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Micro-structured calcium phosphate ceramic for donor site repair after harvesting chin bone for grafting alveolar clefts in children

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A B S T R A C T

Objectives: The purpose of this study was to evaluate the use of synthetic bone graft material as a filling material at the mandibular symphysis donor site of autologous bone in children.
Materials and methods: A blinded patient group comprised 20 patients with unilateral (UCLP) or bilateral (BCLP) cleft of lip and palate, all with an indication for alveolar cleft repair. The study took the form of a prospective randomized clinical trial. We used lateral cephalograms for the measurement of the symphyseal donor area defect both peroperatively and at 12 months postoperatively. The data obtained were digitalized and the treatment outcome expressed in numbers. Comparisons with a previous study were made. Histology of biopsies and CT scans were used for visualising bone formation.
Results: This study demonstrates that the micro-structured, resorbable calcium phosphate ceramic provides good regeneration properties for the repair of a critical size bony defect in children. One year postoperatively, the measurements taken from lateral cephalograms show that there is scarcely any visible residual defect. Histological investigations of the bone biopsies show solid, induced bone formation and almost complete resorption of the micro-structured calcium phosphate.
Conclusions: The findings of this study (novel in children) indicate that micro-structured resorbable calcium phosphate is an excellent alternative to autologous bone. The digital findings showed a restored donor site defect significantly indicating the efficacy (i.e. osteoconductivity and resorbability) of this bone substitute. The biopsy histology demonstrated the overall presence of newly formed vital bone and the resorption of the bone substitute. Its use for grafting the alveolar cleft is currently researched and it may become the new standard.
Clinical relevance: As co-morbidity and prolonged operation time at the donor operation site are inherent to the alveolar cleft repair procedure, the use of the described bone substitute is winning progress.

1. Introduction

The frequency of occurrence of various forms of congenital facial clefts varies throughout the world and between different ethnic groups, local areas and time span (Gundlach and Maus, 2006). In Europe, the occurrence of clefts of lip, alveolus and palate (CLP) among Caucasians has been reported to be somewhere between 0.69 and 2.35 per 1000 births (Andrä et al., 1988). One of the major interventions in the treatment of patients with unilateral (UCLP) or bilateral (BCLP) cleft of lip, alveolus and palate is closure of the alveolar cleft. The importance of this procedure lies not only in the closure of the alveolar cleft in order to allow the eruption of the surrounding teeth and in enabling orthodontic transfer in the grafted bone, but in addition the soft-tissue profile of lip and ala nasi is also improved by the bone correction (Park et al., 2013) and the dental treatment which follows orthodontic treatment. This is of great social importance in every culture in the world. Transplantation of autologous bone is still the gold standard in alveolar cleft repair strategy (Eppley and Sadove, 2000). Using the chin as standard donor site is routine practice in most cleft centres for cleft surgery repair in the Netherlands and well accepted with low objective and subjective morbidity (Freihofer and Kuijpers-Jagtman, 1989; Borstlap et al., 1990; Hoppenreijs et al., 1992; Freihofer et al., 1993; Booij et al., 2005; Raghoebar et al., 2007;

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Weibull et al., 2009; Weijs et al., 2010). Tooth injuries after harvesting bone from the mandibular symphysis have been reported. In 2005 Booij et al. mentioned an endodontic problem that had developed in three lower incisors. Raghoebar et al. in 2007 found subjective changes in sensibility but no noteworthy complaints or discomfort reported by the patients. Weibull in 2009 mentioned an injury percentage of 1% and stated: "it did in general not affect the patient in daily life". Notwithstanding this low morbidity, the patients (and their parents) have to be informed about the risk of objective and subjective disturbances of the sensibility in the chin donor region and the risk of dental pulp necrosis (Booij et al., 2005). In the Netherlands we have observed almost no adverse effects of the chin graft method. Since it began to be used routinely use in 1995 surgeons have built up a thorough experience in harvesting chin bone for repair of unilateral and even bilateral alveolar clefts (Raghoebar et al., 2001; Al-Ani and Nambiar, 2012).

One problem continues to be inherent to harvesting autologous bone: wherever in the body the bone is harvested, it is accompanied to a greater or lesser extent by co-morbidity (Rawashdeh and Telfah, 2008). The question is: can this be avoided?

A resorbable bone substitute is a potential answer to this question. These substitutes have changed from replacement material to resorbable osteoinductive biomaterials (Kolk et al., 2012). Bone substitution with the application of autologous platelet-rich plasma is also considered (Metzler et al., 2012). Transplantation of autologous dental material has been described (Aizenbud et al., 2013).

The bone substitute that we used is a micro-structured resorbable calcium phosphate that has been tested in animal experiments and has been shown to be equally as effective as autologous bone (De Ruiter et al., 2011). The application of bone substitute only, i.e. with no autologous bone and/or cell material or bone morphogenetic proteins (BMP's), for the repair of alveolar clefts in children is new. We wanted to exclude the risk of complications accompanying the use of artificial grafting material for filling clefts in CLP patients. To this end we chose to first investigate micro-structured resorbable calcium phosphate as a filling material in the chin, the Utrecht donor site of autologous bone for repair of the alveolar cleft (Koole et al., 1989) and the only clinically available defect in our patients.

