**Title**: Long term visual and microperimetry outcomes following autologous retinal pigment epithelium choroid graft for neovascular age-related macular degeneration

**Running title:** Long term outcome after RPE-choroid graft

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**ABSTRACT AND KEYWORDS**

**Background**: To describe the 2-4 year visual and microperimetry outcomes of autologous retinal pigment epithelium (RPE)-choroid graft in patients with neovascular age-related macular degeneration (AMD).

**Methods:** In this retrospective cohort study, 12 patients with subfoveal neovascular AMD who had undergone autologous RPE-choroid graft between August 2004 and June 2005 were reviewed. Change in visual acuity (VA), contrast sensitivity (CS), fixation stability and retinal sensitivity on microperimetry after 2-3 years and the rates of late postoperative complications were examined.

**Results**: Patients were followed for 26 to 48 (mean, 39) months. Median preoperative VA (logMAR) was 0.87 but declined to 1.43 (1 year), 1.46 (2 years) and 1.38 (3 years), $p = 0.001$. Median CS (logCS) was 0.75 preoperatively but declined to 0.45 at 2 years. Six patients had serial microperimetry. Fixation stability declined in 1 but improved in 2 patients. All 6 had decline in retinal sensitivity over the graft during follow-up. Retinal detachment did not occur after 12 months but 8 developed epiretinal membrane, 12 had cystic retinal change over the graft and 4 developed recurrent choroidal neovascularisation. However, 10 grafts retained autofluorescence signal at 18 to 48 months of follow-up.

**Conclusions**: Autologous RPE-choroid graft can maintain VA, stable fixation and retinal sensitivity in some patients for over 3 years. The spatial correlation between graft autofluorescence, outer retinal structures on OCT and retinal sensitivity are consistent with photoreceptor cell rescue. However, we caution the use of this technique as there is high complication rate and delayed loss of retinal function.

**Keywords**: AMD; microperimetry; RPE; transplantation; vitreoretinal surgery

## INTRODUCTION

Neovascular age-related macular degeneration (AMD), characterised by leakage of fluid or haemorrhage from choroidal neovascularisation (CNV), can lead to acute and permanent central visual loss. Recent advances in intravitreal anti-vascular endothelial growth factor (VEGF) therapies have shown promise in the treatment of these lesions with over one third of patients gaining 3 lines or more of visual acuity (VA) at 12 month which was maintained at 2 years after initiation of monthly injections.[1,2] However, the role of this therapeutic modality in patients with large submacular haemorrhage, pigment epithelial detachment or retinal pigment epithelial (RPE) rip is uncertain. Although surgical removal of submacular haemorrhage or CNV did not restore vision,[3,4] reconstruction of the RPE defect created by removal of CNV, through macular translocation or autologous RPE-choroid graft, has been shown to rescue visual function.[5-9]

The aim of surgery in AMD is to restore submacular RPE and choroid after removal of the CNV.[10] A previous report showed that autologous RPE-choroid grafts harvested from within the macular region did not maintain retinal function over the long term.[11,12] Similarly, a report of long term outcomes of macular translocation have also raised concerns regarding the ability of extra-macular RPE-choroid in maintaining retinal function after a mean follow up of 38 months.[13] This is an important question, because autologous RPE-choroid grafts are harvested from the equatorial region of the eye, which is populated predominantly by rods and it cannot be assumed that RPE-choroid from this region can sustain foveal cones indefinitely. Maaijwee and colleagues reported that autologous RPE-choroid graft from the equator can stabilise or improve VA at 2 to 4 years.[14] However, VA is a measure of retinal function at the fixation locus and does not provide any information on the ability of the patch graft in supporting central visual field. An alternative method is to measure local retinal sensitivity over the region of the graft using Nidek MP 1 microperimeter.[15,16] Several groups have previously demonstrated, using microperimetry, that retinal function over autologous equatorial RPE-choroid graft may be preserved for up to 20 months postoperatively.[17-20] However, the long term outcome in microperimetry has not been well documented.

We have previously reported the short term outcomes of 12 patients with neovascular AMD who underwent autologous translocation of an equatorial RPE-choroid patch to the macula.[21] We now present the 2 to 4 year outcomes of the same cohort of patients using microperimetry to provide more detailed information on retinal function.

## MATERIALS AND METHODS

### Patients

A total of 12 patients underwent autologous equatorial RPE-choroid graft between August 2004 and June 2005. In this study, we retrospectively reviewed the medical notes and clinical images of these 12 patients to provide the long term follow-up data from a previously published report.[22] All patients studied had visual loss for 2 to 6 (mean of 5) months due to subfoveal neovascular AMD prior to surgery. Preoperatively, all had fixation at the fovea on slit lamp examination. Approval was obtained from the Research Governance of Moorfields Eye Hospital (Institutional review board). This research adhered to the tenets of the Declaration of Helsinki.

**Surgery and follow-up schedule**

The surgical technique is similar to that described by van Meurs and Van Den Biesen.[23,24] Briefly, after a complete 3 port pars plana vitrectomy, a superior equatorial donor site was chosen and surrounded with contiguous argon laser photocoagulation. The CNV was removed through a superonasal or superotemporal macular retinotomy. The graft was cut out with vertical scissors and the overlying retina peeled with forceps. Using an aspirating-reflux spatula, the graft was inserted into the submacular space and manipulated to a subfoveal location. The bleb retinal detachment was then flattened with heavy liquid and exchanged for silicone oil. After a minimum of 2 months, patients underwent phacoemulsification cataract surgery combined with silicone oil removal. Proliferative vitreoretinopathy with retinal break was treated by membrane peeling and gas or oil tamponade. All patients had a 6 month evaluation for functional and structural outcomes as part of the previous study.[25] Thereafter patients were followed every 4 to 6 monthly.

