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RETINAL DISORDERS

Surgery for CNV and autologous choroidal RPE patch transplantation: exposing the submacular space

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Abstract
Background To evaluate the feasibility of transplanting a full-thickness patch of choroid, choriocapillaries, Bruch's membrane and RPE (RPE-choroid FTAP) from the peripheral to the subfoveal area of the same eye, after performing a 180° peripheral retinotomy and removing subfoveal choroidal neovascularization. Thereafter, to study the surgical complications, anatomical outcome and patch perfusion during follow-up.
Methods A retrospective case series of 13 eyes of 13 consecutive patients with a follow-up of 4 to 20 months. All patients suffered from advanced subfoveal choroidal neovascularization and were non-responders to standard care. After performing a complete vitrectomy, a 180° peripheral temporal retinotomy and the removal of subfoveal neovascularization, a FTAP of choroid, choriocapillaris, Bruch's membrane and the RPE were isolated from the mid periphery of the uveal bed, transpositioned under the fovea and covered with the retina. Patients received a complete ophthalmic examination, fluorescein angiography (FA), indocyanin green angiography (ICGA) and optical coherence tomography (OCT) during follow-up.
Results An FTAP could be harvested in every eye and transplanted under the fovea. No intraoperative complications occurred. The FTAP was recognizable at FA, ICGA and OCT at each time point, up to 20 months postoperatively. Perfusion of the choroidal bed were observed into the FTAP during follow-up, from one week after surgery.
Conclusion The creation of an FTAP through a 180° peripheral retinotomy is feasible and safe. The FTAP is vital and perfused. Further studies are needed to collect more data.

Keywords RPE translocation · OCT · Fluorescein angiography · Indocyanin angiography · AMD · CNV removal

Introduction

Age-related macular degeneration (AMD) is the leading cause of legal blindness in western nations in people over 60 years of age [1]. Choroidal neovascularisation (CNV) accounts for 80% of the severe vision loss due to AMD [2]. Therapies like direct laser photocoagulation of the CNV can be useful for extrafoveal lesions, but severe damage to the retina excludes this option in juxta-foveal and subfoveal CNV [3]. Photodynamic therapy (PDT) offers the possibility of treatment in exudative AMD but no improvement in visual acuity, and some degree of retinal damage can occur [4]. Drugs such as vascular endothelial growth factors (VEGF) inhibitors have been introduced recently to treat CNV. Bevacizumab, a full-length recombinant humanized monoclonal antibody against VEGF, used previously for metastatic colorectal cancer [5], has been effective in AMD treatment [6–8]. Pegaptanib [9] and ranibizumab [10, 11] have also been shown to be effective in large clinical

The authors have no conflict of interest.

We have full control of all primary data, and we agree to allow Graefes Archive for Clinical and Experimental Ophthalmology to review our data upon request.

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trials. But there are always some non-responder patients who do not react favourably to such anti-VEGF treatment.

The role of surgery in the treatment of CNV-complicated AMD remains controversial. Although submacular removal of CNV was not favoured in the randomized submacular surgery trials, submacular surgery trial group B revealed that such surgery for haemorrhagic CNV did significantly reduce the risk of severe visual acuity loss and contrast sensitivity loss in comparison to the group observed without any treatment after 24 months of follow-up [12].

Macular translocation surgery (MT) was a technique introduced by Machemer in 1993 and modified by Eckardt in 1999. It was the first surgical approach to demonstrate an improvement in visual acuity [13], although late complications, such as a recurrent CNV or progressive atrophy of the subfoveal RPE, can impair the initial functional improvement [14, 15]. Recently, MT was reported to be beneficial in complicated AMD cases like submacular haemorrhage [16] and RPE tear [17]. These reports demonstrated that the retina could recover some function when relocated to a healthy area of RPE and choroid.

Injection of RPE cells under the fovea was tried after CNV extraction [18]. This approach yielded a poor functional result; RPE cells did not form a functional monolayer, and atrophied. RPE cell transplantation suggested that the fovea needs more than new RPE cells to recover visual acuity.

A newer surgical approach, RPE–choroid transplantation, has been effective in improving vision in some patients and in achieving foveal fixation [19–21]. Stanga et al. in 2002 described subfoveal translocation of an autologous RPE–choroid sheet that was cut from the edge of the RPE defect after CNV extraction. Van Meurs and Van den Biesen first described subfoveal transplantation of an RPE–choroid patch that was isolated from the mid-periphery. These techniques raised concern about the difficulty in correctly positioning the RPE–choroid sheet under the macula, the revascularization of the choroid and choriocapillaries transplanted, and the high risk of postoperative complications, such as proliferative vitreo-retinopathy (PVR) and sub-retinal haemorrhages [22]. One study suggested that an RPE–choroid translocation may be a treatment option for patients with a RPE tear [23]. Furthermore, stabilization or improvement in visual acuity, up to 4 years after surgery, was achieved in patients with exudative AMD treated with an autologous free RPE–choroid graft [21].

We examined a consecutive series of patients who underwent CNV extraction and subfoveal transplantation of a full-thickness patch of choroid, choriocapillaris, Bruch's membrane and RPE (RPE–choroid FTAP). In our study, the macular area was made more accessible and visible by a 180-degree retinotomy that permitted the folding of the temporal retina to expose the macula. We examined the anatomical status of these grafts as well as foveal function postoperatively.

Material and methods

Patients

One eye of 13 consecutive patients with exudative AMD was selected for this study. All patients had clinically active disease with rapid progression to an advanced stage of neovascular AMD at the time of surgery (Fig. 1): the clinical characteristics of these 13 patients are summarized in Table 1. In all patients the treated eye was the most severely affected, and visual acuity (VA) ranged from light perception (LP) to LogMar 0.5. VA of the fellow eye ranged from LogMar 0.5 to LogMar 0. In all the eyes included in this study, less invasive conventional therapeutic options such as thermal laser photocoagulation, verteporfin PDT, intra-vitreal injections of anti-VEGF agents, were not indicated. Patients gave written informed consent regarding their knowledge of the experimental nature of the treatment procedure. Risks and benefits of the therapeutic option were discussed in detail. The study followed the guidelines of the Declaration of Helsinki. The study was approved by the local Medical Ethical Committee.

