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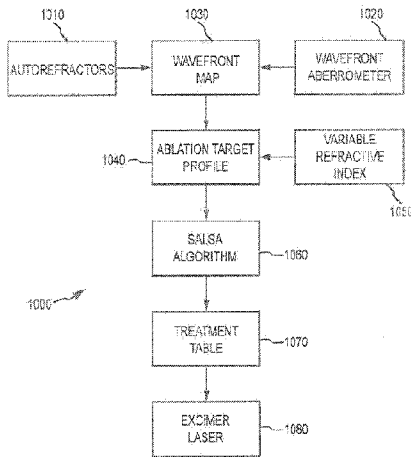


FIG.10

(57) **Abstract:** Systems and methods for fine-tuning refractive shapes for vision treatment are provided. Techniques encompass determining a variable index of refraction for a cornea of the eye, and determining the refractive treatment shape for the eye based on the variable index of refraction. Techniques also encompass determining a variable radius of curvature of an anterior surface of a cornea of the eye, and determining the refractive treatment shape for the eye based on the variable radius of curvature.

## SYSTEMS AND METHODS FOR FINE-TUNING REFRACTIVE SURGERY

### CROSS-REFERENCES TO RELATED APPLICATIONS

5 [0001] This Patent Cooperation Treaty application claims the benefit of priority to U.S. Non-Provisional Application No. 12/627,742, filed on November 30, 2009, which is a continuation-in-part of U.S. Patent Application No. 12/178,127, filed July 23, 2008, which is a nonprovisional of, and claims the benefit of priority to, U.S. Provisional Patent Application No. 60/953,425, filed August 1, 2007. The entire contents of each of the above filings is  
10 incorporated herein by reference for all purposes.

### BACKGROUND OF THE INVENTION

[0002] Embodiments of the present invention relate the field of vision treatment, and in particular to systems and methods for fine-tuning ablation profiles and other treatment  
15 shapes.

[0003] Many current laser correction techniques are based on a nominal value that reflects a constant index of refraction of the corneal stroma. These techniques do not consider the variation that may exist in the refractive index of the corneal stroma. Known techniques are often based on a nominal value, which may be 1.376, for example. Moreover, many current  
20 approaches are based on or employ a nominal value that reflects a constant radius of curvature of the anterior surface of the cornea. This can cause up to about a 2% to 3% error in ablation depth, for example.

[0004] However, such estimations may not accurately represent the actual anatomy of the ocular system, or changes that may occur in the anatomy or the ablation process as the  
25 ablation process is carried out. Hence there is a need for systems and methods that consider a variation in the refractive index, which more closely approximates the ocular anatomy. Moreover, there is a need for systems and methods that consider a variation in the radius of curvature, which more closely approximates the ocular anatomy. Embodiments of the present invention provide solutions for at least some of these needs.

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## BRIEF SUMMARY OF THE INVENTION

[0005] Embodiments of the present invention provide techniques for fine-tuning ablation profiles for both conventional non-wavefront and wavefront-driven refractive surgery. These techniques can be implemented in a variety of laser and aberrometer devices, including  
5 without limitation the VISX WaveScan WaveFront System and STAR S4 Excimer Laser System, the Wavelight Alegretto and Tscherning-based aberrometer; the Alcon Ladarvision lasers and Ladarwave aberrometer; the Bausch and Lomb Zyoptix laser and related aberrometer, and the Zeiss laser and WASCA aberrometer.

[0006] Typically the index of refraction of the corneal stroma is not constant. For example,  
10 the index of refraction may change from about 1.38 at the anterior surface to about 1.373 at the posterior surface of the cornea. Advantageously, embodiments of the present invention encompass techniques that consider such a change in the refractive index. Accordingly, it is possible to obtain an improvement in the accuracy of an ablation profile or treatment shape. In some cases, this involves a consideration of high order aberrations. Moreover, typically  
15 the radius of curvature of the anterior surface of the cornea is not constant. Advantageously, embodiments of the present invention encompass techniques that consider a variable corneal radius of curvature.

[0007] Embodiments of the present invention encompass accurate techniques that take into account a change in refractive index of the corneal stroma. Embodiments of the present  
20 invention also encompass accurate techniques that take into account a customized radius of curvature of the anterior surface of the stroma. These techniques can be implemented in, for example, a VSS refractive treatment.

[0008] In one aspect, embodiments of the present invention encompass systems for determining a refractive treatment shape for an eye of a patient. Systems may include, for  
25 example, an input configured to receive a variable index of refraction for a cornea of the eye, and a processing module comprising a tangible medium embodying machine-readable code that determines the refractive treatment shape for the eye based on the variable index of refraction. In some cases, the refractive treatment shape can be configured to treat hyperopia or myopia. In some cases, the processing module can include a tangible medium embodying  
30 machine-readable code that determines the refractive treatment shape for the eye based on a Munnerlyn shape or a wavefront analysis of the eye. Optionally, systems may include an

ablation system configured to apply the refractive treatment shape to the patient. The variable index of refraction can vary as a function of an ablation depth.

[0009] In some aspects, embodiments of the present invention encompass systems for determining a refractive treatment shape for an eye of a patient, such that the systems include an input configured to receive an instantaneous index of refraction for a cornea of the eye, and a processing module having a tangible medium embodying machine-readable code that determines the refractive treatment shape of a remaining ablation for the eye based on the instantaneous index of refraction. Systems may also include an ablation system configured to apply the refractive treatment shape to the patient. In some cases, systems include sensor or sensing assembly that detects the instantaneous index of refraction. The instantaneous index of refraction can vary as a function of an ablation depth.

[0010] In a further aspect, embodiments of the present invention encompass systems for determining a refractive treatment shape for an eye of a patient, such that a system may include an input configured to receive a variable radius of curvature of an anterior surface of a cornea of the eye, and a processing module with a tangible medium embodying machine-readable code that determines the refractive treatment shape for the eye based on the variable radius of curvature of the anterior surface. Systems may also have an ablation system configured to apply the refractive treatment shape to the patient. In some cases, the variable radius of curvature of the anterior surface of the eye is a function of a radius of curvature of a posterior surface of the cornea. In some cases, the variable radius of curvature of the anterior surface of the eye can vary as a function of an ablation depth.

[0011] In another aspect, embodiments of the present invention encompass systems for determining a refractive treatment shape for an eye of a patient, where a system can have an input configured to receive an instantaneous radius of curvature of an anterior surface of a cornea of the eye, and a processing module with a tangible medium embodying machine-readable code that determines the refractive treatment shape of a remaining ablation for the eye based on the instantaneous radius of curvature of the anterior surface of the cornea of the eye. Systems may also include an ablation system configured to apply the refractive treatment shape to the patient. In some cases, systems include a sensor or sensor assembly that detects the instantaneous radius of curvature of the anterior surface of the cornea of the eye. The instantaneous radius of curvature of the anterior surface of the eye can vary as a

function of an ablation depth. The refractive treatment shape for the eye can be based on a Munnerlyn equation.

[0012] In yet another aspect, embodiments of the present invention encompass methods of determining a refractive treatment shape for an eye of a patient. Methods may include, for example, determining a variable index of refraction for a cornea of the eye, and determining the refractive treatment shape for the eye based on the variable index of refraction. In some cases, the step of determining the refractive treatment shape involves determining a refractive treatment shape of a remaining ablation for the eye based on the variable index of refraction. In some cases, the variable index of refraction for the cornea varies between an anterior portion of the cornea and a posterior portion of the cornea. In some cases, the variable index of refraction for the cornea varies across at least a portion of a corneal stroma. Relatedly, the variable index of refraction for the cornea can vary as a function of corneal stromal depth. The variable index of refraction for the cornea may vary as a linear function of corneal stromal depth. In some cases, the variable index of refraction for the cornea varies as a nonlinear function of corneal stromal depth. The refractive treatment shape can be configured to treat hyperopia. Relatedly, the refractive treatment shape can be configured to treat myopia. In some cases, the refractive treatment shape is determined based on a Munnerlyn shape. In some cases, the refractive treatment shape is determined based on a wavefront analysis of the eye. The variable index of refraction for the cornea of the eye may be determined following application of one or more ablation pulses to the eye. Optionally, the step of determining the variable index of refraction for a cornea of the eye can include determining an instantaneous variable index of refraction for the cornea following application of one or more ablation pulses to the eye, and the step of determining the refractive treatment shape can include determining a refractive treatment shape of a remaining ablation for the eye based on the instantaneous variable index of refraction. Methods may also involve applying the refractive treatment shape to the eye with an ablation system.

[0013] In another aspect, embodiments of the present invention encompass methods of determining a refractive treatment shape for an eye of a patient that include, for example, determining a variable radius of curvature of an anterior surface of a cornea of the eye, and determining the refractive treatment shape for the eye based on the variable radius of curvature. In some cases, the step of determining the refractive treatment shape involves determining a refractive treatment shape of a remaining ablation for the eye based on the variable radius of curvature. In some cases, the variable radius of curvature for the cornea of

the eye is determined following application of one or more ablation pulses to the eye.

Optionally, the step of determining the variable radius of curvature can include determining an instantaneous variable radius of curvature for the cornea following application of one or more ablation pulses to the eye, and the step of determining the refractive treatment shape can include determining a refractive treatment shape of a remaining ablation for the eye based on the instantaneous variable radius of curvature. Methods may also include applying the refractive treatment shape to the eye with an ablation system. In some cases, the variable radius of curvature of the anterior surface of the eye varies as a function of cornea thickness. In some cases, the variable radius of curvature of the anterior surface of the eye is a function of a radius of curvature of a posterior surface of the cornea. In some cases, the variable radius of curvature of the anterior surface of the eye varies as a function of an ablation depth. Optionally, the refractive treatment shape for the eye can be based on a Munnerlyn equation.

**[0014]** In one aspect, embodiments of the present invention encompass systems and methods for determining a refractive treatment for an eye of a patient. Exemplary systems may include an input configured to receive a variable index of refraction for an epithelium of the eye, and a processing module having a tangible medium embodying machine-readable code that determines the refractive treatment for the eye based on the variable index of refraction for the epithelium of the eye. In some cases, the variable index of refraction for the epithelium varies as a function of epithelial depth. In some cases, the variable index of refraction for the epithelium of the eye is about 1.401 at an anterior portion of the epithelium and about 1.380 at a posterior portion of the epithelium.

**[0015]** An exemplary method embodiment of determining a refractive treatment for an eye of a patient may include receiving a variable index of refraction for an epithelium of the eye, and determining the refractive treatment for the eye based on the variable index of refraction for the epithelium of the eye. The variable index of refraction for the epithelium can vary as a function of epithelial depth. In some cases, the variable index of refraction for the epithelium of the eye is about 1.401 at an anterior portion of the epithelium and about 1.380 at a posterior portion of the epithelium.

**[0016]** In another aspect, embodiments of the present invention encompass systems and methods for selecting a patient for treatment with a variable index of refraction surgical procedure. An exemplary system may include an input configured to receive an aberration profile of an eye of the patient. The aberration profile may include a low order aberration

component and a high order aberration component. The system may also include a processing module having a tangible medium embodying machine-readable code that selects the patient for treatment with the variable index refractive surgical procedure based on the aberration profile. An exemplary method of selecting a patient for treatment with a variable index of refraction surgical procedure may include, for example, evaluating an aberration profile of an eye of the patient, where the aberration profile includes a low order aberration component and a high order aberration component, and selecting the patient for treatment with the variable index of refraction surgical procedure based on the aberration profile.

[0017] In still another aspect, embodiments of the present invention include systems and methods for determining a refractive treatment for an eye of a patient. An exemplary system may include an input configured to receive a variable index of refraction for a cornea of the eye, an input configured to receive a wavefront analysis of the eye, and a processing module having a tangible medium embodying machine-readable code that determines the refractive treatment for the eye based on the variable index of refraction and the wavefront analysis of the eye. In some cases, the processing module includes a tangible medium embodying machine-readable code that determines the refractive treatment for the eye independent of a Munnerlyn equation based on the eye. An exemplary method of determining a refractive treatment for an eye of a patient may include, for example, receiving a variable index of refraction for a cornea of the eye, receiving a wavefront analysis of the eye, and determining the refractive treatment for the eye based on the variable index of refraction for the cornea of the eye and the wavefront analysis of the eye. In some cases, the refractive treatment for the eye is determined independent of a Munnerlyn equation based on the eye.

[0018] For a fuller understanding of the nature and advantages of the present invention, reference should be had to the ensuing detailed description taken in conjunction with the accompanying drawings.

#### BRIEF DESCRIPTION OF THE DRAWINGS

[0019] Fig. 1 illustrates a laser ablation system according to an embodiment of the present invention.

[0020] Fig. 2 illustrates a simplified computer system according to an embodiment of the present invention.



- [0021] Fig. 3 illustrates a wavefront measurement system according to an embodiment of the present invention.
- [0022] Fig. 3A illustrates another wavefront measurement system according to an embodiment of the present invention.
- 5 [0023] Figs. 4A and 4B show aspects of an embodiment of the present invention.
- [0024] Fig. 5 shows corneal ablation data according to embodiments of the present invention.
- [0025] Fig. 6 depicts aspects of original maps, reconstructed maps, and residual error according to embodiments of the present invention.
- 10 [0026] Fig. 7 illustrates aspects of residual error according to embodiments of the present invention.
- [0027] Fig. 8 shows aspects of residual error maps according to embodiments of the present invention.
- [0028] Fig. 9 shows aspects of residual maps according to embodiments of the present  
15 invention.
- [0029] Fig. 10 illustrates aspects of a technique that accounts for a variable index of refraction of the cornea or ablated tissue according to embodiments of the present invention.
- [0030] Fig. 11 illustrates aspects of realtime monitoring of a change in refractive index according to embodiments of the present invention.
- 20 [0031] Fig. 12 depicts aspects of a personalized treatment for an individual patient based upon the unique variable refractive index of the patient's cornea according to embodiments of the present invention.

#### DETAILED DESCRIPTION OF THE INVENTION

- 25 [0032] The present invention can be readily adapted for use with existing laser systems, wavefront measurement systems, and other optical measurement devices. Although the systems, software, and methods of the present invention are described primarily in the context of a laser eye surgery system, it should be understood the present invention may be adapted for use in alternative eye treatment procedures, systems, or modalities, such as

spectacle lenses, intraocular lenses, accommodating IOLs, contact lenses, corneal ring implants, collagenous corneal tissue thermal remodeling, corneal inlays, corneal onlays, other corneal implants or grafts, and the like. Relatedly, systems, software, and methods according to embodiments of the present invention are well suited for customizing any of these  
5 treatment modalities to a specific patient. Thus, for example, embodiments encompass custom intraocular lenses, custom contact lenses, custom corneal implants, and the like, which can be configured to treat or ameliorate any of a variety of vision conditions in a particular patient based on their unique ocular characteristics or anatomy.

[0033] Turning now to the drawings, **FIG. 1** illustrates a laser eye surgery system 10 of the  
10 present invention, including a laser 12 that produces a laser beam 14. Laser 12 is optically coupled to laser delivery optics 16, which directs laser beam 14 to an eye E of patient P. A delivery optics support structure (not shown here for clarity) extends from a frame 18 supporting laser 12. A microscope 20 is mounted on the delivery optics support structure, the microscope often being used to image a cornea of eye E.

[0034] Laser 12 generally comprises an excimer laser, ideally comprising an argon-fluorine  
15 laser producing pulses of laser light having a wavelength of approximately 193 nm. Laser 12 will preferably be designed to provide a feedback stabilized fluence at the patient's eye, delivered via delivery optics 16. The present invention may also be useful with alternative sources of ultraviolet or infrared radiation, particularly those adapted to controllably ablate  
20 the corneal tissue without causing significant damage to adjacent and/or underlying tissues of the eye. Such sources include, but are not limited to, solid state lasers and other devices which can generate energy in the ultraviolet wavelength between about 185 and 205 nm and/or those which utilize frequency-multiplying techniques. Hence, although an excimer laser is the illustrative source of an ablating beam, other lasers may be used in the present  
25 invention.

[0035] Laser system 10 will generally include a computer or programmable processor 22.  
Processor 22 may comprise (or interface with) a conventional PC system including the standard user interface devices such as a keyboard, a display monitor, and the like. Processor 22 will typically include an input device such as a magnetic or optical disk drive, an internet  
30 connection, or the like. Such input devices will often be used to download a computer executable code from a tangible storage media 29 embodying any of the methods of the present invention. Tangible storage media 29 may take the form of a floppy disk, an optical

disk, a data tape, a volatile or non-volatile memory, RAM, or the like, and the processor 22 will include the memory boards and other standard components of modern computer systems for storing and executing this code. Tangible storage media 29 may optionally embody wavefront sensor data, wavefront gradients, a wavefront elevation map, a treatment map, a corneal elevation map, and/or an ablation table. While tangible storage media 29 will often be used directly in cooperation with a input device of processor 22, the storage media may also be remotely operatively coupled with processor by means of network connections such as the internet, and by wireless methods such as infrared, Bluetooth, or the like.

