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Success and radiological evaluation of dental implants after augmentation with iliac bone: A long-term study

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Abbreviation

3D	3 Dimensions
ATF-4	Activating transcription factor-4
BMPs	Bone morphogenic proteins
BSM	Bone substituting material
Cbfa1	Core-binding factor alpha1
CEJ	Cement-enamel junction
cm	Centimeter
CSF-1	Colony stimulating factor 1
CT	Computed tomography
DBBM	Deproteinized bovine bone matrix
DCIA	Deep circumflex iliac artery bone flap
Dlx	Distal less homeobox
FGF-23	Fibroblast growth factor-23
Fra	Fos-related antigen
GBR	Guided bone regeneration
GTR	Guided tissue regeneration
ICAM-1	Intercellular adhesion molecule-1
ICC	Interclass correlation coefficient
IGF-I	Insulin-like growth factor I
IGF-II	Insulin-like growth factor II
IL-1	Interleukin 1
Ncm	Newton-centimeter
M-CSF	Macrophage-colony stimulating factor
µm	Micrometer
mm	Millimeter
MSCs	Mesenchymal stem cells MSCs
Msx2	Homeobox protein/gene
NFAT	nuclear factor for activating T cells,
OPG	Osteoprotegerin
Osx	Osterix
PDGF	Platelet derived growth factor
PGE2	Prostaglandin E2
PTFE	Polytetrafluoroethylene PTFE
PTH	Parathyroid hormone
PTHrP	PTH-related protein
RANKL	Receptor activator of nuclear factor-κB ligand (RANKL)
RUNX2	Runt-related transcription factor 2
TGF-β	Transforming growth factor-beta
TNF family	Tumor necrosis factor

Abstract (English)

Objective: The aim of the present study was the analysis of the long-term crestal bone level changes of dental implants after augmentation with an anterior iliac bone graft.

Materials and methods: A total of 32 patients (mean age of 52 years; range 22–70 years) with an atrophied maxillary and mandibular bone volume of less than 5 mm augmented with an autologous iliac bone graft were involved in this study. The healing period was 3 months before implant placement. The patients were monitored with spaced standardised radiological examination at 1, 3, 5 and 10 years for evaluation of peri-implant crestal bone loss. The statistical evaluation was descriptive, and the comparative statistics regarded the influencing factors, such as age, gender and location on the peri-implant resorption rates were analysed with the Mann-Whitney U-test and the Spearman rank-order correlation coefficient.

Results and Discussion: The augmentation was successfully performed in all patients. A total of 150 implants inserted 3 months after jaw augmentation were placed. The mean observation period was 69 months (range 12–165 months; the success rate for maxilla 96%; success rate for mandible 92%), five implants in the maxilla and two implants in the mandible were lost. After 1 year, the mean amount of crestal bone loss was 1 mm, increasing to 1.8 mm at 10 years. There was a significant difference between gender and the amount of crestal bone loss, no significant difference was found between bone loss and the implant system, diameter of implant and patient age. The presented long-term results showed that the peri-implant bone loss rates in the augmented regions were comparable to the rates reported in the literature of non-augmented jaws.

Conclusion: A successful long-term reconstructive procedure can be performed in patients with atrophic maxilla and mandible, with merging of the iliac onlay graft and dental implants. In the long term, the results demonstrated high success rates and stability in the peri-implant bone level after more than 5 years.

Abstract (Deutsch)

Zielstellung: Ziel der vorliegenden Studie war die Auswertung radiologischer periimplantärer Knochenabbauraten nach Augmentation mit avaskulären Beckenkammtransplantaten in hoch atrophen Kiefern.

Material und Methode: In die retrospektive Untersuchung wurden 32 Patienten mit einem Durchschnittsalter von 52 Jahren eingeschlossen, bei denen aufgrund einer extremen Alveolarkammatrophie und einem Knochenvolumen von weniger als 5mm im Ober- bzw./oder Unterkiefer eine Augmentation mit avaskulären Blocktransplantaten durchgeführt worden ist. Nach einer Einheilzeit von 3 Monaten wurden dann die enossalen Implantate inseriert, die als Basis für implantatgetragenen Zahnersatz dienten. Anhand von standardisierten Orthopantomogrammen wurden die periimplantären Knochenabbauraten postoperativ, nach 1, 3, 5 und nach 10 Jahren ausgewertet und verglichen. Die statistische Auswertung erfolgte deskriptiv, die vergleichende Statistik hinsichtlich etwaiger Einflussfaktoren wie Alter, Geschlecht und Lokalisation auf die periimplantären Abbauraten wurden mit dem Mann-Whitney U-test und Spearman rank-order Korrelationskoeffizient geprüft.

Ergebnis und Diskussion: Bei 32 Patienten wurden insgesamt 150 Implantate inseriert. Der mittlere Beobachtungszeitraum betrug 69 Monate (12-165 Monate; Erfolgsrate für den Oberkiefer 96%, Erfolgsrate für den Unterkiefer 92%). Innerhalb des Nachuntersuchungszeitraums gingen 5 Implantate im Oberkiefer und 2 im Unterkiefer zu Verlust. Der periimplantäre Knochenabbau lag 1 Jahr post implantationem durchschnittlich bei 1 mm und nach 10 Jahren bei 1,8 mm. Die Ergebnisse belegen, dass die periimplantären Knochenabbauraten in den augmentierten Regionen vergleichbar zu in der Literatur beschriebenen Abbauraten in nicht augmentierten Kiefern waren.

Zusammenfassung: Bei Patienten mit atrophischem Kiefer konnten nach Augmentation mit kortikospongiösen Beckenkammtransplantaten und zweizeitiger Implantation nach 3 Monaten gute Langzeitergebnisse erreicht werden. Die Ergebnisse zeigen eine hohe Erfolgsraten und stabile periimplantäre Verhältnisse über einen Zeitraum von mehr als 5 Jahren.

1. Introduction

An edentulous or partially edentulous ridge due to missing teeth or the ageing process leads to bone atrophy and significant alteration in the jaw dimensions and morphology (Atwood & Coy, 1971; Araújo & Lindhe 2005). In the first year after tooth extraction, the changes in the alveolar ridge are clinically significant, which is associated with a vertical loss of the alveolar ridge up to 3 mm and up to a 50% width reduction (Schropp et al., 2003; Heberer et al. 2008; Tan et al. 2012).

The reconstruction of severe atrophy in the maxilla and mandible remains the most common practice in oral and maxillofacial surgery. However, dental rehabilitation can successfully be achieved with a dental implant in combination with jawbone augmentation (Nelson et al., 2006 a & b; Heberer et al., 2009; Chiapasco et al., 2012). There are different augmentation procedures involving autogenous, allogenic, xenogeneic and synthetic materials (Vermeeren et al., 1996; Whitmyer et al., 2003; Reinert et al., 2003; Nelson et al., 2006 a&b; Barone et al., 2011; Sbrodone et al., 2014).

An autologous bone graft is considered the “gold standard” for the reconstruction of vertical and horizontal alveolar bone atrophy. It has immunological and biological advantages over allogenic and synthetic bone substitutes as a result of its outstanding combination of osteogenic, osteoinductive, as well as osteoconductive properties, and can be harvested from the intra and extra oral sites (Kao & Scott, 2007; Pape et al., 2010; Fretwurst et al., 2015b; Sakkas et al., 2017). However, limitations of intraoral autografts have been reported, including restricted donor sites, morbidity, and limited availability (Nkenke et al., 2014). All of these drawbacks dictate the choice for using

extraoral donor sites, especially when an extended reconstruction of the jaw is planned and significant amount bone is needed (Zhu et al., 2012; Kilinc et al., 2017).

One of the most common sources of extraoral autogenous bone, mostly corticocancellous bone, is the iliac crest. Other donor sites involve the fibula, calvarium and tibia (Mazock et al., 2003; Dimitriou et al., 2001; Dasmah et al., 2012; Sakkas et al.,2017). Although bone resorption tendency in the graft and morbidity in this donor site are mentioned (Schwartz-Arad & Dori, 2002; Kessler et al., 2005; Fretwurst et al., 2015b), the iliac crest remains the most used extraoral donor site because of its advantages, which include easy access, significant amount and quality of bone containing a high concentration of osteogenic cells preferable for regeneration by osteogenesis (Kessler et al., 2005; Khoury et al., 2007; Schaaf et al., 2010). Authors showed in long-term studies that the reduction in the healing time to 3 months for both graft and implant is enough for osseointegration of the implant and overcoming the resorption tendency (Nelson et al. 2006a; Heberer et.al. 2009). Another strategy suggested is the addition of bone substitutes, may minimize bone resorption after iliac bone grafting (Wiltfang et al., 2014).

In literature, the survival rates of implants, which placed after onlay iliac bone grafting have range from 60% to 100% (according to Kaplan & Meier criteria) with most reported survival rates being at least 90% (Kaplan & Meier 1958; Chiapasco et al., 2006; Boven et al., 2014; Nguyen et al., 2019). Long-term studies concerning quantitative survival rates of dental implant in onlay iliac graft are available. However, a long - term studies for evaluation the qualitative success rate, the peri-implant bone level changes and related influencing parameters do not exist (Verhoeven et al., 2006; Chiapasco et al., 2008, 2014; Sbordone et al., 2012; Boven et al., 2014, Hagn, 2018, Nguyen et al. 2019). This study was aimed to observe the success outcome of

implants and the peri-implant bone level changes as well as their suspected influencing factors in the atrophied jaws after augmentation with onlay grafts which harvested from anterior superior iliac bone, in long-term. The success rate in the current study has been evaluated according to the success criteria of Buser et al. (1990 and 1997).

1.1. Biology of Bone

Bone tissue is a unique type of connective tissue with physiological mineralisation. On the organic level, it has cartilaginous joints, marrow space, **cortical** and **cancellous** bone structures (mineralised tissues) (Seeman et al., 2006; Burr & Akkus, 2014), while on a tissue level, it has both mineralised and non-mineralised tissues, the latter known as osteoid. Additionally, it has three types of cells, **osteoblasts** (bone-forming cells), **osteocytes** (embedded in the mineralising bone matrix) and **osteoclasts** (bone-resorbing cells) (Buckwalter et al., 1996**;** Florencio-Silva et al., 2015).

At the macroscopic level, according to the mechanical and biological requirements, bone is in two forms, either dense (cortical/compact bone) or a meshwork (cancellous/trabecular bone) composed of trabecular struts. There is no histological difference between these two types of bone and they can be distinguished by their amount and distribution of porosity and solid substances (Marx & Garg, 1998; Seeman et al., 2006; Osterhoff et al., 2016; Burr 2019).

Cortical bone is the principal component of the shafts or diaphysis in the long bones of the extremities and on the external sides of flat bone. Compact bone also engulfs the cancellous bone of the body of vertebrates, on the ends of long bones (metaphysis), in the iliac crest, and the skull. It supplies support and protection (Burr, 2019), consisting of multiple Haversian systems or osteons, which have a central tube

carrying a blood vessel, nerves and lymphatics, and are enclosed by several sheets of concentric lamellae (Seeman et al., 2006; Osterhoff et al., 2016). The cortical bone Haversian canals form about 3–5% porosity and increase with ageing and osteoporotic alterations in the skeleton (Burr, 2019). Cancellous bone is located firstly in the metaphyses of the long bones, as well as in the vertebrae, ribs, and iliac crest. It comprises struts and rods of bone, each represents about 200 μm thickness, and form only about 25–30% of the entire tissue volume, with marrow space accounting for the remainder (Burr, 2019).

Cancellous bone derives its primary mechanical benefit from its architecture, which provides structural support without increasing the weight of the entire bone. The gap between the trabecular struts is filled with red marrow in which produces blood cells. Bone lineage cells differentiate into adipocytes, and the bone marrow within the diaphysis will be fattier in nature (i.e., yellow marrow) with ageing. Bone is the primary blood-forming organ, as red marrow is present throughout life in the ends of the bones, vertebrae, iliac crests, and ribs (Marx & Garg, 1998; Burr, 2019).

Excluding articular surfaces, the bone surface is covered with **periosteum**, which is composed of two sheets of specialised connective tissue. The external fibrous layer will give periosteal hardness because it is mainly composed of dense collagenous fibres and fibroblasts, as well as being abundant with nerve fibres and blood supply. The internal layer is in an intimate direct connection with the bone, contains osteogenic cells, and is often referred to as the cambium layer (Marx & Garg, 1998). These osteogenic cells in the cambium layer cause periosteal expansion during growth because of the mechanical factor, as well as during fracture repair (Chanavaz, 1995; Marx & Garg, 1998; Allen et al., 2004; seet al., 2017; Serowoky et al., 2020). In normal situations, these cells are responsible for the production of highly organised lamellar

bone. By differentiation into osteoblast and chondrocytes, these mesenchymal cells located in the cambium will act as bone repair cells (Nakahara et al., 1990; Ito et al., 2001), whereas during pathological situations and in the primary stages of bone repair, they form disorganised woven bone (Krane et al.1977; Burr, 1989; Kannus et al., 1995; Marx & Garg, 1998; Silva & Touhey, 2007; Fuchs et al., 2019).

Bone has a protective function against impact loading, thereby preventing deformities. Additionally, it can absorb and distribute forces by changing bone form without any cracks. It also plays a considerable role in haematopoiesis and mineral metabolic process, hence, is regarded as an endocrine organ (Currey et al., 2003; Burr, 2014).

1.1.1. Composition of Bone

Bone is a complex of organic and inorganic material. The inorganic matrix is composed of mineral (65%), water (10%) and lipids (1%). The hydroxyapatite crystals are forming about 90% of minerals while calcium phosphate and carbonate apatite represent the remaining minerals. The organic part represents 25% of bone composition. It has type I collagen and non-collagenous proteins in percentages of 90% and 10% respectively. These bone components will offer both mechanical and metabolic functions (Boskey 2013; Gasser & Kneissal 2017). It is important to know that these constituents vary with age progression (Boskey & Coleman, 2010), gender, species, and the location (Donnelly et al., 2012), and can be changed by disease and cure (Boskey 2013; Mandair & Morris, 2015).

1.1.2. Bone Cells

Osteoprogenitor cells differentiate from pluripotent mesenchymal cells and are division-active precursors of osteoblasts. They are characterised by a flattened cytoplasm with oval to elongated core and are usually found in the endosteal or periosteal bone surface or the cambium layer of the periosteum (Liebich, 2010; Fuchs et al., 2019).

Osteoblasts are involved in bone formation and can synthesise an osteoid which represents the extracellular matrix. They are specialised basophilic bone cells that can not to divide, which develop from undifferentiated mesenchymal cells and produce large proportions of the organic bone matrix, including 90% type I collagen fibres and about 10% of other proteins (Boskey et al., 1984; Mandair & Morris, 2015). In the active state, they have a cubic shape with a round nucleus, are about 22–30 microns in size and are located endosteal or periosteal bone surfaces (Liebich, 2010). The reduction in metabolic activity flattens the cells, which form a spindle shape. After bone formation, osteoblasts either undergo apoptosis or become entrapped in the mineralised bone matrix then differentiate into osteocytes or become inert cells which can appear on quiescent bone surfaces. The so-called **bone lining cells** are dormant, flat, inactive osteoblasts, and can be reactivated within a short time through osteoinductive signals to contribute to local bone formation processes (Miller & Jee, 1987; Chow et al., 1998; Eriksen, 2010; Kim et al., 2012). However, the bone lining cells are in intimate relationship with matrix-embedded osteocytes via gap crossing and take part in calcium exchange between the bone marrow compartment and the mineralised bone matrix (Dobnig & Turner, 1995; Kim et al., 2012). It has been demonstrated that these cells, which can be found on the bone surfaces, are positive for alkaline phosphatase and ICAM-1 (intercellular adhesion molecule-1), also playing

a crucial role in bone remodelling (Everts et al. 2002).