Surgery

All the eyes in this series were phakic at the time of surgery. The procedure began with phacoemulsification and implantation of an intraocular lens. After the induction of a posterior vitreous detachment by active suction, a complete vitrectomy was performed. A very accurate cleaning of the vitreous base was obtained, using a high-speed electric cutter in order to reduce the risk of both retinal incarceration at the sclerotomy site during surgery and the risk of vitreous base contraction with secondary retinal detachment during the postoperative period. The temporal retina was separated from the RPE by injecting a balanced salt solution (Balanced Salt Solution; Alcon Laboratories, Fort Worth, TX, USA) into the sub-retinal space through a 41-gauge sub-retinal cannula, as described by De Juan [24]. Two or three injections were usually adequate to detach the temporal area. A neural retinal separation to the ora serrata was achieved by repeated fluid–air exchanges. A 180-degree temporal retinotomy was performed with two curved scissors (DORC International), designed for macular translocation surgery; this manoeuvre permits a retinal incision as close as possible to the ora serrata. The CNV was removed after exposing the sub-retinal space with the temporal retina overlying the nasal retina. During this maneuver, the amount of RPE removed with the CNV was usually greater than the area of the CNV measured with FAG and ICGA. The bleeding from the choroidal feeder vessels of the CNV was stopped with gentle pressure or diathermy. A full thickness patch of choroid, choriocapillaries, Bruch's membrane and RPE (RPE–choroid FTAP) was

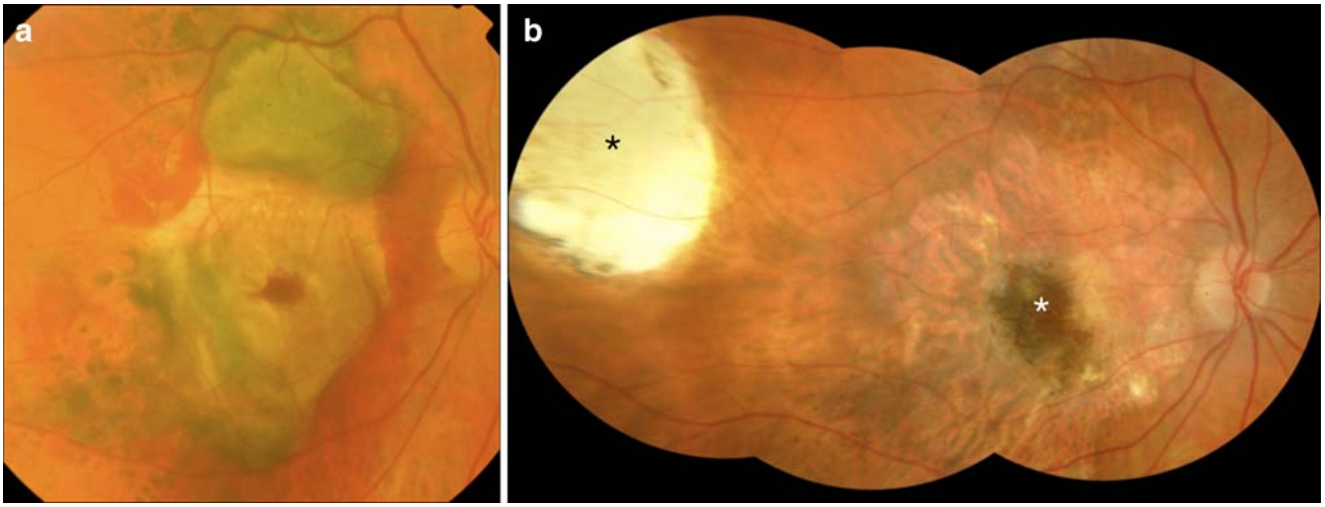

Fig. 1 **a** Preoperative situation of patient no.1. **b** Same patient 1 year after surgery; note the FTAP centered at the fovea (*white asterisk*) and the area of harvesting in the temporal retina (*black asterisk*)

isolated from the mid-periphery of the uveal bed using specially-designed scissors (DORC International). When the patch was fully cut to 360°, choroidal bleeding was controlled by diathermy or intraocular pressure elevation. Perfluorocarbon liquid (PFCL) was injected into the sub-retinal space. The RPE–choroid FTAP was gently pulled to the sub-foveal area. During this manoeuvre the patch was held with forceps at its anterior edge, in order to prevent it from floating free into the vitreous cavity and to avoid damaging it with extensive manipulation. The graft was gently flattened when needed. After waiting some minutes to assure adequate cohesion between the patch and the posterior pole, the PFCL was slowly aspirated from the sub-retinal space in order to avoid fluid turbulences that could displace the patch. The temporal retina was flipped over its original position and the PFCL re-injected into the pre-retinal space to reattach the retina. Peripheral laser endophotocoagulation was performed at the edge of the retinotomy being careful to avoid the pigment epithelium. A PFCL-silicone oil 1000 exchange completed the surgery. Silicone oil was removed 2–3 months postoperatively.

Table 1 Clinical characteristics of patients

	Sex	Eye	Age (years)	Delay (months)	Preoperative situation	Preoperative treatment (type/n°)	Preoperative visual acuity (LogMar)	Postoperative visual acuity (LogMar)	Follow-up (months)	Complications
Patient 1	f	od	63	2	PED-SRH	PDT/1	0.7	0,2	22	none
Patient 2	f	od	70	1	SRH	IVA/1	2.5	2	21	none
Patient 3	f	od	75	3	VH	no	2.5	0,9	20	inferior RD
Patient 4	f	od	80	5	VH	no	3	2	20	none
Patient 5	f	os	74	3	SRH	TPA SF6	2	2	18	none
Patient 6	f	od	68	1	PED-SRH	no	2.5	2	16	none
Patient 7	m	os	64	1	SRH	IVA/1	2	2	15	none
Patient 8	f	od	79	6	fibrotic CNV	PDT/1 IVA/3	2	2	12	none
Patient 9	m	os	84	4	VH-SRH	IVA/5	2.5	2	8	none
Patient 10	f	os	71	1	RPER	IVA/3	0.5	1	8	none
Patient 11	f	os	89	3	SRH	TPA SF6	2	2	6	none
Patient 12	f	os	69	6	Fibrotic CNV	IVA/3	2	1	4	none
Patient 13	f	os	80	1	PED-VH	IVL/3	2.5	0,7	6	none

f: female, m: male; PED: pigmented epithelium detachment, SRH: sub-retinal haemorrhage, VH: vitreous haemorrhage, CNV: choroidal neo-vascularisation, RPER: retinal pigmented epithelium rupture; PDT: photo-dynamic therapy, IVA: intra-vitreal Avastin (bevacizumab), IVL: intra-vitreal Lucentis (ranibizumab) TPA: tissue-type plasminogene activator, SF6: sulfur-hexafluoride; RD: retinal detachment