**Outcome measures**

The main outcome measure was VA at 1, 2 and 3 years. We also examined the change in contrast sensitivity (CS), fixation stability and retinal sensitivity as measured on microperimetry. The type and frequency of late postoperative complications were described.

**Visual function and microperimetry**

All patients had refraction and best-corrected distance VA measurement on the back illuminated ETDRS charts (Lighthouse Low Vision Product, USA) at 4 or 1 m. Letter score corrected to 1 m was converted to logarithm minimal angle of resolution (logMAR).[26] Contrast sensitivity (CS) was measured at 1 m using wall mounted Pelli-Robson contrast sensitivity chart (Clement Clarke Inc., USA). Scoring and stopping rules used are those described by Pelli *et al*.[27] Both ETDRS and Pelli-Robson charts were performed under standard chart luminance of 100 cd/m$^2$ ($\pm$ 15%). The best recorded VA and CS measurements within a 2 month window before or after the exact 12, 24 or 36 months time points following graft were used for analysis of the 1, 2 and 3 year outcomes, respectively.

Locus and stability of fixation was determined during slit-lamp examination by using the five-step fixation task as described by Uppal *et al*.[28] Locus of fixation was noted to be either on or outside the graft. Patients with fixation over the graft also had microperimetry to quantify fixation stability and retinal sensitivity as one of the outcome measures of the short term prospective study reported previously.[29] These patients had follow-up microperimetry if there was subjective decline in central visual function or loss of VA and fixation.

The Nidek MP1 microperimeter, (NAVIS software version 1.7.2, Nidek Technologies, Padova, Italy) was used for fixation analysis and retinal sensitivity measurements. With a 1.27 cd/m$^2$ background luminance, a white or red cross fixation target was used for recording fixation pattern during a 30-second period. Stability of fixation was classified as “stable”, “relatively unstable” or “unstable” based on the proportion of fixation points within 2º or 4º of the gravitational centre of all loci.[30] Using a Goldmann III or V stimulus of 200 ms duration and a 4-2 stair-case strategy, microperimetry tests were performed initially with a customised Cartesian grid pattern to cover the area of the graft. Follow-up examinations were performed at the same test loci by using the follow-up protocol to allow direct comparison of retinal sensitivity. Retinal sensitivity was analysed by calculating (1) the dense scotoma (< 0 dB) size (number of test loci) and (2) the mean retinal sensitivity (dB)

over the graft. The border of the graft was determined on fluorescein and indocyanine green angiographies and superimposed on microperimetry examinations after manual image registration. Only test loci falls within the boundaries of the graft in all follow-up microperimetry examinations were used for these calculations. Microperimetry and fixation maps were overlaid on the fundus image taken at the time of OCT and the fundus autofluorescence image taken within 3 months of the microperimetry for structure-function correlation. A differential map was constructed using the Nidek MP1 software to show change in retinal sensitivity at individual test loci. Those test loci with more than 6 dB of fluctuation in retinal sensitivity were highlighted as they may represent true change. A 6 dB change has been reported as the limit of test-retest variability in normal subjects when Goldmann III size stimulus is used (*IOVS* 2005; 46:ARVO E-Abstract 1561).

**Postoperative complications**

The presence of retinal detachment, macular oedema, subretinal fluid (SRF), CNV, epiretinal membrane (ERM) and atrophy were noted on clinical examination, optical coherence tomography (OCT), fundus autofluorescence imaging and fluorescein angiography.

OCT was performed using the StratusOCT™, software version 4.0 (Carl Zeiss Meditec, Inc., Dublin, CA, USA), the SOCT Copernicus, software version 1.35 (Optopol Technology Sp. Z o.o., Poland) or the 3D OCT-1000, software version 2.12 (Topcon Inc., Tokyo, Japan) to confirm clinical findings of macular thickening, SRF, ERM, cystoid changes and retinal atrophy. We used spectral-domain OCT to allow correlation between retinal sensitivity and intraretinal structures that correspond to the outer plexiform layer and the photoreceptor cell inner/outer segment junction.[31,32] Fundus autofluorescence was assessed by using a scanning laser ophthalmoscope (SLO) – the Heidelberg Retina Angiograph II (HRA II, Heidelberg Engineering GmbH, Dossenheim, Germany). A series of 5 to 15 images over a 30º field was acquired and then aligned and averaged with the image analysis software provided with HRA II (Heidelberg Eye Explorer, Heidelberg Engineering GmbH, Dossenheim, Germany). The pattern and intensity of autofluorescence signal on the graft was assessed qualitatively and correlated with colour fundus image and retinal sensitivity on microperimetry.

**Data analysis**

Data were analysed using SPSS for Windows, version 14.0 (SPSS Inc., Chicago, IL, USA). Median VA and CS at baseline, and the 1, 2 and 3 year time points were calculated. Due to the small sample size, the nonparametric Friedman test was used to determine the significance of change in VA over the 4 time points and Wilcoxon signed ranks test was used for comparison of VA between 1-2 and 1-3 years. A p value of less than 0.05 was considered statistically significant.

