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Autologous Neurosensory Retinal Flap Transplantation in a Porcine Model of Retinal Hole

Madeline E. Olufsen, MD,[1] *Jens Hannibal, MD,*[2,3] *Nina B. Soerensen, MD,*[1] *Anders T. Christiansen, MD,*[1] *Ulrik C. Christensen, MD,*[1] *Grazia Pertile, MD,*[4] *David H. Steel, MD,*[5] *Steffen Heegaard, MD,*[1,6] *Jens F. Kiilgaard, MD*[1,2]

Purpose: Autologous retinal transplantation has been successfully employed in the treatment of large and myopic macular holes that are refractory to standard surgical treatments. Patients transplanted with a peripheral neurosensory retinal graft have shown unexpected improvements in visual acuity. The study aims to investigate if neural integration of the graft takes place in a porcine model of retinal hole.

Design: Experimental animal study.

Subjects: Left eyes of 10 Danish landrace pigs.

Methods: The pigs underwent vitrectomy under general anesthesia, and a subretinal bleb was created within the visual streak on both sites of the optic disc. A retinal hole, approximately 1900 to 4000 microns in size, was cut temporally using a vitrector. A graft of matching size was harvested from the nasal retina. The graft was gently moved toward the retinal hole under perfluoro-n-octane and placed within it. Endolaser was applied around the donor site, and either air or oil tamponade was used. OCT and color fundus photography were performed 2 and 6 weeks after surgery. At the end of follow-up, the eyes were enucleated for histological examination, including immunohistochemical analysis with antibodies against retinal glial cells, photoreceptors, and inner retinal neurons.

Main Outcome Measures: The primary outcome measures were the morphology of the graft and the junctional area between the host and the graft.

Results: Retinal hole closure was achieved in 9 of 10 cases, with the graft remaining in situ in 6 cases. In 4 cases, OCT scans indicated preservation of the outer retinal layers, and in 2 of these cases, there was apparent integration with the adjacent host retina. Corresponding histology confirmed the preservation of the photoreceptor layer in 3 cases, but there was no evidence of graft integration with degeneration of the inner retina in all cases. The distance between the margins of the retinal hole decreased during follow-up, suggesting that the graft contracts and drags the surrounding retina toward the center.

Conclusions: The outer retina of a retinal graft can be preserved, while the inner retina degenerates. No evidence of neuroretinal integration of the graft was observed. The retinal graft serves as a scaffold, promoting the centripetal migration of the edges of the hole, resulting in closure of large retinal holes.

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Permanent loss of retinal cells in the fovea are the main cause of visual loss in patients with refractory macular hole (MH) and age-related macular degeneration. In recent years numerous treatment approaches have been proposed to induce regeneration of retinal cells, especially photoreceptors.[1,2] While earlier studies focused on repairing the damaged tissue, more recent investigations have shown that patients may instead benefit from replacing the damaged tissue with an autologous neurosensory retinal flap transplant.[3–5] Performing the autologous retinal transplantation (ART) procedure, a peripheral retinal graft is harvested from the same eye and placed within the damaged area.

Autologous retinal transplantation was first introduced by Grewal and Mahmoud to assist highly myopic patients with persistent MH despite multiple surgeries.[3] Since then, the procedure has been repeated in several patient case studies globally.[4–10] A multicenter study evaluated its effectiveness and feasibility in the treatment of large refractory MHs in 41 patients, reporting approximately 90% anatomical hole closure and improved vision.[11] Similar findings were subsequently presented in a global consortium with 131 patients undergoing ART for both primary and refractory MH, including MH with retinal detachment.[12]

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The mechanism behind hole closure and improved visual function remains unknown. A generally accepted hypothesis suggests that the retinal graft initially plugs the MH, creating a barrier between the vitreous and the subretinal space. This allows for the removal of subretinal fluid by the retinal pigment epithelium (RPE), thereby promoting MH closure.[13] However, it has been proposed that the graft may exert effects beyond its role as a tissue scaffold and could potentially establish neural connections with the host retina through host-graft synaptogenesis.[3,14]

To investigate this further, research groups have applied different approaches to elucidate the observed visual improvement. High resolution OCT images have suggested that integration of the retinal graft with the host retina may occur with preservation of the outer retinal layers of the graft.[11,12] Multifocal electroretinogram (mfERG), microperimetry, and OCT angiography have suggested some survival of the graft.[15,16] However, mfERG mainly assesses photoreceptors and bipolar cells[17] and does not evaluate neural connections to the brain, and microperimetry have only shown increased signals in the peripheral part of the graft.[16]

Histopathological examination is still the superior way to study retina despite improved imaging techniques. The ideal animal model to investigate macular disease is in foveated animals, often primates, but these are very difficult to justify. To understand the true regenerative potential of ART, we have investigated the anatomical and histological outcomes after ART in an in vivo porcine model of retinal hole. To our knowledge, our study is the first to explore histology after ART and provide mechanistic insights into the role of ART in hole closure.