The critical size defect (CSD) in a child's mandible was never determined and probably never will be. CSD's were originally defined as "the smallest size intraosseous wound in a particular bone and species of animal that will not heal spontaneously during the lifetime of the animal (Schmitz and Hollinger, 1986). However Cooper et al. (2010) stated '*After a review of the existing literature and a critique of the clinical applicability of the models studied, it is suggested that the use of the term "critical-sized-defect" be discontinued*'. The defects following chin bone harvest for alveolar bone closure are obviously not beyond this size. In a previous study (Dik et al., 2010) we have shown that these defects heal spontaneously '*leaving a residual defect* (compared with the original) *of about 14%*'.

1.1. Aim

The aim of this study was to evaluate the safe clinical use of a newly developed calcium phosphate based micro-structured and resorbable bone substitute in children. We used it as a filling material in the autologous chin bone donor site in young patients with a cleft of lip, alveolus and palate (UCLP and BCLP). It was also important to determine the degree of dimensional stability of the micro-structured resorbable calcium phosphate granules used in bone formation and the process of bone graft resorption and remodelling.

2. Material and methods

2.1. Patients

This study was carried out in accordance with the principles expressed in the Declaration of Helsinki. Permission for this study was obtained from the Medical Ethical Committee of the University Medical Centre, Utrecht, The Netherlands (Protocol nr. 06-210).

Before the operation, parents and children were given extensive information about this experimental study. In order to avoid being influenced by the researchers, the parents and children were given the opportunity to speak to an independent but informed physician and to ask any questions they may have had. Patient information forms were developed especially for this study. Patients were included in the study after written informed consent had been obtained. The blinded patient group comprised 20 UCLP and BCLP patients, all with an indication for alveolar cleft repair. The group was sorted by sex and type of cleft (Table 1) and average age at the time of repair surgery (Table 2).

2.2. Material (bone substitute)

The synthetic bone graft material is comprised of 1–2 mm sized micro-structured calcium phosphate particles that contain >90% tricalcium phosphate and <10% hydroxyapatite (RevisiOs BV, The Netherlands) (Fig. 1).

It is a resorbable material for clinical application in bone regenerative surgery. The micro-structured surface of the material renders the material osteoinductive as demonstrated in various preclinical models (Habibovic et al., 2005, 2006; Yuan et al., 2010), without the addition of bone growth factors or other bone inducing agents or cells. These materials have superior ability to accelerate bone healing, compared to non-osteoinductive ceramics.

2.3. Methods

2.3.1. Surgical method

Alveolar cleft repair surgery comprised repair by means of a bone transplant using autologous bone taken from the mandibular symphysis. The bone-harvesting site was then filled with the micro-structured calcium phosphate. The buccal cortical surface of the mandibular symphysis was approached by a horizontal incision in the vestibule of the lower lip in the intercanine region. After making a submucosal flap, an incision was made through the mental muscles on each side and down to the bone. After elevating the muco-periosteal flap the mental nerve was localized bilaterally. Using the position of the apices of the incisors and the germs or roots of the permanent canines as seen on preoperative radiograph, the outline of the bone graft was marked with a fissure burr. The monocortical bone graft was cut out with a reciprocal saw, irrigated

Table 1
Number and gender.

	Male	Female	Total
UCLP	7	5	12
BCLP	6	2	8
Total	13	7	20

Table 2
Average age at time of cleft repair surgery.

	Male	Female
UCLP	11 years 1 month	11 years 2 months
BCLP	12 years 2 months	10 years 9 months

Fig. 1. 1–2 mm sized micro-structured calcium phosphate particles.

with physiological saline solution 0.9%, and harvested using a chisel. To collect the maximum amount of bone, the remaining cancellous bone in the symphysis was harvested using excavators. To refill the harvesting site, a five-wall bony defect, micro-structured calcium phosphate granules, 1–2 mm in size, were mixed with fibrin glue (=human material) and placed in the defect (Fig. 2).

Closure was achieved by approximating the periosteum and both mental muscles to their origins with a Vicryl® 3-0 suture (Ethicon, Johnson & Johnson Intl.). The mucosa was closed with a Vicryl® 4-0 running mattress suture. Directly postoperatively the chin was taped with elastic tape to minimize swelling from oedema and restrict additional haematoma formation. This also served to stabilize the soft-tissue profile of the lower lip with the mandible. The tape was removed after 72 h.

To prevent wound infection, a standard prophylactic antibiotic regime (Clindamicyne, Hameln Pharmaceuticals, 31789 Hameln, Germany, 10 mg/kg per 24 h) was prescribed for 48 h postoperatively. A soft diet was prescribed to prevent wound dehiscence. Oral hygiene was delivered by a dental professional.

2.3.2. Study method

The study took the form of a prospective randomized clinical trial of 20 patients. We followed an established method of using lateral cephalograms (Weibull et al., 2009). These had been taken both peroperatively and at 12 months postoperatively. The area of interest: the mandibular symphysis, was imaged according to the method described by Dik et al. in 2010 (Fig. 3).

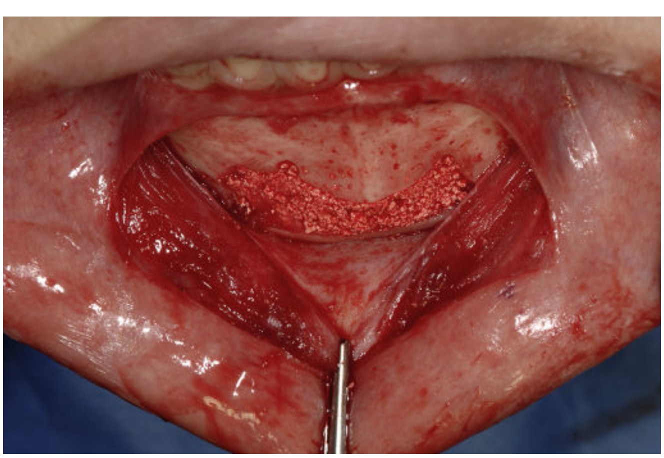

Fig. 2. Micro-structured calcium phosphate granules, 1–2 mm in size, mixed with fibrin glue (=human material) and placed in the symphyseal defect.

