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THE USE OF AUTOLOGOUS TOOTH BONE GRAFT IN ALVEOLAR CLEFT RECONSTRUCTION

PhD thesis

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List of abbreviations

ABG	alveolar bone grafting
ASIS	anterior superior iliac spine
ATB	autologous tooth bone
β-TCP	beta-tricalcium phosphate
CBCT	cone-beam computed tomography
CEJ	cemento-enamel junction
CLP	cleft lip and palate
CT	computed tomography
DFDBA	demineralized freeze-dried bone allograft
DSC	*Dice* similarity coefficient
FDBA	freeze-dried bone allograft
FGF	fibroblast growth factor
GMP	good manufacturing practice
GPP	gingivoperiosteoplasty
HA	hydroxyapatite
HD	*Hausdorff* distance
HU	*Hounsfield* unit
IAN	inferior alveolar nerve

ICBG	iliac crest bone graft
LFCN	lateral femoral cutaneous nerve
L-PRF	leukocyte-platelet rich fibrin
PABG	primary alveolar bone grafting
PDGF	platelet derived growth factor
PLGA	poly (lactic-co-glycolic acid)
PRF	platelet-rich fibrin
PRP	platelet-rich plasma
rhBMP-2	recombinant human bone morphogenic protein 2
SABG	secondary alveolar bone grafting
SLA	stereolithography
STL	standard tessellation language
TABG	tertiary alveolar bone grafting
UCLP	unilateral cleft lip and palate
VEGF	vascular endothelial growth factor
VSP	virtual surgical planning

1. Introduction

1.1 Scientific background

Cleft lip and palate (CLP) are among the most frequent congenital malformations overall with an estimated worldwide incidence of around 1.5-1.7 per 1000 live births, whereas Hungarian data show a cleft prevalence of 2.02/1000 per live births (1). The aetiology of CLP is multifactorial, with both genetic and environmental contributions (2). Maternal age, nutritional deficiencies (e.g.: folic acid), smoking or alcohol abuse during pregnancy, maternal hyperthermia, and certain viral infections are all supposed to affect craniofacial development. In approximately 75% of CLP cases the alveolar ridge is involved, leading to an alveolar cleft (3). The main characteristics of this are:

- Discontinuity of the maxilla
- Collapse of the dental arch segments
- Developmental and growth disturbances of adjacent teeth
- Oro-nasal communication
- Disturbances in nasal morphology.

These anomalies lead to compromised facial aesthetics, difficulties of masticatory function, breastfeeding, swallowing and speech, and overall worse psychosocial well-being. The reconstruction of the alveolar cleft is a crucial step in the treatment of patients with cleft lip and palate, with alveolar bone grafting (ABG) usually being the last primary surgical intervention after cheiloplasty and palatoplasty. The main goals are to stabilize the maxillary dental arch, obliterate the persistent oronasal fistulae, enhance facial symmetry, provide bone for tooth eruption, or dental implant placement, and enhance support of the nasal base (4).

1.2. Timing of alveolar bone grafting

The history of alveolar bone grafting reflects the changes in our understanding of craniofacial growth and function (5). Different approaches are usually categorized based upon the timing of the surgery:

- Primary alveolar bone grafting (PABG): performed before the age of 2, after lip repair but prior to the repair of the palate.
- Secondary alveolar bone grafting (SABG): performed after the age of 2, in patients with mixed dentition (6).
- Tertiary alveolar bone grafting (TABG): performed in patients with permanent dentition.

Early attempts at PABG, performed in infancy, sought to prevent secondary defects, and reduce the number of operations, but were later shown to impair midfacial growth due to premature ossification and scar tissue formation. Gingivoperiosteoplasty (GPP) was proposed as a graftless solution that relied on periosteal induction of bone formation; however, systematic reviews showed inconsistent results, with insufficient bone bridge formation in many patients (7-9). Secondary ABG was introduced in 1972 by *Boyne and Sands* (10), and became the gold standard after landmark studies demonstrated that grafting during the mixed dentition phase, before eruption of the permanent canine, provided optimal arch stability and allowed the physiological eruption of teeth adjacent to the cleft (11). Several studies have also confirmed that this approach does not interfere with the growth and development of the maxilla (12). TABG is generally reserved for late adolescents or adults, usually as a resort for patients who failed to present on time or as an attempt to correct failed grafts or to prepare for prosthetic rehabilitation. While functional rehabilitation (e.g., implant placement) might be feasible, volumetric maintenance of the graft is generally inferior, resorption rates are higher, and orthodontic movements are more limited. TABG is also associated with an increased risk of dehiscence and need for regrafting in wide defects (13).

1.2.1 Timing of secondary alveolar bone grafting and orthodontic considerations

The exact timing of SABG is based on dental development and maxillary growth (14). Though it is always done during the mixed dentition phase, there are two distinct approaches: it is either done at an earlier (4-7 years) or at a later age (8-12 years) (15, 16).

The early SABG approach aims to perform alveolar reconstruction prior to the eruption of the lateral incisor. Advocates of this method argue for improved guidance of erupting incisors and earlier closure of oronasal fistulae (17). Reported advantages include better residual bone volume outcomes at the cleft site; concerns include greater technical difficulty in small alveoli and a possibility of restriction of maxillary growth (18).

Most centres prefer grafting when the root of the cleft-side canine is one-half to two-thirds of its expected final length, usually between the age of 8-12. This approach is associated with the highest rates of successful bone bridging, canine eruption, and long-term stability. Grafting shortly before eruption of the permanent canine allows the canine to erupt through the graft, stimulating remodelling and consolidation of the bone bridge (19-21).

Orthodontic treatment of these patients is often necessary and is usually performed preoperatively. Expansion of the collapsed maxillary segments and alignment of anterior teeth are necessary to open the alveolar cleft site and to improve access. Extraction of any supernumerary or retained teeth around the cleft can be performed prior to or during the same surgery (22).

In bilateral cases stabilization and proper positioning of the premaxilla is critical. Strategies include one-stage bilateral grafting with premaxillary osteotomy and fixation when the premaxilla is protrusive/mobile, these cases, however, carry higher rates of wound breakdown and regrafting. Moreover, the preparation of extended flaps could compromise the vascular supply of the premaxilla and lead to severe complications (23). A staged approach with closure of oro-nasal fistulae and reconstruction of the nasal floor as a first step, followed by alveolar bone grafting in a second intervention might lead to a more predictable outcome (24).

1.3. Flap design

Successful SABG depends on a supple, well-vascularized mucosa capable of tension-free closure. Active infections or poor oral hygiene should be treated before grafting to lower failure risk. In terms of local flap design for alveolar cleft closure, the preferred method is usually the four-flap technique, as described by *Nordin and Abyholm* (25, 26), which provides an ideal soft-tissue closure above the graft. However, in cases of suture loosening due to flap tension, secondary wound healing might occur, and the consequent exposure might lead to the loss of the graft. This classic flap design does not address the width and thickness of keratinized gingiva of the teeth adjacent to the alveolar cleft, where consequent periodontal impairment may develop, resulting in eventual tooth loss.

1.4. Iliac crest bone graft (ICBG)

For decades, autologous bone harvested from the anterior iliac crest has been the gold standard graft for SABG. This donor site provides:

- Abundant corticocancellous bone
- High concentration of osteogenic cells
- Osteoinductive, osteoconductive and osteogenetic properties
- Favourable remodelling capacity in the recipient site

Donor site morbidity however remains a major drawback (27, 28). Possible complications include pain, gait disturbance, fracture of the anterior superior iliac spine (ASIS), nerve injury and paresthesia, especially of the lateral femoral cutaneous nerve (LFCN), hematoma or seroma formation, superficial or deep infection, and aesthetic concerns from scars (29). Meta-analyses and systematic reviews report complication rates between 10–30%, with long-term pain and functional limitation in a subset of patients. Hospitalization time and recovery are also prolonged, raising concerns, especially in children (30). These disadvantages led to the investigation for alternative donor sites and graft types (31, 32).

1.5. Alternative donor sites and biomaterials

Alternatives to the iliac crest aim to reduce donor site morbidity while achieving comparable results to this type of graft (33). These include autologous grafts from various extra- and intraoral donor sites, allografts, xenografts and certain supplementary materials to be used in combination with the grafts, such as platelet rich plasma (PRP), fibrin sealant, leukocyte-platelet rich fibrin (L-PRF) derivatives, etc.

A. Extraoral donor sites:

a. Calvarium (split-thickness). Mainly cortical plates with lower tendency for resorption. Pros: large, flat grafts; scar is hidden in the hairline. Cons: chance of neurosurgical complications; longer operation time; less osteogenic than cancellous iliac bone; unsuitable in very young children.

b. Proximal tibia. Cancellous bone harvested via small incision. Pros: reasonable amount; lower risk of gait disturbance than with iliac crest; low visible scarring. Cons: risk of tibial plateau injury; postoperative discomfort; not ideal for pediatric use.

c. Rib. Curved corticocancellous segments. Pros: structural support. Cons: chest wall pain; risk of pneumothorax; unpredictable remodelling; it is rarely the first choice for SABG.

B. Intraoral donor sites:

a. Mandibular symphysis (chin): Supplies cortico-cancellous blocks/chips. Pros: proximity to recipient site; no visible extraoral scar; short harvest time. Cons: limited volume; risk to lower incisor roots and mental nerve; chance of temporary chin hypoesthesia; potential chin contour change. Best suited for unilateral narrow-to-moderate width clefts, often as a composite graft combined with particulate xenografts to increase volume (34).

b. Mandibular ramus / coronoid process: Dense cortical bone to be used as a block or as particulate chips after processing. Pros: minimal aesthetic impact; good bone quality. Cons: limited cancellous component; risk of trismus or transient inferior alveolar nerve (IAN) paresthesia.

c. Maxillary tuberosity / zygomatic buttress / palatal tori. Provide small particulate volumes for minor defects or in combination with other grafts. Pros: same surgical field; low morbidity. Cons: very limited quantity; variable quality.

All intraoral bone grafts have the advantage of having the same embryologic origin as the maxilla, meaning these grafts contain intramembranous bone. This tends to resorb less and maintain volume better than endochondral bone (e.g.: the iliac crest) in craniofacial sites.

C. Allografts (FDBA/DFDBA) are processed human bone in particulate or block form, usually coming from femoral heads of living donors (35, 36). They offer osteoconductive and osteoinductive properties with no donor site morbidity (37). Their use in alveolar cleft reconstruction is not common, but a study by *Chauvel-Picard et al*. (38) showed that hard-tissue gain after one year was 58.5%

D. Xenografts (e.g., deproteinized bovine bone mineral) are highly osteoconductive with very slow resorption. They are good for space maintenance and act as a scaffold for creeping substitution. In some centres they are commonly used in combination with autografts (39, 40). However, the persistence of particles and limited remodelling capacity generally render these inadequate as monotherapy in cleft patients.

E. Alloplastic / synthetic materials, such as β-TCP, HA/β-TCP, bioactive glass (41, 42), calcium phosphate cements are purely osteoconductive. Pros include unlimited supply, customizable granule size and predictable resorption profiles (43). However, they show inferior integration as standalone graft, and are best used as composites with autografts or PRF.