Methods

Animals and Anesthesia

Left eyes from 10 female domestic pigs (Danish landrace/Duroc/Hampshire/Yorkshire) were used in the study. They weighed between 25 and 30 kg and were approximately 3 months old at inclusion. One pig was excluded from the study due to massive retinal scar tissue formation during follow-up. One of the 9 included animals had ART in 2 retinal holes and therefore 10 retinal holes (10 cases) were included in the study. The pig does not have a macula, but a visual streak, which is a central horizontal band characterized by a high density of ganglion cells and photoreceptors.[18,19] The experiments were conducted within this region. The research protocol followed the Association for Research in Vision and Ophthalmology Statement on the use of animals in ophthalmic and vision research, and permission for the use of pigs was granted by the Danish Animal Experiment Committee (#2019-15-0201-01652). Additionally, the study was conducted in adherence to the principles of the Declaration of Helsinki. All surgical and follow-up procedures were performed under full anesthesia with 2.5% to 3% isoflurane (Attane vet; ScanVet Animal Health A/S). At the end of follow-up the pigs were euthanized using 1 ml/kg Pentobarbital 200 mg/mL (Glostrup Pharmacy). All animal treatments were supervised by a veterinarian.

Surgical Procedure and Follow-Up

Surgeries were performed by experienced vitreoretinal surgeons (G.P. and D.S.). All eyes underwent standard 25-gauge, 3-port lens sparing pars plana vitrectomy (Constellation vitrectomy, totalplus pak 25+, 7500 CPM Ultravit Probe; Alcon) including posterior hyaloid face separation with fluorescein staining of the vitreous. Subretinal blebs were created within the visual streak on both sides of the optic disc to lift the neuroretina from the RPE, thereby preventing damage during the preparation of the graft and the retinal hole. A hole of approximately 1900 to 4000 μm in size was cut temporally using the vitrectomy probe. The selected size was based on a previous study, which indicated that a hole of this dimension would not close spontaneously. A graft of matching size was harvested from the nasal retina using curved scissors (Grieshaber Revolution DSP curved scissors, 25GA, Alcon) and was minimally manipulated to avoid damaging the retinal layers. In 1 pig, retinal holes were created on both sides of the optic disc, with the excised tissue serving as the donor for the opposite hole (cases 3 and 4). Diathermy was applied sparingly to larger vessels near the site. The graft was gently moved with forceps toward the retinal hole under perfluoro-n-octane. The graft was either placed edge to edge with the host retina (n = 8), or with some of the graft tucked under and some above the host retina (n = 2). After ensuring correct graft placement with a microscope-integrated OCT (Zeiss Opmi Lumera 700) it remained under perfluoro-n-octane for 5 minutes, before air-fluid exchange was performed. Endolaser was applied around the graft site. Either air (n = 9) or oil (n = 1) tamponade was used. Sclerostomies were sutured with 7-0 vicryl and chloramphenicol oinment (Kloramfenikol "DAK"; Nycomed) was applied.

Two and 6 weeks after surgery, the eyes were examined by OCT, infrared fundal image, and color fundus photography. The dimension of the basal hole was determined by aligning perioperative video color fundus photography snapshots (Zeiss Opmi Lumera 700) with follow-up infrared images containing a scale bar. This approach was necessary because the presence of air or oil tamponade rendered it impossible to obtain OCT scans immediately after surgery. We chose to use the largest diameter of the hole, as our previous unpublished studies have suggested that retinal graft shrinkage is symmetrical in all directions. At follow-up, the distance between the edges of the original hole was measured on the infrared image at approximately the same location as perioperatively, utilizing the OCT B-scan. If the hole was closed, this distance corresponded to either the graft or a "retinal plug," depending on whether the graft was in place or not. The eyes were enucleated for histology at the end of follow-up.

Histological Procedures

After enucleation the eyes were immediately fixed in paraformaldehyde 4%. Segments containing the optic disc, graft site and donor site were identified, isolated, and embedded in paraffin according to a standard procedure. Five sections of 5 μm were collected every 50 μm through the lesion. Every fifth section was stained with Hematoxylin-Eosin and examined with a light microscope (Axioplan 2, Carl Zeiss). Digital images were obtained with an Axiocam (Axiocam 208 color, Carl Zeiss) using Zen software (Zen blue 3.5, Carl Zeiss Microscope GmbH). Immunohistochemistry was performed on unstained sections containing the graft and donor site. The sections underwent deparaffinization and antigen retrieval (EnvisionFLEX, Target Retrieval Solution,