[0036] Laser 12 and delivery optics 16 will generally direct laser beam 14 to the eye of patient P under the direction of a computer 22. Computer 22 will often selectively adjust laser beam 14 to expose portions of the cornea to the pulses of laser energy so as to effect a predetermined sculpting of the cornea and alter the refractive characteristics of the eye. In many embodiments, both laser beam 14 and the laser delivery optical system 16 will be under computer control of processor 22 to effect the desired laser sculpting process, with the processor effecting (and optionally modifying) the pattern of laser pulses. The pattern of pulses may be summarized in machine readable data of tangible storage media 29 in the form of a treatment table, and the treatment table may be adjusted according to feedback input into processor 22 from an automated image analysis system in response to feedback data provided from an ablation monitoring system feedback system. Optionally, the feedback may be manually entered into the processor by a system operator. Such feedback might be provided by integrating the wavefront measurement system described below with the laser treatment system 10, and processor 22 may continue and/or terminate a sculpting treatment in response to the feedback, and may optionally also modify the planned sculpting based at least in part on the feedback. Measurement systems are further described in U.S. Patent No. 6,315,413, the full disclosure of which is incorporated herein by reference.

[0037] Laser beam 14 may be adjusted to produce the desired sculpting using a variety of alternative mechanisms. The laser beam 14 may be selectively limited using one or more variable apertures. An exemplary variable aperture system having a variable iris and a variable width slit is described in U.S. Patent No. 5,713,892, the full disclosure of which is incorporated herein by reference. The laser beam may also be tailored by varying the size and offset of the laser spot from an axis of the eye, as described in U.S. Patent Nos. 5,683,379, 6,203,539, and 6,331,177, the full disclosures of which are incorporated herein by reference.

[0038] Still further alternatives are possible, including scanning of the laser beam over the surface of the eye and controlling the number of pulses and/or dwell time at each location, as described, for example, by U.S. Patent No. 4,665,913, the full disclosure of which is incorporated herein by reference; using masks in the optical path of laser beam 14 which  
5 ablate to vary the profile of the beam incident on the cornea, as described in U.S. Patent No. 5,807,379, the full disclosure of which is incorporated herein by reference; hybrid profile-scanning systems in which a variable size beam (typically controlled by a variable width slit and/or variable diameter iris diaphragm) is scanned across the cornea; or the like. The computer programs and control methodology for these laser pattern tailoring techniques  
10 are well described in the patent literature.

[0039] Additional components and subsystems may be included with laser system 10, as should be understood by those of skill in the art. For example, spatial and/or temporal integrators may be included to control the distribution of energy within the laser beam, as described in U.S. Patent No. 5,646,791, the full disclosure of which is incorporated herein by  
15 reference. Ablation effluent evacuators/filters, aspirators, and other ancillary components of the laser surgery system are known in the art. Further details of suitable systems for performing a laser ablation procedure can be found in commonly assigned U.S. Pat. Nos. 4,665,913, 4,669,466, 4,732,148, 4,770,172, 4,773,414, 5,207,668, 5,108,388, 5,219,343, 5,646,791 and 5,163,934, the complete disclosures of which are incorporated herein by  
20 reference. Suitable systems also include commercially available refractive laser systems such as those manufactured and/or sold by Alcon, Bausch & Lomb, Nidek, WaveLight, LaserSight, Schwind, Zeiss-Meditec, and the like. Basis data can be further characterized for particular lasers or operating conditions, by taking into account localized environmental variables such as temperature, humidity, airflow, and aspiration.

[0040] FIG. 2 is a simplified block diagram of an exemplary computer system 22 that may  
25 be used by the laser surgical system 10 of the present invention. Computer system 22 typically includes at least one processor 52 which may communicate with a number of peripheral devices via a bus subsystem 54. These peripheral devices may include a storage subsystem 56, comprising a memory subsystem 58 and a file storage subsystem 60, user  
30 interface input devices 62, user interface output devices 64, and a network interface subsystem 66. Network interface subsystem 66 provides an interface to outside networks 68 and/or other devices, such as the wavefront measurement system 30.

[0041] User interface input devices 62 may include a keyboard, pointing devices such as a mouse, trackball, touch pad, or graphics tablet, a scanner, foot pedals, a joystick, a touchscreen incorporated into the display, audio input devices such as voice recognition systems, microphones, and other types of input devices. User input devices 62 will often be used to download a computer executable code from a tangible storage media 29 embodying any of the methods of the present invention. In general, use of the term “input device” is intended to include a variety of conventional and proprietary devices and ways to input information into computer system 22.

[0042] User interface output devices 64 may include a display subsystem, a printer, a fax machine, or non-visual displays such as audio output devices. The display subsystem may be a cathode ray tube (CRT), a flat-panel device such as a liquid crystal display (LCD), a projection device, or the like. The display subsystem may also provide a non-visual display such as via audio output devices. In general, use of the term “output device” is intended to include a variety of conventional and proprietary devices and ways to output information from computer system 22 to a user.

[0043] Storage subsystem 56 can store the basic programming and data constructs that provide the functionality of the various embodiments of the present invention. For example, a database and modules implementing the functionality of the methods of the present invention, as described herein, may be stored in storage subsystem 56. These software modules are generally executed by processor 52. In a distributed environment, the software modules may be stored on a plurality of computer systems and executed by processors of the plurality of computer systems. Storage subsystem 56 typically comprises memory subsystem 58 and file storage subsystem 60.

[0044] Memory subsystem 58 typically includes a number of memories including a main random access memory (RAM) 70 for storage of instructions and data during program execution and a read only memory (ROM) 72 in which fixed instructions are stored. File storage subsystem 60 provides persistent (non-volatile) storage for program and data files, and may include tangible storage media 29 (FIG. 1) which may optionally embody wavefront sensor data, wavefront gradients, a wavefront elevation map, a treatment map, and/or an ablation table. File storage subsystem 60 may include a hard disk drive, a floppy disk drive along with associated removable media, a Compact Digital Read Only Memory (CD-ROM) drive, an optical drive, DVD, CD-R, CD-RW, solid-state removable memory, and/or other

removable media cartridges or disks. One or more of the drives may be located at remote locations on other connected computers at other sites coupled to computer system 22. The modules implementing the functionality of the present invention may be stored by file storage subsystem 60.

5 [0045] Bus subsystem 54 provides a mechanism for letting the various components and subsystems of computer system 22 communicate with each other as intended. The various subsystems and components of computer system 22 need not be at the same physical location but may be distributed at various locations within a distributed network. Although bus subsystem 54 is shown schematically as a single bus, alternate embodiments of the bus  
10 subsystem may utilize multiple busses.

[0046] Computer system 22 itself can be of varying types including a personal computer, a portable computer, a workstation, a computer terminal, a network computer, a control system in a wavefront measurement system or laser surgical system, a mainframe, or any other data processing system. Due to the ever-changing nature of computers and networks, the  
15 description of computer system 22 depicted in FIG. 2 is intended only as a specific example for purposes of illustrating one embodiment of the present invention. Many other configurations of computer system 22 are possible having more or less components than the computer system depicted in FIG. 2.

[0047] Referring now to FIG. 3, one embodiment of a wavefront measurement system 30  
20 is schematically illustrated in simplified form. In very general terms, wavefront measurement system 30 is configured to sense local slopes of a gradient map exiting the patient's eye. Devices based on the Hartmann-Shack principle generally include a lenslet array to sample the gradient map uniformly over an aperture, which is typically the exit pupil of the eye. Thereafter, the local slopes of the gradient map are analyzed so as to reconstruct the  
25 wavefront surface or map.

[0048] More specifically, one wavefront measurement system 30 includes an image source 32, such as a laser, which projects a source image through optical tissues 34 of eye E so as to form an image 44 upon a surface of retina R. The image from retina R is transmitted by the optical system of the eye (e.g., optical tissues 34) and imaged onto a wavefront sensor 36 by  
30 system optics 37. The wavefront sensor 36 communicates signals to a computer system 22' for measurement of the optical errors in the optical tissues 34 and/or determination of an optical tissue ablation treatment program. Computer 22' may include the same or similar

hardware as the computer system 22 illustrated in **FIGS. 1 and 2**. Computer system 22' may be in communication with computer system 22 that directs the laser surgery system 10, or some or all of the components of computer system 22, 22' of the wavefront measurement system 30 and laser surgery system 10 may be combined or separate. If desired, data from wavefront sensor 36 may be transmitted to a laser computer system 22 via tangible media 29, via an I/O port, via an networking connection 66 such as an intranet or the Internet, or the like.

[0049] Wavefront sensor 36 generally comprises a lenslet array 38 and an image sensor 40. As the image from retina R is transmitted through optical tissues 34 and imaged onto a surface of image sensor 40 and an image of the eye pupil P is similarly imaged onto a surface of lenslet array 38, the lenslet array separates the transmitted image into an array of beamlets 42, and (in combination with other optical components of the system) images the separated beamlets on the surface of sensor 40. Sensor 40 typically comprises a charged couple device or "CCD," and senses the characteristics of these individual beamlets, which can be used to determine the characteristics of an associated region of optical tissues 34. In particular, where image 44 comprises a point or small spot of light, a location of the transmitted spot as imaged by a beamlet can directly indicate a local gradient of the associated region of optical tissue.

[0050] Eye E generally defines an anterior orientation ANT and a posterior orientation POS. Image source 32 generally projects an image in a posterior orientation through optical tissues 34 onto retina R as indicated in **FIG. 3**. Optical tissues 34 again transmit image 44 from the retina anteriorly toward wavefront sensor 36. Image 44 actually formed on retina R may be distorted by any imperfections in the eye's optical system when the image source is originally transmitted by optical tissues 34. Optionally, image source projection optics 46 may be configured or adapted to decrease any distortion of image 44.

[0051] In some embodiments, image source optics 46 may decrease lower order optical errors by compensating for spherical and/or cylindrical errors of optical tissues 34. Higher order optical errors of the optical tissues may also be compensated through the use of an adaptive optic element, such as a deformable mirror (described below). Use of an image source 32 selected to define a point or small spot at image 44 upon retina R may facilitate the analysis of the data provided by wavefront sensor 36. Distortion of image 44 may be limited by transmitting a source image through a central region 48 of optical tissues 34 which is

smaller than a pupil 50, as the central portion of the pupil may be less prone to optical errors than the peripheral portion. Regardless of the particular image source structure, it will be generally be beneficial to have a well-defined and accurately formed image 44 on retina R.

[0052] In one embodiment, the wavefront data may be stored in a computer readable medium 29 or a memory of the wavefront sensor system 30 in two separate arrays containing the x and y wavefront gradient values obtained from image spot analysis of the Hartmann-Shack sensor images, plus the x and y pupil center offsets from the nominal center of the Hartmann-Shack lenslet array, as measured by the pupil camera 51 (**FIG. 3**) image. Such information contains all the available information on the wavefront error of the eye and is sufficient to reconstruct the wavefront or any portion of it. In such embodiments, there is no need to reprocess the Hartmann-Shack image more than once, and the data space required to store the gradient array is not large. For example, to accommodate an image of a pupil with an 8 mm diameter, an array of a 20 x 20 size (i.e., 400 elements) is often sufficient. As can be appreciated, in other embodiments, the wavefront data may be stored in a memory of the wavefront sensor system in a single array or multiple arrays.

[0053] While the methods of the present invention will generally be described with reference to sensing of an image 44, a series of wavefront sensor data readings may be taken. For example, a time series of wavefront data readings may help to provide a more accurate overall determination of the ocular tissue aberrations. As the ocular tissues can vary in shape over a brief period of time, a plurality of temporally separated wavefront sensor measurements can avoid relying on a single snapshot of the optical characteristics as the basis for a refractive correcting procedure. Still further alternatives are also available, including taking wavefront sensor data of the eye with the eye in differing configurations, positions, and/or orientations. For example, a patient will often help maintain alignment of the eye with wavefront measurement system 30 by focusing on a fixation target, as described in U.S. Patent No. 6,004,313, the full disclosure of which is incorporated herein by reference. By varying a position of the fixation target as described in that reference, optical characteristics of the eye may be determined while the eye accommodates or adapts to image a field of view at a varying distance and/or angles.

[0054] The location of the optical axis of the eye may be verified by reference to the data provided from a pupil camera 52. In the exemplary embodiment, a pupil camera 52 images



pupil 50 so as to determine a position of the pupil for registration of the wavefront sensor data relative to the optical tissues.

[0055] An alternative embodiment of a wavefront measurement system is illustrated in **FIG. 3A**. The major components of the system of **FIG. 3A** are similar to those of **FIG. 3**.  
5 Additionally, **FIG. 3A** includes an adaptive optical element 53 in the form of a deformable mirror. The source image is reflected from deformable mirror 98 during transmission to retina R, and the deformable mirror is also along the optical path used to form the transmitted image between retina R and imaging sensor 40. Deformable mirror 98 can be controllably deformed by computer system 22 to limit distortion of the image formed on the retina or of  
10 subsequent images formed of the images formed on the retina, and may enhance the accuracy of the resultant wavefront data. The structure and use of the system of **FIG. 3A** are more fully described in U.S. Patent No. 6,095,651, the full disclosure of which is incorporated herein by reference.

[0056] The components of an embodiment of a wavefront measurement system for  
15 measuring the eye and ablations may comprise elements of a WaveScan<sup>®</sup> system, available from VISX, INCORPORATED of Santa Clara, California. One embodiment includes a WaveScan system with a deformable mirror as described above. An alternate embodiment of a wavefront measuring system is described in U.S. Patent No. 6,271,915, the full disclosure of which is incorporated herein by reference. It is appreciated that any wavefront  
20 aberrometer could be employed for use with the present invention. Relatedly, embodiments of the present invention encompass the implementation of any of a variety of optical instruments provided by WaveFront Sciences, Inc., including the COAS wavefront aberrometer, the ClearWave contact lens aberrometer, the CrystalWave IOL aberrometer, and the like.

25 [0057] Embodiments of the present invention encompass techniques that consider the index of refraction for corneal stroma as a function of depth or radial distance, and the radius of curvature variation as a laser ablates deeper and deeper tissue.

[0058] Using a Munnerlyn equation, it can be calculated that as the tissue is being ablated, each diopter of ablation has a smaller value of refractive index and larger value of the radius  
30 of curvature for myopia and a smaller value of the radius of curvature of the cornea for hyperopia, as the ablation goes deeper and deeper. In consequence, for a -6 D ablation, a 2% overcorrection can be estimated. For a +6 D ablation, a 2% undercorrection can be evaluated.

[0059] Excimer laser refractive surgery has been proven as a favorable vision correction means. It is often desirable to achieve a correction or treatment of the low order spherocylindrical error. Moreover, it is also desirable to achieve a favorable outcome of the refractive correction of ocular aberrations. Any small deviation may affect the final outcome of the surgery.

[0060] Embodiments of the present invention encompass techniques that can address factors which may affect a precise correction of low order aberrations or otherwise induce some high order aberrations, preventing a complete or desired correction of ocular aberrations. A methodology used for evaluating the possible error due to an imperfect system is described in G.-m. Dai et al. "System performance evaluation of refractive surgical lasers: a mathematical approach," Appl. Opt. 45, 2124-2134 (2006), which is incorporated herein by reference for all purposes.

#### Variable Index of Refraction of the Cornea

[0061] The refractive index may be dependent on the frequency of light. In some embodiments, only the indices at visible light are considered. In some embodiments, indices at other frequencies are considered. The refractive index of the corneal stroma may be assumed to be a constant by taking an average of the values of the anterior and posterior surfaces of the stroma. This is an approximation. The refractive index of the stroma may vary vertically and horizontally. Aspects of this variation are discussed in M. Dubbelman et al. "The shape of the aging human lens: curvature, equivalent refractive index and the lens paradox," Vis. Res. 41, 1867-1877 (2001), which is incorporated herein by reference for all purposes. The refractive index can be higher toward the periphery of the stroma, and lower toward the center of the stroma. Relatedly, the refractive index can be higher toward the anterior stroma, and lower toward the posterior stroma.

