

# **AN INTELLIGENT SYSTEM FOR DIAGNOSIS OF VARIOUS CONDITIONS OF GLAUCOMA DISEASE IN THE FIELD OF OPHTHALMOLOGY**

A Thesis submitted to Gujarat Technological University

for the Award of

**Doctor of Philosophy**

in

**Computer Science**

by

**Patel Falguniben Bhikhubhai**

Enrollment No.:129990931001

under supervision of

**Dr. Priyanka Sharma**



**GUJARAT TECHNOLOGICAL UNIVERSITY  
AHMEDABAD  
June – 2019**

**© Patel Falguniben Bhikhubhai**

## **DECLARATION**

I declare that the thesis entitled "**An Intelligent System for Diagnosis of Various Conditions of Glaucoma Disease in the Field of Ophthalmology**" submitted by me for the degree of Doctor of Philosophy is the record of research work carried out by me during the period from **December 2012 to December 2018** under the supervision of **Dr. Priyanka Sharma** and this has not formed the basis for the award of any degree, diploma, associateship, fellowship, titles in this or any other University or other institution of higher learning.

I further declare that the material obtained from other sources has been duly acknowledged in the thesis. I shall be solely responsible for any plagiarism or other irregularities, if noticed in the thesis.

Signature of the Research Scholar: .....

Date: 20-6-19

Name of Research Scholar:**Patel Falguniben Bhikhubhai**

Place:**Vadodara**

## **CERTIFICATE**

I certify that the work incorporated in the thesis "**An Intelligent System for Diagnosis of Various Conditions of Glaucoma Disease in the Field of Ophthalmology**" submitted by Smt. **Patel Falguniben Bhikhubhai** was carried out by the candidate under my supervision/guidance. To the best of my knowledge: (i) the candidate has not submitted the same research work to any other institution for any degree/diploma, Associateship, Fellowship or other similar titles (ii) the thesis submitted is a record of original research work done by the Research Scholar during the period of study under my supervision, and (iii) the thesis represents independent research work on the part of the Research Scholar.

Signature of Supervisor:.....

Date: 20-6-19

Name of Supervisor: **Dr. Priyanka Sharma**

Place: **Ahmedabad**

# **Course-work Completion Certificate**

This is to certify that Ms. **Patel Falguniben Bhikhubhai** enrollment no. **129990931001** is a PhD scholar enrolled for PhD program in the branch **Computer Science** of Gujarat Technological University, Ahmedabad.

**(Please tick the relevant option(s))**

- He/She has been exempted from the course-work (successfully completed during M.Phil Course)
- He/She has been exempted from Research Methodology Course only (successfully completed during M.Phil Course)

He/She has successfully completed the PhD course work for the partial requirement for the award of PhD Degree. His/ Her performance in the course work is as follows-

Grade Obtained in Research Methodology (PH001)	Grade Obtained in Self Study Course (Core Subject) (PH002)
<b>BB</b>	<b>BB</b>

Supervisor's Sign

**(Dr. Priyanka Sharma)**

# Originality Report Certificate

It is certified that PhD Thesis titled thesis "An Intelligent System for Diagnosis of Various Conditions of Glaucoma Disease in the Field of Ophthalmology" by Patel Falguniben Bhikhubhai has been examined by us. We undertake the following:

- a. Thesis has significant new work / knowledge as compared already published or are under consideration to be published elsewhere. No sentence, equation, diagram, table, paragraph or section has been copied verbatim from previous work unless it is placed under quotation marks and duly referenced.
- b. The work presented is original and own work of the author (i.e. there is no plagiarism). No ideas, processes, results or words of others have been presented as Author own work.
- c. There is no fabrication of data or results which have been compiled/analysed.
- d. There is no falsification by manipulating research materials, equipment or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- e. The thesis has been checked using EduBirdie and Turnitin (copy of originality report attached) and found within limits as per GTU Plagiarism Policy and instructions issued from time to time (i.e. permitted similarity index<=25%).