The data obtained were digitalized and the treatment outcomes expressed in numbers. Comparisons with a previous study (Dik et al., 2010) were made. Patients from both studies together are a cohort from all newly incoming patients, operated upon by the same surgeons in similar settings. Mean age and sex ratio are also similar in both studies.

2.3.3. Histological methods

In two patients we were able to take a biopsy from the area of the chin from which bone had been harvested and then filled with the micro-structured calcium phosphate more than 18 months previously (Fig. 4).

The two biopsies were taken during re-entry and with strict permission from patients and parents. This mandibular symphysis bone biopsy material was then prepared for histology (Fig. 5).

The biopsies were not decalcified and after dehydration through a graded series of ethanol (Merck) were embedded in cold curing MMA (K-Plast, L.T.I. Bilthoven, The Netherlands). Sections approximately 20 μm thick were made using the Leica SP1600 saw microtome. They were stained with 1% methylene blue and 0.3% basic fuchsin (both Sigma–Aldrich) and mounted on glass slides using UV curing glue (Permacol, Ede, The Netherlands).

2.3.4. Ct scans

On medical indication the CT scans of one patient taken preoperatively, and at 3 months and 1 year postoperatively were available. They were both studied and interpreted visually.

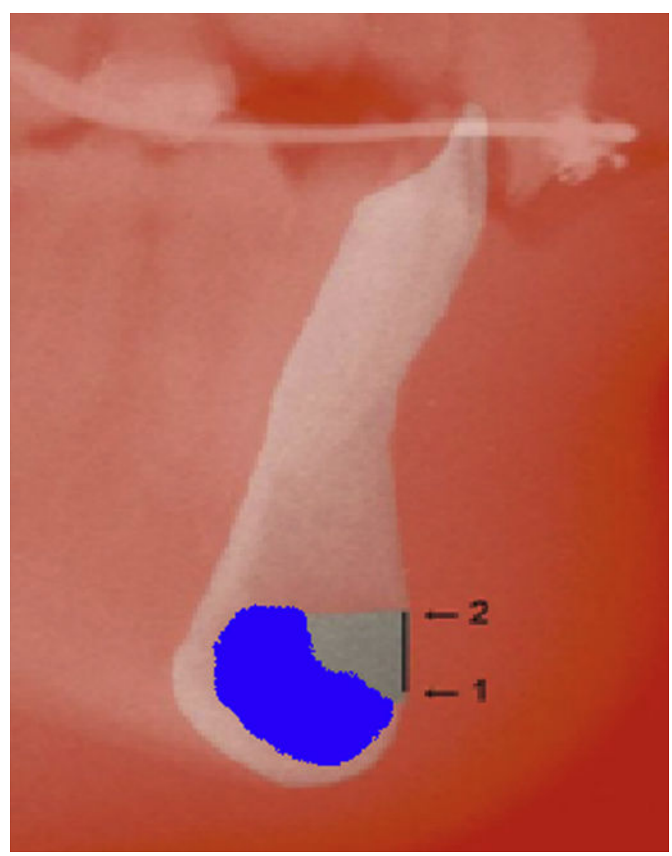

Fig. 3. Digital tracing of the mandibular symphysis showing the bony defect directly postoperatively (grey). Also the cancellous bone marrow harvesting region (blue). Note the straight line from the caudal labial border (1) to the cranial labial border (2).

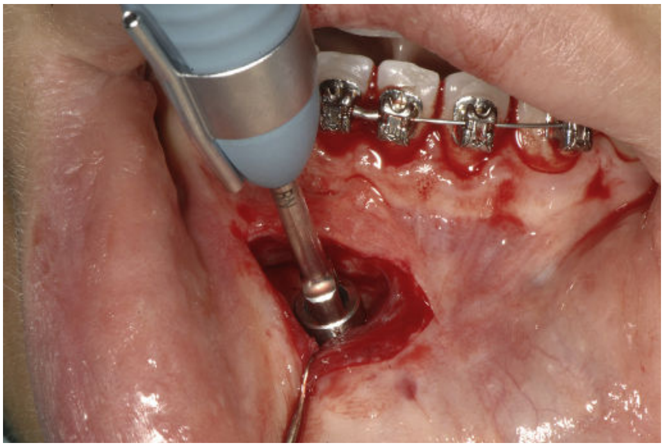

Fig. 4. Taking the biopsy with a hollow drill.

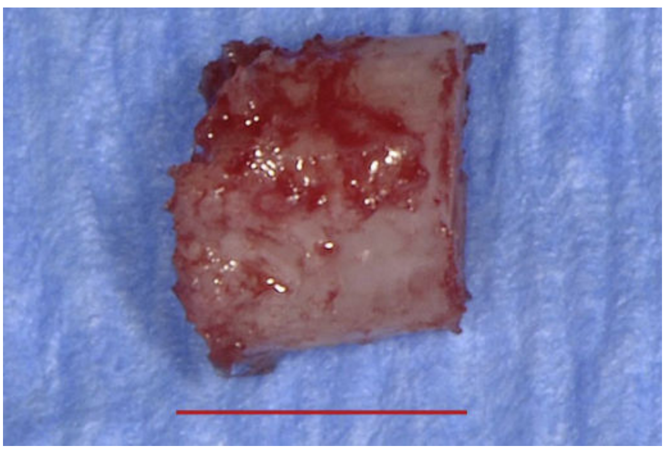

Fig. 5. Specimen of the biopsy material.