Osteoblasts originate from mesenchymal stem cells (MSCs), which can differentiate into osteoblasts, chondrocyte, myoblasts and adipocytes (Caplan & Bruder, 2001). The osteoblast lineage cells can differentiate into preosteoblasts, osteoblasts, bone lining cells, and osteocytes, cells which represent mesenchymal progenitors. There are multiple cytokines that have an important role in osteoblast differentiation, such as hedgehogs, bone morphogenic proteins (BMPs), transforming growth factor-beta (TGF-β), parathyroid hormone (PTH), and WNTs (Lang, 2012; de Gorter & ten Dijke, 2013). During the processes of endochondral and intramembranous ossification, there is a crucial role of Runx2/Cbfa 1 (see Fig. 1) (Ducy et al., 1997; Komori et al., 1998) and Osterix/Sp7 in maintaining and controlling these two activities. According to de Gorter and ten Dijke (2013), osteoblasts establish a mixture of extracellular proteins osteocalcin, osteopontin, osteonectin, bone sialoprotein, alkaline phosphatase, and a huge amount of type I collagen. The calcified bone matrix is considered as a storage cabinet for growth factors, calcium and phosphates. Additionally, these growth factors have an essential role in controlling osteoblastic differentiation and function. These growth factors include insulin-like growth factor I (IGF-I), insulin-like growth factor II (IGF-II), TGF-β, and BMPs (de Gorter & ten Dijke, 2013).

Osteocytes are derived from osteoblasts, have dendritic spurs with mechanoreceptors and a large, mostly oval nucleus. They become entombed through matrix deposition in spaces called lacunae. They are involved in the regulation of phosphate metabolism and secrete FGF-23 (fibroblast growth factor). They are surrounded by calcified bone substance and flattened between lamellar bone layers (Bonewald, 2011). They make about 90% of the bone cells compared to 4–6% osteoblasts and 1–2% osteoclasts, making them the superabundant cell in the bone

matrix and surfaces (Bonewald, 2011). Osteocytes are widely spread on the mineralised bone matrix and by the presence of the dendritic processes, osteoblast and their neighbouring cells, including bone marrow cells, are connected. These dendritic projections are occupied by micro-canals, called canaliculi, filled with fluid, that is, directed toward the surface and blood supply (Knothe Tate et al., 2004; Bonewald, 2011). Figure 1 shows osteoblastogenesis and the principal transcription factors that control the proliferation and differentiation of osteoblast precursors. After bone formation, mature osteoblasts are flattened, forming lining cells over the bone surface. Their fate is either death by apoptosis or they are surrounded by bone matrix, then converted into osteocytes. The transcription factors involved are ATF-4 (activating transcription factor-4), Dlx (distal less homeobox), Fra (Fos-related antigen), Osx (Osterix), and Runx2 (runt-related transcription factor 2).

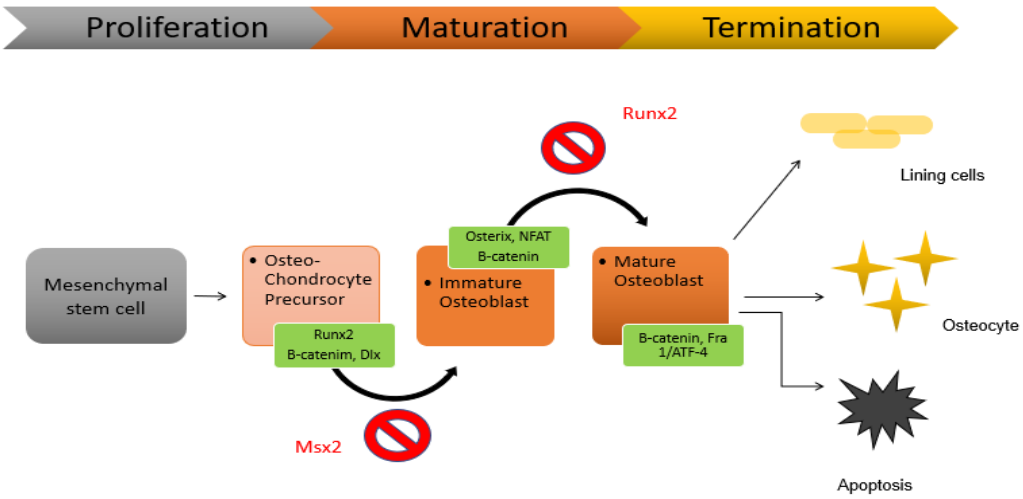


Fig 1 Osteoblastogenesis and fate

Runx2: Runt - Related transcription factor 2, Dlx: Distal less homeobox, ATF- 4: Activating transcription factor-4, Fra: Fos-related antigen, NFAT: Nuclear factor for activating T cells, Msx2: Homeobox protein/gene. (own illustration).

Osteoclasts are amoeboid movable multi-nucleated large cells responsible for bone resorption and they arise from haematopoietic cells in the bone marrow. They are located on bone surfaces, where they form reaction zones, so-called Howship's lacunae, which by their proteolytic enzyme activity enhance the degradation/resorption of intercellular bone substances (Schell et al., 2006). They are regarded as a member of the monocyte/macrophage family according to Suda et al. (1999) and can be produced in vitro from precursors of mononuclear phagocytes. There are two important cytokines in osteoclastogenesis (see Fig. 2), macrophage-colony stimulating factor (M-CSF or CSF-1) (Pixley & Stanley, 2004) and receptor activator of nuclear factor-κB ligand (RANKL) (Suda et al., 1999; Boyle et al., 2003). The latter is a member of the TNF family, basically behaving as a secretory protein from activated T cells (Weitzmann et al., 2000) and is important in priming precursor cells in osteoclastogenesis.

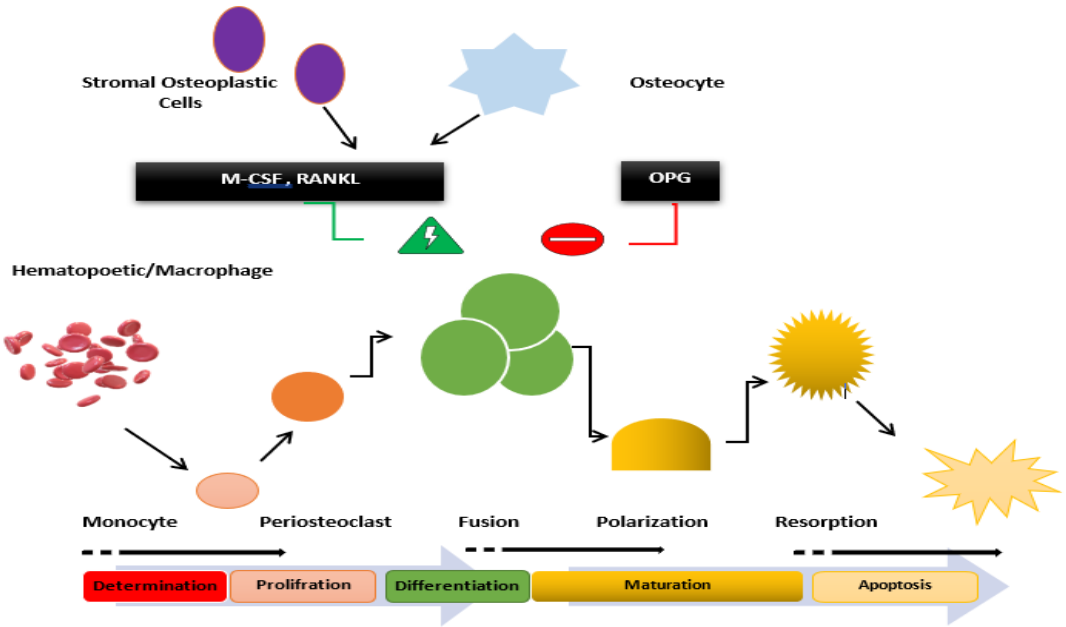


Fig 2 Osteoclastogenesis and apoptosis

M-CSF: Macrophage-Colony stimulating factor, OPG: Osteoprotegerin, RANKL: receptor activator of nuclear factor κappa-B ligand. (own illustration).

Osteoclastogenesis can be activated/controlled by multiple factors like PTH, PTH-related protein (PTHrP), prostaglandin E2 (PGE2), interleukin 1 (IL-1), and 1,25-(OH)2D3 and these stimulators upregulate RANKL expression. Osteoprotegerin (OPG) inhibits osteoclastogenesis through acting as a decoy receptor for RANKL. OPG is a soluble form of the TNF receptor (Kostenuik & Shalhoub, 2001; Liebich, 2010). Activators of OPG include oestrogen, BMP, and TGF-β while it is inhibited by proinflammatory cytokines (Rosen, 2013). Osteoclastic differentiation and activation are regulated by the equilibrium between RANKL and OPG in osteoblast lineage cells (Hofbauer et al., 2000; Boyle et al., 2003; Rosen, 2013). Osteoclast precursor survival, proliferation, differentiation and cytoskeletal rearrangement are regulated by M-CSF.

The process of building and dismantling the bone (modelling/remodelling) is achieved by the balanced interaction of osteoblasts and osteoclast activity and by physiological forces acting on the bone (Frost, 1994). In the absence of stress/loading moments as a mechanical stimulus, there is an increase in osteoclast activity, which is associated with increased absorption of the bone, leading to a continuous volume reduction of the bone. This process has been used as a law of transformation of the bone of the Berlin anatomist and surgeon, Julius Wolf (1892) (Frost, 1994).

Differentiation of osteoclasts is controlled by RANKL and M-CSF, as well as other cytokines produced by osteoblasts and osteocytes that control many stages of osteoclastogenesis, such as precursor proliferation, commitment, differentiation and maturation. Osteoprotegerin OPG which is also secreted by osteoblasts and osteocytes acts as a decoy receptor for RANKL and reduces osteoclast differentiation (Hofbauer et al., 2000; Boyle et al., 2003; Rosen, 2013).

1.2. Basics of bone formation

Bone formation can take place according to various mechanisms:

1. Intramembranous ossification (direct ossification)

2. Endochondral ossification (indirect ossification)

Most parts of the skull, the scapula and clavicula, mandible and maxilla are formed through intramembranous ossification, whereas the remainder of the bones of the skeleton are formed by endochondral ossification (Amir et al., 2006).

The development of intramembranous bone is characterized by proliferation of mesenchymal cells via division-active progenitor cells direct to osteoblasts (Franz-Odendaal, 2011) in the so-called primary ossification centres of the embryonic connective tissue. Mesenchymal connective tissue cells immigrate into the defect via the vascular structures, trigger the synthesis of the bone matrix and differentiate along the osteogenic cell cascade (osteoblast lineage) from osteoprogenitor cells to metabolically active osteoblasts (Zomorodian et al., 2012; Yang et al., 2013; Allen & Burr, 2019). They express hydroxyapatite crystals and are responsible for the formation of osteoids, the synthesis of collagen and the control of mineralization (Gawlitta et al., 2010).

The extracellularly formed collagen fiber enclose the osteoids and create ossification nuclei. The ossification centres then fuse to develop bone trabeculae, which connect to each other and form a templet for later bone matrix mineralization. The mechanical stability of the vascularization network is essential for direct ossification bone development (Claes et al., 2002; Bischoff et al., 2008).

The initial collagen matrix produced in the intramembranous ossification is disorganised and known as woven bone, having an irregular microscopic lamellar

structure of collagen fibres and blood vessels, as well as a lower degree of mineralization. The woven bone is later removed through osteoclastgenesis and replaced by lamellar bone, finally forming the trabecular structures (Burr et al., 1989; Hall et al., 1992; Kannus et al., 1995; Silva & Touhey, 2007; Fuchs et al., 2019).

In contrast to intramembranous ossification, endochondral ossification begins with a condensation of mesenchymal cells which do not develop into osteoblasts but are differentiated into chondroblasts through a specific transcription factor. In endochondral ossification, the cartilage matrix is converted from the inside. This form of ossification plays a role in the emergence of spongy bone inside the long bones and short bones (see Fig. 3). Chondroblasts initiate cartilage matrix synthesis with some of the cells becoming embedded in the matrix that contains mainly collagen II, where these cells differentiate into chondrocytes (Yang, 2013; Allen & Burr, 2019).

The perichondrium is a membranous tissue that encircles the hyaline cartilage and a group of cells switch to the osteoblastic phenotype that build bone matrix within the cartilaginous tissue via RUNX2 (Akiyama et al., 2002). The previous process is responsible for bordering the diaphysis of long bones (primary or diaphyseal ossification center), consequently forming a lamellar structure known as the bone collar. Then, the periosteum substitutes the perichondrium, which is considered as the origin of osteoblasts required for the subperiosteal expansion of the bone collar. Bone collar synthesis and expansion will reduce the availability of nutrients required by the primary cartilage structure, leading to calcification and death of chondrocytes, finally, osteoclasts will eradicate the remnants of the cartilaginous tissue. The bone marrow space is formed by vascular invasion (Kosher et al., 1986; Ornitz et al., 2002; Hartmann et al., 2007; Fuchs et al., 2019).

The same process makes secondary ossification centers at both ends of the long bone in the epiphyses over time. Epiphysis, the cartilage layer, separates the central diaphyseal region that accommodates a bone marrow cavity from the two-secondary ossification centers. Additionally, longitudinal bone growth occurs through the action of the epiphysis or growth plate which forms at the interface of the two ossification centers (see Fig. 3), that is, a primary ossification center in the bone shaft and a secondary ossification center in the epiphyses (Gawlitta et al., 2010; Ignatius et al., 2011; Grimes et al., 2011; Gasser & Kneissal, 2017).

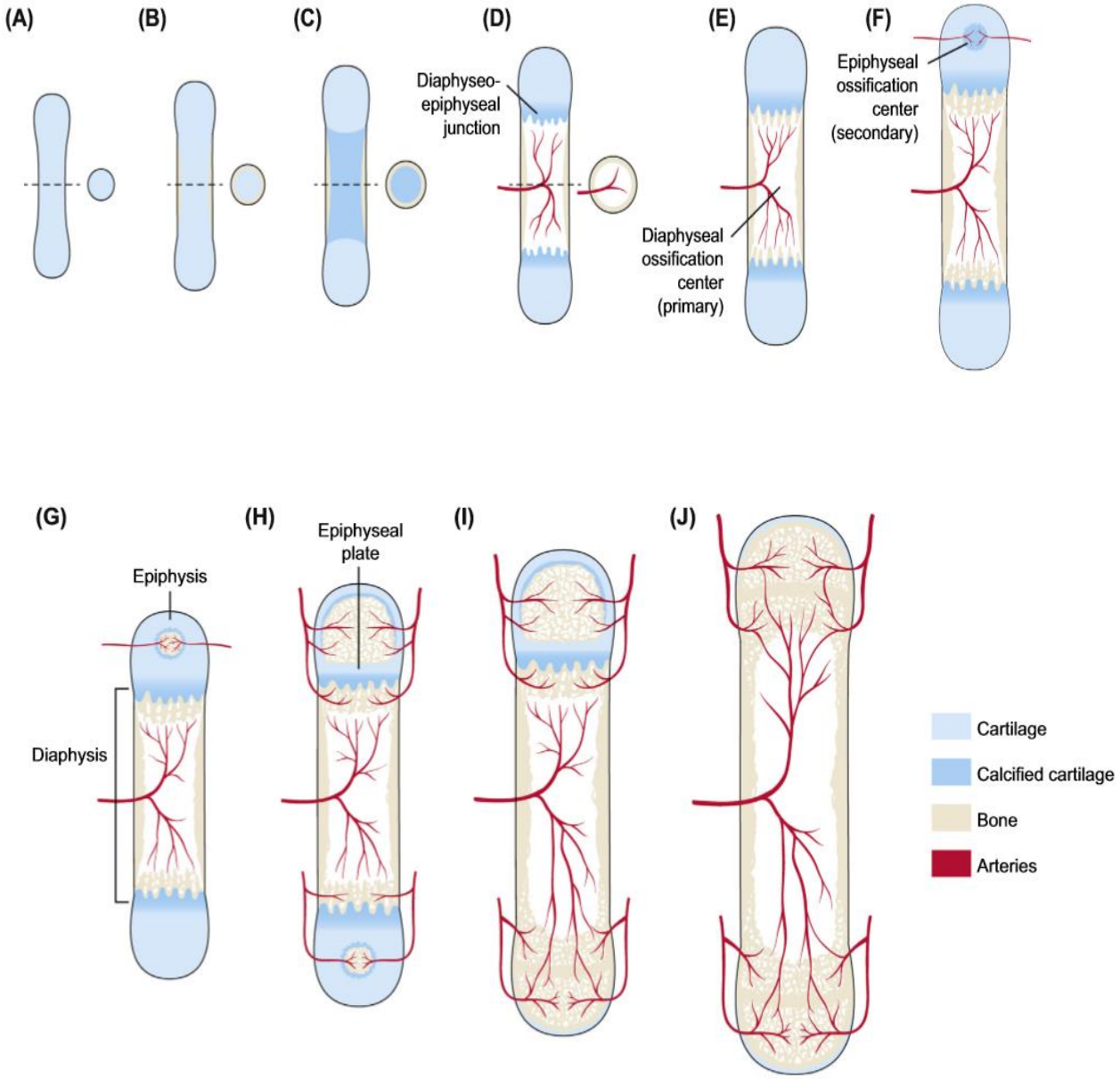


Fig 3 Endochondral Ossification

A & B Foetal hyaline cartilage model develops, **C** cartilage calcifies and the periosteal bone collar forms around the diaphysis, **D & E** primary ossification centres form in the diaphysis, **F** the secondary ossification centre forms in the epiphysis, **G & H** bone replaces cartilage except the articular cartilage and epiphysial plates, **I & J** the epiphyseal plate ossifies and forms the epiphysial line (adapted from **Basic and Applied Bone Biology**, chapter 5, p.87, Allen & Burr 2013, 2019). (the redistribution is permited from publisher *Elsevier / USA*, Licence ID:1104248-2, copy rightsholder: *Elsevier Science & Technology Journals*).