LowpH, #GV805, Dako Omnis) for 1.5 h at 80°C prior to the immunohistochemistry procedure. All primary antibodies were incubated overnight at 4°C. Secondary antibodies were incubated for 2 to 3 hours. To visualize the structural layers in the retinal graft, we used anti-Calretinin (rabbit, code#7699/4, Swant), which stains retinal ganglion cells, horizontal cells, and amacrine cells in the porcine retina.[20] As a marker for cone photoreceptors, we used anti-L/M opsin (rabbit, code#JH492, Kerafast). To identify macroglial cells (Müller glia and astrocytes) we used anti-Glial Fibrillary Acidic Protein (GFAP) (rabbit, code#Z033429-2, Dako).[21] In case where 2 primary antibodies were raised in the same species, we used a combination of streptavidin-conjugated Alexa Flour 488 and Envision (K4002, DAKO) and tyramid-conjungated Alexa 594 dyes (Molecular Probes), as previously described.[22] Images were obtained using an iMIC confocal microscope (Till Pho-tonics, FEI) with an andromeda spinning disk system (FEI). The images were processed in Fiji (ImageJ).

Data Analysis

All histological sections were thoroughly examined by 1 assessor (M.E.O.), and areas of interest were analyzed and discussed within the research group.

Results

OCT Findings

Mean basal hole size was 3214 µm ranging from 1914 to 4000 µm (Table 1). All 10 cases had perioperative OCT performed. Follow-up examinations were performed in all cases after 2 weeks, but only in 9 cases after 6 weeks due to a severe retinal detachment in 1 eye. Other complications included 1 case of iatrogenic cataract in relation to the inferior trocar and 1 case of choroidal neovascularization (in relation to the site of the hole).

Retinal Hole Closure. Hole closure was achieved in 9 of 10 cases within 6 weeks of follow-up (Table 1). The retinal graft was visible and had filled the hole in 6 cases, all of which achieved closure. Interestingly, hole closure was also observed in 3 of 4 cases with a dislocated graft. In these cases, a gliotic retinal plug was present between the original margins of the hole.

In all 9 cases, examined after 6 weeks, the distance between the edges of the original hole had reduced (Table 1). The difference between the size of the basal hole, and the size of the graft or retinal plug, was caused by a central movement of the surrounding retina. Given that the graft covered the hole during surgery (Fig 1A–F), shrinkage of the graft was observed.

In 4 of the 6 cases (Table 1) with a retinal graft in situ, follow-up OCT scans indicated partial preservation of the outer retinal layers, accompanied by varying degrees of inner retinal thinning (Fig 1G–J). Additionally, the graft appeared integrated with the adjacent host retina in 2 of the cases (Fig 1G–H, yellow arrows) with apparent preservation of retinal lamination. In the remaining 2 cases, the retinal graft had lost lamination and appeared gliotic on OCT scans (Fig 1K–L).

Donor Site. Eight donor sites were examined in the study, as 2 retinal holes in 1 eye served as each other's donor. All donor sites closed with a hyperreflective gliotic plug within the follow-up period as shown in Figure 2.

Histopathological Findings

Donor Sites. Hematoxylin-Eosin sections of the donor sites showed closure of the hole with scar tissue (Fig 2B). Immunohistochemistry analyses demonstrated anti-GFAP positive cells, representing macroglial cells (Fig 2C). Identical cell types were found within the retinal plug of the 3 holes that closed without a retinal graft in situ.

Retinal Graft Sites. Preservation of the outer nuclear layer and photoreceptor layer of the grafts were confirmed on Hematoxylin-Eosin-sections in 3 of the 6 cases (Fig 3A, D, G). The RPE appeared intact underneath the grafts. In the

Table 1. Overview of Included Retinal Hole Cases

Case No.	Basal Hole Diameter µm	Distance Between Hole Margins (6 Wks) µm	Hole Status (6 Wks)				
			Closure	*Graft in Situ*	*Partial Preservation*		*Glial Plug or Degenerated Graft*
					OCT	*Histology (PR layer)*	
1	2778	1742	+	+	+	+	-
2	1914	1459	+	+	+	+	-
3	4000	3341	+	+	+	+	-
4	3778	3569	+	+	+	(+)	-
5	2421	1608	+	+	-	(+)	-
6	3625	1421	+	+	-	-	+
7	2547	-	+	-	-	-	+
8	2857	2090	-	-	-	-	-
9	2125	643	+	-	-	-	+
10	2880	1466	+	-	-	-	+

The basal hole diameter and the distance between the original margins of the hole after 6 wks are shown. The status of the hole after 6 wks is shown, including whether hole closure was achieved and if the graft remained in place. The observation of partial preservation of the graft, either on OCT scans or through histological analysis, is shown. In cases 4 and 5, although single PRs were present in the graft, a continuous PR layer was not maintained (Fig 3). Consequently, their preservation is indicated in brackets. Lastly, the presence of a glial retinal plug or a degenerated retinal graft is shown.
PR = photoreceptor.

