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(54) Title: A SYSTEM AND METHOD OF ARTIFICIAL INTELLIGENCE AND TOMOGRAPHY IMAGING OF HUMAN CORNEA

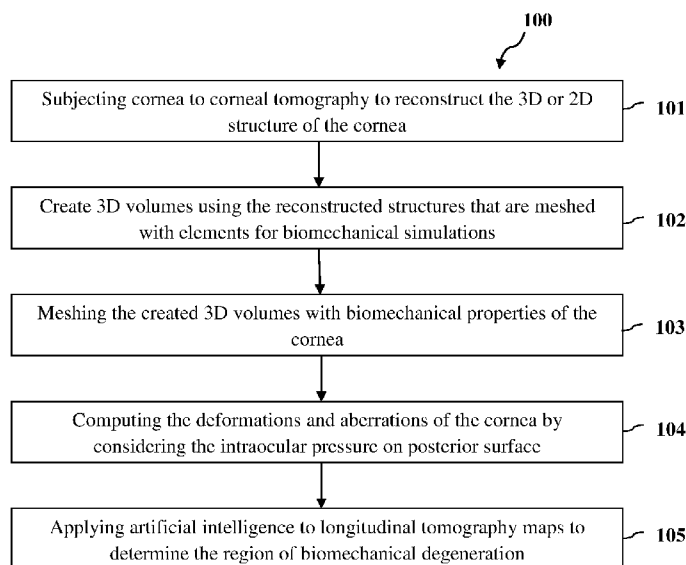


FIGURE 1

(57) Abstract: The invention relates to a system and method of implementation of artificial intelligence and tomography imaging to determine the biomechanical degradation or degeneration in human cornea. The invention relates to a combination tool using artificial intelligence and tomography imaging to map the region of degeneration in the cornea. The method of artificial intelligence and corneal tomography imaging includes analysis of changes in the structure of the cornea, constructing the 3D volumes using corneal tomography, meshing the 3D volumes with the elements for biomechanical simulations by using finite element modules, application of artificial intelligence to determine the region of biomechanical degeneration in cornea. The combination tool of the invention is effective in predicting the progression of the disease by analyzing the chronic steepening of the cornea by quantitating the parameters such as increase in curvature, aberrations of the cornea.



MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,
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- (84) Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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- *in black and white; the international application as filed contained color or greyscale and is available for download from PATENTSCOPE*

TITLE OF THE INVENTION**A system and method of artificial intelligence and tomography imaging of human cornea****DESCRIPTION OF THE INVENTION****5 Technical field of the invention**

[0001] The present invention relates to implementation of artificial intelligence and tomography imaging to determine the biomechanical degradation or degeneration in human cornea. The invention relates to a combination tool using artificial intelligence and tomography imaging to determine the degradation of
10 cornea. The invention also discloses a method of determining the extent of biomechanical degradation in human cornea.

Background of the invention

[0002] Cornea is a transparent anterior part of the eye that covers the iris, pupil
15 and anterior chamber. Cornea has unmyelinated nerve endings that are sensitive to touch, temperature and chemicals. Usually, cornea does not have blood vessels, instead, oxygen dissolves in tears and then diffuses throughout the cornea to keep it healthy. Similarly, nutrients are transported via diffusion from the tear fluid through outside surface and the aqueous humor through the inside surface and
20 also from neurotrophins supplied by nerve fibres that innervate it.

[0003] In human eye, cornea has a diameter of about 11.5 mm and a thickness of 0.5–0.6 mm in the center and 0.6–0.8 mm at the periphery. Cornea is responsible for about 70 percent of the eye's focusing power. The characteristics such as transparency, avascularity and the presence of immature resident immune cells
25 and immunologic privilege make cornea a very special tissue.

[0004] Corneal degradation or degeneration results in several disorders such as keratoconus, pellucid marginal degeneration, where cornea undergoes physical changes. These changes may be inflammatory, structural and biomechanical in nature. It is observed that in these disorders, there is severe thinning of the corneal layer and biomechanical degradation of the cornea. The diseases are progressive in nature, which implies that the severity of the disease increases over time, if left undiagnosed or unmanaged. The progression of the disease results in chronic steepening of the cornea resulting in increase in curvature, corneal aberrations and wave front aberrations.

10 [0005] In order to analyze the progression of the disease, there is requirement of a specific tool to predict the changes in the corneal surface specifically to determine the regions of degradation. These changes are measured using clinical topography and tomography devices. Corneal tomography is a non-invasive medical imaging technique for mapping the surface curvature of the cornea. It is a computer assisted diagnostic tool that creates a three-dimensional map of the surface curvature of the cornea. Corneal tomography is of critical importance in determining the quality of vision and corneal health.

20 [0006] Corneal tomography is used to identify the curvature of the cornea and to identify distortions such as keratoconus, scarring of the cornea or other distortions. It is also used as an aid in fitting contact lenses and in the evaluation of patients undergoing eye surgeries.