Signature of the Research Scholar: ..... Date:20-6-19  
Name of Research Scholar:**Patel Falguniben Bhikhubhai**  
Place:**Vadodara**

Signature of Supervisor: ..... Date: 20-6-19  
Name of Supervisor: **Dr. Priyanka Sharma**  
Place: **Ahmedabad**

## AN INTELLIGENT SYSTEM FOR DIAGNOSIS OF VARIOUS CONDITIONS OF GLA...

an intelligent system for diagnosis of various conditions of glaucoma disease in the field of ophthalmology a thesis submitted to gujarat technological university for the award of [bookmark: \_toc523490664][bookmark: \_toc531330542]doctor of philosophy in [bookmark: \_toc523490665][bookmark: \_toc531330543]computer science by [bookmark: \_toc523490666][bookmark: \_toc531330544]patel falguniben bhikhubhai enrollment no.:129990931001 under supervision of dr. priyanka sharma [image: gujarat technological university ahmedabad september 2018 patel falguniben]

The length of the text: 19242 (No spaces: 16323)

[Check another text](#)

129990931001-AN INTELLIGENT SYSTEM FOR DIAGNOSIS OF VARIOUS  
CONDITIONS OF GLAUCOMA DISEASE IN THE FIELD OF  
OPHTHALMOLOGY.docx

**88.1%** The uniqueness  
of the text

[I NEED PLAGIARISM-FREE CONTENT](#)

### Text matches

Sources:

Similarity index: View in the text:

<https://blog.statsbot.co/ensemble-learning-d1dcd548e936?gi=18cdab808667>

6.4

[Show](#)

<https://statsbot.co/blog/ensemble-learning/>

7.0

[Show](#)

<https://scialert.net/fulltext/?doi=jai.2008.78.85>

5.5

[Show](#)

[Less matches](#)

---

ORIGINALITY REPORT

---

**18%**      **8%**      **14%**      **2%**

SIMILARITY INDEX      INTERNET SOURCES      PUBLICATIONS      STUDENT PAPERS

---

PRIMARY SOURCES

---

<b>1</b>	<b>dbdmg.polito.it</b> Internet Source	<b>3%</b>
<b>2</b>	<b>www.i-scholar.in</b> Internet Source	<b>1%</b>

---

## **PhD THESIS Non-Exclusive License to GUJARAT TECHNOLOGICAL UNIVERSITY**

In consideration of being a PhD Research Scholar at GTU and in the interests of the facilitation of research at GTU and elsewhere, **Patel Falguniben Bhikhubhai** having (Enrollment No.) **129990931001** hereby grant a non-exclusive, royalty free and perpetual license to GTU on the following terms:

a) GTU is permitted to archive, reproduce and distribute my thesis, in whole or in part, and/or my abstract, in whole or in part ( referred to collectively as the “Work”) anywhere in the world, for non-commercial purposes, in all forms of media;

b) GTU is permitted to authorize, sub-lease, sub-contract or procure any of the acts mentioned in paragraph(a);

c) GTU is authorized to submit the Work at any National / International Library, under the authority of their “Thesis Non-Exclusive License”;

d) The Universal Copyright Notice (©) shall appear on all copies made under the authority of this license;

e) I undertake to submit my thesis, through my University, to any Library and Archives.

Any abstract submitted with the thesis will be considered to form part of the thesis.

f) I represent that my thesis is my original work, does not infringe any rights of others, including privacy rights, and that I have the right to make the grant conferred by this non-exclusive license.

g) If third party copyrighted material was included in my thesis for which, under the terms of the Copyright Act, written permission from the copyright owners is required, I have obtained such permission from the copyright owners to do the acts mentioned in paragraph (a) above for the full term of copyright protection.

h) I retain copyright ownership and moral rights in my thesis, and may deal with the copyright in my thesis, in any way consistent with rights granted by me to my University in this non-exclusive license.

i) I further promise to inform any person to whom I may hereafter assign

or license my copyright in my thesis of the rights granted by me to my University in this non- exclusive license.

j) I am aware of and agree to accept the conditions and regulations of PhD including all policy matters related to authorship and plagiarism.