[0062] It is possible to denote  $n(h)$  as the refractive index of the stroma at the ablation depth  $h$ , and the refractive index of the stroma as

$$n(h) = n_0 + \delta h, \quad (1)$$

where the refractive index of the outermost layer of the stroma  $n_0 = 1.38$  and the mean gradient index of the stroma  $\delta = (1.373-1.38)/5.5 \times 10^{-4} = -12.73 \text{ m}^{-1}$ . In Eq. (1), a nominal value of  $550 \text{ }\mu\text{m}$  for the thickness of the cornea can be assumed. For example, when the

stroma is ablated for 50  $\mu\text{m}$ , the refractive index is reduced from 1.38 to  $1.38 - 12.73 \times 50 \times 10^{-6} = 1.379$ . When the entire stroma of 550  $\mu\text{m}$  is ablated, the refractive index can drop to 1.373.

[0063] In some embodiments, instead of using a nominal value of 1.376 for the refractive index of the stroma, it is possible to use Eq. (1) to represent the refractive index of the stroma as a function of the ablation depth  $h$  where  $n_0$  is the refractive index of the stroma at the surface, and is 1.379. For surface ablations, such as LASEK and PRK, Eq. (1) can be used such that  $n_0 = 1.39$  is the refractive index of the anterior surface of the stroma. When it is used for LASIK,  $n_0$  may depend upon the thickness of the LASIK flap. For example, for normal flap thickness of 160 microns,  $n_0$  can be 1.3770. For thin flaps of 110 microns that can be created with IntraLase femtosecond lasers,  $n_0$  can be 1.3776.

[0064] **Table 1** shows the ablation depth for every diopter of myopia and hyperopia for different levels of refractions with a 6 mm optical zone. Optionally, these values can be calculated using the Munnerlyn equation. Relatedly, **Table 1** can provide the basis for an example for a deviation from a Munnerlyn equation on a per diopter situation. For a myopic ablation, the per diopter ablation depth becomes less deep as the ablation progresses. In comparison, for a hyperopic ablation, the per diopter ablation depth becomes deeper as the ablation continues. Hence, there can be a nonlinear relationship between the ablation depth and power, for example. According to some embodiments, the variable index of refraction for the cornea varies as a function of corneal stromal depth. In some cases, the function in Eq. (1) is linear. However, the per-diopter depth of ablation as a function of the ablation depth can be non-linear. **Table 1** shows an ablation depth per diopter as a function of the sphere of myopia and hyperopia. An optical zone  $O = 6$  mm and the pre-surgery corneal radius of curvature  $R_1 = 7.8$  mm are assumed. In some cases, techniques may involve ablation depth per partial diopter as a function of the sphere or myopia or hyperopia. Partial diopters can include half diopters, quarter diopters, and the like. In some cases, partial diopters can be considered as infinitesimally small or approaching zero, for example.

Table 1					
		Myopia		Hyperopia	
Sphere (D)	n	$R_1$ (mm)	Depth ( $\mu\text{m}$ )	$R_1$ (mm)	Depth ( $\mu\text{m}$ )
1	1.3799	7.80	13.310	7.80	13.381

2	1.3797	7.96	13.248	7.64	13.459
3	1.3796	8.13	13.188	7.49	13.541
4	1.3794	8.31	13.130	7.35	13.625
5	1.3792	8.50	13.074	7.21	13.711
6	1.3791	8.69	13.019	7.07	13.800
7	1.3789	8.90	12.967	6.94	13.893
8	1.3787	9.11	12.917	6.82	13.988
9	1.3786	9.34	12.868	6.70	14.086
10	1.3784	9.57	12.821	6.58	14.187

[0065] Based on **Table 1**, it is apparent that for a myopia treatment, the ablation depth can change from about 13.31 microns for the first diopter to about 12.82 microns for the tenth diopter. Similarly, for a hyperopia treatment, the ablation depth can change from about 13.38 microns for the first diopter to about 14.19 microns for the tenth diopter.

5 [0066] As an exemplary illustration, for a -6 D myopic eye it is possible to calculate the deviation of true depth using variable refractive index as compared to using the mean refractive index for  $O = 6$  mm optical zone. Consider for example that a depth per diopter myopia is  $13.43 \mu\text{m}$  so the total depth for a -6 D eye is  $13.43 \times 6 = 80.58 \mu\text{m}$ . To calculate the depth with the variable refractive index, adding the first six values in **Table 1** for myopia, it  
 10 is possible to obtain  $78.97 \mu\text{m}$ . Therefore, the fixed refractive index model over-ablates a -6 D myopic eye by  $80.58 - 78.97 = 1.611 \mu\text{m}$ . This is a 2% overcorrection.

[0067] As an ablation continues, the index of refraction of the resulting anterior stromal layer can change. Hence, a variable index of refraction can vary as a function of ablation depth. In some cases, embodiments of the present invention encompass techniques that  
 15 incorporate a precalculated variable index of refraction. In some cases, embodiments encompass techniques that incorporate an ongoing or instantaneous refinement of the variable index of refraction calculation. In other words, a variable index determination can be used to drive a treatment from the start, and can also be used to form the basis for providing ongoing refinement of a treatment according to a closed-loop process. For example, a method of

determining a refractive treatment shape can include determining an instantaneous index of refraction at one or more times during an ablation treatment, and determining or refining the refractive treatment shape based on the instantaneous index of refraction. Optionally, a method of determining a refractive treatment shape can include determining a variable index of refraction, and determining the refractive treatment shape of the remaining ablation for the eye based on the variable index of refraction. As the ablation progresses, the index of refraction can change as additional material is ablated.

**[0068]** In an open loop approach, a variable index of refraction can be based on a precalculated or predicted value. For example, a look-up table can be constructed such that the depth of the ablation profile can be found based on the refraction of the eye. Optionally, an infinitesimally thin profile can be constructed based upon the Munnerlyn equation or the wavefront-driven parabolic shape and an integration can be performed over the refraction of the eye when determining a final ablation profile. In a closed loop approach, an index of refraction can be monitored in real time during an ablation procedure, and ablation treatment parameters can be adjusted or refined based on the instantaneous refractive index or refractive index change. In some cases, the index of refraction can be measured following the application of one or more ablation pulses applied to the eye. The residual ablation profile can be determined based on the ablated profile and the instantaneous refractive index such that the final ablated profile when the ablation is complete optimally matches the planned ablation profile.

**[0069]** The depth of an ablation and the shape of tissue removed can vary based on the variable index of refraction. Variable index of refractions may vary between different patients. Embodiments disclosed herein provide tissue refractive index measurement and ablation systems suitable for integration with known laser eye surgery systems. Embodiments also encompass techniques that provide diagnostic information before, and/or feedback information during, a corneal resculpting procedure. Information regarding the index of refraction of the cornea or components of the cornea can be used to establish or modify a resculpting laser energy pattern for a corneal tissue surface.

**[0070]** Embodiments encompass systems and methods for measuring or detecting the index of refraction of a corneal or stromal tissue using, for example, a Scheimflug imaging technique. M. Dubbleman et al. discuss a method for determining the refractive index of the crystalline lens in "The shape of the aging human lens: curvature, equivalent refractive index

and the lens paradox,” Vis. Res. 41, 1867-1877 (2001), the entirety of which is incorporated herein by reference for all purposes. Systems may include a processor coupled with, in communication with, or otherwise configured to receive information from the sensor, whereby the processor can generate a refractive index signal indicating the refractive index of the tissue. Relatedly, embodiments encompass systems and methods for resculpting a corneal tissue of an eye. Systems may include an apparatus that directs a pattern of light energy from a laser under the direction of a processor to effect a desired change in an optical characteristic of the eye, and an adjustment module of a system processor can vary the pattern in response to the index of refraction information from a sensor.

10 [0071] In some cases, embodiments encompass compensation techniques for use in a procedure for resculpting a corneal tissue of an eye. A resculpting procedure can selectively direct a pattern of laser energy toward the eye to effect a predetermined change in an optical characteristic of the eye. A compensation method may include sensing or detecting a refractive index of the corneal or stromal tissue of the eye, and adjusting the pattern of laser energy in response to the sensed refractive index. An ablation energy delivery system can be coupled to a processor, the delivery system can direct an ablative energy toward the tissue, and the processor can vary the ablative energy in response to a refractive index signal. The tissue will typically include a corneal tissue of an eye, and the delivery system may include an optical delivery system transmitting photoablative laser energy toward the corneal tissue so as to selectively alter an optical characteristic of the eye. The processor may vary a quantity of change in the optical characteristic of the eye in response to the refractive index signal. For example, the processor may vary a diopter value of the resculpting procedure in response to the index of refraction. Alternatively, the processor may vary the shape of the ablation by altering the ablative energy pattern so as to compensate for local differences in refractive index across the target region of the corneal tissue. In some embodiments, an output device coupled to the processor may show a display in response to the index of refraction signal.

[0072] Systems and methods for sculpting of a corneal tissue of an eye to effect a desired change in an optical property are also provided herein. Such techniques can include sensing or detecting an index of refraction of a stromal tissue of the eye, and determining a desired change in shape of the eye in response to the index of refraction, and in response to the desired change in optical property. A pattern of laser energy can be planned for directing toward the corneal tissue, so as to effect the determined change in shape. A desired change in

optical quality can be determined while the tissue has a initial index of refraction, or a subsequent index of refraction following or during an ablation or resculpting step. The change in optical quality may be determined using any of a variety of standard vision diagnostic systems. Wavefront sensor systems now being developed may also be beneficial for determining a desired change in an optical property, and still further alternative topography and/or tomography systems may also be used. Regardless, rather than simply determining the desired change in shape of the eye from such measurements alone, the desired sculpting or ablation shape can also be based in part on the index of refraction of the eye.

10 [0073] An exemplary method for performing a refractive index compensated photorefractive ablation may be initiated using a predetermined ablation pattern assuming a standard ablation rate. A sensor can be used to determine or evaluate the refractive index of stromal tissue of the eye. The standard ablation rate can be adjusted based on the refractive index, and the adjusted ablation rate can be part of a treatment pattern of ablation energy directed toward the tissue so as to effect the desired change in optical characteristics of eye. The treatment pattern, can include parameters such as the size, location, and/or number of laser pulses directed toward some or all of the treatment region of the eye. One or more of these parameters can be set or adjusted based on the refractive index. In some cases, an algorithm used to calculate a shot pattern so as to effect a desired change in corneal shape may incorporate adjusted ablation rates appropriate for a varying index of refraction.

[0074] As noted above, a refractive index can vary vertically based on stromal depth. A refractive index can also vary horizontally based on a function of radial distance from a central portion of the stroma. Radial dependency of the refractive index can characterize a stroma that has a lower index of refraction in a central portion of the stroma. In some cases, radial dependency can be characterized with the following formula:  $n(r) = n_0 + \lambda r$ , where  $r$  represents the radial distance from a central portion of the stroma, and  $\lambda$  represents the rate of change of the refractive index radially. Thus, it is possible to denote  $n(r)$  as the refractive index of the stroma at the radial distance  $r$ , where the refractive index of a central portion of the stroma is  $n_0$ , which can depend on the ablation depth. On the anterior surface of the cornea, it is about 1.38. On the anterior surface of the stroma, it is about 1.379. On the posterior surface of the stroma, it is about 1.373.

[0075] In some embodiments, techniques involve determining the variability of a refractive index of a patient, and determining a refractive treatment shape based on that variability. These approaches can be used to determine a treatment shape based on modification of a Munnerlyn shape. Optionally, these approaches can be used to determine a treatment shape based on a wavefront analysis.

### Variable Corneal Radius of Curvature

[0076] In one approximation, the corneal radius of curvature can be considered as a constant. Some equations, such as the Munnerlyn equation, can incorporate this assumption. A relationship between the radius of curvature of the anterior surface of the cornea  $R_1$  and the keratometry or keratometric power  $F$  can be expressed by

$$R_1 = \frac{(n-1)[R_2 + (n-n_2)d]}{R_2 F + (n-n_2)(1+Fd)}, \quad (2)$$

where  $n$  and  $n_2$  are the refractive indices of the anterior and posterior surfaces of the stroma or cornea, respectively,  $d$  is the cornea thickness or pachymetry, and  $R_2$  is the radius of curvature of the posterior surface of the cornea. Because the values of  $d$  and  $R_2$  typically vary from eye to eye, the calculated  $R_1$  can also vary.

[0077] **Fig. 4A** illustrates a radius of curvature of the anterior surface of the cornea as a function of pachymetry or cornea thickness ( $R_2 = 6.4$  mm). This figure shows the variability for the calculation of the radius of curvature of the anterior surface of the cornea as a function of the pachymetry, according to some embodiments. **Fig. 4B** illustrates a radius of curvature of the anterior surface of the cornea as a function of the radius of curvature of the posterior surface of the cornea ( $d = 550$   $\mu\text{m}$ ). Refractive indices  $n = 1.3765$  and  $n_2 = 1.336$  are assumed. These figures show the variability for the calculation of the radius of curvature of the anterior surface of the cornea as a function of the radius of curvature of the posterior surface of the cornea, according to some embodiments. It is quite clear that the variability of  $R_2$  gives the variability of  $R_1$ .

[0078] As an exemplary illustration, it is possible to calculate the deviation of the tissue ablation depth for a +1 D hyperopic eye using a 6 mm optical zone, when the radius of curvatures of the anterior and posterior surfaces of the cornea are taken as 6.4 mm and 7.5 mm, respectively. The keratometry and pachymetry are assumed to be 45 D and 550  $\mu\text{m}$ , respectively.



[0079] From Eq. (2), for  $R_2 = 6.4$  mm,  $F = 45$  D, and  $d = 550$   $\mu\text{m}$ , it is possible to obtain  $R_1 = (1.3765-1) \times [0.0064 + (1.3765-1.336) \times 0.00055] / [0.0064 \times 45 + (1.3765-1.336) \times (1+45 \times 0.00055)]$  m = 7.34 mm. Similarly, for  $R_2 = 7.5$  mm, it is possible to obtain  $R_1 = 7.47$  mm. Substituting the two values of  $R_1$  into the Munnerlyn equation Eq. (4), it is possible to  
 5 obtain the depths as 13.73  $\mu\text{m}$  and 13.66  $\mu\text{m}$ , respectively. This example shows that a variability of about 20% on the value of  $R_2$  can lead to about 0.5% mis-correction on the ablation profile.

[0080] Munnerlyn equations for myopia [Eq. (3)], and for hyperopia [Eq. (4)] can be expressed as follows.

$$10 \quad l(r) = \sqrt{R_1^2 - r^2} - \sqrt{\left[\frac{(n-1)R_1}{n-1+SR_1}\right]^2 - r^2} + \sqrt{\left[\frac{(n-1)R_1}{n-1+SR_1}\right]^2 - (O/2)^2} - \sqrt{R_1^2 - (O/2)^2} \quad (3)$$

$$15 \quad l(r) = \sqrt{R_1^2 - r^2} - R_1 + \frac{(n-1)R_1}{n-1+SR_1} - \sqrt{\left[\frac{(n-1)R_1}{n-1+SR_1}\right]^2 - r^2} \quad (4)$$

[0081] Accordingly, embodiments of the present invention encompass techniques where an anterior radius of curvature can be incorporated into a Munnerlyn equation. Anterior optical  
 15 surfaces may vary from person to person, and ablations may effect an anterior surface feature.

[0082] According to some embodiments, as the ablation progresses, the corneal radius of curvature can change. For example, as the ablation continues in a myopia treatment, the radius of curvature of the anterior cornea can become larger and larger. Relatedly, as the ablation continues in a hyperopia treatment, the radius of curvature of the anterior cornea can  
 20 become smaller and smaller. Hence, a variable radius of curvature of the anterior surface of the eye can vary as a function of the ablation depth. Accordingly, embodiments of the present invention encompass techniques that incorporate ongoing or instantaneous refinement of the variable radius of curvature of the anterior surface calculation. In other words, a variable radius of curvature determination can be used to drive a treatment from the start, and  
 25 can also be used to form the basis for providing ongoing refinement of a treatment according to a closed-loop process. For example, a method of determining a refractive treatment shape can include determining an instantaneous radius of curvature of the anterior surface at one or more times during an ablation treatment, and determining or refining the refractive treatment shape based on the instantaneous radius of curvature of the anterior surface. Optionally, a

method of determining a refractive treatment shape can include determining a variable radius of curvature of the anterior surface, and determining the refractive treatment shape of the remaining ablation for the eye based on the variable radius of curvature of the anterior surface. As the ablation progresses, the radius of curvature of the anterior surface can change or vary as additional material is ablated. Thus, embodiments of the present invention encompass techniques for determining a refractive treatment shape that include determining the instantaneous keratometry as the ablation continues, and determining the refractive treatment shape for the remaining ablation based on the instantaneous keratometry.