Table 3
Group statistics.

	duplex_ uni	N	Mean	Std. deviation	Std. error mean
sym_per	Uni	12	43715.00	4180.556	1206.823
	Duplex	8	44165.25	7883.710	2787.313
sym_pos	Uni	12	44994.25	4648.109	1341.794
	Duplex	8	49674.88	6346.719	2243.904
sym_per_mm2	Uni	12	313.3667	29.96975	8.65152
	Duplex	8	316.5875	56.52169	19.98343
sym_pos_mm2	Uni	12	322.5417	33.29249	9.61071
	Duplex	8	356.0875	45.50273	16.08764
def_per	Uni	12	12970.00	2253.532	650.539
	Duplex	8	12133.83	4705.651	1663.699
def_pos	Uni	12	171.88	321.361	92.769
	Duplex	8	249.83	374.688	132.472
def_per_mm2	Uni	12	92.9750	16.15471	4.66346
	Duplex	8	86.9750	33.75355	11.93368
def_pos_mm2	Uni	12	1.2417	2.29722	0.66315
	Duplex	8	1.8000	2.67689	0.94642
perc_per	Uni	12	30.1483	5.10202	1.47283
	Duplex	8	27.6827	9.10290	3.21836
perc_pos	Uni	12	0.4109	0.79544	0.22962
	Duplex	8	0.5417	0.87797	0.31041
perc_original_ def	Uni	12	1.2308	2.15902	0.62325
	Duplex	8	2.7163	4.47436	1.58192

Table 4
Inter-group statistics.

	Study	N	Mean	Std. deviation	Std. error mean
sym_per_mm2	Dik et al., 2010	23	336.6087	45.25156	9.43560
	Present	20	314.6550	41.22643	9.21851
sym_pos_mm2	Dik et al., 2010	23	343.7174	45.47175	9.48151
	Present	20	335.9600	41.09509	9.18914
def_per_mm2	Dik et al., 2010	23	34.9791	27.80065	5.79684
	Present	20	90.5750	24.08170	5.38483
def_pos_mm2	Dik et al., 2010	23	4.8139	5.67292	1.18289
	Present	20	1.4650	2.40291	0.53731
perc_per	Dik et al., 2010	23	10.1704	7.13637	1.48804
	Present	20	29.1621	6.86546	1.53516
perc_pos	Dik et al., 2010	23	1.4152	1.64482	0.34297
	Present	20	0.4632	0.80909	0.18092
perc_original_def	Dik et al., 2010	23	16.2978	18.34148	3.82446
	Present	20	1.8250	3.26065	0.72910

3. Results

3.1. Defect measurements outcome

Table 3 shows the digital measurements in pixels and in mm^2 of the contour of the symphysis (sym) and of the defect (def). Measurements were taken peroperatively (per) and 1 year postoperatively (pos). The total group was divided into unilateral cleft patients (uni) and bilateral cleft patients (duplex). The percentage (perc) of the defect per- and postoperatively was measured and compared with that of the symphyseal contour. The percentage of the residual defect after 1 year was also compared with the original defect (per). The mean defect peroperatively for the unilateral cleft patients was 93 $\pm$ 16 mm^{2,} for the bilaterals 87 $\pm$ 34 mm^2. The mean defect peroperatively (def_per_mm2) for the total group was 91 $\pm$ 24 mm^2. The mean defect postoperatively for the unilateral cleft patients was 1.2 $\pm$ 2.3 mm^2, for the bilaterals 1.8 $\pm$ 2.7 mm^2. The mean defect 1 year postoperatively (def_pos_mm2) for the total group was 1.5 $\pm$ 2.4 mm^2. Table 4 shows the outcomes of the comparison of the current study and a previous study [12]. In this study the average peroperative defect was 35 mm^2 and 4.8 mm^2 1 year postoperatively. The percentage of the residual defect compared with the original defect was 16%. The average defect was 91 mm^2 peroperatively and 1.5 mm^2 1 year postoperatively. The percentage of the residual defect on comparison with the original defect was 1.8%.

3.2. Statistics

Analysis of variance (ANOVA, SPSS 15.0; SPSS, Chicago, Il, USA) was applied to test the null hypothesis that there would be no statistical difference between the results obtained from the radiographs (taken directly (=peroperatively) or one year postoperatively), and between the two independent investigators and three individual tracings. Independent sample t tests were performed to test possible differences in the defects between unilateral and bilateral cleft patients (peroperatively and 1 year postoperatively). The independent sample t test was used to compare the present results with those of our previous study (Dik et al., 2010). One-sample t tests were performed to test whether after 1 year the defect differed from zero (Tables 5 and 6). Pearson's correlation coefficients were calculated to determine possible relationships between the age of a patient and the residual defect after 1 year, and a relationship between the defect peroperatively and 1 year later. In addition, we studied a possible relationship between sex and the defect after 1 year. A p-value of less than 5% was considered significant.

Table 5
One-sample statistics.

