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Feasibility and Utility of Microscope-Integrated Intraoperative OCT for Vitreoretinal Surgery: The DISCOVER Study 7-Year Results

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OBJECTIVE To assess the role of microscope-integrated intraoperative OCT (iOCT) in the management of vitreoretinal surgical diseases.

PURPOSE The feasibility and utility of iOCT on ophthalmic surgery has been demonstrated in preliminary studies evaluating microscope integration of OCT and have suggested a potential role for OCT in vitreoretinal surgery. The purpose of the DISCOVER study is to assess the feasibility and potential utility of microscope-integrated iOCT systems in ophthalmic surgery with a large prospective study.

METHODS The DISCOVER study is a prospective IRB-approved multi-surgeon investigational device study for evaluating microscope-integrated iOCT. Three integrated systems are utilized: the RESCAN 700 (Carl Zeiss Meditec, Germany), the Leica EnFocus (Leica, Germany), and the Cole Eye Integrated Prototype (Cleveland, OH). The study also includes digitally-enabled intraoperative OCT utilizing the NGENUITY system (Alcon, USA) and ARTEVO (Carl Zeiss Meditec). Surgeons utilized iOCT system during various surgical milestones. Clinical characteristics, adverse events, and iOCT workflow feedback were collected. The impact on surgical decision-making was assessed with a standardized surgeon feedback form.

RESULTS At 7 years, 1690 eyes were enrolled in the vitreoretinal arm. The most common surgical indications were retinal detachment (RD) (429), epiretinal membrane (311), macular hole (213), uveitis (135), proliferative diabetic retinopathy (123), vitreous

hemorrhage (122), and dislocated intraocular lens (73). In 1648 eyes (97.5%), iOCT imaging was successfully obtained. Digitally enabled intraoperative OCT with 3D surgical systems was also successful. Overall, iOCT provided perceived valuable feedback in 984 (58%) cases and altered surgical approach in 424 (25%) cases. The most common procedural changes based on iOCT were guidance regarding membrane peeling, including the identification of residual membranes, visualization of surgical dissection planes, and confirmation of complete membrane removal. The system interfered with surgery in 3% of cases, most frequently due to iOCT software malfunction that resulted in surgical delay. No adverse events were attributed to the iOCT system.

CONCLUSION This extensive prospective clinical study demonstrates that iOCT provides valuable information to the surgeon and impacts surgical decision-making in a significant number of cases. These findings were consistent and durable over the entirety of the study. Future randomized clinical trials are being planned to further explore the role of iOCT in ophthalmic surgery.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

10/11/2021 4:21PM

A Comparison of Superficial Macular Anatomic Changes Following ILM peeling Using a Micro-Vacuum Pick (MVP) Versus Forceps

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OBJECTIVE Does ILM peeling with a Micro-Vacuum Pick (MVP) result in less iatrogenic superficial macular changes than retinal foreceps?

PURPOSE To compare superficial macular anatomic changes which have been previously termed dissociated optic nerve fiber layer (DONFL) – a potential measure of tractional trauma to the retina following ILM peeling – using standard surgical forceps versus a novel surgical device, the micro-vacuum pick (MVP)

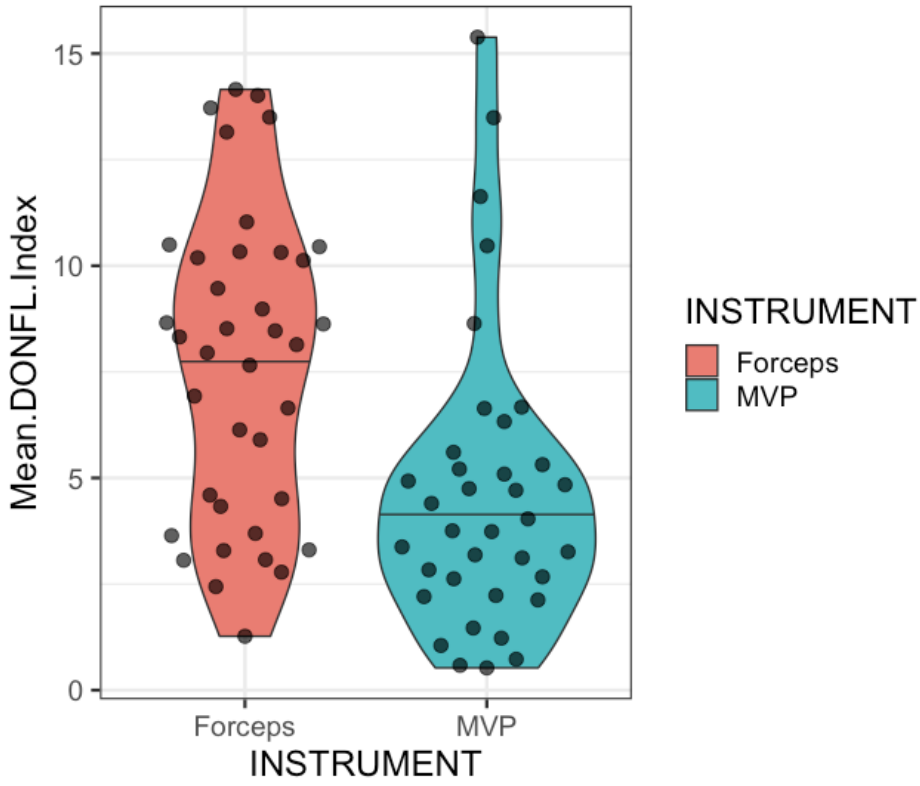
METHODS In this retrospective cohort study, consecutive eyes undergoing ILM peeling for either epiretinal membrane (ERM) or macular hole (MH) using the MVP were identified as well as a matched number of eyes using forceps. En-face OCT images at the level of the nerve fiber layer measuring 2x2 disc areas centered on the fovea were generated for the 3- and 6-month postoperative visits. Two masked graders manually measured the areas of DONFL. The percentage of the imaged area showing DONFL was termed the DONFL index. DONFL severity was additionally measured using a qualitative DONFL severity scale. DONFL severity as well as visual and anatomic outcomes were compared in the MVP and forceps groups.

