# On minimally invasive approaches to sinus lift procedures

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To Ingrid, Joel and Jens

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### Abstract

**Aims:** The overall aim of the present thesis was to evaluate implant survival and bone regeneration after minimally invasive sinus lift procedures.

**Material and methods:** In *study I*, 61 patients were prospectively evaluated 12 to 60 months after two different methods of locally bone harvesting methods adjacent to the maxillary sinus lift procedure.

In *study II*, spherical, hollow, and perforated hydroxyapatite space-maintaining devices (HSMD) with a diameter of 12 mm were manufactured for this pilot study. Three patients with a residual bone height of 1–2 mm and in need of a sinus augmentation procedure prior to implant installation were selected for the study. In *study III*, 14 consecutive patients in need of maxillary sinus floor augmentation were included. Preoperative CBCT with titanium screwposts as indicators at the intended implant positions was used to visually guide the flapless surgical procedure. Twenty one implants all with a length of 10mm and a diameter of 4.1 and 4.8mm were inserted and followed clinically and with CBCT for 3, 6 and 12 months postoperatively. In *study IV*, 24 consecutive patients were included and provided with 30 sinus lift procedures. Three procedures for lateral sinus lift were used: Lateral sinus lift with replacement of bone window and without bone graft (BW), lateral sinus lift and covering osteotomy site with a collagen membrane and without bone graft (CM) and lateral sinus lift with autogenous bone graft (ABG). Experimental implants were retrieved after 7 months of healing and analyzed by microcomputed tomography (µCT).

**Results:** In *study I* the survival rate of implants after a follow-up of 12 to 60 months was 98.8% using locally harvested bone grafts at the site of the maxillary sinus augmentation. There was no significant difference in marginal bone loss on the mesial and distal sides of the implant when baseline to 1-year registration was compared with baseline to final registration. During the same time, graft height decreased significantly on the distal apical side of the implants.

A HSMD used in a two stage sinus lift procedure can produce a void for a blood clot and new bone formation and subsequent implant installation (*study II*).

There was minimal marginal bone loss after flapless, CBCT-guided osteotome sinus floor elevation with simultaneous implant installation during the follow-up verified by CBCT. The implants penetrated on average 4.4mm (SD 2.1mm) into the sinus cavity and the mean bone gain was 3mm (SD 2.1mm) (*study III*).

All three methods for lateral sinus lift surgery in *study IV* were equal when new intra sinus bone formation was compared using data from  $\mu$ CT. Implants apices were seldom covered with bone at the time of retrieval.

**Conclusions:** Bone grafts can be locally harvested at the site of the maxillary sinus augmentation procedure to enable placement, successful healing, and loading of 1 to 3 implants (*study I*).

A HSMD used in sinus lift procedures can produce a void for blood clot and new bone formation and subsequent implant installation (*study II*).

Flapless transalveolar sinus lift procedures guided by preoperative CBCT can successfully be used to enable placement, successful healing and loading of one to three implants in residual bone height of 2.6–8.9mm. There was minimal marginal bone loss during the 3–12 months follow-up (*study III*).

With regards to lateral sinus lift procedure, high degree of bone-to-implant contact was found regardless of the surgical technique utilized. With regards to lateral sinus wall formation only the autogenous Bone Graft (ABG) group consistently regenerated a completely ossified bony wall (*study IV*).

**Keywords:** autogenous bone graft, bone formation, clinical study, cone beam computed tomography, dental implants, flapless surgery, hydroxyapatite, osteotome technique, partially dentate maxillae, sinus lift surgery

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# Preface

This thesis is based on the following studies, which will be referred to in the text by their Roman numerals (I-IV):

Ι Johansson L-Å, Isaksson S, Lindh C, Becktor J, Sennerby L. Maxillary sinus floor augmentation and simultaneous implant placement using locally harvested autogenous bone chips and bone debris: A prospective clinical study. J Oral Maxillofac Surg 2010; 68:837-844 Johansson L-Å, Isaksson S, Adolfsson E, Lindh C, Sennerby L. Π Bone regeneration using a hollow hydroxyapatite space-maintaining device for maxillary sinus floor augmentation – A clinical pilot study. Clin Implant Dent Relat Res 2012; 14:575-584 Ш Fornell J, Johansson L-Å, Bolin A, Isaksson S, Sennerby L. Flapless, CBCT-guided osteotome sinus floor elevation with simultaneous implant installation. I: radiographic examination and surgical technique. A prospective 1year follow-up. Clin Oral Implants Res 2012; 23:28-34 Johansson L-Å, Isaksson S, Bryington M, Dahlin C. IV Evaluation of bone regeneration after three different lateral sinus lift procedures using micro-computed tomography of retrieved experimental implants and surrounding bone: a clinical, prospective and randomized study.

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# Introduction

The main reasons for loss of teeth are caries and periodontal disease. Periodontal disease is often bilaterally symmetrical and with a predictable order of likelihood of tooth loss according to position in the arch with greater loss of maxillary premolars and molars and least loss of mandibular cuspids <sup>1-6</sup>. Caries and its sequelae remain the principal reason for all tooth loss other than for lower incisors which are extracted mainly for periodontal reasons <sup>7</sup>. Even if the prevalence of edentulism continues to decline, in the western world, the loss of teeth in the posterior upper jaw will still be a quite common reason for patients requiring dental care <sup>8</sup>.

After tooth loss the alveolar process of the maxilla resorbs vertically and horizontally to become progressively smaller (Fig. 1) <sup>9-12</sup>. Reich and coworkers <sup>13</sup> studied a historical skeletal material from a population without modern prosthetics. They found that atrophy of the jaw evidently does occur, displaying similar patterns of resorption in a population without modern prosthetics, where the negative effect of ill-fitting dentures was excluded. According to Wolff's Law and the Mechanostat Model <sup>14-15</sup>, disuse and a loss of mechanical stimulation results in the reduction of bone mass. This effect was originally demonstrated for limb bones. Whether a lack of mechanical strain has the same impact on the alveolar process of the jaw and other skull bones remains to be studied in detail. The magnitude and pattern of alveolar bone loss shows great individual variation <sup>16</sup>. The duration of edentulousness has a significant influence on the rate of residual ridge resorption with significantly higher amounts of alveolar bone height decrease in those patients who had lost the last remaining teeth more recently <sup>17</sup>.

*Figure 1.* After tooth loss the alveolar process of the maxilla resorbs vertically and horisontally to become progressively smaller.

#### Anatomy, physiology of the maxillary sinus

The maxillary sinuses develop symmetrically at about the  $12^{th}$  week of intra-uterine life from the embryonic infundibulum region of the middle meatus between the medial and inferior concha nasalis. Until the eruption of the permanent teeth the sinus cavities are insignificant in size. At the end of growth, the sinus cavities have expanded in the maxillary bone in all three dimensions probably caused by the slight positive intra-sinus pressure due to the small size of the nasal openings. Another possible reason for expansion can be the physiology of the mucosal sinus membrane with presence of osteoclasts <sup>18</sup>. The volume of the maxillary sinus increases up to the age of 20 years. It appears that volume changes with age might be related to skeletal size and physique <sup>19</sup>. Loss of teeth in the posterior maxilla may also induce an expansion of the maxillary sinus. The tendency towards pneumatization is significantly higher after molar as compared with premolar extraction <sup>20-21</sup>.

The combination of resorption of the alveolar process and pneumatization of the maxillary sinus may lead to difficulties to insert dental implants and necessity to perform sinus lift surgery to increase bone volume (Fig. 1, 2a).

The respiratory epithelium lining the maxillary sinus is classified as ciliated, pseudostratified columnar epithelium. Three types of cells are recognized: ciliated cells, goblet cells and basal cells (Fig 2b)<sup>22</sup>. The association of epithelium, the loose connective tissue and the periosteum is called the Schneiderian membrane. The ciliated cells are columnar epithelial cells with specialized ciliary modifications. Goblet cells, so named because they are shaped like a wine goblet, are columnar epithelial cells that contain membrane-bound mucous granules and secrete mucus, which helps maintain epithelial moisture and traps particulate material and pathogens moving through the airway. The cilia of the respiratory epithelium beat in concert cranially, effectively moving secreted mucus containing trapped foreign particles toward the oropharynx, for either expectoration or swallowing to the stomach where the acidic pH helps to neutralize foreign material and micro-organisms. The basal cells are small, nearly cuboidal cells thought to have some ability to differentiate into other cells types found within the epithelium. For example, these basal cells respond to injury of the airway epithelium, migrating to cover a site denuded of differentiated epithelial cells, and subsequently differentiating to restore a healthy epithelial cell layer.