F. Bone morphogenic proteins (rhBMP-2) are potent osteoinductive factors delivered on an absorbable collagen sponge. They yield outcomes close to ICBG bone fill in selected cases while avoiding a donor site (44, 45). However, their use is considered off-label in children in many jurisdictions, moreover they are linked to dose-dependent oedema, airway swelling, and ectopic bone formation (46, 47). Their cost is also higher compared to other grafts.

G. Platelet rich plasma/fibrin (PRP/PRF) are autologous platelet concentrates. PRF supports tissue repair initiation through containment of growth factors, cytokines and adhesion proteins that have a role in the haemostatic cascade, connective tissue synthesis, and angiogenesis (48, 49). PRF also improves the natural healing potential of hard and soft-tissues by containing growth factors, such as VEGF, FGF, PDGF, and modulating pain and inflammation. There is however inconsistent evidence for added bone volume as standalone graft, they are best used as adjuncts, combined with other types of grafts, particularly with alloplastics or xenografts which only have osteoconductive properties (50).

H. Tissue-engineering strategies such as collagen/PLGA scaffolds, decellularized matrices (51, 52), and stem-cell–based constructs show strong preclinical performance (53, 54). Clinical use is limited by regulatory hurdles, cost, and need for standardized, GMP-compliant workflows. Early clinical feasibility studies suggest potential as adjuncts, not replacements.

1.6. Autologous tooth bone (ATB)

Auto-tooth bone is an autologous graft material, originally developed in Korea by *Kim et al.* in the early 2010s, which is derived from extracted teeth (55, 56). The idea is to process extracted teeth into particulate or block grafts through chemical and mechanical preparation (57). Unlike synthetic grafting materials, ATB possesses both osteoconductive and osteoinductive properties, promoting rapid new bone formation and remodelling. This material is composed of an incompletely demineralized dentin matrix, which contains type I collagen, similarly to alveolar bone, as well as BMPs and calcium phosphate, all of which are key components of bone regeneration. The mineral components of ATB consist of four stages (types) of calcium phosphate: hydroxyapatite, tricalcium phosphate, octacalcium phosphate, and amorphous calcium phosphate. When using ATB for guided bone regeneration, *Kim et al.* found that after 3 months, most of the graft underwent resorption, and excellent bone healing was observed, which occurred as a result of osteoinduction and osteoconduction. Regarding the histomorphometric analysis of the samples collected during the 3–6-month healing period, new bone formation was detected in 46–87% of the area of interest, and excellent bony remodelling was achieved. ATB has been successfully applied so far in periodontal regenerative surgery (58), alveolar ridge preservation (59), preprosthetic surgery, and implantology. There are also case reports presenting successful outcomes in alveolar cleft reconstruction, *Jeong et al.* (60) were able to place a 3 mm-wide implant with 45 Ncm insertion torque 3.5 months after ABG using ATB (61).

1.7. The role of virtual surgical planning

Virtual surgical planning (VSP) has become a valuable auxiliary technique in the management of craniofacial malformations and cleft surgery, particularly so in alveolar bone grafting (62). These techniques utilize preoperative three-dimensional (3D) imaging, most commonly cone-beam computed tomography (CBCT), to generate accurate virtual models of the maxillofacial area. These models allow the surgeon to assess the morphology of the alveolar cleft, the number and position of adjacent teeth, and the relationship with critical structures such as the nasal floor and maxillary sinus (63).

One of the main advantages of VSP is the ability to visualize the shape and quantify the volume of the alveolar defect, which helps to estimate the required graft material more precisely and aids in the selection of an appropriate donor site. Virtual simulations also enable the surgeon to plan the ideal size and contour of the graft, with consideration of future orthodontic tooth movement or implant placement (64-66). In complex cases, patient-specific surgical guides or 3D-printed anatomical models may be fabricated, allowing more precise intraoperative execution of the planned procedure (67, 68).

During the postoperative phase, the virtual surgical plan also gives the opportunity to evaluate outcomes better. Pre- and postoperative 3D datasets can be compared to assess bone fill, graft resorption, and integration with surrounding bone.

Despite the benefits, VSP in alveolar cleft repair has certain limitations. The need for advanced imaging equipment, specialized surgical planning software, and medical-grade 3D printers may increase costs (69). Furthermore, the use of CBCT comes with radiation exposure, although this is generally justified in the context of cleft care where repeat radiographic assessments are indicated. In summary, VSP can improve the precision and predictability of alveolar cleft reconstruction by helping preoperative assessment, enhancing intraoperative accuracy, and standardizing the evaluation of outcomes.

1.8. Assessment of surgical outcomes

Alveolar bone grafting is considered successful when it achieves sufficient bone fill in the alveolar cleft. However, the goal of grafting is not only radiographic bone fill, but there are also clinical and functional considerations: eruption of adjacent teeth, orthodontic alignment, lack of residual fistulae, prosthetic feasibility, and long-term stability (70).

The proper assessment of surgical outcomes remains challenging. A postoperative evaluation is crucial not only to measure the success of the procedure, but also to enable the early detection of graft resorption or displacement, which are among the most frequent complications of alveolar bone grafting. The earliest assessment methods, such as the use of *Bergland and Chelsea* (71, 72) scales, relied on a two-dimensional approach, using intraoral X-rays. Over time, with the emergence of computed tomography (CT) and especially cone-beam computed tomography (CBCT) technologies, several 3D evaluation methods have been developed to assess the outcomes of ABG (63, 73). While 2D methods are limited by structural overlaps and cannot provide volumetric data, and tend to overestimate graft volume, 3D techniques using CT overcome these limitations (74, 75). Moreover, CBCT is often preferred over conventional CT for evaluating bone grafts due to its lower radiation exposure and its ability to accurately estimate the graft volume. Three-dimensional radiological imaging helps assess the presence and spatial location of the bone graft (76). It allows the size and location of graft resorption to be precisely specified. It can also help to evaluate the process of teeth eruption in the grafted area (77). CBCT has certain limitations in comparison with CT examination. Firstly, the *Hounsfield* unit (HU) scale cannot offer a credible assessment of bone quality. Another drawback to CBCT is a documented underestimation of bone volume.

2. Objectives

Despite its status as the gold standard in alveolar cleft reconstruction ICBG is associated with significant donor site morbidity and high resorption rates. ATB offers an autologous and biologically active alternative grafting material with osteoconductive and osteoinductive properties, which also eliminates the need for an extraoral donor site.

This thesis evaluates the use of ATB and ICBG in alveolar bone grafting of patients with cleft lip and palate. For precise comparison of the outcomes modern CBCT-based assessment methods, such as volumetric subtraction analysis and the *Stasiak* rank scale are being implemented. Both short- and long-term radiological data are presented and interpreted to support the findings of the research, and to contribute to the international evidence base guiding future clinical protocols.

Through this research, the aim is to reduce patient morbidity, improve clinical outcomes, and advance the field of cleft care by integrating surgical innovation with state-of-the-art radiological evaluation.

The objectives of this doctoral thesis are grounded in the findings and methodology of two key studies: the retrospective pilot study by *Molnár et al.*(78), and the retrospective cohort study by *Würsching et al.*(79). These articles provide the scientific foundation for defining the specific research aims of this work.

Primary objectives:

- The evaluation of short-term volumetric hard-tissue gain after using ATB for SABG in patients with UCLP by 3D subtraction analysis based on preoperative CBCT and 3 months postoperative control images.
- The evaluation of long-term volumetric stability and resorption patterns of ATB compared to ICBG in secondary alveolar bone grafting of patients with unilateral cleft lip and palate, using standardized CBCT-based analysis.

Secondary objectives:

- To validate the efficacy of the surgical procedure and volumetric stability of the graft, by calculating the ratio between the actual volumetric hard-tissue gain and the planned hard-tissue volume.

- Assessment of the similarity between the planned and actual hard-tissue morphologies by calculating the *Dice Similarity Coefficient* (DSC) and *Hausdorff Distance* (HD).

- Assessment of the success of permanent canine eruption through ATB compared to ICBG.

- To evaluate the prevalence of short- and long-term surgical complications in each group.
- To assess the relationship between initial defect volume and outcome scores.
- To evaluate intra- and interrater reproducibility of the *Stasiak* scale.

Hypothesis:

- Volumetric analysis and clinical outcomes show that ATB can be integrated into SABG protocols with comparable short-term outcomes to ICBG.

- ATB demonstrates volumetric stability and functional outcomes equivalent to ICBG over long-term follow-up, while minimizing donor site morbidity.

3. Methods

3.1 Study design and ethical approval

This thesis integrates the outcomes of two complementary clinical studies: a retrospective pilot study and a retrospective longitudinal cohort study. Both studies were approved by Semmelweis University's Regional and Institutional Committee of Science and Research Ethics (Approval Number: SE RKEB 251/2020). The study protocol was submitted and approved by the U.S. National Library of Medicine (www.clinicaltrials.gov; trial registration number: NCT05971914). The research plan was compiled following the legislation in force and the Declaration of Helsinki from the World Medical Association (reference number: 23/2002. V.9.). Surgical interventions were undertaken with the understanding and written consent of each subject's caregiver.

3.2 Patient selection and characteristics

All the enrolled patients for both studies were being treated for cleft lip and palate at the Centre of Facial Reconstruction at the Pediatric Center of Semmelweis University, Budapest.

3.2.1. For the pilot study of *Molnár et al*., all the patients underwent SABG surgery between August of 2021 and April of 2022. Only patients exhibiting a complete unilateral cleft lip and palate (UCLP) were recruited for this study. The exclusion criteria were:

a) major relevant general medical conditions or syndromic cases,

b) systemic use of steroids,

c) current or previous intravenous bisphosphonate treatment,

d) acute infection at the operation site,

e) any previous attempts at alveolar bone grafting.

In every case the development of the cleft-side canine was considered during planning of the surgery, as was the need for orthodontic treatment. All the patients included in the study required orthodontic maxillary expansion. The development of the canine was followed using periapical X-rays. Only once the canine's root development was between one-third and two-thirds of its expected final length, was the decision made to proceed with surgery. At this point CBCT scans were taken for surgical planning. Each patient was required to have presented at least three deciduous teeth, which were scheduled for extraction, as in the pilot study every patient underwent SABG using autologous tooth bone graft. All enrolled patients were examined by two independent dentists to assure that tooth removal was in accordance with the patients' age and orthodontic planning.

3.2.2. For the cohort study by *Würsching et al.* patients who had undergone secondary alveolar bone grafting between 2020 and 2023 were recruited. Inclusion criteria were complete UCLP without other congenital deformities, ABG surgery using either an iliac crest cancellous bone graft or ATB from deciduous or supernumerary teeth, and CBCT imaging at least one year after grafting.

The exclusion criteria were:

a) bilateral clefts,

b) any previous attempt at bone grafting,

c) the use of any other type of grafting material (e.g., xenografts, other donor site),

d) and a lack of long-term follow-up CBCT.

The STROBE checklist was implemented during the preparation of this manuscript.

3.3 Preoperative imaging and 3D virtual planning

For precise assessment of the alveolar cleft anatomy, and to measure the required volume of the graft, the regular preoperative work-up of these patients always included a CBCT scan.