## RESULTS

**Visual function and microperimetry**

All patients from the initial case series were followed for two or more years (mean: 39, range: 26 to 48 months). Last observation carried forward (from 26 and 33 months, respectively) was used for the 3 year VA in 2 patients. Figure 1, a box plot, shows the change in VA over 3 years. The median preoperative VA was 0.87 logMAR. Median VA (logMAR) at 1, 2 and 3 years were 1.43, 1.46 and 1.38, respectively. Friedman test showed

significant decline in VA over the 4 time points ($\chi^2$ = 16.4, $p$ = 0.001) but there was no significant change from 1 - 2 years, and 1 - 3 years (Wilcoxon signed ranks test, $p$ = 0.2 and $p$ = 0.1, respectively). At 2 and 3 years, 1 (8%) eye gained 3 or more lines of VA, 5 (42%) remained within 3 lines of baseline VA and 6 (50%) lost 3 or more lines of VA (Figure 1). After 2 years, 2 of 12 (17%) eyes had VA of 0.7 logMAR or better. In 2 patients (4 and 8), VA declined during the second and third year. The median CS at baseline, 1 and 2 years were 0.75, 0.75 and 0.45 logCS respectively.

Six patients (4, 5, 7, 8, 9 and 11) demonstrated fixation over the graft. They had the baseline microperimetry tests at various time points ranging from 9 to 31 months post-operatively. The most recent follow-up microperimetry tests were performed between 26 and 48 months post-operatively. Using a small (1-2º) cross fixation target, we found that fixation stability declined in 1 patient (from stable to unstable) and improved in another 2 (from unstable to relatively unstable or stable) during follow-up (Table 1 and Figure 2). However, mean sensitivity over the graft declined (loss of 0.1 to 8.4 dB) and dense scotoma over the graft enlarged (increment of 1 to 13 test loci) in all 6 tested eyes (Table 1, Figures 3 and 4).

**Postoperative complications**

At the 2 and 3 year follow-up visits, all patients were pseudophakic with no axial media opacity. Within the first 12 months, 5 patients (42%) developed 7 retinal detachments. The 2 re-detachment in 2 patients occurred after gas tamponade and were repaired under oil. No retinal detachment occurred after the first 12 months although 1 patient still had oil in situ at 33 months. Four patients (33%) had recurrent CNV, extending peripherally from the edge of the graft, occurring between 6 and 28 months postoperatively.

ERM was present in 8 patients (67%) but all 12 patients had intraretinal cysts over the graft accompanied by variable degrees of retinal atrophy or thickening (Figure 3). OCT sections through regions with retinal sensitivity over the graft showed intact outer retinal structures (Figures 3 and 4). In areas without retinal sensitivity, retinal thickness was either reduced with loss of the reflective bands representing the plexiform layers (retinal atrophy) or thickened accompanied by intraretinal cysts (cystoid macular oedema). In some regions, intraretinal cysts were present without retinal thickening (atrophic macular cysts).

Autofluorescence signal was observed over the graft in the 10 patients examined after 1 year (18 – 48 months). Patchy areas of reduced autofluorescence over the graft corresponded to masking by RPE hyperplasia and subretinal fibrosis. Regions of the graft with homogenous autofluorescence signal did not necessarily predict retinal sensitivity. Although there was no significant loss of graft autofluorescence over time, the surrounding area without autofluorescence signal enlarged during follow-up due to either progressive RPE atrophy or fibrosis of CNV.

All 6 patients with fixation over the graft had early or late postoperative complications except for patient 5 who had no complications and also had the best long term visual outcome (Table 1). Decline in fixation stability and VA in patients 4 and 8 were associated with the development of atrophic macular cysts or cystoid macular oedema at the locus of fixation (Table 1, Figures 3 and 4).

## DISCUSSIONS

The combination of fundus autofluorescence imaging, spectral-domain OCT and microperimetry provided a detailed assessment of graft and retinal function in patients undergoing autologous RPE-choroid graft. We found that VA, fixation stability and retinal sensitivity can be sustained beyond 3 years with autologous RPE-choroid grafts harvest from the equatorial region. There was however a gradual decline in VA and retinal function based on microperimetry. This was associated with late cystic retinal changes associated with retinal atrophy, macular oedema, RPE atrophy or CNV recurrence from the edge of the graft.

Maaijwee et al. reported the visual outcomes in a cohort of 83 patients followed up for 24 to 48 months.[33] They found the mean VA improved from 0.95 logMAR at baseline to 0.89 logMAR at 1 and 2 years and 0.79 logMAR at 3 years (n = 84, 45 and 24 patients, respectively). They showed, with a Kaplan-Meier plot that the percentage of eyes loosing < 3 ETDRS lines was 70-80% at 1 year and stabilises at around 50% at 2 to 4 years. Also, 6 of 45 (13%) and 4 of 24 (17%) eyes had VA of 6/24 or better at 2 and 3 years. Although our result showed an overall decline in VA, we also had similar percentages of eyes with < 3 lines loss (50%) and VA of better than 6/24 (17%). Hence our results are comparable to this largest series despite higher rate of retinal detachment (42% compared to 8%) and more frequent recurrence of CNV (33% compared to 13%).