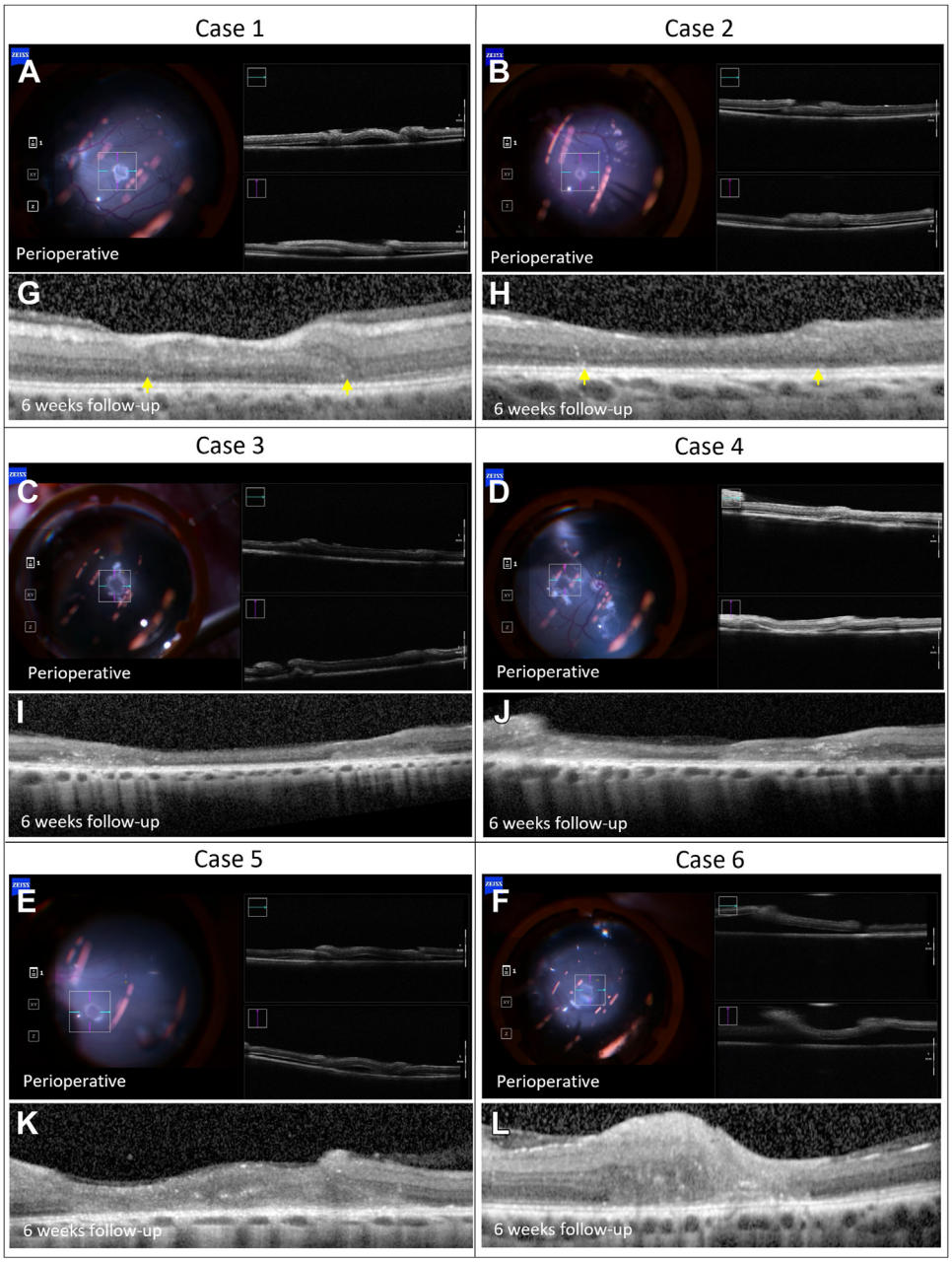

Figure 1. Retinal imaging of holes closed with a retinal graft in situ. Perioperative and follow-up OCT. **A** to **F**, Perioperative OCT shows correct placement of the graft within the retinal holes. **G** to **J**, The follow-up examinations show partial preservation of the outer retinal layers and thinning of the inner retina in cases 1 to 4. In cases 1 and 2 the graft appears integrated with the surrounding host retina (**G**–**H**, yellow arrows). **K** to **L**, In cases 5 and 6 the retinal graft appeared gliotic with a loss of lamination.

junction area between the graft and the adjacent host retina there was an accumulation of cell nuclei, which suggested that there was no connection between the graft and host retina laminations (Fig 3A, black arrow). In 2 cases, the photoreceptor layer had degenerated with gliotic tissue underneath (Fig 3J, M), while the remaining case showed complete degeneration of the graft (Fig 3P).