Pre- and postoperative evaluation

At each examination, best-corrected visual acuity (BCVA) testing (in Snellen lines) and a comprehensive ophthalmic examination were performed. BCVA was converted to its LogMar equivalent for the analysis. Each patient was tested with a confocal scanning laser ophthalmoscope (Heidelberg Retina Angiograph [HRA]; Heidelberg Engineering, Heidelberg, Germany) for autofluorescence (AF). An argon blue laser (488 nm) was used for excitation; emitted light was detected above 500 nm (barrier filter). To amplify the autofluorescence signal several images can be aligned and a mean image calculated by using image analysis software [25, 26]. Fluorescein (FA) and indocyanine green angiography (ICGA) were performed using the same scanning laser ophthalmoscope (HRA). Dynamic angiography of the early phase of FA and ICGA was used to define the perfusion of the graft. The early fluorescence in FA in the graft area was compared with the surrounding area as described by Maaijwee [27] (Fig. 2). The dynamic early phase of ICGA was used to study the filling of the choroidal vessels. If there was a choroidal structure in the patch, it was examined to see if the vessels ran parallel to one another forming a ladder-like pattern [27], and to ascertain if their orientation differed from that of the surrounding area. Optical coherence tomography (OCT) was performed in five patients. One was examined with Stratus OCT (Carl Zeiss Meditec, Inc) and four with HRA Spectralis (Heidelberg Engineering, Heidelberg, Germany).

Results

Of 13 consecutive patients treated with an RPE–choroid FTAP in our series, eight patients completed a 1-year follow-up. Mean follow-up was 13 months, ranging from 4 to 22 months. Mean age of the 13 patients (11 females and two male) was 74.63±7.8 (mean ± standard deviation) years (the range was 63–89 years). The preoperative delay after onset of symptoms in the operated eye ranged from 1 month to 6 months.

Surgery

No major intraocular complications occurred. The haemorrhage from the harvesting zone of the choroidal patch could be controlled by increasing the intraocular pressure and/or by intraocular coagulation at the edge of the choroid, paying attention to avoid the contact with the patch in order to prevent its shrinkage. The choroidal patch was properly positioned under the fovea in all the eyes. PFCL turned out to be very useful in controlling the right position of the patch.

Postoperative complications

One eye (Patient 3) had an inferior retinal detachment 2 days after surgery with incomplete silicone oil filling. A complete silicone oil tamponade and aspiration of the sub-retinal fluid facilitated retinal reattachment. In patient 10, 2 months postoperatively, we drained sub-retinal fluid, and we filled the eye with gas (SF6) to alleviate the progressive accumulation of fluid and obtain a permanent contact between the patch and the original choroid. Revascularisation and flattening of the FTAP was achieved.

Imaging

Postoperative angiograms were performed in all 13 patients: both FA and ICGA images were obtained. Angiograms were scheduled at 1 month, 3 months, 6 months and 1 year after surgery. In addition, six of 13 patients were examined 1 day after surgery, six patients 1 week, and 4 patients 2 weeks after surgery. None of the patients

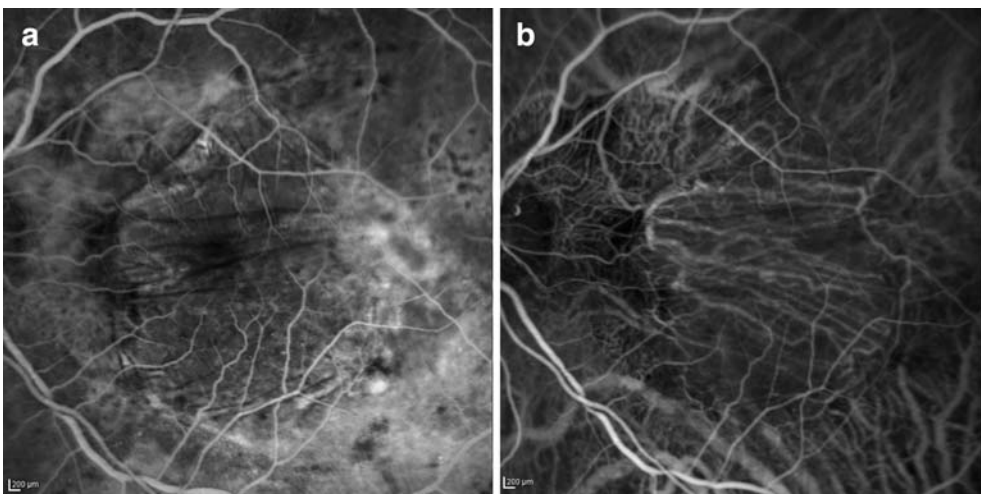

Fig. 2 Revascularisation of the FTAP of the same patient. **a** Early phase of FA showing fluorescence on the patch similar to fluorescence of sane surrounding retina. **b** Early phase of ICGA showing ladder-like structure of the choroidal bed

examined at day 1 showed signs of revascularization. In FA and ICGA, the macula area presumably occupied by the FTAP appeared dark, with no early or late fluorescence in either FA or ICGA. One month after the operation, early fluorescence at FA and a distinct choroidal bed of the patch at ICGA were clearly visible on dynamic angiography in 11 patients. Two patients without vascularisation of the patch at 1 month showed a complete fluorescence on FA and a ladder-like choroidal structure on ICGA at the 3-month examination. Twelve patients maintained patch vascularisation until the last follow-up. One patient (Patient 6) showed revascularisation at 1 month after surgery, but lost early fluorescence on FA and ladder-like structure on ICGA at 3 months after surgery.

