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ORIGINAL ARTICLE OCULOPLASTIC

Orbital Fat Injection: Technique and 5-Year Follow-Up

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Abstract

Background Orbital volume loss, early or late, is common after placement of an orbital implant or dermis fat graft, and there is currently no satisfactory long-lasting solution. Hyaluronic fillers are relatively easy to administer but are prone to migration and are temporary. Cannula-based orbital fat grafting has not gained the status of standard of care because of perceived low likelihood of success in the near term. This paper describes a technique for fat volume augmentation, its rationale, long-term follow-up, and a description of a complication unique to fat grafting in the orbit.

Methods Ten consecutive subjects with acquired anophthalmic enophthalmos were enrolled in two IRB (institutional review board)-approved protocols (10.27 and 12.01) undergoing a single session of autologous fat grafting to the orbit using a closed blunt cannula technique. Preoperative photography and non-contrast MRIs (magnetic resonance imaging) were obtained prior, immediately after, and at 1 year after injection. Yearly postoperative photography was performed on subjects with successful results.

Results Three of five subjects in IRB 10.27 clearly showed a clinically apparent increase in orbital volume at 1 year. One subject who failed to show improvement also sustained inadvertent injection into three extraocular muscles; she subsequently volunteered to enter IRB 12.01. Three of five subjects in IRB 12.01 did benefit, showing volume increase at 1 year, including the subject who had experienced intramuscular injection in 10.27. One subject in IRB 12.01 was lost to follow-up. Of the total of ten subjects enrolled, three showed no improvement and one was lost to follow-up; six subjects showed volume improvement at 1 year with two retaining the correction at 5 years and four showing variable diminution over 2–5 years. With the exception of the subject who sustained injection into extraocular muscles, none experienced complications.

Conclusion A modified technique is recommended for orbital fat injection distinct from methods used elsewhere in the body. Theoretical limits of volumetric enhancement temper expectations in orbital fat grafting and should inform surgical planning. Cannula-based orbital fat grafting can be done safely and result in a gain of orbital fat volume at 1 year and in some cases up to 5 years.

Level of Evidence IV This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Orbital atrophy · Fat grafting · Anophthalmos · Complication · Longevity

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Introduction

Orbital volume loss is common after placement of an integrated orbital implant or dermis fat graft. Non-integrated implants such as Pyrex beads [1], silicone spheres or plates, and hydrogel pellets [2] are subject to migration and require open surgery, as do fixated implants; soft tissue fillers are temporary and can be subjected to migration as well as tissue reaction [3]. Successful and long-lasting cannula-based orbital autologous fat augmentation could avoid these limitations.

Smith and Petrelli [4] introduced the dermis fat graft for orbital volume enhancement in 1978, and variations of this approach have been published over the years [5]. Illouz [6, 7] pioneered blunt cannula lipo-harvesting and grafting beginning in 1977, and innovations by Coleman [8] and Amar [9] improved outcomes and morbidity for blunt cannula autologous facial fat grafting and as a general technique.

Whereas dermis fat graft survival depends on the reperfusion of a preexisting intact capillary network by extraocular muscle arterioles, survival of injected fat requires anchoring and neovascularization of micro-aggregated cells that depend on "nutrient diffusion" until vascularization is re-established. As a free graft, injected fat ideally should be evenly distributed three-dimensionally within a tissue bed, in a pattern that maximizes cell survival. Whole tissue grafts (advancement, pedicled, etc.) are planned by matching surface areas on a one-to-one ratio; volumetric grafting with micro-aggregated cells must be in some reduced fractional proportion to the volume of the recipient tissue bed.

The purpose of this study was to demonstrate the safety, efficacy, and longevity of orbital fat grafting in a series of ten consecutive subjects: five with and five without platelet-rich plasma (PRP).

Of ten consecutive cases enrolled in this prospective study, one was lost to follow-up, six had positive results of at least one year (Tables 1, 2), and one sustained a complication. Five cases are shown to illustrate.