These scans were acquired using a NewTom VGi evo® device with a 12 cm × 8 cm field of view, and a 200 µm voxel size (NewTom, Cefla S.C., Imola, Italy). CBCT data were also acquired at the 3-month follow-up for the pilot study, and at least one year postoperatively for the cohort study. Digital imaging and communications in medicine (DICOM) datasets were imported into the 3D Slicer open-source image-processing software (www.slicer.org) Baseline and follow-up CBCT scans were segmented utilizing a semi-automatic segmentation method in the 'Segment Editor' module of 3D Slicer (80, 81). Separate binary label maps were generated for the bone of the maxilla. The maxilla was segmented utilizing the region-growing tool 'Grow from seeds', and thereafter the 'Watershed' tool was used to segment all the teeth separately (82). The software automatically generated 3D models of binary label maps, with real-time rendering. (Figure 1.)

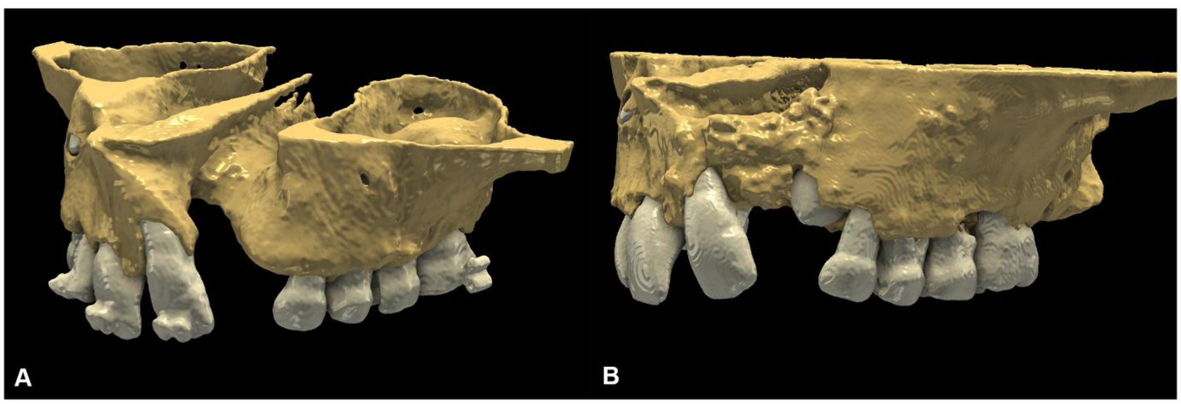

Fig. 1. Segmented 3D models of CBCT datasets: (A) virtual model of baseline hard-tissue conditions; (B) virtual model of 3-month follow-up hard-tissue conditions.

Based on the extent and morphology of the cleft the desired shape of the nasoalveolar graft was also designed in 3D Slicer. Since every case was unilateral, the non-cleft side anatomy was used as a reference during graft planning. The upper border of the defect was taken as the lowest part of the piriform aperture on the non-affected side, while the lower border was taken as the cementoenamel junction (CEJ) of the neighbouring teeth. The buccal and palatal borders were determined by a line connecting the most buccal and palatal points of the alveolar process, next to the defect. This also gave us the opportunity to determine the exact volume of the graft in cm^3. This facilitated preoperative planning because the maximum amount of material the ATB machine can produce is approximately 3 cm^3. The achievable volume of the ATB could be predicted based on the volume of the deciduous teeth, which was a limiting factor, since in case the number and condition of removable deciduous teeth was not sufficient the iliac crest graft had to be used.

After planning, the model was exported as a standard tessellation language (STL) file. As the final step, a grafting template was constructed using an open-source computer-aided design (CAD) software (Blender®; Blender Foundation, Amsterdam, The Netherlands), as described by Fábián et al. (67, 69) (Figure 2.) The designed parts were manufactured with a stereolithography (SLA) 3D printer (Phrozen Shuffle XL; Phrozen, Hsinchu City, Taiwan) using class I biocompatible, surgical-grade resin (Dental SG; NextDent BV, Soesterberg, The Netherlands). These 3D printed models enabled intraoperative visualization of defect dimensions and gave guidance for graft shaping. This ensured optimal defect filling, minimized graft waste, and standardized intraoperative workflows.

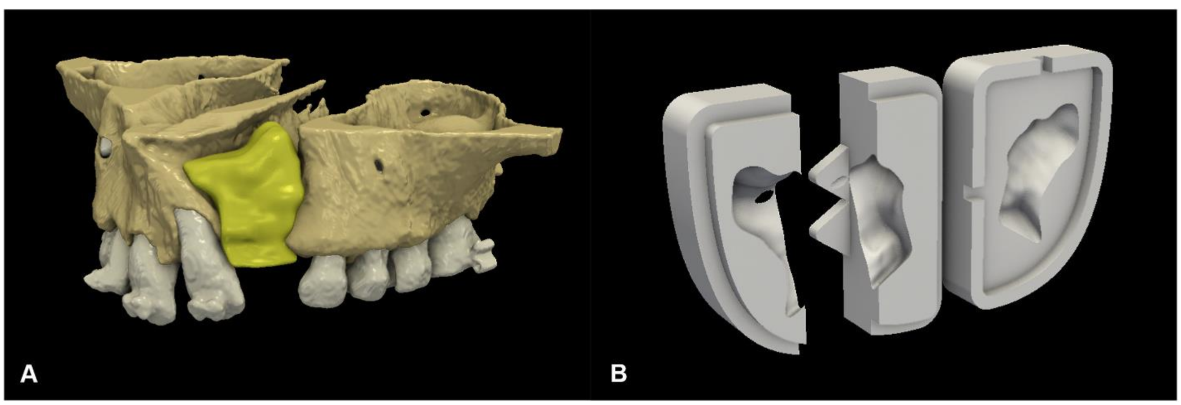

Fig. 2. Preoperative virtual planning: (A) digital 3D plan of cleft reconstruction; (B) CAD-modelled grafting template.

3.4 Surgical protocols

3.4.1. Preparation of the ATB graft and preparation of the recipient area

Teeth were extracted under general anaesthesia with the gentle application of forceps and elevators. Extracted teeth were prepared immediately after removal, according to the

Bonmaker® protocol (Korea DentalSolution Co Ltd, Busan, Korea) (Figure 3.) The outer surface of the teeth was debrided with diamond-coated burs (55, 56). Following the removal of pulp tissue, carious lesions and restorations, the crowns and roots were both ground in the Bonmaker® tooth grinder. After grinding, the tooth particles (particle size: 425–1500 µm) underwent disinfection and preparation via proprietary A, B, and C liquids inside the Bonmaker® device. Between patients, the equipment underwent a regular disinfection cycle, according to the manufacturer's instructions.

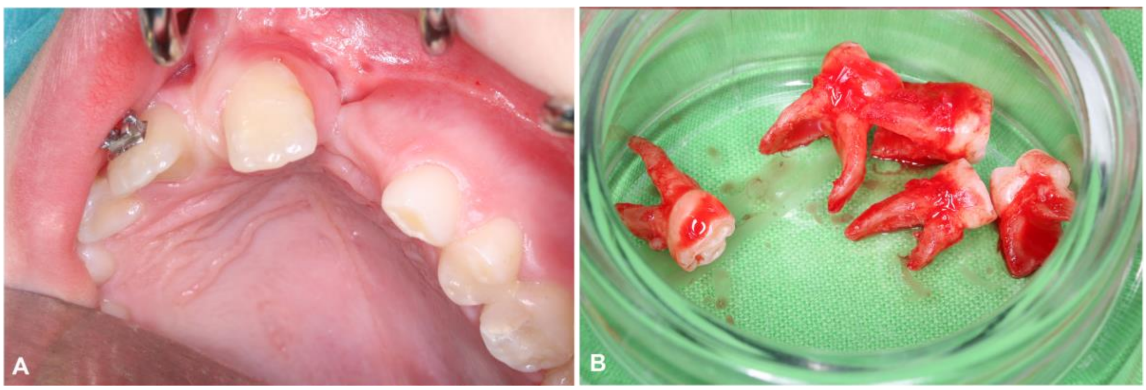

Fig. 3. Baseline clinical situation and tooth extraction: (A) baseline clinical situation; (B) extracted deciduous teeth.

During the preparation and disinfection procedure (which usually took 30–35 minutes), flap preparation and exploration of the alveolar cleft and oronasal fistula were carried out. Articaine hydrochloride 4% with 0.0001% epinephrine (Ultracain DS Forte; Sanofi-Aventis, Paris, France) was used for local anaesthesia. A full-thickness incision was made starting at the ipsilateral maxillary tuberosity, continued in a continuous intrasulcular incision along all teeth located distally from the oronasal fistula, with a no. 15 blade (Aesculap; Braun AG, Tuttlingen, Germany). At the level of the cleft and the oronasal fistula (located in the lateral incisor position), the incision was continued along the alveolar crest in full-thickness, followed by a split-thickness incision at the mucogingival junction of the adjacent central incisor, and continued vertically in the midline labial frenulum. Subsequently, the area of keratinized gingiva around teeth located distally from the cleft was elevated in full thickness with blunt dissection. Flap elevation was continued by sharp dissection apically from the mucogingival junction of the distal teeth, as well as at the loose mucosa over the central incisor, where the keratinized gingiva was left untouched. The periosteal layer of the complete hemimaxilla was then exposed, followed by excision of the epithelial down growth in the oronasal fistula, which was closed with resorbable monofilament sutures (Chirmax Monolac 5/0) by approximating adjacent scar tissue margins. Scar tissue in the cleft area was outlined by mesial, distal, and palatal incisions to allow for nasal repositioning, exposing the bony cleft and creating a secluded space for graft insertion (Figures 4. and 5).

