiographs when available and excluded from analysis afterward due to inconsistencies. Missing data were imputed using MICE and the MID procedure, followed by mixed-effects regression models. Mixed-effects models handled the multilevel structure of the data appropriately via inclusion of random effects for office and patient. However, complex statistical modelling, which was not contemplated a priori to the data collection, also demands for larger samples. With hindsight, nearly three years of acquisition in 12 specialized dental offices finally resulted in

**TABLE 3** Associations with relative bone loss from mixed-effects (including random intercepts for office and patient) linear regression models ($n = 66$)

| Fixed effects | B (95% CI) | | *p*-value |
|---|---|---|---|
| Age at implantation, years | 0.07 (−0.55; −0.69) | | 0.82 |
| Sex | | | 0.44 |
| Female | 0 (reference) | | |
| Male | 5.05 (−7.76; 17.87) | | |
| Current smoking | | | 0.68 |
| No | 0 (reference) | | |
| Yes | −3.17 (−18.45; 12.12) | | |
| Jaw | | | 0.01 |
| Maxilla | 0 (reference) | | |
| Mandible | 17.31 (3.91; 30.72) | | |
| Location | | | 0.06 |
| Incisor or canine | 0 (reference) | | |
| Premolar or molar | −14.53 (−29.35; 0.29) | | |
| Implant length, mm | −2.79 (−5.50; −0.08) | | 0.04 |
| Usage of bone substitute material | | | 0.99 |
| No | 0 (reference) | | |
| Yes | −0.01 (−19.23; 19.22) | | |
| Survival time, years | −0.17 (−1.35; 1.02) | | 0.78 |
| **Random effects** | | **Estimate** | **Standard error** |
| Office | | 2.96 | 4.95 |
| Patient | | 20.12 | 2.36 |
| Residual | | 6.03 | 1.96 |

*Note:* Missing value imputation was performed on patient and implant level using MICE and an MID approach. Detailed information and an overview of the imputed values for this regression model are given in Tables S1 and S3.

Abbreviations: B, linear regression coefficient; CI, confidence interval.

regression samples comprising 140 and 66 explants. Subsequent studies planning extensive statistical analyses should therefore perform a priori sample size calculations considering the possibility of high exclusion rates.

Reasons for implant removal were not clear, although we asked for implants removed due to peri-implantitis. Some of the implants were removed only one month after insertion. Based on this observation, we assume that no common definition of peri-implantitis was present in the mind of specialists (Tomasi & Derks, 2012); it even seems that peri-implantitis did not need to come along with a certain degree of bone loss. For our main analysis, we excluded early failures and damaged implants to only consider bone loss from peri-implantitis affected implants. Though the mean bone loss (66.2%) at which implants were explanted was in accordance with the literature, its wide variation and differentiation between the jaws showed that the profession has no universally accepted threshold beyond which an implant cannot be preserved. In general, a larger study population would be needed and more factors such as prosthetics, periodontitis, prior treatment attempts, number of missing teeth, and number of inserted and explanted implants should be collected to obtain more conclusive results.

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## CONFLICT OF INTEREST

The authors declare no conflicts of interest. Offices, which worked with Nobel implants, received a new replacement implant for a Nobel explant.

## AUTHOR'S CONTRIBUTIONS

T.K., L.J. conceived the idea; L.J. collected the data; F.W. measured the implants and radiographs; C.P. and B.H. performed the statistical