**[0083]** As an ablation continues, the anterior corneal radius of curvature can change. Hence, a variable index of refraction can vary as a function of the anterior corneal radius of curvature. In some cases, embodiments of the present invention encompass techniques that incorporate a precalculated variable anterior corneal radius of curvature. In some cases, embodiments encompass techniques that incorporate an ongoing or instantancous refinement of the variable anterior corneal radius of curvature calculation. In other words, a variable anterior corneal radius of curvature determination can be used to drive a treatment from the start, and can also be used to form the basis for providing ongoing refinement of a treatment according to a closed-loop process. For example, a method of determining a refractive treatment shape can include determining an instantaneous anterior corneal radius of curvature at one or more times during an ablation treatment, and determining or refining the refractive treatment shape based on the instantaneous anterior corneal radius of curvature. Optionally, a method of determining a refractive treatment shape can include determining a variable anterior corneal radius of curvature, and determining the refractive treatment shape of the remaining ablation for the eye based on the variable anterior corneal radius of curvature. As the ablation progresses, the anterior corneal radius of curvature can change as additional material is ablated.

**[0084]** In an open loop approach, a variable anterior corneal radius of curvature can be based on a precalculated or predicted value. For example, this value can be based on the keratometry measurements of the eye. Optionally, an infinitesimally thin profile can be constructed based upon the Munnerlyn equation or the wavefront-driven parabolic shape and an integration can be performed over the refraction of the eye to determine a final ablation profile. In a closed loop approach, an anterior corneal radius of curvature can be monitored in real time during an ablation procedure, and ablation treatment parameters can be adjusted or refined based on the instantancous anterior corneal radius of curvature or anterior corneal

radius of curvature change. In some cases, the anterior corneal radius of curvature can be measured following the application of one or more ablation pulses applied to the eye.

[0085] The depth of an ablation and the shape of tissue removed can vary based on the variable anterior corneal radius of curvature. Variable anterior corneal radius of curvatures may vary between different patients. Embodiments disclosed herein provide tissue radius of curvature measurement and ablation systems suitable for integration with known laser eye surgery systems. Embodiments also encompass techniques that provide diagnostic information before, and/or feedback information during, a corneal resculpting procedure. Information regarding the anterior corneal radius of curvature can be used to establish or modify a resculpting laser energy pattern for a corneal tissue surface.

[0086] Embodiments encompass systems and methods for measuring or detecting the anterior corneal radius of curvature. Systems may include a processor coupled with, in communication with, or otherwise configured to receive information from the sensor, whereby the processor can generate an anterior corneal radius of curvature signal indicating the anterior corneal radius of curvature. Relatedly, embodiments encompass systems and methods for resculpting a corneal tissue of an eye. Systems may include an apparatus that directs a pattern of light energy from a laser under the direction of a processor to effect a desired change in an optical characteristic of the eye, and an adjustment module of a system processor can vary the pattern in response to the anterior corneal radius of curvature information from a sensor.

[0087] In some cases, embodiments encompass compensation techniques for use in a procedure for resculpting a corneal tissue of an eye. A resculpting procedure can selectively direct a pattern of laser energy toward the eye to effect a predetermined change in an optical characteristic of the eye. A compensation method may include sensing or detecting an anterior corneal radius of curvature, and adjusting the pattern of laser energy in response to the sensed anterior corneal radius of curvature. An ablation energy delivery system can be coupled to a processor, the delivery system can direct an ablative energy toward the tissue, and the processor can vary the ablative energy in response to an anterior corneal radius of curvature signal. The tissue will typically include a corneal tissue of an eye, and the delivery system may include an optical delivery system transmitting photoablative laser energy toward the corneal tissue so as to selectively alter an optical characteristic of the eye. The processor may vary a quantity of change in the optical characteristic of the eye in response to the

anterior corneal radius of curvature signal. For example, the processor may vary a diopter value of the resculpting procedure in response to the anterior corneal radius of curvature.

Alternatively, the processor may vary the shape of the ablation by altering the ablative energy pattern so as to compensate for local differences in anterior corneal radius of curvature across the target region of the corneal tissue. In some embodiments, an output device coupled to the processor may show a display in response to the anterior corneal radius of curvature signal.

**[0088]** Systems and methods for sculpting of a corneal tissue of an eye to effect a desired change in an optical property are also provided herein. Such techniques can include sensing or detecting an anterior corneal radius of curvature, and determining a desired change in shape of the eye in response to the anterior corneal radius of curvature, and in response to the desired change in optical property. A pattern of laser energy can be planned for directing toward the corneal tissue, so as to effect the determined change in shape. A desired change in optical quality can be determined while the tissue has a initial anterior corneal radius of curvature, or a subsequent anterior corneal radius of curvature following or during an ablation or resculpting step. The change in optical quality may be determined using any of a variety of standard vision diagnostic systems. Wavefront sensor systems now being developed may also be beneficial for determining a desired change in an optical property, and still further alternative topography and/or tomography systems may also be used. Regardless, rather than simply determining the desired change in shape of the eye from such measurements alone, the desired sculpting or ablation shape can also be based in part on the anterior corneal radius of curvature.

**[0089]** An exemplary method for performing an anterior corneal radius of curvature compensated photorefractive ablation may be initiated using a predetermined ablation pattern assuming a standard ablation rate. A sensor can be used to determine or evaluate the anterior corneal radius of curvature. The standard ablation rate can be adjusted based on the anterior corneal radius of curvature, and the adjusted ablation rate can be part of a treatment pattern of ablation energy directed toward the tissue so as to effect the desired change in optical characteristics of eye. The treatment pattern, can include parameters such as the size, location, and/or number of laser pulses directed toward some or all of the treatment region of the eye. One or more of these parameters can be set or adjusted based on the anterior corneal radius of curvature. In some cases, an algorithm used to calculate a shot pattern so as to effect a desired change in corneal shape may incorporate adjusted ablation rates appropriate for a varying anterior corneal radius of curvature.

[0090] Embodiments of the present invention may involve fine-tuning techniques that incorporate wavefront and topographic features of an optical system. Exemplary approaches for determining shapes and features of the topography of a corneal of the eye are discussed in, for example, U.S. Patent Application Nos. 11/769,054 and 12/119,293 filed June 27, 2007 and May 12, 2008, respectively, which are incorporated herein by reference for all purposes.

### **Compensation of Corneal Biomechanics and Healing**

[0091] Techniques that involve cutting a flap with a microkeratome may cause a change of the high order aberrations. In some laser ablations, an increase of the high order aberrations can be dominated by the spherical aberrations. In general, when the pre-operative high order root mean square (RMS) error of the aberrations is low, ocular aberrations can tend to increase after surgery. On the other hand, when the pre-operative high order RMS error is high, ocular aberrations can tend to decrease. The increase of the spherical aberration post-surgery may not be all due to the biomechanics and healing, neglect of some of the effects discussed in this section may also cause an increase in spherical aberrations.

[0092] To compensate for the induction of ocular aberrations due to biomechanics and healing, mechanical and optical models have been proposed. For example, one way to account for the induction of ocular aberrations is to treat the biomechanical and healing effects as a low pass filtering process. When a flap is laid onto an ablated structure, some of the sharper, or higher spatial frequency, features can be smoothed. Similarly, when the ablated cornea heals, some of the smaller structures, whether it is due to the flap cut or due to the gaps between the laser pulses, can also be smoothed out.

[0093] Another approach, which can be useful in addressing the effect of a flap cut, for example, is to use mechanical models. Before the LASIK flap is cut, the tension of the lamellae is maintained between the interlamellar crosslinking, and the corneal internal fluid and intraocular pressures. After the flap is cut, the lamellar segments at the edge of the cut lose the tension, hence making the peripheral cornea to expand. This in turn can increase the interlamellar spacing, causing the edge of the cut to bulge and the central ablation area to flatten. After the flap is put back, the lost tension at the edge of the flap may not be able to recover. Therefore, the deformation of the cornea due to the flap cut may remain. Optically, this can create a phase advance at the center of the cut and a phase lag at the periphery, or the induction of a positive spherical aberration. With modeling, such as with finite element

method, for example, a prediction of the corneal surface deformation after flap cut is possible.

### Determination of Treatment Shape

[0094] In some embodiments, systems and methods may involve producing a treatment shape in a variety of steps. For example, an optical region shape can be determined, either by Munneryn equations or wavefront techniques. In some cases, aspects of the shape can be smoothed by pixel averaging, or by spatial averaging of depth.

[0095] Once the desired ablation shape has been determined, a next step is to define the parameters of the actual laser ablation required to administer the treatment ablation profile. A particularly useful way of determining these parameters is by using an ablation equation, such as the one shown below.

$$AblationShape = \sum_{n=1}^{TotalPulses} (PulseShape_n \otimes Position_n)$$

[0096] In brief, this equation is based on the principle that a treatment ablation is the sum of each of the individual laser pulses. This equation has been empirically verified on a variety of materials including plastic, and bovine, porcine, and human corneal tissue.

[0097] In this equation, the *AblationShape* variable represents the desired ablation shape. In this sense, it is a known variable. The target shape can be, for example, a simple sphere, an ellipse, a cylinder for treating myopia or hyperopia, or even a saddle for treating mixed astigmatism. The target shape can be any arbitrary shape, such as the map from a wavefront type device or any other topography system.

[0098] The *PulseShape* variable, which is also a known variable, represents the ablation shape of each laser pulse size to be used. The *PulseShape* typically varies for different ablated materials, such as plastic, animal cornea, or human cornea. The *PulseShape* also typically varies for each laser pulse diameter. An example of this type of ablation data is shown in **Fig. 5**. This figure shows different shapes of craters expected from a single laser pulse. There is a unique description for every unique pulse shape or size to be used. By systematically measuring the shape which each laser pulse ablates onto a specific target material, it is possible to generate such basis data for a variety of materials, such as tissue or plastic. For a given material, at a given diameter, the shape is generally consistent from laser system to laser system.

[0099] A fixed spot laser may have only one description, while a variable spot laser could have as many as desired. There is no requirement that the crater shape be flat, round, or symmetric. As long as it can be described mathematically or with an array of data, it can be incorporated in the equation.

5 [0100] In order to create the ablated surface, it is useful to determine the locations where each of the laser pulses will be applied. The *Position* variable, which represents the exact position of every laser pulse, is an unknown variable. This variable is calculated by solving the ablation equation. Put another way, the output is a set of instructions for creating the target ablation shape using the laser pulses. This is sometimes called a treatment table. The  
10 treatment table consists of a list of individual pulses, each containing the size and offset, or position, to be used for that pulse. When the laser fires according to the instructions in the treatment table, the target shape will be created.

[0101] The target ablation shape is a theoretical construct; it is a mathematically perfect representation of a desired ablation outcome. Put another way, while the application of  
15 thousands of specifically placed brief laser pulses can create an actual ablation shape that approaches the ideal target ablation shape, in the end it is still an approximation thereof.

[0102] Therefore, solving for the *Position* variable can allow for the formulation of a corresponding ablation shape that approaches the target ablation shape as closely as possible. In this way each of the thousands of pulse positions are individually determined so as to  
20 minimize the difference between the ideal target ablation shape and the actual resulting ablation shape. In a system for ablating tissue using a scanning laser, a presently preferred computational technique for achieving this goal employs simulated annealing.

[0103] Other mathematical approaches include, for example, the SALSA Algorithm. SALSA is an acronym for Simulated Annealing Least Squares Algorithm. It is an algorithm  
25 that solves an equation having over 10,000 unknowns. The algorithm finds the best solution by selecting: the number of pulses, the size of each pulse, and the location of each pulse. It is an exact algorithm, and makes no statistical assumptions.

[0104] Simulated Annealing is a recent, proven method to solve otherwise intractable problems, and may be used to solve the ablation equation discussed above. This is more fully  
30 described in PCT Application No. PCT/US01/08337, filed March 14, 2001, the entire disclose of which is incorporated herein by reference. See also W. H. Press et al., "Numerical Recipes in C" 2<sup>nd</sup> Ed., Cambridge University Press, pp. 444-455 (1992). This

approach is also further discussed in co-pending U.S. Patent Application No. 09/805,737, the entire disclosure of which is incorporated herein by reference.

[0105] Simulated annealing is a method used for minimizing (or maximizing) the parameters of a function. It is particularly suited to problems with very large, poorly behaved function spaces. Simulated annealing can be applied in the same way regardless of how many dimensions are present in the search space. It can be used to optimize any conditions that can be expressed numerically, and it does not require a derivative. It can also provide an accurate overall minimum despite local minima in the search space, for example.

### Epithelial Index of Refraction

[0106] Embodiments of the present invention can also generate or administer treatments which take into account the index of refraction in the epithelial tissue layer, which may be different from the index of refraction in the corneal stroma. Hence, the index of refraction can be considered to vary as a function of tissue depth, in terms of a depth or distance below an anterior tissue surface that includes the epithelial layer. In some cases, the epithelial index of refraction may be greater than the stromal index of refraction. The epithelial index of refraction may be variable, or it may be constant.

[0107] Accordingly, it is possible to denote  $n(h)$  as the refractive index of the tissue at the ablation depth  $h$ , and the refractive index of the tissue as

$$n(h) = n_0 + \delta h,$$

where the refractive index of the outermost layer of the tissue or epithelium is  $n_0 = 1.401$  and the mean gradient index is  $\delta = (1.38-1.401)/50\mu\text{m} = -0.00042/\mu\text{m}$  for an epithelial ablation. For a PRK procedure, the refractive index of the outer tissue can be  $n_0 = 1.38$  and the mean gradient index can be  $\delta = -0.000015/\mu\text{m}$ . For a LASIK procedure involving a 160  $\mu\text{m}$  LASIK flap thickness, the refractive index of the outer tissue can be  $n_0 = 1.3776$  and the mean gradient index can be  $\delta = -0.000015/\mu\text{m}$ . For a LASIK procedure involving a 110  $\mu\text{m}$  LASIK flap thickness, the refractive index of the outer tissue can be  $n_0 = 1.3784$ .

[0108] Embodiments which factor in the index of refraction of the epithelial tissue are well suited for use with certain. For example, some techniques involve ablating the epithelium prior to eye chart testing, clinical testing, contrast sensitivity testing, and the like. In some instances, surgeons or operators perform or administer an "epithelium shape" for temporary experiments, such as presbyopia evaluation, by ablating a very fine or thin shape only on the



epithelium. For example, because the epithelial layer is often about 50 microns in thickness, such treatments may involve ablating to a depth that is less than about 50 microns, or that otherwise does not extend into the stroma. Over the course of a few days following the ablation, the epithelium recovers as the epithelial ablation heals, and fills back in with new regenerated epithelium. Treatment or evaluation procedures which involve epithelial ablation can be configured to account for the index of refraction of the epithelial layer, which can be about 1.401. By using the index of refraction of the epithelial layer, the surgeon or operator can accurately estimate or calculate the parameters of the administered ablation. According to some embodiment, epithelial ablations may be incorporated into procedures which test hypothetical treatment shapes such as multifocal presbyopic shapes.

### **Patient Selection**

[0109] In some instances, an aberration analysis of a patient eye can be used when selecting the patient for a refractive treatment. Certain wavefront-driven treatments may not correct high order aberrations (HOAs) for a variety of reasons, such as the biomechanical effect and healing, dehydration during the ablation, imperfect treatment targets, or the deviations of the hardware components from their preferred situations during the surgery. It has now been discovered that techniques of compensating for a variable index of refraction as discussed herein can have a significant impact on reducing high order aberrations following surgery, and thus a patient may be selected based on the extent to which the patient's eye presents high order aberrations.

[0110] Current wavefront-driven refractive surgery techniques for determining target ablation profiles are typically based on a nominal value of the refractive index of the cornea. Embodiments of the present invention present laser systems and methods for refractive surgery can take into account a variable index of refraction for conventional or wavefront-driven ablations, thus reducing the possibility that early pulses may be over-ablating the tissue (because the estimated nominal index of refraction is greater than the variable index of refraction for that depth) or that final or later pulses may be under-ablating the tissue (because the estimated nominal index of refraction is less than the variable index of refraction for that depth). In the absence of such compensation techniques, high myopia and high hyperopia can be under-corrected, and such results were observed in clinical outcomes.

[0111] Embodiments of the present invention provide approaches to address these situations. For example, improved techniques can take into account a variable index of

refraction that is higher on the surface and gradually decreases as ablation continues to greater depths. Such approaches may be particularly useful when applied to refractive treatments involving high corrective ablation depths. In an exemplary technique, differential ablation layers can be considered for the refractive index of that layer, making the ablation depth dependent upon the ablation depth. Relatedly, in a real-time monitoring system, the observed profile deviation can be compensated by the knowledge of the refractive index of a certain depth. Optionally, an ablation target profile can be designed using personalized refractive index profile of the patient.