1.3. Osteogenesis of defect or fracture healing

The bone has a special property, that is, the ability to regenerate without scarring, with a complete restoration of structure and function (Cornell & Lane, 1992). The healing time of defects is characterised by being the same as bone formation and bone resorption (Einhorn, 1998; Cho et al., 2002; Byrne et al., 2011). There are different types of the bone healing depending on the size of the defect. In primary healing, there is sufficient vascularisation for the defect ends and they are in intimate contact or fixed to each other without dislocation (Marsell & Einhorn, 2011). Primary healing of fractures occurs by either contact or gap healing, recreating a lamellar bone structure which has successful anatomical and biomechanical properties. Direct bone healing can happen in the case of anatomical repair of the fractured pieces with a hard fixation, leading to a valuable reduction in the interfragmentary force. To achieve mechanical continuity, bone on one side of cortex should fuse with bone on the other side. The term contact healing of fusion between bones occurs when the gap between fragments is less than 0.01 mm and the interfragmentary force is less than 2% (Shapiro, 1988). Hulse stated that in this situation, cutting cones are established at the ends of the osteons nearest the fracture site (Slatter et al. 2003). Osteoclasts are found at the tips of the cutting cones and these cells cross the fracture line to form longitudinal holes about 50–100 μm/day. These cavities are topped up with bone tissue from osteoblasts located at the back of the cutting cones. This occurs during the concurrent formation of bone fusion and reestablishment of Haversian systems formed in an axial direction (Kaderly, 1991; Sumner-Smith et al. 2002). Osteoblast's precursors are carried by the blood vessels passing through the reformed Haversian systems. After that, the osteons will undergo maturation into lamellar bone by direct remodelling, leading to healing of the fracture without a periosteal callus (Greenbaum, 1993; Einhorn, 1998).

The main difference between gap and contact healing is that in the first, the bony union and Haversian remodelling do not occur at the same time. It happens when there is stability with an anatomical reduction, although the gap should be less than 800 µm to 1 mm (Kaderly, 1991). In this procedure, the fracture region is deposited with lamellar bone which is directed perpendicularly to the long axis, and it needs a secondary osteonal reconstruction, which differs from contact healing (Schenk, 1994).

The primary bone structure is exchanged by longitudinal revascularized osteons holding osteoprogenitor cells, which differentiate into osteoblasts and form lamellar bone no-ball sides of the gap (Shapiro et al., 1988). The formed lamellar bone is characterised by mechanical weakness and is deposited in a perpendicular direction to the long axis. This primary process lasts between 3 and 8 weeks, before a secondary remodelling similar to the contact healing surge with cutting cones occurs. This process is not as substantial as endochondral remodelling but is important for complete restoration of both biomechanical and anatomical characteristics of the bone (Shapiro, 1988).

Secondary fracture healing occurs due to the continuity interruption (more than 0.5 mm fracture gap) and rupture of the surrounding vessels, that lead to the development of a hematoma, which is characterised by platelet aggregation and activation of the locally acting coagulation cascade, which enhances stabilisation of the blood clot. The distribution of molecular mediators, such as platelet derived growth factor (PDGF) and transforming growth factor-ß (TGF-ß, induces migration of neutrophil granulocytes, mast cells, macrophages, endothelial cells, fibroblasts and other chemotactic factors (Fazzalari, 2011). Simultaneously, local inflammatory mediators (IL-1, IL-6) activate proteolytic enzyme cascades, followed by vasodilation and excessive capillary influx (Remedios, 1999). In this stage, granulation begins with the immigration of

mesenchymal cells and proliferation of fibroblast-rich granulation tissue (Philip et al., 2005; Bielby et al, 2007). The mesenchymal progenitor cells differentiate according to their developmental cascade into fibro-, chondro- or osteoblasts and organise the fibrin giascaffold in the fracture gap (Marsell & Einhorn, 2011). Between two to three weeks, soft callus arises and after mineralisation of the basic substance, it will be followed by the formation of woven bone. The woven bone is converted into lamellar bones through the interaction of osteoblasts and osteoclasts to achieve complete consolidation (Giannoudis et al., 2011).

The phases of defect healing apply to every bony area in the human skeleton, even to tooth-bearing structures of the maxillary facial bones. Teeth are lost, either through traumatic, cariogenic or inflammatory causes, and immediately after tooth extraction, the healing cascade arises in the alveolar socket. Scientific research has shown that the dimensional resorptive changes (which will be described in the next sections) occur in the alveolar ridge after tooth extraction causing a clinical problem in the prosthetic rehabilitation of the jaw (Schropp et al., 2003; Nahles et al., 2014).

1.4. Alveolar Bone

The alveolar bone is that part of the maxilla (upper jaw) or mandible (lower jaw) which supports the teeth (see Fig. 4 & 5). The alveolar bone grows in combination with the growth and eruption of the teeth. The alveolar bone process is formed from cells of the alveolar bone proper (dental follicle) and cells associated with tooth development. The alveolar bone in combination with the root cementum and periodontal ligament constitutes the periodontium of the tooth, which has an important role in the distribution and relief (resorption) of the outer acting forces, such as mastication (Lindhe et al., 2008).

Alveolar bone is composed of two parts: firstly, the alveolar process of the maxilla and the mandible, which represents the home of the developing tooth buds, then receives the root of the tooth after eruption. The alveolar process provides structural stability for teeth. There is no need for this part of bone if the teeth are lost, then it will be subjected to resorption. Secondly, the alveolar bone proper represents the bone that surrounds the tooth socket, which forms the site of attachment of the periodontal tissue and its related tooth (Chu et al., 2014).

The alveolar process has two layers, the outer layer (cortical bone) and the inner layer (cancellous bone) (see Fig. 4 & 5). Nerves and blood vessels run through the alveolar process to supply the bone and teeth. The cortical bone of the alveolar process is thicker in the mandible than in the maxilla. The alveolar crest at the coronal border of the socket is formed by the fusion of the alveolar bone proper with the cortical bone of the process. In healthy people, the alveolar crest is nearly 1–2 mm below the cement-enamel junction (CEJ) of the tooth. Interdental bone is the alveolar bone between two teeth and the interradicular septum is the bone between the roots (Carranza & Newman, 2006; Chu et al., 2014).

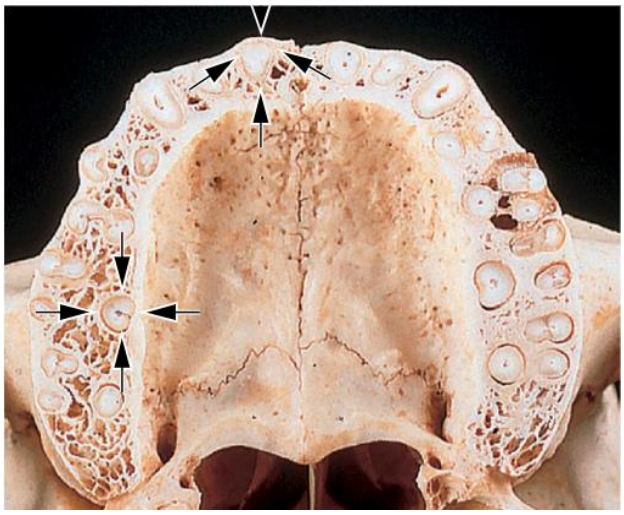


Fig 4 Alveolar bone cross section through the maxilla

The cross section through the maxilla at the mid root level, the arrows illustrate the wall of the socket which is lined with cortical bone and cancellous bone (adapted from **Clinical Periodontology and Implant Dentistry Book,** 5th edition, p.35). (The permission is acquired from publisher *Blackwell Munksgaard / UK*, Licence ID:1104248-1, copy rightsholder: *John Wiley & Sons – Books*)

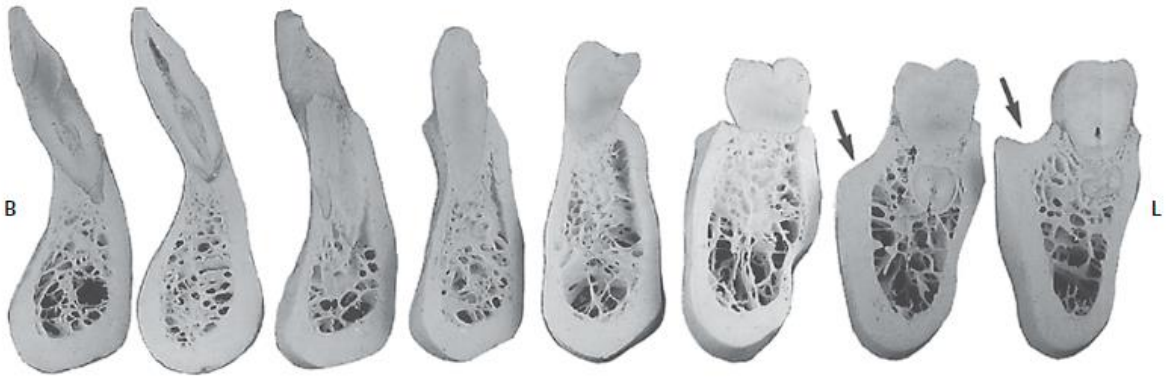


Fig 5 Alveolar bone vertical section through various regions of the mandible

The represents a vertical section through various regions of the mandible, B & L indicate buccal and lingual aspects, arrows show *linea obliqua* (adapted from **Clinical Periodontology and Implant Dentistry,** 5th edition, p.36). (The permission is acquired from publisher *Blackwell Munksgaard / UK*, Licence ID:1104248-1, copy rightsholder: *John Wiley & Sons – Books*).

1.5. Resorptive changes of the alveolar bone

Post extraction resorptive changes take place in both horizontal and vertical dimensions (Atwood & Coy, 1971; Schropp et al., 2003; Tallgren, 2003; Sargolzaie et al., 2018). After tooth loss, the total height of the alveolar bone can decrease up to 60% after 2 years of being load free (Cawood & Howell, 1988). The dimensional changes take place differently in the lower and upper jaws, and are particularly pronounced in the buccal alveolar walls, with 50% occurring in the first three months (Schropp et al., 2003; Petaibunlue et al., 2019). Tan and colleagues declared that a horizontal alveolar bone loss of about 29–63% and vertical bone loss of 11–22% occur within the first three to six months (Tan et al., 2012). Typical jaw atrophy (centripetal form in the maxilla, centrifugal in the mandibula) in case of non-existent residual tooth stock leads to a transversal shift of the mandibulo-maxillary relationship (Heberer et al., 2008). Many conditions can lead to bone resorption before tooth extraction, such as traumatic lesion of bone and teeth, periapical lesion and progressive periodontal disease, with traumatic tooth extraction being the most common cause of bone loss (Jahangiri et al., 1998; Chen et al., 2004; Irinakis & Tabesh, 2007). The actual cause stands and the extent behind the resorptive changes are still unknown. Systemic conditions e.g., osteoporosis, renal disease and endocrine disorders may play a role in enhancing bone loss by changing normal physiological processes and metabolism (Atwood, 1962, 2001; Irinakis & Tabesh, 2007; AlSheikh et al., 2019). The main goals of reconstruction and augmentation are the restoration of a sufficient bony situation, both in the horizontal as well as vertical dimension to the placement of the dental implant in an ideal prosthetic position (Nahles et al., 2014).

1.6. Reconstruction of resorptive changes of the alveolar bone

Depending on the size of the defect, bone regeneration of the alveolar bone and pre-implant preparation of various concepts, such as onlay technique, Le-Fort osteotomy technique, distraction osteogenesis, as well as guided tissue regeneration (GTR procedure) and guided bone regeneration (GBR procedure) with a necessary combination of surgical intervention. In the case of onlay bone grafting, autologous grafts are mostly used to repair vertical, horizontal or combined progressively alveolar bone defects. In the interpositional technique, such as Le-Fort osteotomy or sandwich technique, the interposition of the autogenous bone graft is to compensate sagittal discrepancies between the upper and lower jaws. Distraction osteogenesis as further procedures are also used in the orthognathic surgery, as well as to correct atrophic changes in the jaws (Hidding et al., 2000; Nahles et al., 2014). Other possibilities for bone regeneration are GTR and GBR procedures. Originally, GTR procedures were used in periodontal surgery for the regeneration of the periodontium. Later, the indication was extended with the possibility of regeneration of bone defects (GBR procedure) (Rose & Rosenberg, 2001; Bremm et al., 2004). The concept of GTR involves the application of a membrane to achieve a physical barrier between the soft tissue and bone tissue, thus preventing the growth of rapidly generating cells of soft tissue into the placed graft (Zellin et al. 1996; Lindhe et al., 2008). At the same time, the blood clot is stabilised and the gained space used to support the mineralisation of the mesenchymal tissue (Zellin et al., 1996; Lindhe et al. 2008). GBR is useful in reconstruction of the horizontal defect of the alveolar bone or one wall bone defect around the implant body as in the dehiscence defect and fenestration. It is used in a one-stage procedure (augmentation and implantation simultaneously) when primary stability and correct 3D position is acquired. In such cases, GBR will include

autogenous bone collected from a neighbouring area with a bone scraper to cover the exposed implant surface. Bone substituting material (BSM) is utilised to cover these autogenous bones graft, then a membrane is placed on the top or both mixed to directly cover this defect. Autogenous bone can also be mixed with BSM and used in sinus augmentation (Buser et al., 1995; Budihardja & Mücke., 2019).

The barrier function can be achieved through non-resorbable as well as resorbable membranes. Non-resorbable membranes mainly consist of polytetrafluoroethylene (e-PTFE-Teflon) and are preferred because of their simple application. They are mostly used in large bone defects that are augmented (Chiapasco et al. 2006). A significant drawback of using a non-resorbable membrane is the need for a second surgical procedure for its removal. Having an additional surgery is mostly associated with concerns over patient acceptance, time, cost, and possible morbidity associated with any surgical procedure besides the probability of acquiring an infection which may consequently result in dehiscence (Tatakis et al., 1999; Chiapasco et al. 2006).

During the last decades, resorbable membranes have been increasingly used in bone augmentation. The advantage of these membranes is the residue-free metabolism, a second intervention to remove the membrane is therefore unnecessary (Bunyaratavej & Wang, 2001; Nahles et al. 2014). Resorbable membranes are tissue-compatible and permeable for vascular proliferation (Kozlovsky et al., 2009).

