



Three-dimensional Assessment of Autologous Calvarial Bone Grafting for Alveolar Clefts Reconstruction in Pediatric Population: A Retrospective Study

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Abstract: Reconstruction of alveolar clefts using cancellous bone graft is associated with a high rate of resorption. The aim of this study was to evaluate the osseointegration capacity of cortical calvarial bone grafting using 3-dimensional imaging assessment for alveolar cleft reconstruction in pediatric population. All alveolar bone grafting procedures performed between January 2015 and October 2017 in the maxillofacial surgery department of Lille University Hospital were included. All patients were evaluated clinically and by 3-dimensional imaging before bone grafting and at 3 months after surgery. Cleft and bone graft volumes were assessed using Horos software, v. 3.3.5, through a segmentation process. The bone filled ratio at 3 months after surgery was calculated. A total of 48 alveolar bone grafting procedures were performed in 37 patients: 3 unilateral cleft lip and alveolar, 20 unilateral cleft lip and palate, and 25 bilateral full cleft lip and palate (3 patients had only unilateral surgery). The mean bone filled ratio was $72.27\% \pm 23.65\%$, 81% for unilateral cleft lip and alveolus, $75.4\% \pm 20.6$ for unilateral cleft lip and palate, and $65.5\% \pm 30$ for bilateral complete cleft lip and palate ($P = 0.1981$). Calvarial bone grafting seems to be a relevant alternative to other donor sites for alveolar cleft reconstruction.

Key Words: alveolar bone grafting, autogenous bone graft, calvarial bone graft, cleft lip and palate

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During cleft treatment, satisfactory alveolar ridge reconstruction is essential for supporting tooth eruption, eliminating oronasal fistula, creating bony support for the alar base, stabilizing the premaxilla, facilitating orthodontic treatment, and improving aesthetic outcome. Many changes have been introduced in the treatment of alveolar cleft over the past century in the attempt to decrease the impact of midfacial growth,¹ to improve alveolar bone integration, and to reduce donor site morbidities. The surgical protocol for reconstruction of alveolar clefts varies in terms of timing,² type of bone graft, the donor site, and the use of allogeneic material.^{3,4}

At the time of this writing, gingivoperiosteoplasty (GPP) combined with cancellous autologous bone grafting is considered the gold standard for alveolar cleft reconstruction.^{5,6} The increasing use of 3-dimensional (3D) imaging assessment has revealed a high rate of resorption of cancellous bone grafts. Several surgical teams have explored whether inclusion of a cortical component in the bone graft can prevent bone resorption and optimize bone density.^{7,8}

The aim of this study was to evaluate calvarial cortical bone volume (BV) remaining in the cleft area and to calculate the bone filled ratio (BFR) by comparing preoperative and third month postoperative 3D imaging cone-beam computed tomography (CBCT) or multislice computed tomography (MSCT).

MATERIAL AND METHOD

Protocol

All alveolar bone grafting procedures performed in pediatric population for cleft reconstruction between January 2015 and November 2017 were considered for inclusion in this retrospective study. Patients were included regardless of the age and the type of cleft: unilateral cleft lip and alveolus (UCLA), unilateral cleft lip and palate (UCLP), and bilateral complete cleft lip and palate (BCLP). The inclusion criteria were treatment with GPP combined with autogenous calvarial bone grafting and completion of ≥ 1 -year clinical follow-up with 3D imaging at 3 months after surgery. The exclusion criteria were previous alveolar bone graft procedure or incomplete follow-up records (clinical and radiologic).

Information on age, sex, dental agenesis, state of eruption of the incisors and the canine, bucconasal fistulae, and prior GPP, were collected during preoperative examination.

Each patient underwent preoperative orthodontic treatment to open the gap, increase transversal dimension of the maxilla, and stabilize the premaxilla (for bilateral cleft). For all patients, the alveolar bone graft procedure was performed as soon as the space is considered adapted to the surgery.

The BV required was assessed using preoperative 3D imaging (MSCT or CBCT) after completion of the orthodontic preparation.