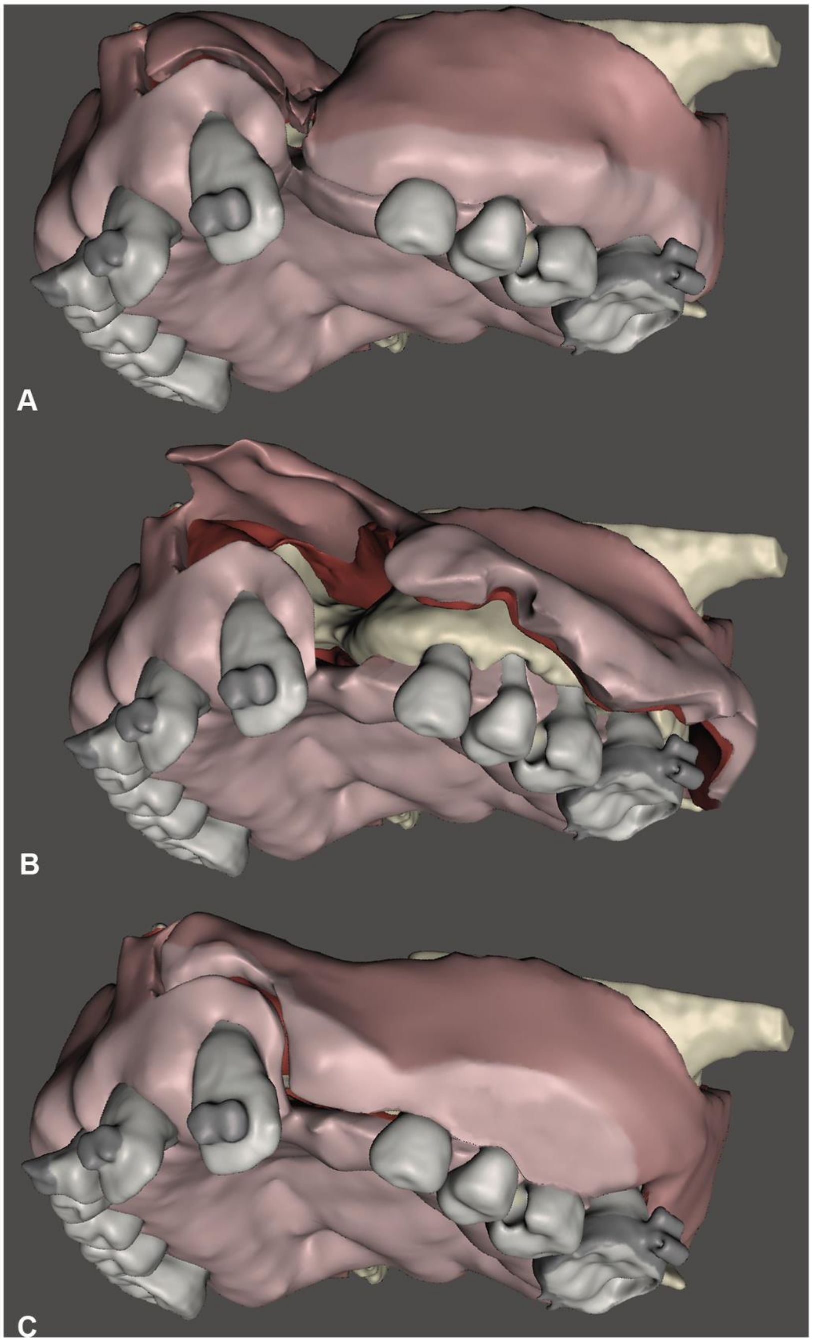

Fig. 4. Schematic presentation of the split-thickness papilla curtain flap: (A) initial incision (light pink: keratinized mucosa, dark pink: mobile mucosa); (B) flap elevation (red: periosteum); (C) mesially shifted flap closure.

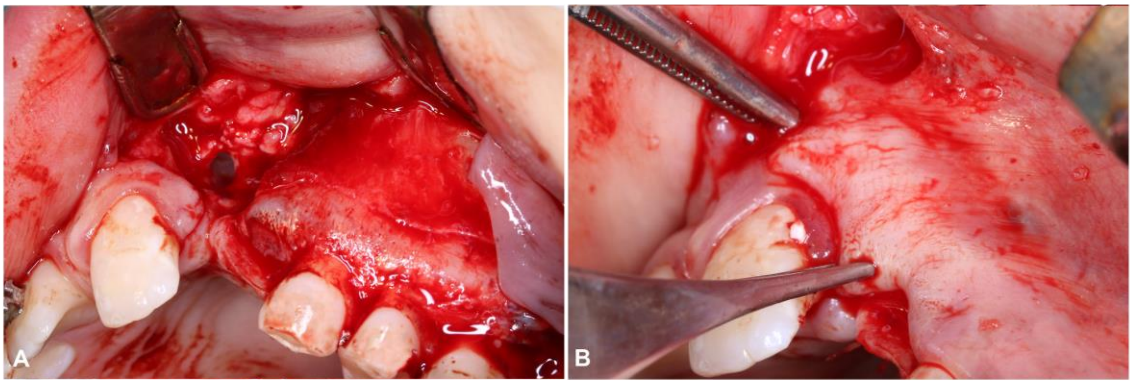

Fig. 5. Intraoperative situation: (A) surgical access of the UCLP; (B) tension-free mesial flap advancement.

Ready-to-use ATB was mixed with fibrin sealant (Tisseel®; Baxter, Glenview, Illinois, USA) in the digitally planned and 3D-printed grafting templates to obtain a sticky ATB graft that matched the shape and extent of the bony defect (83). The sticky ATB graft was then inserted in the alveolar defect (Fig. 6). Following cleft augmentation, the split-thickness papilla curtain flap was repositioned by shifting all buccal surgical papillae mesially to the adjacent or the second-adjacent interproximal space, depending on the horizontal extent of the cleft. Next, the papilla in the close vicinity of the oronasal fistula was relocated to the level of the mesial vertical incision in the midline frenulum (Fig. 7).

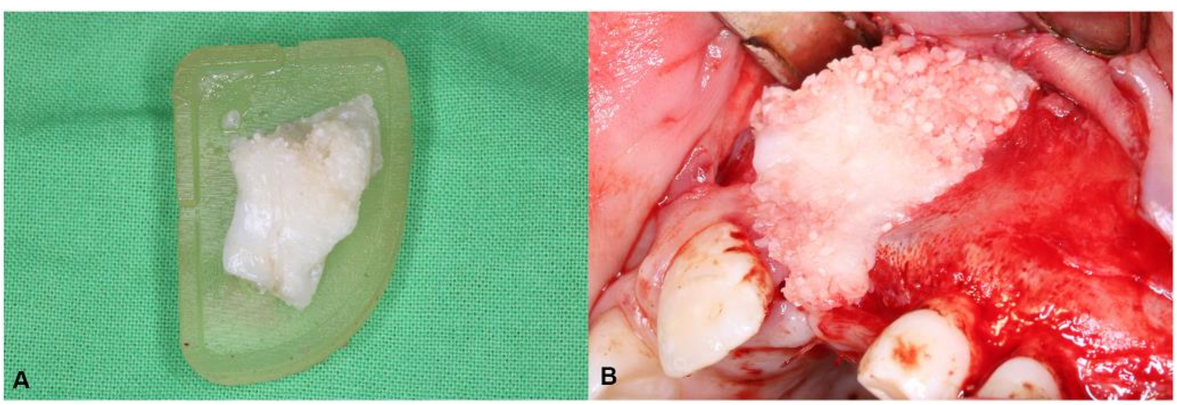

Fig. 6. Hard-tissue reconstruction of the UCLP: (A) the mixture of fibrin sealant and ATB particles was shaped by the 3D-printed grafting template to prepare the sticky ATB graft; (B) reconstruction of the UCLP with the sticky ATB graft.

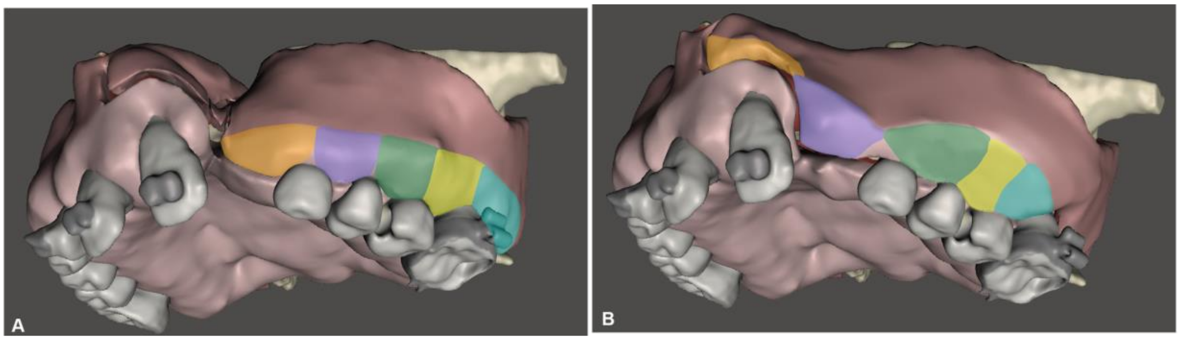

Fig. 7. Schematic demonstration of the mesial papilla shift: (A) preoperative state (the first interdental papilla is located distally to the alveolar cleft, marked in purple); (B) Postoperative state (the interdental papilla, marked in purple, was shifted mesially to cover the area of the alveolar cleft).

As a result, healthy continuous keratinized gingiva was shifted over the cleft to cover the grafted area and to ensure simultaneous reconstruction of the distorted vestibulum and lacking keratinized tissues. To stabilize the tension free split-thickness papilla curtain flap, suturing was carried out with resorbable monofilament sutures (Chirmax Monolac 5/0), utilizing circumdental double sling sutures and single interrupted mucosal sutures (Figure 8A).

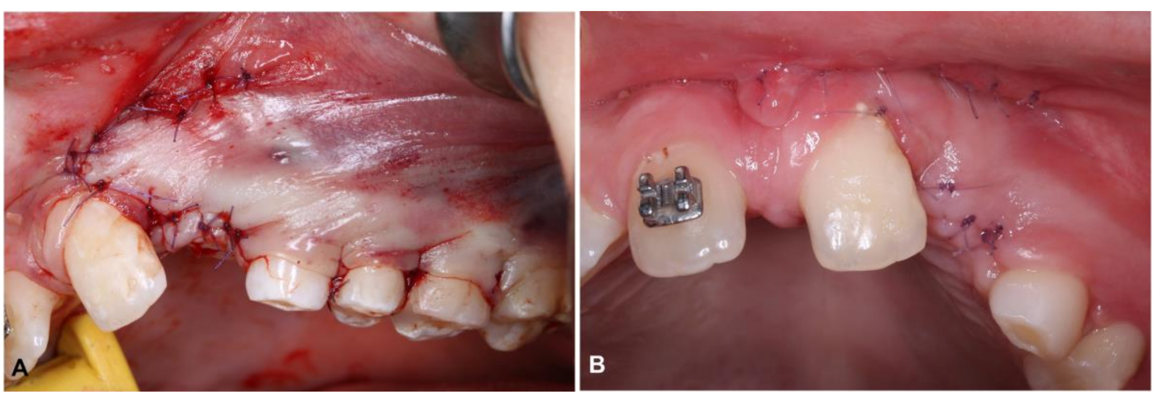

Fig. 8. Wound closure and postoperative control: (A) wound closure with primary intention; (B) 2-week postoperative control.

3.4.2. Harvesting the iliac crest bone graft

In cases where the number of extractable teeth was deemed insufficient for the preparation of ATB, cancellous bone from the iliac crest was used instead. In these cases, a two-team approach was chosen to reduce the operation time. The skin was draped and prepared, leaving the anterior superior iliac spine (ASIS) and the anterior iliac crest exposed. Before incision, local anaesthetic was administered (2% Lidocaine with 0.01% Epinephrine). The skin incision was approximately 2 cm long and respected the patient's relaxed skin tension lines. During the early adolescent age, when secondary alveolar bone grafting is performed, the iliac crest is usually still covered by a layer of cartilage, which was incised in a rectangular shape. This piece was elevated medially, hinged on the inner edge of the iliac crest. Curettes were used to harvest cancellous bone chips. These were inserted into the 3D-printed mold and were mixed with Tisseel fibrin glue, as described above, to give the graft better morphological stability. After the setting of the fibrin glue, the graft was removed from the mold, preserving the shape designed preoperatively, and was ready to be transferred to the cleft site. A collagen sponge was inserted into the donor area to promote hemostasis. The retracted cartilage was repositioned, and the wound was closed in layers. No drains were used.