Fixation over graft may be considered a sign of success as it indicates that the translocated RPE is able to support central visual function. Using various techniques to study fixation, previous studies have also shown 40 to 74% of eyes achieved fixation over the graft.[34-39] Similar to that reported by Maaijwee et al., we also found that fixation stability may worsen or improve during follow-up.[40] The reason for worsening of fixation stability may be related to delayed cystic change or atrophy whereas improvement in stability may be related to adaptation to eccentric fixation and viewing.[41,42] Treumer *et al*. reported microperimetry outcome in 5 of 10 patients between first and second year (< 20 months).[43] They found that the mean sensitivity improved by 2 or more dB in 2 eyes and lost 2 dB in 1 eye. In our series, all 6 patients had a decline in mean retinal sensitivity but only 1 had significant change (> 2 dB loss) due to cystoid macular oedema over the graft associated with recurrent CNV (patient 8). However, loss of 6 or more dB in local retinal sensitivity at some point over the graft was noted in all tested eyes. This loss in local retinal sensitivity may be due to primary retinal atrophy, progressive dysfunction of the grafted RPE or test-retest variability in microperimetry (*IOVS* 2005; 46:ARVO E-Abstract 1561).[44] Nevertheless, we have shown that some residual retinal sensitivity can be maintained over the graft for more than 3 years in some cases. The demonstration of structures which correspond to outer plexiform and nuclear layers on spectral-domain OCT in regions over the graft where there is retinal sensitivity is consistent with the extensive literature on photoreceptor cell rescue by RPE transplantation.[45] Fundus autofluorescence signal, from the fluorophores within the RPE, is an indirect measure of outer segments renewal and lipofuscin clearance.[46,47] The loss of retinal sensitivity over regions of the graft where autofluorescence signals remain may be explained by a combination of (1) prolonged retention of lipofuscin within the translocated equatorial RPE, (2) pre- or intra-operative loss of photoreceptor cells and (3) postoperative retinal atrophy (patient 4) or oedema (patient 8).

Late postoperative complications were common. Although retinal detachment did not occur after 12 months, some degree of ERM was present in the majority which may represent mild forms of proliferative vitreoretinopathy. Peeling of the ERM or ILM is unlikely to have improved the overall outcome as our results

were similar to previous series where the ILM was frequently peeled at the time of removal of oil.[48] By using spectral-domain (in 9 patients) or time-domain OCT (in 3 patients), we were able to detect retinal atrophy associated with cystic change within the retina over all grafts. The high rate of cystic change compared to previous studies may be related to use of dense raster B-scan instead of the 6 radial B-scan protocols.[49] Intraretinal cysts over the graft may occur as a consequence of recurrent CNV, compromised RPE, leaky perifoveal retinal capillaries, graft ischaemia, retinal atrophy or RPE atrophy (causing retinal cysts). Even with fluorescein and indocyanine green angiographies, it was difficult to determine the contribution of each process to the intraretinal cystic change. Patchy loss of autofluorescence signal over the graft was related to pigmentation and fibrosis as previously reported.[50,51] The enlarging rim with absent autofluorescence signal (due to progressive RPE atrophy or fibrosis of recurrent CNV) surrounding the graft is of particular concern as this may compromise choice of preferred retinal locus if foveal fixation over the graft is lost (which occurred in 12 of 64 eyes during follow up in the study by Maaijwee et al.[52]).

The main limitations of this study are its retrospective design and small sample size. We were unable to provide microperimetry data on all patients at regularly spaced time interval during follow-up since we did not routinely perform this investigation. Nevertheless, the data presented here provided some information on the long term visual outcomes and enabled correlation between fixation/retinal sensitivity with OCT/autofluorescence features in cases where retinal sensitivity is most likely to be present over the graft. The small sample size also does not provide the statistical power required to confirm previous reports of associations between visual outcome and pre- or intra-operative features.[53,54]

In conclusion, autologous equatorial RPE-choroid grafts can support VA, stable fixation and retinal sensitivity in some patients for over 3 years. The spatial correlation between fixation, retinal sensitivity, presence of structures corresponding to photoreceptor cell layer on OCT and autofluorescence signal on the graft suggest that equatorial RPE-choroid is able to support macular photoreceptor cells. We did however note a high rate of late postoperative complications including progressive decline in retinal function and cystic changes developing within the retina overlying the grafts. It will be important to determine if these changes are related to AMD disease progression, surgical trauma or a fundamental inability for equatorial RPE-choroid grafts to sustain the high metabolic activity of macular photoreceptors. In view of these long term results, we caution the use of this technique for treatment of neovascular AMD.

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**TABLE**

**Table 1. Microperimetry outcomes in six patients**

| Patient number | Number of Test loci over graft†, stimulus size* | First MP | | | | Second MP | | | | Early and late postoperative complications | Time points for the 2 MP tests (months) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | VA (logMAR) | Fixation stability | Mean RS† (dB) | DSS† (loci) | VA (logMAR) | Fixation stability | Mean RS† (dB) | DSS† (loci) | | |
| 4 | 21, V | 0.32 | Stable | 1.8 | 12 | 1.62 | Stable | 1.2 | 15 | CNV, CMO, AMC | 23, 42 |
| 5 | 35, III | 0.64 | Stable | 1.4 | 20 | 0.54 | Stable | 0.6 | 27 | None | 16, 40 |
| 7 | 19, III | 1.00 | Stable | 0.4 | 14 | 1.00 | Stable | 0.3 | 18 | EGH, CNV, CMO, ERM | 20, 30 |
| 8 | 18, V | 0.68 | Stable | 9.2 | 1 | 1.22 | Relatively unstable | 0.8 | 14 | EGH, CNV, CMO, SRF | 9, 29 |
| 9 | 19, III | 0.82 | Unstable | 2.4 | 9 | 0.92 | Stable | 1.7 | 10 | RD, ERM, CMO | 31, 40 |
| 11 | 13, III | 1.54 | Unstable | 1.5 | 11 | 1.56 | Relatively unstable | 0.6 | 12 | EGH, CNV, ERM, CMO | 17, 26 |

* Equivalent Goldmann perimetry target size.