Immunohistochemistry analyses verified the preservation of long- and middle wavelength-sensitive cones (L/M) opsin positive cone photoreceptors within the retinal grafts in the 3 cases (Fig 3B, E, H). Single L/M opsin positive cone photoreceptors were visible within retinal rosettes of the other 2 cases (Fig 3K, N). Anti-Calretinin staining, representing ganglion cells, amacrine cells, and horizontal cells, showed preserved retinal structure of the surrounding retina. In contrast, the anti-Calretinin positive cells of the retinal grafts had partially vanished, and the degenerated inner retina was infiltrated with glial cells (Fig 3B, E, H, K, N). No connection was observed between the residual anti-Calretinin positive cells of the graft and the host retina (Fig 3B, E, white arrows).

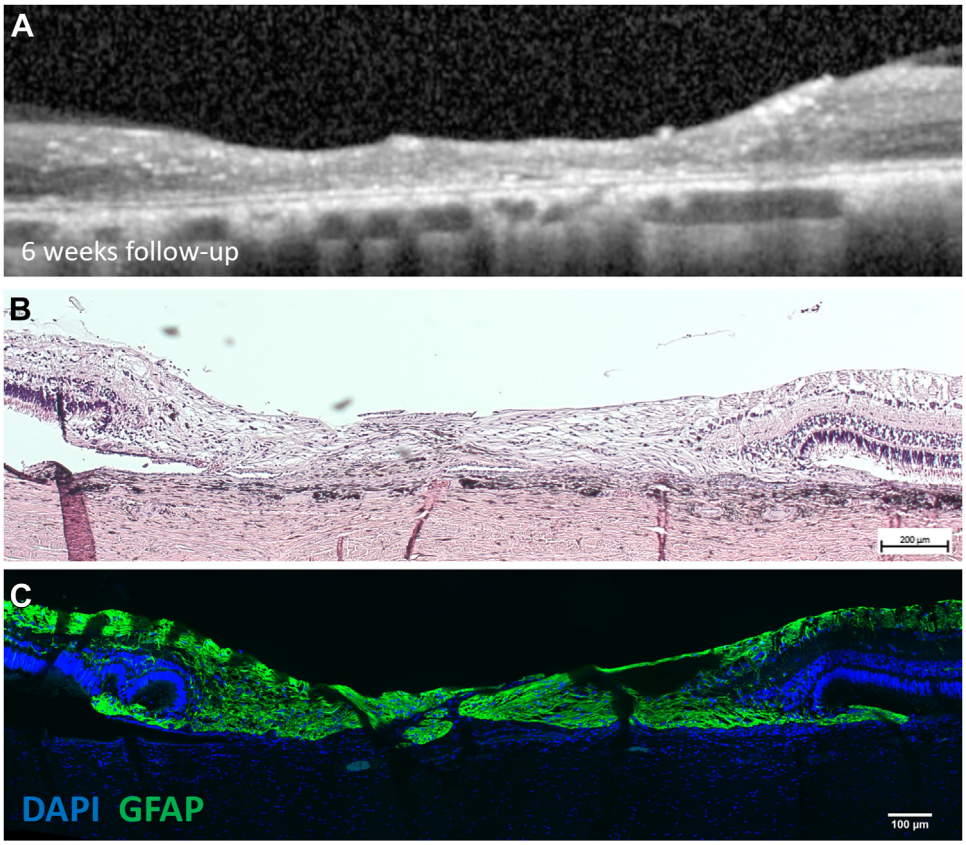

Figure 2. Retinal imaging and histology of the donor site. OCT scans of a donor site (case 2) showed closure with a hyperreflective gliotic plug (**A**). The corresponding histology showed scar tissue (**B**), which was positive for anti-GFAP (astrocytes and Müller glia) (**C**). DAPI = 4′,6-diamidino-2-phenylindole; GFAP = glial fibrillary acidic protein.

There were a few anti-GFAP positive macroglial cells present in the junctional area between the graft and the host in the cases (cases 1−2) with apparent integration on OCT images (Fig 3C, F, white arrows). In the 2 cases with only a few preserved photoreceptors (cases 4−5), gliosis was evident beneath the graft (Fig 3L, O). In the 2 cases that served as each other's donors (cases 3−4), gliosis was observed beneath the adjacent retina (Fig 3I, L). The latter cases had endolaser prior to the creation of the retinal hole. Thus, laser induced RPE damage may explain the gliosis.