3.5 Postoperative care

Postoperative systemic antibiotic therapy (875/125 mg amoxicillin/clavulanic acid twice a day, or 300 mg clindamycin four times a day in cases of penicillin allergy) was prescribed. Patients were advised to clean the area gently with an ultra-soft toothbrush and rinse with a 0.2% chlorhexidine-digluconate mouthwash for two weeks after surgery. Sutures usually resorbed 3–4 weeks after surgery (Figure 8B.). Clinical follow-up intervals included early inspection (7–10 days), intermediate controls (3 and 6 months), and extended follow-up (1 year and beyond, yearly controls up to 3–5 years). Clinical assessments included soft-tissue healing, eruption of adjacent teeth, and complications such as infection, dehiscence, or graft loss.

3.6 Radiological assessment and outcome measures

3.6.1 CBCT subtraction method

Following the segmentation of both preoperative and 3-month follow-up CBCT scans, spatial registration was carried out to validate volumetric and morphological hard-tissue changes. Registration of DICOM datasets was performed using the 'General Registration (Elastix)' module, which is an automatic intensity-based medical image registration algorithm (84). After spatial registration, the preoperative 3D model of the maxilla was subtracted from the postoperative 3D model (80, 81, 85). Subsequently, the hard-tissue difference between the two time points could be visualized and evaluated in 3D. The volumes of the newly formed hard-tissues were calculated and compared with the preoperatively planned volumes. The primary outcome of this investigation was the evaluation of volumetric hard-tissue gain by 3D subtraction analysis. The secondary outcomes of the study were:

- Validation of the efficacy of the surgical procedure and volumetric stability of the graft, by calculating the ratio between the actual volumetric hard-tissue gain and the planned hard-tissue volume
- Assessment of the similarity between the planned and actual hard-tissue morphologies by calculating the *Dice Similarity Coefficient* (DSC) and *Hausdorff Distance* (HD).

DSC is a spatial overlap index and a reproducibility validation metric. The value of DSC ranges from 0, indicating no spatial overlap between two sets of binary segmentation results, to 1, indicating complete overlap (69, 86). HD is the longest distance from a point in one of the two models to its closest point in the other model, meaning that the lower the HD value the more the two models overlap. To calculate DSC and HD the Slicer RT extension of 3D Slicer was used.

3.6.2 CBCT-based qualitative scoring (*Stasiak)*

In the second study assessment of the surgical outcomes was performed following the protocol described by *Stasiak et al.,* namely using a CBCT-based qualitative scoring system that relies on the presence and the relative dimensions of the bony bridge between the medial and lateral side of the alveolar cleft in four different vertical positions along the central incisor. This method was chosen instead of the volumetric subtraction analysis, because of the longer follow-up time. Years after the SABG surgery the initial anatomical circumstances in the vicinity of the alveolar cleft are prone to change. The reasons behind this are further growth of the maxilla, eruption of teeth into the graft and changes of tooth positions due to orthodontic movements. These changes render the use of the subtraction analysis unreliable.

The evaluation began by reorienting the images along the long axes of the central incisors on each respective side. The cementoenamel junction (CEJ) served as the reference point for determining four measurement levels: 3 mm, 5 mm, 7 mm, and 9 mm. The CEJ was defined as the most apical point of the enamel in the midsagittal section of the incisor. The next step involved examining the presence or absence of a bone bridge through the continuous analysis of the region. Next, the alveolar bone was ranked at the designated levels by identifying the narrowest points between the central incisors and canines, using a horizontal scale, as follows:

• 0 = No alveolar bone bridge;

• 1 = The thickness of the alveolar bone bridge < ½ of the labiolingual width of the central incisor's root;

• 2 = The thickness of the alveolar bone bridge ≥ ½ of the labiolingual width of the central incisor's root and less than the labiolingual width of the central incisor's root;

• 3 = The thickness of the alveolar bone bridge is at least the labiolingual width of the central incisor's root. (Figure 9.)

Score	CBCT cross-sectional image (cleft side is on the left side)	Description
0		No alveolar bone bridge.
1		Thickness of the alveolar bone bridge < ½ of the labiolingual width of central incisor's root.
2		Thickness of the alveolar bone bridge ≥ ½ of the labiolingual width of central incisor's root and less than the labiolingual width of central incisor's root.
3		Thickness of the alveolar bone bridge amounts to at least the labiolingual width of central incisor's root.

Fig. 9. Horizontal scale for bone fill assessment, as described by *Stasiak et al.* (87-89)

To assess the overall bone quality, the rank scores for each level were summed up for each side. The total score was interpreted using an interval scale, as follows:

• 0 = Failure;

• 1–4 = Poor outcome;

• 5–8 = Moderate outcome;

• 9–12 = Good outcome.

A score of 0 was assigned when no bone bridge was present. In cases where a narrow bone bridge existed but fell between or above the designated measurement levels (3, 5, 7, or 9 mm), a modified evaluation was applied. This involved conducting scoring at the actual bone bridge level and attributing the score to the nearest standard level. Additionally, for cases with severe root resorption of the central incisors, classification using the horizontal scale was still performed at the 9 mm level. However, the assessment was adjusted by comparing the root width, measured 0.5 mm below the apex, to provide a more accurate evaluation.

3.7 Statistical analysis

For *Molnár et al.*'s pilot study the primary focus was to determine the amount of hard-tissue change rather than determining absolute baseline and follow-up values. Therefore, only descriptive statistics were used. Data were expressed as mean value ± standard deviation.

For *Würsching et al.*'s cohort study the *Kappa* correlation coefficient with linear weights was used for the intra-rater and inter-rater reproducibility measurements of the *Stasiak* score system. To test the normality of the acquired data, the *Shapiro–Wilk* test was used. The non-parametric *Wilcoxon* signed-rank test was used for a comparison of the cleft-side and non-cleft-side bone volume. The non-parametric *Mann–Whitney U* test was used to compare the *Stasiak* score and the patient's age at the time of surgery of the iliac crest group and the ATB group. S*tudent's* t-test was used to compare the initial defect volume of the two groups. As a prerequisite to the *Student's* t-test the *Shapiro–Wilk* test was used to confirm that the volume data were normally distributed in both groups, and *Levene's* test was used to show the homogeneity of the variances. The correlation between the bone defect volume and the outcome score was analyzed separately for the iliac crest and ATB groups, using *Spearman's* rank correlation. Statistical significance was set at $p < 0.05$. The data were collected in Microsoft Excel (Microsoft, Washington, CA, USA). Statistical analyses were performed using SPSS version 30.0. (IBM Corporation, Redmond, WA, USA).

4. Results

4.1 Study cohorts

Pilot study: Seven consecutive SABG cases reconstructed with particulate ATB graft using a split-thickness papilla curtain flap were recruited for the pilot study. All cases exhibited UCLP requiring secondary alveolar reconstruction during mixed dentition. Five patients were male, two were female. The patients were aged 9–11 years, with a mean age of 10.43 ± 0.79 years. Two defects were located on the right side and five on the left. In total, 35 deciduous teeth and two supernumerary teeth were extracted and utilized for preparation of the ATB graft. In every case, the patient's own teeth provided enough material for proper reconstruction of the alveolar defect, using an average of 4.75 ± 2.49 teeth per patient. Patient demographic data are shown in Table 1. Orthodontic preparation was completed prior to surgery according to the centre's protocol. No patients were lost to follow-up within the early assessment window.

Table 1. Patient demographic and surgical data.

Patient	Age	Sex	No. of extracted teeth	Surgical area location
1	11	M	4	Right side
2	10	M	5	Right side
3	11	M	10	Left side
4	11	F	4	Left side
5	10	M	4	Left side
6	9	M	5	Left side
7	11	F	5	Left side
Mean ± st. deviation	10.43 ± 0.79	n/a	5.29 ± 2.14	n/a

Retrospective cohort study: During the examination period, a total of 42 ABG surgeries were performed in our department. In 12 cases, the defect was bilateral; in 30 cases, the defect was unilateral. In 14 cases, an ATB graft was used; in 25 cases, the donor site was the iliac crest; in three cases, the donor site was the chin. Long-term CBCT data was available for 39 patients; three patients were lost to follow-up. Twenty-one participants exhibiting UCLP were found to be eligible and were enrolled in the current study (Figure 10.). Thirteen patients were male, eight were female. Their age at the time of surgery was between 8 and 14 years; the mean age was 10.4 ± 1.7 years. Sixteen defects were located on the left side and five on the right side. In eleven cases, the donor site for the graft was the iliac crest. In the other 10 cases, a total of 53 deciduous teeth and 4 supernumerary teeth were extracted and utilized for the preparation of the ATB graft. In these cases, the patient's own teeth provided enough material for the proper reconstruction of the alveolar defect, using an average of 5.3 ± 2.26 teeth per patient. The mean follow-up time was 30 ± 13.1 months.

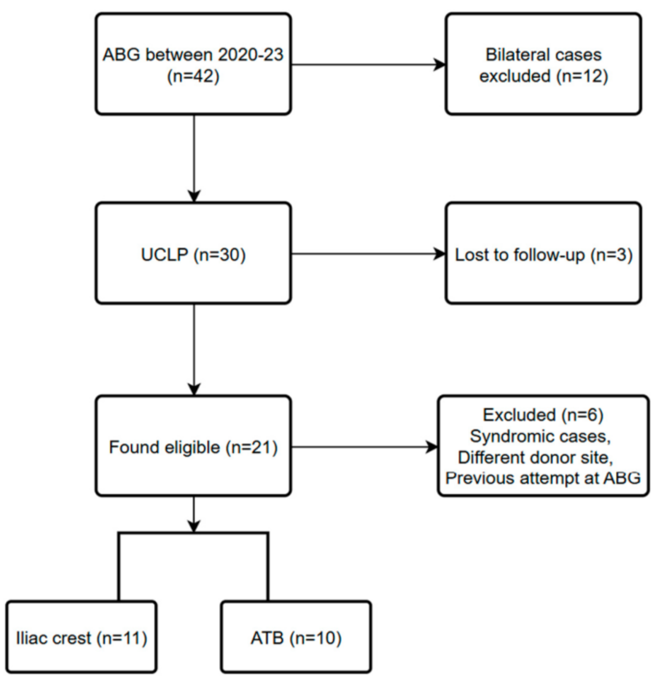

Fig. 10. STROBE flowchart.

4.2 Clinical and radiological outcomes after 3 months follow-up (pilot study)

4.2.1 Soft-tissue healing and local events

Clinical follow-up focused on soft-tissue integrity over the graft, control of oedema, oral hygiene, and the presence of minor dehiscence, or any adverse events. All patients were able to leave the hospital on the first postoperative day without any major complaints and could return to normal daily activity shortly after surgery. Initial wound healing was uneventful in all the seven cases. No unexpected adverse patterns were described within the early window. The quality of keratinized tissues was favourable, fully eliminating any muscle pull or vestibular distortions over the cleft. During the follow-up period, eruption of the cleft-side canine was observed in one patient.

4.2.2 Early volumetric hard-tissue gain

Planned graft volumes averaged 1.14 $cm^3 \pm 0.36$ cm^3, whereas hard-tissue gain, as measured on the 3-months follow-up CBCT scans, averaged 0.65 $cm^3 \pm 0.26$ cm^3 (Figure 11.). The primary outcome data are summarized in Table 2.