Surgical Procedure

All surgeries were performed by 2 experienced surgeons: Pr J.Ferri or Dr S.Touzet-Roumazeille. The alveolar bone graft procedure was performed in 2 phases. The first phase consisted of calvaria bone graft (CBG) harvesting as described by Touzet et al.⁹ The external cortical bone was harvested with a 1.2-mm side-cutting bur. Narrow strips, 5 to 15 mm in width, oriented in the coronal direction, were split using a thin osteotome. The strips were harvested from the parietal bone, along with cancellous bone obtained using a bone scraper.¹⁰ The outer table was then reconstructed using granules of beta-tricalcium phosphate. The second phase of the procedure consisted of a classical GPP.¹¹ Then the cortical part of the bone graft was set up in formwork, with the placement of the first bone strip at the nasal floor and a second at the vestibular wall as shown in the Figure 1. All the volume of the alveolar cleft was filled by the parietal bone strips and the harvested diploe mixed with bone marrow sample from the iliac bone. All procedures were performed by the same surgeon.

Clinical Follow-up

All patients received perioperative prophylactic antibiotic therapy with amoxicillin plus clavulanic acid, or clindamycin in case of penicillin allergy. Patients were clinically evaluated on the day 10 after surgery and then at the end of the sixth week, sixth month, and 12th month. At each follow-up we assessed the mucosal healing, looking for wound dehiscence, swelling, or infection. Residual Bucconasal fistulae were assessed at 6 months. Orthodontic treatment was restarted at 3 months after surgery after 3D assessment by CBCT or MSCT.

Data Acquisition

The anatomic limits of the alveolar cleft were defined according to Oberoi et al.¹² The cranial limit was at the most inferior part of the pyriform aperture and the caudal limit at the cemento-enamel junction of the teeth adjacent to the cleft. The lateral boundaries were delimited by parasagittal planes passing through the distal cusp and the mesial cusp of the mesial tooth and the lateral tooth, respectively, adjacent to the cleft.

As Shown in the Figure 2, the cleft volume (CV) was assessed using the Feichtinger et al.¹³ technique: a segmentation process was used to delineate a region of interest on each slice of the 3D image. Software was used to calculate the areas of each slice. The CV was calculated as

$$CV = (A_1 \times \text{slice thickness}) + (A_2 \times \text{slice thickness})$$

The residual BV was assessed by the same procedure in such a way as to circumscribe the volume of bone tissue grafted into the initial cleft defect.

Bone volume was calculated as

$$BV = (A1 \times \text{slice thickness}) + (A2 \times \text{slice thickness})$$

The BFR was calculated as

$$BFR = (BV/CV) \times 100$$

All measurements were carried out by 2 assessors. Intrarater and inter-rater reproducibility were assessed using the Pearson correlation coefficient, which was, respectively, evaluated at 0.97 and 0.96 as shown in the Figure 3.

The BV and BFR were then compared between subgroups: patients with prior GPP, patients with lateral incisor agenesis, patients with preoperative bucconasal fistulae and according to the state of dental eruption. All the patients who undergone alveolar bone grafting before incisor eruption were classified in the Early Secondary Alveolar Bone Grafting, patients who benefited alveolar bone grafting after incisor eruption and before canine eruption were classified in the Late Secondary Alveolar Bone Grafting Group and patients who undergone bone grafting after canine eruption were classified in the Tertiary Alveolar Bone Grafting group.

Software

All measurements and calculations were made using Horos medical viewer software version 3.3.5 (<https://horosproject.org/>).

Statistical Analysis

Qualitative variables were summarized as frequencies and percentages, and gaussian numerical variables as the mean (and SD) or as the median (and interquartile range). The normality of distribution of the numerical variables was checked graphically and tested using the Shapiro-Wilk test. Comparisons of the BFR between different population subgroups were performed using a mixed linear model to account for repeated measurements per patient. The normality of the model residuals was verified. The statistical analysis was carried out by the Biostatistical Methodology Unit of the Lille University Hospital. Bilateral tests were carried out with a level of significance of 5%. Statistical analysis was carried out using SAS software version 9.4 (SAS Institute).

Research Ethics

This retrospective research work was carried out in accordance with the ethical standards outlined in the Declaration of Helsinki. All data were anonymized, and the “Comission Nationale de l’Informatique et Libertés” (CNIL) declaration was performed in accordance with French law.