1.7. Bone augmentation procedure in oral cavity

1.7.1. General background

Human bone grafts or bone substitute materials are used in augmentative procedures to fulfil various requirements:

- osteogenesis, osteoinduction, osteoconductive

- biocompatibility

- porosity

Osteogenesis is the ability to form new bones, that is, the osteogenic capability of osteoblasts derived from an autogenous graft and nourished by diffusion to form new viable bone tissue (Budihardja & Mücke, 2019). **Osteoinduction** is the procedure of new bone formation by stimulating mesenchymal cell differentiation into osteogenic cells (Kenley et al., 1993). Cytokines, such as BMP and TGF, modulate bone matrix osteoinductive properties to enhance neoangiogenesis (Budihardja & Mücke, 2019), while osteoinductive proteins (e.g., BMP cytokines) induce the regulatory mechanisms and guide cell differentiation (Xiao et al., 2007). **Osteoconduction** is the presence of a structure as guidance or scaffold to enable the growth of bone tissue. The presence of these conductive effects enables the neogenesis of the bone through the proliferation of blood vessels (Davies, 2003; Budihardja & Mücke , 2019).

Autologous bone has a unique property in comparison with other augmentation materials, that is, it combines osteoinductive, osteoconductive and osteogenic properties, which is not the case for bone substitutes and composite materials. Hence, autologous bone grafts are the “gold standard” because of all the previously mentioned characteristics and lack of immunological response. Accordingly, it is regarded as the

most convenient material for bone regeneration procedures (Chiapasco et al., 2006; Sbordone et al., 2014; Sakkas et al., 2017).

With regard to biocompatibility, bone substitute materials are expected to be non-toxic, teratogenic or carcinogenic. Furthermore, they should not provoke pro-inflammatory reactions and there should be no rejection of the bone graft (Nahles et al., 2014). The porosity of the bone substitute material influences vascularisation, with the size and interconnection of the pores determining bone reconstruction (Eggli et al., 1988; Kirmeier et al., 2007).

1.7.2. Human bone grafts

There are different types of human bone grafts, with autologous bone being the gold standard due to its biological value (Zijderveld et al., 2005; Artzi et al., 2005; Sakkas et al., 2017). Depending on the extent of the atrophic area, the bone graft can be selected from the intraoral (chin, retromolar, tuber) or extraoral donor sites (ilium, fibula calvarial) for transplantation into the defective area (Nelson et al., 2006 a,b; Beck-Broichsitter et al., 2015). Many studies have demonstrated the successful integration of autologous grafts as a result of active remodelling (Nelson et al., 2006 a,b). However, the limited availability, morbidity in the donor site and the resorption of grafts post augmentation are considered disadvantages of autologous bone grafts (Lundgren et al., 1997; Sbordone et al., 2011; Guarnieri et al., 2019). (see Table 1)

Table 1 Types of bone graft materials

Bone graft	Source	Advantages	Disadvantages
Autografts "Gold standard"	Donor site and recipient site are from the same individual	Osteogenic, osteoinductive and osteoconductive properties; no risk of immunological rejection or infection transmission	Pain and morbidity in the donor site; limited quantity and availability
Allograft	Donor and recipient are genetically different but belong to the same species	(Osteoinductive) and osteoconductive properties without donor site morbidity; high availability	Absence of osteogenic properties; risk of an antigenic response and disease transmission
Xenograft	Donor and recipient are genetically non-identical and belong to different species	osteoconductive properties; low cost; high availability	Absence of osteogenic properties; risk of an antigenic response and disease transmission
Alloplastic	Biological materials synthesised in a laboratory	Osteoconductive properties; low cost; high availability	Minimal risk of rejection

Allogeneic graft augmentation is achieved between the same species (donor and recipient) which are not genetically identical. Furthermore, processing of the allogenic graft requires certain procedures, such as cryopreservation, lyophilisation and deproteinization (Misch et al., 1993; AlGhamdi et al. 2010; Sakkas et al., 2017). Allogenic grafts are highly biocompatible, easily applicable, yield good postoperative results, with no donor site morbidity and are readily obtainable (Margonar et al., 2010; Sakkas et al., 2017). They remain critical from an ethical aspect, and there is the possibility of cellular and humoral rejection and the risk of infection transmission (Glass et al. 2008). Allogenic grafts providing osteoconductive properties through structural porosity have advantages, such as their availability and avoidance of morbidity at the donor site (Zimmermann & Moghaddam, 2011; Oryan et al., 2014).

1.7.3. Xenogenic and Synthetic bone replacement materials

Xenogenic bone substitution materials are derived from animals (bovine, porcine) and act osteoconductively. According to the literature, xenogenic substitution materials have a low risk of infection transmission and are similar to allografts, with a low rate of morbidity because there is no need for a second surgical intervention. These materials are subjected to demineralisation and deproteinisation via thermal and chemical treatments using sodium hydroxide (Hönig et al., 1999; Ausenda et al., 2019).

Alloplastic bone substitution materials are biocompatible synthetic materials, including calcium carbonate, tricalcium phosphate, hydroxyapatite, bioglass and calcium-coated polymers (Budihardja & Mücke, 2019).

1.8. Vascular and Avascular autografts

1.8.1. Vascular Autogenous Graft

The bone graft is taken with its arteries and veins and anastomosed with blood vessels of the recipient area (usually neck vessels) by microsurgery procedure. There are considerable benefits by using this method. For instance, there is less cellular ischaemia and fast growth in the area due to the direct blood nutritional supply. Both of bone and soft tissue can be gathered in this bone graft (Mitchell, 2006; Steel & Cope, 2015). Nonetheless, this method has some drawbacks including the need for highly skilled operator hands, a complicated surgical operation in addition to being a relatively expensive procedure. Generally, this type of graft is usually used in the reconstruction of large defects of the maxilla or mandible, post tumour resection and other malignant lesions. Fibula and iliac bone are the most common areas used for harvesting the graft (Brown et al., 1996; Mücke et al., 2009, 2013). The consideration of donor site morbidity is mentioned and discussed intensively in literature, as after DCIA harvesting, which can be included mobility reduction of hip joint and lumbar spine as well as persistent sensory disturbance (Rendenbach et al., 2019). A permanent deficiency in ankle joint motion and persistent pain may occur after fibula harvesting (Rendenbach et al., 2018).

1.8.2. Avascular Autograft

1. **Intraoral**: symphysis, retromolar region, tuber maxillae and Crista zygomaticoalveolaris.

2. **Extraoral**: iliac crest, calvaria, head of tibia, fibula and ribs.

1.9. Harvesting of autogenous bone from Intraoral sites

Intraoral autogenous bone is regarded as main origin for donor bone graft as it possesses osteogenic, osteoconductive, and osteoinductive properties. Moreover, the cortical bony nature has an important advantage in providing mechanical resistance. Intraoral autogenous bone is used to repair alveolar bone defects, either the horizontal, vertical, or a combination of the two (Neukam & Mosgau, 2004; Clementini et al., 2011). However, because of the small size of the harvested intraoral boney piece, the intraoral graft can only be used to reconstruct a small to medium size bony lesions (Schwartz-Arad & Dori, 2002; Nkenke et al., 2014).

Grafts can be collected in the form of:

• bone graft, including cortical and cancellous bone.

• cancellous bone alone.

Intraoral autogenous bone grafts can be gathered from the following regions: symphysis mandible, retromolar (ramus) area, the anterior wall of the sinus, tuber maxillae, edentulous region, mandibular tori, and crista zygomaticoalveolaris. Generally, both retromolar and symphysis regions can give a large volume of bone, whereas only a small amount of bone can be obtained from other intraoral bony tissues (Proussaefs et al., 2002; Neukam & Mosgau, 2004; Zouhary et al., 2010).

1.9.1. Harvesting bone from the Mandibular symphysis.

The mandibular symphysis can provide a reasonable quantity of a graft of both cortical and cancellous bone characteristics. Accordingly, this is considered as a positive to promote graft healing. However, harvesting bone from this site should be performed carefully to avoid sensitivity issues ad compromising the vitality of the adjacent teeth (Nkenke et al., 2001). Other postoperative complications may occur including ptosis

in the chin, which may affect the patient's aesthetic profile when the bone is collected from this region (Hunt et al.,1999; Montazem et al., 2000).

1.9.2. Harvesting bone from the Mandibular retromolar area (Ramus)

Generally, retromolar and symphysis regions in the oral cavity can provide a valuable quantity of bone for grafting (Proussaefs et al., 2002; Zouhary et al., 2010; Clementini et al. 2011). The external oblique ridge is preferred because it offers a sufficient quantity of mandibular bone blocks grafts. The close proximity of the donor and graft sites, the reduction of the required time for anaesthesia and the procedure, minimal donor site morbidity, the absence of cutaneous scarring and less hospital admission time, result in favourable conditions for augmentation utilising autogenous bone grafts. Additionally, intraoral bone grafting is preferable when only limited amounts of bone are required (Khoury et al., 2007; Klijn et al., 2010; Nkenke et al., 2014; Voss et al., 2016). In addition to the osteogenic, osteoconductive, and osteoinductive properties of retromolar bone, the cortical bony structure has outstanding mechanical resistance features. The horizontal or vertical bony defects, as well as a combination of them, can be repaired by using a retromolar donor site (Neukam & Mosgau, 2004; Clementini et al., 2011; Khoury et al., 2007,2009, 2015; Budihardja & Mücke, 2019). However, the relatively limited amount of bone that could be gained from this donor site means this approach is only suitable for treating small to moderate bone defects (Schwartz-Arad & Dori, 2002; Budihardja & Mücke, 2019). Multiple grafting procedures can be distinguished depending on the size and shape of the bony defect. The bone from this donor site can be used in different forms, such as block bone grafts or particulate bone, with both successful for augmentation procedures of alveolar ridge deficiencies (Aloy-Prósper et al., 2011; Dasmah et al., 2012; Voss et al., 2016).

Harvesting bone from the mandibular ramus should be performed by elevating the outer plate, which consists mainly of cortical bone. The purpose behind this way of the bone harvesting is that to eradicate the risk of causing trauma to the mandibular canal or any teeth located in the mandibular cancellous area (Nkenke et al., 2001). However, because the retromolar bone blocks consist mainly of cortical bone with a small amount of cancellous bone, this may make it more resistant to revascularisation, consequently negatively affect its regeneration potential (Khoury et al., 2015). Accordingly, the harvested thick bone block was divided with a micro saw into two thin bone blocks as in the shell technique of the grafting procedure (Khoury et al., 2007; Khoury et al., 2015). The splitting procedure will increase the number of bone blocks, providing more surfaces in a different form. Moreover, it will enhance revascularisation and regeneration (Khoury et al., 2007). Bone blocks may be fixated in the form of a single monocortical block or utilising the bone shell technique (both vestibular and lingual aspects are rebuilt by applying bone block), in which space is left between the bone graft and the recipient site, which is then filled with cancellous bone. This technique allows for more osteoconductivity of the graft (Khoury et al., 2007).

Reconstruction of the atrophied jaw is challenging as vertical bone reconstruction is more difficult than horizontal bone reconstruction. Intraoral donor sites can provide bone grafts to achieve augmentation of small to moderate bony defects and the retromolar bone graft is regarded as a convenient graft for this purpose. Both bone blocks and particulated bone graft can be gathered from this site and if multiple cancellous bones are required, it is optimal to use the symphysis area for this purpose. The success rate of augmentation from intraoral donor sites is high if performed by experienced surgeons using the correct technique (Khoury et al., 2007; Nkenke et al., 2014; Voss et al., 2016; Budihardja & Mücke, 2019).

1.10. Harvesting of autogenous bone from Extraoral sites

1.10.1. Harvesting bone from Calvaria

Skull cortical bone has the highest mineral density of the human body in comparison with other extraoral cortical bones, higher than that obtained from the mandible. (Cordaro & Terheyden 2014, 2019). Therefore, the skull bone is less susceptible to resorption and this resistance to resorption exceeds that of the other extraoral cortical bone (Mertens et al., 2012; Chiapasco et al.2013), promoting healing in the intraoral recipient site. It can be harvested under general anaesthesia from the parietal bone on both sides of the sagittal suture, which is considered as an area of great thickness (Cordaro & Terheyden 2014, 2019).

The thickness of blocks harvested from the dipole ranges between 4–5 mm thick and this includes cortical bone. During osteotomies, bone chips are gathered by a bone trap. It has been stated by some scientists that using pieces of pericranium is important as a source of natural collagen membrane (Chiapasco et al., 2013). Authors reported a high success rate up to 96% of implants placed in augmented jaw with calvarium bone (Chiapasco et al., 2013). The morbidity of the donor region can be lowered if the graft is carefully obtained and the resulting donor defects are rapidly refilled with newly formed bone. However, grafting from the calvarial sites could result in severe complications, intracerebral haemorrhage which is a life-threatening condition, intracranial penetration and fracture of the skull (Scheerlinck et al., 2013). Accordingly, bone collection from the skull region should be conducted by skilled maxillofacial surgeons who can deal with any probable complications. An advantage of this procedure is that the scar is disguised by the hair (Condaro & Terheyden, 2014, 2019).

1.10.2. Harvesting bone from the iliac crest

The iliac bone, both the anterior and posterior iliac crest, is one of the most commonly used extraoral donor sites for harvesting avascular autologous cortical and cancellous bone grafts for bone reconstruction (Kessler et al., 2005; Pape et al., 2010). Bone from the iliac crest is rich in cancellous material, which contains many vital cells that promote osteoconductive, osteoinductive and osteogenic/proliferative effects that result in high healing and regenerative capacity compared to other donor sites (Springer et al., 2004; Khoury et al., 2007). Moreover, the iliac crest can be utilised in a variety of clinical situations in the maxilla and mandible, including defects with a large discontinuity of the mandible because it obtains an adequate bone volume for prosthetic rehabilitation and facial aesthetic standardisation (Pogrel et al., 1997; Springer et al., 2004; Chiapasco et al., 2008). Nonetheless, these iliac crest grafts can be harvested as a bicortical block, monocortical block, or particulate material composed of cancellous bone and bone marrow. The specificity of the required surgical procedure and the site to be repaired will determine the shape and size of the graft. Specific methods are used for the maxilla and mandible and on some occasions, the same technique can be applied for both jaws. The surgeon should reform the harvested piece of iliac bone to fit and be suitable according to the required shape and position considering the prosthetic position of the abutment (Kademani et al., 2006; Khoury et al., 2007). As mentioned before, a bone graft from the hip donor site can be harvested from both the anterior and posterior iliac crest (Kessler et al., 2005). In a CT measurement study, Kilinc et al. suggested that corticocancellous bone, as well as a more cancellous bone graft, could be harvested with the posterior approach. While harvesting from the anterior one, it is possible to obtain a larger cortical as well as a bicortical bone graft (Kilinc et al., 2017), as confirmed by Engelsted and Mores (2010),

who reported that the collected cancellous bone graft from the posterior iliac bone was larger than that from the anterior iliac bone graft. Generally, the iliac bone provides an adequate volume of cortical, corticocancellous and cancellous bone graft (Kessler et al., 2005). Regarding the morbidity and complications after bone grafting of both approaches, the literature has discussed discomfort, pain, functional disorders, gait disturbances, herniation and sensory disturbances (Banwart et al., 1995; Arrington et al.,1996; Kalk et al., 1996; Ahlmann et al., 2002; Kessler et al., 2005; Barone et al., 2011; Dimitriou et al.,2011; Fretwurst et al., 2015b; Ou et al. 2015, Suda et al., 2018), with some reports of more postoperative complaints after grafting from the anterior iliac crest compared to the posterior iliac crest (Kessler et al., 2005). In contrast, Fretwurst et al. reported a high acceptance of up to 95% in patients with harvesting procedures from the anterior iliac crest, as well as a lower postoperative rate of complaints (Kalk et al., 1996; Ahlmann et al., 2002; Fretwurst et al., 2015b). Postoperative complications in the iliac donor site are avoidable, especially as some authors have described safe surgical techniques for bone harvesting and wound closure (Arrington et al., 1996; Dimitriou et al., 2011; Fretwurst et al. 2015b). In the literature, harvesting bone from the posterior iliac crest is associated with fewer postoperative complications but some authors argue that the posterior approach has drawbacks, that the harvesting is limited to only monocortical blocks and the patient should be repositioned to prepare the intraoral recipient site, which elongates the operation/anaesthesia time and increases the costs (Chan et al., 2001; Kessler et al., 2005). Although some authors reported that the volume of cancellous bone which is gained from the posterior approach is larger than that from the anterior (Kessler et al., 2005; Engelsted & Mores, 2010), other authors prefer the anterior approach which permits harvesting larger mono and/or bicortical bone grafts, as it is less time-

consuming and the patient does not have to be repositioned to prepare the recipient oral and maxillofacial region (Fretwurst et al., 2015b; Kilinc et al., 2017).