Study		N	Mean	Std. deviation	Std. error mean
	def_pos_mm2	0[a,b]			
Dik et al., 2010	def_pos_mm2	23	4.8139	5.67292	1.18289
Present	def_pos_mm2	20	1.4650	2.40291	0.53731

[a] t cannot be computed because the sum of case weights is less than or equal 1.
[b] t cannot be computed. There are no valid cases for this analysis because not all case weights were positive.

Fig. 6C shows a higher magnification (100×) of a typical bone structure. an osteon with Haversian channel in the top right.

Fig. 6D shows a 200× magnification of the tricalcium phosphate remnant, (yellow square) which is in direct contact and fully embedded within the newly formed bone.

Fig. 7A shows an overview of the entire biopsy taken from patient 3.058.885 at 40× magnification. The yellow square indicates remnants of the implanted micro-structured calcium phosphate material. The open structure in between the bone is filled with bone marrow.

Table 6
One-sample test.[a]

Study		Test value = 0					
		t	df	Sig. (2-tailed)	Mean difference	95% Confidence interval of the difference	
						Lower	Upper
Dik et al., 2010	def_pos_mm2	4.070	22	0.001	4.81391	2.3608	7.2671
Present	def_pos_mm2	2.727	19	0.013	1.46500	0.3404	2.5896

[a] No statistics have been computed for one or more split files.

3.3. *Histological evaluation of human mandibular symphysis bone biopsies*

Fig. 6A shows an overview at 40× magnification of the biopsy taken from patient 2.000.401. Bone is stained red/pink in this image and the yellow square indicates the presence of a remnant of the implanted tricalcium phosphate material.

Fig. 6B was taken at a magnification of 100× magnification and shows (yellow square) a remnant of the implanted tricalcium phosphate material fully embedded within the bone. The open structure in between the bone is filled with bone marrow (white).

Fig. 7B is taken at a magnification of 100×s and shows the presence of remnants of the implanted tricalcium phosphate material fully embedded within the bone (yellow squares).

Fig. 7C shows a higher magnification (100×s) of a blood vessel in the bone.

Fig. 7D shows a 200× magnification of a tricalcium phosphate remnant, (yellow square) which is in direct contact with the newly formed bone.

Fig. 7E shows a 200× magnification of the blood vessel. In both patients the bone structure resembles the normal bone structure, with only very small remnants of the implanted calcium phosphate ceramic.

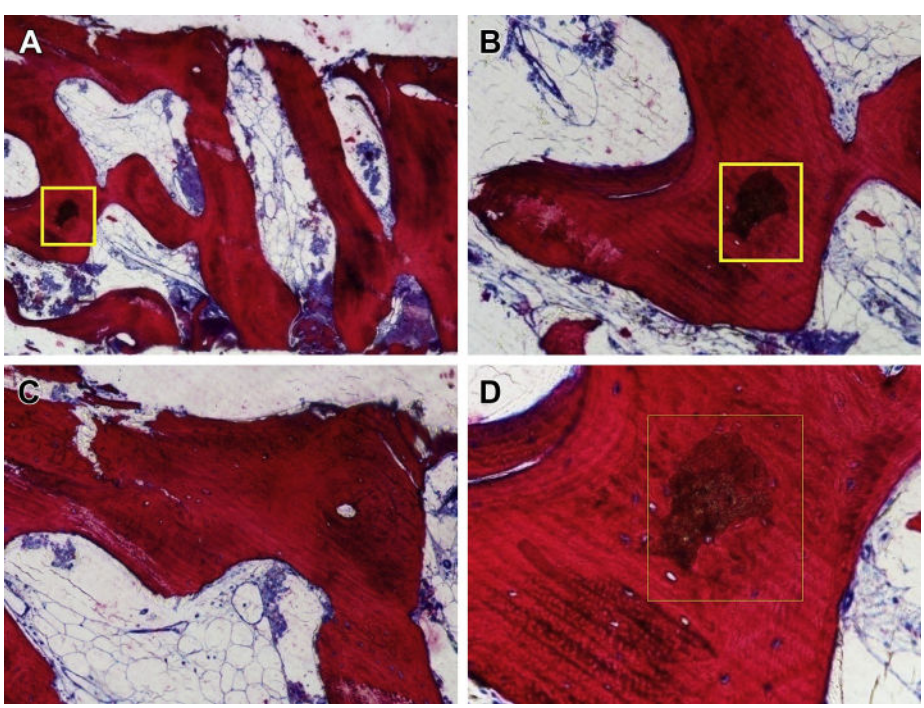

Fig. 6. A: 40×s magnification. Bone is stained red/pink in this image and the yellow square indicates the presence of a remnant of the implanted tricalcium phosphate material. B: 100×s magnification of a CaP remnant (yellow square) fully embedded within the bone. The open structure in between the bone is filled with bone marrow (white). C: 100×s magnification of a typical bone structure; an osteon with Haversian channel in the top right. D: 200×s magnification of the tricalcium phosphate remnant, (yellow square) which is in direct contact and fully embedded within the newly formed bone.