RESULTS

Patient and Cleft Characteristics

The study sample included 37 patients (11 females, 26 males; mean age, 10.3 years \pm 2.9), with a total of 48 alveolar bone grafting procedures as shown in the Supplemental Table 1, Supplemental Digital Content 1, <http://links.lww.com/SCS/E365>. The procedures included 3 UCLA, 20 UCLP, and 25 BCLP (3 patients were grafted on only one side). In this sample, 26/48 clefts (54.2%) have had prior GPP procedure without alveolar bone grafting. With the regard to the timing of the alveolar bone grafting procedure, there were 4 (8%) early secondary alveolar bone graftings, 26 (54%) late secondary alveolar bone graftings, and 18 (38%) tertiary alveolar bone graftings.

Intraoperative and Postoperative Outcomes

Preoperative clinical examination revealed 26 (54%) bucconasal fistulae and 25 (52.1%) lateral incisor agenesis. No



FIGURE 1. Photograph showing the osteosynthesis of calvarial grafts on the vestibular wall.

intraoperative complications occurred. Mean hospitalization was for 2.4 ± 0.6 days. During follow-up there were 4 (8%) early complications (wound dehiscence at graft site), 1 (2%) late complication (bone loss with late exposure), and 11/26 (42%)

buconasal fistulae recurrences. Osteosynthesis material removal had to be performed in 13 (27%) cases.

Three-dimensional Assessment

The mean CV was $0.8 \pm 0.3 \text{ cm}^3$. The cleft size varied according to the cleft type: $1.04 \text{ cm}^3 \pm 0.29$ for UCLA, $0.95 \text{ cm}^3 \pm 0.31$ for UCLP, and $0.62 \text{ cm}^3 \pm 0.27$ for BCLP. The mean residual BV of the graft at 3 months after surgery was $0.6 \pm 0.3 \text{ cm}^3$: $0.87 \pm 0.21 \text{ cm}^3$ for UCLA, $0.71 \pm 0.27 \text{ cm}^3$ for UCLP, and $0.41 \pm 0.21 \text{ cm}^3$ for BCLP as shown in the Supplemental Table 2, Supplemental Digital Content 2, <http://links.lww.com/SCS/E366>. According to the cleft type, the BFR was 81% for UCLA, $75.4\% \pm 20.6$ for UCLP, and $65.5\% \pm 30$ for BCLP ($P = 0.1981$).

According to the type of procedure, the BFR was $74.5\% \pm 22.0\%$ for early secondary alveolar bone grafting, $66.7\% \pm 22.8\%$ for late secondary alveolar bone grafting, and $75.2\% \pm 19.6\%$ for tertiary alveolar bone grafting ($P = 0.1881$). As shown in the Supplemental Table 3, Supplemental Digital Content 3, <http://links.lww.com/SCS/E367>, the Subgroup analysis showed significantly lower BFR in the group with history of previous GPP than in the group without (63.37% versus 79.04%; $P = 0.0259$). However, BFR did not statistically differ between patients with different types of cleft or alveolar bone grafting procedures, or between patients with and without lateral incisor agenesis or preoperative buconasal fistula.