25 [0007] The greatest advantage of corneal tomography is its ability to detect irregular conditions that are usually invisible to conventional testing methods. Corneal tomography produces a detailed, visual description of the shape and power of the cornea, which provides the details regarding the condition of the corneal surface. These details are used to diagnose, monitor and to treat various eye conditions. They are also used in fitting contact lenses and for planning surgery, including laser vision correction.

[0008] The US Application No. **US09565851** titled “*Systems and methods for imaging corneal profiles*” discloses systems, methods and apparatus for generating images of portions of the patient's eye such as the anterior surface of the cornea. The methods and apparatus of the present invention are particularly useful for directly imaging the profile of the ablated region of the cornea. These methods and apparatus are helpful to image the exterior edge of the eye to characterize the profile of ablated corneas and to determine the spatial variance of tissue ablation rates during the surgical procedures. The methods and apparatus also provide provisions for generating one or more images depicting the profile of the ablated region of the cornea. The profile is registered with a pre-ablation profile to provide feedback regarding the true ablation properties of the eye. This feedback permits the laser system to be programmed with a laser ablation algorithm based on the measured ablation properties of the eye. However, the tool is silent with respect to the specific region as a target for intervention.

[0009] The US Application No. **US07931271** titled “*Method and apparatus for imaging and analysis of corneal tissue*” discloses a method and apparatus for in vivo imaging of corneal tissue. In general, the method comprises providing a laser beam having a substantially planer configuration. The substantially planar laser beam is directed through a cross-sectional portion of the cornea of a patient, so as to illuminate the cross-sectional portion and cause the laser beam to be scattered by molecules in the corneal tissue. Then, at least a portion of the scattered laser light is detected so as to form a cross-sectional image of the corneal tissue. In general, the planar configured laser beam exhibits a slit-like cross-sectional dimension having essentially the same width dimension over the depth of field within which the largest depth dimension of the eye extends. These unique characteristics of the illumination beam permit the formation of clear, in-focus images detected at the image detection plane. The method and apparatus of the invention are utilized to produce in-focus cross-sectional images from which the optical density of corneal tissue is precisely measured. The method and apparatus of the invention are useful for objectively measuring the optical density of corneal

tissue as well as precisely measuring the physical dimensions such as thickness and curvature of the cornea and its correct spatial relationship within the eye. However, the invention is silent with respect to the imaging on complete corneal tissue and to quantitate the extent of distortions of cornea in order to identify the progression of the disease.

5 [0010] The existing methods or tools of tomography are useful in identifying the distortions in the corneal tissue. However, the available methods are not useful for quantitative measurement and to identify the specific regions of biomechanical degradation. The degradation of the corneal tissue may be due to inflammatory, structural or biomechanical changes. It is crucial to analyze the biomechanical changes in the corneal tissue by the existing methods or apparatus.

10 [0011] Hence, there is a requirement of the combination tool to analyze the biomechanical degradation of the corneal tissue. The analysis and biomechanical degradation of the corneal tissue also helps in analyzing the progression of the disease. There is a requirement of a tool that analyzes the specific region as target for intervention such as transplant and corneal crosslinking.

Summary of the invention

15 [0012] The invention provides a system with a combination of artificial intelligence and corneal tomography to determine the regions of degradation in human cornea. The system comprises corneal tomography, finite element simulation module and artificial intelligence module. Corneal tomography helps in analyzing the anterior and posterior corneal surfaces with elevation and curvature and in reconstruction of 3D (Dimensional) or 2D surface of the cornea. Corneal tomography also provides elevation data of the corneal surface and layers in terms of point cloud. These surfaces are useful to create 3D volumes that are meshed with elements for biomechanical simulations. The imaging tool further comprises finite element simulation module. The 3D volumes constructed using corneal tomography is populated with biomechanical properties of the cornea. The finite element simulations help in computing the deformations. Finite element

simulation module also utilizes ray tracing for computing aberrations. The artificial intelligence module uses longitudinal tomography maps of the same eye or a single cross-section tomography of the patient eye referenced to a normative database of corneal shape to determine the region of biomechanical degeneration.

- 5 [0013] The invention also discloses a method of implementing artificial intelligence and corneal tomography in combination to analyze the corneal tomography of the patient and use biomechanical simulation with finite element modeling to determine the region of degradation in human cornea.

[0014] The analysis of physical changes in cornea helps in analyzing the severity
10 of the disease and acts a marker for progression of the disease. The method disclosed in the invention helps in analyzing the corneal diseases. The method of artificial intelligence and corneal tomography imaging includes analysis of changes in the structure of the cornea, constructing the 3D volumes using corneal tomography, meshing the 3D volumes with the elements for biomechanical
15 simulations by using finite element modules, application of artificial intelligence to determine the region of biomechanical degeneration in cornea. The tool compares corneal tomography at different follow-up visits of the patient and use biomechanical simulation with finite element modeling to determine the region of degradation by analyzing the spatial area and location of the disease.