At the 1-week follow-up, two out of six patients examined (Patients 2 and 12) had complete revascularisation of the FTAP, and two others (Patients 1 and 13) presented a relatively dark FTAP on ICGA, with an incomplete choroidal bed. At the 2-week follow-up, one patient (Patient 9) out of four had a complete revascularisation, and one (Patient 11) showed an incomplete choroidal bed on ICGA. One month after surgery, patients with incomplete revascularisation (Patients 1, 11 and 13) showed total early fluorescence on FA and well-defined choroidal structure on ICGA (Fig. 3).

When complete vascularisation was achieved, dynamic angiography on ICGA revealed vessels starting at the margin of the FTAP, with radiating minor branches of choroidal vessels (Fig. 4). These were thought to be FTAP feeder-vessels, and were detected in seven out of 13 eyes. In five cases, more than one was seen, arising from diverse locations. Feeder-vessels seemed to grow in FTAP sites in contact with the healthy and original underlying choroidal vasculature.

One case (patient 10) reported blurred vision 2 months after surgery. He had no sign of vascularisation at the 1-month follow-up. Ophthalmoscopically there was a large amount of sub-retinal fluid around and beneath the FTAP. FA revealed a focal area of intra-retinal staining, with indistinct borders located juxta-foveally. At the same point, ICGA revealed a focal area of intense hyper-fluorescence, a hot spot. Both FA and ICGA resembled the angiographic characteristics of a retinal angiomatous proliferation [28] (RAP) (Fig. 5). We considered this to be an attempt at revascularisation of the FTAP starting from the retina.

In all patients, the RPE–choroid FTAP presented autofluorescence from the first exam. Autofluorescence remained constant during follow-up. Scattered black spots of no autofluorescence were detectable on the surface of every RPE–choroid FTAP (Fig. 6).

The RPE–choroid FTAP had a brown velvet appearance on initial observation. Irregular hyper-pigmentation could be seen at the margins and scattered on the patch (Fig. 7). This hyper-pigmentation tended to progress in all patients. A progressive contraction of the graft was noted in four eyes. The position of the RPE–choroid FTAP did not change during follow-up. In one patient (Patient 6), the RPE–choroid FTAP presented a wrinkled nasal margin from surgical day 1; this area corresponded to a site lacking fluorescence in FA and ICGA. This was the same FTAP that had lost vascularisation at the 3-month follow-up; the original macular choroidal vessels became visible on ICGA and FA (Fig. 8).

The dimension of the patch under the fovea was always noticeably smaller than the site of harvesting in the mid-periphery of the retina. Some amount of haemorrhage was present in all patients at the site of harvesting; blood disappeared 1 month after surgery in one patient (Patient 6), at 3 months in ten patients and at 6 months in two patients (Patients 4 and 5). In one patient (Patient 5), there was a progressive enlargement of the haemorrhage from the mid-periphery reaching the posterior pole at the 3-month follow-up, but the blood completely disappeared 6 months postoperatively. Nine patients haemorrhaged at the margin

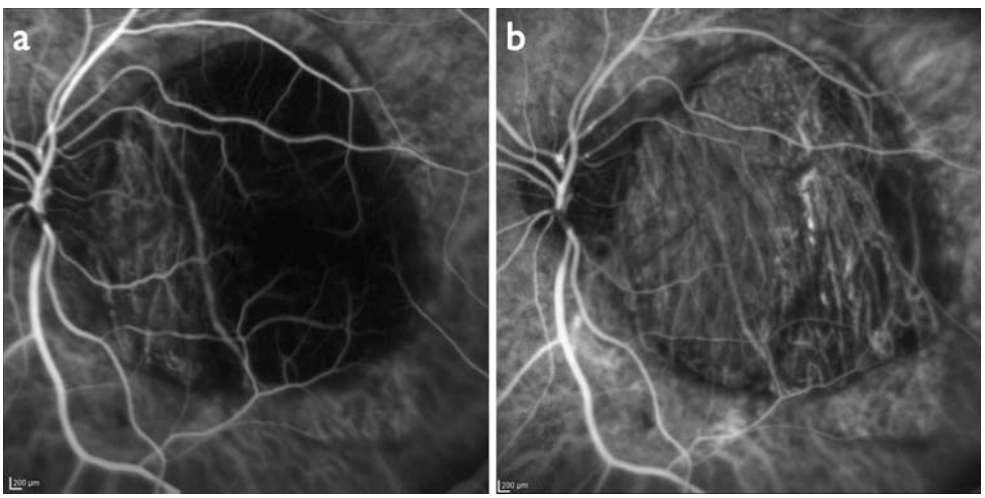

Fig. 3 Progressive revascularisation of the FTAP. Same patient, same ICGA phase. **a** Two weeks after surgery, a partial fill of the choroidal bed is visible. The dark side of the FTAP is still avascular. **b** At 1 month, FTAP is fully vascularized