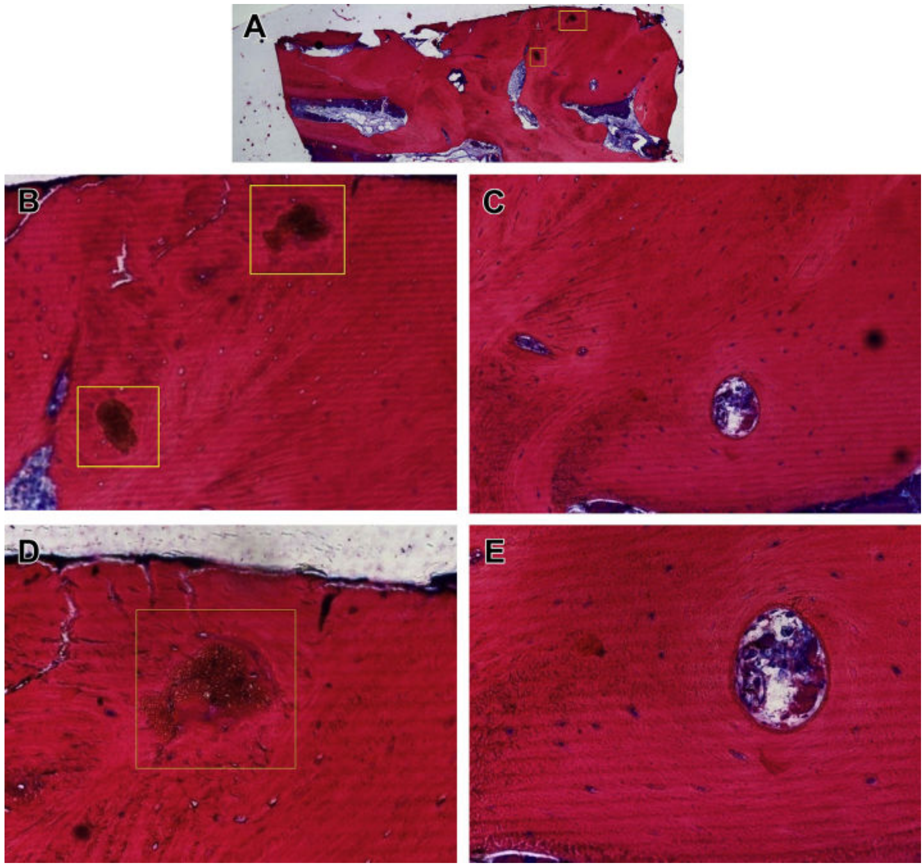

Fig. 7. A: An overview of the entire biopsy taken from patient 3.058.885 at 40×s magnification. The yellow squares indicate remnants of the implanted micro-structured calcium phosphate material. The open structure in between the bone is filled with bone marrow. B: Magnification of 100×s. It shows the presence of remnants of the implanted tricalcium phosphate material fully embedded within the bone (yellow squares). C: Higher magnification of 100×s of a blood vessel inside the bone. D: 200×s magnification of a tricalcium phosphate remnant (yellow square) in direct contact with the newly formed bone. E: 200×s magnification of the blood vessel inside the bone.

3.4. 3D CT scans

3D CT scans of one patient were available. Figs. 8 and 9 show the preoperative mandibular symphyseal harvesting site. Figs. 10 and 11 show the symphysis 3 months postoperatively. Figs. 12 and 13 show it 1 year postoperatively including reoccurrence of a mental protruberance

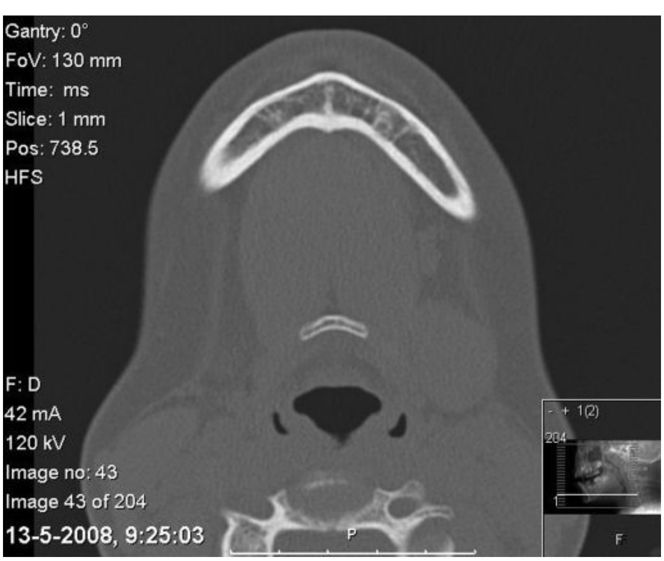

Fig. 8. Axial image of the harvesting site preoperatively.

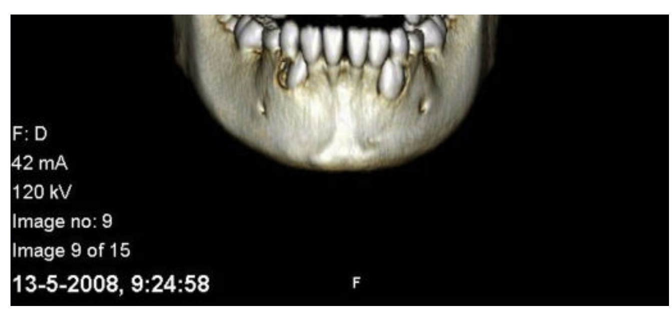

Fig. 9. Frontal image of the harvesting site preoperatively.

4. Discussion

This study demonstrates that the micro-structured, resorbable calcium phosphate ceramic provides excellent regeneration properties for the repair of the chin bone harvesting defect in children. Horch, in five bony wall defects as well, showed this after the surgical removal of large pathological jaw defects (Horch et al., 2006). Naudi performed mandibular reconstructions in rabbits using β-TCP in combination with recombinant bone morphogenetic protein (Naudi et al., 2012).

