PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: BARRY J. SCHINDLER
GREENBERG TRAURIG, LLP
500 CAMPUS DRIVE, SUITE 400
FLORHAM PARK, NEW JERSEY 07932

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	07 JAN 2019

Applicant's or agent's file reference	FOR FURTHER ACTION
144861-011801/PCT	See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 18/48910	30 August 2018 (30.08.2018)	31 August 2017 (31.08.2017)

International Patent Classification (IPC) or both national classification and IPC
IPC(8) - A61N 5/06,5/067; A61F 9/007, 9/008,9/013 (2018.01)
CPC - A61N 5/06, A61N 5/0613, A61N 5/0622, A61N 2005/0648, A61N 2005/0659, A61N 2005/0661, A61N 2005/0662, A61N 2005/067; A61F 9/007, A61F 9/00781, A61F 9/0079, A61F 9/008, A61F 9/00802, A61F 9/00804, A61F 9/00814, A61F 9/00821, A61F 9/00823, A61F 9/00825, A61F 9/00827, A61F 9/013, A61F 2009/00842, A61F 2009/00861, A61F 2009/00863, A61F 2009/00872, A61F 2009/00885, A61F 2009/00891

Applicant SERDAREVIC, OLIVIA

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	12 December 2018	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a)).

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

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Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	2-9, 15, 16, 19, 23-26	YES
	Claims	1, 10-14, 17, 18, 20-22	NO
Inventive step (IS)	Claims	16, 24	YES
	Claims	1-15, 17-23, 25, 26	NO
Industrial applicability (IA)	Claims	1-26	YES
	Claims	NONE	NO

2. Citations and explanations:

Claims 1, 10-14, 17, 18 and 20-22 lack novelty under PCT Article 33(2) as being anticipated by US 2015/0297342 A1 AMO Gronigen B.V. (hereinafter AMO).

Regarding claim 1, AMO teaches a device, wherein the device is configured to redirect light away from a fovea or another retinal fixation region to at least two other spatially separated retinal regions (Fig. 4A and para [0013], [0110], improve vision where there is a loss of retinal function (e.g., a loss of foveal vision), the intraocular lens comprising: a redirection element configured to redirect incident light along a deflected optical axis which intersects a retina of a user at a preferred retinal locus. . .Accordingly, multiple PRLs may be appropriate and an IOL can be configured to redirect incident light to the appropriate PRLs using multiple zones and/or multiple redirection elements, as described herein), wherein the at least two other spatially separated retinal regions are different from the fovea or the another retinal fixation region, thereby to produce a retinal irradiance distribution modification (IDM) (para [0013], [0110], illustrated in figure 4A, improve vision where there is a loss of retinal function (e.g., a loss of foveal vision), the intraocular lens comprising: a redirection element configured to redirect incident light along a deflected optical axis which intersects a retina of a user at a preferred retinal locus. . .Accordingly, multiple PRLs may be appropriate and an IOL can be configured to redirect incident light to the appropriate PRLs using multiple zones and/or multiple redirection elements, as described herein).