In the remaining case (case 6) with a graft in situ, the structural retinal lamination had disappeared, and the graft mainly consisted of anti-GFAP positive macroglial cells (Fig 3Q).

Discussion

In this study, we observed that the outer retina of autologous retinal grafts can survive under optimal conditions. OCT scans indicated partial preservation of the outer retinal layers in 4 of 6 cases with a retinal graft in situ. Histological analysis confirmed an intact L/M opsin producing photoreceptor layer in 3 cases, while the inner retina had partially degenerated. In the remaining cases, varying degree of photoreceptor degeneration and gliosis of the grafts were observed. Surgically induced RPE damage may have contributed to photoreceptor degeneration, as the RPE is crucial for their maintenance.[23] Suboptimal conditions leading to gliosis might also be related to the size of the graft. If the graft is too small or dislocates after surgery, glial ingrowth may occur between the graft and the host retina. Conversely, neuroretinal contact between the graft and host may minimize gliosis, as seen in cases 1 and 2. In the 2 cases (case 4 and 5) where gliosis was evident beneath the graft, it likely affected the choroidal blood supply to the graft, resulting in photoreceptor degeneration.

Whilst the outer retina survived in some cases, we observed inner retinal degeneration with varying degree of gliosis in all cases. Unlike the outer retina, which can survive through choroidal oxygen diffusion, the survival of the inner retina depends on retinal neovascularization or vascular anastomosis between the graft and the host retina within a short timeframe. It is known that perfluoro-n-octane facilitates the diffusion of oxygen, and its initial use for an extended period may positively affect the oxygenation of the inner retina. However, this effect would require a supine position, which is not possible in an awake pig. Although OCT angiography or fluorescein angiography were not performed in this study, we did not observe any vascular