20 [0015] The invention helps in analyzing the axial curvature before treatment with keratoconic pattern. The treatment results in change of the axial curvature from the keratoconic to astigmatism pattern and the difference in the axial curvature post treatment is illustrated. The system and method of combination of artificial intelligence and tomography imaging is useful in determining the biomechanical
25 degradation in human cornea. The combination tool of the invention is effective in predicting the progression of the disease by analyzing the chronic steepening of the cornea by quantitating the parameters such as increase in curvature, aberrations of the cornea.

Brief description of drawings

[0016] FIG 1 illustrates the method of imaging the cornea using the combination tool.

[0017] FIG 2 illustrates the axial curvature of a patient cornea measures during different timelines.

5 [0018] FIG 3 illustrates the predicted curvature of cornea at the same time points.

[0019] FIG 4 illustrates the axial curvature of the cornea before and after treatment.

[0020] FIG 5 illustrates the consistency of axial curvature of the cornea as predicted by theoretical biomechanical simulation models.

10 Detailed description of the invention

[0001] In order to more clearly and concisely describe and point out the subject matter of the claimed invention, the following definitions are provided for specific terms, which are used in the following written description.

15 [0021] The term “*Corneal Tomography*” refers to a technique for displaying a representation of a cross section of a cornea using X-rays or ultrasound.

[0022] The term “*Artificial Intelligence*” refers to the development of computer systems that are capable of performing tasks normally requiring human intelligence such as visual perception, speech recognition, decision-making, and translation between languages.

20 [0023] The invention provides a system with a combination of artificial intelligence and corneal tomography to determine the regions of degradation in human cornea. The system is an automated tool, which is the combination of artificial intelligence and corneal tomography. The system comprises corneal tomography, finite element simulation module and artificial intelligence module.

[0024] The invention also discloses a method of implementing artificial intelligence and corneal tomography in combination to analyze the corneal tomography of the patient and use biomechanical simulation with finite element modeling to determine the region of degradation in human cornea.

5 [0025] Corneal tomography is a non-invasive medical imaging technique for mapping the surface curvature of the cornea, which helps in the assessment of the corneal shape. The technique of corneal tomography helps in analyzing the anterior and posterior corneal surfaces with elevation and curvature. Corneal tomography helps in reconstruction of 3D (Dimensional) or 2D surface of the
10 cornea. Corneal tomography provides elevation data of the corneal surface and layers in terms of point cloud. These surfaces are useful to create 3D volumes that are meshed with elements for biomechanical simulations.

[0026] The tool also comprises finite element simulation module. The 3D volumes, constructed using corneal tomography, are populated with
15 biomechanical properties of the cornea. The finite element simulations help in computing the deformations. Finite element simulation module also utilizes ray tracing for computing aberrations. Since the finite element model is generally built for normal corneas, modifications to the material model are implemented to model disease related changes. Further, finite element models include fiber
20 dependent hyperplastic material models.

[0027] The combination tool further comprises the artificial intelligence module, which uses longitudinal tomography maps of the same eye or a single cross-section tomography of the patient eye referenced to a normative database of corneal shape to determine the region of biomechanical degeneration.

25 [0028] The invention further includes the method of implementation of artificial intelligence and corneal tomography imaging to determine the regions of biomechanical degradation in cornea.

[0029] Cornea exhibits physical changes such as inflammatory, structural and biomechanical changes, which leads to degeneration or degradation of the corneal tissue leading to several corneal diseases such as keratoconus, pellucid marginal degeneration etc. The analysis of such physical changes helps in analyzing the severity of the disease and acts a marker for progression of the disease. The method disclosed in the invention helps in analyzing the corneal diseases.

[0030] The method of artificial intelligence and corneal tomography imaging includes analysis of changes in the structure of the cornea, constructing the 3D volumes using corneal tomography, meshing the 3D volumes with the elements for biomechanical simulations by using finite element modules, application of artificial intelligence to determine the region of biomechanical degeneration in cornea.