†Test loci over the graft were selected for calculation of mean retinal sensitivity and dense scotoma size.

AMC, atrophic macular cysts; CNV, choroidal neovascularisation; CMO, cystoid macular oedema; dB, decibel; DSS, dense scotoma size; EGH, early graft haemorrhage; ERM, epiretinal membrane; logMAR, logarithm of minimum angle of resolution; MP, microperimetry; RD, retinal detachment; RS, retinal sensitivity; SRF, subretinal fluid; VA, visual acuity.

## FIGURE LEGENDS

**Figure 1**. Visual acuity (VA) change over 3 years. (A) A box plot showing median, quartiles and range in VA at baseline 1, 2 and 3 years. (B, C and D) Three scatter graphs comparing baseline VA with post-operative VA at 1, 2 and 3 years.

**Figure 2.** Fixation stability change in 6 patients whose grafts supported fixation. Inserts show percentage of fixation locus within 2º and 4º of gravitational centre of all fixation loci during a 30 second recording. (A, B) Patient 4 had stable fixation stability despite loss of acuity at 48 months. (C, D) Patient 5 had stable fixation for up to 40 months. (E, F) Patient 7 had stable fixation for up to 30 months despite recurrent CNV supratemporal to the graft. (G, H) Patient 8 had decline in stability due to cystoid macular oedema secondary to recurrent CNV temporal to the graft. (I, J) Patient 9 had improvement in fixation stability at extrafoveal locus on the patch at 40 months. (K, L) Patient 11 had improvement in fixation stability also at extrafoveal locus on the patch at 26 months.

**Figure 3**. Serial microperimetry in patients 4 and 5. Microperimetry tests are displayed as interpolated maps and differential maps on the autofluorescence image taken around the time of the most recent microperimetry. Borders of the grafts are marked and loci with greater than 6 dB increment (green) or decline (pink) are highlighted on the differential map. (A, B, C and D) In patient 4, the mean retinal sensitivity (Goldmann V size stimulus) over the graft decline from 5.3 dB at 12 months to 1.8, 1.8 and 1.2 dB at 23, 32 and 42 months, respectively. (E) Local retinal sensitivity change between 23 and 42 months overlaid on autofluorescence image. (F) Visual acuity (VA) at corresponding time points over 4 years showed steady decline between 1 and 3 years and rapid decline after 3 years. (G) Optical coherence tomography through fixation showed foveal cyst causing rapid decline in VA after 3 years and intact retinal structure in the nasal macula (region marked by white bar) corresponding to regions with retinal sensitivity. (H, I, J and K) In patient 5, the mean retinal sensitivity (Goldmann III size stimulus) over the graft declined from 1.4 dB at 16 months to 0.2 dB then improved to 2.3 dB and again declined to 0.6 dB at 25, 32 and 40 months, respectively. (L) Local retinal sensitivity change between 16 and 40 months overlaid on autofluorescence image. (M) VA change over 3 years at corresponding time points. (N) Optical coherence

tomography through fixation locus showed a smooth foveal depression with intact outer retinal structures in the foveal region.

**Figure 4**. Serial microperimetry in patients 7, 8, 9 and 11. Microperimetry tests are displayed as interpolated maps and differential maps on the autofluorescence image taken around the time of the most recent microperimetry. Borders of the grafts are marked and loci with greater than 6 dB increment (green) or decline (pink) are highlighted on the differential map. (A-E) The graft in patient 7 supported retinal sensitivity (Goldmann III size stimulus) and stable visual acuity (VA) over its nasal region which was associated with presence of autofluorescence signal and outer retinal structures (marked by white bar) in the same region at 20 and 30 months. (F-J) Patient 8 had marked loss of retinal sensitivity (Goldmann V size stimulus) and VA due to cystoid macular oedema between 9 and 29 months. (K-O) Patient 9 had retinal sensitivity (Goldmann III size stimulus) over superior half of the graft associated with homogenous pattern of autofluorescence signal and intact outer retinal structures in the same region at 31 and 40 months. (P-T) Patient 11 had retinal sensitivity (Goldmann III size stimulus) over the inferior pole of the graft and stable but poor VA associated with faint autofluorescence signal and intact outer retinal structures in the same region at 17 and 26 months.