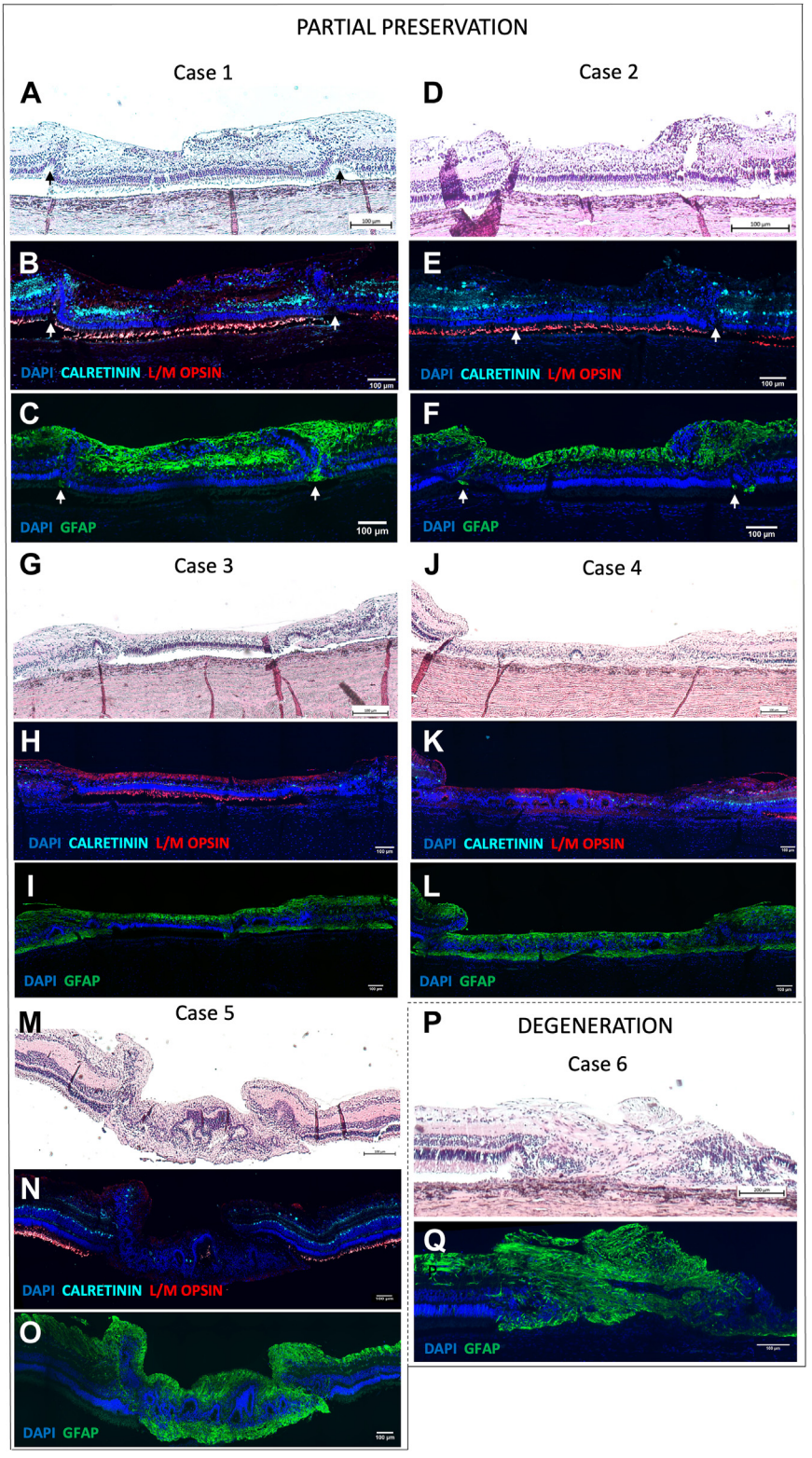

Figure 3. Histology of retinal holes closed with a retinal graft in situ. HE sections of cases 1 to 3 (**A**, **D**, **G**) show preservation of the outer retinal layers, more specifically the outer nuclear layer and photoreceptor layer, and the retinal pigment epithelium appeared intact beneath the graft. There was an accumulation of cell nuclei in the junction area between host and graft (**A**, black arrows). HE section of cases 4 and 5 (**J**, **M**) showed partial degeneration of the photoreceptors and gliotic tissue beneath the graft. Anti-LM opsin positive cone photoreceptors was preserved throughout the graft in cases 1 to 3 (**B**, **E**, **H**). In cases 4 and 5, only single L/M positive cells was present (**K**, **N**). Anti-Calretinin positive cells (ganglion cells, amacrine cells, and horizontal cells) had partially vanished within the grafts. No connection was observed between the residual cells of the graft and the adjacent host retina (**B**–**E**, white

channels in the degenerated inner retina. Tabandeh recently demonstrated graft survival in 2 patients who underwent ART for giant MHs.[15] OCT angiography and fluorescein angiography showed reperfusion and vascularization of the grafts 6 weeks after surgery.[15] Similarly, Kitahata et al and Takeuchi et al also reported blood flow within retinal grafts on OCT angiography examinations 6 and 10 months after surgery, respectively.[24,25] It was hypothesized that the graft initially becomes ischemic, triggering angiogenic pathways leading to neovascularization and vascular anastomosis between the graft and host retina over time.[15,24] As the formation of new vessels takes ≥6 weeks, they were not observed in our study. However, by 6 weeks, the inner retina had already degenerated in all cases. We postulate that the inner retinal vessels within the grafts observed in humans are aberrant within gliotic tissue. Therefore, even if neoangiogenesis occurs, it does not necessarily imply preservation of the inner retina or its transformation into functional retinal tissue.

In our study, OCT images suggested preserved retinal layering; however, histological analysis confirmed preservation of only the outer retinal layers, while the inner retina primarily consisted of gliotic scarring. Additionally, OCT images suggested alignment of the retinal layers of the graft in cases 1 and 2, but the histological examination revealed gliotic tissue around the retinal graft. There was no connection between the residual retinal neurons (anti-Calretinin positive) of the graft and the host retina.

Several patient studies have suggested anatomical integration of the graft in OCT scans.[3,6,8,11,12,26,27] Similar to our finding of outer retina survival, microstructural regeneration of the external retinal layers of the graft, more specifically the ellipsoid zone (EZ) and the external limiting membrane, has been observed during follow-up.[11,12,27] Myodis et al observed alignment of the neurosensory layers in 13 of 131 patients, where the retinal layers between the graft and host appeared to anatomically aline.[12] Interestingly, they observed that restored EZ and alignment of the neurosensory layers was associated with visual improvement,[12] supporting the hypothesis of neuroretinal integration of the graft. This may be explained by ectopic synaptogenesis, wherein functional connections between donor photoreceptors and host bipolar or horizontal cells are established, as seen in earlier animal studies.[12,28] Additionally, it is possible that the transplanted and preserved rod photoreceptors rescue the dormant host cone photoreceptors located at the borders of the MH, akin to previous observations in a pig model for retinitis pigmentosa.[29] Reactivation of cone photoreceptors and their migration toward the graft, akin to the process of foveation,[30] could explain the reconstruction of the EZ band and part of the delayed visual improvement observed.