Materials and Methods

Institutional Review Board (IRB) 10.27: Autologous Fat Augmentation of Orbital Volume Using a Closed Cannula Technique and IRB 12.01: Augmentation of Orbital Volume with Autologous Fat and Platelet Rich Plasma (PRP) enrolled ten consecutive patients (five each) with acquired anophthalmic enophthalmos. Informed consent complied with Helsinki protocols. In all cases, persistent volume deficits prompted the referral to this study after their prosthetic shells had been optimized by the subjects' ocularist prior to enrollment. Each patient underwent non-contrast MRI (magnetic resonance imaging) [Philips (Best, Netherlands) Achieva Integra Quasar Dual 3 Tesla] of the orbits before, immediately after, and at least 1 year after fat injection. Standardized medical studio photography was done pre-injection for all study subjects and yearly thereafter for successful cases. Success was defined by the visible appearance of volume enhancement at 1 year. Each subject underwent a single intra-orbital injection session by the author after standard hand lipo-harvesting and centrifugation at 3000 rpm for 3 min. No local anesthesia was used in the orbit. After centrifugation and decantation, a net of 4–6 cc of fat was then divided among four-six 1.0 cc Luer Lok syringes for injection and then injected depending on correction objectives. For subjects in protocol 12.01, ten cc of blood was drawn and processed to obtain platelet-rich plasma using a Selphyl kit provided by Aesthetic Factors (Wayne, NJ). The ratio of PRP to harvested fat mixed immediately prior to injection was 1:3, producing a thickening of the combination and representing 3/4 cc of actual fat in each 1 cc syringe.

Injection Technique

A small conjunctival bleb (0.1–0.2 cc) was created in the infero-temporal fornix using 1% lidocaine with epinephrine 1:100,000. A sharp awl was used to create a puncture through the conjunctival bleb to allow access to the orbital space with a curved cannula (18 g with an 80 degree angle and a working length of 35 mm) attached to a 1 cc Luer Lok syringe loaded with fat. I.V. sedation was increased for the orbital injection. From the infero-lateral quadrant, the tip of the cannula was maneuvered from lateral to medial, working inferior, medial, posterior, and superiorly around the orbit, injecting with each withdrawal within and without the cone, exchanging 1.0 cc fat-loaded syringes while leaving the cannula in the orbit to minimize trauma. When present, attempts were made to seed established dermis fat grafts. No pre-septal fat was placed. Each 1 cc of fat was distributed using 3–4 passes per syringe. A soft eye patch was placed, and the patient was discharged under ambulatory protocol.

Table 1 IRB 10.27

Case	1	2	3	4[a]	5
Age	63	69	57	59	60
Status	Phthisis OD	IOI OD	DFG OD	DFG OS	Phthisis OS
Injection	6 cc fat	5 cc fat	4 cc fat	4 cc fat	5 cc fat
Longevity (years)	$2 > x < 5$	5+	$2 > x < 3$	0	0

DFG dermis fat graft, *IOI* integrated orbital implant

[a]Cases 4 and 10 are the same subject who was 1 year older at the time of her second procedure

Table 2 IRB 12.01

Case	6[b]	7	8	9	10[a]
Age	67	51	56	64	60
Status	Phthisis OD	Phthisis OD	IOI OS	SS OD	DFG OS
Injection	5 cc fat + PRP	5 cc fat + PRP	5 cc fat + PRP 5	5 cc fat + PRP	5 cc fat + PRP
Longevity (years)	0	$2 > x < 5$	0	5+	$2 < x > 3$

DFG dermis fat graft, *IOI* integrated orbital implant, *SS* silicone sphere

[a]Cases 4 and 10 are the same subject who was 1 year older at the time of her second procedure

[b]Lost to follow-up before 1 year

Postoperative Care

IV Ancef 1 Gm was infused intra-operatively and oral antibiotics continued for 5 days post-injection. Oral non-narcotic analgesia was sometimes used for the first 24–48 h. The prosthetic shell was left out for a minimum of 2 weeks after injection, after which a thin temporary shell was used until 6 weeks post-injection when a new permanent shell was made.