analysis; and T.K. and F.W. led the writing. All listed authors critically revised the manuscript.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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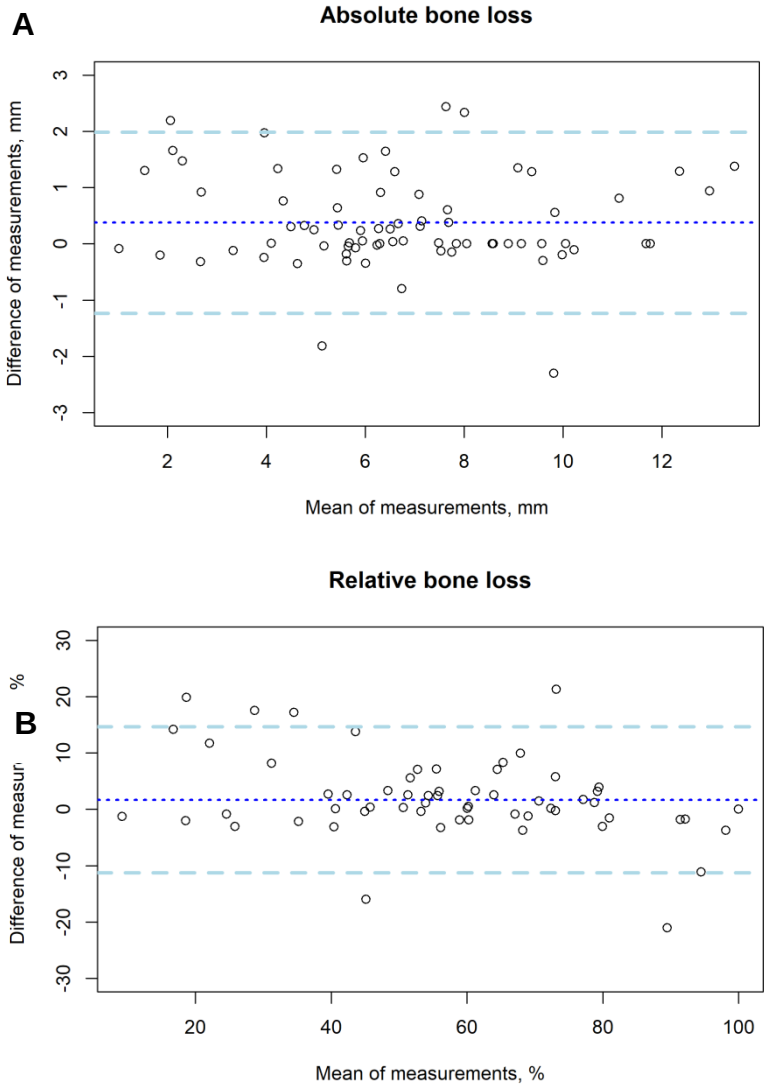
## 7.3 Supplemental Appendix of the Publication




**Suppl. Figure 1.** Bland-Altman plots for main measurements of absolute bone loss (A) and relative bone loss (B) vs. complete replication performed by the same examiner with different software.

**Suppl. Table 1.** Overview of missing value imputation on patient and implant level using MICE†

| Variable | Scale | Missing values | Imputation method | Imputation level | Comments |
|---|---|---|---|---|---|
| Age at implantation | metrical | 43 | predictive mean matching | patient | Multiple implants within patients with missing age at implantation had identical dates of implantation. |
| Sex | dichotomous | 6 | logistic regression | patient | |
| Smoking | dichotomous | 23 | logistic regression | patient | |
| Jaw | dichotomous | 7 | logistic regression | implant | |
| Location | dichotomous | 7 | logistic regression | implant | |
| Implant length | metrical | 48 | predictive mean matching | implant | |
| Bone replacement material | dichotomous | 43 | logistic regression | implant | |
| Survival time | metrical | 19 | predictive mean matching | implant | MID‡ -> deletion of 19 implants / imputed values for analyses having survival time as outcome |
| Relative bone loss | metrical | 93 | truncated regression with restricted range [0;1] | implant | MID‡ -> deletion of 93 implants / imputed values for analyses having relative bone loss as outcome |
| Dental practice | nominal | 0 | - | - | |

† Multiple imputation by chained equations: missing values in multiple variables were filled in iteratively by using chained equations, a sequence of univariate imputation methods with fully conditional specification of prediction equations.
‡ Complete multiple imputation followed by deletion of imputed outcomes.

**Suppl. Table 2.** Imputed information for mixed-effects linear regression analyses on survival time (n=140).

| Variable | Complete | Imputed |
|---|---|---|
| Age at implantation | 116 | 24 |
| Sex | 139 | 1 |
| Smoking | 123 | 17 |
| Jaw | 136 | 4 |
| Location | 136 | 4 |
| Implant length | 99 | 41 |
| Bone substitute material | 111 | 29 |
| Relative bone loss | 61 | 79 |
| Dental office | 140 | 0 |

**Suppl. Table 3.** Imputed information for mixed-effects linear regression on relative bone loss (n=66).

| Variable | Complete | Imputed |
|---|---|---|
| Age at implantation | 51 | 15 |
| Sex | 65 | 1 |
| Smoking | 59 | 7 |
| Jaw | 66 | 0 |
| Location | 66 | 0 |
| Implant length | 65 | 1 |
| Bone substitute material | 49 | 17 |
| Survival time | 61 | 5 |
| Dental office | 66 | 0 |

## 7.4 Eidesstattliche Erklärung

Hiermit erkläre ich, dass ich die vorliegende Dissertation selbständig verfasst und keine anderen als die angegebenen Hilfsmittel benutzt habe.

Die Dissertation ist bisher keiner anderen Fakultät, keiner anderen wissenschaftlichen Einrichtung vorgelegt worden.