There have been a lot of speculations about the function of the paranasal sinus. Some of the theories are: lightening of the skull, add resonance to speech, humidifying and warming of inspired air, regulation of intranasal pressure, increasing surface area of olfaction, contribute to facial growth, shock absorbing in trauma and immunologic defence (Fig. 2a).



Figure 2a. Frontal view of maxillary sinus in relation to other structures.



*Figure 2b.* The maxillary sinus pseudostratified columnar epithelium with ciliated cells, goblet cells and basal cells (with permission from Science Photo Library)

The vascularization of the antero-lateral wall of the maxillary sinus coming from the maxillary artery from the external carotid artery and consist of an intra-osseous anastomosis

between the dental branch of the posterior superior alveolar artery (alveolar antral artery) and the infraorbital artery <sup>23-24</sup>. This anastomosis which is radiographically evident in 50% of cases is located halfway up the lateral sinus wall <sup>25-28</sup>. The alveolar antral artery has a diameter of 2.5-3mm and supplies the sinus membrane and the antero-lateral wall of the sinus <sup>26, 29</sup>. This vessel can present a risk of bleeding during surgery even if it mostly self resolves due to reactive contraction of the vessel <sup>24-27, 29-30</sup>. Testori and colleagues reported a case involving ligation of a blood vessel with a nearly 3-mm diameter in the lateral wall of the maxillary sinus <sup>31</sup> (Fig. 3a, 3b).

The presence of maxillary sinus septa may complicate sinus elevation procedures, especially when they are not diagnosed prior to surgery (Fig. 4). Pommer and coworkers <sup>32</sup> found in a systematic review and meta-analysis that septa were present in 28.4% of 8923 sinuses investigated. Prevalence was significantly higher in atrophic sinuses compared with dentate maxilla. Septa were located in premolar, molar and retromolar regions in 24.4%, 54.6% and 21.0% respectively. The orientation of the septa was: transverse in 87.6%, sagittal in 11.1% and horizontal in 1.3% of cases. Septa height measured 7.5 mm on average. Complete septa (dividing the sinus into two separate cavities) were found in only 0.3%. Other rare conditions included multiple septa in one sinus (4.2%) and bilateral septa (17.2%). Septa diagnosis using panoramic radiographs yielded incorrect results in 29% of cases. While sinus septum strengthen the bony structure they may cause perforation of the sinus membrane during a sinus elevation surgery <sup>33-35</sup>. Sinus septa can be found in any of the maxillary sinus regions regardless of dentition. The panoramic radiograph can lead to false positive and falsenegative findings in the visualization of septa. Therefore, whenever a maxillary sinus lift is planned, a thorough study of the affected sinus using CT could be recommended <sup>32, 36-40</sup>.



**Figure 3a.** from Servier medical art. **3b.** PSAA posterior superior alveolar artery, IA infraorbital artery, MA Maxillary artery, AR alveolar ridge, ANS anterior nasal spina. The lateral maxilla is supplied by branches of the posterior superior alveolar artery and the infraorbital artery that forms anastomosis in the bony lateral wall, which also supplies the Schneiderian membrane <sup>27</sup>.



Figure 4. Frontal, horisontal and sagittal view of septa in CBCT

#### Bone

#### Macroscopic structure and chemical composition of bone

Bone tissue is a highly developed supporting tissue. The skeletal structure provides protection for the vital organs of the body: the skull protects the brain; the ribs protect the heart and lungs. It is unlike any other connective tissue in that the extracellular matrix becomes calcified by calcium phosphate. Besides its excellent mechanical behavior, bone is a dynamic tissue with a remarkable healing potential <sup>41-42</sup>. Bone consists of about 65% mineral (mostly hydroxyapatite  $Ca_{10}(PO_4)_6(OH)_2$ ), 25% organic matrix, and 10% water. Collagen type I represents about 90% (dry weight) of the organic phase. The remaining 10% are non-

collagenous proteins of these osteocalcin is the most abundant, and its concentration in serum is closely linked to bone metabolism <sup>43</sup>.

The skeleton consists of two macroscopic types of bone: cortical or compact bone and cancellous or trabecular bone. Cortical bone can be seen in the long bones and the surface of the flat bones. Cancellous bone is a lacework surrounding the bone marrow of most flat bones and the metaphyseal region of long bones. Bone envelopes are bone surfaces that have different behavioral and functional properties. The three bone envelopes are called: 1) The periosteal envelope which covers the outside surface of bone, 2) The endosteal envelope which is divided between the endocortical and trabecular and 3) The Haversian envelope that includes Volkmann's canal surfaces. Bones are characterized anatomically as long bones (e.g. humerus, femur), flat bones (many bones of the skull), irregular bones (such as vertebrae). Long bones increase in length by endochondral ossification. Flat bones develop by the process of intramembranous bone formation. The shapes of individual bone are genetically determined, but biomechanical forces induced by muscle pull, gravity, and joint function modify the structure in health and disease <sup>44</sup>.

#### Microscopic structure of bone

There are three types of bone based on the orientation of the collagen fibrils. These are: woven bone, lamellar bone, and an intermediate type – the primary parallel-fibered bone. Bone is formed by osteoblasts which are derived from local osteoprogenitor mesenchymal cells. These cells cover all active bone-formation sites and are responsible for synthesizing osteoid, the unmineralized bone matrix. Woven bone is formed more rapidly than lamellar bone, and the interval between osteoid deposition and mineralization is short. Woven bone is not usually found in people aged over 14 except for some specific locations including the vicinity of sutures of flat bones of the skull, in tooth sockets, and some tendon insertions. Woven bone also develops temporarily in cases of bone fracture and repair <sup>44</sup>.

Osteocytes form from osteoblasts that become embedded in bone matrix as it is being deposited. The cells are found within bone lacunae, and they communicate with each other and the overlying tissue by canaliculi through which they extend tenuous cytoplasmic processes. The critical transport distance to keep the osteocytes alive is  $100\mu m$  (0.1mm). This explains why osteons, the structural metabolic unit of compact bone, rarely has a wall thicker than  $100\mu m$ . The osteocytes participate in the calcium homeostasis of the body fluids. The total surface for calcium exchange in the human skeleton has been calculated to be somewhere between 300 and 500 m<sup>2</sup><sup>44</sup>.

Osteoclasts are the largest of the bone cells (20-100µm diameter) and are multinuclear (with up to 50 nuclei). Osteoclasts are involved in bone resorption and can be found on the eroding surfaces of bone, often in cavities known as Howship's lacunae. The osteocytic cell membrane closest to the bone undergoing resorption has multiple invaginations and is known as the "ruffled border". The cells are very metabolically active, possessing large numbers of mitochondria (resulting in the acidophilia during histlogical staining) and have well-developed Golgi bodies. Osteoclasts secrete the enzyme acid phosphatase, which is involved in the erosion of the bony matrix. More specifically the enzyme is known as Tartrate-resistant Acid Phosphatase or TRAP and histochemical localization of TRAP enzymatic activity is a useful marker for identifying osteoclasts in sections. Osteoclasts originate from the hemopoietic system. The precursors are probably granulocyte-macrophage progenitor cells <sup>44</sup>.

#### Development and growth of bone

Bone formation depends on two important prerequisites: Abundant blood supply and mechanical support <sup>44</sup>. Osteoblasts can only function in the vicinity of blood vessels and bone can only form on a mechanically stable surface. These principles are seen in early bone development where connective tissue serve as a template for bone deposition in intramembranous ossification and endochondral ossification takes place in growth cartilages. During growth, thickening of bones and modeling of their shape is based on formative and resorptive activities by the periosteal and endosteal envelopes. This is achieved by periosteal apposition and endosteal resorption. Modeling and remodeling continues after cessation of growth. The trabecular framework of the cancellous bone undergoes profound changes as a result of the prevailing functional load "according to Wolff's law"<sup>15</sup>. The mechanism of this functional adaptation is not fully understood. Systemically, bone remodeling is activated by trauma to the bone or implant insertion.