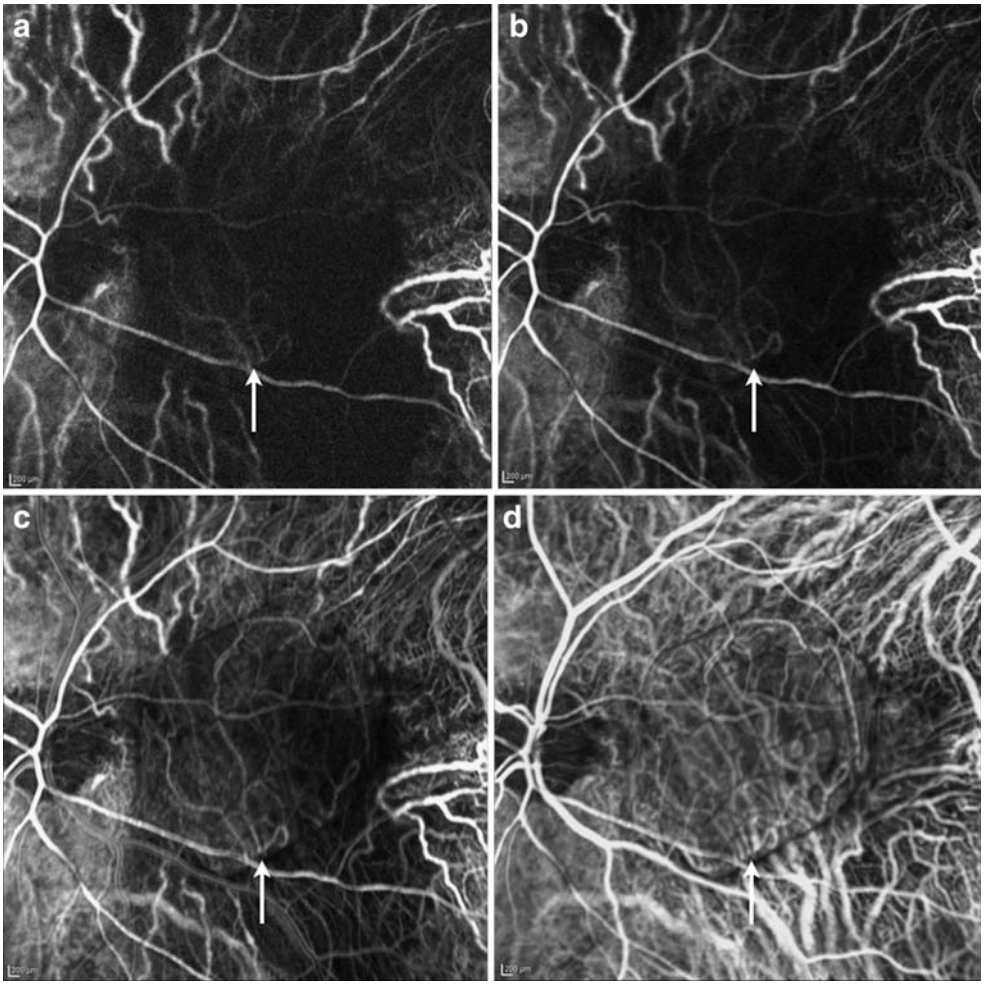

Fig. 4 ICGA frames of the same patient during dynamic angiography of the early phase: note the starting position of the feeder vessels (*white arrow*) at the margin of the FTAP. **a** Fifteen sec, **b** 20 sec, **c** 25 sec, **d** 30 sec

of the FTAP with no or very little haemorrhaging over the patch; blood progressively diminished, and had disappeared at the 3-month follow-up in eight eyes and at the 6-month follow-up in the remaining eyes.

OCT was performed on five patients (Patients 1, 9, 10, 11, 12) 1 week after surgery and at the scheduled time of angiography. Seven days after surgery, OCT revealed a dome-shaped FTAP in four of these five patients. We believe this was due to fluid accumulation under the patch (Fig. 9). In one patient (Patient 1), the FTAP was flat but its margins were elevated from the surrounding, original macular RPE-choroidal complex. At this same time sub-retinal fluid (SRF) was detected in three patients, which was typically located around the FTAP and under the fovea. Three months after surgery, all five patients had a flat FTAP on OCT with no SRF. All patches showed elevated margins at the macular RPE–choroidal complex, which decreased progressively during follow-up. The OCT of patient 1, 1 year after surgery, revealed a totally flat posterior pole with margins of FTAP completely integrated with the surrounding choroidal bed (Fig. 10).

Visual outcome

Mean preoperative visual acuity (VA) was LogMar 1.9 (range PL +, logMar 0.5). In our 13 patients, four had a VA of hand motion (HM: logMar 2.5) and four of count fingers (CF: logMar 2). Three patients had a VA ≥ LogMar 1 before surgery.

At the final follow-up, mean VA was LogMar 1.6 (range logMar 2 to logMar 0.2); eight patients had a VA of CF. Five patients had a VA ≥ LogMar 1. One patient alone (Patient 10) experienced a loss of ≥ 3 lines in VA from logMar 0.5 to logMar 1. Eight patients had a slight improvement in acuity, four remained unchanged and one became slightly worse (Fig. 11).

Discussion

FTAP transplantation can be performed through a peripheral 180° retinotomy, which provides better accessibility to, and visibility of the macula. This approach is characterized