Regarding claim 10, AMO teaches the device of claim 1, comprising at least one of an intraocular lens (IOL), an intraocular lens accessory device (IOLAD), or any combination thereof for insertion in a phakic, aphakic or pseudophakic eye, including IOLs and IOLADs positioned in the sulcus or capsular bag, anterior chambers IOLs and IOLADs, iris-fixated IOLs and IOLADs and transscleral-sutured IOLs and IOLADs (Fig. 4A and para [0009], [0071], ophthalmic devices (such as, for example, IOLs, contact lenses, etc.) that take into consideration the retinal structure and image processing capabilities of the peripheral retina. . . providing a piggyback lens in addition to an existing lens in the eye. The existing lens can be an IOL (e.g., standard IOL) that provides good foveal vision and/or the natural lens; the addition to the lens understood as phakic); wherein the IOL or IOLAD includes, at least one of i. central, paracentral or peripheral regions that are spatially separated, with or without overlapping of the regions, to modify radii of curvature, indices of refraction, diffraction, scattering or a combination thereof in any or all of the regions (para [0094], [0110], The various surface characteristics can include curvatures, surface sags, radius of curvatures, conic constant, axial thickness, area of the optical zone, diffractive features, echelletes and/or prismatic features provided with the optic, etc. . .multiple PRLs may be appropriate and an IOL can be configured to redirect incident light to the appropriate PRLs using multiple zones and/or multiple redirection elements, as described herein),
ii. two or more prisms (para [0112], The redirection elements can include, for example and without limitation, a simple prism. . . multiple redirection elements and/or multiple modifications can be made to the IOL; para [0010] refractive structures such as prisms),
iii. light-steering structures, including, but not limited to, at least one reflector within each paracentral region and at least one optical fiber, within at least one paracentral region, or iv. any combination thereof for light redirections away from the fovea or the another retinal fixation region to the at least two other spatially separated retinal regions and wherein the IOL or IOLAD is configured to produce the retinal IDM of claim 1 before insertion in the eye, or, by means of a light source, after insertion in the eye (Fig. 4A and para [0009], [0110], Various embodiments disclosed herein include ophthalmic devices (such as, for example, IOLs, contact lenses, etc.) that take into consideration the retinal structure . . .multiple PRLs may be appropriate and an IOL can be configured to redirect incident light to the appropriate PRLs using multiple zones and/or multiple redirection elements, as described herein).

Regarding claim 11, AOM teaches the device of claim 1, comprising an extraocular device configured to produce the retinal IDM of claim 1 and including spectacles and contact lenses to redirect light away from the fovea or the another retinal fixation region to the at least two other retinal regions, by means of radii of curvature, refractive indices, diffraction, scattering, light-steering structures, including, but not limited to, at least one reflector within each paracentral region and at least one optical fiber, within at least one paracentral region, or any combination thereof (para [0035], [0094], The methods and systems described herein to focus incident light at a region of the peripheral retina around the fovea can also be applied to spectacle lenses, contact lenses. . . The various surface characteristics can include curvatures, surface sags, radius of curvatures, conic constant, axial thickness, area of the optical zone, diffractive features, echelletes and/or prismatic features provided with the optic, etc), wherein the contact lens is corneal, scleral or any combination thereof and wherein the contact lens configured for retinal IDM may be worn for retinal IDM by a subject (para [0013], [0035], a deflected optical axis which intersects a retina of a user at a preferred retinal locus. . .The methods and systems described herein to focus incident light at a region of the peripheral retina around the fovea can also be applied to spectacle lenses, contact lenses) or may be utilized for screening or customization of retinal IDM with a non-contact lens device prior to the non-contact lens device being used for retinal IDM treatment on a subject.

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Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
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Box No. V.2. Citations and Explanations:

Regarding claim 12, AMO teaches the device of claim 1, wherein the IDM device is configured to produce at least one of
i. an improvement of vision in an eye or both eyes of a subject (para [0015], implemented in a method for improving vision where there is no or reduced foveal vision using an intraocular lens and a redirection element having a tailored slope profile),
ii a stabilization of vision in an eye or both eyes of a subject,
iii. an amelioration of a visual symptom in an eye or both eyes of a subject with an ophthalmic condition, disease, injury or disorder,
iv a reduction, compared to an untreated control group, of a rate of vision loss in an eye with a vision loss from an ophthalmic condition, disease, injury or disorder or v. any combination thereof, wherein the improved vision is for at least one of the following: visual acuity, hyperacuity, contrast sensitivity, vernier acuity, depth of focus, color vision, peripheral vision, night vision, light adaptation, dark adaptation, stereoacuity, face recognition, vision-related quality of life, or any combination thereof (para [0027], Various implementations disclosed herein are directed towards an intraocular device (e.g., an intraocular lens, an ophthalmic solution, a laser ablation pattern, etc.) that improves visual acuity and contrast sensitivity for patients with central visual field loss).

Regarding claim 13, AMO teaches the device of claim 1, configured to treat or compensate for at least one symptom of aretinal condition, disease, disorder, injury or degeneration including, but not limited, to a macular degeneration, macular scar, a macular edema, a macular hole, a macular pucker, a light-induced retinal injury, an epiretinal membrane, a retinal detachment sequela, a central serous retinopathy, a diabetic retinopathy, a retinal vascular disorder, a retinal genetic disorder, and a retinal nutritional disorder (para [0028], the device is configured to provide sufficient contrast sensitivity for light focused at the fovea for patients with early stages of macular degeneration).