#### Bone regeneration

Regeneration is commonly understood as replacement of lost tissues in the body by equally highly organized elements. Many tissues undergo a physiologic regeneration, i.e. a continuous replacement of cells or tissue elements. Examples of such cells and tissues are blood cells, epithelia, glands and endometrium. Reparative regeneration takes place when tissue are lost because of injury or disease. Bone has the unique potential to restore its original structure if abundant blood supply and mechanical stability is secured. The regeneration closely repeats the pattern of growth and development of bone. Growth factors are released when a bone lesion occurs. Example of bone lesions are fracture, insertion of implants or interruption of blood supply. Bone harbors many growth factors. Some growth factors are produced by bone cells (insulinlike growth factor [IGF], transforming growth factor [TGF], fibroblast growth factor [FGF], platelet-derived growth factor[PDGF]). Others are synthesized by bone-related tissues (interleukin-1 [IL-1], tumor necrosis factor a [TNFa]. There are also bone inducing factors of importance, such as Lacroix's osteogenin and the bone morphogenetic proteins (BMP)<sup>44</sup>. Osteoinduction is the process by which bone formation is induced. It is a phenomenon regularly seen in any type of bone healing process<sup>45</sup>. Osteoinduction in its classical concept implies initiation of heterotopic bone formation in sites where bone physiologically does not normally exist. If ossification is activated in contact with existing bone this is called orthotopic bone induction. Factors that impair bone regeneration are: 1) Failure of vascularity, 2) Mechanical instability, 3) Oversized defects, and 4) Competitive tissues of high proliferative activity<sup>44</sup>.

The distance of which the blood vessel can branch and allow complete bridging by woven bone healing of a defect is called the "osteogenic jumping distance" <sup>46</sup>. The osteogenic jumping distance is around 1 mm for rabbit cortical bone and is species specific. Larger gaps or holes will take longer time to complete repair. Bone filling of larger defects is facilitated by osteoconduction, ie, by offering a framework or scaffold for bone deposition. There are certain conditions that will influence the osteoconduction: 1) Biocompatibility of the scaffold and 2) The external and internal structure of the scaffold should favor tissue ingrowth and bone deposition <sup>44</sup>.

#### Guided bone regeneration

Guided Bone Regeneration (GBR) includes the application of occlusive membranes, which mechanically exclude non-osteogenic cell populations from the surrounding soft tissues, thereby allowing osteogenic cell populations originating from the parent bone to inhabit the osseous wound <sup>44, 47-48</sup>. The mechanism of healing by guided bone regeneration is also referred to in sinus lift publications even when a membrane is not used. This is especially common in papers presenting results after maxillary sinus membrane elevation and simultaneous placement of implants without the use of membranes, bone grafts or bone substitutes (Fig. 5.) <sup>49-51</sup>.



*Figure 5*. *Maxillary sinus membrane elevation and simultaneous placement of implants without the use of bone grafts or bone substitutes.* 

- 1. Creating and removal of a bone window in the lateral sinus wall
- 2. The sinus membrane is dissected free from the bone walls and the implant is installed.
- *3. The removed bone window is replaced creating a closed compartment that is filled with blood.*
- 4. New bone formation

#### Importance of implant surface topography and chemistry

Titanium (Ti) is today the most successful clinical implant metal used, especially in dental implantology. Ti is resistant to corrosion and the titanium surface will instantly form a thin (2-17 nm) oxide film when exposed to atmospheric oxygen  $^{52}$ . The original Brånemark titanium implant had a minimally rough surface imparted by machining. Today most implants have a surface that is modified with varying techniques. The surface roughness seems to have a positive impact on integration of implants into the bone  $^{53}$ . A preferable way of evaluation of surface roughness is by 3D evaluation, i.e. average roughness over a surface (the Sa value). There is a positive relationship between surface roughness and bone-to-implant contact up to a certain roughness threshold. Surface roughness is also described by Sdr which is the surface enlargement if a given surface is flattened out. Animal experiments of a moderately roughned surface with a Sa value of about 1.5µm and a Sdr value of ~50% promotes the

strongest bone response. The defunct plasma-sprayed surfaces were too rough invoking an impaired bone response <sup>53-57</sup>. Others have also demonstrated increased plaque indices and bone resorption with plasma-sprayed implants compared to moderately rough controls <sup>58-59</sup>. While implant micro roughness seems to be an important factor for the bone response <sup>60</sup> the benefits of nanometer-level roughness are still to be evaluated <sup>53</sup>. The clinical impact of surface hydrophilia is also not fully assessed.

#### Biomechanical considerations in bone regeneration

Bolind and coworkers <sup>61-62</sup> demonstrated lower bone-to-implant contact for unloaded compared to loaded implants. The possibility to achieve bone anchorage of clinical implants in irradiated tissue was also studied by this group. Implants with longer healing times demonstrated the possibility of achieving integration even in this compromised patient group. Functional loading of an implant generates greater loading on the marginal bone than around the apical part of the implant <sup>63-65</sup>. The influence of loading on intra-sinus bone remodeling after sinus lift procedures has not been thoroughly studied but it can be anticipated that functional loading can have a stabilizing effect on the maintenance of the intra-sinus bone <sup>66-67</sup>.

#### Bone regeneration after sinus lift surgery

Even with the well established clinical effectiveness of sinus lift procedure there are still questions regarding the origin of newly formed bone, the influence of the surrounding tissues, the contribution and fate of the graft material, and the volume of new bone necessary for a successful treatment <sup>68</sup>. Earlier histologic observations of biopsy specimens implicated the contiguous endosteum of the sinus floor (the residual bone) and the elevated periosteum as possible sources for the newly generated bone <sup>69</sup>. There are different opinions as to whether residual bone height affects implant survival or the graft result itself. In retrospective studys, Wheeler et al. <sup>70-71</sup> noted that alloplasts had a high implant-retention rate except when the preoperative bone height was <3 mm. In contrast, a 2003 review by Wallace and Froum <sup>72</sup> noted that the influence of the residual bone height in the lateral- window technique was unknown. In a study by Price et al. <sup>68</sup>, the influence of the residual bone height was evaluated as a potential variable by comparing samples with <4 mm to samples with ≥4 mm. The range of vertical height dimension was considerable (0.5 to 7.0 mm), but there was no associated difference in new bone formation found in any zone of the graft compartment. They concluded that new bone was derived from a combination of de novo appositional and

intramembraneous formation in which cells evolved from the regeneration of vascular and perivascular tissues that grew inward at a uniform rate from the entire periphery, but this proposal requires further investigation.

Jensen and coworkers <sup>73</sup> using minipigs, found that the volume of autogenous bone grafts from the iliac crest and the mandible was reduced significantly after maxillary sinus floor augmentation. The graft volume was better preserved after the addition of Bio-Oss and the volumetric reduction was significantly influenced by the ratio of Bio-Oss and autogenous bone <sup>74</sup>. The authors also found that early bone-to-implant contact formation was more advanced with autogenous bone. No differences between the use of mandibular or iliac bone grafts were observed since the bone-to-implant contact was not significantly influenced by the origin of the bone graft.

There has been considerable clinical controversy about the role of the graft material in the sinus lift procedure. The discussion has usually been limited to osteogenic capacity, osteoinductivity, or osteoconduction. Also an alternative function of graft materials as space holders has been gaining interest in the literature. Experiments, in which the sinus membrane was elevated and allowed to rest on simultaneously placed implants, indicated that creating a space with a blood clot alone could lead to bone deposition on an implant <sup>50, 75-78</sup>. Sohn et al. <sup>79-80</sup> found a faster and greater new bone formation was observed in sites that received no grafting material. The repositioned bony window may accelerate new bone formation earlier versus placement of a collagen membrane. Srouji et al. found that the Schneiderian membrane has an osteogenic potential <sup>81</sup>. On the other hand Scala et al. <sup>82</sup> found that bone formation started from the parent bone of the sinus floor and extended toward the apex of the implants. However, this coronal proliferation of bone did not ever exceed 4.5mm, indicating the limitation dictated by the Schneiderian membrane collapsing over the implant apex (Fig. 6).



Figure 6. The invading vascular sprouts are accompanied by osteoprecursor cells from the bone marrow. The organization of the hematoma by granulation tissue follows the basic pattern of wound healing.



"Faster and greater new bone formation was observed in sites that received no grafting material. The repositioned bony window may accelerate new bone formation earlier versus placement of a collagen membrane"<sup>80</sup>.



"Bone formation started from the parent bone of the sinus floor and extended toward the apex of the implants. However, this coronal proliferation of bone did not ever exceed 4.5mm, indicating the limitation dictated by the Schneiderian membrane collapsing over the implant apex"<sup>83</sup>.