[0112] The original target in OPD without adjustment (e.g. cosine effect or scaling factor) was sliced into a number of very thin (differential) layers. Within each layer, the refractive index was considered as constant. For each layer, the OPD of the thin layer was converted to tissue depth with the refractive index of that layer. The following formula was used:

$$n_i = n_0 - k \cdot h$$

[0113] In this formula,  $n_0$  is the refractive index of the anterior surface of the stroma and can be assumed as 1.380,  $k$  is the rate of change and is  $0.000015/\mu\text{m}$  of tissue depth, and  $h$  is the distance of that layer in microns below the anterior surface of the stroma. With this new approach, a new volume of tissue can be reconstructed. This volume can be compared to the original volume which is determined based on a refractive index of 1.377, which is a nominal value commonly used in the industry. **FIG. 6** graphically illustrates the original map (left column), the reconstructed map (middle column), and the residual error (right column) when the sliced layers are in  $1 \mu\text{m}$  (top row),  $0.1 \mu\text{m}$  (middle row), and  $0.05 \mu\text{m}$  (bottom row). As shown here, when  $0.1 \mu\text{m}$  layers are used, the residual error, or difference between the original map and the reconstructed map, can be considered as negligible. Such  $0.1 \mu\text{m}$  layers were used for analyses provided herein.

[0114] The original map of **FIG. 6** corresponds to the true shape or input that is prescribed for application to the eye. When using a  $1 \mu\text{m}$  slice, there is a relatively higher amount of error, as evidenced by the noticeable bands or patterns of the residual error result at the top right corner of the figure. As the slice becomes thinner, the difference between the original shape and the reconstructed shape becomes smaller, and the error appears random. These results can be used to evaluate the reduction in error when using a variable index of refraction as a function of depth.

[0115] With the above model validation, error evaluations for the following three types of input were performed: (1) pure Zernike polynomials with one micron of OPD wavefront error; (2) 8 typical refractions ranging from +6 D to -12 D; (3) 5 ocular wavefronts with little low order refractive errors but normal HOAs.

5 [0116] Errors can be introduced when a variable index of refraction of the cornea is not taken into account. The three situations discussed below provide exemplary techniques for evaluating error that may be introduced when a variable refractive index of the cornea is not considered. First, it was observed that for pure Zernike terms with one micron OPD  
10 wavefront error, high order aberrations such as RMS and PV are in the order of 0.04 and 0.15 microns, respectively. This corresponds to about 5% error in terms of RMS. Second, for 8 low order only cases, the refractions range from +6 D to -12 D, and the error without consideration of variable refractive index gives about 0.1 micron RMS and 0.3 micron PV error, or on average about 1% error in terms of RMS. Third, for 5 random wavefront with  
15 low refractive error but normal HOAs, the RMS and PV are about 0.5 and 0.13 microns, respectively. This corresponds to about 10% error in terms of RMS. In addition, very little residual low order refractive error is observed. An unexpected and surprising result was discovered. That is, a primary effect of not compensating for a variable refractive index is that high order aberrations were not fully corrected. Hence, it was discovered that accounting for a variable index of refraction can have a significant impact on reducing HOAs following  
20 surgery.

[0117] FIG. 7 shows the residual error due to the use of a nominal refractive index of the stroma, with each Zernike term having 1 micron of wavefront error in OPD. Each of the 25 boxes represents a residual error for a particular Zernike term from a typical Zernike pyramid. When a variable index of refraction is not considered, there is an error of about 5%  
25 for the pure Zernike polynomials.

[0118] The respective RMS and PV error in OPD, as well as the RMS error as a percentage of the input wavefront RMS, are shown in Table 2, which corresponds to the results provided in FIG. 7. As depicted in this table, the percentage can be about 5%.

<b>Table 2</b>			
<b>Zernike</b>	<b>RMS</b>	<b>PV</b>	<b>Percent</b>
z3	0.049	0.137	4.9%
z4	0.051	0.131	5.1%
z5	0.047	0.144	4.7%
z6	0.044	0.141	4.4%
z7	0.044	0.138	4.4%
z8	0.044	0.138	4.4%
z9	0.044	0.141	4.4%
z10	0.041	0.144	4.1%
z11	0.042	0.134	4.2%
z12	0.048	0.128	4.8%
z13	0.043	0.137	4.3%
z14	0.039	0.142	3.9%
z15	0.039	0.149	3.9%
z16	0.040	0.133	4.0%
z17	0.042	0.143	4.2%
z18	0.042	0.143	4.2%
z19	0.040	0.133	4.0%
z20	0.039	0.149	3.9%
z21	0.038	0.146	3.8%
z22	0.039	0.130	3.9%
z23	0.043	0.141	4.3%
z24	0.044	0.132	4.4%
z25	0.041	0.132	4.1%
z26	0.040	0.133	4.0%
z27	0.037	0.141	3.7%

[0119] The second case is for pure low order only refractions. The 8 refractions used in this experiment ranged from -12 D to +6 D and covered spherical myopia, spherical hyperopia, myopic astigmatism, hyperopic astigmatism, as well as mixed astigmatism. The residual error maps are shown in **FIG. 8**.

- 5 [0120] The corresponding RMS and PV error in OPD, the residual spherical equivalent (SE) in diopters, as well as the RMS as a percentage of the input wavefront RMS error, are given in **Table 3**. As depicted here, the percentage is around 1%.

Rx	RMS	PV	SE	Percent
-12 DS	0.153	0.329	0.000	1.2%
-8DS/-4DCx48	0.167	0.332	0.013	1.5%
-6DS	0.083	0.249	0.000	1.2%
-3DS/-1DCx111	0.056	0.228	-0.003	1.3%
-2DS/+4DCx83	0.045	0.221	-0.006	1.2%
+3DS	0.043	0.202	0.000	1.0%
+4DS/+3DCx165	0.083	0.321	0.008	1.0%
+6 DS	0.087	0.261	0.000	1.0%

[0121] With these low order aberration refractions, the undercorrection was about 1%, which is less than the results observed with high order aberration and pure Zernike polynomials shown in FIG. 7 and Table 2. In instances with very high hyperopia or myopia, many of the random errors may be canceled out, thus providing a lower error for the refractive case, or low order aberrations.

[0122] In the third situation, 5 input wavefronts with little low order error and normal high order aberrations were used. The residual maps are shown in FIG. 9. The corresponding RMS and PV error in OPD, the residual SE, and the RMS as a percentage of input wavefront RMS, are listed in Table 4. As shown here, the percentage is as high as about 10%, indicating a higher degree of error.

Case	RMS	PV	SE	Percent
1	0.040	0.137	0.001	8.3%
2	0.053	0.133	-0.001	9.9%
3	0.048	0.131	0.000	12.4%
4	0.038	0.132	0.000	8.3%
5	0.041	0.138	0.001	8.6%

[0123] These higher error results are more akin to the first situation, which involves high order aberration and pure Zernike polynomials. It can be seen that by accounting for a variable index of refraction, it is possible to avoid or reduce error when devising a vision treatment for correcting or ameliorating ocular aberrations having very fine structural details.

[0124] FIG. 10 provides an illustrative flow chart for a technique that considers a variable index of refraction of the cornea or ablated tissue. System 1000 can include an autorefractor module 1010 that can produce low order aberration information, optionally in the format of wavefront data or a wavefront map, and a wavefront aberrometer module 1020 that can produce low order and high order aberration information, in the format of wavefront data or a

wavefront map. Information from autorefractor module 1010 or wavefront aberrometer module 1020, or both, can be transmitted to a wavefront map module 1030. In turn, wavefront map information from wavefront map module 1030 can be transmitted to an ablation target profile module 1040. System 1000 also includes a variable refractive index module 1050. Variable index of refraction information from variable refractive index module 1050 can be transmitted to ablation target profile module 1040, which generates ablation target profile information, optionally based on a combination of the wavefront map information and the variable index of refraction information. The ablation target profile information can be transmitted from the ablation target profile module 1040 to a SALSA algorithm module 1060, which can generate SALSA algorithm information based on the ablation target profile information. The SALSA algorithm information can then be transmitted to a treatment table module 1070, which can generate treatment table information based on the SALSA algorithm information. The treatment table information can then be transmitted to an excimer laser module 1080.

#### 15                    **Personalized Refractive Index and Realtime Monitoring**

[0125] Embodiments of the present invention encompass systems and methods that account for a personalized refractive index during a pre-operative examination, and that provide realtime monitoring of the refractive index change during a surgical procedure. In addition, embodiments encompass a feedback system for real-time monitoring of the ablation depth, and for adjustment of ablation profiles during the ablation procedure. Furthermore, 20                    embodiments encompass techniques for designing a customized ablation target profile that is based on personalized refractive index of the cornea or ocular tissue. As such, systems and methods are discussed which take into account the person-to-person variability in the index of refraction when generating a customized ablation target.

25                    [0126] **FIG. 11** illustrates a system 1100 that can provide realtime monitoring of a change in refractive index at various levels of cornea or tissue as the ablation goes deeper into the tissue. Aspects of this approach may be incorporated into personalized treatment systems and methods. System 1100 includes an initial treatment table module 1110 and an excimer laser module 1120. Initial treatment table information can be transmitted from initial treatment 30                    table module 1110 to excimer laser module 1120. Ablation energy is transmitted from laser module 1120 toward a human cornea 1103. System 1100 also includes an EyeCam

profilometer module 1140 that can determine or evaluate the cornea profile. Optionally, the cornea profile may be evaluated with an optical coherence tomography (OCT) apparatus.

[0127] System 1100 includes a comparison module 1150 that compares the cornea profile with a treatment target profile. Comparison information can be transmitted from comparison module 1150 to a treatment target profile adjustment module 1160. System 1100 also includes a variable refractive index module 1170. Variable index of refraction information can be transmitted from variable refractive index module 1170 to treatment target profile adjustment module 1160. Treatment target profile adjustment information can be generated by treatment target profile adjustment module 1160, optionally based on a combination of comparison information transmitted from comparison module 1150 and variable index of refraction information transmitted from variable refractive index module 1170. According to some embodiments, variable index of refraction information can be transmitted from variable refractive index module 1170 to initial treatment table module 1110. Relatedly, initial treatment table module 1110 may generate initial treatment table information based on the variable index of refraction information.

[0128] System 1100 also includes an adjusted treatment target module 1180. Adjusted treatment target information can be generated by adjusted treatment target module 1180 based on treatment target profile adjustment information transmitted from treatment target profile adjustment module 1160. Adjusted treatment target information can be transmitted from adjusted treatment target module 1180 to laser module 1120 as indicated by arrow A. Optionally, the ablation procedure may be terminated, as indicated by arrow B.

[0129] FIG. 12 illustrates a system 1200 that provides a personalized treatment for a patient. For example, system 1200 can generate a treatment for an individual patient based upon the unique variable refractive index of the patient's cornea. Pre-operative examination techniques can be used to measure the refractive index of the patient's cornea which is to be ablated. Accordingly, system 1200 may include or be coupled with a pre-operative exam module 1210. As shown here, pre-operative exam module 1210 may include a pre-operative ocular module 1220 having a clinical module 1222 and a wavefront aberrometer module 1224. In some cases, wavefront aberrometer module 1224 may include features of a WaveScan system. Relatedly, pre-operative exam module 1210 may include a refractive index module 1230 having an Abbe refractometer module 1232 and a personalized refractive index profile module 1234. In some cases, refractometer module 1232 can be configured to

provide refractive index information instantaneously, or in realtime during a treatment procedure. Clinical module 1222 may include an autorefractometer device, a keratometry device, a pachymetry device, or any combination thereof. Clinical information can be transmitted from clinical module 1222 to wavefront aberrometer module 1224, and wavefront  
5 aberrometer information can be transmitted from wavefront aberrometer module 1224 to a wavefront map module 1240. Optionally, pre-operative ocular information can be transmitted from pre-operative ocular module 1220 to wavefront map module 1240. Similarly, refractometer information can be transmitted from refractometer module 1232 to personalized refractive index profile module 1234, and personalized refractive index profile  
10 can be transmitted from personalized refractive index profile module 1234 to an ablation target profile module 1250. Optionally, refractive index information can be transmitted from refractive index module 1230 to ablation target profile module 1250.

[0130] Ablation target profile module 1250 can receive wavefront map information transmitted from wavefront map module 1240. According to some embodiments, ablation  
15 target profile module 1250 can generate ablation target profile information based on wavefront map information transmitted from wavefront map module 1240, refractive index information can be transmitted from refractive index module 1230, or both. In turn, ablation target profile information can be transmitted from ablation target profile module 1250 to SALSA algorithm module 1260. SALSA information can be generated by SALSA algorithm  
20 module 1260 and transmitted to treatment table module 1270. Treatment table information can be generated by treatment table module 1270 and transmitted to excimer laser module 1280.

[0131] Aspects of systems 1000 or 1100 shown in **FIGS. 10 and 11**, respectively, can be incorporated into system 1200 shown in **FIG. 12**. Similarly, aspects of systems 1100 or 1200  
25 shown in **FIGS. 11 and 12**, respectively, can be incorporated into system 1000 shown in **FIG. 10**. Likewise, aspects of systems 1000 or 1200 shown in **FIGS. 10 and 12**, respectively, can be incorporated into system 1100 shown in **FIG. 11**.

[0132] Embodiments of the present invention provide systems and methods for determining a treatment target for a patient, based on a variable or customized index of refraction.  
30 Treatment targets may incorporate ablation depths calculated based on such variable or customized indexes, and may be based upon optical correction shapes or ablation volumes that are divided into layers, wherein each layer presents a constant index of refraction. For



each layer, the optical effect can be converted into a tissue depth according to the index of refraction for that layer. In this way, an entire optical surface can be converted to a tissue volume, which can be used to determine a pulse treatment protocol. Relatedly, optical volumes for ablation can be estimated when determining an optical surface that is applied to the eye in an ablation procedure. Treatments involving a high correction can incorporate an ablation with deeper pulses. In some cases, a treatment protocol may involve early pulses administered at a relatively lower rate, and later pulses administered at a higher rate. Optionally, deeper ablations may be achieved by using the same laser pulse rate, with a higher correction effect or scaling factor. For example, if the correction surface is deeper, then the scaling factor can be increased. Such adjustments can be performed by a treatment target adjustment module such as the treatment target profile adjustment module shown in **FIG. 11**. In some cases, an adjusted treatment target may be based upon an increased number of pulses per unit volume. For example, in general terms, whereas a -4D correction may involve 500 pulses, a -10D correction may involve 500 pulses for the first -5D and 550 pulses for the second -5D. Further, the adjustments can be implemented in smaller increments. For example, the adjustments can be carried out for every micron in OPD. According to such refining techniques, target ablation profiles can be modified to take into account of the variability of the refractive index of the eye tissue, optionally in a personalized or customized implementation.

#### 20 **Variable Index of Refraction and Wavefront Analysis**

[0133] Embodiments of the present invention provide systems and methods for administering a wavefront-driven refractive surgery onto a variable refractive index cornea. Relatedly, embodiments encompass systems and methods for determining a refractive treatment for the eye based on a variable index of refraction and a wavefront analysis of the eye, independent of a Munnerlyn equation.

[0134] The methods and apparatuses of the present invention may be provided in one or more kits for such use. The kits may comprise a system for profiling an optical surface, such as an optical surface of an eye, and instructions for use. Optionally, such kits may further include any of the other system components described in relation to the present invention and any other materials or items relevant to the present invention. The instructions for use can set forth any of the methods as described above.

2010324562 31 Oct 2014

**[0135]** Each of the above calculations or operations may be performed using a computer or other processor having hardware, software, and/or firmware. The various method steps may be performed by modules, and the modules may comprise any of a wide variety of digital and/or analog data processing hardware and/or software arranged to perform the method steps described herein. The modules optionally comprising data processing hardware adapted to perform one or more of these steps by having appropriate machine programming code associated therewith, the modules for two or more steps (or portions of two or more steps) being integrated into a single processor board or separated into different processor boards in any of a wide variety of integrated and/or distributed processing architectures. These methods and systems will often employ a tangible media embodying machine-readable code with instructions for performing the method steps described above. Suitable tangible media may comprise a memory (including a volatile memory and/or a non-volatile memory), a storage media (such as a magnetic recording on a floppy disk, a hard disk, a tape, or the like; on an optical memory such as a CD, a CD-R/W, a CD-ROM, a DVD, or the like; or any other digital or analog storage media), or the like.

**[0136]** All patents, patent publications, patent applications, journal articles, books, technical references, and the like discussed in the instant disclosure are incorporated herein by reference in their entirety for all purposes.

**[0137]** While the above provides a full and complete disclosure of the preferred embodiments of the present invention, various modifications, alternate constructions and equivalents may be employed as desired. Therefore, the above description and illustrations should not be construed as limiting the invention, which can be defined by the appended claims.