Signature of the ResearchScholar:\_\_\_\_\_

Name of Research Scholar:**Patel Falguniben Bhikhubhai**

Date: 20-6-19

Place:**Vadodara**

Signature of Supervisor:\_\_\_\_\_

Name of Supervisor:**Dr. Priyanka Sharma**

Date: 20-6-19

Place: **Ahmedabad**

Seal:

# Thesis Approval Form

The viva-voce of the PhD Thesis submitted by Smt. Patel Falguniben Bhikhubhai (Enrollment No. 129990931001) entitled thesis "An Intelligent System for Diagnosis of Various Conditions of Glaucoma Disease in the Field of Ophthalmology" was conducted on Thursday, 20<sup>th</sup> June, 2019 at Gujarat Technological University.

**(Please tick any one of the following option)**

- The performance of the candidate was satisfactory. We recommend that he/she be awarded the PhD degree.
- Any further modifications in research work recommended by the panel after 3 months from the date of first viva-voce upon request of the Supervisor or request of Independent Research Scholar after which viva-voce can be re-conducted by the same panel again.

(briefly specify the modifications suggested by the panel)

- The performance of the candidate was unsatisfactory. We recommend that he/she should not be awarded the PhD degree.

(The panel must give justifications for rejecting the research work)

---

Name and Signature of Supervisor with Seal

1) (External Examiner 1) Name and Signature

---

2) (External Examiner 2) Name and Signature

3) (External Examiner 3) Name and Signature

## **ACKNOWLEDGMENT**

The journey of carrying out my research work has been an enlightening process for me. It has not only been a breathtaking academic exercise but has also added immense value to growth of my personality by helping me to develop newer perspectives.

With this, it gives me great pleasure to express my feelings of gratitude towards my guide **Dr. Priyanka Sharma**, who helped me in overcoming all the impediments and timely completion of this work. She has always been an utmost source of wisdom and a lighthouse that guided my ship-like research through the turbulent waterfronts of discoveries till its anchorage ashore. I also wish to hereby thank **Dr. Hemant Patel**, my brother, an eminent ophthalmologist and a person par excellence for endowing me with conscientious insights into the field of medical ophthalmology.

During this journey, the role of **Dr. D. B. Choksi** and **Dr. S. K. Vij** as DPC members and reviewers has been extremely commendable. I shall always carry high regards for their well-informed guidance and critical evaluations in correcting my work, time and again.

I wish to render a very special gratitude to my husband **Dr. Amol Ranadive** and our daughter **Nishka** who have been a source of strength and encouragement throughout the research.

I would also like to specially thank my colleague **Dr. Ashutosh Sandhe** and my other research fellow colleagues for extending a colossal support and encouragement to me throughout this journey.

# **ABSTRACT**

Disease diagnosis system in medicine is a peculiar form of clinical data processing coming from a range of clinical as well as atomized systems. However, it is more complicated in medicine than in other areas, because of medical terms, semantic relations and amount of data. Reaching a full proof diagnosis in Ophthalmology, is never an easy job for a clinician. There are number of examinations performed using various diagnostic instruments, in order to diagnose the problem from the symptoms described by the patient. Result of each examination needed to be inferred separately, because of the variation in representations and their significances. For accurate diagnosis, the results of number of examinations are to be inferred in a contextual conjunction. This is again a complicated task forming the diagnosis.

Glaucoma, an eye diseases is prevailing in aging population. It causes an irreversible loss of vision. There is a distinct need of Computer aided solutions for diagnosis purposes. (Madhulika J., 2015)<sup>184</sup>The rising concern for the treatment of this disease is increasing looking at the propagation of glaucoma cases in past few recent years. It is majorly widespread in urban aging population. According to an estimation, 79 million individuals all over the world would be affected by glaucoma by year 2020. (R. Bock et. al., 2010)<sup>185</sup>(G. Joshi et. al., 2011)<sup>186</sup> In a decade, the estimation shows a 33% increase in the number of people affected by glaucoma. (R. Saxena et. al., 2013)<sup>187</sup> Thus, screening for glaucoma is crucial, owing to the nature, for the early detection and enabling effective treatment in early stages to prevent permanent blindness. (Madhulika J., 2015)<sup>184</sup>

According to Glaucoma society of India, glaucoma is the second leading cause of blindness in India. The major challenge posed by Indian population is the number of people getting affected by glaucoma. At present, 12 million people in India are affected by glaucoma which is expected to increase to 16 million by 2020 (R. Saxena et. al., 2013)<sup>187</sup>. The number of patients per ophthalmologist is around 2 to 3 lakhs in India. Thus apart from cost, lack of manpower in terms of skilled technicians poses major challenge in such scenarios.