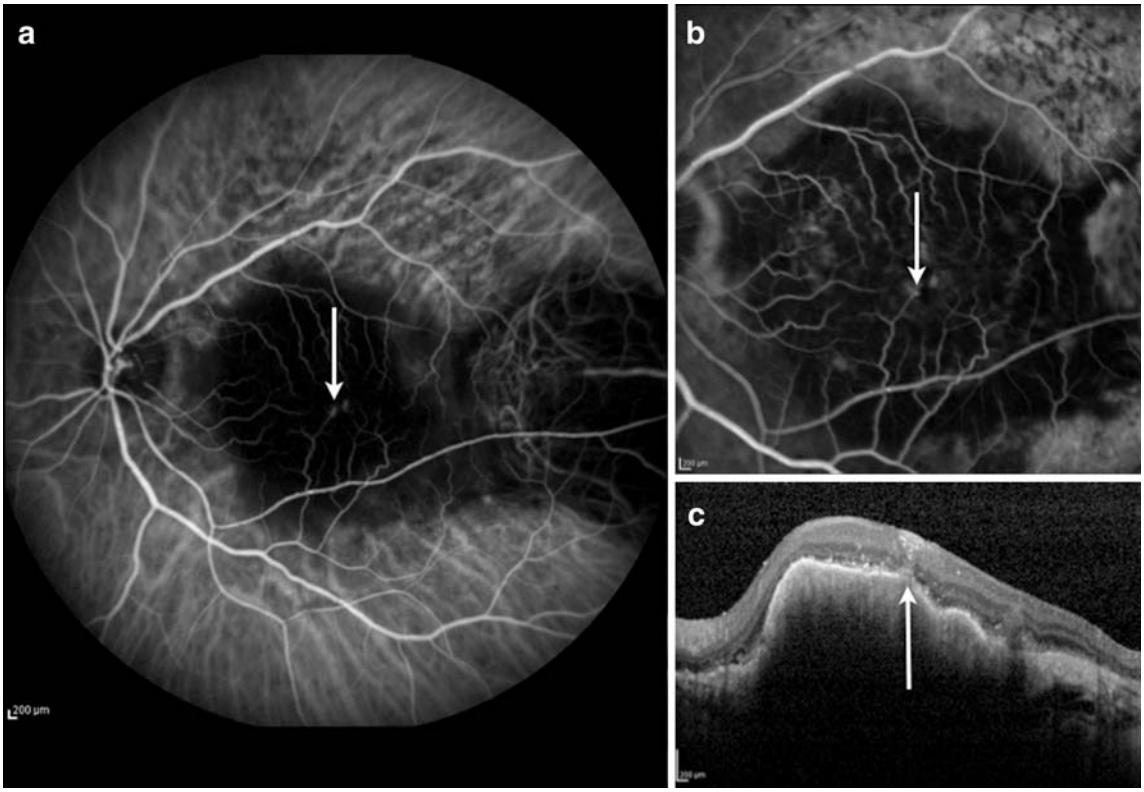

Fig. 5 Patient 10 had no sign of revascularisazion, but in both ICGA (**a**) and FA (**b**) showed an hyperfluorescence spot (*white arrow*), a RAP-like lesion. **c** OCT of the same lesion demonstrated fluid under the FTAP and a transretinal lesion (*white arrow*)

by folding the temporal retina onto the nasal retina, with the creation of a wide surgical field at the posterior pole. During CNV excision, direct observation allows the surgeon to preserve as many healthy RPE cells as possible and to gently dissect the CNV from the retina. Bleeding of feeder vessels can easily be controlled by diathermy or increasing intra-ocular pressure. In patients with advanced ARMD, where considerable photoreceptor damage has already occurred, preservation of these receptors is essential, making complete control of the manoeuvres in contact with the outer retina crucial. Similar results have now been described using a similar procedure by two other groups [29, 30].

The use of PFCL, during FTAP translocation, allows the surgeon to keep the graft flat and to control movements

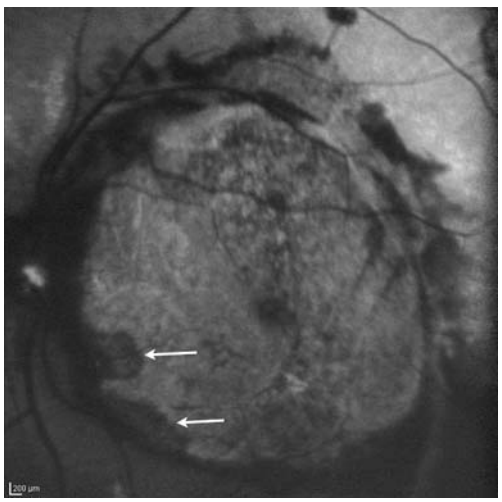

Fig. 6 Autofluorescence of a Patch: note black spots on the margin (*white arrows*) due to manouvres with forceps during transplantation

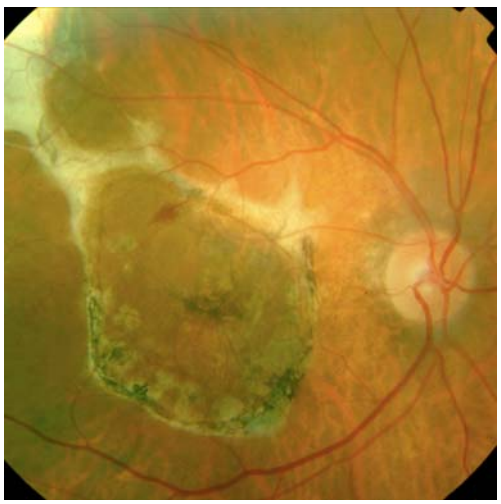

Fig. 7 FTAP: 6 months after the operation there is visible hyperpigmentation of the margin. In this case, some degree of pigment is visible also in the center of the graft

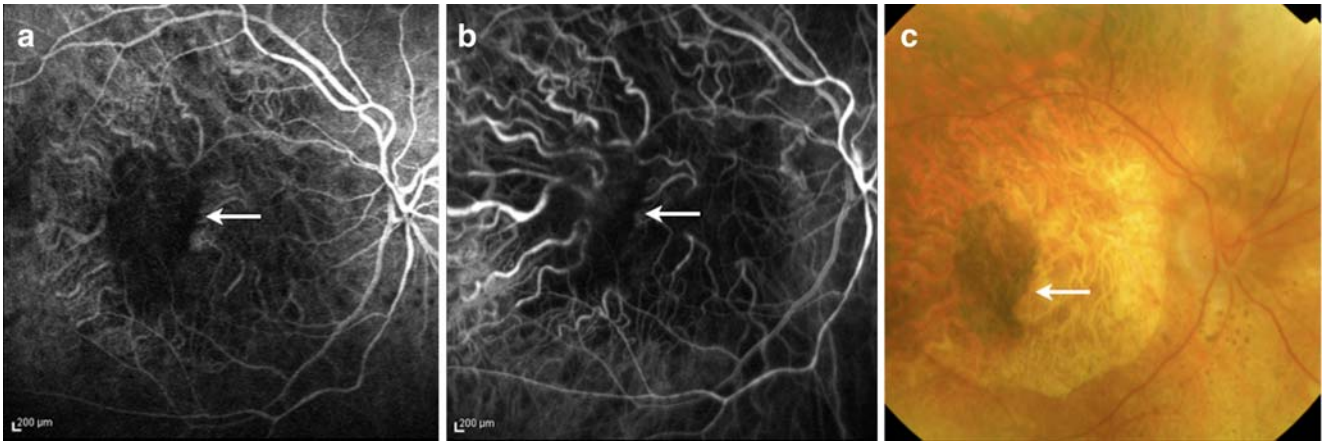

Fig. 8 Three months after surgery, no sign of vascularisation was seen either in FA or ICGA. **a** FA. **b** ICGA: note the visible original choroidal vessels of the macula. **c** Color. *White arrows* showing the wrinkled nasal margin of the FTAP

with a single forceps in contact with the tissue. As RPE is a single layer of cuboidal cells, the mere pressure of the forceps can cause irreversible damage. With our technique, there is no need to fold the patch or to stress it through a small posterior retinotomy. The FTAP remains flat under the PFCL and can be gently transferred to the sub-macular area. This is an unusual use of PFCL. De Queiroz et al. showed that short-term injection of PFCL into the sub-retinal space is not associated with significant retinal toxicity in experimental eyes [31]. As a result of its high surface tension, PFCL tends to form a bubble. Therefore, it is possible to visually control the complete removal of this heavy liquid before the retina is repositioned over the choroidal patch. Nevertheless, a thin layer of PFCL could potentially stick on the RPE and express its silent toxicity over the long run. OCT imaging does not show any suspicious alteration of the signal at the level of the interface RPE-photoreceptors in the area that came in