Regarding claim 14, AMO teaches the device of claim 1, configured to treat or compensate for at least one symptom of glaucoma or another neuro-retinal disorder (para [0004], [0006], improve overall vision where there is a local loss of retinal function (e.g., loss of central vision due to a central scotoma),. . .Other retinal disorders affect younger patients. Examples of such diseases include Stargardt disease and Best disease. Also, a reverse form of retinitis pigmentosa produces an initial degradation of central vision).

Regarding claim 17, AMO teaches the device of claim 1, wherein the IDM device is configured to redirect light from one or more dysfunctional areas to at least two functional areas (para [0110], a patient can have a first PRL for reading, a second PRL when navigating, and a third PRL when talking and doing facial recognition, etc. Accordingly, multiple PRLs may be appropriate).

Regarding claim 18, AMO teaches the device of claim 1, wherein the IDM device is further configured to
i. decrease by at least 0.1 % retinal irradiance from the field of view on spatially separated retinal areas within at least one of a foveal area or non-foveal area, and
ii. increase by at least 0.1 % retinal irradiance from the field of view on at least one retinal area with viable cells, wherein the at least one retinal area is different from the foveal area or the non-foveal area of i (para [0099], [0110], piggyback lens configured for reading can be configured to increase the average MTF for a range of spatial frequencies and locations from 0.41 to 0.81. . . Accordingly, multiple PRLs may be appropriate and an IOL can be configured to redirect incident light to the appropriate PRLs using multiple zones and/or multiple redirection elements).

Regarding claim 20, AMO teaches a method utilizing a device, wherein the device is configured to redirect light away from a fovea or another retinal fixation region to at least two other spatially separated retinal regions (Fig. 4A and para [0013], [0110], improve vision where there is a loss of retinal function (e.g., a loss of foveal vision), the intraocular lens comprising: a redirection element configured to redirect incident light along a deflected optical axis which intersects a retina of a user at a preferred retinal locus. . .Accordingly, multiple PRLs may be appropriate and an IOL can be configured to redirect incident light to the appropriate PRLs using multiple zones and/or multiple redirection elements, as described herein), wherein the at least two other spatially separated retinal regions are different from the fovea or the another retinal fixation region, thereby to produce a retinal irradiance distribution modification (IDM) (para [0013], [0110], illustrated in figure 4A-1, improve vision where there is a loss of retinal function (e.g., a loss of foveal vision), the intraocular lens comprising: a redirection element configured to redirect incident light along a deflected optical axis which intersects a retina of a user at a preferred retinal locus. . .Accordingly, multiple PRLs may be appropriate and an IOL can be configured to redirect incident light to the appropriate PRLs using multiple zones and/or multiple redirection elements, as described herein).

Regarding claim 21, AMO teaches the method of claim 20, comprising optically modifying a retinal irradiance distribution by means of light redirections from the fovea or the another retinal fixation region to the at least two other spatially separated retinal regions (Fig. 4A and para [0013], [0110], improve vision where there is a loss of retinal function (e.g., a loss of foveal vision), the intraocular lens comprising: a redirection element configured to redirect incident light along a deflected optical axis which intersects a retina of a user at a preferred retinal locus. . .Accordingly, multiple PRLs may be appropriate and an IOL can be configured to redirect incident light to the appropriate PRLs using multiple zones and/or multiple redirection elements, as described herein), wherein the IDM is accomplished using
i. a device that produces changes in corneal or lenticular radii of curvature, refractive indices, diffraction, scattering or any combination thereof in one or both eyes of a subject by means of a process or device, including, but not limited to, corneal photovitrification, corneal photodisruption, corneal photoionization, corneal photodissociation, corneal photoablation, laser thermal keratoplasty, corneal crosslinking, conductive keratoplasty, intralenticular photodisruption and a corneal inlay or any combination thereof,
ii. an intraocular lens configured for retinal IDM (para [0009], include ophthalmic devices (such as, for example, IOLs, contact lenses, etc.) that take into consideration the retinal structure and image processing capabilities of the peripheral retina to improve vision),
iii. a contact lens configured for retinal IDM (para [0009], include ophthalmic devices (such as, for example, IOLs, contact lenses, etc.) that take into consideration the retinal structure and image processing capabilities of the peripheral retina to improve vision),
iv. spectacles configured for retinal IDM, or
v. any combination thereof configured to produce IDM; (claim 21 continued)