In the 1970s, iliac crest bone grafts were utilised to reconstruct jaw atrophy due to early missing teeth or the ageing process and to improve prosthetic rehabilitation without implant insertion, resulting in almost complete resorption of the autogenous graft (Curtis et al., 1977). The resorption tendency of the iliac bone graft was intensively described in the literature, especially when the bone graft was not properly and punctually loaded after augmentation (Vermeeren et al., 1996; Verhoeven et al., 2006; Cordaro & Terheyden, 2014, 2019). Some studies showed that bone grafts that have a membranous origin, such as mandibular symphysis and ramus, demonstrated less resorption tendency than endochondral bone grafts like the iliac crest and tibial plateau (Smith & Abramson, 1974; Dolanmaz et al., 2015). However, other authors suggested that the morphology, the ratio of cortical to the cancellous bone and the microarchitecture of the bone graft are the determinants of bone loss behaviour and survivability of the bone graft (Ozaki & Buchmann, 1998; Sugg et al., 2013). Authors reported in the observation time of up to 5 years, there was 50% bone loss (mostly in the first year) of the graft volume and around implants after augmentation with a one-step iliac bone graft (Vermeeren et al., 1996; Verhoeven et al., 2006). In the early 1990s, some problems were reported with the one-step technique comprising insufficient implant positioning for prosthetic rehabilitation and tissue dehiscence, by which patients suffered from peri-implantitis as well as aggressive bone resorption. Accordingly, this necessitated a second surgical intervention, so this technique was not recommended by some authors (Nyström et al., 1993; Vermeeren et al., 1996; Van der Maij et al., 2004; Verhoeven et al., 2006). Since then, the timing of the implant placement, whether simultaneous or delayed, has been extensively discussed in the

literature (Lundgren et al., 1997; Sjöstrom et al., 2006; Verhoeven et al., 2006). By the end of the 1990s, the two-stage method was established, with Lundgren et al. (1999) demonstrating that waiting for bone graft regeneration through revascularisation and delayed implant placement improved the osseointegration of the implant. Furthermore, other authors recommended waiting for 4–6 months to perform the second surgical intervention for implant placement (Schliephake et al., 1997; Lundgren et al., 1997). However, numerous studies have reported that the initial bone resorption occurred in the first six months (Nyström et al., 1995). Long-term studies showed that three months of healing for both the graft and the implants is sufficient for the revascularisation of graft and the secure insertion of rough-surfaced dental implants, as well as the loading of the implants, similar to that achieved in non-augmented jaws (Raghoebar et al., 2003, Nelson et al., 2006 a, b; Heberer et al., 2009).

In the last three decades, many oral and maxillofacial surgery centres, surgeons and authors have utilised and described this donor site and its indications. The iliac bone crest is considered the gold standard under the autogenous bone graft applied in dental implantology and has a wide spectrum of usage. It has also been established that the two-step technique is the standard approach for the treatment of atrophied jaws, as well as the waiting before implant placement for 3 months after augmentation for successful graft healing and revascularisation. However, no long-term study to date has evaluated this protocol or whether there is an individual influence on the peri-implant bone level changes and the iliac graft resorption tendency.

2. Aim of Study

This study aimed to evaluate crestal bone level changes around dental implants placed in onlay bone grafts harvested from the anterior superior iliac rim in the long term. Moreover, the present study analysed some parameters like gender, age of the patients as well as type and diameter of the dental implants that may influence the peri-implant bone level changes.

3. Methodology

This study was approved by the local ethical committee of the Charité Medical University Berlin, Germany. (Ethics number: EA2/135/13).

3.1. Study design and sample

A total of 32 patients (22 female and 10 male) with a mean age of 52 years (range, 22-70 years) underwent maxillary or mandibular onlay augmentation with iliac bone grafts and were re-examined. All patients were partially edentulous or edentulous and showed a severe resorption of the alveolar ridge with a remaining bone volume of $\geq$ 5 mm in height.

Onlay grafting with corticocancellous bone from the anterior superior iliac crest was performed in all patients. In this study, corticocancellous bone blocks with a cortical rim of $\leq$ 4 mm were harvested from the median margin of the anterior iliac crest.

3.2. Exclusion criteria

The exclusion criteria were age less than 18 years, periodontitis, smoking, history of immunosuppression, irradiation, or chemotherapy, and participation in other studies.

3.3. Surgical procedure

Bone harvesting and bone augmentation were performed under general anaesthesia while the implant placement was done under local anaesthesia. The collection of bone from the iliac crest was conducted by two expert surgeons according to a standardised protocol as follows: the selected iliac crest was positioned in the ordinary style to form the anterior part of the crest and to approach the anterior iliac spine. The surgical incision was made 1 cm behind the anterior iliac spine in a posterior direction following the iliac crest. An incision was performed in the midcrest of the rim to cleft the musculotendinous aponeurosis of the tensor muscle of the fascia lata and the oblique

abdominal muscles avoiding harming the muscle fibres. The median cortical plate of the anterior rim was exposed directly by pulling back the iliac muscle subperiosteally. After raising the iliac muscle, the donor area was exposed with a retractor (see Fig. 6). Two vertical and two horizontal bone incisions were made by an oscillating surgical saw (Aesculap, B. Braun Melsungen AG, Melsungen, Germany) and osteotomes (Gebrüder Martin GmbH & Co. KG, KLS Martin Group, Tuttlingen, Germany) to harvest a corticocancellous bone block. A superior horizontal bone incision was made midcrestally and the inferior horizontal bone incision was achieved with a curved osteotome (Fig. 7). The iliac bone block was harvested in a way to have two cortical layers, which were angulated with each other (Fig. 8). Following harvesting of the corticocancellous bone block from the inner table, extra cancellous bone was extracted utilizing curettes being cautious to avoid perforating the lateral cortical plate. The harvested cancellous bone will be used when sinus lifting was planned simultaneously. The shape and size of the onlay bone grafts were made according to the needed size and dimensions. Suturing was made in three sheets including the muscle layer, the subcutaneous and intracutaneous layers (2-0 Vicryl®, 4-0 Vicryl® and 5-0 Ethilon®, Ethicon, Norderstedt, Germany). The oral part of the operation began with a crestal incision in the attached gingiva of the edentulous alveolar crest with three vertical releasing incisions. In the edentulous region of jaw, corticocancellous bone blocks were fixated on the labial and occlusal part of the alveolar ridge, so that the two cortical walls were occlusal and vestibular. Microscrews were applied to fix each bone block (Modus 1.5, Medartis, Umkirch, Germany) (see Fig. 9). Iliac cancellous bone was applied to fill the gaps between the blocks. The bone grafts were shielded with periosteum and the passively mobilised mucosa (tension free) was sutured utilizing a running suture and attached with interrupted sutures (5-0

Monocryl, Ethicon, Norderstedt, Germany). The patients were given an intravenous antibiotic regimen (Unacid 2 g or 600 mg clindamycin when the patient is allergic to penicillin) during the operation and a postoperative oral antibiotic (Unacid 2 g 2x1 or 300 mg clindamycin three times a day) for seven days after the procedure. All patients are supplied with an elastic abdominal bandage (Helios® Leibbandage Spezial Typ B, med.kontex GmbH, Teonisvorst/Krefeld, Germany) for one week and were hospitalised for 2–3 days. The iliac sutures were removed after ten days.

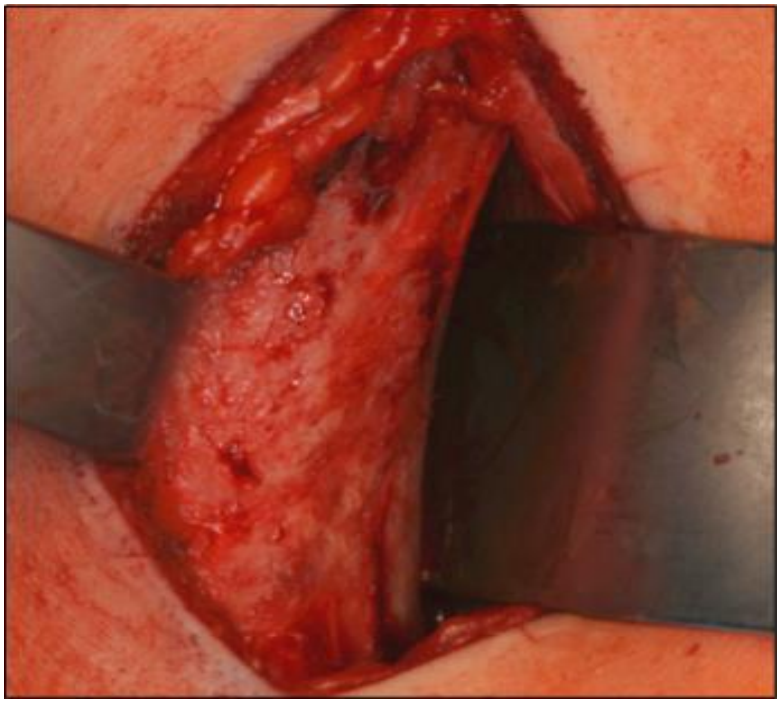


Fig 6 The exposed median cortical plate of the anterior superior rim of iliac spine.

(*From Charité University Medicine of Berlin, CVK- Oral & Maxillofacial Surgery)*

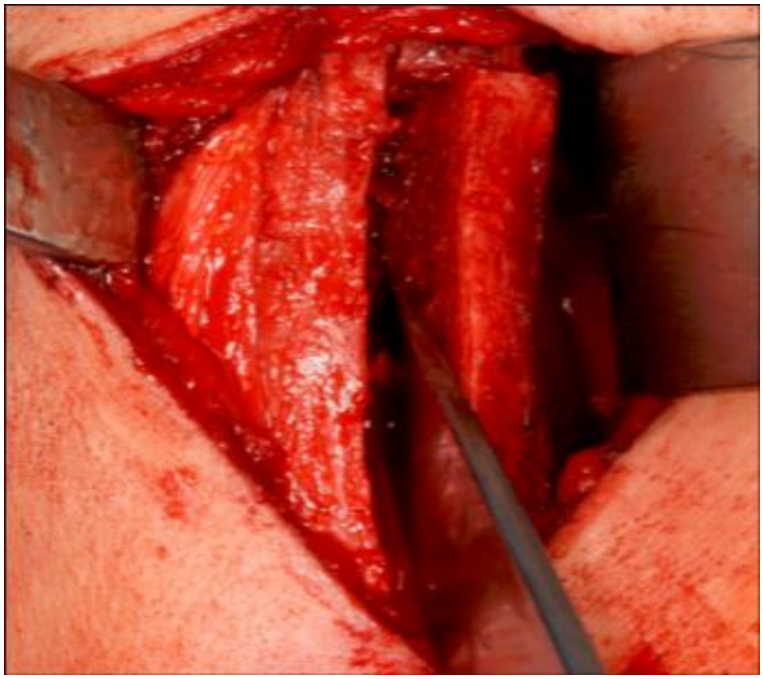


Fig 7 The mobilized bone graft after horizontal and vertical bone incision with surgical saw.

(From Charité University Medicine of Berlin, CVK- Oral & Maxillofacial Surgery).

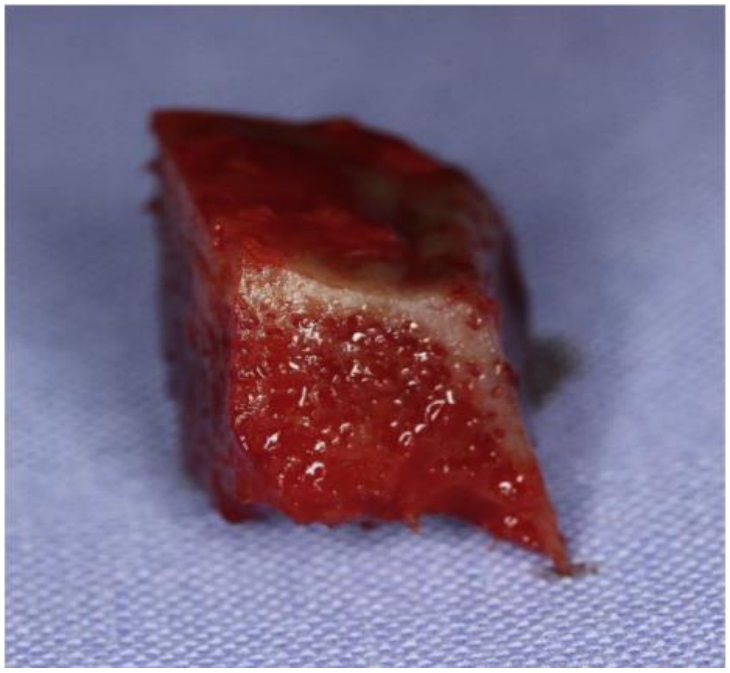


Fig 8 The harvested corticocancellous iliac graft with two curved cortical walls and cancellous internal part before preparation for intraoral fixation.

(From Charité University Medicine of Berlin, CVK- Oral & Maxillofacial Surgery)

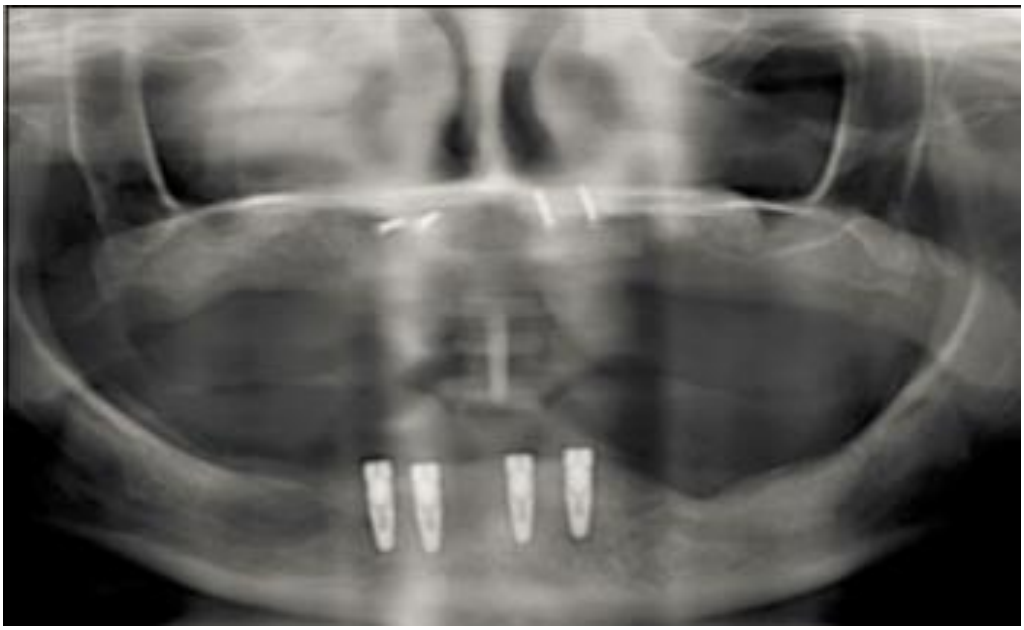


Fig 9 Bone graft fixation in the maxilla with multiple microscrews.

(From Charité University Medicine of Berlin, CVK- Oral & Maxillofacial Surgery)

(Modus 1.5; Medartis, Umkirch, Germany)

Postoperative clinical evaluation was performed after 1, 3, 10, and 30 days as well as after 3 months. The clinical examination included observing complications such as inflammation, mucosal erythema, wound dehiscence and loss of bone grafts. Orthopantomograms (standardised radiographic examinations) were performed before and immediately after the surgical procedure, after 1, 3, 5, and 10 years.

3.4. Implant placement

After three months of healing, the microscrews were removed and the dental implants placed by making a mucoperiosteal flap in the area of the previous incision line used in the grafting procedure (see Fig. 10).