"Histologically, the process of new bone formation resembled a combination of de novo appositional and intramembraneous ossification. The findings suggested a passive role for the graft material and implicated the ingrowth of vascular and perivascular tissues as the most logical source of osteogenic capacity"<sup>68</sup>.

#### Diagnostic imaging and sinus lift surgery

In 2011, the EAO (European Academy of Osseointegration) held a consensus workshop on radiological guidelines in implant dentistry. Previous EAO guidelines from 2002 were updated and expanded to include cone beam computed tomography (CBCT) <sup>84-85</sup>. CBCT can offer cross-sectional imaging and 3D reconstructions at potentially lower radiation doses compared to medical multi-slice CT. By using panoramic views of the posterior maxilla there is the risk of underestimating the amount of bone available for implant placement. CBCT provides more accurate measurements of the available bone volume <sup>86-87</sup>. CBCT can also provide information on arterial channels in the lateral sinus wall, the presence of septa and pathology of the maxillary sinus <sup>88</sup>.

In the literature, little data is available on the thickness of healthy sinus membranes. An average thickness of 1 mm with considerable inter-subject variation have been reported. There seems to be an association between thickness of the antral mucosa and periodontal phenotype <sup>89</sup>. Mucosal thickening of 2 mm is considered a reliable threshold for pathological mucosal swelling of the Schneiderian membrane <sup>90</sup>. Mucosal thickening of more than 2 mm can be grouped according to criteria from Soikkonen and coworkers <sup>91</sup>: 1) Flat: shallow thickening without well defined outlines, 2) Semi-aspherical: thickening with well-defined outlines rising in an angle of more than 30° from the floor or the walls of the sinus, 3) Mucocele-like: complete opacification of the sinus, 4) Mixed flat and semi-aspherical thickenings, 5) Other mucosal thickenings types or pathological findings. A high prevalence of mucosal thickening in paranasal sinuses in asymptomatic patients has been reported <sup>92-95</sup>. Because of the complex anatomy in the posterior maxilla, cross-sectional imaging has been proposed as the standard diagnostic imaging method for preoperative planning of dental implant placement <sup>84-85, 96</sup>. CBCT can be regarded as a first choice for three-dimensional imaging of the posterior maxilla due to less radiation administrated to the patient compared to CT <sup>97-98</sup>.

#### Pathology of the maxillary sinus

Maxillary sinus disease may increase the difficulty of performing sinus lift surgery and the risk of developing postoperative complications <sup>99-101</sup>. Pathological conditions in the nasal-maxillary complex should be considered a contraindication for sinus floor elevation <sup>102</sup>. Sinus diseases that might interfere with the performance of sinus lift surgery include acute/chronic rhinosinusitis, sinusitis of odontogenic origin, odontogenic cysts, pseudocysts, mucoceles, and

retention cysts<sup>103</sup>. Although, recent reports have demonstrated that pseudocysts of the maxillary sinus are not a contraindication for sinus augmentation <sup>104-108</sup>.

Maxillary sinusitis of odontogenic origin account for approximately one tenth of total maxillary sinus diseases <sup>109-110</sup>. A careful dental and periodontal examination in the vicinity of the sinus should be executed to rule out any odontogenic lesions responsible for maxillary sinusitis. Periodontal therapy of upper premolars and molars will significantly reduce swelling of maxillary sinus mucosa in patients with periodontal disease <sup>111-113</sup>.

Clinical evidence suggests that maxillary sinus augmentation procedures if performed in a healthy maxillary sinus have limited permanent effects on sinus physiology <sup>101, 114</sup>.

#### **Osseointegrated dental implants**

Today, the use of dental implants is a well-documented treatment for replacing missing teeth. Historically, osseointegration of titanium dental implants was developed and scientifically documented by Brånemark and co-workers <sup>115-116</sup> and by Schroeder and co-workers <sup>117</sup>.

Albrektsson et al. have discussed factors for dental implants success: adequate implant material, design and surface quality, correct bone quality, delicate surgical technique and appropriate loading conditions for the implants were all deemed important <sup>118</sup>. The survival and success rates for implant treatment have reached very high levels even in patient with deficient bone quality and volume. Reviews of clinical follow-up studies show that survival rates around 95% can be expected on all indications over a 5-year period of time <sup>119-120</sup>.

#### Different methods in maxillary sinus lift surgery

The reduced vertical bone height in the posterior maxillary region is often a major obstacle to placement of dental implants. Elevation of the maxillary sinus floor is an option to solve this problem. Various surgical techniques have been presented to access the sinus cavity and elevate the sinus membrane.

The two main techniques of sinus floor elevation for dental implant placement are: a twostage technique with a lateral window approach, followed by implant placement after a healing period, and a one-stage technique using either a lateral or transalveolar approach. The decision to use one or two-stage techniques is based on the amount of residual bone available and the possibility of achieving primary stability for the inserted implants.

#### Lateral approach with grafting materials

Boyne & James<sup>121</sup> were the first authors to publish a study on elevation of the maxillary sinus floor in patients with large, pneumatized sinus cavities. They described a two stage procedure, where the maxillary sinus was grafted using autogenous particulate iliac bone at the first stage of surgery. After approximately 3 months, a second stage surgery was performed in which blade implants were placed and later used to support the prosthetic constructions. Since then, numerous articles have been published regarding different grafting materials and modifications of this technique.

Wallace and Froum <sup>72</sup> published in 2003 a systematic review on the effect of maxillary sinus floor elevations and the survival of dental implants. The criteria for review included human studies with a minimum of 20 interventions, a follow-up time of one year of functional loading and with an outcome variable of implant survival being reported. The main results reported in this study were:

- 1. The survival rate of implants placed in sinuses augmented with the lateral window technique varied between 61.7% and 100%, with an average survival rate of 91.8%.
- 2. Implant survival rates compared favorably with reported survival rates for implants placed in the non-grafted posterior maxilla.
- 3. Rough surfaced implants had a higher survival rate than machined surface implants when placed in grafted sinuses.
- 4. Implants placed into sinuses augmented with particulate autografts showed higher survival rates than those placed in sinuses that had been augmented with block grafts.
- 5. Implant survival rates were higher when barrier membranes were placed over the lateral window.
- 6. The utilization of grafts consisting of 100% autogenous bone or the inclusion of autogenous bone as a component of composite grafts did not affect implant survival.

Pjetursson et al. <sup>122</sup> also reviewed the effect of residual bone height. Their criteria for review included human studies with a minimum of 10 patients and a mean follow-up time of at least 1 year or more after functional loading. Patients had a mean residual bone height at site of implant placement of up to 6 mm. Both one-stage surgery and two-stage surgery were utilized in the totally 48 included studies. Autogenous bone grafts were used in 23 of the 48 studies. In 19 studies a combination of particulate autogenous bone and various bone

substitutes were used. In 12 studies, various bone substitutes were used alone. The following conclusions were drawn from this systematic review:

- The estimated annual failure rate was 3.5% [95% confidence interval (CI): 2.5%–
  4.9%] translating into a 3-year implant survival of 90.1% (95% CI: 86.4%–92.8%).
- However, when failure rates was analyzed on the subject level, the estimated annual failure was 6.04% (95% CI: 3.87%–9.43%) translating into 16.6% (95% CI: 10.9%–24.6%) of the subjects experiencing implant loss over 3 years.
- 3. The annual failure rate of machined surface implants (6.9%) was significantly (p < 0.0001) higher than that for rough surface implants (1.2%)
- 4. The annual failure rate was significantly higher (4.0% versus 0.7%) (*p*=0.001) when membrane was not used to cover the lateral window after the grafting procedure.
- 5. In rough surface implants the 3-year survival rates ranged between 96.3% and 99.8% depending on the grafting material used.
- 6. The lowest annual failure rate (0.1%) of rough surface implants was observed using autogenous particulated bone graft.
- The annual failure rates of rough surface implants were similar using bone substitutes (1.1%) and combinations of autogenous bone and bone substitutes (1.1%)

Handschel et al. <sup>123</sup> concluded in a review that autogenous bone seemed to be more effective than bone substitutes during the early phase of healing, but after 9 months, no statistically significant differences were detected between the various grafting materials. Tong et al. <sup>124</sup> in a metaanalysis for implants placed in grafted maxillary sinuses found similar survival rates whether autografts, allografts or alloplastic grafting material were used.

