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ORIGINAL ARTICLE • SPINE - BIOMATERIALS

Clinical and radiographic evaluation of bioactive glass in posterior cervical and lumbar spinal fusion

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Abstract

Introduction Spinal surgery of degenerative painful segments is a valuable treatment option in the management of chronic cervical and low back pain. The surgery consists in stabilizing and fusing painful vertebral segment(s). The objective of the study was to report our experience with 45S5 bioactive glass (BAG) to obtain inter-vertebral fusion in the context of posterior spine surgery.

Material and method In this retrospective study, 30 patients with a wide range of degenerative and traumatic conditions of the cervical or lumbar spine underwent spinal fusion utilizing a synthetic bone graft substitute of BAG (GlassBone™, Noraker, Lyon-Villeurbanne, France). The pain was evaluated by VAS score, and graft consolidation was assessed on according radiographic images at 1-year post-op.

Results All patients underwent posterior spinal fusion either in the cervical or the thoraco-lumbar spine. Multi-level fusions represented the majority of the cohort (43% of patients with more than seven levels treated). Radiographic imaging demonstrated excellent fusion rates (93%) at final follow-up, equivalent to the outcomes reported in the literature for autogenous bone, with excellent bone bridging and no spinal implant loosening. Only two cases of non-union were encountered. Additionally, 90% of the patients demonstrated recovery at 1 year after surgery with a pain reduction of 60%.

Conclusion The results of this retrospective study suggest that the 45S5 BAG may be an interesting alternative option to autologous graft, in terms of safety and bone fusion efficiency.

Level of evidence IV Retrospective study

Keywords Spinal surgery · Bone graft · Bioactive glass · Spinal fusion

Introduction

Cervical or low back pain represents the second leading cause of office visit, after respiratory infections, and the third leading cause of disability between the age of 45 and 65. Overall, 80% of the population experiences one or more episodes of back pain at some point in their life [1, 2]. Spinal fusion is commonly performed when treating degenerative, traumatic and scoliotic conditions. The surgery consists in joining two or more vertebrae into one single structure. The goal is to stabilize and fuse painful vertebral segment(s), reducing back pain. Although it is a subject of debate in the community, most surgeons consider that a successful outcome of fusion is characterized by a solid bridge of bone across the spinal segment instrumented.

Bone graft material can be taken from the patient's iliac crest (autograft bone) during the spine fusion surgery, harvested from cadaver bone (allograft bone), or manufactured (synthetic bone graft substitute). Autogenous bone graft is still considered as the gold standard for spinal fusion with confirmed effectiveness for more than 50 years [3]. The effectiveness of autogenous bone is generally attributed to two inherent properties: osteoconduction, as autogenous bone gives the adequate biological environment for new bone to grow; and osteoinduction, which is the ability to promote bone formation at a site where bone formation does not "naturally" occur. The harvested bone graft provides both a physical support for bone ingrowth and a biological reservoir of osteogenic cells, growth factors, cytokines and other naturally present substances that induce bone formation.

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However, graft harvested on the iliac crest (primary source of autologous bone) may lead to site morbidity such as increased blood loss and operative time, and post-surgery residual chronic pain, infection, fracture, loss of sensation or haematoma [4–6]. Alternative bone substitutes can be used to replace autograft, such as allograft or synthetic bone substitute, which are known to be osteoconductive. However, in the synthetic category, only bioactive glasses can potentially match the osteoinductive properties of autogenous bone due to their osteostimulative properties [7–9]. The latter is given by the ability of bioactive glasses to resorb, delivering silicic acid, calcium and phosphate ions to the surrounding osteoprogenetic cells, due to their very unique structure. Soluble silicate has notably demonstrated its role in up-regulating collagen synthesis [8, 9], osteoblastic metabolism [10], promoting osteoinductive gene expression, which in turns translates into faster bone formation. [9–11].