[0031] FIG 1 illustrates the method of imaging the cornea using the combination tool. The cornea is imaged using a combination tool comprising corneal tomography, finite element simulation module and artificial intelligence module. The method (100) of imaging starts with step (101) of subjecting the cornea to corneal tomography to reconstruct the 3D or 2D structure of the cornea. The 3D structures are constructed by obtaining the elevation data of the corneal surface and layers in terms of point cloud. These point clouds are easily reconstructed using commercial 3D computer aided drafting packages or other open source tools. At step (102), the reconstructed structures are used to create 3D volumes that are meshed with elements for biomechanical simulations. At step (103), the 3D volumes created are meshed with biomechanical properties of the cornea. The biomechanical properties determine the fiber dependent, anisotropic, hyperelastic behavior of the cornea. At step (104), the deformations of the cornea are computed by considering the intraocular pressure as the mechanical load on the posterior surface of the cornea and aberrations are computed by analyzing the change in curvature and surface wave front of the cornea. Ray tracing is also used for computing aberrations. At step (105), artificial intelligence is applied to longitudinal tomography maps to determine the region of biomechanical

degeneration. The artificial intelligence determines the region of biomechanical degeneration in the cornea as function of 3-D coordinates. The different metrics such as area, perimeter and volume of the degenerate zone within the cornea are calculated to analyze the biomechanical degradation.

- 5 [0032] The tool compares corneal tomography at different follow-up visits of the patient and use biomechanical simulation with finite element modeling to determine the region of degradation by analyzing the spatial area and location of the disease. Corneal tomography is either anterior surface curvatures and aberrations, and/or the same of sub-epithelium corneal layers such as the
- 10 Bowman's surface. In case where patients' follow-up visits are not available, the regions of the degeneration are determined from a general database of normal patient tomography.

[0033] Since the finite element model is generally built for normal corneas, modifications to the material model are implemented to model disease related

15 changes. Most of the degenerations lead to loss of collagen, the material model properties of the disease eyes are considered to be a fraction between 0 and 1 of the same for normal corneas. Thus, 0 indicates total loss of biomechanical strength and 1 indicates no loss.

[0034] In order to determine the regions of biomechanical degeneration, the

20 artificial intelligence module uses longitudinal tomography maps of the same eye or a single cross-section tomography of the eye referenced to a normative database of corneal shape. In case of use of longitudinal tomography maps of the same eye, artificial intelligence compares the corneal curvature and aberrations between the normal state before the onset of progression and the state where the

25 eye has progressed to the disease. Since the assumption that disease is caused by biomechanical weakness, the artificial intelligence modulates the material properties in the finite element model to derive the diseased shape of the cornea. In case of use of single cross-section tomography of the eye referenced to a normative database of corneal shape, the artificial intelligence compares the

corneal curvature and aberrations between the normal state of an age matched eye with curvature and thickness representative of the population and the state where the eye has progressed to the disease. Further, in both the cases, the modulations are achieved by implementing optimization routines such as Nelder-Mead search,
5 Levenberg-Marquedt gradient method. The artificial intelligence determines spatial map of region of biomechanical degeneration in the diseased state of the cornea. The optimization algorithms minimize the difference between the predicted curvature from finite element simulations and the measured curvature from cornea in the progressed state of the disease. This is an iterative process and
10 continues till the difference becomes smaller than a predefined tolerance.

[0035] FIG 2 illustrates the axial curvature of a patient cornea measures during different timelines. The axial curvature of the cornea is measured using corneal tomography during different time periods. The result shows the steeping of the cornea with time. FIGs 2a, 2b and 2c illustrates the axial curvature of cornea in
15 August 2015, July 2016 and December 2016 respectively indicating the steeping of the cornea evidencing the progression of the disease with time.

[0036] FIG 3 illustrates the predicted curvature of the cornea at the same time points using the artificial intelligence.

[0037] FIG 3a and FIG 3b indicate the degeneration of cornea.

20 [0038] FIG 3c and FIG 3d indicate the corresponding regions of cornea with biomechanical degeneration in July 2016 and December 2016, respectively. The magnitude of the material properties in the degenerate zone is lower than the magnitude of the same in the non-degenerate zone. Further, the size of the degenerate zone increased from July 2016 to December 2016 due to progression
25 of the disease. The same cornea is treated with corneal crosslinking by treating only the degenerate zone as predicted by the artificial intelligence.

[0039] FIG 4 illustrates the axial curvature of the cornea before and after treatment.

[0040] FIG 4a illustrates the axial curvature after treatment with a regular astigmatism pattern.

[0041] FIG 4b illustrates the axial curvature before treatment with keratoconic pattern. The treatment results in change of the axial curvature from the
5 keratoconic to astigmatism pattern and the difference in the axial curvature post treatment is illustrated.

[0042] FIG 4c highlights the region of profound flattening indicating a decrease of -2D surrounded by an annular zone of sharp steepening in excess of +4D.