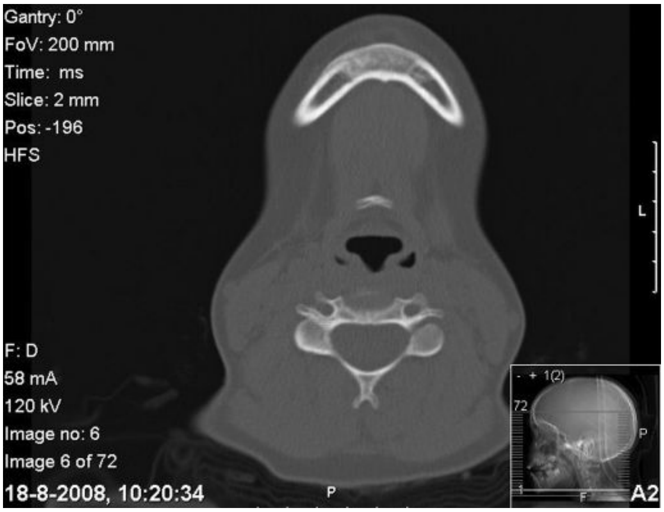

Fig. 10. Axial image of the repaired symphysis 3 months postoperatively with grafting material (micro-structured calcium phosphate) still visible.

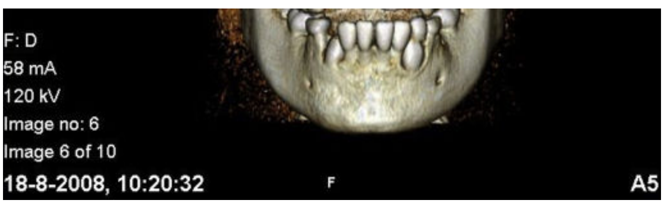

Fig. 11. Frontal image of the repaired symphysis 3 months postoperatively and no grafting material (micro-structured calcium phosphate) visible.

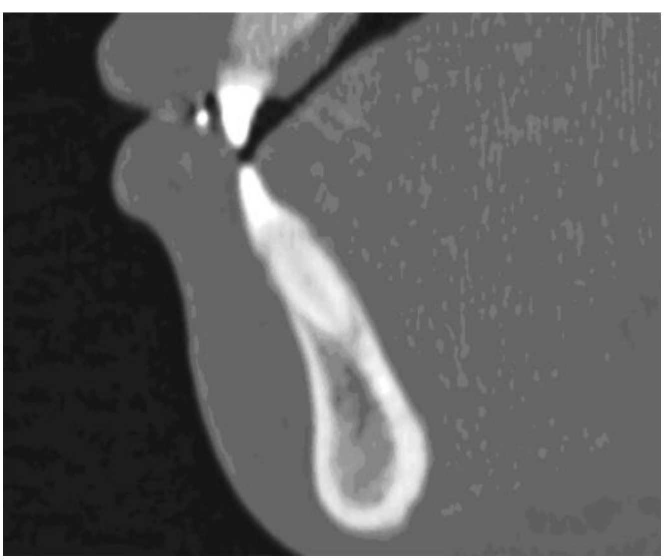

Fig. 12. Sagittal image of the repaired symphysis 1 year postoperatively.

Fig. 13. Frontal image of the repaired symphysis 1 year postoperatively.

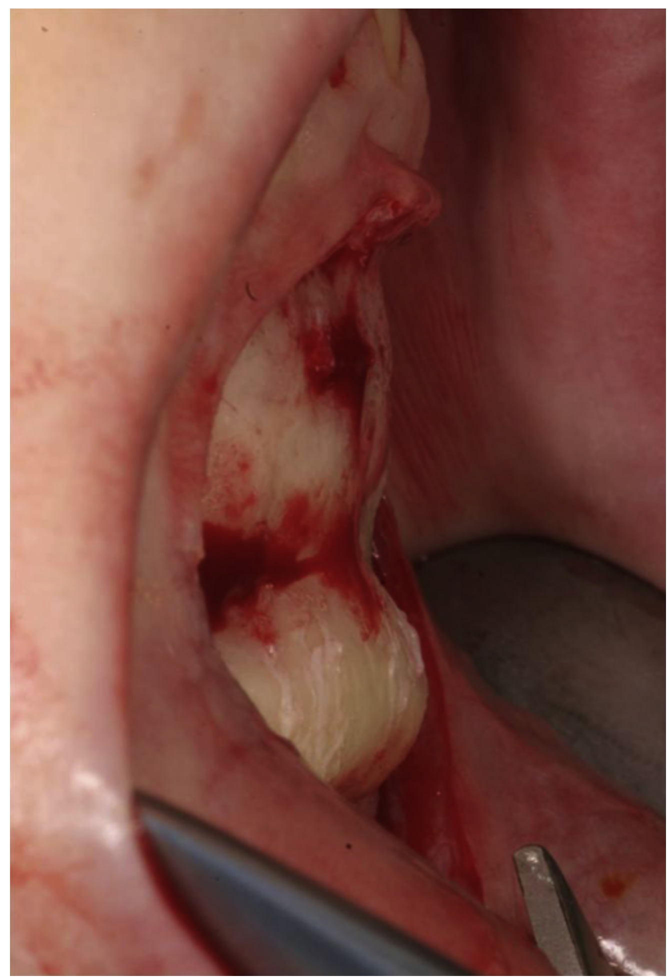

Fig. 14. The hollow-curved mandibular symphysis shows a non-regenerated bone defect at the time of secondly harvesting chin bone for a redo of alveolar cleft repair.