Among all 32 patients, a total of 150 implants were placed according to manufacturer's surgical protocol; 99 were Camlog RootLine implants (Camlog Biotechnologies, Wimsheim, Germany), 18 were Straumann Tissue Level implants, 10 were Straumann

Bone Level implants (Straumann AG, Basel, Switzerland), and 23 were Steri-Oss implants (Nobel Biocare Deutschland GmbH, Cologne, Germany). The bone level Straumann, Camlog and Steri-Oss were inserted equicrestally. All Tissue level Straumann implants were positioned with the smooth-rough border at the crestal bone level (see Fig. 12). The mucoperiosteal flaps were closed with running sutures and secured with randomly interrupted sutures (5-0 Monocryl, Ethicon, Norderstedt, Germany).

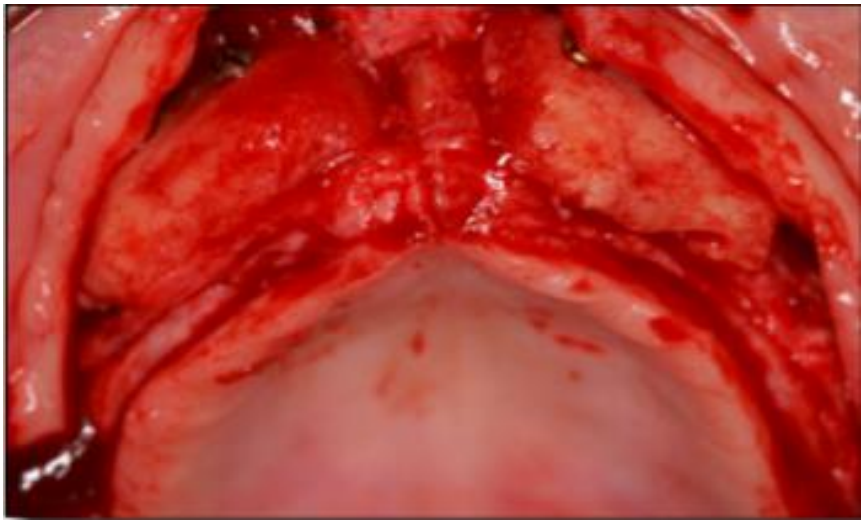


Fig 10 The exposed maxilla for implant placement after 3 months.

(From Charité University Medicine of Berlin, CVK- Oral & Maxillofacial Surgery)

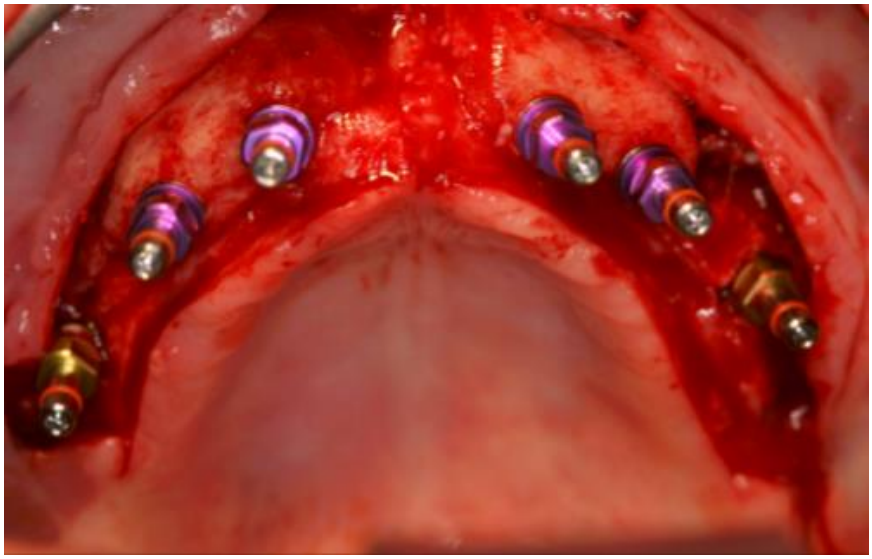


Fig 11 The initial implant position directly after implant insertion

(From Charité University Medicine of Berlin, CVK- Oral & Maxillofacial Surgery)

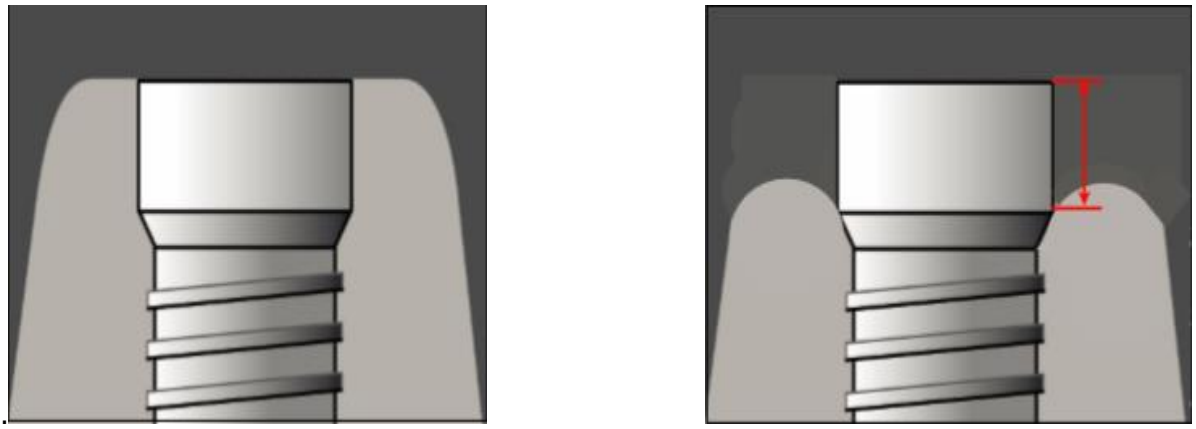
The duration of unloaded healing of the maxillary implants was 12 weeks, 8 weeks for mandibular implants. At loading, the stability of the implant was re-examined with a torque ratchet. If the torque of the implant was **<** 35 Ncm, then the prosthetic treatment was initialised. All patients are supplied with a splinted prosthetic treatment and were either restored with a removable denture seated on individually fabricated bars or with fixed bridges.

3.5. Radiographic and clinical evaluation

All patients received spaced standardised radiological examination for evaluation of peri-implant crestal bone loss. The quantitative evaluation of the crestal bone loss was analysed on routine orthopantomographs as described previously (Go'mez-Roman et al., 1997; Semper et al., 2010; Heberer et al., 2011; Nack et al., 2014). Conventional radiographs (Orthophos Plus, Sirona, Bensheim, Germany) were not digitised and were analysed using a previously published method (Semper et al., 2010; Heberer et al., 2011). Digital orthopantomographs (Orthophos XG 5/Ceph, Sirona, Bensheim,

Germany) were analysed with Kodak Dental Imaging Software 6.8 (Carestream Dental, Stuttgart, Germany). The measurement of the vertical changes in the marginal bone was performed at the described time points t0 (postoperatively = baseline), t1 (after 1 year), t2 (after 3 years), t3 (after 5 years), and t4 (after 10 years) five times at mesial (m) and distal (d) sites of the implant (see Fig. 12 A & B). To eliminate radiographic distortions, the values were adjusted with respect to the original length of the implant.

The interpretation of the values of the mesial and distal sites was performed separately, and the mean values for all sites (mesial/distal) were determined as follows: m1/d1 = value of mesial/distal bone contact from the reference point after 1 year; m2/d2 = value of mesial/distal bone contact from the reference point after 3 years; m3/d3 = value of mesial/distal bone contact after 5 years; and m4/d4 = value of mesial/distal bone contact from the reference point after 10 years. Bone level changes were analysed by subtracting the values of bone loss from the initial postoperative value.



A B

Fig 12 Implant position and bone loss value

A: The initial postoperative implant position, **B**: the measurement of bone loss value (Gómez-Roman et al.,1995) at 1, 3, 5 and 10 years

The success outcome of the implants was clinically investigated and analyzed according to certain success criteria as well described by Buser et al. 1990. The implants were regarded successful when fulfil the success criteria.

These “criteria are:

- Absence of persistent subjective complaints, such as pain foreign body sensation and / or dysesthesia.
- Absence of recurrent peri-implant infection with suppuration.
- Absence of mobility.
- Absence of continuous radiolucency around the implant.’’

(Buser et al., 1990; Buser et al., 1997).

3.6. Statistical analysis

The interclass correlation coefficient (ICC) was used to determine the intra observer reliability using SPSS16.0 software (SPSS Inc., Chicago, IL, USA). Besides the descriptive evaluation of the data, the correlation between the diameter, age, gender, and localisation with mesial and distal bone level changes was analysed using the Mann-Whitney U-test and the Spearman rank-order correlation coefficient. The mesial and distal site were analysed separately. Statistical analysis was performed using SPSS 13.0 software (SPSS Inc.) and SAS version 9.1 (SAS Institute Inc., Cary, NC, USA). A P-value of < 0.05 was considered statistically significant.

4.Results

A total of 150 implants were placed (23 Steri-Oss, 99 Camlog and 28 Straumann). The mean observation period of all implants was 69 months (range, 12e165 months). A total of 88 implants (maxilla, 83, mandible, 5) were followed up for more than 5 years, and 29 implants were followed up for 13 years. The mean observation period of the maxilla with 125 implants (23 Steri-Oss, 82 Camlog implants, 20 Straumann) was 75 months (range 12–165 months) and the mandible with 25 implants (17 Camlog implants, 8 Straumann implants) had a mean follow-up of 42 months (range 12–91 months).

In this current study, the clinical evaluation and success outcome of implants placed on the augmented maxilla and mandible has been analysed according to the success criteria of Buser et al. 1990. The implants regarded successful when there is no mobility, no continues peri-implant radiolucency, no recurrent peri-implant infection with putrid secretion and absence of persistent symptoms such as pain, sensation of foreign body or dysesthesia (Buser et al. 1990).

During the observation period, seven implants (five maxillary and two mandibular implants) were lost. Two implants in the lower jaw were lost prior to loading due to a failed osseointegration. No second implant insertion was performed. One implant was lost in the maxilla after 6 years and four maxillary implants after 8 years due to peri-implantitis. The survival success rate of the implants was 95% (maxilla, 96%; mandible, 92%).

The mean values of bone level changes over time are listed in table 2 & 3. There was a mean crestal bone loss of 2 mm (range 0.5–4 mm) in female patients and 1 mm (range, 0.5–2 mm) in males documented after 10 years.

Of all implants, 92 had a follow-up of five or more years, with the mean values of bone level changes during this period listed in table 2 & 3. There was a significant difference between gender (Fig. 13) ($P_{mesial+distal}<0.01$) in the crestal bone loss after 10 years, but no significant difference between the diameter of the implants ($P_{mesial} = 0.26$, $P_{distal} = 0.68$), implant systems ($P_{mesial} = 0.37$, $P_{distal} = 0.15$), and age ($P_{mesial} = 0.13$, $P_{distal} = 0.68$). The length, diameter, frequency, and manufacturer of the implant systems used are shown in Table 4.

Table 2 mean crestal bone loss for all implants over 120 months

***** *Bone level (mm)*

Time	**T1 (**1Year)		**T2** (3Years)		**T3 (**5Years)		**T4 (**10Years)	
Peri-implant	Mesial*	Distal*	Mesial*	Distal*	Mesial*	Distal*	Mesial*	Distal*
Maxilla	0,9 (0 - 3.3)	0.9 (0-3.5)	1.4 (0 - 4.3)	1.4 (0 - 4.4)	1.8 (0.1 - 4)	1.7 (0.2-3.7)	1.8 (0.4 - 4)	1.8 (0.4-3.8)
Mandible	1 (0 - 3.2)	1 (0.1-3.3)	1.1 (0.2-2.7)	1 (0.2-2.7)	1.8 (0.5-3)	1.5 (0.4-2.8)		

Table 3 mean crestal bone loss regarding gender for all implants after 120 months

***** *Bone level (mm)*

Time/ location	**T4 / Mesial***		**T4 / Distal***	
Gender	Male	Female	Male	Female
Peri -implant bone loss / level*	1 (0.4-1.9)	2 (0.6-3.9)	1 (0.4-1.5)	2 (0.6-3.8)
Number of implants	9	30	9	30

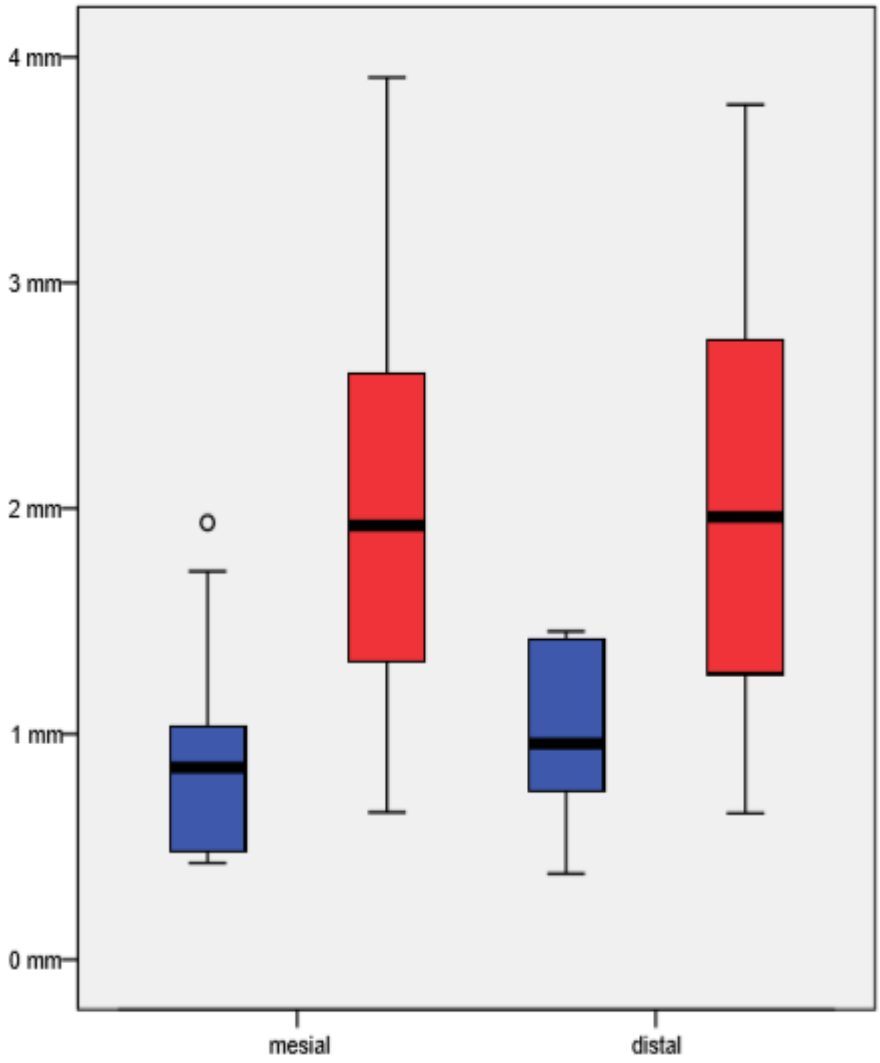


Fig 13 Comparison of bone loss between males and females

Diagram showing the significant differences of the bone loss between M-Male and F-Female.

Table 4 lengths, diameters, frequencies, and manufacturers of implant system used.

	Diameter	Frequency	%	Length	Frequancy	%
Steri - Oss	3.3	4	17.4	10	1	4.3
	3.8	14	60.9	12	14	60.9
	4.5	5	21.7	14	4	17.4
				16	4	17.4
	Total	23	100	Total	23	100
Camlog	3.8	63	63.4	9	4	4.0
	4.3	33	33.3	11	45	45.5
	5.0	2	2	13	45	45.5
	6.0	1	1	16	5	5.0
	total	99	100	Total	99	100
Straumann	3.3	2	7.1	10	17	60.7
	4.1	26	92.9	12	11	39.3
	total	28	100	Total	28	100

Table 5 mean peri-implant bone resorption according to implant system after 10-years follow – up, T4.