**FIGURE 1**

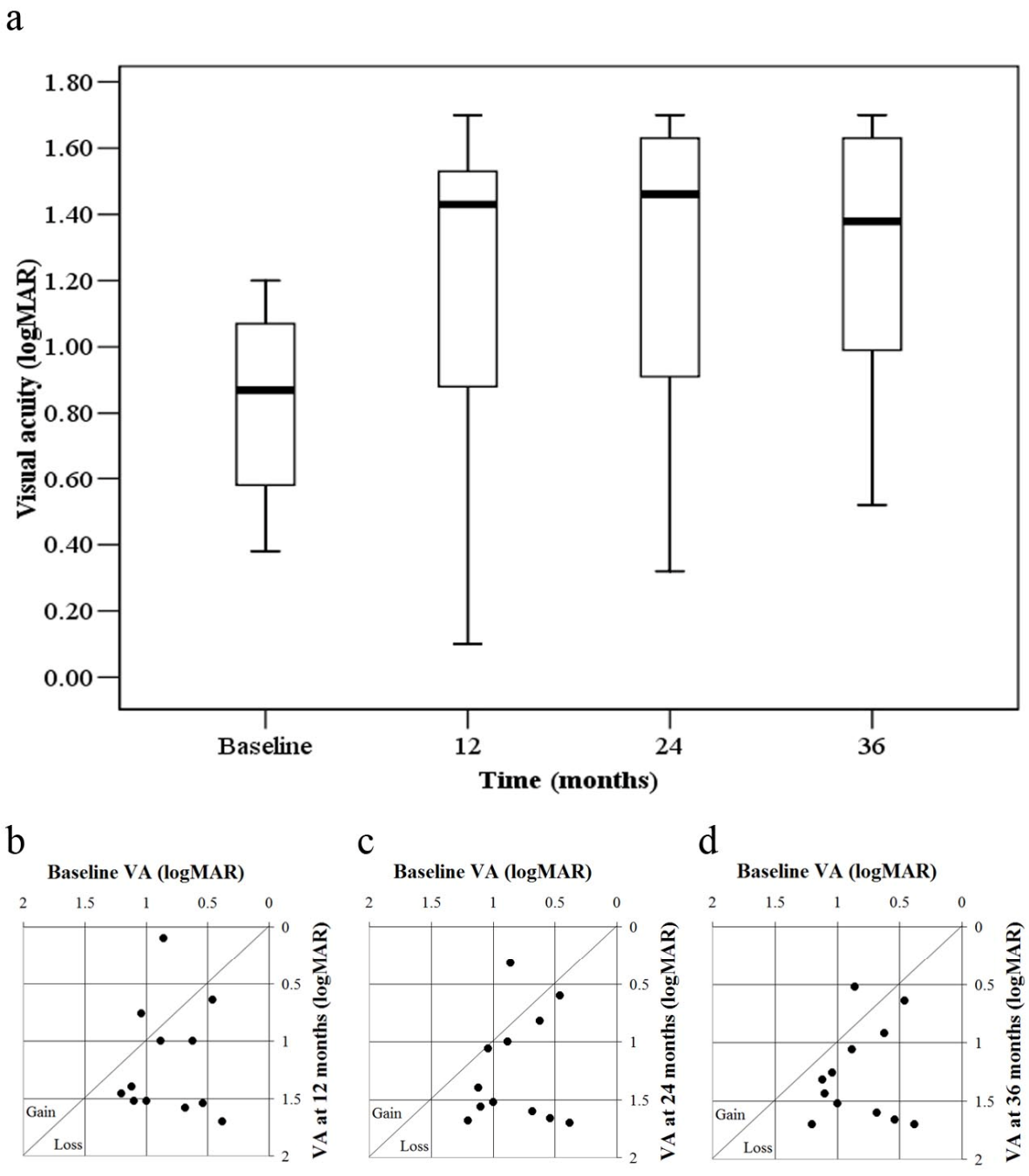

a
1.80
1.60
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
Visual acuity (logMAR)
Baseline
12
24
36
Time (months)
b
Baseline VA (logMAR)
2
1.5
1
0.5
0
0
0.5
1
1.5
2
VA at 12 months (logMAR)
Gain
Loss
c
Baseline VA (logMAR)
VA at 24 months (logMAR)
Gain
Loss
d
Baseline VA (logMAR)
VA at 36 months (logMAR)
Gain
Loss