A comparative study of 45S5 bioactive glass (in wt %, 45% SiO_2, 24.5% CaO, 24.5% Na_2O and 6.0% P_2O_5, Particle size: 90 to 710 µm) versus iliac crest autograft for spinal fusion in adolescent idiopathic scoliosis has already been reported with a group of 88 patients. The results showed fewer infections and fewer mechanical failures in the bioactive glass group. [16] While this study was an elegant proof of concept, the efficacy of 45S5 bioactive glass remains to be proven with other indications. To our knowledge, this retrospective study is the first clinical report on utilization of bioactive glass in posterior spinal surgery for various conditions (degenerative, trauma, deformities, cervical disorders, etc.) in an adult population. The primary outcome was the graft consolidation after 1-year post-surgery with radiographic imaging. The pain was also evaluated with patients who have completed the visual analogue scale (VAS) score before and after the surgery. Complications were also recorded (general, infectious, neurological and mechanical).

It was hypothesized that 45S5 bioactive glass could be an alternative to autogenous bone with comparable fusion rates than the other bone substitutes for any indication in spine fusion.

Materials and methods

Research protocols

Medical records were reviewed for all patients consecutively treated with GlassBone™ (45S5 bioactive glass (BAG) with a particle size from 1 to 3 mm manufactured by Noraker, France) from January 2015 to October 2015 and confirmed from operating room records. Patients were operated for degenerative diseases, trauma or spinal deformities in the lumbar or cervical spine. All patients that underwent posterior fusion needed instrumentation. Indications for surgery are summarized in Table 1 for all patients. Demographic data, co-morbidities, pre- and post-operative pain levels and neurological status were recorded. Operative data included location and quantity of graft, intraoperative complications, blood loss and duration of operation. Pre- and post-operative data included clinical evaluation (pain evaluation, presence of complication), CT scans with sagittal and coronal reconstructions, at 6 and 12 months.

Table 1 Demographic data and indications for posterior spinal fusion for 30 patients from 22 to 85 years old (mean 63 years old)

Entry	Value (*n*)	Percentage (%)
Demographic		
Male	11	37
Female	19	63
Indication for spinal fusion		
Trauma	5	17
Degenerative	16	53
Deformity	6	20
Cervical spine	3	10
Number of levels		
1 or 2	5	17
3 to 6	12	40
> 6	13	13
Nicotine use		
Smoker	3	10
Non-smoker	27	90

Surgical technique

All patients from January to October 2015 with indications for a posterior spinal fusion procedure were operated by the author and consecutively included in the study. Appropriate decompressive surgery was performed as the clinical pathology dictated, with subsequent fixation using posterior instrumentation as appropriate. The blister packaging was opened in sterile conditions, and at the time of the surgery, the 45S5 BAG granules were then put in a stainless steel sterile container to be moistened with saline serum and mixed with local autologous bone at a 50:50 volume ratio (see Fig. 1).

The composite mixture was used for the posterior fusion and after adequate decortication, placed between adjacent facets and lamina along all the constructs (Fig. 1b to e). A drain was placed, and the wound was closed in a standard way.

Results

Thirty patients have been enroled in the study. Average age at the time of surgery was 63 years old (22 to 85 years old, 11 males, 19 females). Five patients underwent one or two