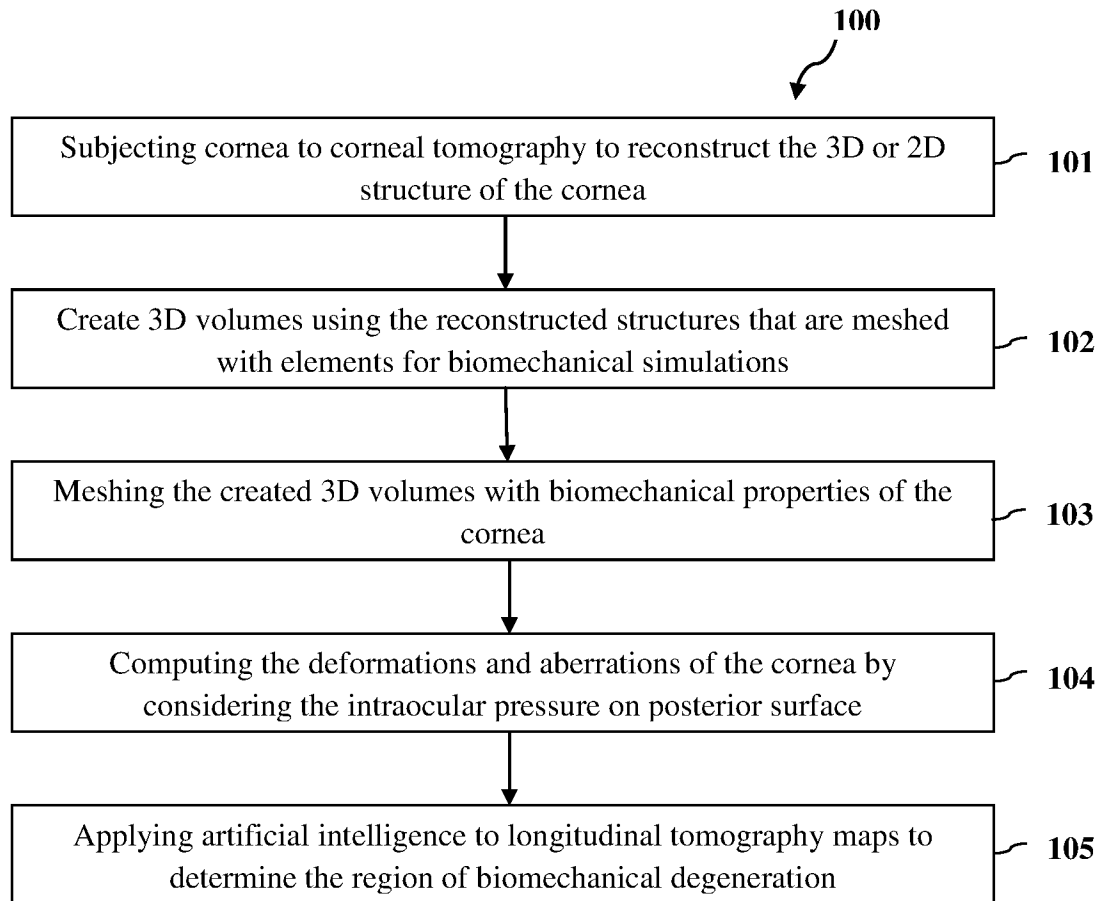
[0043] FIG 5 illustrates the consistency of axial curvature of the cornea as
10 predicted by theoretical biomechanical simulation models. The observations from FIG 4 are in consistent with the theoretical simulations of outcomes of corneal crosslinking in corneas of patients by treating only the degenerate zone as illustrated in FIG 5.

[0044] The system and method of combination of artificial intelligence and
15 tomography imaging is useful in determining the biomechanical degradation or degeneration in human cornea. The combination tool of the invention is effective in predicting the progression of the disease by analyzing the chronic steepening of the cornea by quantitating the parameters such as increase in curvature, aberrations of the cornea. The tool compares corneal tomography at different time
20 periods and use biomechanical simulation with finite element modeling to determine the region of degradation by analyzing the spatial area and location of the disease.

Claims:**We claim,**

- 5 1. A system to determine one or more regions of biomechanical degradation of human cornea, the system comprises:
- a. a corneal tomography to map the surface curvature of cornea;
 - b. a finite element simulation module to compute one or more
10 deformations in cornea; and
 - c. an artificial intelligence module to determine one or more regions of biomechanical degeneration in cornea.
- 15 2. The system as claimed in claim 1, wherein the corneal tomography analyses the anterior and posterior corneal surfaces with elevation and curvature to reconstruct 3D (Dimensional) or 2D structure of the cornea.
- 20 3. The system as claimed in claim 1, wherein the finite element simulation module utilizes ray tracing for one or more computing aberrations after populating with biomechanical properties of the cornea.
- 25 4. The system as claimed in claim 1, wherein the artificial intelligence module determines biomechanical degeneration by using longitudinal tomography maps of the same eye or a single cross-section tomography of the eye referenced to a normative database of corneal shape.
- 30 5. A method to determine one or more regions of biomechanical degradation of human cornea, the method **(100)** comprises the steps of:
- a. subjecting cornea to corneal tomography for reconstructing
the 3D or 2D structure of cornea **(101)**;
 - b. creating one or more 3D volumes using the reconstructed
structures **(102)**;