Esposito et al.<sup>125</sup> concluded in a review article that bone substitutes such as Bio-Oss and Cerasorb appear to be as effective as autogenous bone grafts for augmenting atrophic maxillary sinuses, therefore they could be used as a replacement for autogenous bone grafting. They also concluded that there is no evidence that the addition of platelet-rich plasma (PRP) treatment to autogenous bone grafts or bone substitutes improves the outcome of sinus lift procedures for implant rehabilitation.

#### Lateral approach without grafting material

An early study by Boyne <sup>78</sup> 1993 with monkeys revealed that implants protruding into the maxillary sinus following elevation of the sinus membrane without grafting material exhibited spontaneous bone formation below the sinus membrane. In 1997 Ellegard et al. <sup>75</sup> presented a study in periodontally compromised patients where following a sinus floor elevation, the sinus

membrane was allowed to "settle" on the implants, thereby creating a void which would be filled with coagulum. They concluded from the estimation of the survival rates that the sinus lift technique could be used successfully.

In 2004, Lundgren et al. <sup>51</sup> presented a modification of the previously described technique in a study with twelve sinus elevations in 10 patients. The bone window was cut with a reciprocating saw and removed. The Schneiderian membrane was elevated and often sutured to the bony wall to create and maintain a space. Dental implants were installed where the apex protruded for at least 5 mm into the maxillary sinus. A blood clot was allowed to fill the space underneath the sinus mucosa. The formation of new bone within the space was verified by computed tomography. Implant survival was 100% after 12 months of loading. This has been supported by several studies demonstrating bone formation merely from blood clots <sup>50, 126-130</sup>. Riben and Thor <sup>131</sup> found in a review of studies using the graftless technique high implant survival rates and concluded that the technique is considered to be cost-effective, less timeconsuming and has lower morbidity.

However, Scala et al. <sup>83</sup> found some limitations with this technique. Their animal study showed that the void initially occupied by the coagulum shrank substantially. This lead to the collapse of the sinus mucosa onto the implant surface and the newly formed bone never exceeded 4.5 mm. They also found no influence of the Schneiderian membrane on bone formation apical to the implants.

#### Transalveolar technique

A less invasive transalveolar technique for sinus floor elevation with immediate implant placement was first suggested by Tatum <sup>132</sup> (1986) and later developed as an osteotome technique by Summers in 1994 <sup>133</sup>. The osteotome technique has been modified by several authors and the success of sinus floor elevation with this technique has been reviewed by Tan et al. <sup>134</sup>. The following conclusions were drawn from this systematic review:

- 1. The estimated annual implant failure rate was 2.5% (95% CI: 1.4–4.5%). This translated into a 3-year implant survival of 92.8% (95% CI: 87.4–96.0%).
- 2. The survival rate appeared to decrease with decreasing residual bone height.
- Analysis on the subject-level revealed an estimated annual failure of 3.71% (95% CI: 1.21–11.38%), translating to 10.5% (95% CI: 3.6–28.9%) of the subjects experiencing implant loss over 3 years.

4. Perforation of the sinus membrane occurring in 3.8% of the procedures was the most frequently reported complication. The mean incidence of post-operative graft infection was 0.8%.

The authors also concluded that the survival rates of implants placed in transalveolar sinus floor augmentation sites are comparable to those in non-augmented sites.

There is still controversy regarding the necessity of a grafting material in order to maintain the space for new bone formation after elevating the sinus membrane utilizing the transalveolar technique. Nedir et al. <sup>135</sup> found that implant protrusion into the sinus decreased from  $4.9\pm1.9$  mm after surgery to  $1.5\pm0.9$  mm after 5 years when no grafting material was used.

Pjetursson et al. <sup>136</sup> compared a group of 164 implants installed by the transalveolar technique with no grafting materials being placed with another group of 88 implants installed by the transalveolar technique where deproteinized bone material was placed. The authors reported a gain of radiographic bone height of 1.7 and 4.1 mm, respectively, when assessing these parameters on digitized periapical radiographs.

Esposito et al. <sup>125</sup> found in a review that if residual alveolar bone height is 3 to 6 mm, a crestal approach to lift the sinus lining and place 8 mm implants may possibly lead to fewer complications than a lateral window approach to place implants at least 10 mm long.

#### Minimally invasive surgery

A minimally invasive surgical procedure has been defined in general surgery as a procedure that is carried out with the smallest damage possible to the patient. When there is minimal damage of biological tissues at the point of entrance of instrument(s), the procedure is called minimally invasive <sup>137</sup>. Today minimally invasive surgeons are continuing to determine and redefine how much can be accomplished through smaller incisions and with minimal surgical stress. For the patient there are some obvious advantages with a less invasive surgical approach such as less postoperative pain, quicker recovery and economic gain due to shorter convalescence. However, the safety and effectiveness of each procedure must be demonstrated with randomized controlled trials.

#### Alternative to sinus lift surgery

#### Short implants, tilted implants, zygoma implants

Instead of using different sinus augmentation techniques short implants have been proposed. Short implants are defined as implants with an intrabony length of 5-8 mm<sup>138</sup>. Some authors consider implants of 7-10 mm to be short<sup>139</sup>. Finite element (FEA) analyses have shown that the occlusal forces are distributed primarily to the crestal bone rather than evenly throughout the entire surface area of the implant. This supports the biomechanical rationale for using short implants<sup>140</sup>.

It is obvious from earlier literature that turned (machined) short implants fail more often than longer implants <sup>141</sup>. On the other hand recent studies where textured-surfaced implants have been used show survival rates of short implants comparable with those obtained with longer ones <sup>138</sup>. Ten Bruggenkate and coworkers <sup>142</sup> found in a multicenter study of 126 patients followed up from 1 to 7 years that implants with a length of 6 mm had a comparable quality of survival as longer implants. Still they recommended that shorter implants be used in combination with longer implants, especially when used in less dense bone that is often seen in the maxilla. Das Neves and coworkers <sup>139</sup> found in a systematic review of 16344 implants a total failure rate of 4.8%. Implants 3.75 mm wide and 7 mm long failed at a rate of 9,7%, compared to 6.3% for 3.75\*10-mm implants. The use of implants 4 mm in diameter appeared to minimize failure in these situations. Long-term prognosis of using 5 mm long implants as an alternative to bone augmentation is unknown<sup>143</sup>. Pieri and coworkers<sup>144</sup> compared in a randomized clinical trial clinical and radiographic outcomes of 6 mm implants in patients having 6 to 7 mm residual bone with standard-length implants ( $\geq 11$  mm) placed simultaneously with a sinus augmentation procedure. They found that both techniques had similar clinical and radiographic outcomes at 3 years control.

Other alternatives to sinus lift surgery are placing implants in a disto-angulated direction in order to avoid the maxillary sinus <sup>145-146</sup>. In some situations implants can be placed in the pterygomaxilla <sup>147-148</sup>. Zygoma implants have also been used as an alternative to sinus augmentation procedures (Fig. 7) <sup>149-150</sup>.





*Figure 7. Examples of different ways of avoiding sinus surgery: short implants, tilted implants, implants in the pterygomaxilla and zygoma implants* 

Studies have also been presented where alveolar socket augmentation has decreased the dimensional alterations of the alveolar ridge, increasing the possibility of inserting implants without the need for a sinus augmentation procedure <sup>151</sup>.

### **Complications in sinus lift surgery**

#### General considerations

According to the literature, the incidence of development of maxillary sinusitis after an augmentation of the sinus floor ranges from 0% to 20% <sup>18, 152-156</sup>. Timmenga and coworkers <sup>101, 114, 157-158</sup> found that the incidence of maxillary sinusitis after bone grafting was very low in patients without preexisting sinus problems. Transient sinusitis only developed in patients with a predisposition for sinusitis but these symptoms ceased after appropriate treatment. Sinus drainage does not seem to be compromised in healthy persons after sinus floor augmentation. The authors also found that an accidental perforation of the mucous lining of the maxillary sinus did not result in sinusitis postsurgically. The authors also concluded that only patients suffering from previous symptoms of sinusitis or predisposing factors should be evaluated preoperatively to rule out structural drainage problems. The authors also recommended nasendoscopic evaluation for patients with a history of frequent sinusitis to rule out the presence of an obstructive phenomenon before undergoing a sinus lifting procedure. Pommer and coworkers <sup>159</sup> found that the maxillary sinus membrane, even in healthy clinical conditions, undergoes morphologic modifications after sinus floor elevation, yet membrane

reactions demonstrate significant variability. They recommended future research on the effect of augmentation surgery on maxillary sinus physiology.