**FIGURE 2**

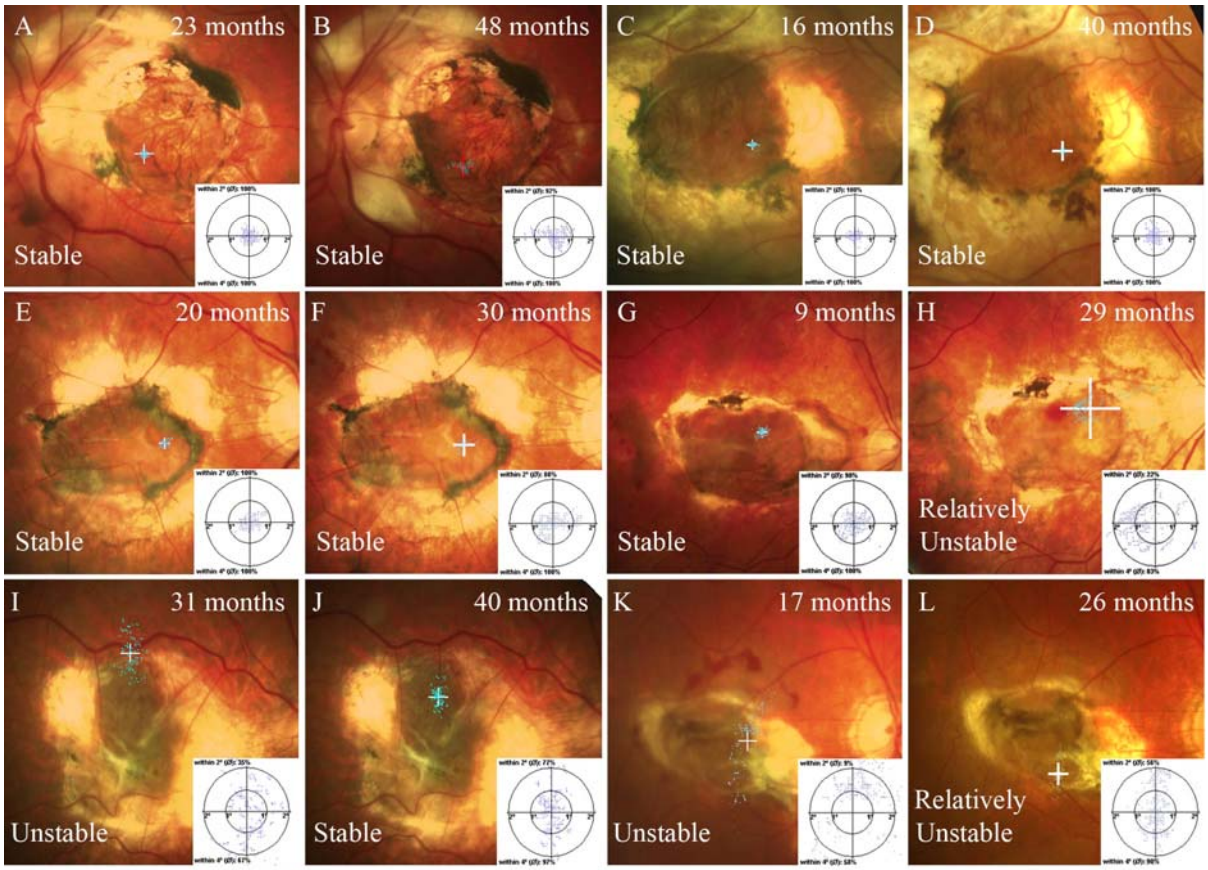

A
23 months
Stable
B
48 months
Stable
C
16 months
Stable
D
40 months
Stable
E
20 months
Stable
F
30 months
Stable
G
9 months
Stable
H
29 months
Relatively
Unstable
I
31 months
Unstable
J
40 months
Stable
K
17 months
Unstable
L
26 months
Relatively
Unstable