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(claim 21 continued) wherein the IDM device is configured to produce at least one of an improvement of vision in an eye or both eyes of a subject, a stabilization of vision in an eye or both eyes of a subject, an amelioration of a visual symptom in an eye or both eyes of a subject with an ophthalmic condition, disease, injury or disorder, a reduction of a rate of vision loss compared to an untreated control group in an eye or both eyes of a subject with vision loss from an ophthalmic condition, disease, injury or disorder, or any combination thereof, wherein the improved vision is for at least one of the following: visual acuity, hyperacuity, contrast sensitivity, vernier acuity, depth of focus, color vision, peripheral vision, night vision, light adaptation, dark adaptation, stereoacuity, face recognition, vision-related quality of life, or a combination thereof (para [0010], a system and method relating to providing ophthalmic lenses that can improve visual acuity and/or contrast sensitivity when there is a loss of central vision by focusing incident light onto an area on the peripheral retina around the fovea or at a region of the peripheral retina where vision is best); and
wherein the IDM treats or compensates for at least one symptom of a retinal degeneration, a retinal disorder, including but not limited to, a macular scar, a macular edema, a macular hole, a macular pucker, an epiretinal membrane, a retinal detachment sequela, a central serous retinopathy, a diabetic retinopathy, a retinal genetic disorder, a retinal nutritional disorder, a retinal vascular disease, glaucoma or another neuroretinal disorder, amblyopia or a combination thereof (para [0006], [0027], Other retinal disorders affect younger patients. Examples of such diseases include Stargardt disease and Best disease. Also, a reverse form of retinitis pigmentosa produces an initial degradation of central vision. . .The device can be configured to improve visual acuity and contrast sensitivity for patients with AMD through correction of the optical errors for the still healthy retina that the patient uses for viewing).

Regarding claim 22, AMO teaches the retinal IDM method of claim 21, further comprising i. decreasing by at least 0.1 % retinal irradiance from the field of view on spatially separated retinal areas within at least one of a foveal area or non-foveal area, and ii. increasing by at least 0.1 %i retinal irradiance from the field of view on at least one retinal area with viable cells, wherein the at least one retinal area is different from the foveal area or the non-foveal area of I (para [0099], [0110], piggyback lens configured for reading can be configured to increase the average MTF for a range of spatial frequencies and locations from 0.41 to 0.81. . . Accordingly, multiple PRLs may be appropriate and an IOL can be configured to redirect incident light to the appropriate PRLs using multiple zones and/or multiple redirection elements).

Claims 2 and 4-9 lack an inventive step under PCT Article 33(3) as being obvious over AMO in view of US 2017/0007395 A1 (Peyman).

Regarding claim 2, AMO teaches the device of claim 1, wherein the device in one or both eyes of a subject at least one of ·
i. radii of curvature,
ii. refractive indices,
iii. diffraction (para [0030], the optics included in various implementations of the device described herein can be diffractive to provide near vision),
iv. scattering, or v. any combination thereof for light redirections away from the fovea or the another retinal fixation region to two or more other retinal regions (Fig. 4A and para [0110], Accordingly, multiple PRLs may be appropriate and an IOL can be configured to redirect incident light to the appropriate PRLs using multiple zones and/or multiple redirection elements, as described herein). AMO does not teach the device modifies in a cornea or a naturally occurring crystalline lens, by means of processes or devices including corneal photovitrification, corneal photodisruption, intralenticular photodisruption, corneal photoionization, corneal photoablation, photothermal keratoplasty, corneal crosslinking, conductive keratoplasty and corneal inlay or any combination thereof. However Peyman teaches a device modifies in a cornea or a naturally occurring crystalline lens, by means of processes or devices including corneal crosslinking (para [0266], the photosensitizer is applied inside the pocket, the cornea 1100 of the eye is irradiated using ultraviolet (UV) radiation 1112 so as to activate cross-linkers in the portion of the tissue bounding the pocket 1106). It would have been obvious to a person having ordinary skill in the art to use the device modifies in a cornea or a naturally occurring crystalline lens, by means of processes or devices including corneal crosslinking of Peyman in the device of AMO, because the disclosure of Peyman would have prevented corneal ectasia (para [0022], activate cross-linkers in the portion of the tissue bounding the pocket and thereby stiffen the cornea and prevent corneal ectasia of the cornea. . . the cross-linking of the tissue bounding the pocket does not adhere the lens implant to the tissue bounding the pocket so that the lens implant is capable of subsequently replaced if needed).