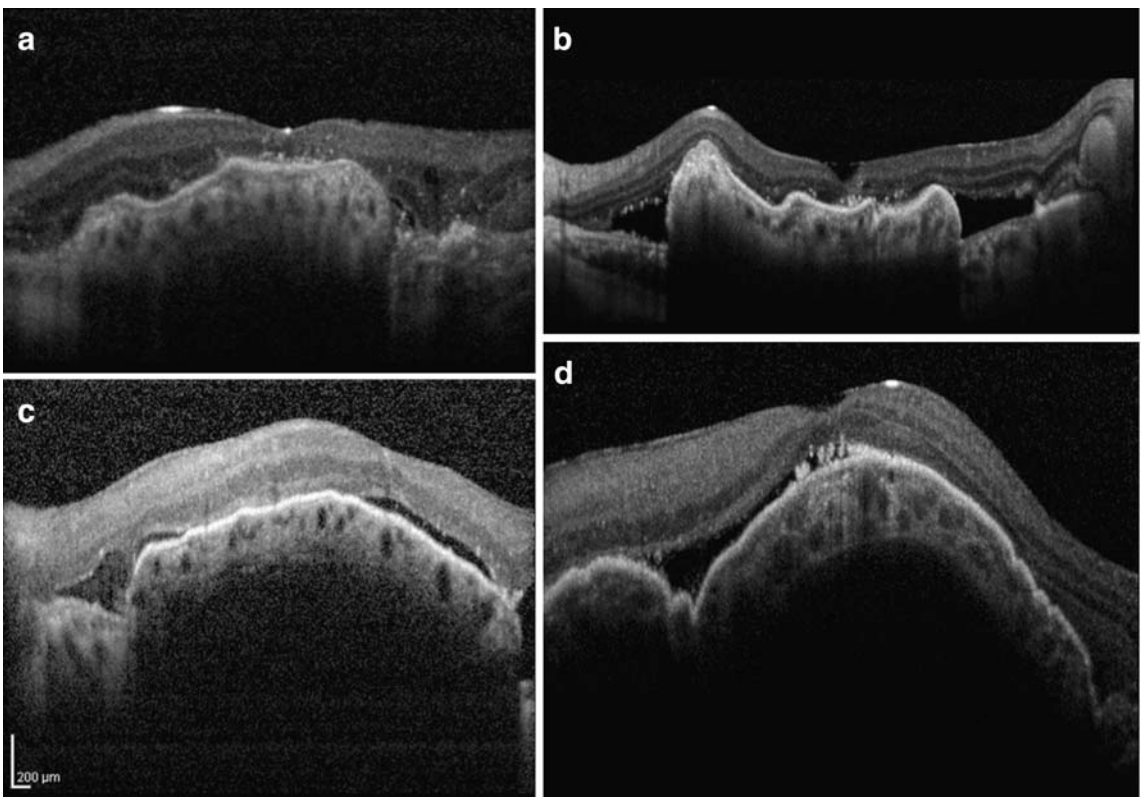

Fig. 9 One week after surgery, four patients examined with HRA Spectralis OCT: note the elevation of the FTAP (dome-shaped), probably due to fluid accumulation under the patch. Sub-retinal fluid is visible at the margin or between FTAP and retina

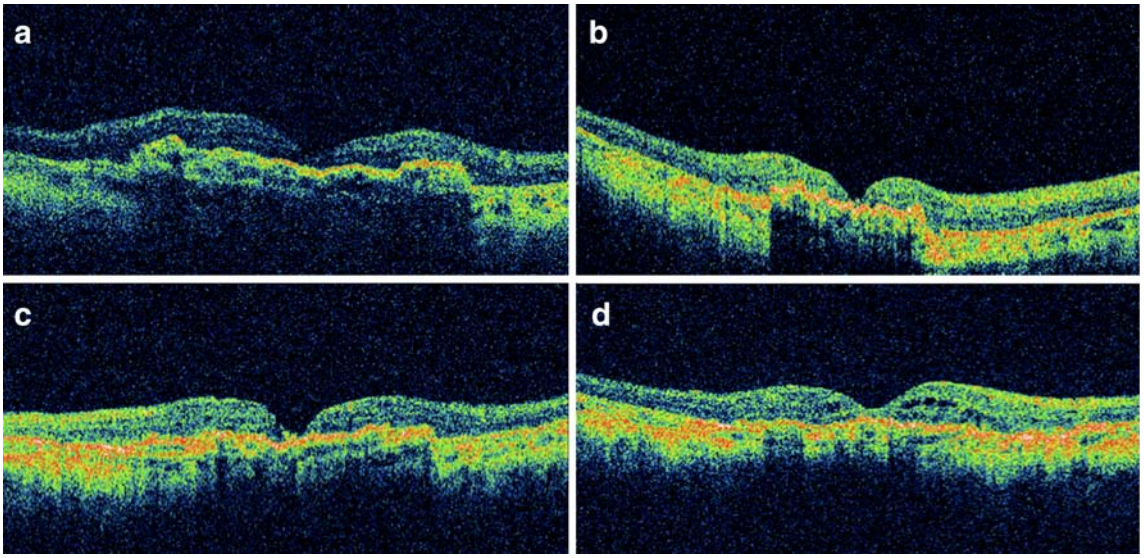

Fig. 10 Progressive integration of the FTAP to the nearby original choroid. **a** Seven days after surgery. **b** One month after surgery. **c** Three months after surgery. **d** One year after surgery

contact with PFCL. Moreover, the good visual outcome in some patients seems to rule out a significant toxicity connected with the use of heavy liquid in the sub-retinal space.