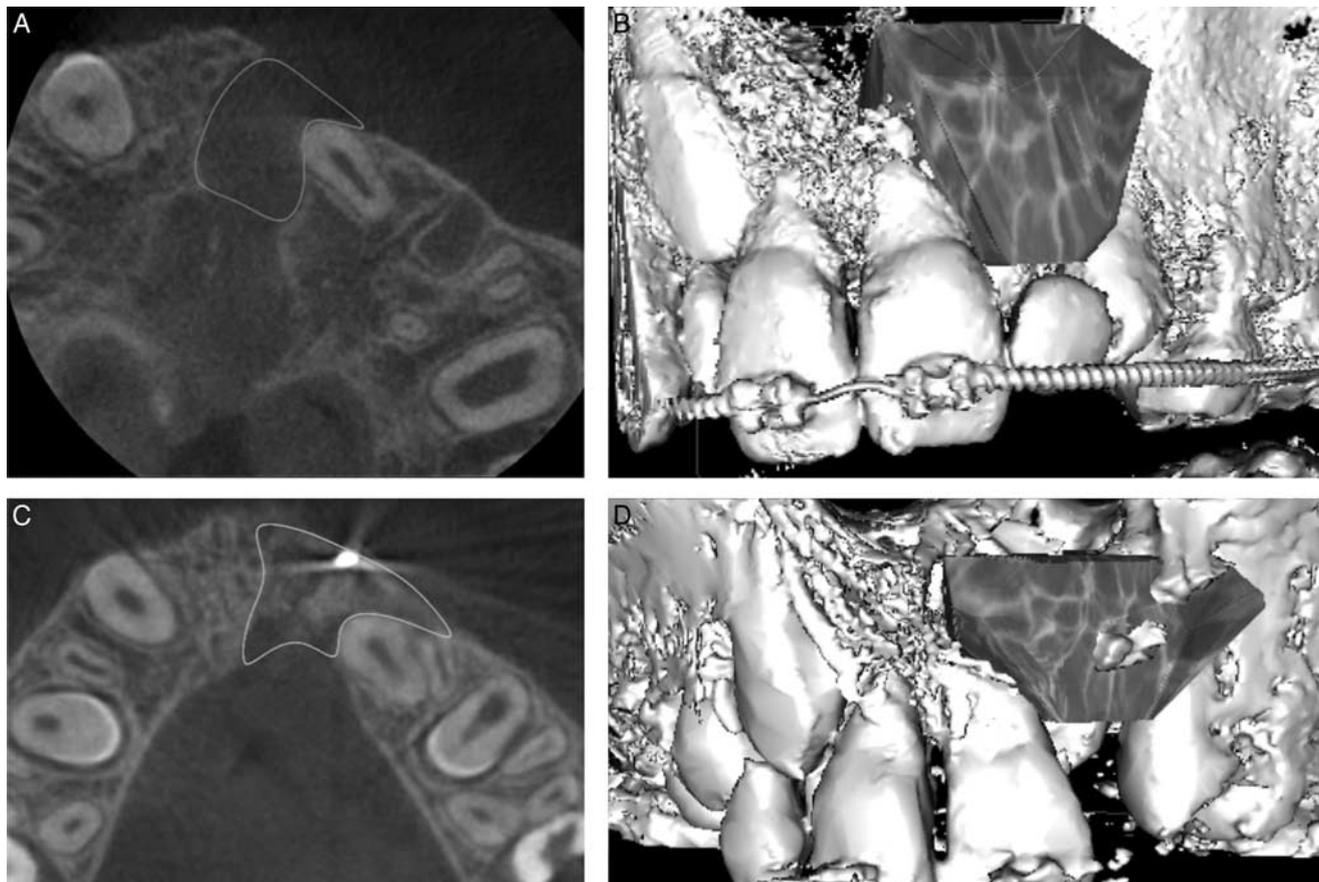


FIGURE 2. Case of an 11-year-old boy who undergone a tertiary alveolar bone grafting. (A) Delineation of a region of interest in axial plane of the cleft site; (B) 3D reconstruction of the volume of the cleft; (C) Delineation of a region of interest in axial plane of the residual bone graft at 3 months postoperatively; (D) 3D reconstruction of the volume of the alveolar graft at 3 months postoperatively. 3D indicates three-dimensional.

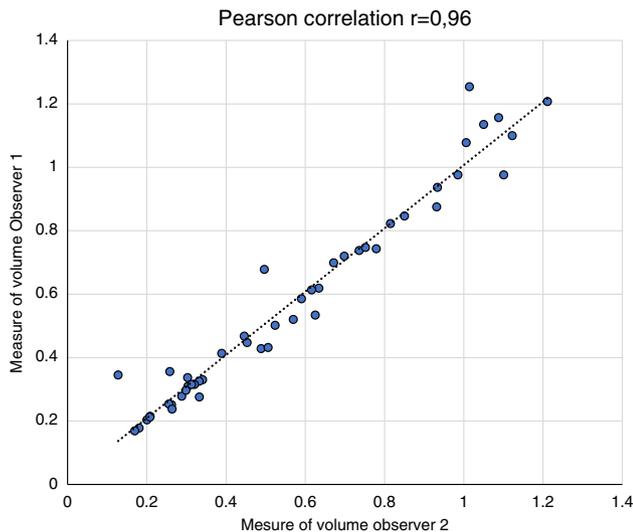


FIGURE 3. Measure of the Pearson correlation coefficient to evaluate the interobserver reliability.