Regarding claim 4, AMO teaches the device of claim 1. AMO does not teach a corneal cross-linking treatment, including an ultraviolet light source, laser thermal keratoplasty laser or corneal CPV laser or other light emitting source and photosensitizer, or other photoactivation system with photoactivation agents. However Peyman teaches a corneal cross-linking treatment, including an ultraviolet light source and photosensitizer (para [0266], the photosensitizer is applied inside the pocket, the cornea 1100 of the eye is irradiated using ultraviolet (UV) radiation 1112). It would have been obvious to a person having ordinary skill in the art to use the corneal cross-linking treatment, including an ultraviolet light source and photosensitizer of Peyman in the device of AMO, because the disclosure of Peyman would have prevented corneal ectasia (para [0022], activate cross-linkers in the portion of the tissue bounding the pocket and thereby stiffen the cornea and prevent corneal ectasia of the cornea. . . the cross-linking of the tissue bounding the pocket does not adhere the lens implant to the tissue bounding the pocket so that the lens implant is capable of subsequently replaced if needed).

Regarding claim 5, AMO teaches the device of claim 1. AMO does not teach the device comprising a laser source including at least one of a femtosecond laser, a nanosecond laser, a laser source for photodisruption, a laser source for photoionization or a laser source for photodissociation. However Peyman teaches a femtosecond laser (para [0179], Laser 500 is preferably an ultra-short pulse laser, such as a femto, pico, or attosecond laser). It would have been obvious to a person having ordinary skill in the art to use the femtosecond laser of Peyman in the device of AMO, because the disclosure of Peman would have allowed high surface quality and accuracy (para [0179], Cuts or ablation performed using ultra short pulse lasers can have very high surface quality with accuracy better than 10 microns, resulting in more precise cuts than those made with mechanical devices or other lasers).

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Box No. V.2. Citations and Explanations:

Regarding claim 6, AMO teaches the device of claim 1. AMO does not teach the device comprising a laser source for corneal ablation. However Peyman teaches a laser source for corneal ablation (para [0179], Ultra short pulse lasers are desired since they are capable of ablating or vaporizing corneal tissue beneath the surface of the cornea). It would have been obvious to a person having ordinary skill in the art to use the laser source for corneal ablation of Peyman in the device of AMO, because the disclosure of Peyman would have allowed high surface quality and accuracy (para [0179], Cuts or ablation performed using ultra short pulse lasers can have very high surface quality with accuracy better than 10 microns, resulting in more precise cuts than those made with mechanical devices or other lasers).

Regarding claim 7, AMO teaches the device of claim 1. AMO does not teach the device comprising a thermal corneal laser source. However Peyman teaches a thermal corneal laser source (para [0019]. The electrodes emit a radio frequency wave or laser light, thereby heating the surface of the cornea). It would have been obvious to a person having ordinary skill in the art to use the thermal corneal laser source of Peyman in the device of AMO, because the disclosure of Peyman would have corrected presbyopic and hyperopic errors (para [0019], since the cornea can generally only be shrunk in response to thermal coagulation, this method is exclusively used for presbyopic and hyperopic correction of refractive errors).