**FIGURE 3**

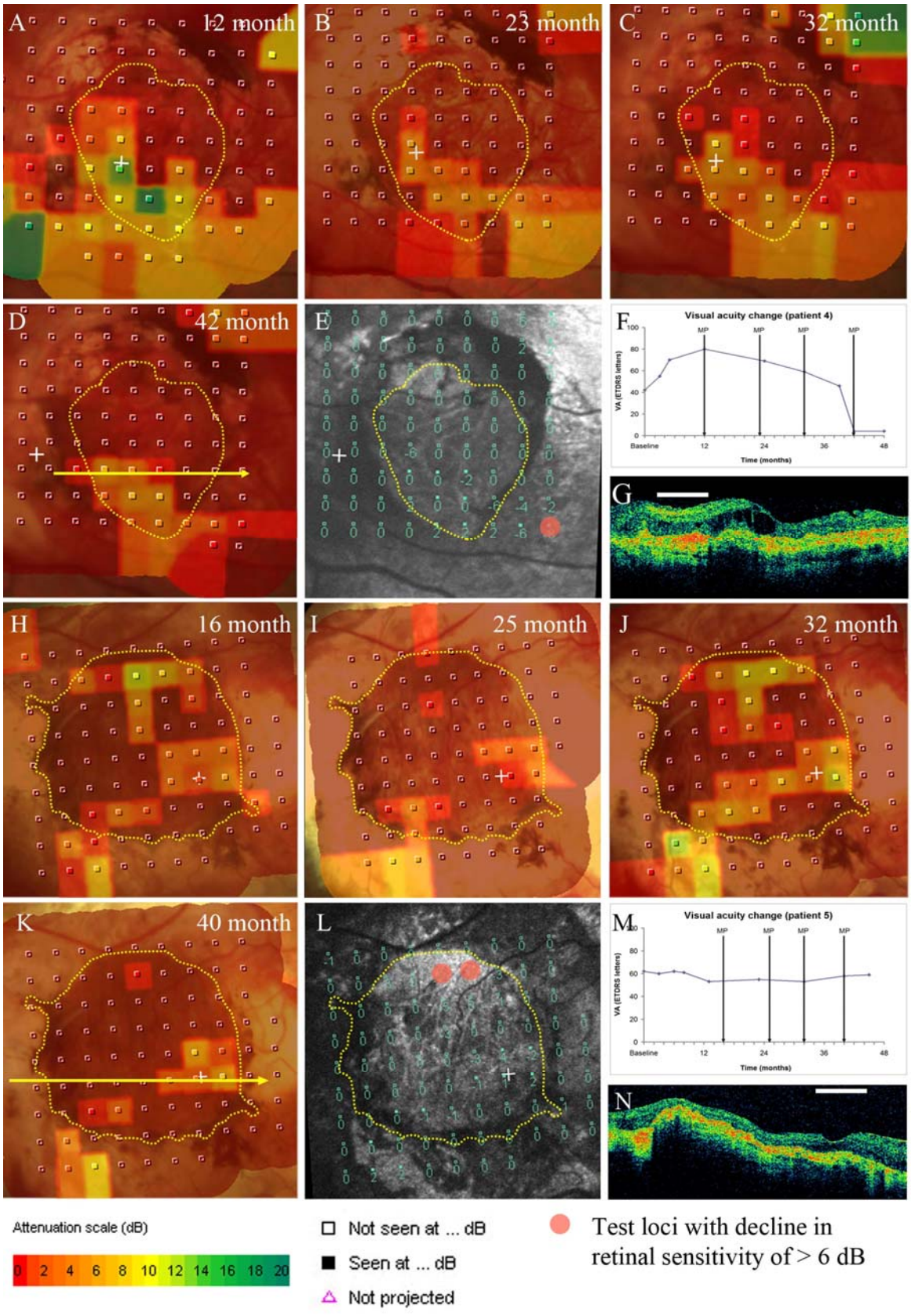
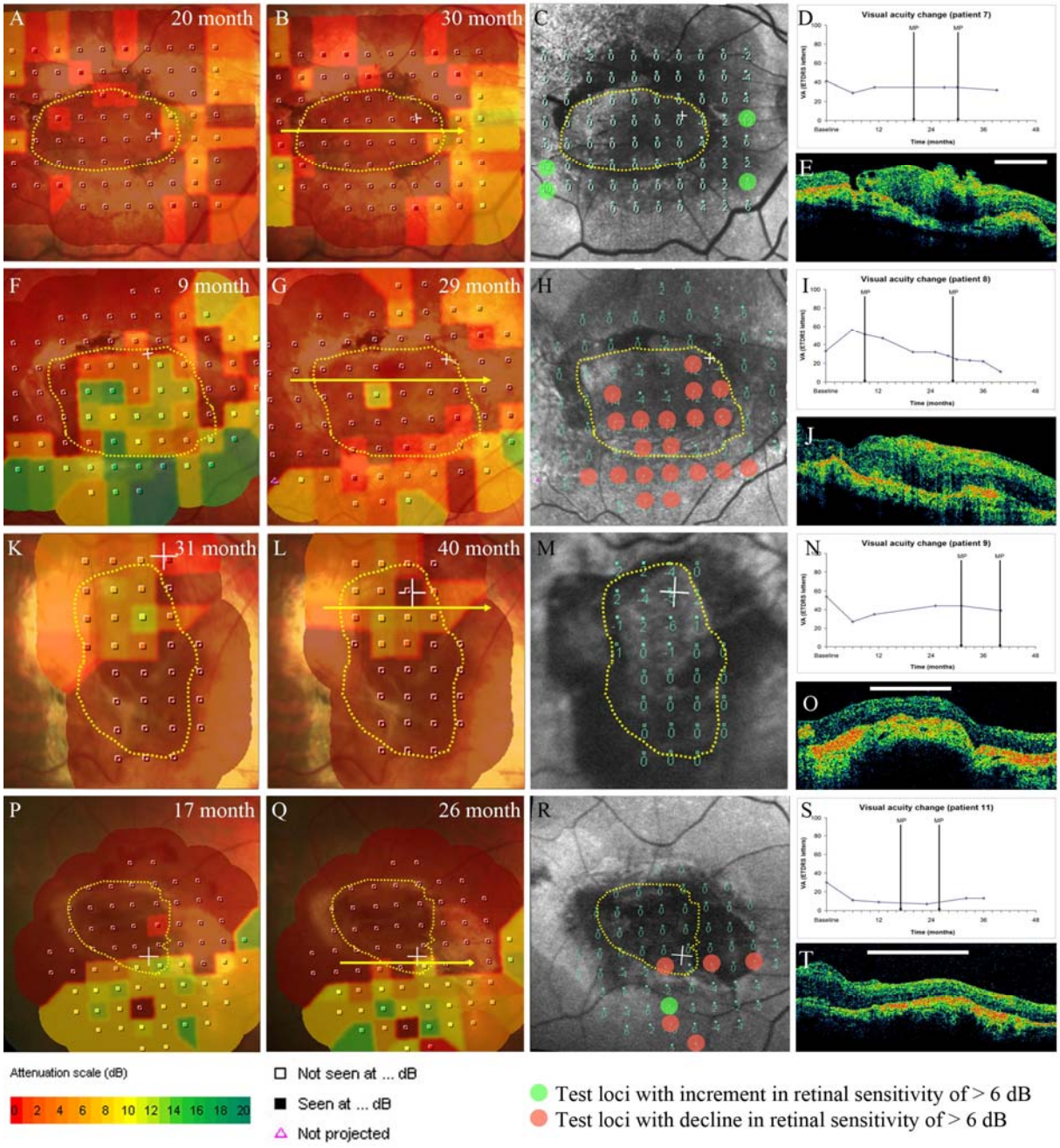

A
12 month
B
23 month
C
32 month
D
42 month
E
F
Visual acuity change (patient 4)
VA (ETDRS letters)
Time (months)
Baseline
12
24
36
48
MP
G
H
16 month
I
25 month
J
32 month
K
40 month
L
M
Visual acuity change (patient 5)
N
Attenuation scale (dB)
0 2 4 6 8 10 12 14 16 18 20
Not seen at ... dB
Seen at ... dB
Not projected
Test loci with decline in retinal sensitivity of > 6 dB

**FIGURE 4**


A
20 month
B
30 month
C
D
Visual acuity change (patient 7)
E
F
9 month
G
29 month
H
I
Visual acuity change (patient 8)
J
K
31 month
L
40 month
M
N
Visual acuity change (patient 9)
O
P
17 month
Q
26 month
R
S
Visual acuity change (patient 11)
T
Attenuation scale (dB)
0 2 4 6 8 10 12 14 16 18 20
Not seen at ... dB
Seen at ... dB
Not projected
Test loci with increment in retinal sensitivity of > 6 dB
Test loci with decline in retinal sensitivity of > 6 dB