DISCUSSION

Main Results

To the best of our knowledge, our series is the only one that provides a reproducible 3D evaluation of CBG for alveolar cleft reconstruction. The bone filled ratio in our series is higher than those reported in previous studies on cancellous grafts as shown in the Supplemental Table 4, Supplemental Digital Content 4, <http://links.lww.com/SCS/E368>. Whereas Touzet-Roumazeille et al¹⁴ found BFR of 61.89%, most recent studies have reported BFR <50%.^{13,15,16} Some of the earlier studies that performed 3D evaluation of alveolar grafts found higher BFR.^{12,17}

The CV in our series is consistent with that reported in other studies in patients with UCLA and UCLP. The CV values for BCLP patients varies widely in previous studies. Oberoi et al¹² reported CV of only 0.82 cm³ for both sides combined, whereas Denny¹⁷ found a much larger mean CV of 1.68 cm³ for both sides. Difference between studies can be explained by age differences between the populations studied or by differences in the definition of the CV. In addition, the measurements depend on the method used for assessment.

The 3-dimensional Assessment Method

Alveolar bone graft integration was earlier evaluated by 2D radiography on Bergland scale or Chelsea scale.¹⁸ After development of the 3D assessment method, several authors¹⁹ Some authors²⁰ reported a high resorption rate (49%–50%) of iliac crest bone graft for secondary alveolar bone grafting. Cone-beam computed tomography or MSCT imaging permits calculation of CV (or bone defect), BV, dimensions of the graft, BFR (or augmentation ratio), resorption rate, tooth movement, and bone density. Numerous radiologic protocols have been proposed²¹ for measuring resorption, varying in terms of measurement technique, modality used (CBCT or MSCT), assessment criteria, and examination schedules. The variety of methods used and parameters assessed can make comparison between studies difficult.

The measurement can be processed manually (segmentation process)^{12,13} or through a semiautomatic process.^{22,23} Semiautomated measurement protocols reduce operator subjectivity

and save significant time, but may have limitations in asymmetric case studies (eg, BCLP) and in the integration of anatomic changes related to facial growth or dental eruption.^{23,24} The segmentation technique used in our series is the most widely used, and its reproducibility has been proved.^{21,25}

Bone filled ratio and resorption rate are the 2 most commonly used parameters to assess graft osseointegration. The resorption rate calculation requires comparison of the immediate postoperative 3D images with follow-up images. We preferred to calculate the BFR so that we could compare our results with those of previous studies and also limit the number of radiologic examinations. However, it must be noted that, compared with resorption rate, BFR tends to underestimate osteointegration of grafts. Indeed, the protocol assume that the entire volume of the cleft gap has been filled by the bone graft, but does not consider soft tissue limitations such as a lack of laxity due to presence of scar tissue. It is important to emphasize that BFR does not assess real bone resorption. It is therefore not possible to state that the use of cortical bone formwork reduces the risk of alveolar bone graft resorption; to do so it would be necessary to compare immediate postoperative 3D imaging with follow-up imaging. Most of the resorption occurs during the first year, with relative stability thereafter,¹³ The resorption takes place in both the sagittal (nasal cavity floor) and the coronal plane (vestibular wall), but the resorption kinetics remain unclear. Most studies have evaluated bone integration at 6 months or 1 year after surgery. We chose to control BV at 3 months before restarting any orthodontic treatment. Evaluation performed late should look for tooth movement (eruption of lateral incisor or canine mesialization) that could result in measurement errors due to a change in the anatomic limits used to calculate the BFR and the absence of a visible boundary between the graft and the maxillary bone.

In the present study, some bias may arise from the fact that the measurements were made by a single operator. Outlining the cleft site is relatively easy for unilateral cases but it can be complicated for bilateral cases because of the projection and rotation of premaxilla combined with maxillary contraction. In addition, the 3D images were produced on different machines (MSCT and CBCT), with the protocol (thickness of slices, voxel size) left to the radiologist's discretion. Multislice computed tomography images vary significantly in quality and resolution from CBCT images and so the results could vary with the modality used.²⁵

Graft Choice

The debate about the choice of alveolar bone graft concerns both the type of bone harvested (cortical or cancellous) and the donor site (calvaria, iliac crest, mandibular, and tibial).