Regarding claim 8, AMO teaches the device of claim 1. AMO does not teach the device comprising a radiofrequency emitting device. However Peyman teaches a radiofrequency emitting device (para [0019], The electrodes emit a radio frequency wave or laser light, thereby heating the surface of the cornea). It would have been obvious to a person having ordinary skill in the art to use the radiofrequency emitting device of Peyman in the device of AMO, because the disclosure of Peyman would have corrected presbyopic and hyperopic errors (para [0019], since the cornea can generally only be shrunk in response to thermal coagulation, this method is exclusively used for presbyopic and hyperopic correction of refractive errors).

Regarding claim 9, AMO teaches the device of claim 1. AMO does not teach the device comprising a corneal inlay for insertion in a cornea. However Peyman teaches a corneal inlay for insertion in a cornea (para [0168], a modified method does not necessarily need to be performed on the cornea, but can be performed on a separate lens or inlay 430. Inlay 430 is preferably a substantially circular polymeric or synthetic inlay). It would have been obvious to a person having ordinary skill in the art to use the corneal inlay for insertion in a cornea of Peyman in the device of AMO, because the disclosure of Peyman would have corrected refractive error in the eye (para [0168], inlay or blank that has a predetermined thickness and a first side 432 and a second side 434 and is positioned under the flap adjacent second surface 26 to correct refractive error in the eye).

Claim 3 lacks an inventive step under PCT Article 33(3) as being obvious over AMO in view of US 2015/0133901 A1 Serdarevic et al. (hereinafter Serdarevic).

Regarding claim 3, AMO teaches the device of claim 1. AMO does not teach the device comprising a laser or other light emitting source for corneal photovitrification. However Serdarevic teaches a laser or other light emitting source for corneal photovitrification (para [0002], [0093], [0114], methods and devices for photovitrification that utilize a photon source to produce vitrification of corneal tissue. . .the at least one photon source is a semiconductor diode laser that produces at least one photon output . . .methods of use of devices and/or systems can be used in vivo cornea of an in situ human eye for corneal photovitrification). It would have been obvious to a person having ordinary skill in the art to use the laser or other light emitting source for corneal photovitrification of Serdarevic in the device of AMO, because the disclosure of Serdarevic would have helped improve vision (para [0038], corneal optical aberrations by the instant invention can also be used to improve vision in these cases with ectasia).

Claim 15 lacks an inventive step under PCT Article 33(3) as being obvious over AMO in view of the article entitled "Phakic Intraocular Lens Implantation for Treatment of Anisometropia and Amblyopia in Children: 5-year Follow-up" by Alio et al. (hereinafter Alio).

Regarding claim 15, AMO teaches the device of claim 1. AMO does not teach the device configured to treat or compensate for at least one symptom of amblyopia. However Alio teaches a device configured to treat or compensate for at least one symptom of amblyopia (Abstract, To evaluate the safety and effi cacy during 5-year follow-up of phakic intraocular lens (PIOL) implantation to correct high anisometropia in amblyopic children). It would have been obvious to a person having ordinary skill in the art to use the device configured to treat or compensate for at least one symptom of amblyopia of Alio in the device of AMO, because the disclosure of Alio would have allowed a positive long term impact on visual acuity (Abstract, Phakic IOL implantation in children with anisometropic amblyopia showed a positive long-term impact on visual acuity).

Claims 19 and 23 lack an inventive step under PCT Article 33(3) as being obvious over AMO in view of US 2011/0306919 A1 Latina et al. (hereinafter Latina).

Regarding claim 19, AMO teaches the device of claim 18. AMO does not teach wherein treatment with the IDM device produces in a treated eye at least one of the following: i. an increase in retinal sensitivity in a retinal region, ii. a decrease in the rate of retinal sensitivity loss compared to an untreated control group, iii. a decrease in the rate of photoreceptor loss compared to an untreated control group, iv. a decrease of the area of photoreceptor loss, v. a decrease of drusen volume, vi. a regeneration of retinal cells, vii. any combination thereof. However Latina teaches a treatment produces in a treated eye, regeneration of retinal cells (para [0055], a q-switched Nd:YAG laser, the cells in the irradiated tissue are induced to proliferate and cause repair and/or regeneration of the tissue. . . The cells to be targeted may express an endogenous chromophore (e.g., retinal epithelium)). It would have been obvious to a person having ordinary skill in the art to combine the regeneration of Latina in the device of AMO, because AMO teaches it would be beneficial to halt the degradation of the retina (para [0006], If the degradation of the retina can be halted a sustained vision benefit can be obtained with an IOL), and the disclosure of Latina which could be achieved with the disclosure of Latina (para [0003], proliferation and growth, and thereby results in a healing effect on atrophied or diseased tissue, while avoiding cell damage and cell death).