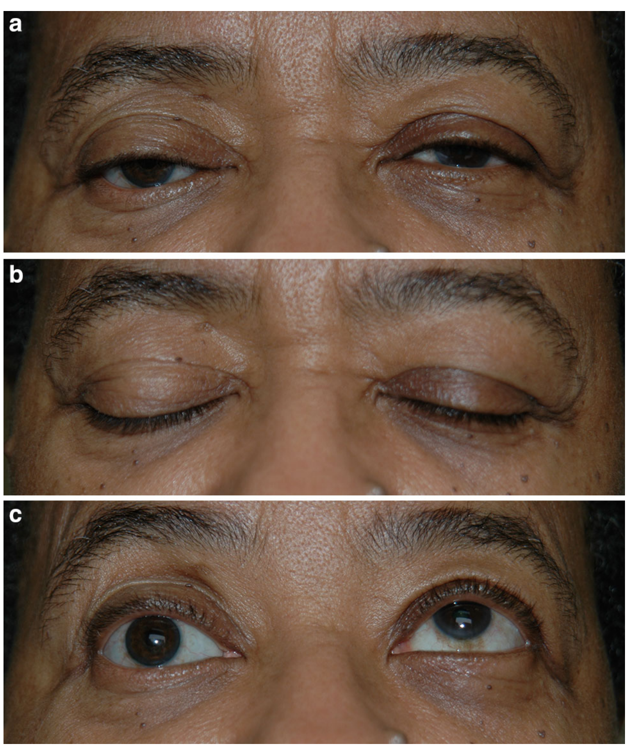

Fig. 1 Pre-injection in primary gaze (**a**), eyelid closure (**b**) with loss of right upper lid fold. Upgaze best shows the superior sulcus volume deficit (**c**)

Results

In all ten cases enrolled, injections were performed uneventfully, except as reported in case #4, with no oil cysts or hemorrhage present on post-injection MRIs. Cases with positive results are shown, with case #4 showing the only complication encountered.

IRB 10.27

Case #2 (Fig. 1a–c) is a 69-year-old woman with an integrated orbital implant on the right, loss of superior eyelid

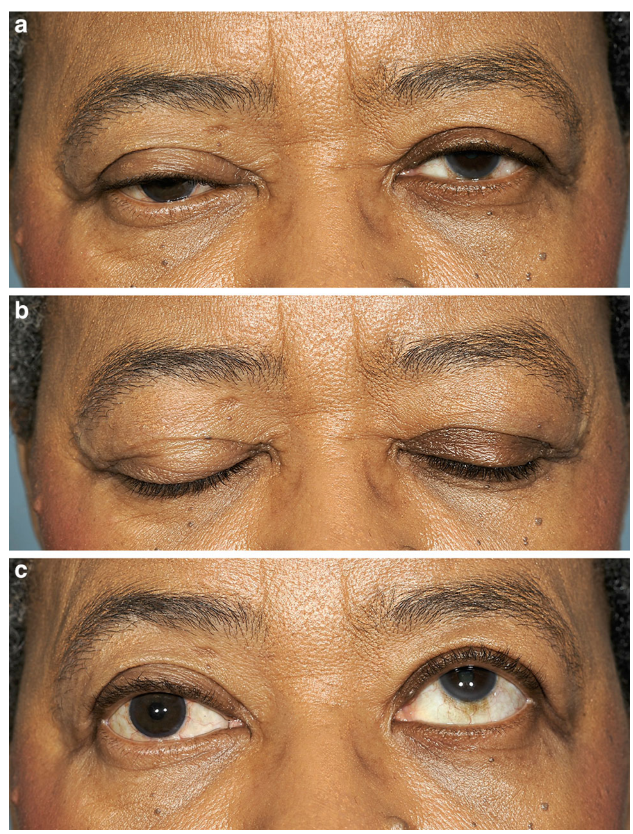

Fig. 2 Two years post-injection of 5 cc in **a** primary, **b** closure, and **c** upgaze

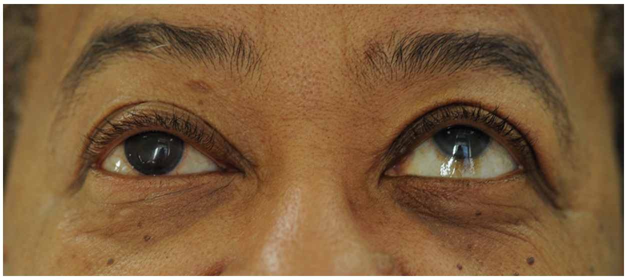

Fig. 3 Preservation of superior sulcus correction at 5 years

volume and ptosis. Her volume deficit is best appreciated in ungaze as shown in Fig. 1c. Figure 2a–c shows volume correction 2 years after she underwent injection of 5 cc of fat, and Fig. 3 shows maintenance of volume at 5 years in upgaze when compared with Fig. 1c.