**[0138]** Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

**[0139]** The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as, an acknowledgement or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

## WHAT IS CLAIMED IS:

1. A system for determining a refractive treatment for an eye of a patient, the system including:

- 5 an input configured to receive a function representing a variable index of refraction for an epithelium of the eye, wherein the function includes an index of refraction term  $n(h)$  that varies according to an epithelial depth term  $h$  according to the formula

$$n(h) = n_0 + \delta h$$

wherein  $n_0$  represents an index of refraction constant and  $\delta$  represents a gradient index; and

- 10 a processing module including a non-transitory computer readable medium embodying machine-readable code that determines the refractive treatment for the eye based on the function representing the variable index of refraction for the epithelium of the eye.

- 15 2. The system according to claim 1, wherein the variable index of refraction term  $n(h)$  is about 1.401 at an anterior portion of the epithelium and about 1.380 at a posterior portion of the epithelium.

3. A method of determining a refractive treatment for an eye of a patient, the method including, through the use of a computer processor:

receiving a function representing a variable index of refraction for an epithelium of the eye, wherein the function includes an index of refraction term  $n(h)$  that varies according to an epithelial depth term  $h$  according to the formula

$$n(h) = n_0 + \delta h$$

- 25 wherein  $n_0$  represents an index of refraction constant and  $\delta$  represents a gradient index; and

determining the refractive treatment for the eye based on the function representing the variable index of refraction for the epithelium of the eye.

4. The method according to claim 3, wherein the index of refraction term  $n(h)$  is about 1.401 at an anterior portion of the epithelium and about 1.380 at a posterior portion of the epithelium.

5 5. A system for selecting a patient for treatment with a variable index of refraction surgical procedure, the system including:

an input configured to receive an aberration profile of an eye of the patient, wherein the aberration profile includes a low order aberration component and a high order aberration component; and

10 a processing module comprising a non-transitory computer readable medium embodying machine-readable code that selects the patient for treatment with the variable index refractive surgical procedure based on the aberration profile, wherein the variable index of refraction surgical procedure is based on:

a first function representing a variable index of refraction for a cornea of the eye,  
15 wherein the first function includes a variable index of refraction term  $n(h)$  that varies according to a corneal stromal depth term  $h$  according to the formula

$$n(h) = n_0 + \delta h$$

wherein  $n_0$  represents a stromal index of refraction constant and  $\delta$  represents a stromal gradient index,

a second function representing a variable index of refraction for an epithelium of  
20 the eye, wherein the second function includes a variable index of refraction term  $n(h)$  that varies according to an epithelial depth term  $h$  according to the formula

$$n(h) = n_0 + \delta h$$

wherein  $n_0$  represents a tissue index of refraction constant and  $\delta$  represents a tissue gradient index, or

a third function representing a variable index of refraction for a central portion of a  
25 stroma of the eye, wherein the third function includes an index of refraction term  $n(r)$  that varies according to a corneal stromal radial distance term  $r$  according to the formula

$$n(r) = n_0 + \lambda h$$

wherein  $n_0$  represents an index of refraction constant and  $\lambda$  represents a refractive index radial rate of change.

2010324562 31 Oct 2014

6. The system according to claim 5, wherein the variable index of refraction surgical procedure is based on the first function including the term that varies according to the corneal stromal depth term  $h$ .

5 7. The system according to claim 5, wherein the variable index of refraction surgical procedure is based on the second function including the term that varies according to the epithelial depth term  $h$ .

8. The system according to claim 5, wherein the variable index of refraction surgical procedure is based on the third function including the term that varies according to the corneal stromal radial distance term  $r$ .

9. A method of selecting a patient for treatment with a variable index of refraction surgical procedure, the method including, through the use of a computer processor:

15 evaluating an aberration profile of an eye of the patient, wherein the aberration profile comprises a low order aberration component and a high order aberration component; and

selecting the patient for treatment with the variable index of refraction surgical procedure based on the aberration profile, wherein the variable index of refraction surgical procedure is based on:

a first function representing a variable index of refraction for a cornea of the eye, wherein the first function comprises a variable index of refraction term  $n(h)$  that varies according to a corneal stromal depth term  $h$  according to the formula

$$n(h) = n_0 + \delta h$$

25 wherein  $n_0$  represents a stromal index of refraction constant and  $\delta$  represents a stromal gradient index,

a second function representing a variable index of refraction for an epithelium of the eye, wherein the second function includes a variable index of refraction term  $n(h)$  that varies according to an epithelial depth term  $h$  according to the formula

$$n(h) = n_0 + \delta h$$

30 wherein  $n_0$  represents a tissue index of refraction constant and  $\delta$  represents a tissue gradient index, or

2010324562 31 Oct 2014

a third function representing a variable index of refraction for a central portion of a stroma of the eye, wherein the third function includes an index of refraction term  $n(r)$  that varies according to a corneal stromal radial distance term  $r$  according to the formula

$$n(r) = n_0 + \lambda h$$

wherein  $n_0$  represents an index of refraction constant and  $\lambda$  represents a refractive index radial rate of change.

10. The method according to claim 9, wherein the variable index of refraction surgical procedure is based on the first function including the term that varies according to the corneal stromal depth term  $h$ .

10

11. The method according to claim 9, wherein the variable index of refraction surgical procedure is based on the second function including the term that varies according to the epithelial depth term  $h$ .

15 12. The method according to claim 9, wherein the variable index of refraction surgical procedure is based on the third function including the term that varies according to the corneal stromal radial distance term  $r$ .

13. A system for determining a refractive treatment for an eye of a patient, the system including:

20

an input configured to receive a function representing a variable index of refraction for a cornea of the eye, wherein the function includes:

an index of refraction term  $n(h)$  that varies according to a corneal stromal depth term  $h$  according to the formula

$$n(h) = n_0 + \delta h$$

25 wherein  $n_0$  represents a stromal index of refraction constant and  $\delta$  represents a stromal gradient index,

an index of refraction term  $n(h)$  that varies according to an epithelial depth term  $h$  according to the formula

$$n(h) = n_0 + \delta h$$

wherein  $n_0$  represents a tissue index of refraction constant and  $\delta$  represents a tissue gradient index, or

an index of refraction term  $n(r)$  that varies according to a corneal stromal radial distance term  $r$  according to the formula

$$n(r) = n_0 + \lambda h$$

5 wherein  $n_0$  represents an index of refraction constant and  $\lambda$  represents a refractive index radial rate of change;

an input configured to receive a wavefront analysis of the eye; and

a processing module comprising a non-transitory computer readable medium embodying machine-readable code that determines the refractive treatment for the eye  
10 based on the variable index of refraction and the wavefront analysis of the eye.

14. The system according to claim 13, wherein the processing module includes a non-transitory computer readable medium embodying machine-readable code that determines the refractive treatment for the eye independent of a Munnerlyn equation based on the eye.  
15

15. The system of claim 13, wherein the function includes the term that varies according to the corneal stromal depth term  $h$ .

16. The system of claim 13, wherein the function includes the term that varies  
20 according to the epithelial depth term  $h$ .

17. The system of claim 13, wherein the function includes the term that varies according to the corneal stromal radial distance term  $r$ .

25 18. A method of determining a refractive treatment for an eye of a patient, the method including, through the use of a computer processor:

receiving a function representing a variable index of refraction for a cornea of the eye, wherein the function includes;

an index of refraction term  $n(h)$  that varies according to a corneal stromal depth  
30 term  $h$  according to the formula

$$n(h) = n_0 + \delta h$$

2010324562 31 Oct 2014

wherein  $n_0$  represents a stromal index of refraction constant and  $\delta$  represents a stromal gradient index,

an index of refraction term  $n(h)$  that varies according to an epithelial depth term  $h$  according to the formula

$$n(h) = n_0 + \delta h$$

5 wherein  $n_0$  represents a tissue index of refraction constant and  $\delta$  represents a tissue gradient index, or

an index of refraction term  $n(r)$  that varies according to a corneal stromal radial distance term  $r$  according to the formula

$$n(r) = n_0 + \lambda h$$

10 wherein  $n_0$  represents an index of refraction constant and  $\lambda$  represents a refractive index radial rate of change;

receiving a wavefront analysis of the eye; and

determining the refractive treatment for the eye based on the variable index of refraction for the cornea of the eye and the wavefront analysis of the eye.

15 19. The method according to claim 18, wherein the refractive treatment for the eye is determined independent of a Munnerlyn equation based on the eye.

20. The method of claim 18, wherein the function includes the term that varies according to the corneal stromal depth term  $h$ .

20

21. The method of claim 18, wherein the function includes the term that varies according to the epithelial depth term  $h$ .

22. The method of claim 18, wherein the function includes the term that varies according to the corneal stromal radial distance term  $r$ .

25

23. A system for determining a refractive treatment for an eye of a patient, substantially as herein described with reference to the accompanying drawings.

30 24. A method for determining a refractive treatment to an eye of a patient, or, a method



2010324562 31 Oct 2014

of selecting a patient for treatment with a variable index of refraction surgical procedure, substantially as herein described.