RESULTS Seventy-four consecutive eyes underwent ILM peeling with either the MVP (36/74; 48.6%) or forceps (38/74; 51.4%) by a single surgeon. The two methods of DONFL severity measurement were strongly correlated (Spearman's $\rho = 0.9$, $p < 0.001$). At 6 months postoperatively, the mean DONFL index for the forceps group was 7.7 ± 3.5% vs 4.7 ± 3.9% for the MVP ($p < 0.001$, $R2 = 0.15$). The median DONFL index was similarly

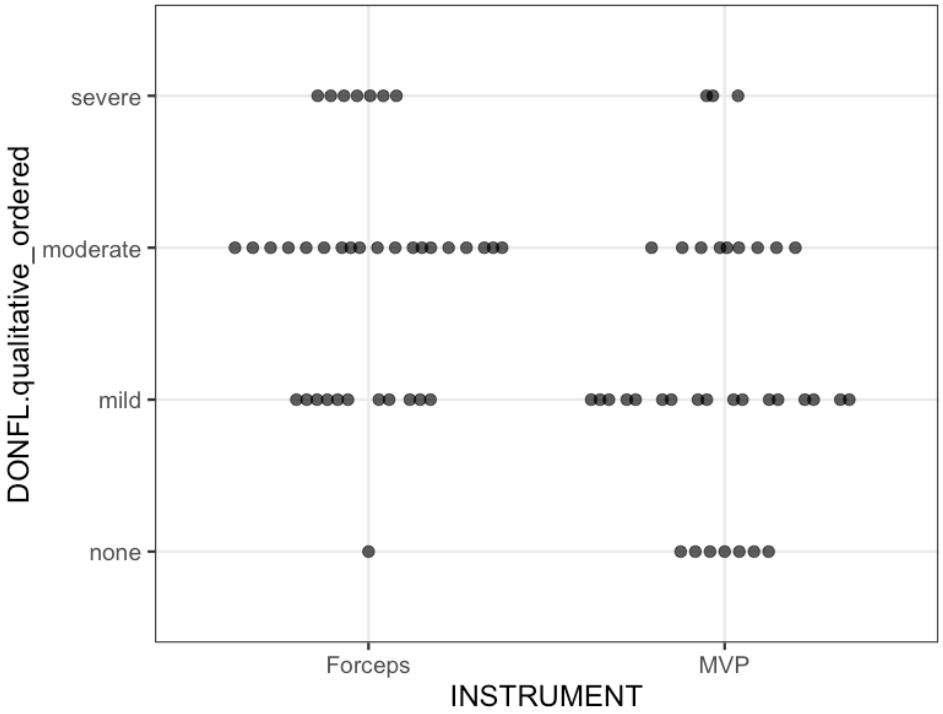
lower for the MVP (8.2% vs 3.9%, p = 0.001). By qualitative analysis 26/38 eyes (68.5%) in the forceps group had either moderate or severe DONFL at 6 months postoperatively compared to 12/36 eyes (33.3%) in the MVP group (p = 0.001). In the MVP group, median qualitative severity of DONFL was mild, whereas in the forceps group the median severity of DONFL was moderate. Subgroup analyses of eyes with ERM yielded similar results. A similar trend was also seen in eyes with MH. Visual outcomes and macular hole closure rates were similar between the groups.