Case #4 (Figs. 4a, b, 5, 6, 7) is a 58-year-old woman who underwent enucleation of her left eye for rubeotic glaucoma related to Von Hippel-Lindau syndrome with placement of a silicone sphere in 1978, followed by removal of the sphere and placement of a dermis fat graft in 1982. In 1987, a stacked silicone plate was placed to compensate for progressive fat atrophy, after which subsequent serial enlargements of her prosthetic shell were used for volume enhancement.

Injection of the orbit was difficult because of increased scarring and the presence of the silicone block. Her dermis fat graft was encapsulated and impervious to cannula seeding. After starting the injection from the infero-temporal approach, working around the dermis fat graft, the silicone block prevented access to the anterior-medial orbit. A second access was created medially just above the level of the medial rectus to complete the injection of 4 ccs. The cannula passes through the medial access were constrained by the silicone plates and the encapsulated dermis fat graft, which behaved much like a retained globe, limiting the cannula motions through the medial access to a more anterior–posterior direction.

The patient reported considerable orbital pain upon awakening from sedation and required overnight pain management with intravenous narcotics and anti-emetics. She was discharged to home the following morning with oral narcotic analgesia and NSAIDS for another 7 days, followed by NSAIDS alone for 3–4 weeks. Figure 6 is a coronal cut of her pre-injection MRI. The immediate (within 24 h) post-injection MRI showed fresh fat deposition in the medial rectus, superior rectus and superior oblique muscles (Fig. 7) that was still present on MRI 1 year post-injection. Her 1-year clinical result was disappointing, showing no visible volume improvement. Pre-injection is shown in Fig. 4a, b. One year post-injection is shown in Fig. 5a and b.

IRB 12.01

Case #7 is a 51-year-old woman with a phthisical globe from prior injury in Fig. 8a, b who underwent injection of 5 cc of 1:3 PRP to fat. She is shown in Fig. 9a, b at 1 year with full correction of her deficit and in Fig. 10a, b at 2 years after injection with maintained symmetry, and at 5 years Fig. 11a, b with some volume diminution.

Fig. 4 Deep superior sulcus volume deficit on the left in **a** primary and **b** closure with lagophthalmos

Fig. 5 **a**, **b** One year post-injection of 5 cc. No apparent improvement

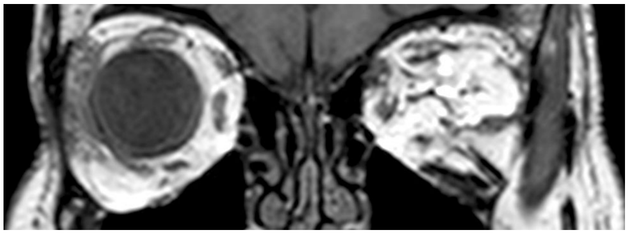

Fig. 6 Pre-injection MRI showing silicone plates and encapsulated dermis fat graft

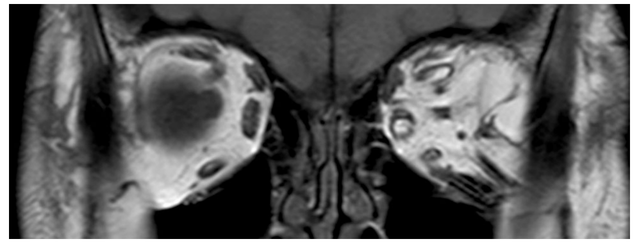

Fig. 7 Immediate post-injection MRI showing fat density within the medial rectus, superior rectus and superior oblique

Case #9 is a 64-year-old man with right orbital volume deficiency and cicatricial entropion after traumatic enucleation with a migrated silicone sphere that is fixed in the anterior-inferior-lateral orbit (Fig. 12a, b). He received 5 cc of 1:3 PRP to fat. He is shown in Fig. 13a, b at 1 year, and Fig. 14a, b at 5 years post injection. The improvement in his volume correction most apparent in upgaze is shown in Fig. 15a, b.