Diagnosis of glaucoma is dependent on various findings such as IOP (if IOP > 21 mm Hg (High Eye Pressure and Glaucoma [online])<sup>1</sup>, it is considered as a suspicious case for glaucoma), optical nerve cupping and visual field loss. Detection and diagnosis of Glaucoma is performed through various tests such as Tonometry, Ophthalmoscopy, Perimetry, OCT, Gonioscopy and Pachymetry. (Diagnosing Glaucoma)<sup>189</sup>

Artificial neural networks are finding many uses in the medical diagnosis application. Artificial neural networks provide a powerful tool to analyze and model complex clinical data for a wide range of medical applications. Most applications of artificial neural networks to medicine are classification problems; that is, the task is on the basis of the measured features to assign the patient to one of a small set of classes.(R. Dybowski and V. Gant, 2007)<sup>2</sup>. An artificial neural network a part of artificial intelligence, with its ability to approximate any nonlinear transformation is a good tool for approximation and classification problems. (S. Kajan,

---

<sup>1</sup>"High Eye Pressure and Glaucoma", accessed on, <http://www.glaucoma.org/gleams/high-eye-pressure-andglaucoma.php6>

<sup>2</sup>R. Dybowski and V. Gant, Clinical Applications of Artificial Neural Networks, Cambridge University Press, 2007.

2009)<sup>3</sup>(M. Negnevitsky, 2005)<sup>4</sup> (B. D. Ripley, 1996)<sup>5</sup>Multilayer perceptron (MLP), a feed-forward, back-propagation network, is the most frequently used ANN technique in glaucoma research. (Rumelhart DE et. al., 1986)<sup>6</sup>

The primary focus of this research is to develop an intelligent diagnostic system for Glaucoma- an eye related disease, from the data obtained through clinician by various examination devices or equipment used in ophthalmology. The data is used as training set to multi-classifier, developed using hybridization of various techniques of Artificial Intelligence. The classification is done by a hybrid approach using Artificial Neural Network, Naïve Bayes Algorithms and Decision Tree Algorithms. A design/development of a new technique or algorithm is required for such diagnosis and it is tested for its efficacy. Using the algorithms and techniques of Neural Network, Naïve Bayes Algorithm and Decision Tree based classifiers, the proposed hybrid technique is anticipated to intelligently analyze and perform diagnosis for patient's visionary predicaments, thus lessening the intervention of medical practitioners in terms of decision making.

---

<sup>3</sup>S. Kajan. GUI for classification using multilayer perceptron network, Technical Computing Prague, 2009.

<sup>4</sup>M. Negnevitsky, Artificial Intelligence. Pearson Education Limited, 2005.

<sup>5</sup>B. D. Ripley. Pattern recognition and neural networks. Cambridge university press, 1996. 403 s. ISBN 0-521-46086-7.

<sup>6</sup>Rumelhart DE, Hinton G, Williams R, Learning representations of back-propagation errors. Nature. 1986; 323:533–536.

# Table of Contents

	Page
<b>1. Introduction</b>	<b>1</b>
<b>1.1. Intelligent Systems</b>	<b>1</b>
<b>1.2. An Ophthalmic Condition-Glaucoma</b>	<b>12</b>
<b>1.3. Diagnosis of Glaucoma</b>	<b>35</b>
<b>1.4. Organization of the Thesis</b>	<b>41</b>
<b>2. Literature Review</b>	<b>43</b>
<b>2.1. Intelligent System in Disease Diagnosis</b>	<b>43</b>
<b>2.2. Artificial Intelligent Techniques in Glaucoma Diagnosis</b>	<b>64</b>
<b>2.3. Research Gap</b>	<b>77</b>
<b>3. Research Methodology</b>	<b>82</b>
<b>3.1. Objectives</b>	<b>82</b>
<b>3.2. Obtaining and pre-processing data</b>	<b>83</b>
<b>3.3. Artificial Neural Network</b>	<b>85</b>
<b>3.4. Decision Tree</b>	<b>93</b>
<b>3.5. Naïve Bayes Algorithm</b>	<b>96</b>
<b>3.6. Ensemble Method for classification</b>	<b>99</b>
<b>3.7. Ensemble FGLAUC-99</b>	<b>102</b>
<b>4. Result and Discussions</b>	<b>110</b>
<b>4.1. Experimental setup</b>	<b>110</b>
<b>4.2. Result and Discussion</b>	<b>113</b>
<b>5. Conclusions, Major Contributions and Scope of Future Work</b>	<b>141</b>
<b>5.1. Conclusion</b>	<b>141</b>
<b>5.2. Major Contribution-aligned to objectives</b>	<b>142</b>
<b>5.3. Scope of Future Work</b>	<b>144</b>
<b>6. List of References</b>	<b>145</b>
<b>7. List of Publications</b>	<b>166</b>