4.2.3 Morphometric accuracy and shape agreement

The ratio between actual and planned graft volume ranged between 34.17% and 108.21%, resulting in an average ratio of 59.92% ± 24.35%. (Table 3.) Agreement between planned and realized 3D contours yielded a mean **DSC** of **0.43 ± 0.20** and a **HD** of **1.83 ± 0.77 mm**, reflecting only partial overlap of the reconstructed alveolar volume with the intended design at 3 months follow-up (Figure 12.) Surface deviation maps highlighted systematic positive deviations (overfill bulges) on the buccal side, and negative deviations (underfill) at the nasal floor and the palatal aspect of the defect.

Table 2. Planned and achieved volumetric hard-tissue gain.

Patient	Planned hard tissue gain (cm^3)	Hard tissue gain at 3-month follow-up (cm^3)
1	0.82	0.48
2	1.65	1.15
3	1.03	0.35
4	0.61	0.66
5	1.44	0.7
6	1.26	0.75
7	1.17	0.49
Mean ± st. deviation	1.14 ± 0.36	0.65 ± 0.26

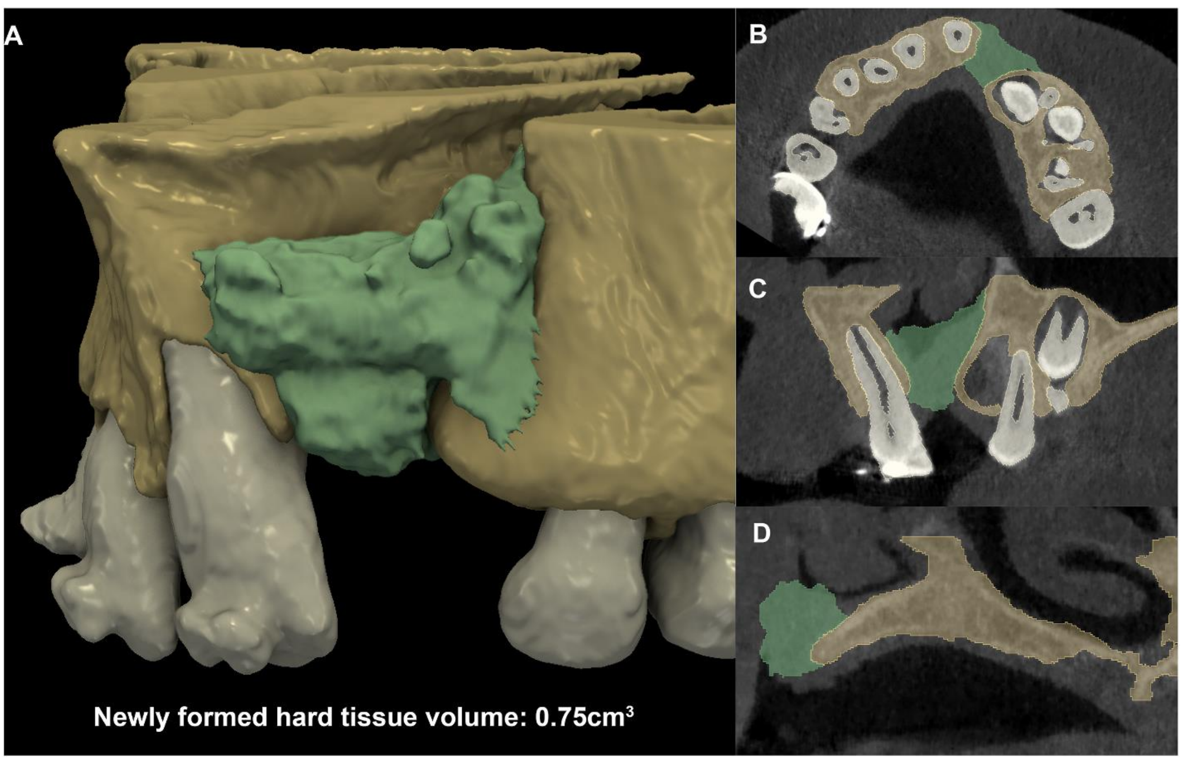

Fig. 11. Volumetric evaluation of the newly formed hard-tissues: (A) 3D view; (B) axial view; (C) coronal view; (D) sagittal view.

Table 3. Volumetric and morphological stability of the graft.

Patient	Achieved volume/ planned volume ratio (%)	Dice similarity coefficient (DSC)	Hausdorff distance (HD) average (mm)
1	58.36	0.65	0.97
2	69.27	0.57	1.56
3	34.17	0.25	2.31
4	108.21	0.41	1.91
5	48.40	0.14	3.24
6	59.55	0.65	1.10
7	41.49	0.36	1.70
Mean ± st. deviation	59.92 ± 24.35	0.43 ± 0.2	1.83 ± 0.77

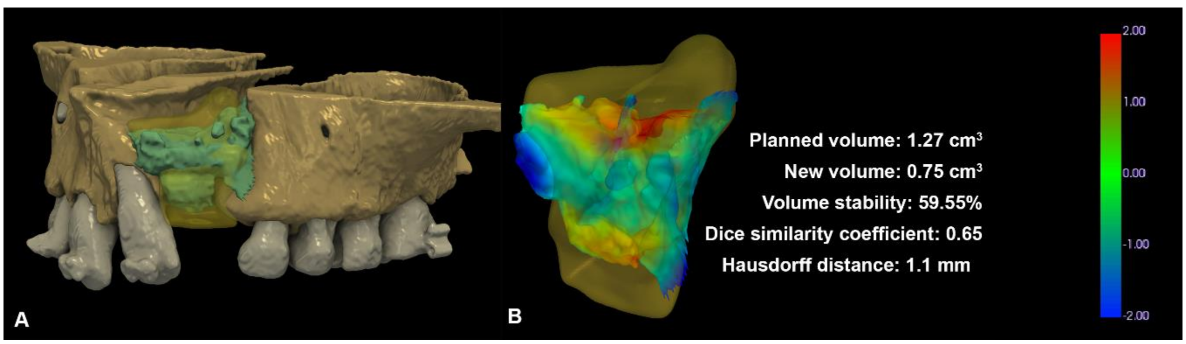

Fig. 12. Relationship between planned outcome and actual outcome:(A) 3D virtual model of planned and actual outcome (planned in transparent yellow, actual in green); (B) colormap model visualizing the morphological differences between the newly formed hard-tissues and the morphology of the planned outcome.

4.3. Long-term outcomes based on CBCT evaluation (cohort study)

4.3.1. Descriptive statistics

The mean volume of the initial defect in the iliac crest group was 0.927 cm^3 (SD = 0.316 cm^3) and, in the ATB group, it was 1.176 cm^3 (SD = 0.449 cm^3). The mean age at the time of surgery in the iliac crest group was 10.9 years (SD = 2.1 years) and, in the ATB group, it was 9.9 years (SD = 1.2 years). There was no obvious difference between the occurrence of early (dehiscence) or late (fistula) complications. In one patient, a severe periodontal defect also developed on the distal surface of tooth 21, which led to extraction. In the ATB group, canine eruption did not happen in two cases during the observed period, whereas no such problems were observed in the other group (Tables 4. And 5.).

Table 4. Descriptive statistics of the iliac crest group.

Iliac crest	**Vdefect (cm3)**	**Dehiscence**	**Fistula**	**Canine**	**Stasiak score**	**Age at surgery (years)**	**Follow-up (months)**
Patient 1.	1.085	no	no	erupted	11	9	58
Patient 2.	1.492	yes	fistula	erupted	9	14	24
Patient 3.	0.973	no	no	erupted	0	14	41
Patient 4.	0.578	no	no	erupted	9	12	36
Patient 5.	0.504	yes	no	erupted	11	13	14
Patient 6.	0.916	no	no	erupted	0	10	49
Patient 7.	0.973	no	no	erupted	9	8	18
Patient 8.	0.788	no	fistula	erupted	6	10	24
Patient 9.	0.512	no	no	erupted	8	9	52
Patient 10.	1.295	no	no	erupted	0	10	12
Patient 11.	1.079	yes	no	erupted	1	11	56

Table 5. Descriptive statistics of the ATB group.

ATB	Vdefect (cm3)	Dehiscence	Fistula	Canine	Stasiak score	Age at surgery (years)	Follow-up (months)
Patient 12.	1.994	no	no	not erupted	0	10	28
Patient 13.	0.819	no	no	erupted	9	9	25
Patient 14.	1.653	yes	no	erupted	10	8	20
Patient 15.	1.03	no	no	erupted	7	11	20
Patient 16.	1.226	yes	21 def.	erupted	2	11	26
Patient 17.	0.609	no	no	erupted	11	11	28
Patient 18.	1.438	no	no	not erupted	3	8	29
Patient 19.	1.256	no	no	erupted	11	10	25
Patient 20.	1.169	no	fistula	erupted	2	11	25
Patient 21.	0.565	no	no	erupted	9	10	23

4.3.2. Radiographical assessment

The measurements on both the cleft and non-cleft sides were performed three times by two observers in all the patients, and during each instance, all the 168 sites were measured. The first observer performed the measurements twice during a 4-week period, and the second observer performed the measurements only once. Finally, a consensus reading was performed by both observers.

On the cleft side of the iliac crest group, fifteen sites were classified as 0, four sites as 1, ten sites as 2, and thirteen sites as 3. On the cleft side of the ATB group, twelve sites were classified as 0, five sites as 1, ten sites as 2, and thirteen sites as 3. On the control side, no 0 or 1 scores were obtained. There were six sites classified as 2 and seventy-eight sites as 3.

The surgical outcome showed a high level of variability. The mean total score on the cleft side in the **iliac crest** group was **5.8 (SD: ± 4.6)**; in the **ATB** group, the mean total score on the cleft side was **6.4 (SD: ± 4.2)**. (Figure 13.). On the non-cleft side, the mean total score was 11.7 (SD: ± 0.5). In the **iliac crest** group, the results showed 27% failure, 9% poor, **18% moderate**, and **46% good** results of the surgical procedure. In the **ATB** group, the results were 10% failure, 30% poor, **10% moderate**, and **50% good**. The alveolar bone was classified as good in all the patients on the non-cleft side.