We did not use laser photocoagulation around the area of FTAP creation. Excess bleeding from the harvesting zone occurred in one patient with our technique. Direct laser photocoagulation of the RPE surrounding the graft site is advisable in order to coagulate choroidal vessels, presumably the source of the haemorrhages. Prophylactic treatment before cutting the patch is not indicated, as it can cause graft shrinkage.

Proliferative vitreo-retinopathy (PVR) is described as the most frequent complication in sub-macular surgery procedure, irremediably affecting visual outcome. Recent studies have found significant incidences of this complication: revision surgery was required in five of 12 patients in a series by Joussen [32], and PVR was present in three of 21 patients in a series by Zhizhong [29]. In a long-term evaluation, Maaijwee noted an 8% incidence of retinal detachment (seven of 84 patients) associated, however, with a 90% rate of cellophane or macular pucker [21]. The formation of epiretinal membrane on the posterior pole, though partially due to the presence of silicone oil, may be considered an abortive form of PVR; this reinforces the premise that the control of vitreoretinal proliferation is of considerable importance in the outcome of these patients. No PVR occurred in our series.

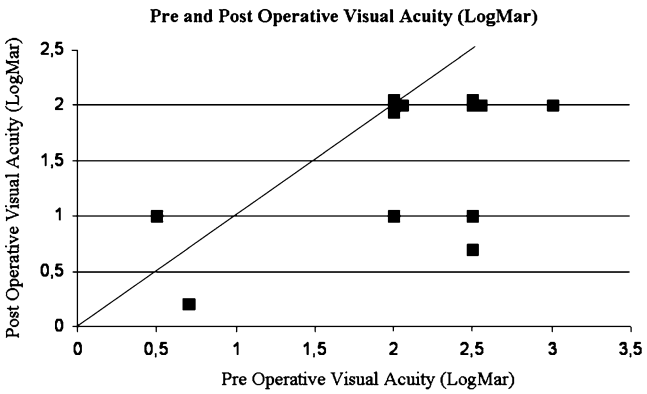

Fig. 11 Diagram of pre- and postoperative visual acuity (LogMar)

The incidence of PVR is most likely related to the acquisition of technique and to the learning curve necessary to perform these procedures. We benefitted from our surgeon's (GP) long experience in macular translocation (MT) surgery; both techniques are similar in many aspects. An extensive, precise anterior vitrectomy and 360° peripheral retinotomy play an important role in preventing PVR. In our surgical approach with phacoemulsification, the anterior vitreous can be thoroughly cleaned while avoiding traction on the anterior boundary of the retinotomy. Gentle removal of CNV from the retina and preservation of healthy RPE cells from the posterior pole reduce the diffusion of cells that can be a cause of an epiretinal membrane.

Above all, the presence of functioning FTAP is critical. Autofluorescence evaluates the presence of lipofuscin and, even if present in all our patches, we do not think it gives much information about graft vitality. Autofluorescence does provide the visualisation of iatrogenic damage on the surface of the FTAP. We noted some black areas without autofluorescence correlating with the signs of the forceps used to manoeuvre the patch.

FTAP vascularisation is essential for a successful surgery. Angiography with ICGA is the best method of evaluating the choroidal circulation. Maajiwee's observa-

tion was confirmed in our study: vascularised choroidal vessels of the patch run parallel to one another and differ from the radially arranged choroidal vascular system in the macula area [27]. Dynamic angiography with ICGA clearly revealed progressive filling of these vessels, and in some cases localized feeder vessels. We call a feeder vessel what is probably a large choroidal artery arising from the connection between the patch and the original choroid or choriocapillaris. These feeders originate at the margin of the graft in correspondence with the visible original choroidal bed. It is likely that the connection lies under the patch in an area in which transplanted choroid is in contact with a healthy choriocapillaris of the macula area. Evidence of bridging vessels emanating vertically from recipient bed to the edge of the graft, as reported by Maajiwee in pigs [33], can likewise be postulated in the human eye. This suggests that, during CNV removal, choroidal structure should be left unharmed as much as possible, and that the dimension of the graft must be large enough to connect to an area of preserved choroid.

In our study, one FTAP lost vascularisation after 3 months of follow-up (Patient 6); the patch was quite small, and complicated by wrinkling of the nasal margin. A wrinkled region of the patch is unlikely to achieve vascularisation. The revascularisation rate seems to remain high in all the previous series; Maajiwee reported graft vascularisation in 29 out of 31 patients [27].

We found that revascularisation is a progressive event that takes time for completion. Patients 1, 11 and 13 had a partially filled choroidal bed on ICGA taken 1 week or 2 weeks after surgery. This partially-filled choroid was closest to the feeder vessel. Complete revascularisation was present at the 1-month examination. There are two possible explanations:

- The choroidal vessels collapsed after harvesting and, despite high perfusion pressure in the choroidal bed, re-opening time depended on the distance from the feeder vessel.
- The FTAP choroidal bed needs more than one feeder to be fully perfused.

Before revascularisation, patch survival may be accomplished through plasmatic diffusion, as in skin transplantation [34]. The time necessary for complete revascularisation varied in our series. To more fully understand this process, repeated postoperative dynamic angiography should be started at day 1.

Interestingly, revascularisation arose from new-vessel formation, although no recurrence of CNV was reported in our 13 patients. In a large series reported by Maajiwee of 84 eyes, CNV recurred in 11 [21]. A smaller series of patients reported no recurrence of CNV [35, 36]. Despite the likelihood of significant VEGF production necessary for new-vessel creation in the patch, no recurrent CNV was observed. The stimuli for patch revascularisation were obvious. Patient 10 showed no signs of revascularisation, and developed a RAP-like lesion. A large amount of fluid had accumulated under the FTAP, confirmed by OCT examination. This fluid kept the graft in contact with the neural retina but away from the recipient choroidal bed. The attempt at retinal-graft anastomosis may suggest that there was a strong stimulus for revascularization, in this patient, inducing growth of a new vessel from the retinal side. Restoring contact between the patch and the original choroidal bed by SF6 filling, head positioning and drainage of sub-retinal fluid, permitted a choroid–choroid anastomosis and revascularisation.

Twelve of 13 eyes achieved stable or improved VA. In this study, the potential for visual improvement of the presented technique remains difficult to assess, because the patients in which we analyzed the feasibility of this approach had very advanced disease.

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