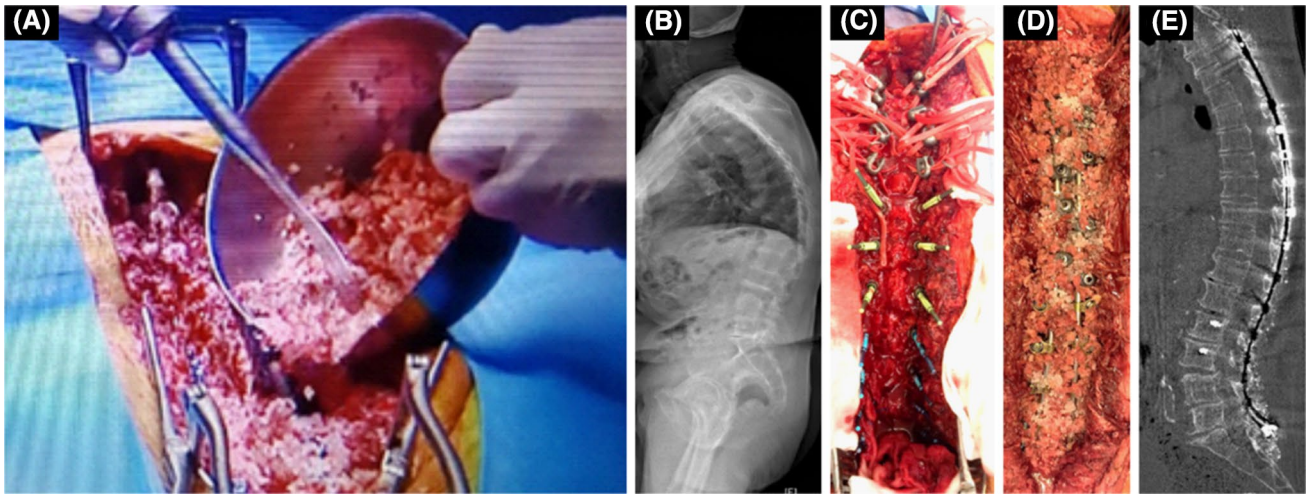

Fig. 1 **a** Mix of GlassBone with local autologous bone and saline serum place on the decorticated posterior elements of the spine; followed by an illustration of the surgery steps where a long instrumentation to treat thoraco-lumbar spinal deformity with sagittal imbalance. The composite bone graft/autologous bone was placed along the construct from T3 to pelvis. **b** Pre-operation X-ray; **c** positioning of the instrumentation; **d** composite placed between facets and lamina; and **e** post-operation X-ray

Table 2 Operative data recorded during surgery given with their standard deviation

# of levels (*n*)	# of patients (*n*)	Graft volume (cc)	Blood loss (mL)	Surgical time (min)
1 or 2	5 (17%)	12.4 ± 3.5	368 ± 181	182 ± 53
3 to 6	12 (40%)	15.1 ± 6.2	654 ± 496	174 ± 68
> 6	13 (43%)	22.2 ± 8.0	1112 ± 597	259 ± 62

levels fusions, 12 patients underwent three to six levels fusions, and 12 patients underwent more than seven levels fusion. Two patients were smokers (Table 1).

Operative data, such as the duration of operation, blood loss and GlassBone™ volume, are highly dependent of the number of levels treated, as shown in Table 2.

After surgery, four complications and one death were reported (see Table 3): 1 mechanical complication (3.8%), 3 infections after surgery (staphylococcus, 10%). There are no serious adverse events relating specifically to the use of 45S5 BAG. These four patients were re-operated successfully (graft consolidation and patient recovery).

For cervical procedures (three patients, one or two levels), fusion was evaluated using CT scans at 6 and 12-months post-surgery (case report Fig. 2). Fusion was acquired for one patient (33%) and is in good progress for two patients (67%). No patient showed average fusion nor pseudarthrosis. After few months, one patient died (for cardiac event) and the two other patients, who were in good progress, acquired complete fusion 1 year after surgery. Patient recovery is good for the two patients (100%) (Table 4).

For lumbar procedures (27 patients, two to ten levels), fusion was evaluated using CT scans at a minimum of 12-month post-op (Figs. 3 and 4). Fusion was acquired for 22 patients (82%) and in good progress for three patients

Table 3 Details of the type of complications encountered post-surgery

Complication	# of patient	Percentage (%)
General	0	0.0
Mechanical	1	3.3
Infection	3	10.0
Neurological	0	0.0
Mortality	1	3.3
Total	5	16.7

(11%) (Table 4). Two patients presented with pseudarthrosis (7%). These patients exhibited material failure after operation, necessitating the replacement of the hardware because of persistent pain. After the revisions, residual pain was not significant. Recovery was observed for all patients except for two patients. (7%: Two described above with pseudarthrosis, one of whom CT scans demonstrated a good bone consolidation, and one of whom where the pain experienced did not seem to be linked with the surgery.)