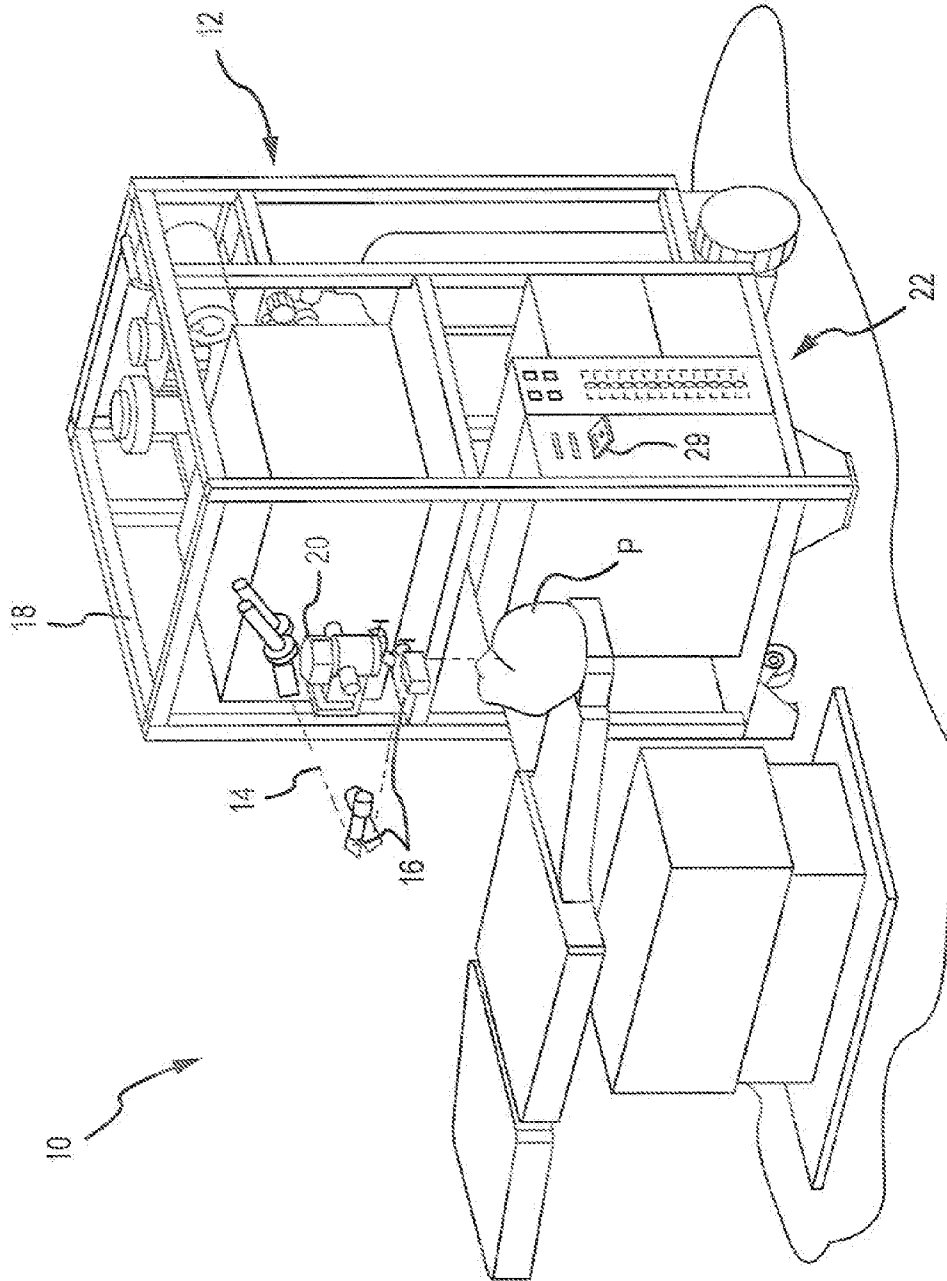


FIG. 1

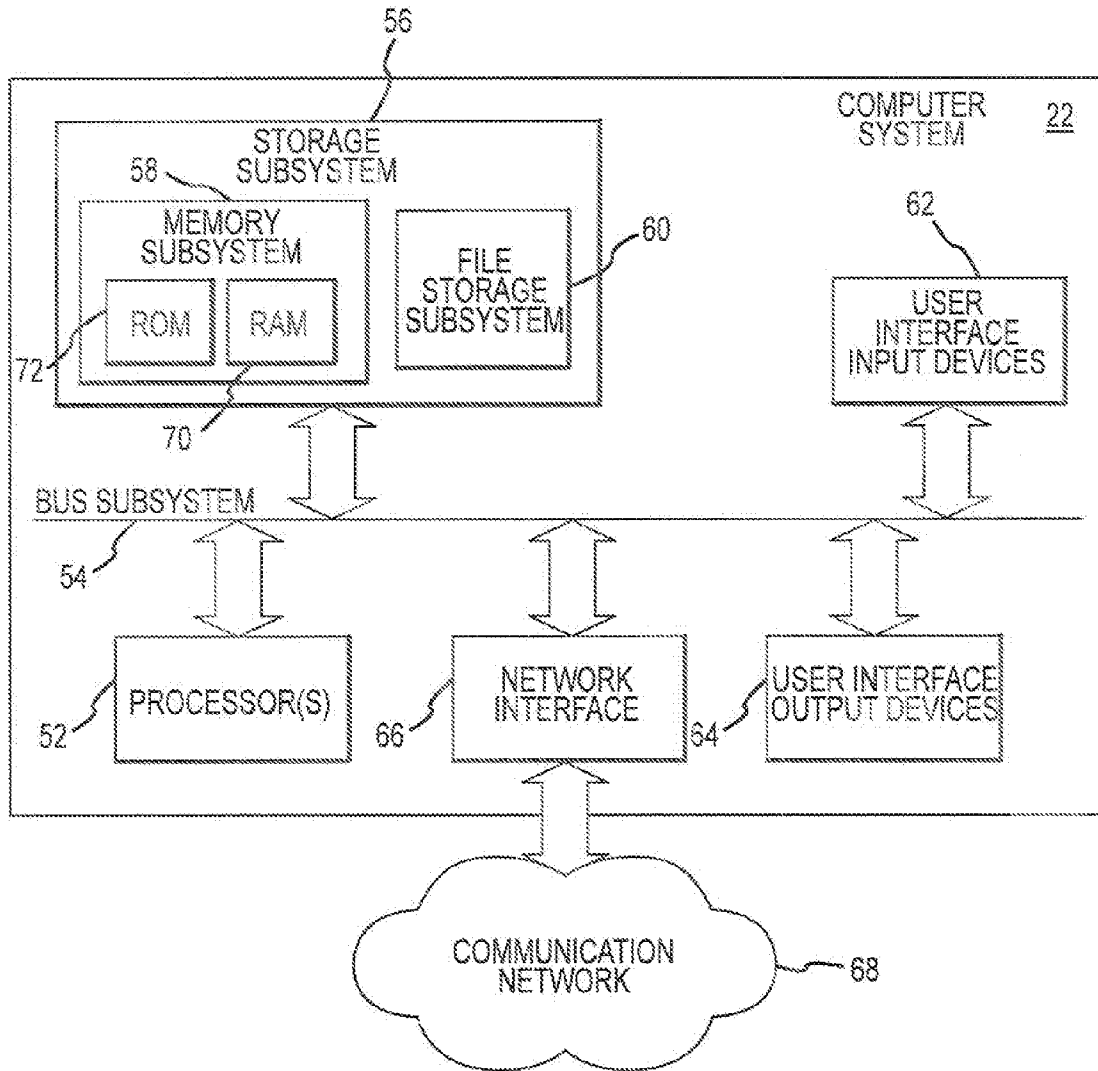


FIG.2

3/12

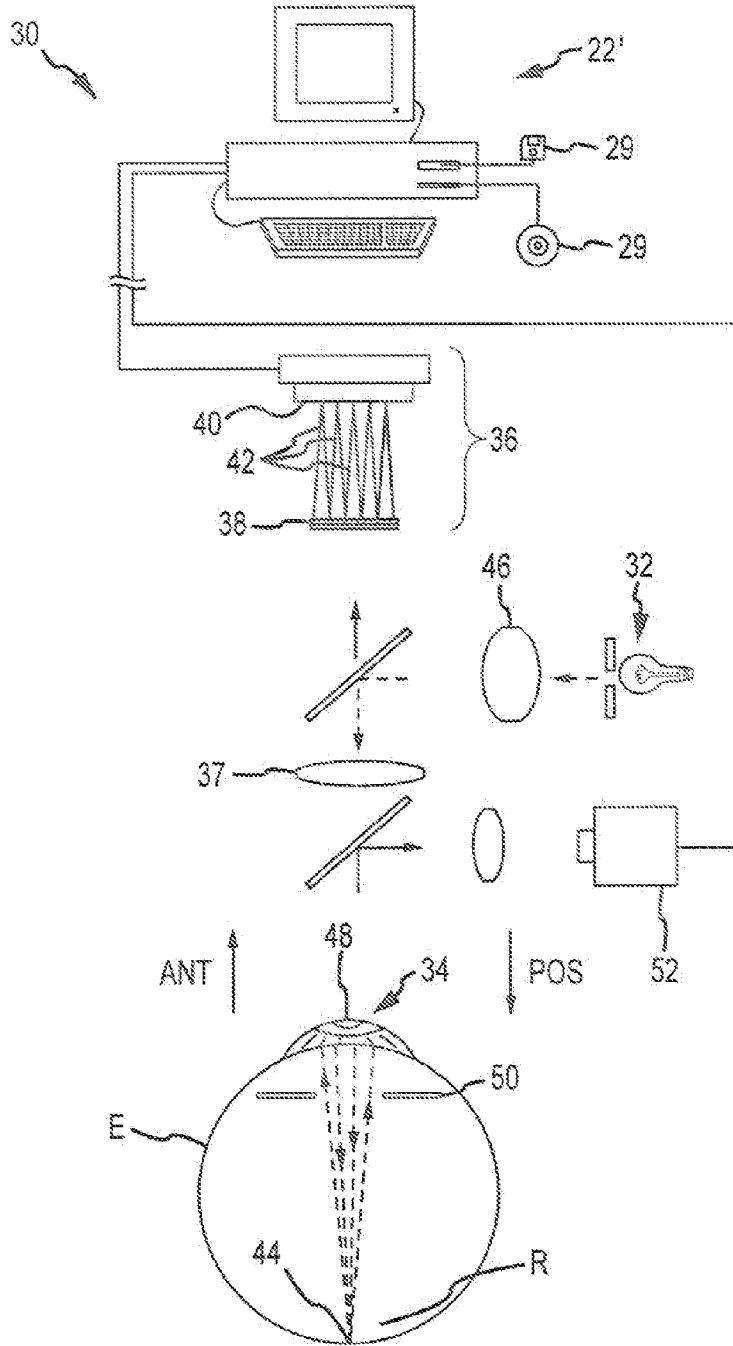


FIG.3

4/12

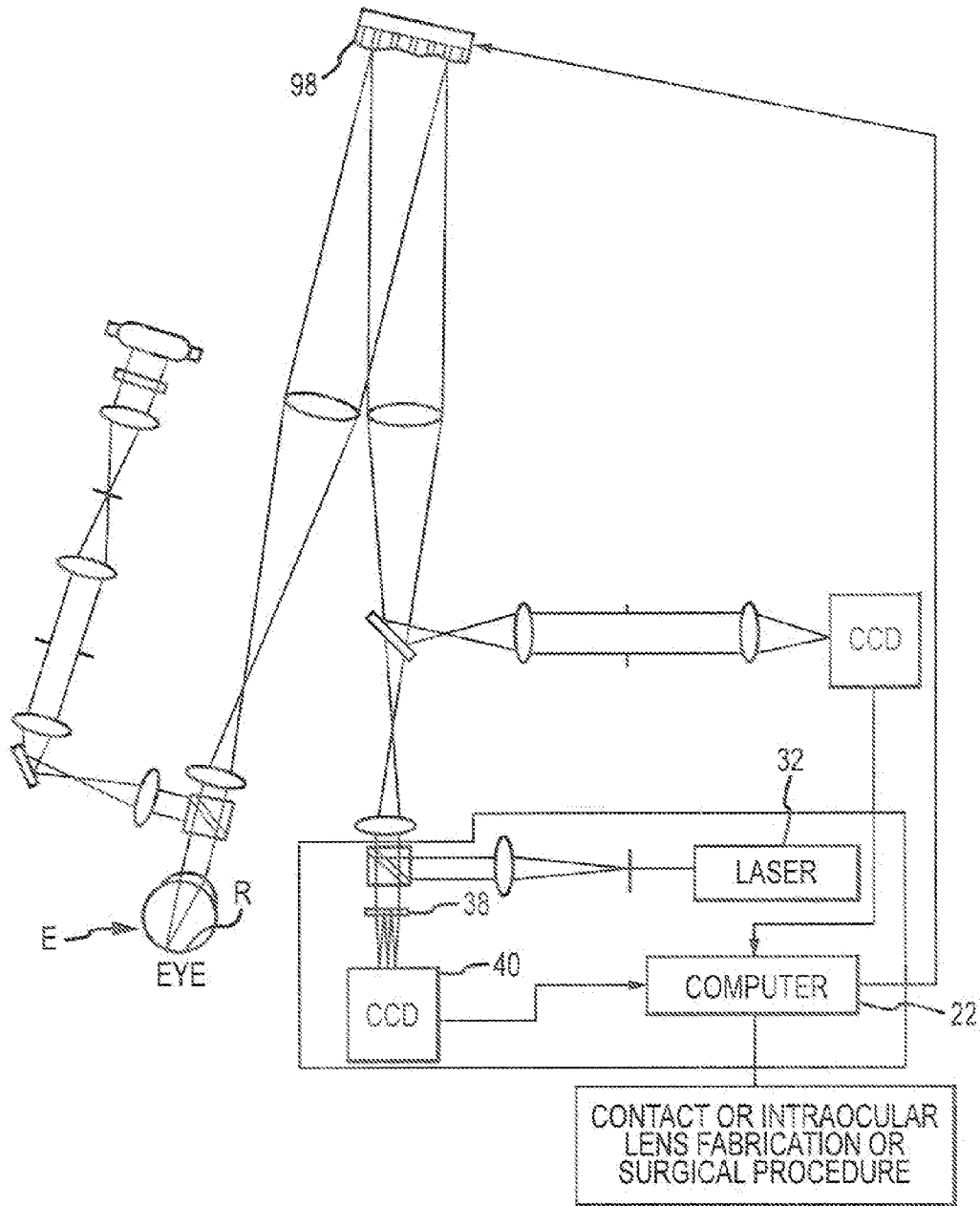


FIG.3A

5/12

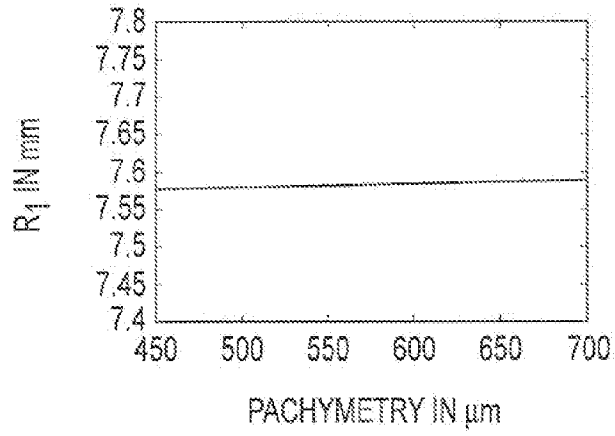


FIG.4A

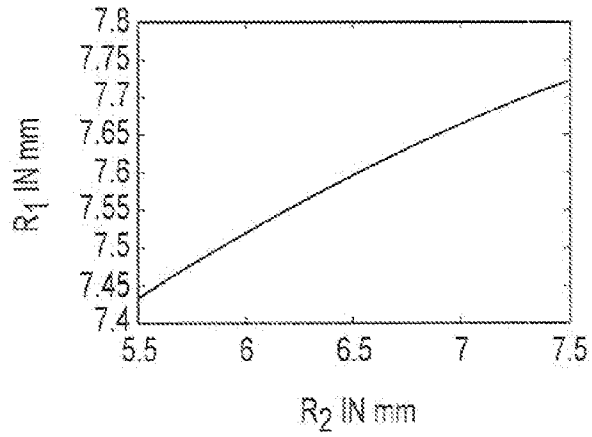
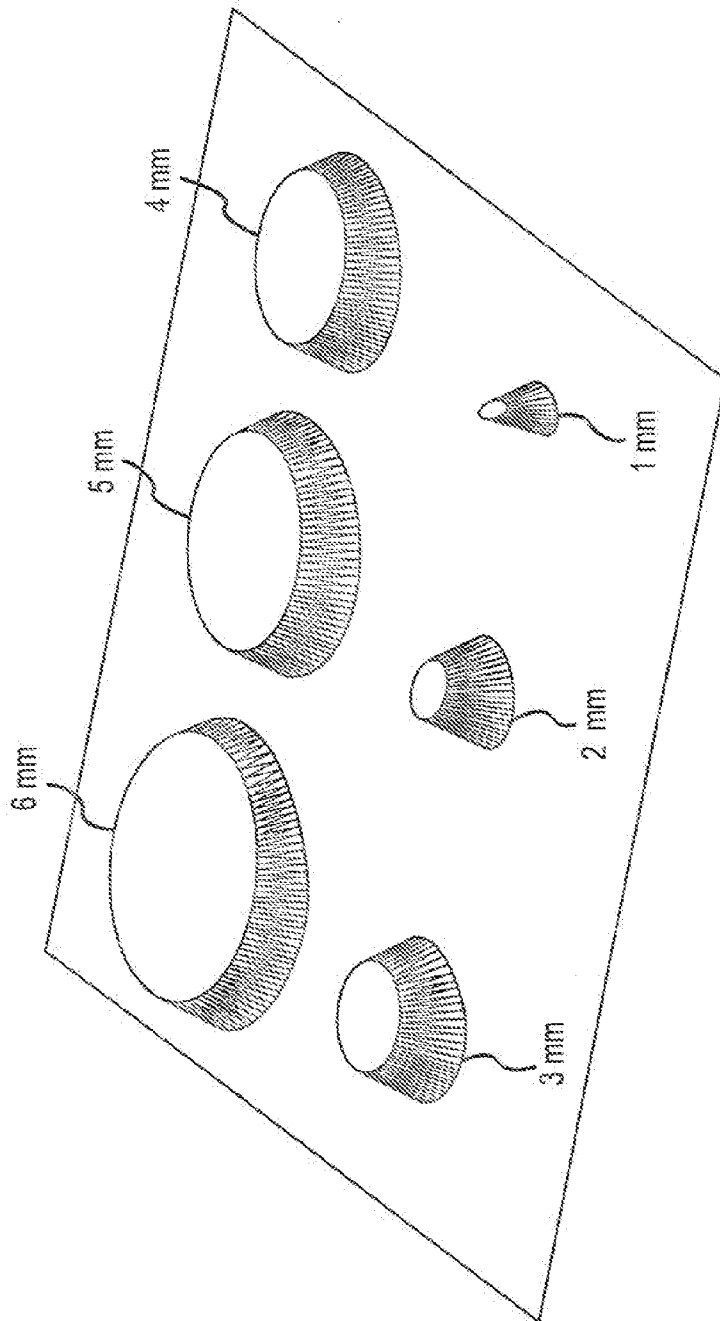