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Continuation of:
Box no. V.2. Citations and Explanations:

Regarding claim 23, AMO teaches the retinal IDM method of claim 22. AMO does not teach the method further comprising producing in a treated eye at least one of the following: i. an increase in retinal sensitivity in a retinal region, ii. a decrease in the rate of retinal sensitivity loss compared to an untreated control group, iii. a decrease in the rate of photoreceptor loss compared to an untreated control group, iv. a decrease of the area of photoreceptor loss, v. a decrease of drusen volume, vi. A regeneration of retinal cells, or vii. any combination thereof. However Latina teaches a treatment produces in a treated eye, regeneration of retinal cells (para [0055], a q-switched Nd:YAG laser, the cells in the irradiated tissue are induced to proliferate and cause repair and/or regeneration of the tissue. . . The cells to be targeted may express an endogenous chromophore (e.g., retinal epithelium)). It would have been obvious to a person having ordinary skill in the art to combine the regeneration of Latina in the device of AMO, because AMO teaches it would be beneficial to halt the degradation of the retina (para [0006], If the degradation of the retina can be halted a sustained vision benefit can be obtained with an IOL), and the disclosure of Latina which could be achieved with the disclosure of Latina (para [0003], proliferation and growth, and thereby results in a healing effect on atrophied or diseased tissue, while avoiding cell damage and cell death).

Claims 25 and 26 lack an inventive step under PCT Article 33(3) as being obvious over AMO in view of Latina and further in view of WO 2017/046358 A1 to Medterials Inc (hereinafter Medterials).

Regarding claim 25, AMO and Latina teach the retinal IDM method of claim 23. Neither AMO nor Latina teach the method further comprising treating an eye by the retinal IDM of claim 23 in combination with sequentially administering, either before or after retinal IDM treatment, genetic, epigenetic, optogenetic or stem cell therapy for treating a retinal disorder. However Medterials teaches administering, a genetic, epigenetic, optogenetic or stem cell therapy for treating a retinal disorder (pg. 1, ln 28-33, treating the retina with specific gene and cell therapies, a therapeutic agent is often desired to be injected in the subretinal space). It would have been obvious to a person having ordinary skill in the art to use the administering, a genetic, epigenetic, optogenetic or stem cell therapy for treating a retinal disorder of Medterials in the method of AMO, because the disclosure of Medterials would have helped to treat many different conditions (pg. 16, ln 32-pg. 17, ln 15; the treatment of a variety of ocular diseases and conditions including inflammation, infection, macular degeneration, retinal degeneration, neovascularization, proliferative vitreoretinopathy, glaucoma, and edema).