VAS scores were collected preoperatively and postoperatively at 1 year for 20 patients. One-year post-surgery

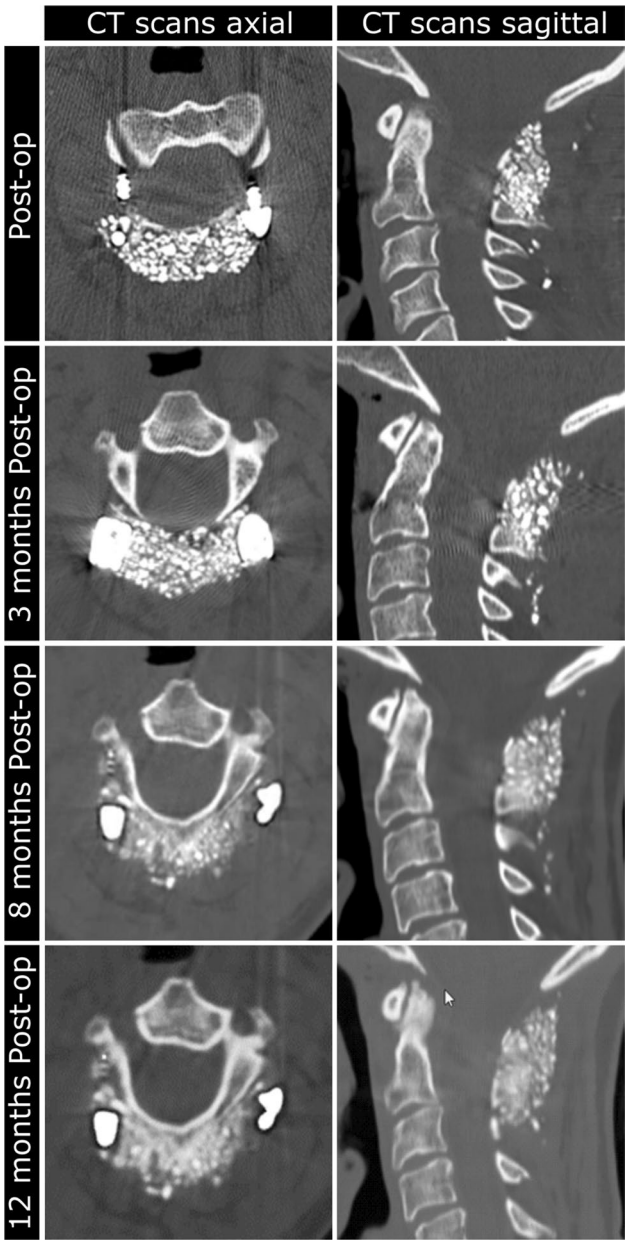

Fig. 2 Post-surgery CT scans of laminectomy with C1–C2 posterior fusion using a mixed of local bone and GlassBone

Table 4 Graft consolidation for 29 patients. One patient was excluded for this study (see Table 3)

Graft consolidation	12 m post-op cervical (*n*)	1 y post-op for T-L-S (*n*)
Acquired	2 (100%)	22 (82%)
In progress	0	3 (11%)
Pseudarthrosis	0	2 (7%)
Mediocre	0	0

T-L-S thoraco-lumbar-sacral

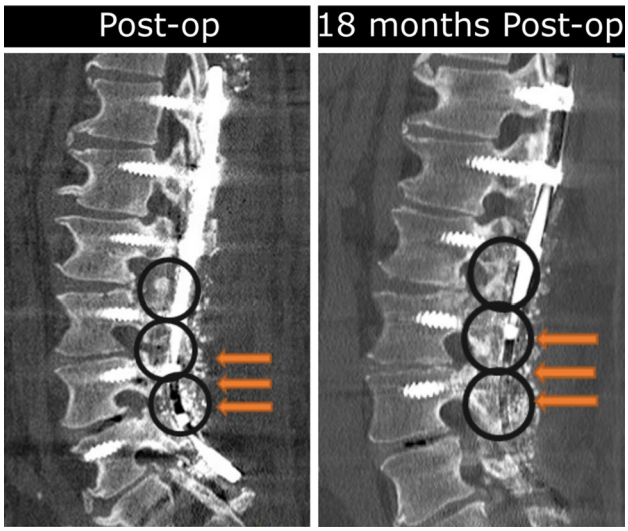

Fig. 3 Granules of bioactive glass are well-visible (orange arrow) immediately just after operation, and gap between posterior arches is visible (black circle). After 18 months, granules are less visible, and a bone bridging has formed with remodelling of the graft (color figure online)

pain decreased by 60% according to the score. The mean pre-operative score was 7.5 [4–10], and the mean post-operative score was 3 [0–7].

Case report (see Fig. 2)

This case consisted of a 47-year-old female, with major osteophytic arthritis at C1–C2 joint, confirmed by CT scan. She is a smoker with a 50 packs a year history.