#### Membrane perforation

A common complication of maxillary sinus floor elevation is perforation of the sinus membrane. This complication has been reported as a complication occurring 10% to 60% of sinus floor elevation procedures <sup>160-165</sup>. In a review article, Vina-Alumina and coworkers <sup>166</sup> reported that in maxillary sinus lift procedures with membrane perforation an implant survival rate was 88.6%, and in maxillary sinus lifts with intact membranes the survival rate rose to 98%. They found no consensus if a perforated membrane should be repaired, but the method of choice according to the majority of authors was a resorbable membrane. In the case of a large perforation, there was no consensus either, although the majority of authors choose to abandon the procedure. Oh and Kraut <sup>167</sup> examined retrospectively the effect of sinus membrane perforation with regards to graft survival and implant integration. A total of 175 sinuses were augmented with 115 of the membranes being reported as intact at the time of surgery. A total of three infections occurred in patients who sustained perforated sinuses and one infection occurred in a patient who had an intact sinus. All four infections resolved after culture sensitivity and placement of the patient on an appropriate antibiotic for 10 days. Of 438 dental implants placed in the augmented sinuses, five implants failed, four of which were associated with perforated sinuses and one which was not associated with a perforated grafted sinus. The authors concluded that perforation of the Schneiderian membrane does not cause negative long-term effects on sinus bone grafts and dental implants. However, more studies correlating the size of sinus membrane perforation with the type of repair performed are needed. Several authors have reported a lower Schneiderian membrane perforation rate during sinus elevation using piezosurgery. Seoane and coworkers <sup>168</sup> found that the use of a piezoelectric device reduced the frequency of membrane perforation among surgeons with limited experience. Toscano and coworkers <sup>169</sup> had no perforations of the Schneiderian membrane during the piezoelectric preparation of 56 lateral antrostomies, whereas two perforations were noted during subsequent membrane elevations using hand instrumentation. In both instances, membrane perforations were associated with sinus septa. The overall sinus perforation rate was 3.6% with this technique.

#### Benign paroxysmal positional vertigo

Benign paroxysmal positional vertigo is an unusual complication of osteotome sinus floor elevation. The condition is characterized by short, often recurrent episodes of vertigo that are triggered by certain head movements <sup>170-177</sup>. It can be idiopatic or secondary to a number of underlying conditions such as head injury, viral labyrinthitis, stapes surgery, and chronic suppurative otitis media <sup>178</sup>. Sohn and coworkers recommended the use of piezoelectric internal sinus elevation technique to reduce or eliminate the risk of postoperative positional vertigo <sup>179</sup>.

#### Displaced implant into sinus cavity

If there is lack of supporting bone, the placed implant may not have enough primary stability and may migrate into the maxillary sinus. Displaced implants must be removed <sup>180</sup>(Fig. 8).



*Figure 8.* From the moment of intraoral radiograph to panoramic view one implant has been lost and one has migrated from the initial intrasinus position to a new position.

#### **Economical considerations**

There are many treatment options for sinus floor elevation with substantial differences in cost. Listl and Faggion <sup>181</sup> tried to identify the most cost-effective approach to sinus lifting on the basis of currently available evidence. The authors used two systematic reviews to identify clinical outcome data from lateral sinus floor elevation and the transalveolar technique <sup>122, 134</sup>. After calculating the cost for these procedures Listl and Faggion concluded that if there are no financial restrictions on a sinus lift the optimum treatment strategy is the lateral approach with autogenous particulate bone and a resorbable membrane. When monetary resources for sinus-floor elevation are scarce, the decision depends on the initial bone height at the implant site. In cases where bone height is sufficiently high, the most cost-effective option is the

transalveolar technique without bone grafting. In cases where bone height is comparably low, it is most cost-effective to rely on a lateral approach with as much autogenous particulate bone as available. Thereby, clinicians should only refrain from membrane application if monetary resources are markedly scarce.

Truedsson et al. <sup>182</sup> compared the estimated cost for sinus augmentation with iliac graft to sinus augmentation with local bone graft. They concluded that provided an augmentation with local bone graft could be used the economic gain is substantial and postoperative morbidity is greatly reduced.

This introduction gives a fundamental background of sinus lift surgery to enable implant installation in the posterior maxilla when vertical bone height is reduced.

# **Objectives**

The overall aim of the present thesis was to evaluate implant survival and bone regeneration after minimally invasive sinus lift procedures.

### Specific aims

- To prospectively evaluate the status of implants, marginal bone loss, and outcome of maxillary sinus floor augmentation in patients undergoing maxillary sinus lift and simultaneous implant placement with the use of bone grafts harvested adjacent to the actual surgical site (*Study I*).
- To prospectively evaluate bone formation by using a spherical, hollow and perforated hydroxyapatite space-maintaining device in a two-stage sinus lift procedure where residual alveolar bone height was ≤2 mm (*Study II*).
- To prospectively evaluate a simplified technique for flapless, CBCT-guided osteotome sinus floor elevation technique suitable for the installation of one to three implants (*Study III*).
- To prospectively evaluate the amount of bone regeneration following three lateral sinus elevation treatment modalities using micro-computed tomography (µCT) (*Study IV*).

# Material and methods

#### Study I

Patients in need of maxillary sinus floor augmentation to enable implant placement were enrolled in 2 different groups. In group A, a "bone trap" was used to harvest bone debris during implant preparation with additional bone collected by further drilling adjacent to the implant sites. In group B, a "bone scraper" was used to harvest cortical bone chips from the zygomatic buttress and from the lateral sinus wall before opening of a bony window (Fig. 9). All patients were provided with a fixed partial denture after a healing period of 3 to 6 months. A total of 61 patients with 81 Straumann implants (Institut Straumann AG, Basel, Switzerland) were assessed, with 17 patients (20 implants) in group A and 44 patients (61 implants) in group B.



### Figure 9.

- *a* Bone chips harvested from zygomatic buttress with bone scraper
- **b** Bone scraper with bone chips
- *c* Bone harvested with bone collector
- *d* Bone collector with collected bone debris

#### Study II

Hydroxyapatite space-maintaining devices (HSMDs) with a diameter of 12 mm were manufactured for this pilot study (Fig 10). Three patients with a residual bone height of 1–2 mm, as verified clinically and radiographically, and in need of a sinus augmentation procedure prior to implant installation were selected for the study. The HSMD and bone formation was evaluated by cone beam computed tomography (CBCT) 6 months after augmentation procedure. Implants were installed 6 to 9 months after augmentation. The implant sites were prepared by a trephine drill to obtain a specimen of HSMD and bone for histological evaluation. After implant installation, the condition of the sinus membrane adjacent to the HSMD was evaluated endoscopically. After an additional 8 weeks, fixed partial prostheses were fabricated.



*Figure 10*. Surgical technique to install the hydroxyapatite space-maintaining device (HSMD).

*a* The sinus mucosa with paper thin bone wall is carefully elevated.*b*, *c* The hollow and perforated HSMD is installed under the intact sinus mucosa which is

visible beyond the device.

*d* 6 months of healing showing integrated HSMD filled with new bone.

#### Study III

Fourteen consecutive patients in need of maxillary sinus floor augmentation were enrolled in this study. Preoperative CBCT with a titanium screwpost as an indicator at the intended implant position was used to visually guide the flapless surgical procedure. Twenty one implants all with a length of 10mm and a diameter of 4.1 and 4.8mm were inserted and followed clinically and with CBCT for 3, 6 and 12 months postoperatively (Fig 11). All patients were provided with permanent prosthetic constructions 8–12 weeks after implant surgery.





months after prosthetic loading; f Frontal view 12 months after prosthetic loading



Figure 12. Measurements in CBCT a-c=reference distance a-d=marginal bone distance a-b=apical-intrasinusal bone distance

#### Study IV

24 consecutive partially dentate patients with a mean age of 64 years were included in the study and provided with 30 sinus lift procedures. The following three procedures for lateral sinus lift were used: Lateral sinus lift with replacement of bone window and without bone graft (BW), lateral sinus lift and covering osteotomy site with a collagen membrane and without bone graft (CM) and lateral sinus lift with autogenous bone graft (ABG) (Fig 13). Experimental implants were retrieved after 7 months of healing and analyzed by micro-computed tomography (Fig 14).