Ich erkläre, dass ich bisher kein Promotionsverfahren erfolglos beendet habe und dass eine Aberkennung eines bereits erworbenen Doktorgrades nicht vorliegt.

Datum Unterschrift

## 7.5 Zusammenfassung in deutscher Sprache

**Zielsetzungen:** Es fehlen klare Leitlinien, wann ein Implantat entfernt werden sollte. Ziel dieser Studie war es, das Ausmaß des periimplantären Knochenverlusts bei der Explantation durch Spezialisten zu bewerten.

**Material und Methoden:** Fachärzte für Implantologie wurden gebeten, Implantate, die aufgrund von Periimplantitis explantiert wurden, mit entsprechenden klinischen Informationen zu versehen. In den Fragebögen wurden Alter, Geschlecht, Rauchgewohnheiten, Implantatlage, Verwendung von Knochenersatzmaterialien und Implantatmarke abgefragt. Frühe Misserfolge (Überlebenszeit <12 Monate) wurden gesondert analysiert. Die Implantate wurden vermessen, und der Knochenverlust und die Art des Knochenverlustes wurden anhand von Röntgenbildern beurteilt. Für die Art des Knochenverlusts wurde eine bivariate Analyse durchgeführt, und für das Ausmaß des Knochenverlusts und die Überlebenszeit wurden kovariatenbereinigte Modelle mit gemischten Effekten ausgewertet.

**Ergebnisse:** Zwölf Zahnarztpraxen stellten 192 Explantate von 161 Patienten mit 99 zugehörigen Röntgenbildern zur Verfügung. Die meisten Implantate waren von vertikalem Knochenverlust betroffen (51,1 %), gefolgt von kombiniertem horizontalem und vertikalem Knochenverlust (22,3 %), periimplantärem Spalt (11,7 %), horizontalem Knochenverlust (10,6 %) und nur in wenigen Fällen von einer apikalen Entzündung (4,3 %). Bei dreiunddreißig (17,2 %) Explantaten handelte es sich um frühe Misserfolge. Die Art des Knochenverlustes stand in signifikantem Zusammenhang mit der Überlebenszeit und der Implantatmarke. Die Implantatmarke zeigte ebenfalls eine signifikante Korrelation mit einem frühen/späten Implantatversagen. Mit Ausnahme der frühen Misserfolge war der kombinierte horizontale und vertikale Knochenverlust zusätzlich signifikant mit dem Rauchen assoziiert, und die Lokalisation, gruppiert nach Schneidezahn, Eckzahn, Prämolar und Molaren, zeigte einen signifikanten Zusammenhang mit der Art des Knochenverlusts. Darüber hinaus betrug die durchschnittliche Überlebenszeit 9,5 ± 5,8 Jahre mit einem absoluten und relativen Knochenverlust von 7,0 ± 2,7 mm bzw. 66,2 ± 23,7 %. Späte Ausfälle wurden mit einem durchschnittlichen Knochenverlust von 50,0 % mit 5,44 mm Restknochen im posterioren Oberkiefer und 73,8 % mit 2,89 mm Restknochen in anderen Bereichen entfernt. In vollständig angepassten Modellen mit gemischten Effekten blieb nur das Alter bei der Implantation (B=-0,19; 95% CI: -0,27 bis -0,10) ein signifikanter Faktor für die Überlebenszeit. Die Implantate wiesen einen signifikant höheren relativen Knochenverlust auf, wenn sie im Unterkiefer positioniert waren (B=17,3; 95% CI: 3,91 bis 30,72) oder wenn sie kürzer waren (B=-2,79; 95% CI: -5,50 bis -0,08).

**Schlussfolgerungen:** Obwohl der durchschnittliche Knochenverlust (66,2 %), bei dem die Implantate explantiert wurden, mit der Literatur übereinstimmte, zeigten die große Varianz und die Differenzierung zwischen dem posterioren Oberkiefer und anderen Lokalisationen, dass es in der Fachwelt keinen allgemein akzeptierten Schwellenwert gibt, über den hinaus ein Implantat nicht erhalten werden kann.

## 7.6 Danksagung

Am Ende dieses Lebensabschnittes möchte ich mich herzlich bei den folgenden Personen bedanken, die die Erstellung dieser Arbeit ermöglichten.

An erster Stelle steht mein Doktorvater Herr Prof. Dr. Thomas Kocher, der mit eindrucksvoller Geschwindigkeit Texte korrigierte und mit Erfahrung und Expertise immer die adäquate Richtung vorgab.

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