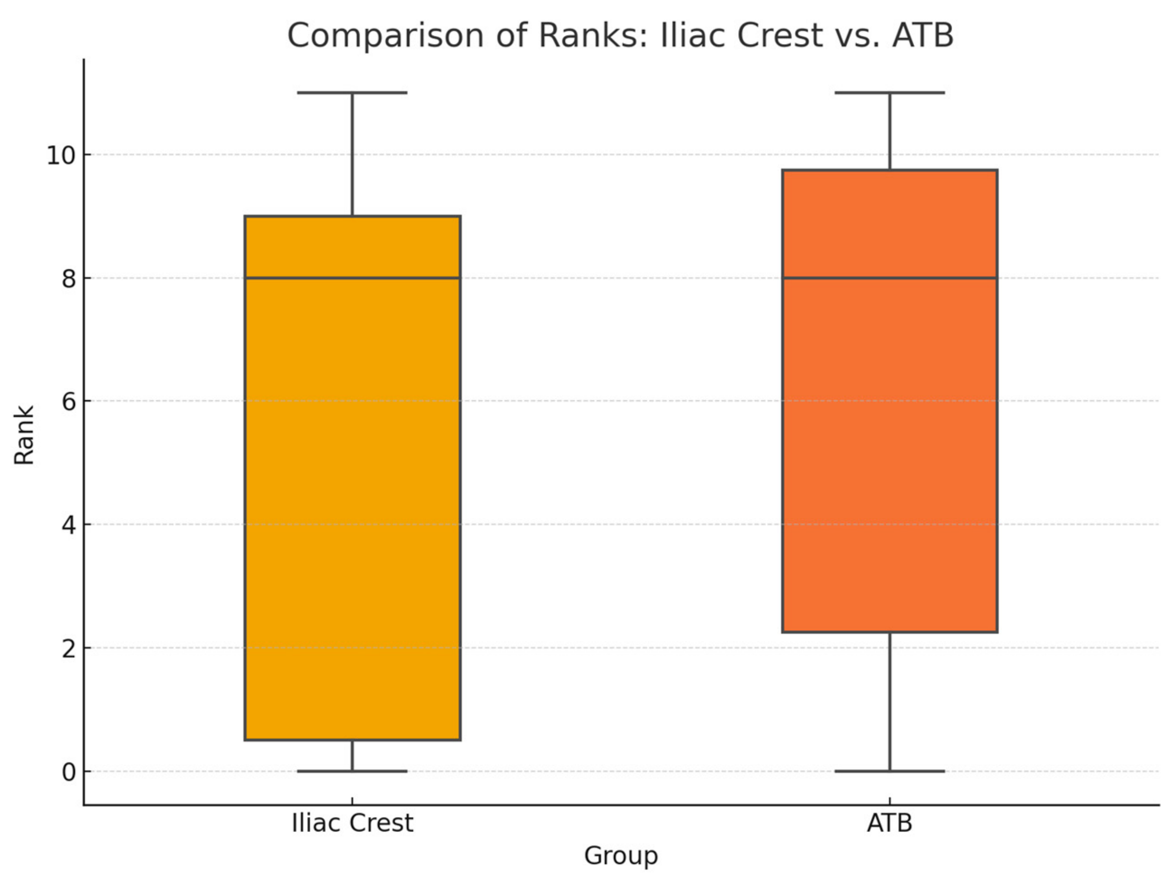

Figure 13. Comparison of the mean of the rank scores on the cleft side

4.3.3 Statistical analysis

Regarding all the statistical measurements, a 95% confidence interval was adopted. The *Wilcoxon* signed-rank test showed statistically significant (ATB: $p = 0.002$, iliac crest: $p = 0.005$) differences between the cleft- and non-cleft-side measurements, which was independent of the type of graft being used. The linearly weighted *Kappa* coefficient result was 0.85 for intra-rater and 0.82 for inter-rater reproducibility. These results showed the excellent reproducibility of the method published by *Stasiak et al*.

The *Mann–Whitney U* test showed **no significant** differences between either the ***Stasiak* scores** ($U = 47.5$, $p = 0.617$) or the **age** at the time of surgery ($U = 67.5$, $p = 0.388$) of the two groups. A comparison of the defect volumes between the two groups was performed using an independent sample *Student*'s t-test. Prior to the analysis, the assumptions for parametric testing were evaluated: *Shapiro–Wilk* tests confirmed that the volume data were normally distributed in both the iliac crest ($p = 0.61$) and ATB ($p = 0.86$) groups, and *Levene's* indicated the homogeneity of the variances ($p = 0.36$). The *Student's* t-test revealed **no statistically significant** difference in the mean **defect volume** between the iliac crest group and the ATB group ($t(df) = −1.48$, $p = 0.155$).

The correlation between the initial bone defect volume and the outcome *Stasiak* score was analysed separately for the iliac crest and ATB groups, using *Spearman's* rank correlation. In the **iliac crest** group, a **weak negative** correlation was observed ($\rho = −0.19$, $p = 0.58$), while the **ATB** group showed a **moderate negative** correlation ($\rho = −0.36$, $p = 0.31$). However, neither correlation reached statistical significance ($p > 0.05$). Scatter plots with trendlines are used to illustrate the inverse relationship between the defect volume and outcome score in both groups. (Figure 14).

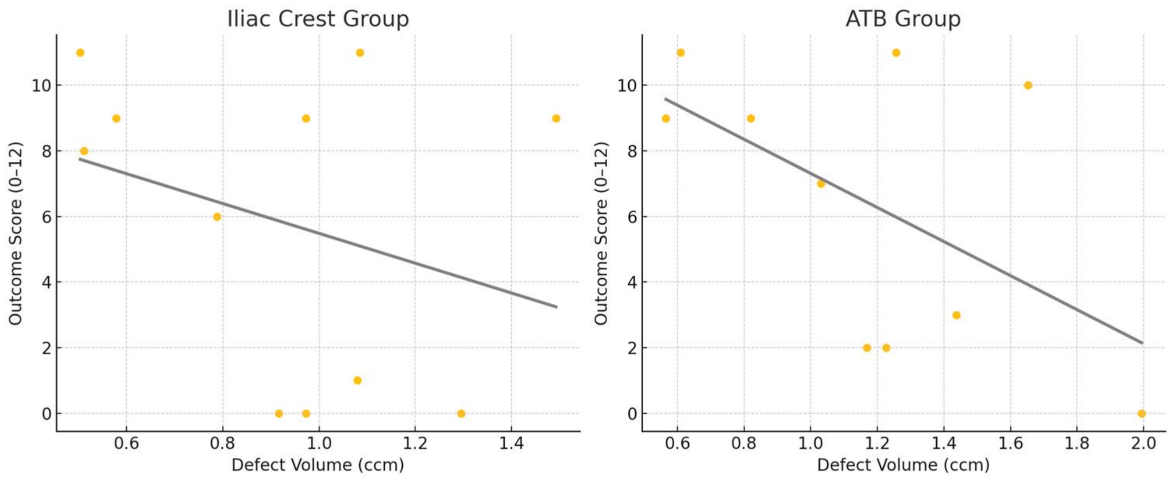

Figure 14. Correlation between initial defect size and outcome score.

5. Discussion

This thesis integrates two complementary datasets: an early pilot series employing CBCT subtraction analysis after autologous tooth bone-based SABG, and a comparative cohort assessing long-term morphology with a CBCT rank scale in ATB versus iliac crest bone graft.

In the first study the efficacy of a 3D-planned ATB graft in conjunction with a split-thickness papilla curtain flap was evaluated for secondary alveolar bone grafting of patients exhibiting UCLP. Autologous tooth bone grafts can effectively restore damaged alveolar bone using autologous tissue and offer solutions to several challenges associated with other grafting materials, such as insufficient osteoconduction, a lack of osteoinduction, sterilization concerns, and the risk of disease transmission. This type of graft is commonly used in preprosthetic and periodontal regenerative surgery.

Although there have been previous case reports describing the use of ATB during SABG (60, 90, 91) these were single case reports. To the best of our knowledge, this was the first study to report clinical and 3D-radiographic data demonstrating favourable defect fill in alveolar clefts, utilizing ATB in a series of patients. Although graft resorption was observed, the amount lost was in line with what can be expected from the use of iliac crest, according to the literature (92).The average volume of the remaining graft at the 3-month follow-up was well above 50% when compared with the planned graft volume. In one case, the actual graft volume even exceeded the planned volume by 8%, thereby suggesting that ATB graft could have an advantageous effect on bone regeneration. The relatively low average DSC value (0.43 ± 0.2) and the high HD (1.83 mm ± 0.77 mm) indicated a low correlation between the preoperatively planned graft shape and the actual graft shape at 3-months follow-up. This phenomenon could be observed regardless of graft volume stability, and even cases with high graft stability showed a moderate morphological similarity to the planned graft shape. According to the 3D reconstructed images, this was due to buccal displacement of the graft during healing. In most cases, sufficient palatal fill could not be achieved, and the ATB graft did not reach the nasal base. This was most probably due to the pressure applied on the graft by the nasal and palatal flaps. This suggests a need for further modifications to the flap design on the palatal aspect, or perhaps use of a rigid barrier on the palatal/nasal aspect in conjunction with the graft. A similar approach was adopted by *Ishii et al.* (93) who positioned a rigid cortex bone plate on the palatal aspect to compensate for the pressure applied by the nasal/palatal flaps, and to maintain a safe, secluded space. Limitations of the current study included the relatively low sample size, due to the pilot nature of the examination, and the lack of histological information on graft integration. Although histological evaluations have been performed previously (94) , only tissue integration of the ATB particles could be assessed in this current study. With the aid of 3D technology, quantitative radiographic evaluation was possible; however, the inability to perform qualitative, histological evaluation was a significant limitation.

The Bonmaker® device is suitable for preparing extracted teeth and obtaining ATB particulate grafting material. As confirmed by previous radiographic and histological studies (94, 95) ATB powder may act as a resorbable scaffold and a space-maintaining device to facilitate the healing of alveolar cleft defects. After the preparation of the ATB powder and its mixture with fibrin sealant, a sticky ATB graft was acquired with excellent intraoperative handling properties. The time required for the harvesting of a hip graft is comparable to ATB preparation. Nevertheless, the ATB protocol has two benefits: (i) approximately half of the duration - 20 min - is fully automatic, executed by the Bonmaker® device, which does not require user interaction, thus allowing medical personnel to undertake other activities during the surgery; and (ii) ATB preparation is straightforward — it does not require a highly qualified physician, with nurses fully capable of handling the graft preparation. The estimated costs for the presented surgical approach were as follows: 3D printing 5 EUR, Bonreagent 35 EUR, fibrin glue 100 EUR. The use of these auxiliary techniques increased the costs for the operation itself, although these expenses were not considered to be exceptionally high. On the other hand, avoidance of an extraoral donor site may reduce hospitalization time, as all patients in our study were discharged from hospital on the first postoperative day. This was in contrast with the study by *Brudnicki et al.* (30), who stated the mean length of hospitalization postoperatively was 2.9 days and varied from 1 to 8 days. Most patients were discharged on the second (66 cases) or third day (102 cases) following the procedure. In higher-income countries, where the cost of hospital stay is more expensive, the use of these auxiliary techniques may lower the overall costs of the treatment, but exact calculations to support this statement were beyond the scope of our study. To ensure the compaction and tight fit of the grafting material inside the cleft, 3D preoperative planning was successfully utilized to manufacture a 3D-printed grafting template to shape the sticky ATB graft before insertion. Closure of the oronasal fistula was achieved in all cases.

Modifications of the original four-flap design, to improve certain aspects of the technique - for example, minimizing injury to the dental papillae and periodontium of the involved dentition, or increasing the amount of attached gingiva surrounding the canine - have been described previously (*L´opez-Cedrún et al.,*(96)). Most of these modifications continue to use a full thickness mucoperiosteal flap, and the suture line remains directly above the graft. The novel split-thickness papilla curtain flap aims to ensure the following: (a) tension-free wound closure without compromising flap circulation, via vertical or horizontal releasing incisions; (b) that a sufficient amount of keratinized gingiva is rotated mesially to surround the tooth on the mesial side of the cleft (usually the lateral or mesial incisor). It also has the benefit of shifting the suture line from directly above the grafted area to a more mesial position, where the sutures will rest on the well vascularized periosteal surface of the premaxilla. The nasal and palatal mucosa on the mesial side of the cleft is still elevated in full thickness, as previously described and now widely applied. The presented flap design resulted in primary-intention wound healing in 100% of the cases, with minimal pain and ooedema, as well as excellent, inflammation-free, early wound healing. These pilot results indicated the applicability of the split-thickness papilla curtain flap, and in our experience, this modification showed superior results compared with the traditional mucoperiosteal flap approach. Nevertheless, this needs to be further investigated in future comparative clinical studies. The application of ATB as an autogenous grafting material provides a cost- and time-effective alternative for patients. Its application with the split-thickness papilla curtain flap proved to be an effective surgical approach with a low duration, while providing favourable hard and soft-tissue conditions. This report introduces the early results of a pilot study regarding the use of ATB in alveolar cleft reconstruction, combined with a split-thickness papilla curtain flap. Although the results were favourable, the study had its limitations - namely the short follow-up period and relatively small sample size.