## List of Figures

Figure 4. 17 Ensemble of Naïve Bayes, SMO and Random Forest.....	132
Figure 4. 18 Ensemble of Naïve Bayes, MLP and RF .....	133
Figure 4. 19 Ensemble of MLP and RF.....	133
Figure 4. 20 Ensemble of MLP, Naïve Bayes and J48 .....	134
Figure 4. 21 Diagnosis of Condition of Glaucoma .....	135
Figure 4. 22 Classification plot by ensemble method with MLP, J48 and Naïve Bayes.....	137

## List of Tables

Table 1. 1 Global Estimates by WHO of Visual Impairments, 2010 .....	21
Table 1. 2 Global Estimates of Visual Impairment in people by Age, 2010 .....	22
Table 3. 1 Glaucoma Diagnosis with 2 classes.....	81
Table 3. 2 Glaucoma Diagnosis with 4 classes.....	81
Table 3. 3 Glaucoma Diagnosis with 7 classes.....	82
Table 4. 1 Demographic profile of patients' age groups.....	115
Table 4. 2 Demographic profile of patients gender gropus .....	116
Table 4. 3 Demographic profile of patients' age group wise gender groups .....	116
Table 4. 4 Area Under the Curve for 2-classes.....	118
Table 4. 5 Area Under the Curve for 4-classes.....	119
Table 4. 6 Area Under the Curve for 7-classes.....	122
Table 4. 7 Comparison of different group of classifiers .....	130
Table 4. 8 Comparison of different ensembles .....	135
Table 4. 9 AUC for ensemble of MLP and RF .....	136
Table 4. 10 AUC for ensemble of MLP, Naïve Bayes and J48.....	136
Table 4. 11 Comparison of performance of algorithms for glaucoma diagnosis .....	138

# **CHAPTER – 1Introduction**

## **1.1 Intelligent Systems**

Intelligent systems can be employed as a supportive tool to the medical practitioner, in medical diagnosis. Specially, in India, a country with vast rural areas and absolute shortage of doctors. Intelligent systems can also be used extensively in the field of medical diagnosis to diminish cost and diagnostic issues such as dynamic perturbations, shortage of physicians, etc.

An intelligent system can be understood as an information system that offers answers to queries concerned with the information accumulated in the Knowledge Base (KB), which is a repository of human knowledge.(Ghosh J. and Mukhopadhyay S. 2002)<sup>7</sup>

Modelling an intelligent system in the medical sphere increasingly recognized the significance of the elucidation potential of the system. In one of the surveys with the potential users of a medical diagnostic system, advocated that the explanation capability is the most imperative capability to recognize the clinical decision tool (Teach, R.L. and Shortliffe, E.H. 1981)<sup>8</sup> (Wallis, J.W. and Shortliffe, E.H., 1982)<sup>9</sup>

In the preceding few years, the field of Artificial Intelligence (AI) has witnessed an unprecedented research attention towards assimilating

---

<sup>7</sup> J. Ghosh, S. Mukhopadhyay, 2011, “Role of Certainty Factor in Rough-Fuzzy Rule Generation”, International Journal of Computer Science, Engineering and Applications (IJCSEA) Vol.1, No.6, pp. 49-61.