Case #10 is, despite the complication of painful extraocular muscle injection from her first orbital fat injection, the woman of case # 4 in 10.27 who is volunteered to enter protocol 12.01. She underwent uneventful injection of 5 cc fat + PRP with 2-year result as shown in Fig. 16a, b after which her result started to fade at 3 years. She exited the study after sustaining orbital trauma necessitating removal of her silicone plates.

Consecutive results for IRB 10.27 and 12.01 are shown in Tables 1 and 2, where 0 equals no improvement at 1 year. The expression $2 > x < 3$ or $2 > x < 5$ means that the full improvement at 1 year was still present at 2 years but slowly faded to minimally present or absent at three or 5 years as illustrated in Case 7.

Discussion

Acquired enophthalmos ensues from a variety of causes [10, 11] that have been traditionally ascribed to three categories: structural abnormality, fat atrophy, and traction.

Therapeutic approaches to correct acquired anophthalmic enophthalmos have been legion, but fall into two broad categories. Reducing the inner dimensions of the boney orbital space with subperiosteal Pyrex beads, silicone beads [12], liquid silastic [13], silicone plates [14], glass wool [15], porous polyethylene implants [16], subperiosteal [17] and apical intraorbital cartilage [18], bone grafting [19], and others [20] seek to correct enophthalmos by displacing the orbital contents anteriorly. Directly injectable soft-tissue fillers, while easy to administer, are subject to migration [21, 22], tissue reaction, and are temporary [23, 24] with reports of lasting 1–1.5 years. The multitude of approaches reported over past decades carries the implication that the physiology of progressive anophthalmic enophthalmos remains poorly understood.

The first description of orbital injection of autologous fat for correction of acquired enophthalmos by Hunter and Baker [25] in 1994 used a 14-gauge needle. Using a sharpened 16-gauge cannula, Hardy [26] reported success in a retrospective review of 13 orbits engrafted (3 with second injections) with a mean follow-up of 14.5 months, but without presenting any data. Some of these cases included sighted eyes as also described by Cervelli in a single case report [27] that only included 3 months of follow-up. In the current study, a 1-year threshold as a minimum criterion of success was deemed necessary to justify an OR procedure when compared to office-injectable soft tissue fillers.

The loss of the globe would be expected to decrease orbital hemodynamics and present a challenge to cannula-based fat grafting. However, an angiographic study failed to show changes in hemodynamics after 30 weeks in a simian model of enucleation [28]. Paradoxically, the companion study [29] showed increased orbital fat in all subjects as early as 4 weeks after enucleation, a condition unknown in humans. Failing to prove a circulatory basis for post-enucleation atrophy, the authors speculated that 'redistribution of the orbital soft tissues' might be a cause. The technique of evisceration with an integrated spherical implant would seem to belie this notion. Whether relevant or not, the only procedural variation from the human condition in the study was the absence of a prosthetic shell postsurgically.

Fat grafting to the orbit using a closed cannula technique is a conceptual extension of fat grafting performed

Fig. 8 Pre-injection of 5 cc fat + PRP to the right orbit in **a** primary **b** lid closure

Fig. 9 **a**, **b** One year after injection. There is improved fullness of the upper lid and improvement in lid fold

elsewhere in the body, but has unique features that are in distinction to methods developed by Amar or Coleman. Access to the orbital space is constrained by four boney walls and often limited in the anterior approach by integrated/non-integrated spheres. The medial origin of the optic canal and annulus of Zinn within the orbit results in more crowding of the medial orbit by the optic nerve, medial rectus and the oblique muscles, while the distance between the lateral and inferior rectus muscles, the shallow valley in the anterior orbital floor lateral to the inferior optic canal, and the suspension of the globe by Lockwood's ligament make the infero-temporal quadrant the easiest point of entry. The presence of integrated orbital implants, optic nerve (when present), and extraocular muscles present obstacles to the advancement of a cannula, requiring some maneuvering. The first case reported here presents a clear indication that injection into the extraocular muscles is to be avoided because of the risk of acute, intense pain, and prolonged discomfort, while not adding meaningfully to volume enhancement. This first documented case of extraocular muscle fat injection suggests a refinement to avoid this complication.