Lateral sinus lift with replacement of bone window and without bone graft (BW)

Lateral sinus lift and covering osteotomy site with a collagen membrane and without bone graft (CM)

Lateral sinus lift with autogenous bone graft (ABG)

Figure 13. Three different procedures for lateral sinus lift surgery



**Figure 14.**  $\mu$ CT analysis of buccal (left) and lingual (right) side of the implant and matched histology section from the same area. Lack of mineralized bone have been set to <0.05 mm (green color). Note that bone is missing on some tops of the threads but fills the bottom of the threads. Arrow indicate residual bone height.

# **Results**

#### Study I

One implant was lost (in group B, bone-scraper) before loading. The survival rate after a follow-up of 12 to 60 months was 98.8%. Due to the ability to harvest a greater volume of bone using a bone-scraper, longer implants was usually placed in this group (Fig. 15).



Figure 15. Distribution of mean residual bone height and implant lengths in different regions

There was no significant difference in marginal bone loss on the mesial and distal sides of the implant when baseline to 1-year registration was compared with baseline to final registration. During the same time, graft height decreased significantly on the distal apical side of the implants.

#### Study II

Bone formation verified by CBCT was found around and inside the HSMD in all three patients after 6 months. Despite the fact that residual bone before augmentation was ≤2 mm, 12-mm-long implants with diameter of 4.8 mm could be inserted with preservation of an intact and healthy sinus membrane verified endoscopically (Fig. 17). Bone formation inside HSMDs was noted histologically in two out of three HSMDs (Fig. 16). Implants were stable and without any marginal bone loss after 1 year of prosthetic loading.



**Figure 16** A. Light micrograph showing overview of remnants of the device (HA) and new bone (NB). Arrow points to areas of displaced HA particles from trephining the specimen. Left = orally. **B**, Close up of rectangle (Fig. 16A) showing direct contact between new bone and the device (arrows) as well as bone formation (NB) inside the pores of the device (HA).



*Figure 17.* Endoscopic picture of healthy sinus mucosa adjacent to the HSMD at the time of implant installation

#### Study III

Ten (47.6%) implants were inserted in residual bone of 2.6–4.9mm and 11 (52.3%) implants were inserted in residual bone of 5–8.9mm. No implants were lost after surgery and follow-up. There was minimal marginal bone loss during the follow-up verified by CBCT (Fig. 18,19). The implants penetrated on average 4.4mm (SD 2.1mm) into the sinus cavity and the mean bone gain was 3mm (SD 2.1mm).





#### Study IV

One implant was found not to be integrated at time of implant retrieval. This implant belonged to group CM and was excluded when calculating bone-to-implant contact (BIC %) and intrasinus bone levels. The integrity of the lateral sinus bony wall was determined at the time of implant removal. In group ABG all lateral sinus walls were ossified. In Group BW one lateral sinus wall and in group CM two lateral sinus walls were not completely ossified. There were no statistical differences in BIC% between the groups: 93.5% (BW), 92.0% (CM) and 93.5% (ABG). Additionally no statistical differences were found in apical-intrasinus bone

levels between the groups. When surfaces were compared within the same implant a statistical difference was found between the apical buccal distance and the apical lingual distance. The mean apical buccal distances/apical lingual distances were 0.6mm/1.2mm for the BW group, 0.5mm/0.8mm for the CM group and 0.6mm/0.8mm for the ABG group (p = 0.003)(Table 1).

Table 1 **BW** (*Lateral sinus lift with replacement of bone window and without bone graft*), **CM** (*Lateral sinus lift and covering osteotomy site with a collagen membrane and without bone graft*). **ABG** (*Lateral sinus lift with autogenous bone graft*) Table showing residual bone height and sinus width from apex of implant to buccal cortex (A-B) and from apex of implant to lingual cortex (A-L) before implant retrieval (CBCT-values) and total surface of implant covered with bone (BIC%) and intrasinus bone levels on the buccal, lingual, mesial and distal sides (µCT -values). Values in bold differ within the group.

<b>CBCT</b> values (mm)					µCT values (mm)			
	Residual	Sinus	width	DICA	Apical-	Apical-	Apical-	Apical
	bone	A-B	A-L	BIC%	Buccal	lingual	mesial	distal
BW								
( <b>n=10</b> )								
Mean	4.3	6.3	7.5	93.5	0.6	1.2	0.7	0.9
Max	6.8	9.6	10.9	100.0	1.3	3.2	1.4	4.4
Min	2.5	2.3	5.3	87.6	0.0	0.0	0.0	0.0
SD	1.3	2.1	1.7	3.3	0.4	0.8	0.4	1.3
СМ								
( <b>n=9</b> )								
Mean	3.5	7.4	6.8	92.0	0.5	0.8	0.6	0.8
Max	6.0	11.5	11.0	97.0	0.8	1.4	1.4	1.7
Min	2.0	4.1	4.6	83.6	0.0	0.0	0.0	0.0
SD	1.3	2.4	1.9	4.1	0.3	0.4	0.4	0.5
ABG								
( <b>n=10</b> )								
Mean	4.3	6.8	7.2	93.5	0.6	0.8	0.6	0.6
Max	5.3	9.5	10.5	97.4	1.6	1.7	1.1	1.3
Min	2.8	4.7	3.5	87.7	0.3	0.1	0.0	0.1
SD	0.9	1.7	2.4	3.3	0.4	0.5	0.4	0.3
P value	0.201	0.511	0.722	0.502	0.835	0.199	0.708	0.794

## Discussion

The presented studies demonstrate that a minimally invasive approach can successfully be used in sinus lift surgery. The oral cavity is an excellent source of autogenous bone graft for several bone regeneration techniques. In *study I* we could minimize the surgical trauma by harvesting autogenous bone next to the site for implant installation and by that avoiding an extra surgical approach for augmenting the sinus floor. Two different harvesting methods to

collect bone were used. The use of a bone scraper has proved to be of special interest to obtain amounts of bone that are required in most sinus augmentation procedures <sup>183-186</sup>. Due to the ability to harvest a greater volume of bone using a bone-scraper compared with a bone trap, longer implants were usually placed in that group compared with the bone trap group. Yang and coworkers measured the lateral sinus wall thickness using CT. The mean thickness from the first premolar to second molar was 1.69±0.71, 1.50±0.72, 1.77±0.78 and 1.89±0.85 mm respectively <sup>187</sup>. We found by collecting bone from the lateral sinus wall and zygomatic buttress that the opening in the lateral sinus wall could be minimized and still have a good access to elevate the sinus membrane. This is today one standard method in our clinic for lateral sinus lift procedures. There are different techniques presented creating a bone window in the lateral sinus wall. If the bone window is going to be replaced a piezo surgery equipment is recommended to use making a more stable replacement of the bone window (study IV). The piezo surgery technique is technically more demanding and time-consuming due to the need of creating a larger opening compared with the technique used in study I especially if the lateral sinus wall is thick. In *study IV* we recorded the integrity of the lateral sinus wall when experimental implant was retrieved. When using the same technique as described in study I we found that all lateral sinus walls were ossified.

When residual bone is  $\leq 2$  mm at the intended position of implant placement there is a risk that implant stability is impossible to attain without previous augmentation. A lot of methods have been presented for sinus lift procedures using the lateral sinus wall approach. The compartment created between the floor of the maxillary sinus and the elevated sinus membrane is typically filled with autografts, allografts, xenografts, alloplasts, or combinations of different graft materials. Recently studies have reported successful sinus augmentation via the lateral window approach with membrane elevation alone. Cricchio and coworkers <sup>49</sup> tested a resorbable dome shaped polylactide space-making device in an animal model. Sites with simultaneous implant placement and using this dome showed bone formation along the implant surface, but sites with delayed implant placement showed minor or no bone formation. The authors concluded that the reason for lack of bone formation was displacement of the space maintaining device when no implant was inserted to stabilize the device during healing. In study II we used a spherical, hollow, and perforated hydroxyapatite spacemaintaining device, in a two-stage sinus lift procedure. The regenerated bone volume could be limited to the intended implant position and no additional grafting material was needed. Other shapes of the device were initially discussed, but the spherical device appeared to be clinically easy to handle and needed no further stabilization after installation. The hollow perforated

device is easily filled with blood from the wound area and the osteoinductive properties of the surrounding bone and sinus membrane can stimulate new bone formation inside and around the perforated spherical device. The characteristics of the hydroxyapatite material with respect to resorption can be modified to obtain a desirable resorption rate of the device. The tested device showed only a minor tendency to resorb 6 to 9 months after installation.