One year postoperatively, the measurements taken from lateral cephalograms show that there is scarcely any visible residual defect. This is in contrast with the results from our previous study (Dik et al., 2010) and the Weibull study in 2009 that states: '*at radiographic* (lateral cephalograms) *examination bone healing after chin graft harvesting did not regenerate to the preoperative level*'. This is demonstrated in Fig. 14, showing a non-regenerated bone defect along the hollow-curved mandibular symphysis at the time of secondly harvesting of chin bone for a redo of the alveolar cleft repair at later age. The main reason for the use of the accepted method of lateral cephalogram assessment in this study was the non-availability of 3-D radiographic imaging in our previous retrospective study (Dik et al., 2010). For comparison reasons we performed this similar method and assessed the defect two-dimensionally as depicted in Fig. 14 three-dimensionally. In future studies cone-beam computed tomography should be the assessment method of choice (Kim et al., 2012a,b).

The histological investigations of the two bone biopsies show proof of solid, induced bone formation and almost complete resorption of the micro-structured calcium phosphate.

The data from the results of both per- and postoperative visual-imaging show no difference between patients with a unilateral and bilateral alveolar cleft. We had expected this as repair of a bilateral alveolar cleft generally requires the harvesting of more autologous bone than repair of a unilateral alveolar cleft (Jia and Mars, 2000).

Statistical tests showed that there were no significant differences between the groups (p-values >5%). It was striking that the peroperative defects measured in this study appeared to be larger than those in the previous study (Dik et al., 2010). This difference proved significant ($p = 0.000$). The explanation for this can be found in the visibility of the defect on lateral skull radiograph. The presence of the calcium phosphate material peroperatively marks the defect better.

The size of the defect after 1 year is also different in each study. Both show a significant residual defect. However, in the previous study ($t = 4.1$; $p = 0.001$) the residual defect was significantly larger than in this study ($t = 2.7$; $p = 0.013$). This means that the residual defect is nearer to nil despite the much larger original defect. The final defect is significantly smaller than found by the previous study ($p = 0.019$). At 1 year the percentage of the final defect compared with the original defect is also different in each study: 14 % previously and now 1.8%. This means that the final defect percentage of the original defect is now much smaller than in the last study ($p = 0.001$). For this reason we can conclude that micro-structured resorbable calcium phosphate fills the defect better than Spongostan which is normally used.

The bone biopsies of the symphysis from these two patients after 1 year show that the implanted micro-structured calcium phosphate granules have almost been fully resorbed and replaced by viable bone normal histological appearance. These results indicate the biocompatibility and efficacy of this novel synthetic bone graft. This shows that the revascularization that was responsible for the changing process of remodelling of the bone substitute had taken place. If we were to transpose these data to the alveolar cleft itself, it is only in a vital bone setting that tooth movement can be initiated throughout the activation time of the orthodontic forces. These forces initiate a remodelling process in the tension and pressure sides of the bone surrounding the tooth. It is the characteristic properties of the fibrous periodontal ligamental joint between a tooth and its socket – the gomphosis – that allow for the attachment and load bearing characteristics of a tooth (Nishihara and Nakagiri, 1994; Ho et al., 2007). Functional loading is of the utmost importance for the preservation of the newly-acquired of bone. However, in order for this process to take place, bone must be present.

A question asked frequently by the parents of patients was: Why don't you put the bone substitute directly into the alveolar cleft itself? This question should be seen in its social context. Dutch patients like to be actively involved in their treatment and their doctors are happy to articipate in shared transparent decisions about treatment. Our decision not to do this was a considered one. As the implantation of bone substitute in general and this micro-structured, resorbable calcium phosphate ceramic in particular is new in children, we wanted to first safely test it at a less critical site than the alveolar cleft.

The Dent-Scan CT views taken preoperatively, three-months postoperatively and 1-year postoperatively show a real restoration of integrity of the mandibular symphysis following peroperative filling with the micro-structured calcium phosphate bone graft. The compact contour of the defect that was caused by harvesting autologous chin bone to repair the alveolar cleft in the upper jaw was completely healed after 3 months. After 3 months some remains of ceramic granules are still visible in the cancellous bone. The 1-year postoperative scan demonstrates complete healing and progressive resorption of the micro-structured calcium phosphate granules and a reoccurrence of a mental protruberance because of muscular loading of the bone.

On the grounds of these results and of the results from an earlier animal study (De Ruiter et al., 2010), the Medical Ethics Committee has given permission for these micro-structured and resorbable calcium phosphate granules to be grafted directly into the alveolar cleft. A new-coned beam computer tomogram (CBCT scan) radiography protocol is currently investigating bone quality and bone quantity (Kim et al., 2012a,b).

5. Conclusions

The findings of this study have illustrated the biocompatibility and efficacy of a new class of micro-structured, resorbable calcium phosphate granules, as well as its dimensional stability throughout remodelling. Histological examination of biopsies indicates the overall presence of newly formed vital bone and the resorption of the bone substitute, an absolute requirement for maintaining shape and volume of bone for the orthodontic moving of teeth.

The use of micro-structured calcium phosphate bone grafts in alveolar cleft repair is now warranted. At such time harvesting autologous bone elsewhere in the body, and by extension its inherent concomitant morbidities is avoided. This will be a significant improvement in patient management.

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