The best way to intentionally enter a muscle is at its origin or insertion, where it is relatively fixed, and in the plane and direction of the muscle fibers [30], analogous to venipuncture. This is a characteristic of the Amar FAMI technique. Once in the orbit, passes in a generally coronal plane, maneuvering laterally to medially, superiorly and inferiorly, oblique or perpendicular to the anterior–posterior orbital axis allow the muscles and optic nerve to be displaced by a blunt-tipped cannula (Fig. 17).

Orbital fat volumes are inherently small, even more so with acquired atrophy or scarring from earlier procedures, providing a limited graft bed for seeding. MRI data [31] on normal orbital fat volume has been reported as about 20 cc (estimated by total orbit volume minus extraocular muscles and optic n). Carpeneda [32, 33] demonstrated that cannula-harvested and injected human fat autografts showed adipocyte graft survival in a subcutaneous adipose tissue bed at 60 days in a zone up to 1.5 mm from the edge of the host/graft interface. This led to a model of expected graft survival based on the width of the graft as an ideal sphere or cylinder. Adipocytes more than 1.5 mm from the tissue bed did not survive until revascularization, limiting potentially viable graft diameters to 3 mm. Even in with this theoretically optimized approach, graft survival peaked at 40%. Coleman utilized these data to create his "micro-cannulation" technique to deposit 0.1 cc spherical aliquots of fat in multiple passes, in multiple directions and layers, to help improve graft survival, with variable amounts of overcorrection. This approach is not practical in the orbit where access is limited and anatomic obstacles complicate maneuvering.

Extending Carpeneda, one could consider engrafting the orbital fat bed as a mathematical packing problem. The graft bed could be imagined as a sphere into which either smaller fat spheres or cylinders are placed, each separated

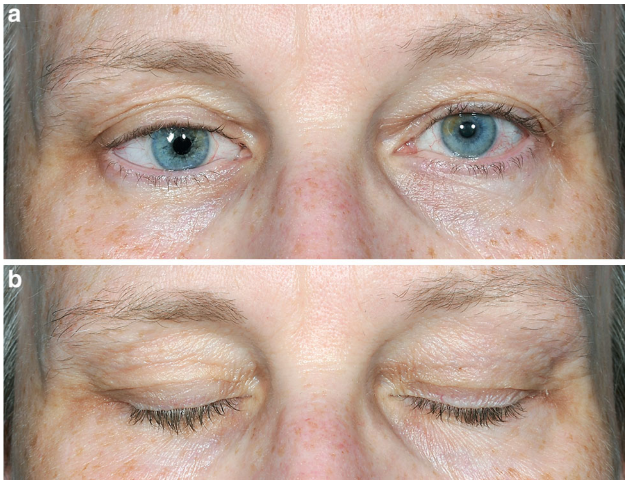

Fig. 10 **a**, **b** Two years after injection symmetrical correction is maintained

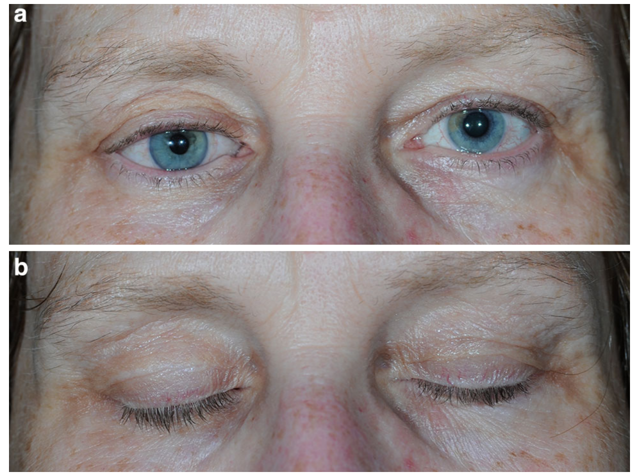

Fig. 11 Five years after injection there is some diminution of the correction in **a** primary and **b** lid closure

by some interval consistent with providing contact with a perfused tissue bed. A model can be approximated by "cylinder in the sphere" calculations. Basically, the largest cylinder (V_c) that can be contained in a sphere (V_s) of radius R is:

$$V_c = 4\pi \text{ divided by } {}^3\sqrt{3}$$

or more simply:

$$V_c = V_s \text{ divided by } \sqrt{3}.$$

For a sphere of volume 20 cc, R = 1.68, the maximum cylinder volume is 11.5 cc. Introducing separation of 2 mm between individual 2 mm diameter cylinders to provide graft bed contact reduces the total injectable cylindrical volume by 2/3, to 3.8 cc. Introducing similarly spaced smaller cylinders outside the larger cylinder but still within the sphere would be additive of about 1.6 cc making the total injected volume that can be placed, with interval spacing, into a spherical volume of 20 cc, a maximum of about 5.4 cc.