CONCLUSION ILM peeling with the MVP resulted in lower DONFL severity compared to forceps though visual outcomes were similar in both groups. The severity of DONFL was consistent if measured subjectively or quantitatively. DONFL may indicate tractional stress on the retina during ILM peeling. Whether anatomic differences translate to differences in retinal sensitivity or function remains to be seen.

IRB APPROVAL No — I received a determination that the study/activity qualified for **exempt status or that it did not require IRB approval** from an IRB or another authorized oversight body *(IRB Exemption Letter may be requested)*.



Violin plot showing the distribution of DONFL index in eyes following ILM peeling with either forceps or the MVP



Distribution of qualitative DONFL severity in eyes undergoing ILM peeling with either forceps or the MVP

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One Year Follow-up in a Phase 1/2a Clinical Trial of an Allogeneic RPE Cell Bioengineered Implant for Advanced Dry Age-Related Macular Degeneration

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OBJECTIVE Is it safe and feasible to surgically deliver a stem-cell derived composite implant for replacement of RPE in subjects with advanced dry age-related macular degeneration and geographic atrophy?

PURPOSE To report one-year follow-up in a Phase 1/2a clinical trial testing a composite subretinal implant having polarized human embryonic stem cell-derived RPE cells on a synthetic substrate in subjects with advanced non-neovascular age-related macular degeneration.

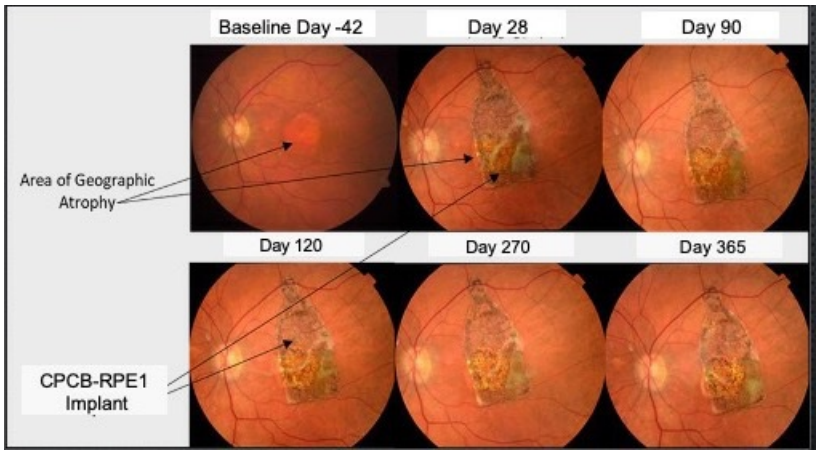
METHODS A single-arm, open label, prospective, non-randomized, Phase 1/2a study was conducted using a single surgical intervention on the worse-seeing eye (BCVA 20/200 or worse) of up to 20 pseudophakic subjects with advanced dry AMD with GA involving the fovea. All subjects underwent baseine and follow-up clinical evaluation, OCT and fundus photography as well as a single surgical intervention using commercially available vitrectomy instrumentation. The main endpoint was safety assessed at 365 days by ophthalmic and systemic exams. Low-dose tacrolimus immunosuppression was utilized for 68 days in the peri-implantation period. A data safety monitoring committee reviewed all results.

RESULTS Sixteen eyes of 16 subjects in 2 cohorts (BCVA Cohort 1 < 20/200 and Cohort 2

20/80-20/400) were recruited into the study. The treated eyes of all subjects were legally blind with a baseline BCVA of ≤ 20/200 . There were no unexpected serious adverse events. Four subjects in Cohort 1 had serious ocular adverse events including: hemorrhage, edema, focal retinal detachment, or RPE detachment. Surgically related serious adverse events were essentially eliminated in Cohort 2 with minor modifications to surgical technique. Although this study was not powered to assess efficacy, treated eyes from 4 subjects showed an increased BCVA of >5 letters (6-13 letters). A larger proportion of treated eyes experienced >5 letter gain when compared to the untreated eye (27% vs 7%, p=NS) and a larger proportion of nonimplanted eyes demonstrated > 5 letters loss (47% vs 33%, p=NS).

CONCLUSION At one-year, the surgical delivery of this composite implant is safe and well-tolerated. Surgical delivery of the implant is feasible on an outpatient basis can be performed with commercially available vitrectomy equipment. Preliminary visual acuity findings demonstrate promising signs of efficacy that need to be investigated in future trials.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.



Fundus photographs of a subject with geographic atrophy before and after subretinal surgical delivery of a composite monolayer of stem cell-derived RPE on a biosynthetic parylene membrane through 365 days of follow-up.