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- 30
- c. meshing the created 3D volumes with biomechanical properties of the cornea (**103**);
 - d. computing one or more deformations of the cornea by considering the intraocular pressure as the mechanical load on the posterior surface of the cornea and one or more aberrations by analysing the change in curvature and surface wave front of the cornea (**104**); and
 - e. applying artificial intelligence to longitudinal tomography maps to determine the region of biomechanical degeneration (**105**).
6. The method as claimed in claim 5, wherein the 3D structures of cornea are constructed by obtaining the elevation data of the corneal surface and layers in terms of point cloud.
7. The method as claimed in claim 5, wherein the biomechanical properties determine the fiber dependent, anisotropic, hyperelastic behavior of the cornea.
8. The method as claimed in claim 5, wherein the artificial intelligence determines the region of biomechanical degeneration as function of 3-D coordinates by analysing metrics such as area, perimeter and volume of the degenerate zone within the cornea.
9. The method as claimed in claim 5, wherein the method predicts the progression of the disease by analyzing the chronic steepening of cornea by quantitating the parameters such as increase in curvature and aberrations of cornea.

**FIGURE 1**

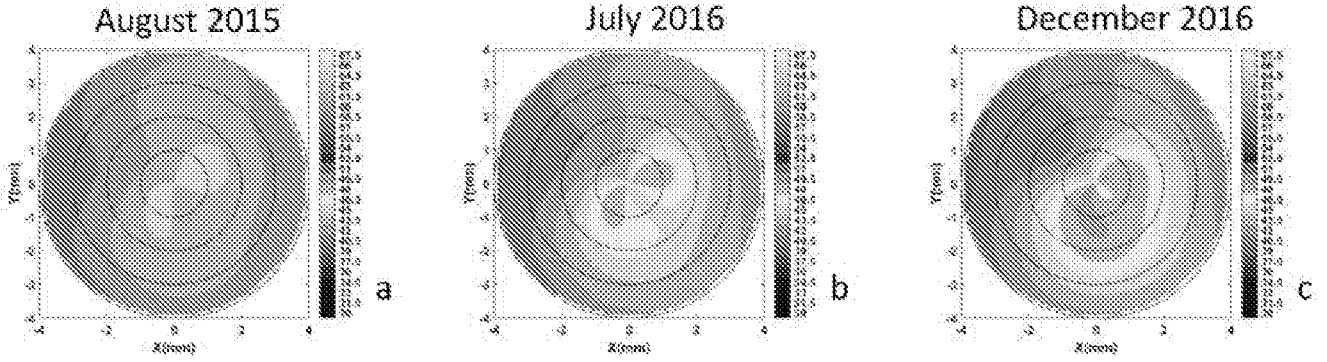


FIGURE 2

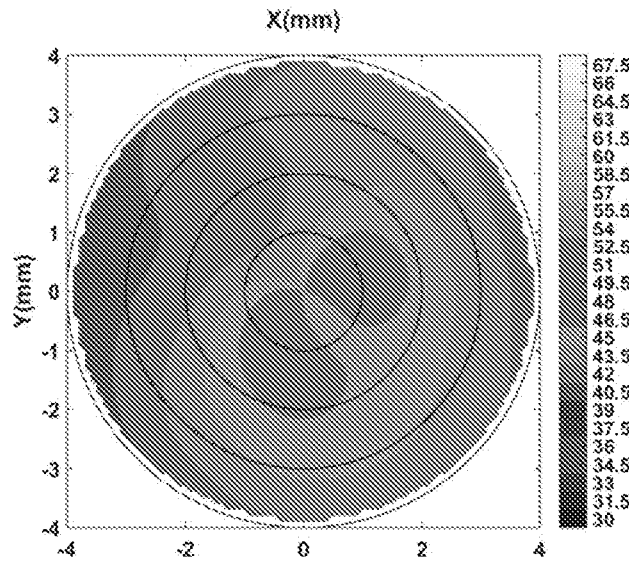


FIGURE 3a

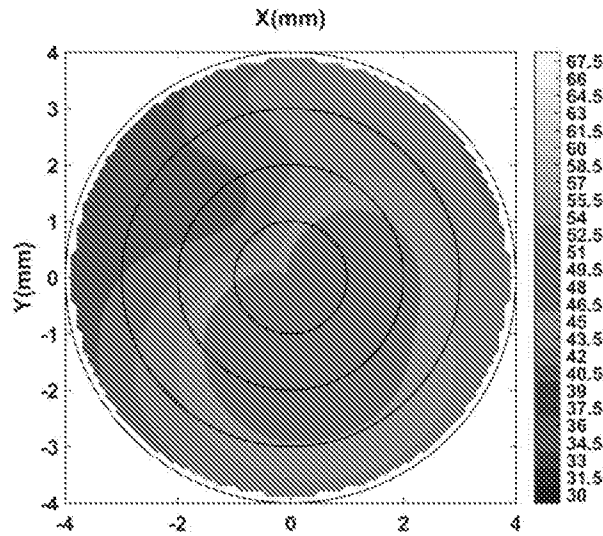


FIGURE 3b

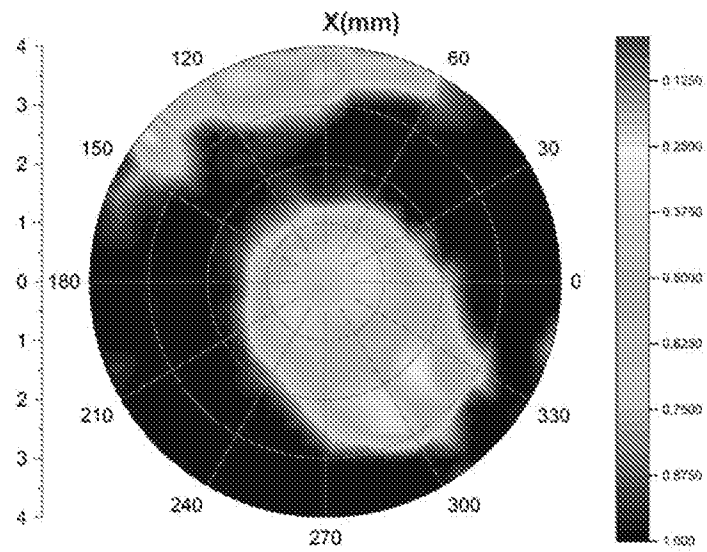


FIGURE 3c

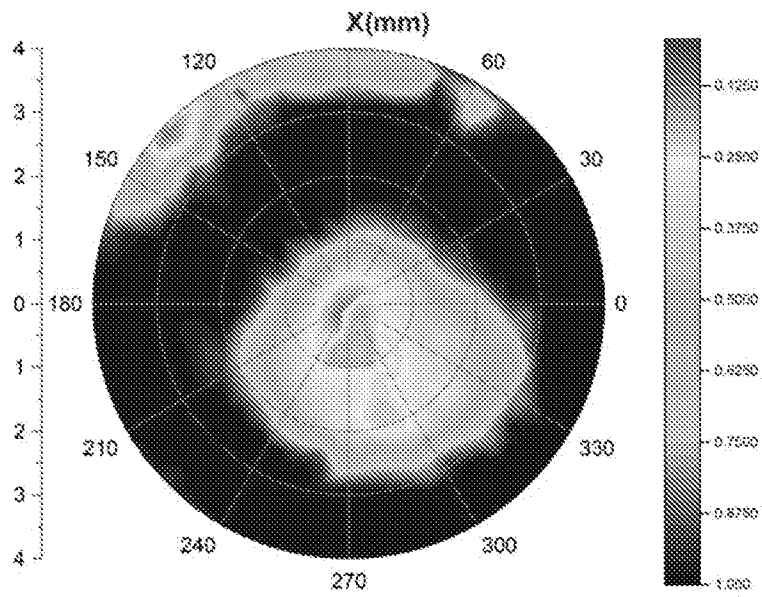


FIGURE 3d

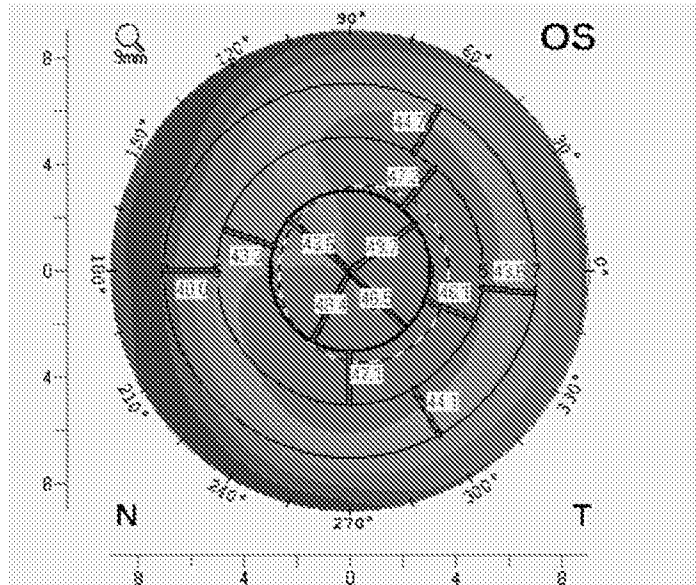


FIGURE 4a

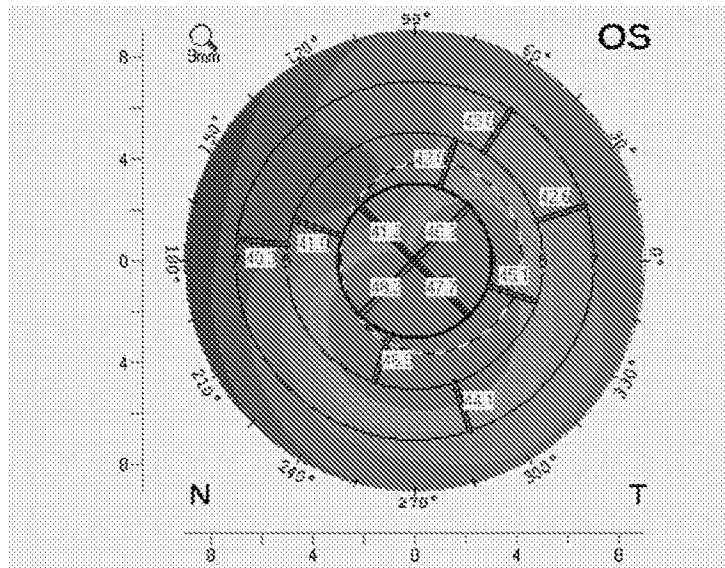


FIGURE 4b

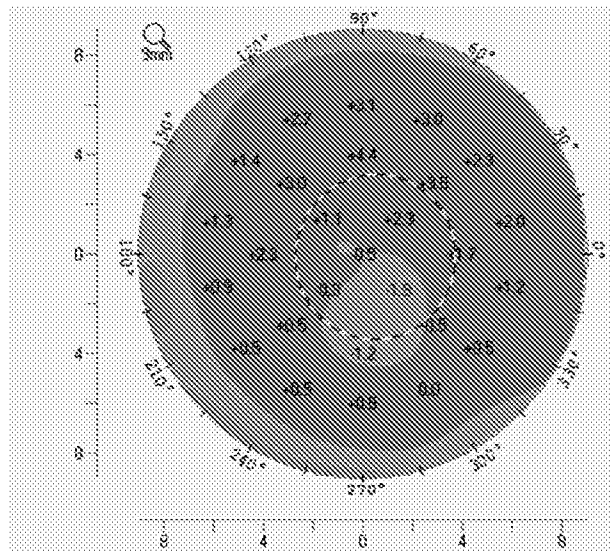


FIGURE 4c

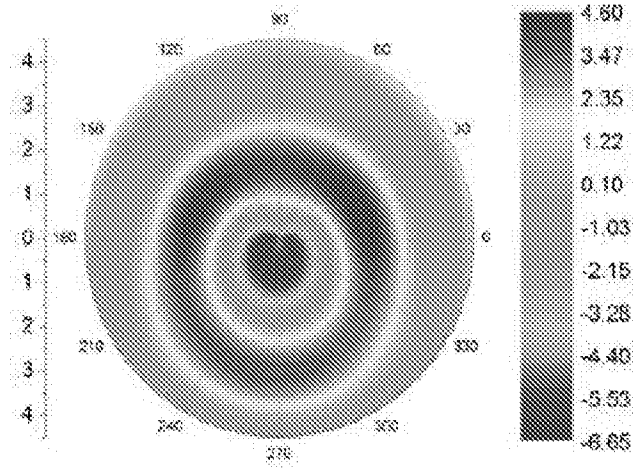


FIGURE 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2018/051716

A. CLASSIFICATION OF SUBJECT MATTER
A61B8/13,G16H30/00 Version=2018.01

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61B, G16H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Databases: TotalPatent One, IPO Internal Database

Keywords: cornea surface, finite elements, 3D, curvature, keratogram

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US20160364543 A1 (CLEVELAND CLINIC FOUND US) 15 December 2016 (15-12-2016) Abstract, Claims 1, 16 ; Paragraphs [0018-0027], [0034], [0040], [0042], [0044, [0049]; figures 2-4	1-4
Y	EP2704095 (A1) (CONSEJO SUPERIOR INVESTIGACION ES) 05 March 2014 (05-03-2014) Paragraphs [0010], [0018], [0021], [0034]; figures 3A, 3B	1-4

Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent but published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 18-05-2018	Date of mailing of the international search report 18-05-2018
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Name and mailing address of the ISA/ Indian Patent Office Plot No.32, Sector 14, Dwarka, New Delhi-110075 Facsimile No.	Authorized officer Devendra Kumar Deshmukh Telephone No. +91-1125300200
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2018/051716

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

- 1. Claims Nos.: 5-9
because they relate to subject matter not required to be searched by this Authority, namely:
The subject matter of claim 5-9 relates to a method for treatment of the human and diagnostic methods, which does not require an international search by the International Searching Authority in accordance with PCT Article 17(2)(a)(i) and [Rule 39.1(iv)].
- 2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
- 3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

- 1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
- 2. As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
- 3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
- 4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

- Remark on Protest**
- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
 - The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
 - No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

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EP 2704095 A	05-03-2014	US 9593933 B2	14-03-2017