The patient underwent posterior C1–C2 laminectomy with posterior fusion. Bone substitute GlassBone (16 cc) was mixed with patient's local bone and then placed between C1 and C2 posterior arches.

As early as 3-month post-op, cervical pain decreased by 80%. CT scans demonstrated early fusion with formation of a bone bridge between posteral C1 and C2 vertebras.

At 8- and 12-month post-op, a bone bridge of excellent quality was observed with a decreasing of the radio-opacity of GlassBone granules and progressive creation of a bony bridge. No complication was reported.

Discussion

The ideal bone graft substitute should be osteoconductive and osteoinductive potential similar to autologous graft. It would also need to be readily available, easy to apply, cost-effective and non-immunogenic, with no risk of viral or bacterial contamination [12]. 45S5 BAG is a synthetic bone graft that supports bone formation with its osteoconductive

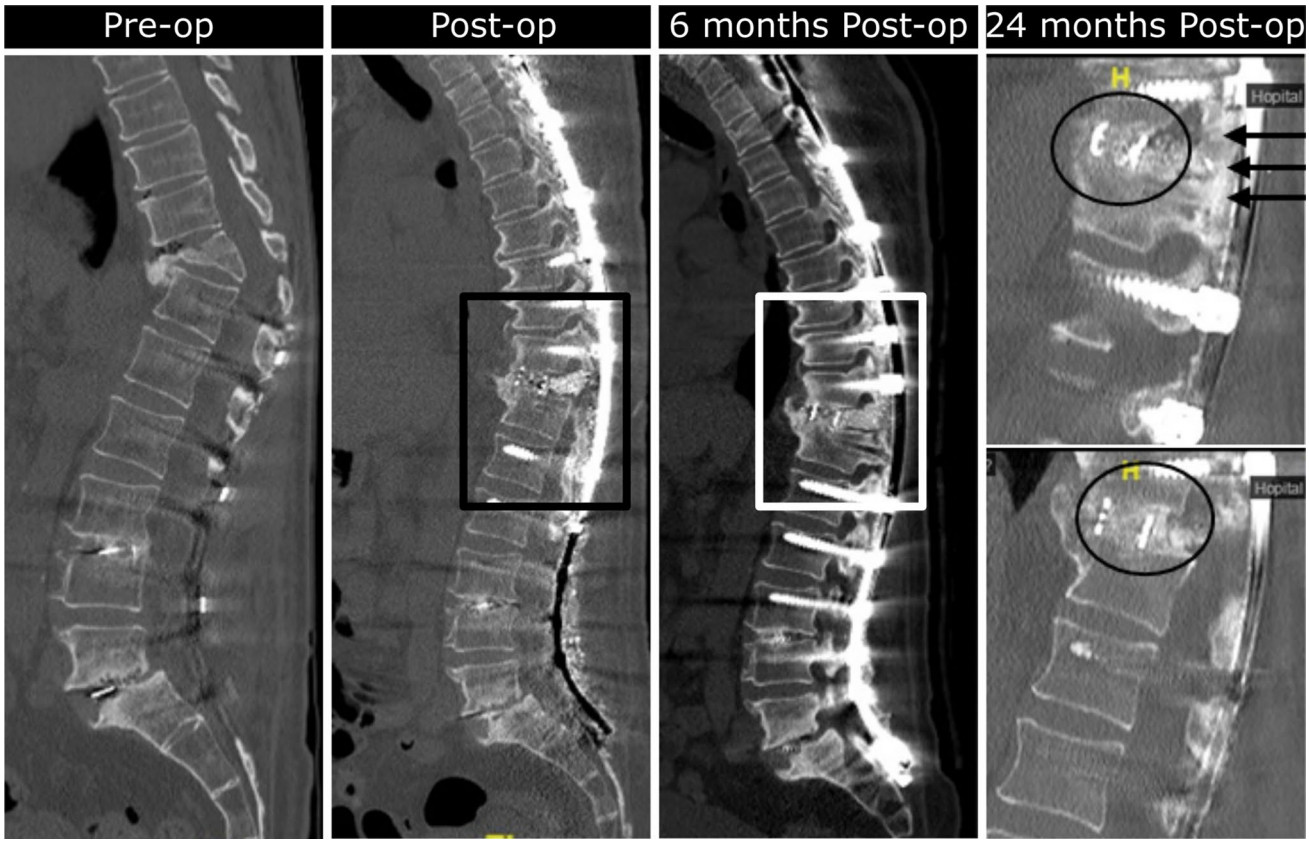

Fig. 4 Patient was operated by VCR (vertebral column resection) to treat PJK (proximal junctional kyphosis). The granules are visible immediately after surgery along the instrumentation. At 2 years after surgery, a bone bridging is clearly visible inside the vertebral cage and through the disc space