Regarding claim 26, AMO and Latina teach the retinal IDM method of claim 23. Neither AMO nor Latina teach further comprising treating an eye by the retinal IDM of claim 23 in combination with sequentially administering topically, intraretinally, via intravitreal injections, via implants or via iontophoresis, either before or after retinal IDM treatment, a therapeutically effective amount of at least one of the following for treating a neuro-retinal disorder, including glaucoma:
i. an intraocular pressure-lowering agent, including but not limited to a miotic, an alpha or alpha/beta adrenergic agonist, a beta-blocker, a Ca2+ channel blocker, a carbonic anhydrase inhibitor, a chlolinesterase inhibitor, a prostaglandin agonist, a prostaglandin, a prostarnide, a cannabinoid, or any cornbination thereof;
ii. a ganglion cell-neuroprotective or neuroregenerative agent, including but not limited to a rho-kinase inhibitor, an adenosine receptor agonist or a glutarnate antagonist; or
iii. any combination thereof. However Medterials teaches administering via intravitreal injections a therapeutically effective amount of at least one of the following for treating a neuro-retinal disorder, including glaucoma (pg. 1, ln 28-33, pg. 16, ln 32-pg. 17, ln 15, a therapeutic agent is often desired to be injected in the subretinal space. . .treatment of a variety of ocular diseases and conditions including inflammation, infection, macular degeneration, retinal degeneration, neovascularization, proliferative vitreoretinopathy, glaucoma, and edema):
i. an intraocular pressure-lowering agent, including but not limited to a miotic, an alpha or alpha/beta adrenergic agonist, a beta-blocker, a Ca2+ channel blocker, a carbonic anhydrase inhibitor, a chlolinesterase inhibitor, a prostaglandin agonist, a prostaglandin, a prostarnide, a cannabinoid, or any cornbination thereof (pg. 16, ln 32-pg. 17, ln 15; antihypertensive agents such as prostaglandin analogs, beta blockers, alpha agonists, and carbonic anhydrase inhibitors). It would have been obvious to a person having ordinary skill in the art to use the administering via intravitreal injections a therapeutically effective amount of at least one of the following for treating a neuro-retinal disorder, including glaucoma an intraocular pressure-lowering agent, including but not limited to a miotic, an alpha or alpha/beta adrenergic agonist, a beta-blocker, a Ca2+ channel blocker, a carbonic anhydrase inhibitor, a chlolinesterase inhibitor, a prostaglandin agonist, a prostaglandin, a prostarnide, a cannabinoid, or any cornbination thereof of Medterials in the method of AMO, because the disclosure of Medterials would have helped to treat many different conditions (pg. 16, ln 32-pg. 17, ln 15; the treatment of a variety of ocular diseases and conditions including inflammation, infection, macular degeneration, retinal degeneration, neovascularization, proliferative vitreoretinopathy, glaucoma, and edema).

Claims 16 and 24 meet the criteria under PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the subject matter claimed.

The prior art for claim 16 is exemplified by AMO.

Regarding claim 16, AMO teaches the device of claim 1. AMO does not teach wherein the IDM device is configured to produce, without requiring perceptual or oculomotor training, a natural awareness in a treatment subject of one or more alternate functional visual pathways and a natural sensorimotor learning.

The prior art made of record does not disclose or fairly suggest the claimed subject matter, specifically he IDM device is configured to produce, without requiring perceptual or oculomotor training, a natural awareness in a treatment subject of one or more alternate functional visual pathways and a natural sensorimotor learning. Further, the prior art, whether taken alone or in combination, fails to disclose or suggest the particular arrangement of these parts as required by the claims.

The prior art for claim 24 is exemplified by AMO and Latinal.

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 18/48910

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of:
Box No. V.2. Citations and Explanations:

Regarding claim 24, AMO and Latina teach the retinal IDM method of claim 23. Neither AMO nor Latina teach the method further comprising treating an eye by the retinal IDM of claim 23 in combination with sequentially administering, either before or after retinal IDM treatment, a therapeutically effective amount of a vascular endothelial growth factor (VEGF) antagonist, including, but not limited to, aflibercept, ranibizumab, bevacizumab and brolucizumab, wherein the VEGF antagonist is administered via intravitreal injections, orally, topically, intraretinally, via implants or via iontophoresis and wherein the combination therapy is for treating or ameliorating a neovascular ocular disease, including macular degeneration, choroidal neovascularization and diabetic retinopathy.

The prior art made of record does not disclose or fairly suggest the claimed subject matter, specifically sequentially administering, either before or after retinal IDM treatment, a therapeutically effective amount of a vascular endothelial growth factor (VEGF) antagonist, including, but not limited to, aflibercept, ranibizumab, bevacizumab and brolucizumab, wherein the VEGF antagonist is administered via intravitreal injections, orally, topically, intraretinally, via implants or via iontophoresis and wherein the combination therapy is for treating or ameliorating a neovascular ocular disease, including macular degeneration, choroidal neovascularization and diabetic retinopathy. Therefore claim 24 meets the criteria under PCT Article 33(2)-(3).

Claims 1-26 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.