FIG.4B



CORNEAL ABLATION DATA

FIG.5

7/12

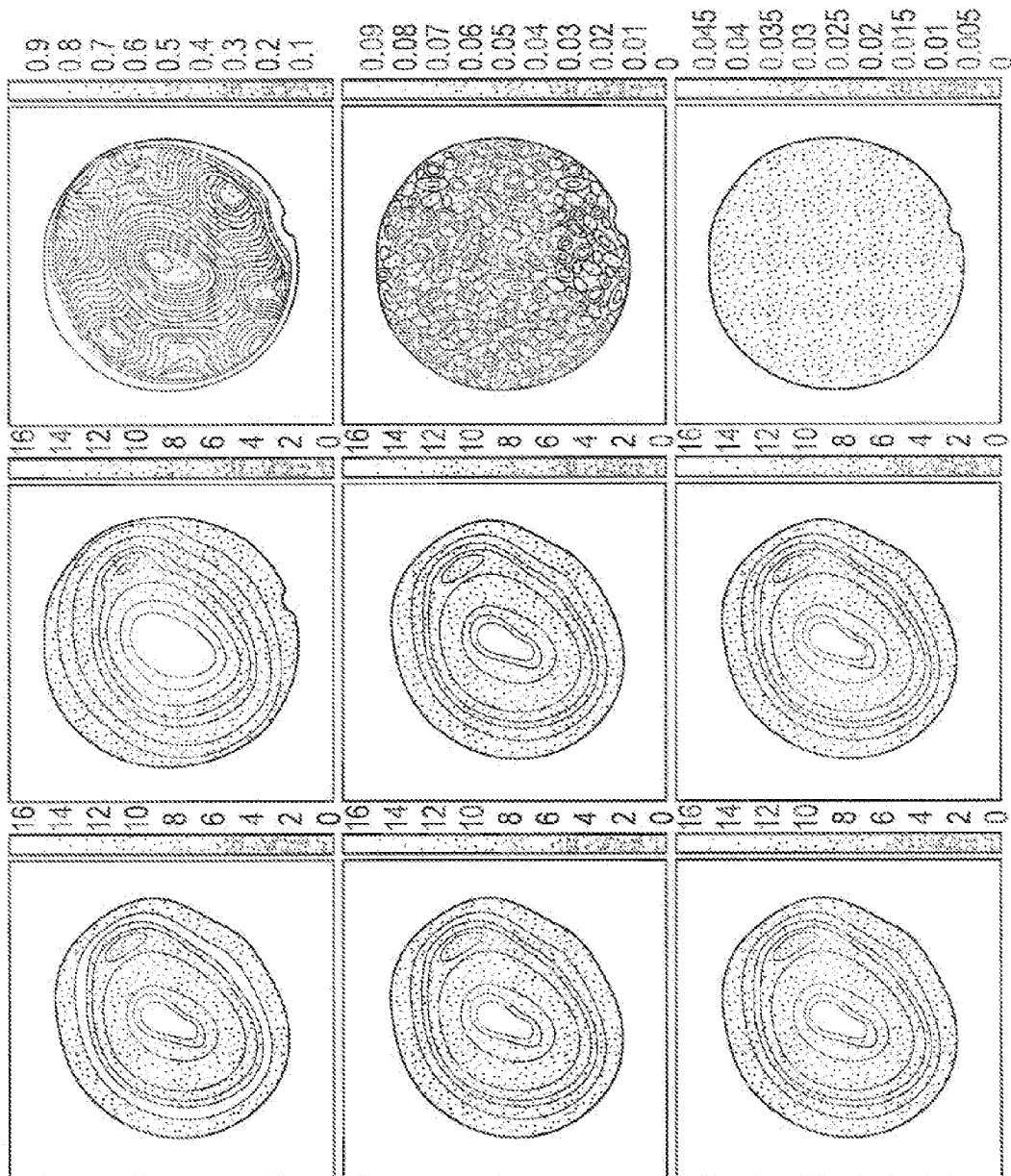


FIG.6



8/12

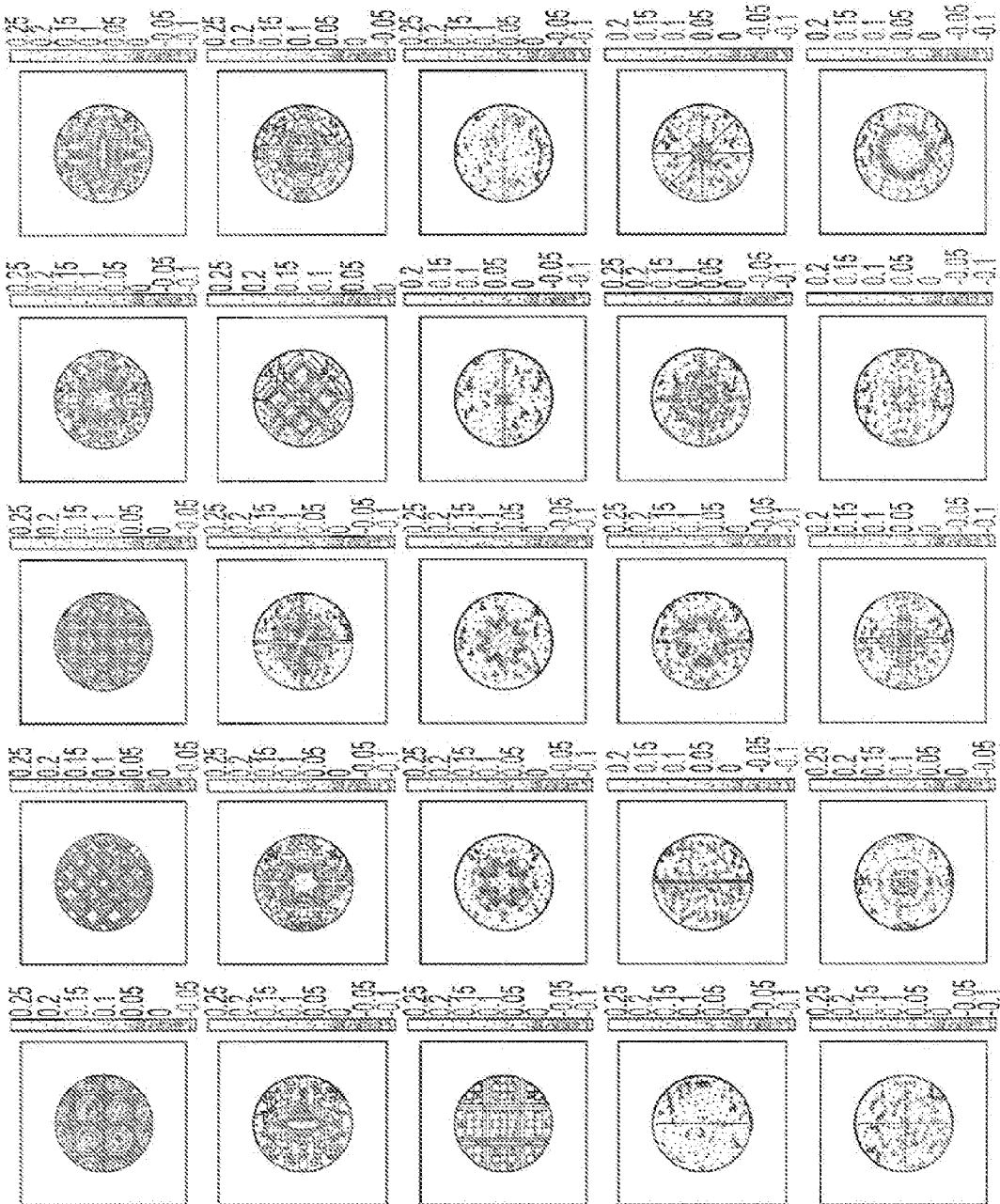


FIG.7

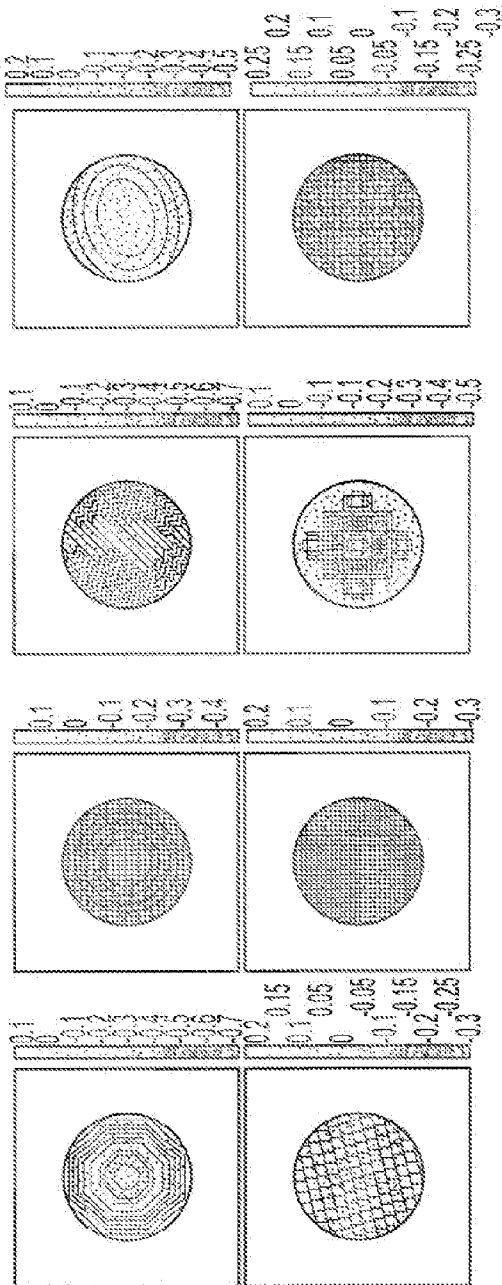


FIG. 8

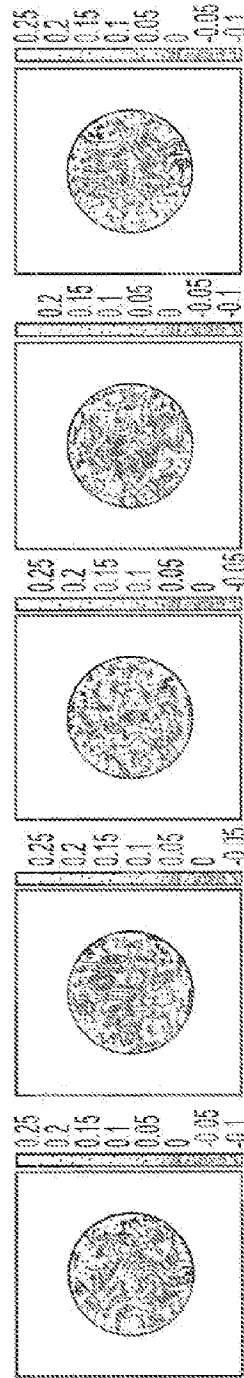


FIG. 9

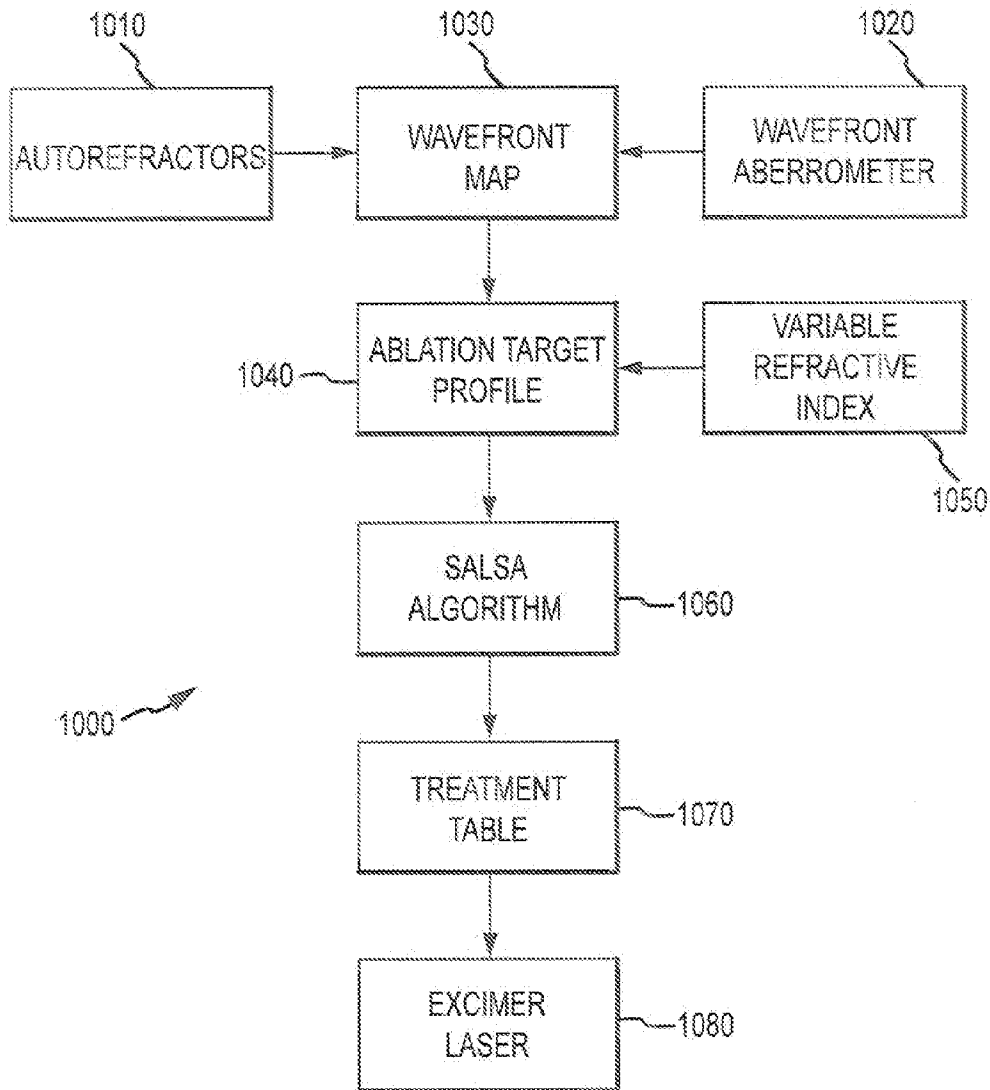


FIG.10

11/12

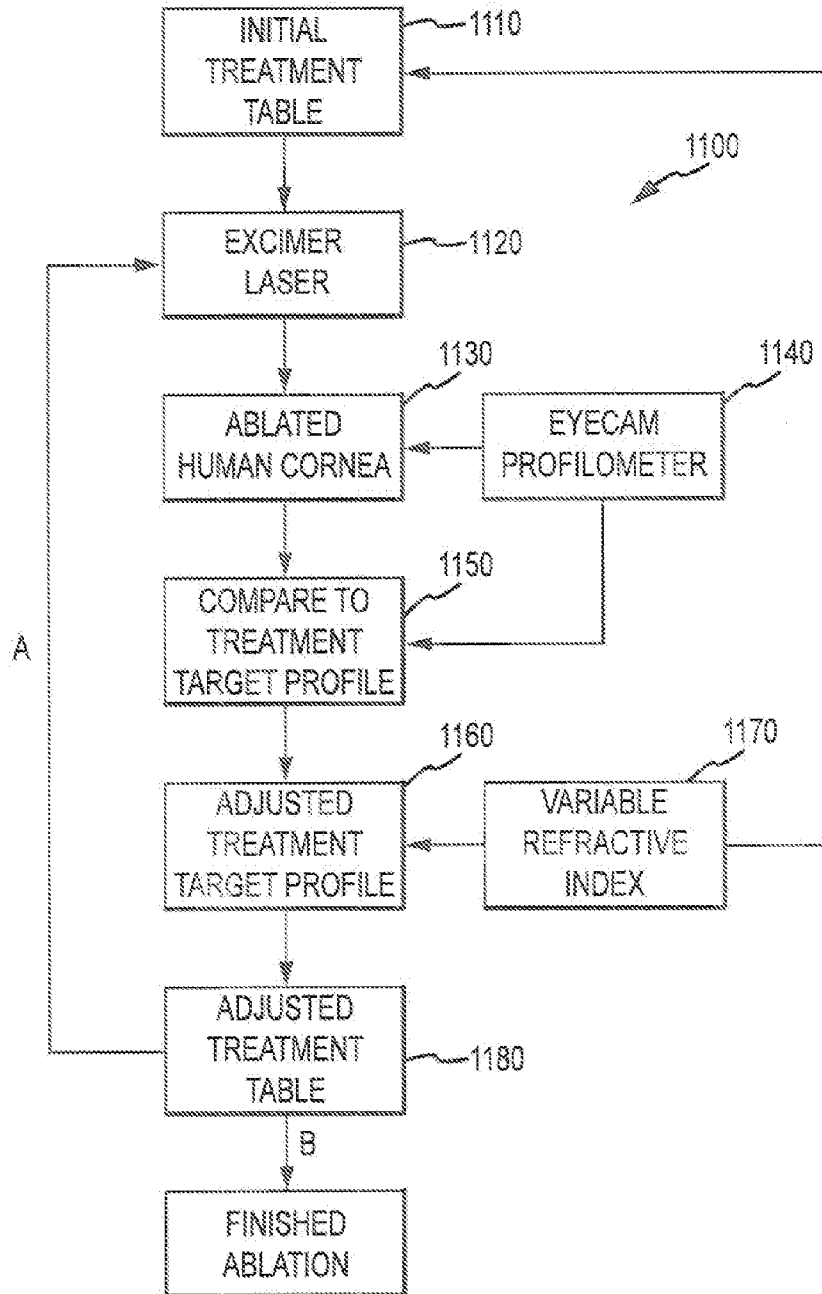


FIG.11

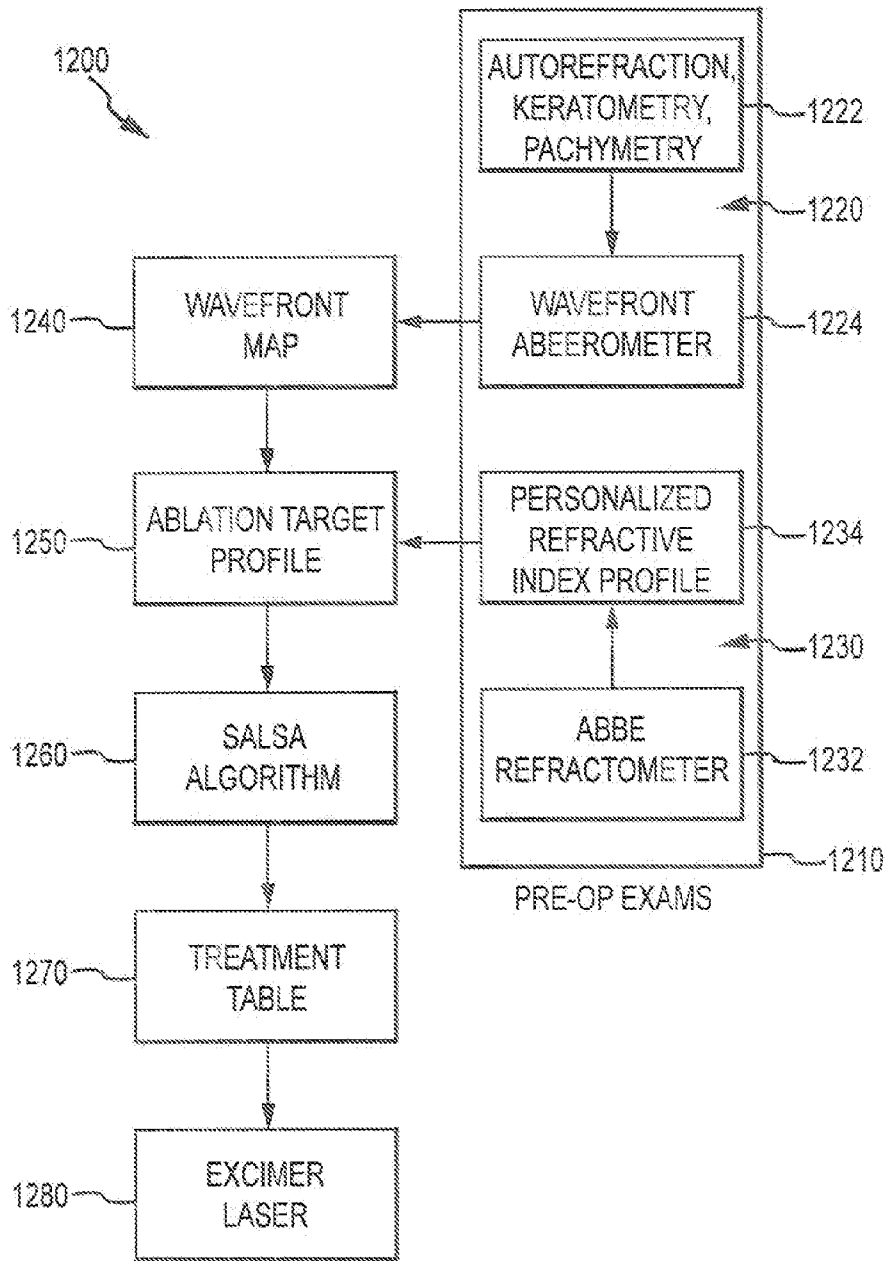


FIG.12