In the second study, the long-term outcomes of using ATB for alveolar bone grafting in patients with a unilateral cleft lip and palate were compared to the results achieved by using the iliac crest as a donor site. There was no randomization during allocation of patients to the study and the control groups, ATB was the preferred method in the cases where the number of deciduous teeth was adequate. For the rest of the patients, the donor site was the iliac crest, in which a two-team approach was adopted to optimize the surgical time. To achieve the proper amount of graft material according to the preoperative planning, an average of 5.3 ± 2.26 teeth per patient were used. As the early loss of deciduous teeth can lead to complications during eruption of the patients' permanent teeth, our aim was to avoid unnecessary and early extractions. This means, however, that the roots of these teeth were usually partially or completely resorbed, leading to less graft volume per extracted tooth. This also means that the amount of graft that can be prepared using this method is usually only sufficient for small to medium sized unilateral clefts, so no bilateral cases were treated this way, and they were excluded from this study.

Alveolar bone grafting is considered successful when it achieves sufficient bone filling in the alveolar cleft. The eruption of adjacent teeth, particularly the canine, through the grafted bone is also a critical indicator of treatment success (97). Additionally, the lack of oronasal fistulae, healthy periodontal tissues around teeth adjacent to the graft site, and the maintenance of alveolar bone stability and continuity over time are also essential criteria. A recent meta-analysis by *Jahanbin et al.* showed that the total percentage of bone filling after 1 year, according to CBCT, was about 63.38% (70). Due to the limited sample size in this study, it is not possible to conclude whether there is a significant difference between the rate of early or late complications between the two groups. However, the fact that canine eruption in the iliac crest group happened in every case and, in the ATB group, there were two cases out of ten where it did not, needs to be addressed. This must be followed on a longer-term basis and regarding a larger sample size, as the failure of the canines to spontaneously erupt leads to further surgical interventions, which is a factor that must be considered when choosing ATB as a potential graft material.

CBCT is increasingly used to evaluate the results of ABG, due to its ability to provide detailed 3D imaging with lower radiation than conventional CT, replacing conventional methods based on 2D X-rays. While several CBCT-based methods exist, none have achieved universal recognition (63, 98, 99). Volumetric assessments quantify bone fill, but lack spatial specificity, limiting their value regarding clinical decision making. Grading scales using 2D measurements at vertical levels, such as those by *Soumalainen and Liu* (76, 100), offer partial localization, but are affected by the dental eruption status and have limited generalizability. Assessment approaches are generally classified as continuous (e.g., bone volume or resorption rates) or categorical (e.g., bone height/width). Continuous methods, while quantitative, lack standardized clinical thresholds and fail to identify critical bone deficits impacting orthodontic outcomes. *Stasiak et al.* introduced a more advanced, clinically applicable method that divides the cleft into defined zones, enabling the precise localization of bone presence and resorption (87-89). It uniquely considers the impact of bone loss on adjacent teeth and considers root resorption. This spatially detailed approach supports more informed decisions about regrafting and orthodontic planning, representing a major improvement to CBCT-based ABG evaluations. This method was implemented in the current study, and proved to be reliable and reproducible, with excellent rates of intra- and inter-rater reliability. The results show that there are no significant differences between the outcomes of the two groups based on the *Stasiak* scale and, in both groups, at least 60% of the cases fell into the moderate or good category, meaning no regrafting was deemed necessary. In terms of the other cases, approximately 40% of the cases where the outcome fell into the poor or the failure category, regrafting or prosthetic rehabilitation needed to be considered on an individual basis.

6. Conclusions

Synthesizing the early pilot data after 3 months follow-up and the evidence supported by the longer-term cohort study, autogenous tooth bone (ATB) emerges as a feasible and promising alternative to iliac crest cancellous bone for secondary alveolar bone grafting of patients with cleft lip and palate, particularly in unilateral defects during the mixed dentition.

Short-term integration dynamics from the pilot series show that at 3 months, mean hard-tissue gain after ATB grafting was approximately 60% of the planned volume, indicating substantial, early mineralized fill within the defect. Notably one case slightly exceeded planned volume, consistent with active bone regeneration and favourable scaffold behaviour. Soft-tissue healing was uneventful in all seven cases, with primary closure and improved keratinized tissue coverage—outcomes attributable in part to the split-thickness papilla curtain flap, which relocates healthy gingiva over the graft while moving the suture line off the grafted zone.

However, the morphological assessment of the pilot data showed that despite satisfactory volumetric gains, the "shape fidelity" of the healed graft to the preoperative plan was modest, with a tendency toward buccal displacement and insufficient palatal and nasal fill which most likely could be attributed to pressure by the palatal and nasal flaps. This suggests that technical modifications, e.g., the use of rigid palatal/nasal barrier membranes or cortical plates may further optimize 3D architecture where it matters for orthodontic eruption paths and nasal base support.

The cohort study documented no statistically significant difference in cleft-side bone quantity between ATB and iliac crest groups, while differences between cleft and non-cleft sides persisted, with both groups remaining inferior to the contralateral healthy side independently of graft type. The evaluation method demonstrated excellent intra- and inter-rater reliability, strengthening the validity of these comparisons. Clinically, at least 60% of cases in both groups achieved moderate-to-good *Stasiak* categories - thresholds generally consistent with avoiding regrafting and supporting continued orthodontic care - whereas the remainder required individualized consideration for regrafting or prosthetic planning. Together, these findings position ATB as a clinically acceptable option for long-term alveolar reconstruction outcomes, not inferior to iliac crest, without exposing the child to an extraoral donor site.

There are, however, certain limitations to both studies. The long-term cohort remains modest (n = 21) with nonrandomized allocation between ATB and iliac crest. The small number of patients renders the statistical assessment of early and late complications (e.g.: lack of canine eruption) unreliable. The pilot series is also small (n = 7), descriptive, and lacks histological evaluation; while prior work supports ATB's osteoinductive/osteoconductive behaviour, tissue-level integration within cleft sites over time remains to be investigated more rigorously. The pilot's early shape drift also proves that "volume met" doesn't necessarily mean optimal architecture. Moreover, the cohort's primary endpoint only used a categorical scale, lacking a continuous, volume-based assessment of long-term integration of the graft. These constraints underline the need for larger, controlled, and methodologically harmonized studies.

As a conclusion, given comparable long-term radiographic outcomes to iliac crest in this cohort and favourable early healing profiles, ATB may be considered as a first-line option when sufficient tooth-derived graft volume is obtainable, and the surgical team is trained in the workflow.

7. Summary

The two studies this thesis is based upon examine autogenous tooth bone as a graft for secondary alveolar bone grafting in patients with unilateral cleft lip and palate.

The first pilot study details the operative concept on a small cohort of seven patients: extracted deciduous and supernumerary teeth were processed into particulate ATB graft. Mixing it with fibrin sealant inside a 3D-printed mold based on virtual surgical planning yielded a “sticky” block that improved handling and fit. Soft-tissue closure employed the split-thickness papilla curtain flap, which shifts keratinized gingiva over the graft and moves the suture line away from the grafted zone. Patients were discharged on the first postoperative day, and early healing was uneventful with favourable soft-tissue conditions. Three-month radiographic outcomes based on CBCT subtraction analysis showed that planned graft volume averaged 1.14 ± 0.36 cm^3 and measured hard-tissue gain averaged 0.65 ± 0.26 cm^3 (≈60% realization). Morphological similarity between planned and achieved grafts was moderate (mean DSC: 0.43 ± 0.20; mean HD: 1.83 ± 0.77 mm), with a consistent trend toward buccal displacement and insufficient palatal/nasal fill.

The second, retrospective cohort study by *Würsching et al.*, included 21 patients exhibiting UCLP treated with either ICBG (n=11) or ATB (n=10). Outcomes were assessed on long-term CBCT (mean follow-up was 30 ± 13 months) using the grading system published by *Stasiak et al.* Key findings were, that bone on the cleft side remained significantly less than the contralateral non-cleft side in both groups (ATB $p=0.002$; iliac crest $p=0.005$), yet there was no significant difference between the two groups on the cleft side (*Mann–Whitney U*=47.5, $p=0.617$). At least 60% of cases in each group achieved moderate or good outcomes on *Stasiak* grading. On average, approximately 5 teeth provided sufficient ATB volume for unilateral defects. To sum up, the data support that ATB is a feasible alternative to iliac crest for unilateral alveolar cleft reconstruction, delivering short- and long-term CBCT outcomes comparable to iliac crest, while avoiding donor-site morbidity, although neither material fully restores the cleft to the contralateral healthy side.

8. New statements of the thesis

1. A digitally planned ATB graft using deciduous and supernumerary teeth, combined with fibrin sealant produced substantial early hard-tissue fill of the alveolar cleft in patients with UCLP. Volumetric stability however didn't necessarily mean reliability in graft morphology
2. The split-thickness papilla curtain flap is a practical modification to the *Nordin-Abyholm* 4-flap technique, that relocates keratinized mucosa over the graft and achieves uneventful early healing.
3. Autogenous tooth bone yields long-term radiographic and clinical outcomes comparable to iliac crest for unilateral alveolar cleft grafting.
4. Initial defect size showed no significant correlation with categorical outcome regardless of the type of graft.
5. ATB enables unilateral alveolar cleft reconstruction without extraoral donor morbidity and can be proposed as a patient-friendly first-line option in select cases.

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10. Bibliography of the candidate's publications

Publications related to the thesis:

- Würsching, T., Mészáros, B., Sólyom, E., Molnár, B., Bogdán, S., Németh, Z., & Nagy, K. (2025). Long-Term Results of Autologous Tooth Bone Grafting in Alveolar Cleft Reconstruction: A Retrospective Cohort Study. *Biomedicines*, *13*(7), 1735. https://doi.org/10.3390/biomedicines13071735
  IF: 3.9, Q1

- Molnár, B., Würsching, T.*, Sólyom, E., Pálvölgyi, L., Radóczy-Drajkó, Z., Palkovics, D., & Nagy, K. (2024). Alveolar cleft reconstruction utilizing a particulate autogenous tooth graft and a novel split-thickness papilla curtain flap - A retrospective study. *Journal of cranio-maxillo-facial surgery*, *52*(1), 77–84. https://doi.org/10.1016/j.jcms.2023.10.006
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- Würsching, T., Kesztyűs, A., Pottel, L., Swennen, G., & Nagy, K. (2025). Comparison of two methods for segmentation of the nasoalveolar defect and design of a three-dimensional surgical template in patients with cleft lip and palate: a retrospective study. *International journal of oral and maxillofacial surgery*, *54*(10), 897–903. https://doi.org/10.1016/j.ijom.2025.05.006
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