<sup>8</sup> Teach, R.L. and Shortliffe, E.H. 1981, “An analysis of physician attitudes regarding computer-based clinical consultation systems”, Comput. Blomed. Res. 14, pp. 542-558.

<sup>9</sup> Wallis, J.W. and Shortliffe, E.H., 1982, “Explanatory power for medical expert systems: studies in the representation or causal relationships for clinical consultations”, Meth. Info. Med. 21, pp.127-136.

various computing paradigms viz. Genetic Algorithms (GAs), Fuzzy Systems and ANNs to breed more efficient hybrid systems. The intent is to make available, agile information processing systems that can make the most of the tolerance for imprecision, uncertainty, approximate reasoning and partial information to attain tractability, robustness, low solution cost and close resemblance with human like decision making (Pal et al 2000)<sup>10</sup>. This research emphasizes on a hybrid algorithm for an efficient computer aided medical diagnosis. This chapter establishes various steps in computer aided medical diagnosis using soft computing techniques. Moreover alongside, the motivation for carrying out this research, various phases of research and contributions are also discussed hereafter.

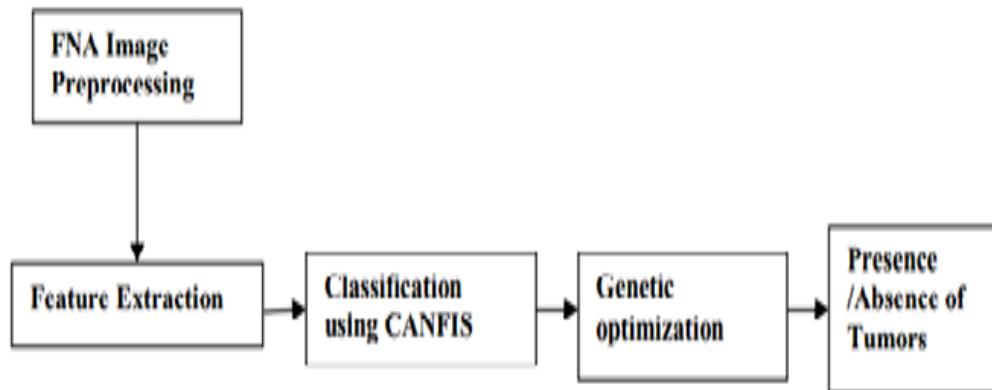
Computer aided medical diagnosis combines the areas of computer science, image processing, pattern recognition and AI techniques and all their performance and consistency depends on a number of factors together with segmentation, feature selection, reference database size, computational efficiency etc.,(Bin Zheng 2009)<sup>11</sup>. Computer-Aided Diagnosis (CAD) is a practice in medicine that supports medical practitioners in interpretation of medical condition related images. Imaging techniques in mammography, Computerized Tomography (CT), X-ray, Magnetic Resonance Imaging (MRI), and UltraSound (US) diagnostics acquiesce a great deal of information, which a radiologist may have to analyse and assess meticulously in a short time period. As depicted in Figure 1.1, the Breast cancer diagnosis has been dealt with using machine learning algorithms, such as linear programming, decision tree (Breiman

---

<sup>10</sup>Pal S.K., Dillon T.S. and Yeung D.S. (2000), "Soft Computing in Case Based Reasoning", Springer-Verlag, U.K.

<sup>11</sup> Park S.C., Pu J. and Zheng B. (2009), "Improving performance of computer-aided detection scheme by combining results from two machine learning classifiers", Academic Radiology, No. 16, No.3, pp 266-274.

1984)<sup>12</sup> (Mangasarian et al 1995)<sup>13</sup> and neural networks (Xin Yao and Yong Liu 1996)<sup>14</sup>(Abbass2002)<sup>15</sup>.



**Figure 1. 1 Block Diagram of Computer Aided Diagnosis<sup>14</sup>**

AI is actually the intelligence of machines and also the field of computer science which intends to build such intelligence. Computational Intelligence (CI) is viewed as an all-inclusive framework to devise and scrutinize intelligent systems with an emphasis on all ground rules of autonomy, learning, and reasoning (Duch 2007)<sup>16</sup>. The thought is to reflect on such robust computing systems that are capable to learn and deal with new situational conditions using reasoning, generalization, association, abstraction, and discovery capabilities (Eberhart et al 1996)<sup>17</sup>. The paradigm of CI is revealed in Figure 1.2.