properties, while also being osteostimulative, showing higher osteoblastic activity than with calcium–phosphate ceramics [7–11]. In animal studies, mix of autograft and 45S5 BAG produced results comparable to those of autograft alone for non-healing calvarial defects and spinal fusion [13, 14]. This synthetic bone graft therefore presents characteristic close to an ideal bone graft.

To our knowledge, this is the first clinical report on utilization of 45S5 BAG in posterior spinal surgery for various conditions (degenerative, trauma, deformities, cervical disorders) in an adult population. The only adult study was reported by Frantzen et al. but in a strict indication (degenerative spondylolisthesis) using another bioactive glass composition with a higher silica content than 45S5 BAG (53.9 versus 46.1 mol % for 45S5), which in turn could potentially translate into a lower bioactivity and a lack of long-term resorption [15, 26].

The use of 45S5 BAG, with a particle size ranging from 90 to 710 µm, has been clinically reported for spine surgery [16–18]. Ilharreborde et al. and Ameri et al. reported separate studies of multi-level spinal fusion in adolescent patient suffering from idiopathic scoliosis. Complete fusion was observed 32-month post-surgery with 45S5 BAG used alone in both cases (no local autologous bone used). Seddighi et al. reported the anterior fusion of cervical spine in patients with degenerative cervical disc disease using PEEK cages filled with 45S5 BAG and autologous bone harvested locally during discectomy. A rate of spine fusion of 91.3% for single level and 80% for multi-level was observed after 6 months.

Even though the present report is looking at a larger particle size range of 45S5 BAG, above 1 mm, rate of fusion at 1 year was in between these reported for the idiopathic scoliosis, 32-month post-surgery and the anterior fusion of cervical spine, 6-month post-surgery. CT imaging provided objective confirmation that good clinical outcome was achieved, with evidence of good fusion by bridging bone (93% of bone fusion) and no sign of spinal implant loosening. In addition, fusion rates reported here are comparable with reports evaluating instrumented lumbar fusions using autologous graft, with fusion rates between 40 to 90% [19–23]. It is noteworthy to mention that the success rate for fusion above seven levels (46% of the patient treated) was high, with regard to conventional methods of treatment [24].

Two patients suffered from post-surgical infection (7.6%), rate in agreement with the literature, and were successfully re-operated [25].

Despite the fact that this cohort is retrospective, including a limited number of patients with a wide range of degenerative and traumatic conditions of the cervical and lumbar spine, conclusion can be drawn, with regard to the literature, with the following claims: (1) the particle size of 45S5 BAG when above 90 µm has little effect on the rate of fusion and that it is solely due to the inherent property of the glass; (2) the rate of fusion using 45S5 BAG is independent to the indication, if the site is free of pathogen prior to surgery.

Additional prospective studies are needed to confirm these preliminary findings, but our findings are encouraging for use of bioactive glass in posterior spinal fusion.

Conclusion

This study confirms that the use of 45S5 BAG mixed with local autograft represents, potentially, an alternative to autologous graft harvested in the iliac crest region, or other bone substitutes that are solely osteoconductive for posterior spinal fusion. No changes were required to the standard surgical techniques, and results at 6 and 12 months from the treatment of degenerative or trauma spine disorders were highly encouraging, with respect to pain, neurological status and function. At 12-month follow-up, high levels of bony fusion using 45S5 BAG were observed, in combination with various surgical spinal techniques. Imaging results supported clinical pictures of solid fusions. Additional prospective studies are ongoing to confirm these preliminary results.

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Compliance with ethical standards

Conflict of interest The author would like to declare a conflict of interest as he is a consultant for Noraker.

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