Expressing micro-aggregated fat through an 18-g cannula typically yields cylinders of 2–3 mm diameter. An injection of 5.4 cc at a 40% optimal survival rate results in net retained fat of about 2.2 cc. Biologic factors may extend the range of results (up or down), but geometric considerations alone place a theoretical upper limit on the amount of fat injected beyond which little or no benefit should be expected. Fortunately, even the retention of small amounts (1–2 cc) of fat to orbital volume can make a visible difference.

Overcorrection has been used to compensate for incomplete removal of local anesthetic, oil, blood cells, non-viable fat cells, and the empiric (but variable) 40% survival rate, but might risk fat necrosis and oil cysts in a tissue bed that must recover with only a rudimentary lymphatic endowment [34].

As with any tissue graft, success is dependent on absolute immobilization, or "anchoring", of surfaces between cells to establish microvascular connection to the graft bed. Fibrin gels have been used in plastic surgery since first described in 1915 [35], and as a tissue glue since 1944 [36] although not in wide use until platelet-rich plasma (PRP) preparations were developed in the early 1990s [37]. Platelet-rich plasma (PRP) has been used in a wide variety of therapeutic settings, both as a source of alpha-granule growth factors and as a platelet-rich fibrin matrix in cosmetic [38, 39] and reconstructive surgery [40]. Results have been variable. IRB 12.01 was initiated to seek any advantage that might improve results in a clinical situation with currently suboptimal reconstructive options; however, no increased success, either by response to injection or longevity, with PRP can be claimed in this small study. The reduced number of cells injected (as a fraction of total volume) in the PRP group is noted and may point to some increased efficiency, but there was no increase in the overall success rate.

Volume improvement at 1 year was used as a minimum requirement for success in this study as generally accepted for facial fat grafting and as a comparison to reported longevity for hyaluronic fillers. Withholding pre-septal fat injection in this study was deliberate to avoid confounding the results when the pathologic process is clearly orbital. In each protocol 3 of 5 (six of 10 total) showed volume improvement at 1 year: in 4 cases the improvement was

Fig. 12 Pre-injection of 5 cc fat + PRP to the right orbit in **a** primary and **b** closure

Fig. 13 Improvement in upper lid fullness and fold in **a** primary and **b** lid closure

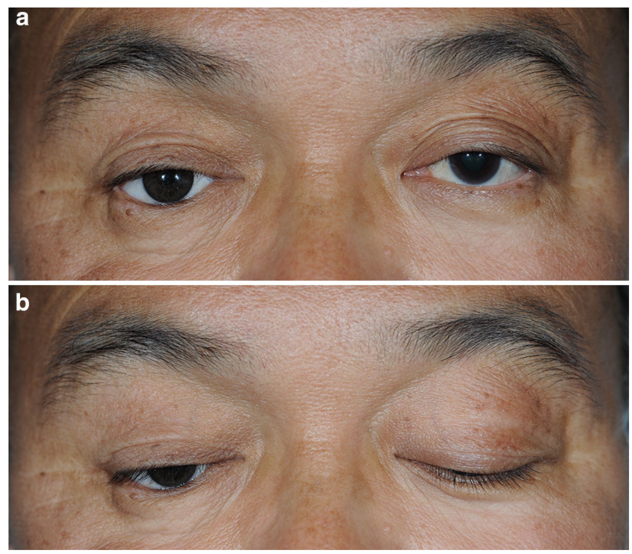

Fig. 14 **a**, **b** Five years post-injection with stable volume correction

apparent up to 5 years, and in 2 cases volume correction was maintained at 5 years. Fat grafting results, generally, are notoriously variable when compared to whole tissue grafting [41] even as the same risk factors for age, variations in graft preparation and surgical technique, smoking, general health, and recipient bed mobility contribute to resorption and failure. Consecutive subject recruitment is arguably a form of randomization, and success and failure in this study appear to be random, which implies factor(s) exist that have yet to be addressed. Immobilizing the extraocular muscles with botulinum toxin would allow better adherence to a cardinal principle of tissue grafting, possibly increasing the chances of success.