In our study, all cases exhibited shrinkage of the graft during the follow-up period, accompanied by a centripetal migration of the surrounding retina, resulting in a reduction of the original lesion. These findings, combined with the lack of neural integration, suggest that the visual improvement observed in patients may largely result from the centralization of the host photoreceptors. This could also explain the functional improvement seen in microperimetry, which is observed only in the peripheral graft.[16] Lumi et al[16] reported OCT, mfERG, and microperimetric findings after ART in 4 patients with chronic refractory MH. All cases achieved hole closure, restoration of EZ, and minor visual improvement. The mfERG and microperimetric findings revealed active function of the peripheral, but not central, part of the graft after 2 years of follow-up.[16]

It is crucial to emphasize that our follow-up period was relatively short, given that patient studies have documented a gradual visual improvement during the first 12 months.[27] In a patient study with 6 months follow-up, Ding et al reported significant visual improvement at the last visit but not in the initial months.[6] This time dependent visual improvement suggests that further restoration of the graft may occur over time through migration of host photoreceptors toward the graft, continuous graft shrinkage, cone rescue, or by the formation of functional connections between the graft and the host.

Retinal hole closure was achieved in 9 of 10 cases, despite graft dislocation in 4 cases. The high occurrence of graft dislocation might be attributed to vigorous postoperative movements of the animal's head during recovery from anesthesia or surgically induced RPE damage impairing pump function and graft adherence. Interestingly, 3 of 4 cases with dislocated grafts still achieved hole closure through the formation of a glial plug. Previous findings in untreated retinal holes in the same porcine model demonstrated that spontaneous closure occurred in holes <1380 μm, whereas larger holes remained unclosed with minimal glial reaction.[31] Unlike the earlier study, which used no tamponade, this study employed air or oil tamponade. Additionally, gliosis might have been induced by laser application at the donor site and surgical damage to the RPE at the graft site. Retinal hemorrhage around the holes may have also promoted closure, as seen in patients treated with autologous blood clot for MH.[32] These factors likely contributed to the closure of larger holes by glial plug formation in this study.

The major limitation of this study is the relatively short follow-up period, as earlier mentioned. The rapid weight gain of landrace pigs poses challenges for prolonged studies. Therefore, an alternative approach for long-term follow-up could involve using minipigs. Additionally, there were variations in the surgical techniques, particularly concerning the placement of the graft, choice of tamponade, and application of laser. The study provides important histological insights into the early postoperative phase after the ART procedure and raises questions about the theory of retinal graft restoration and integration based on OCT findings in patients.

arrows). Few anti-GFAP positive macroglial cells (astrocytes and Müller glia) were present in the junctional area between the graft and adjacent retina in cases 1 and 2 (**C**, **F**, white arrows). In cases 3 and 4, gliosis appeared beneath the adjacent retina (**I**, **L**). In cases 4 and 5, gliosis was evident beneath the retinal graft (**L**, **O**). The degenerated inner retinal tissue was infiltrated with glial cells in all cases. In case 6, the graft had degenerated (**P**) and mainly consisted of anti-GFAP positive macroglial cells (**Q**). DAPI = 4′,6-diamidino-2-phenylindole; GFAP = glial fibrillary acidic protein; HE = Hematoxylin-Eosin; L/M OPSIN = long- and middle wavelength-sensitive cones.

The outer retina of a retinal graft can be preserved, while the inner retina degenerates. There is no evidence of neuroretinal integration of the graft. The retinal graft serves as a scaffold for centripetal migration of the edges of the hole and allows for closure of large retinal holes. Long-term animal studies, e.g., in minipigs, are needed to examine retinal graft integration and remodeling over time.

Footnotes and Disclosures

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[1] Department of Ophthalmology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark.

[2] Faculty of Health and Medical Sciences, Institute of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark.

[3] Faculty of Health Sciences, Department of Clinical Biochemistry, Bispebjerg and Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark.

[4] Department of Ophthalmology, IRCCS Sacro Cuore Don Calabria Hospital, Verona, Italy.

[5] Bioscience Institute, Newcastle University, Newcastle Upon Tyne, UK.

[6] Department of Pathology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark.

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All authors have completed and submitted the ICMJE disclosures form.

The authors have made the following disclosures:

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Author Contributions:

Conception and design: Olufsen, Soerensen, Christiansen, Kiilgaard, Hannibal

Data collection: Olufsen, Hannibal, Christiansen, Pertile, Steel, Kiilgaard

Analysis and interpretation: Olufsen, Hannibal, Soerensen, Christiansen, Pertile, Steel, Heegaard, Kiilgaard

Obtained funding: Olufsen

Overall responsibility: Olufsen, Hannibal, Soerensen, Christiansen, Christensen, Pertile, Steel, Heegaard, Kiilgaard

Abbreviations and Acronyms:
ART = autologous retinal transplantation; **EZ** = ellipsoid zone; **GFAP** = glial fibrillary acidic protein; **mfERG** = multifocal electroretinogram; **MH** = macular hole; **RPE** = retinal pigment epithelium.

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Correspondence:
Madeline Evers Olufsen, MD, Department of Ophthalmology, Rigshospitalet, Inge Lehmanns Vej 8, Copenhagen 2100, Denmark. E-mail: madeline.evers.olufsen@regionh.dk.

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