In study III we used preoperative CBCT and titanium screwpost indicators at the intended implant positions to visually guide flapless implant installation in combination with an osteotome sinus lift technique. The use of an in-office CBCT offers many advantages to the surgeon performing implant surgery or bone grafting. Most studies using CT or CBCT in flapless implant surgery describe surgical guides being used for precise implant position, angulation and depths of insertion. In this study we presented a simple and cheaper alternative when installing one to three implants in the lateral segments of the maxilla. Our study shows minimal marginal bone loss as recorded at 3, 6 and 12 months postoperatively. The advantages of a flapless approach have been described by Jeong and colleagues and You and colleagues <sup>188-189</sup>. They found that gingival inflammation, height of junctional epithelium and bone loss around non-submerged implants can be reduced when implants are placed without flap elevation. In a clinical study by Leblebicioglu and colleagues <sup>190</sup>, implants were installed extending into the sinuses of 40 patients using an osteotome technique with no graft or cushion material. The authors reported a mean gain of alveolar bone height in scanned panoramic radiographs of  $3.9 \pm 1.9$ mm (residual bone <9mm) apically around exposed mesial and distal implant surfaces following 6 months of healing. Pjetursson and colleagues <sup>136, 191</sup> recently presented a study concerning transalveolar maxillary sinus floor elevation using osteotomes with or without grafting material. In their material, the residual bone height was 7.5mm and the implants penetrated on average 3.1mm into the sinus. The measured mean radiographic bone gain using the transalveolar technique without grafting material was 1.7mm compared with 4.1mm when grafting material was used. In our study, the mean residual bone was 5.6mm. Implants protruded in average 4.4mm into the sinus and the measured mean radiographic bone gain was 3mm. The difference in results can be explained by the fact that remodeling occurs with time and the study by Pjetursson and colleagues had longer followup. In study I using a lateral window technique grafted with locally harvested bone chips, the mean vertical apical-intrasinus bone distance was 0.81mm mesially and 0.86mm distally after 1 year. In study III, corresponding figures were 1.7mm mesially and 1.5mm distally after the same period. Obviously, there is likely to be less bone after 1 year around the apical part of an implant placed with a transalveolar osteotome technique compared with implants placed with a lateral window technique and grafted with locally harvested bone chips. In *study III*, only 33.3% of the implants showed a mean bone gain of 80-100% of the initial sinus elevation after 12 months. This could not be explained by differences in residual bone height and/or amount of sinus elevation. A reason for this difference could be unobserved, accidental membrane perforation decreasing the potential for new bone formation. With the surgical technique used in study III, the implant was used to lift the membrane after the osteotomes were inserted to a depth not exceeding the height of the residual bone. The clinical significance of these results in the long run will be analyzed. A decrease in bone volume will always occur around the apical part of implants placed in grafted sinus areas. This pneumatization is also obvious around the apical part of natural teeth protruding in to the maxillary sinus cavity. Even when sinus floor augmentation is performed with an autogenous bone/xenograft mixture and simultaneous placement of dental implants, a progressive sinus pneumatization occurs <sup>66, 192</sup>. Zijderveld and colleagues concluded <sup>193</sup>, when using a lateral window approach that both B-TCP (B -tricalcium phosphate) and mandibular bone grafts resulted in radiographic reduction of the vertical height over the 5-year period following maxillary sinus floor elevation. After an initial height reduction in the first 18 months, subsequent changes were minimal. No significant differences were observed between the two types of grafting material. It is important to preserve the marginal bone support because this bone is not only crucial for giving the initial stability to the implant but also for withstanding most force when the implant is loaded later on. Provided that marginal bone loss can be avoided, equilibrium is probably established between the effects of continuous sinus pneumatization, resorption of the graft and stimulation of the bone that supports the implant. Functional loading of an implant generates greater loading on the marginal bone than around the apical part of the implant  $^{63-65}$ .

In *study IV* we compared the amount of bone regeneration following three lateral sinus elevation treatment modalities using  $\mu$ CT. In this study we found no difference in new intrasinus bone formation between the three different lateral sinus lift procedures calculated by 3D  $\mu$ CT. Neither was any difference of intra-sinus bone formation recorded when bone levels on the buccal, lingual, mesial and distal sides of the implant were compared between the three methods but more bone was recorded on the buccal-apical aspects of the implant compared to the lingual-apical aspect of individual implants. A reason for this difference could be greater osteoinductive potential on the buccal side than on the lingual side of the implant after creation of a bone window on the buccal side. Sohn and colleagues <sup>80</sup> reported that the repositioned bony window may accelerate new bone formation earlier during healing versus

placement of a collagen membrane grafting material in the sinus. The bucco-palatal width of the sinus has been reported to influence this potential <sup>194-195</sup>. Our study does not support this conclusion as we found no correlation between implant distance to the sinus wall and adjacent bone formation heights.

The Schneiderian membrane has been found to have an osteogenic potential which can contribute to the development of successful sinus augmentation techniques <sup>196-198</sup>. Other authors have not been able to clinically document this potential. Scala and coworkers <sup>82-83</sup> found that new bone formation was limited to an area close to the parent bone and originated from the sinus walls and septa while there was no evidence of participation of the Schneiderian membrane in this bone formation. On the lingual side of retrieved implants in our study, bone was thinner but still present inside the implant threads but was missing on the top of the threads (Fig. 14). Price and coworkers<sup>68</sup> found that new bone formation resembled a combination of de novo appositional and intramembraneous ossification and that graft material had a passive role, implying that the ingrowth of vascular and perivascular tissues are the most logical source of osteogenic capacity. By avoiding scaffolding fillers made from biological and/or synthetic materials, with or without additional particulated autogenous bone, a shorter healing time for optimal bone formation can probably be expected <sup>123</sup>.

Experimental implants in our study were never loaded before removal. The adjacent implants were loaded 3-5 months after implant installation. The experimental implant was retrieved after 7 months of healing. This means that adjacent implants to the experimental implant were loaded 2-4 months before experimental implant was retrieved. The influence of loading on intra-sinus bone remodeling has not been thoroughly studied but it can be anticipated that functional loading can have a stabilizing effect on the maintenance of the intra-sinus bone <sup>66-67</sup>. Most examined implants in our study were not covered with bone on the apical side at the time of removal (Fig. 14). This has also been reported in autopsy studies <sup>199-200</sup>. Since BIC% values were equal in the three different lateral sinus lift procedures in this study total bone volume regenerated by using different techniques has to be further investigated. One limitation of  $\mu$ CT is that while it is very good at determining BIC it fails to measure the total bone formation within the sinus. Thus further studies are required to assess total sinus bone formation with regards to different sinus lift techniques. Unfortunately given the use of multiple implants in this study, CBCT artifacting precludes such analysis.

# Conclusions

#### Study I

Bone grafts can be locally harvested at the site of the maxillary sinus augmentation procedure to enable placement, successful healing, and loading of 1 to 3 implants.

#### Study II

A hydroxyapatite space-maintaining devices (HSMD) used in sinus lift procedures can produce a void for blood clot and new bone formation and subsequent implant installation.

#### Study III

Flapless transalveolar sinus lift procedures guided by preoperative CBCT can successfully be used to enable placement, successful healing and loading of one to three implants in residual bone height of 2.6–8.9mm. There was minimal marginal bone loss during the 3–12 months follow-up.

#### Study IV

Three different lateral sinus lift procedures were compared using micro-computed tomography of retrieved implants with surrounding bone. The procedures were: Lateral sinus lift with replacement of bone window and without bone graft (BW), lateral sinus lift and covering osteotomy site with a collagen membrane and without bone graft (CM) and lateral sinus lift with autogenous bone graft (ABG). All three procedures showed equal high degree of bone-to-implant contact. Implant distance from the initial sinus wall had little effect on adjacent implant bone formation, regardless of method used. The examined implants apices were seldom covered with bone at the time of removal. The integrity of the lateral sinus bony wall was determined at the time of implant removal. With regards to lateral sinus wall formation we found that only the Autogenous Bone Graft (ABG) group consistently regenerated a completely ossified bony wall. While this study found no method to be superior with regards to bone-to-implant contact, further studies are required to assess total bone formation volume within the grafted sinus.

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