Limitations arise from the relatively small number of cases available to a single practitioner and the lack of a method to reliably measure small differences in orbital fat volumes. The available tools for quantitative measurement of volume enhancement were not practical [42] or reliable enough to capture the relatively small improvements in orbital volume seen with a single fat grafting session. As cited above, a meticulous volumetric MRI study [31] of orbital structures showed standard deviations too large to accurately measure net orbital fat graft retention (theoretically 1–2 cc) to be a useful technique for this study. Hence, the reliance on careful photography in different eyelid positions, while acknowledging the standard caveat of observer bias.

Many cases of anophthalmic enophthalmos, including some in this series, have volume deficits uncorrectable by a single orbital injection; nonetheless, cannula-based fat grafting to the orbit can be successful and long-lasting, even if optimal algorithms have yet to be developed.

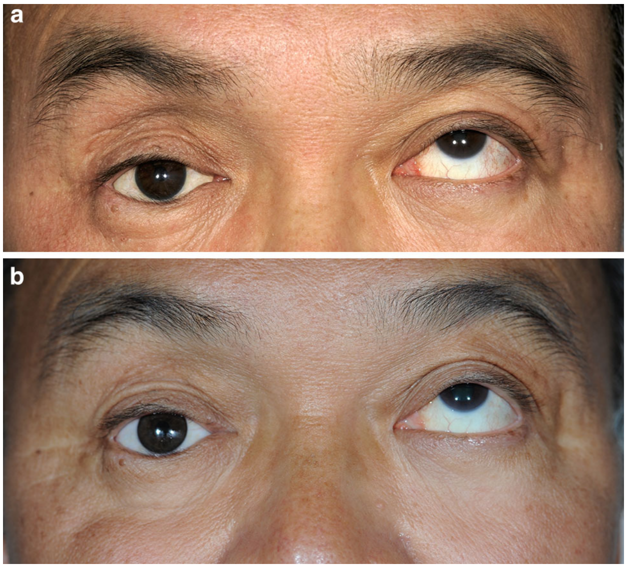

Fig. 15 Maintenance of sulcus filling five years post-injection (**b**) compared to pre-injection (**a**) in upgaze

Fig. 16 Case # 4 as Case #10 two years after second injection with fat + PRP in **a** primary and **b** lid closure. Compare to Fig. 5a, b

Conclusion

Injection of autologous fat into the orbit can be safe and effective but requires a technique adapted to the anatomy. In six cases of ten subjects, initial correction of the volume deficit was seen at 1 year, with persistence of correction of 2–5 years in four cases and maintenance of volume correction in two cases to 5 years.

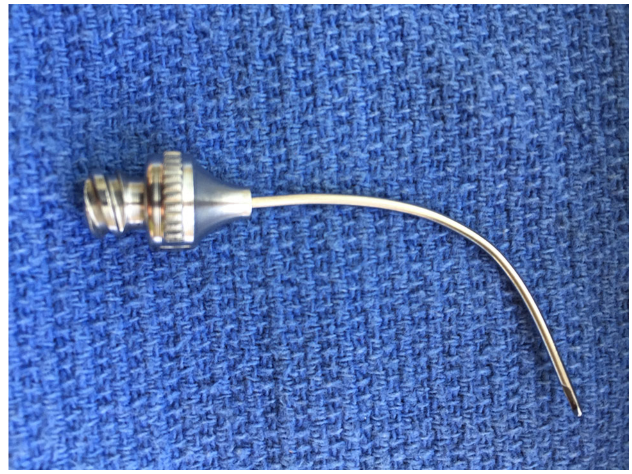

Fig. 17 Amar # 1 cannula used in all cases. Curved profile enables more coronal plane motions within the orbit

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Compliance with Ethical Standards

Conflict of interest The author declares that he has no conflicts of interest to disclose.

Ethical Standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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