Cancellous bone grafts have been traditionally preferred for their faster revascularization. It has long been accepted that the osteointegration capacity is related to the speed of revascularization of the graft. This precept is now being questioned in view of the significant resorption rate observed for these grafts.²⁶ Some authors^{7,8} proved that addition of a cortical element in the graft does not increase the risk of complications at the grafted site. Mikoya and colleagues proposed an original technique of mandibular cortical bone grafting without cancellous bone filling. Their results reinforce the idea of an osteo-inductive et osteoconductive power of membranous cortical graft with 92.6% self-erupted canine at the grafted site.

Donor site morbidity is an important issue influencing bone graft choice. Calvarial bone graft is often criticised for the theoretical risk of neurological damage and the small amount of cancellous bone available. Many authors have reported the use of the calvarial bone since Tessier et al²⁷ that was the first to

popularized this bone. Numerous studies have shown that calvarial harvesting is a safe technique in experienced hands.^{10,28–30} The relatively small amount of cancellous bone can be compensated for by using a specific tool (bone scraper.¹⁰) This tool allows the harvesting of all the diploic bone remaining in contact with the inner table of the calvaria and also allows the harvesting of thin strips of cortical bone from the surface around, which will constitute a filling material for the cortical bone formwork. Doing so whatever the calvaria thickness a good amount of bone is available. In addition, the entire cancellous bone is embedded with a bone marrow sample from the iliac bone. A certain amount of liquid is obtained exactly as it is obtained when performing a Myelogram. The trochar went through the skin to reach the iliac crest. The cortical bone is then perforated and it arrives in the cancellous area. Then the liquid is harvested by suction. The aim of this liquid is to enrich the calvarial bone adding BMP and stem cells that are particularly present in this “bony liquid”.

Although the scar is longer than for iliac harvesting, it is often better tolerated.³⁰ Some teams have described a residual palpable depression at the donor site,⁹ which can be prevented by using Beta Tricalcium phosphate granula for donor site reconstruction.³¹

A special feature of our technique is the use of osteosynthesis material to stabilize the cortical bone formwork. There is a potential risk of tooth root or germ damage and, in addition, the titanium screws could be an obstacle for tooth eruption. In 13 (27%) of our patients, the osteosynthesis material had to be removed under local anesthesia. Thus, an additional intervention was needed in children who had already undergone multiple operations. It needs to be noted that the material removal can be performed under local anesthesia in older patients.

Timing of Alveolar Bone Grafting

The optimal timing of surgery is debated. Early secondary alveolar bone grafting has been reported to produce a better outcome in terms of BFR,¹⁵ and early mechanical graft site loading through dental eruption could result in less resorption.^{15,19,32} Because of a high frequency of lateral incisor agenesis, the optimal time of alveolar bone grafting may be just before the eruption of teeth adjacent to the cleft.^{33,34} In our subgroup analysis, we did not detect significant difference between the different age-groups.

One of the interesting aspects of this study was that alveolar bone grafting was performed at different ages, and hence the number of late secondary and tertiary alveolar bone graftings. Moreover, we had to manage some previously operated alveolar cleft sites with scarred soft tissues. As expected, subgroup analysis showed significant differences in residual BV between patients with prior gingival surgery and patients without, emphasizing the importance of surrounding soft tissue quality.

The Limitations of the Study

The study has some limitations. Firstly, this work corresponds to a retrospective study and the low number of patients included is linked to a lack of data in the follow-up files. Second, the absence of a control group makes it impossible to assess the superiority of CBG over cancellous bone grafts. Third, all measurements were performed by a single assessor, which exposes a bias in the measurements although the technique used has been validated by previous studies. This study, like many current studies, is based on the measurement of residual BVs. However, as soon as an alveolar graft allows the eruption of teeth or the placement of an implant while ensuring the closure of the bucco-nasal fistula, it should be considered a success.

CONCLUSION

The use of Calvarial bone graft for the reconstruction of alveolar clefts seems to be a serious alternative to the use of cancellous bone grafts for alveolar cleft reconstruction. The results of this study highlight the importance of the quality of the surrounding soft tissue on the osseointegration of the bone graft. It would be interesting to study the impact of the use of a cortical calvarial bone graft on tooth eruption and prosthetic rehabilitation in cases of lateral incisor agenesis.

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