Implant system	Steri-Oss	Camlog	Straumann
Number of implants	23	16	0
T4 / Mesial Peri -implant bone loss in mm	0.9 (0.4 – 3.9)	1 (0.5 -3.9)	
T4 / Distal Peri-implant bone loss in mm	0.9 (0.4 – 3.8)	0.9 (0.8 – 3.4)	

5. Discussion

Population ageing and the overall number of infections, trauma and cancer of the maxilla and mandible are increasing, which can result in alveolar and basal bone loss necessitating advanced surgical and prosthetic reconstructive treatment (Maiorana et al., 2005). Typically, a collapse of the ridge tissue appears within the first three months after tooth extraction (Schropp et al., 2003) and this alteration in the architecture of the soft tissue and bone morphology can make the functional and aesthetic rehabilitation of the oral cavity more difficult, whether via conventional dentures or with an implant-supported prosthesis. Therefore, an adequate bone volume is needed for the insertion of dental implants for confirming primary stability (Misch et al., 1994; Castagna et al., 2013). In cases with severe alveolar atrophy, the treatment strategy demands a significant reconstruction by utilising autogenous bone grafts harvested from extraoral donor sites (Maiorana et al., 2005).

The present study evaluated the success rate of implants and radiographical data of bone level changes in peri-implant regions in thirty-two partially edentulous and edentulous patients. Initially, all patients had severely atrophied maxilla and mandible requiring bone augmentation before implant placement. The analysis revealed a high success rate after ten years, with a mean value of 95%, and a relatively stable peri-implant bone level of 1–2 mm during the observation period. In jaws that were augmented with iliac bone grafts, the bone resorption rate around implants was comparable to areas augmented with autogenous bone grafts harvested from other donor sites as well as around the implants in native non-augmented bones.

The graft quality

In the current study, a strategy was adopted to overcome the well-known tendency of endochondral bone (iliac bone graft) for resorption. The protocol involved only harvesting a corticocancellous block containing mainly cortical curvature. As described in the methodology section, the corticocancellous iliac bone block was harvested from the medial inner table of the ilium. The outer two cortical layers faced the periosteum and represented the later occlusal and vestibular aspects of the jaws. The inner cancellous layer faced the recipient bone after its manipulation to adapt the jaw surfaces. This concept has been discussed and investigated in numerous studies (Nelson et al. 2006a; Heberer et al., 2008). With no regard to the available amount of bone graft, bone density is considered a crucial factor for successful osseointegration which will improve the primary stability of dental implants (Esposito et al., 1998).

In general, several studies clarified that the embryologic origin of bone plays a major role in determining the rate and behaviour of bone resorption and survivability. The superior preservative property of membranous over endochondral bone has been highlighted in many studies and provides evidence about its favourable clinical use as an onlay grafting material in the craniofacial skeleton. Ozaki (1998) reported that the cortical bone is a superior onlay grafting material, regardless of the embryologic origin of its donor site (Ozaki & Buchmann, 1998). The resorption tendency of iliac crest bone grafts might be related to the quality and microarchitecture of the graft, as it is now obvious that the amount of cortical bone is crucial for the maintenance of the graft volume rather than the native embryologic origin (Ozaki & Buchmann, 1998; Ozaki et al., 1999; Heberer et al., 2008). Lundgren et al. (1997) stated that both cortical thickness and density of the donor bone are essential factors that could affect bone resorption pattern. The corticocancellous iliac grafts should be harvested with a thick

resorption-resistant cortical bone to maintain sufficient graft volume after the initial resorption, thereby enables placement of long implants with optimum primary stability (Lundgren et al., 1997). Indeed, Heberer et al. (2008) reported that the harvested thick cortex iliac bone blocks with a large proportion (72%) of cortical bone resulted in a mean 1.2 mm low bone resorption after 3 months of healing.

Simultaneous or delayed

This study verified the two-step technique which involves augmentation of the atrophied jaw, followed by implant placement after a primary healing period of 3 months in contrast to the one-step technique allowing insertion of the dental implants at the same time as jaw augmentation with a bone graft. Many previous studies have discussed and compared the one and two-step approaches, observing bone-implant interference when studying its related influence on the successful outcome (Lundgren et al., 1999; Yerit et al., 2004; Tosun et al., 2018). There are issues associated with the one-step technique, such as insufficient implant positioning for prosthetic rehabilitation and tissue dehiscence, which lead to poor primary implant stability and poor prosthetic orientation (Nyström et al., 1993; Vermeeren et al., 1996; Van der Maij et al., 2004). Also, a high rate of marginal bone loss is associated with the one-step approach (Vermeeren et al.,1996; Tosun et al., 2018). Nonetheless, the one-step method has some advantages, a single operation is more preferable to the patient and more cost-effective as well as being more time-efficient, thereby accelerating patient's rehabilitation (Yerit et al., 2004; van der Meij et al., 2005). However, the simultaneous method is still controversial given the high prevalence of complications (Vermeeren et al., 1996; Verhoeven et al. 1997). Dehiscence is the most frequent complication and can happen directly after augmentation. This wound dehiscence is accompanied by infection, resulting in comprehensive bone loss in the peri-implant area, which may

lead to graft and implants loss. Other challenges include difficulties in angulation and positioning of the implants as well as unexpected resorption at the augmented sites (Vermeeren et al., 1996; Schliephake et al., 1997; Verhoeven et al., 1997; van der Maij et al., 2005; Boven et al., 2014).

Lundgren et al (1999) preferred the second step method and described it in their histomorphological and morphometric analyses study of ten patients. They placed two micro-implants in the corticoancellous iliac graft and six months later (at ordinary implant placement), one micro-implant was retrieved with a trephine drill and a new one was placed in the graft. At the abutment surgery six months later, the remaining two micro-implants were removed in the same way and three bone specimens were histomorphologically analysed in the different healing periods (0–6, 0–12 and 6–12 months). The authors concluded better osseointegration of titanium micro-implants in the augmented maxilla with an onlay iliac bone graft after 6 months from augmentation. They showed that during the healing time in the two-step technique, the graft was revascularised comprising regenerated bone and bone marrow at the time of implant placement. This is in contrast to the one-step technique when the implant is placed into virtually non-viable bone. Other studies reported a striking difference in the survival and success rates between simultaneous and delayed implant placement in the augmented jaw. Yerit et al. (2004) compared the one and two-step technique after horseshoe Lefort I osteotomy with an iliac bone graft, finding that the 5-year survival rate of simultaneous implant placement was 87% in contrast to the delayed implant placement of 91%. Although their patients were satisfied after prosthetic rehabilitation, they concluded that the two-step technique was the method of choice. Sjöstrom et al. (2006) applied radiological examination and resonance frequency analysis measurement six months after grafting and implantation in a three-

year follow-up survey, showing predictable and stable long-term results of 29 atrophic edentulous maxilla augmented with an anterior iliac bone graft and treated with delayed implant placement. In the long-term ten-year observational study of Schliephake et al. (1997), they reported a noticeable difference in the success rate between primary and secondary implant placement on an augmented jaw with a combined inlay and onlay iliac bone grafts of 67.6% and 96.6%, respectively. Tosun et al. (2018) also reported that the delayed approach is a credible method with a high success rate and less bone resorption.

By contrast, the healed augmented alveolar bone in the two-step approach permits more adjustment in the alveolar bone before implant placement. The visual inspection of the graft after primary healing and the initial resorption permits implant placement within the optimum depth (epicrestal, supracrestal and subcrestal according to implant system manufacturer requirement). Conversely, implants placed simultaneously to bone graft, which may undergo a huge bone loss that threatens the graft and implant success outcome, was also suggested by Lundgren et al. (1997). Furthermore, the two-step approach enables implant placement with navigation systems utilising 3D planning and a surgical guide splint. All the above enables good primary stability and optimum positioning of the dental implant, which are the most important requirements for successful dental rehabilitation of edentulous or partially edentulous patients (Yerit et al., 2004). In this study, the two-step technique was performed with implant insertion three months after grafting, with functional prosthetic loading after another three months. At loading, the stability of the implants was re-examined utilising a torque ratchet and the prosthodontic treatment was initialised only when the torque value was greater than 35 Ncm. Many studies have debated the most appropriate duration of healing time before implant placement, discussing whether a longer healing time

means better bone integration and revascularisation. However, there will be more bone graft loss when it is not punctually and adequately loaded. It has been shown that three months of healing for both the graft and the implants are sufficient to ensure revascularisation of the graft, as well as secure insertion and loading of rough-surfaced dental implants (Nelson et al., 2006 a, b; Heberer et al., 2008). Nelson et al. (2006a) concluded that there was an adequate bony structure for secure implant placement after a healing period of three months in their histomorphometric evaluation, reporting that the amount of newly formed bone after three months was comparable to that formed after 4–5 months of healing. Furthermore, it was possible to prevent the onset of graft resorption by shortening the healing time before implantation. Tosun et al. (2018) indicated that implant placement three months after onlay iliac bone grafting is more reliable and results in a higher success rate and less bone resorption compared with simultaneous implant placement.

The success rate and resorption behaviour reported in these studies are in line with the present study findings, hence, the two-step technique is regarded as a standard technique in dealing with the placement of dental implant after jaw augmentation with an onlay iliac bone graft. Autologous bone blocks can be incorporated in the recipient site within three months (Heberer et al., 2008), so, it is not useful to wait for more than six months before implant placement because the graft may undergo resorption at the periosteal surface if it is not promptly and sufficiently loaded (Nelson et al., 2006 a, b; Heberer et al., 2008; Cordaro et al., 2011; Cordaro & Terhyeden 2014, 2019).

Success rate

It is generally accepted that osseointegration is a basic requirement for successful implantation. "Osseointegration" is defined as living and organised bone tissue in direct contact with a functionally loaded implant without any intervening connective tissue (Brånemark, 1983). It is important to know the consequences if an implant is no longer fully osseointegrated, therefore, success and survival rates were discussed and determined in several clinical studies to evaluate dental implant destiny. However, comparison and definitions of these two terms can differ significantly from one another The first step in determining a success rate is to define success criteria and many of the clinical and radiological success criteria for implants to date are negative criteria, the absence of which indicates success and the occurrence of which indicates failure (Albrektsson et al., 1986; Buser et al., 1990; Misch et al., 2008).

In this current study, the clinical evaluation of implants placed on the augmented maxilla and mandible has been done according to the success criteria of Buser et al. 1990. The clinical evaluation was made after 1, 3, 10, and 30 days after augmentation as well as 3 and 6 months, then annually up to 10 years post-implantation. The evaluation included the assessment of complications such as inflammation, mucosal erythema, wound dehiscence, loss of bone grafts and implant mobility. The radiographical examination (panoramic x-ray) was performed before and directly after augmentation and implantation, then at 3 months, 6 months, 1 year, 3 years, 5 years and 10 years. In this observational study, the implants were described as successful when there was no mobility, no continuous peri-implant radiolucency, no recurrent peri-implant infection with putrid secretion and absence of persistent symptoms such as pain, feeling of foreign body or dysesthesia (Buser et al., 1990). In this study, good bone graft integration in the recipient site, the high implant success rate (mean: 95%)

and the mean value of peri-implant bone loss confirmed the success criteria of Albrektsson et al. (1986) and Buser et al. (1990).

The present study results are in line with several long-term follow-up studies which have reported a high success rate of implants after augmentation with an iliac bone graft (Nyström et. al., 2009; Chiapasco et al., 2008; Boven et al., 2014; Nguyen et al., 2019). The prospective study of Nyström et al. (2009) observed in the long-term the success outcome of 334 implants in 44 patients who received an onlay and inlay bone grafts harvested from the anterior iliac bone crest. All patients waited six months for graft healing before implant placement and another 6 months for osseointegration before prosthetic rehabilitation. After 11 years of follow-up, the success rate was 90%. The study of Nyström et al. confirmed the treatment outcome of the current study and even the current work has a better success rate after treatment of both atrophic jaws. Chiapasco and colleagues showed an implant success rate of 93.7% and a survival rate of 96.7% among 60 implants, which were placed after 4–7 months in the reconstructed mandible with ilium or calvarium bone after benign tumour resection. No information about the success rates regarding the different augmentation procedure was given. The sixteen patients were subjected to a follow-up of (mean: 94 months, range: 36–132 months) after rehabilitation with a fixed prosthesis and 14 of them were fully satisfied (Chiapasco et al., 2008). Boven et al. reported a survival rate of 98.7% in a five-year observational study involving forty edentulous patients who received two implants four months after augmentation with an onlay iliac bone graft in the intraforaminal area and overdenture for each one. The good results of Boven et al. included a stable marginal bone loss of 0.6 +/- 0.7 mm, high patient satisfaction and stable clinical parameters, which correspond with the success rate criteria of Albrektsson et al. and Buser et al. However, the high survival rate was not regarded

as a fully successful outcome, maybe because some patients suffered from sensitivity disturbances due to mental nerve damage during mandible augmentation, which is inconsistent with the success criteria of Albrektsson (1986) and Buser (1990). The two studies are in agreement with the results of the current study, particularly for the success rate, which included the general prosthetic rehabilitation outcome and patient acceptance of general complaints regarding donor and recipient sites.

Nguyen and colleagues (2019) achieved a 100% success rate of implants placed in the augmented maxilla and mandible with an anterior iliac bone graft, followed by a removable and fixed dental prosthesis. The implant placement was performed 4–6 months after augmentation and implants healing expended to 3–5 months, which was ended by the initiation of prosthetic rehabilitation. After a mean observation period of 50 months (range, 12–62 months), they concluded that a combination of the iliac onlay bone graft and dental implants resulted in satisfactory reconstruction and a reliable long-term prognosis (Nguyen et al., 2019). Although they reported a higher success rate than that of the current study, the comparison is limited because they utilised a small sample (only seven patients with 29 implants).

Another study reported a lower success rate of dental implant placed in an augmented jaw with ilium in the long-term. Nyström et al. (2002) achieved a success rate of 74.6–85%, which was considered at the date of publication as a high success rate. The patients gained augmentation of the atrophied maxilla with an iliac bone graft and placement of dental implants, followed by a fixed prosthesis. All patients in their study underwent radiological investigation with computer tomography. The low success rate might be due to all patients undergoing the one-stage approach as well as more than one graft failure occurred in some patients, which induced inflammation that resulted

in dehiscence of the covering soft tissue, consequently leading to a high marginal bone loss or in some cases, complete loss of the graft.

For comparison, studies have reported implant success rates in the non-augmented bone of 84% to 98.7% with follow-up periods ranging between 2 and 15 years (Albrektsson et al., 1986; Buser et al., 1997; Pikner et al., 2009; Mertens et al. 2012; Degidi et al., 2012). The long-term study of Degidi and colleagues (2012) compared the survival rate of implants placed in healed and post-extractive sites, with success rates of 98.05% and 96.52%, respectively. They measured the success of the implant according to the criteria of Albrektsson et al. (1986) and Misch et al. (2008). The survival rate of Degidi et al. (2012) is in the line with the current study but is limited to compare because they utilised the one system (TiUnite implants) and the post-extractive group demonstrated a low success rate of restoration, which affected the peri-implant soft and hard tissue. Nonetheless, the current study reported a better outcome in comparison to Degidi et al., especially as the qualitative success rate was intensively explored in this study studied. The 11-year study of Mertens et al. (2012) studied the outcome of patients (15) and implant (94) level after the restoration of the edentulous maxilla (non-augmented) with an implant-supported fixed prosthesis, reporting a success rate of 92% according to Albrektsson's criteria (1986). The current results indicated a higher mean of success rate even when compared with the success rate of implants placed in the native non-augmented jaw like that of Mertens et al. (2012). In the present work, the 150 implants success rate during long-term follow-up was comparable to the success and survival rate of dental implants placed in the native non-augmented jawbone. The success rate assessment may not be profound or significant without an evaluation of the peri-implant bone level changes, therefore, the bone resorption rate was measured around the implants in this study.

Peri-implant bone resorption

The stable peri-implant bone level is regarded as a crucial factor to assess dental implant outcomes measured by clinical and radiological parameters (Lang et al., 2012; Lang & Zitzmann, 2012). Marginal bone loss is very important in dental implantology because the peri-implant bone is necessary for implant stability and plays an important role in aesthetic outcomes. The presence of sufficient bone in the peri-implant area has a direct impact on soft tissue integrity, consequently, this will improve both hygienical and aesthetical aspects (Nisapakultorn et al., 2010; Negri et al., 2014). Only a few long-term studies have evaluated the peri-implant bone level changes after onlay iliac crest bone grafting (Sjöstrom et al., 2006; Nyström et al., 2009; Boven et al. 2014). In the present study, the peri-implant bone level was radiographically measured and examined regarding the reference point as mentioned before in the methodology section. In the current work, the insertion level of 23 Steri-Oss Nobel Biocare, 99 RootLine Camlog (machined surface,1.4 mm), 10 Straumann implants (bone level) was equicrestally and 18 Straumann implants (tissue level) were placed with the smooth-rough border at the crestal bone level (supracrestally, implant-abutment interference 2.8 mm above the crestal bone). Frequently, the implant platform was placed either equicrestally or surpracrestally and sometimes subcrestally according to the manufacturer's instructions. A two-year observational study of 120 implants with various systems, insertion levels and different internal connections reported that the placement of implant supracrestally revealed low marginal bone resorption compared to crestally placed implants (Augustin-Panadero et al., 2019). Based on a systematic review, implants placed equicrestally revealed more peri-implant bone resorption (Schwarz et al., 2014). Chiapasco and colleagues (2014) conducted a comparative study of 95 bone level and 97 tissue level Straumann implants, comparing

radiographically the peri-implant bone level of the implants in 50 patients within a follow-up period ranging from 12–68 months. All patients received jaw reconstruction treatment with a different autogenous bone graft (iliac bone, calvarium and retromolar) and they demonstrated that regardless of the type of bone graft, the tissue level implants (supracrestal) indicated lower peri-implant bone resorption. In the present study, there was no significant difference in peri-implant bone level changes among the different implant systems used but only 18 tissue level implants were analysed in the present study.

Therefore, the implant insertion level and the implant-abutment junction are decisive factors having a direct impact on marginal bone loss. In the current investigation, the major crestal bone loss appears within the first year, with an average loss of less than 1 mm. Other studies investigated the marginal bone loss around implants that were placed in augmented jaws with anterior iliac crest bone (Nyström et al., 2009; Boven et al., 2014; Tosun et al., 2018; Nguyen et al., 2019). In the long-term prospective study of Nyström et al. (2009), they observed for 11 years the successful outcome and marginal bone resorption around 334 implants in 44 patients that received onlay and inlay bone grafts harvested from the anterior iliac bone crest. All patients were treated with the two-step approach, waiting six months for both implant placement and prosthetic restoration. By the end of their observation, the mean bone resorption was 2.4 mm after 10 years, 1.8 mm in the first year. Hence, the present study findings are in agreement in more than one aspect despite the present study having more positive points, that is, the success rate was higher, the peri-implant bone loss was less over 10 years and both jaws were treated.

Boven et al. (2014) observed the peri-implant bone resorption of implants placed after 4 months from augmentation with an iliac bone graft in the interforaminal area in 40

patients, showing that the mean peri-implant bone loss of implants in the augmented area was comparable with those placed in the non-augmented mandible. They observed the peri-implant bone level radiologically with OPTG and demonstrated an accumulative mean radiographic marginal bone loss of 0.6 ± 0.7 mm over five years. Although the authors only reconstructed the mandible, their data agree with those of the current study regarding the bone loss rate. However, the comparison is still limited because only bone level changes in the mandible were evaluated and information about the implant insertion level is missing. Tosun et al. (2018) reported that the mean resorption values on the buccal, lingual, mesial, and distal sides of the implants were 1.08 mm, 0.36 mm, 0.30 mm, and 0.25 mm respectively, (mean 0.49 mm) in the delayed implantation after 3 months from augmentation with an anterior iliac bone graft. Despite this study reporting a lower rate of marginal bone loss, it is difficult to directly compare to the current study as they only examined 61 implants of 10 patients for 29 months and only inserted one implant system (Straumann Standard Plus, Switzerland), with the radiological examination performed with a Cone-Beam CT at 29 months after implantation. Nguyen et al. (2019) measured the peri-implant bone changes mesially and distally of 29 implants inserted in the maxilla and mandible after augmentation with anterior iliac crest bone. Although they inserted two implant types, bone level and tissue level Straumann implants, they found no significant difference in the marginal bone loss at the end of the observation period (1.12 ± 0.50 mm). The value and nature of the marginal bone loss in the present study are comparable to that of Nguyen et al. Furthermore, the observation time in the current study was much longer than that of Nguyen et al. (mean, 50 months), with a higher number of implants (150) compared.

Duttenhoefer et al. (2015) evaluated and observed the successful outcome of graft and dental implants, as well as the peri-implant bone level changes in augmented jaws with

non-vascular fibula up to 15 years. The 39 dental implants in 8 patients revealed a high success rate of 97% and a low peri-implant bone reduction of 1.4 mm mesially and distally after 10 years, with their results fulfilling the success criteria of Buser. The highest rate of bone resorption occurred in the first year after implant placement (about 0.7 mm), with no subsequent significant marginal bone reduction thereafter according to radiological examination up to 15 years. The bone loss nature, the low peri-implant bone resorption and the high success outcome of Duttenhoefer et al. are comparable to the current work. Although their results are better than these of the current study, their observations included only eight patients.

Voss et al. (2016) evaluated the long-term (10 years) success of implants after grafting with particulate bone harvested from the retromolar area and peri-implant bone loss. They inserted 164 implants in the maxilla and mandible, reporting a mean bone loss of 2.47 mm and 2.50 mm mesially and distally, respectively. They concluded that the primary stability of the implant has a direct impact on bone resorption, especially as some implants were inserted simultaneously while other implants were placed 4–6 months after augmentation. These results confirm the two-step technique induces high primary stability and are in line with the present study, especially as they utilised several implant systems in both jaws and followed up patients for up to 10 years. However, the peri-implant bone loss in the current study is lower than that of Voss et al (2016) considering that a large number of implants were placed simultaneously with bone grafting in their work. The comparable results of the last two studies in addition to the current study confirm the suggestion of Ozaki and Buchmann (1998), who demonstrated that the cortical bone and its 3D microarchitecture is a superior onlay grafting material, regardless of the donor site and embryologic origin. The comparison of the current study with the results of the above-mentioned augmentation studies

demonstrates that the current results are comparable with the good outcome of long-term as well as short-term studies (Nelson et al., 2006 a, b; Nystöm et al., 2009; Boven et al., 2014; Voss et al., 2016; Tosun et al., 2018; Nguyen et al., 2019).

The present study results demonstrate that the implants placed in augmented bone have similar bone level changes compared to implants inserted in non-augmented regions. In the 10-year prospective study of Degidi et al. (2012), they surveyed 210 TiUnite implants in 59 patients and radiographically evaluated the accumulated mean peri-implant bone loss, 1.93 mm and 1.98 mm in healed and post-extractive sites respectively. The value of marginal bone loss confirmed the results of the current study, especially as they measured the difference in bone level mesially and distally in the long term. However, they did not define the level of implant insertion exactly (slightly above crestal level). In the study of Mertens and colleagues (2012), they performed an annual radiographical examination of 94 implants in 15 patients and showed relatively stable mesial and distal bone level loss of 0.88 mm after 11 years, which is comparable with the success rate of the present study. They reported a lower marginal bone loss in comparison to the current study but the comparison is still limited especially as they only utilised one implant system (TiO blast TM, Astra Tech AB, Mölndal, Sweden) in the non-augmented maxilla and did not state the insertion level of the implants. In the 10-year observation study of Pikner and colleagues (2009), they included 640 patients treated with 3,462 Brånemark implants and excluded patients with augmentation and overdentures, finding that the worst bone loss occurred in the first year, then slowed down thereafter. They recorded a mean marginal bone loss of 2.1 mm in the mesial and distal aspect, reporting that the implants placed close to the midline of the mandible in edentulous jaws showed a higher bone loss in comparison to implants in other positions.

The present study findings are in agreement with the above studies regarding the peri-implant bone loss rate and its nature. The present study showed that there is no effect of patient age, as confirmed by Mertens et al. (2012), Digidi et al. (2012), Voss et al. (2016) and Pikner et al. (2009), whereas Hugoson and Laurell (1993) observed an increased occurrence of marginal bone loss in natural dentation of older age groups.

It has been observed that gender has a significant effect on the treatment outcome, as there was a notable bone loss in females compared with males after 10 years. This could be attributed to hormonal factors that may influence bone physiology. Manolagas et al. (2013) discussed the role of oestrogens and androgens in bone health and preservation, stating that sex steroid hormones can preserve the balance between bone accretion and resorption through changes in osteoclastogenesis and osteoblastogenesis. Osteoporosis and compromised systemic bone metabolism may affect bone remodelling and osseointegration or maintenance of osseointegration of implants (Chrcanovic et al., 2015a). Osteoporosis is a common condition in postmenopausal women due to the reduction in the level of oestrogen which is responsible for inducing early and late forms of osteoporosis in women after menopause and elderly men (Riggs, 2000). Theoretically, all the above outweigh the hypothesis that female patients face more peri-implant bone resorption than male patients, thereby confirming the findings of the current study. The aforementioned study of Nyström et al. (2009) found that female patients after 11 years showed a higher rate of failure implant of 11% than male, while male patients had more marginal bone resorption. They also demonstrated that smokers had a lower success rate and more bone resorption.

According to a systematic review and meta-analysis of Chrcanovic et al. (2015a), the insertion of implants in male patients influenced the marginal bone loss and survival

rate of implants. They reviewed 91 publications, including 27, 203 and 25,154 implants in males and females, respectively, with male patients having a slightly lower survival rate and more marginal bone loss. Negri and colleagues (2014) concluded after 36 months of clinical and radiographical investigation of 632 implants in 252 patients, that patient gender and age significantly affected the marginal bone loss around the implants, with elderly men suffering from more peri-implant bone resorption around implants placed in the maxilla, in contrast to the present study. However, their observational period was shorter, and smokers were not excluded from their study.

The clinical trial of Chrcanovic et al. (2015b) further suggested that smoking has a statistically significant effect on influencing implant failure rates. A survey in the United States (2005–2014) found that the smoking prevalence within the adult population was higher among males than females (Jamal et al., 2014), which may account for the difference between the results of the above two studies and the results of the current study, especially as smoking was an exclusion criterion in the present work.

It is difficult to anticipate the impact of patient gender on marginal bone loss around the implants because of the limited number of studies regarding the marginal bone loss. Although the survival and success outcome of osseointegrated implants are well discussed and reported extensively, the effects of gender are still unknown (Chrcanovic et al., 2015a). The impact of gender demonstrated in the present study cannot be compared to other studies, hence further scientific studies are necessary to confirm this finding.

6. Conclusion

In previous capital, there was a trail to compare the results of this study with other results. This comparison dealt with studies that observed the outcome and peri-implant bone level changes in patients who had undergone implant placement after augmentation with an iliac bone graft, non-vascular fibula and retromolar bone graft or non-augmented jaws. The treatment outcome and findings were discussed and compared, as well as their related parameters in both jaws for short-term and long-term studies, revealing that the results of the present study are comparable with the good results of the aforementioned studies. At the same time, the patients who participated in this study suffered from extreme atrophy in both jaws and achieved successful implant-dependent prosthetic rehabilitation in the long-term. It is important to note that the assessment of success does not depend only on the presence and stability of the implants, many parameters defined the success rate.

In summary, this retrospective study demonstrated a high implant success rate (96% in maxilla and 92% in mandible) of implants that were placed into the augmented atrophic jaws which have been built up by utilising an onlay bone graft harvested from the anterior iliac bone crest. The peri-implant bone level changes in augmented jaws were comparable with those of non-augmented jaws. These results confirm the choice of the autogenous iliac crest graft as the "gold standard" for the reconstruction of the extremely atrophied upper and lower jaw.

7. References

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8. Eidesstattliche Versicherung

„Ich, Mohammed Al-Ghrairi, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: „Langzeitverlauf periimplantärer Knochenabbauraten nach Augmentation mit autologen Beckenkammtransplantaten bei extremer Alveolarkammatrophie.“
„ Success and radiological evaluation of dental implants after augmentation with iliac bone: A long-term study'' selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren/innen beruhen, sind als solche in korrekter Zitierung kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) werden von mir verantwortet.

[Für den Fall, dass Sie die Forschung für Ihre Promotion ganz oder teilweise in Gruppenarbeit durchgeführt haben:] Ich versichere ferner, dass ich die in Zusammenarbeit mit anderen Personen generierten Daten, Datenauswertungen und Schlussfolgerungen korrekt gekennzeichnet und meinen eigenen Beitrag sowie die Beiträge anderer Personen korrekt kenntlich gemacht habe (siehe Anteilserklärung). Texte oder Textteile, die gemeinsam mit anderen erstellt oder verwendet wurden, habe ich korrekt kenntlich gemacht.

Meine Anteile an etwaigen Publikationen zu dieser Dissertation entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem/der Erstbetreuer/in,

angegeben sind. Für sämtliche im Rahmen der Dissertation entstandenen Publikationen wurden die Richtlinien des ICMJE (International Committee of Medical Journal Editors; www.icmje.og) zur Autorenschaft eingehalten. Ich erkläre ferner, dass ich mich zur Einhaltung der Satzung der Charité – Universitätsmedizin Berlin zur Sicherung Guter Wissenschaftlicher Praxis verpflichte.

Weiterhin versichere ich, dass ich diese Dissertation weder in gleicher noch in ähnlicher Form bereits an einer anderen Fakultät eingereicht habe.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§§156, 161 des Strafgesetzbuches) sind mir bekannt und bewusst.“

Datum Unterschrift

Anteilserklärung an etwaigen erfolgten Publikationen

Mohammed Al-Ghrairi hatte folgenden Anteil an den folgenden Publikationen:

Publikation 1: Fretwurst T, Nack C, Al-Ghrairi M, Jan-Dirk Raguse, Andreas Stricker, Reiner Schmelzeisen, Katia Nelson, Susanne Nahles. Long-term retrospective evaluation of the peri-implant bone level in onlay grafted patients with iliac bone from the anterior superior iliac crest. Journal of Cranio-Maxillo-Facial Surgery. 2015;43(6):956-960.

Beitrag im Einzelnen:

1. Idee, Vorbereitung der Studie:

Herr Mohammed Al-Ghrairi war an der Vorbereitung (Auswahl der zu untersuchenden Parameter, statistische Analysemöglichkeiten) der publizierten Studie beteiligt. Des Weiteren erstellte er Einwilligungs- und Aufklärungsbögen für die zu untersuchenden Patienten.

2. Durchführung der Studie:

Die Untersuchung und Befundung der Patienten, sowie die Aktensichtung- und Auswertung der Patientendaten.

3. Aufbereitung der Daten zur Vorbereitung der statistischen Analyse:

Herr Mohammed Al-Ghrairi bereitete die Daten auf und erstellte die SPSS-Tabelle für die statistische Analyse.

4. Verfassen der Publikation, Literaturrecherche:

Herr Mohammed Al-Ghrairi führte die Literaturrecherche durch. Die Auswahl, Beschreibung und Deutung der Ergebnisse erfolgte in Rücksprache mit Herrn PD Dr.Tobias Fretwurst und Frau Prof. Dr. Susanne Nahles.

_____

Unterschrift, Datum und Stempel des/der erstbetreuenden Hochschullehrers/in

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Unterschrift des Doktoranden/der Doktorandin

9. Curriculum vitae (Lebenslauf)

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

10. List of Publication

- Susanne Nahles, Claudia Nack, Mohammed Al-Ghrairi, Andreas Stricker, Bodo Hoffmeister, Katia Nelson. **Langzeitverlauf periimplantärer Knochenabbauraten nach Augmentation mit autologen Beckenkamm-transplantaten bei extremer Alveolarkammatrophie.** Vortrag, 62. Kongress der DGMKG, 31.05 - 02.06.2012 Freiburg.

- Tobias Fretwurst, Claudia Nack, Mohammed Al-Ghrairi, Jan-Dirk Raguse, Andreas Stricker, Reiner Schmelzeisen, Katia Nelson, Susanne Nahles. **Long-term retrospective evaluation of the peri-implant bone level in onlay grafted patients with iliac bone from the anterior superior iliac crest.** Journal of Cranio-Maxillo-Facial Surgery. 2015;43(6):956-960.

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