---

<sup>12</sup>Breiman L. (1984), “Classification and Regression Trees”, Wadsworth International group, Belmont, California.

<sup>13</sup>Mangasarian O.L., Street W.N. and Wolberg W.H. (1995), “Breast cancer diagnosis and prognosis via linear programming”, Operations Research , Vol. 43, No.4, pp. 570-577.

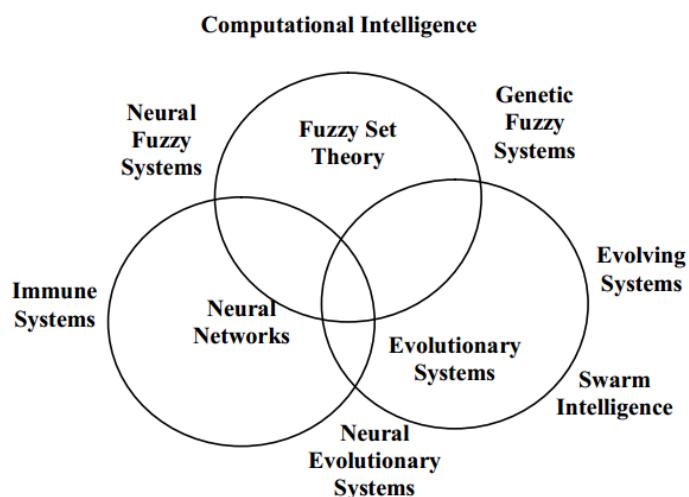
<sup>14</sup>Xin Yao and Yong Liu (1996), “Neural networks for breast cancer diagnosis”, Proceedings of the 1999 Congress on Evolutionary Computation, IEEE Press, Vol. 3, pp. 1760-1767.

<sup>15</sup>Abbass H.A. (2002), “An evolutionary artificial neural networks approach for Breast Cancer Diagnosis”, Artificial Intelligence in Medicine, Vol.25, No.3, pp.265-281.

<sup>16</sup>Duch W. (2007), “What is computational intelligence and Where it is going”, W.Duch and J.Mandziuk (Eds.), Challenges for Computational Intelligence, pp. 1 -13, Springer Verlag, Heidelberg.

<sup>17</sup>Eberhart R.C., Simpson P.K. and Dobbins R.W. (1996), “Computational Intelligence PC Tools”, Academic Press, Boston, MA

Emerging as an independent field by itself, CI in the present times consists of evolving systems (Angelov 2002)<sup>18</sup>, swarm intelligence (Kennedy and Eberhart 2001)<sup>19</sup> (Dorigo and Stutzle 2004)<sup>20</sup>, immune systems (Castro and Timmis 2002)<sup>21</sup>, and other varieties of naturally oriented (viz., biologically inclined) computational systems. A key concern in CI is behavioural adaptation as a strategy to manage varying environments and deal with unanticipated situations.



**Figure 1. 2The Paradigm of CI<sup>18</sup>**

CI demonstrates remarkable associations with machine intelligence (Mitchell et al 1997)<sup>22</sup>, statistical learning (Tibshirani et al 2001)<sup>23</sup> and

---

<sup>18</sup>Angelov P.P. (2002), "Evolving Rule-Based Models- A tool for design of Flexible Adaptive Systems", Physica-Verlag, Springer Verlag, Heidelberg.

<sup>19</sup> Kennedy J. and Eberhart R.C. (2001), "Swarm Intelligence", Morgan Kaufmann Publisher, San Francisco, CA.

<sup>20</sup>Dorigo M. and Stutzle T. (2004), 'Ant Colony Optimization', MIT Press, Cambridge, MA.

<sup>21</sup> Castro L.N.De. and Timmis J. (2002), "Artificial Immune Systems : A New Computational Intelligence Approach", Springer, Heidelberg

<sup>22</sup> Hong X. and Mitchell R.J. (2007), 'Backward elimination model construction for regression and classification using leave-one-out criteria' International Journal of Systems Science, Vol. 38 , No.2, pp. 101 – 113.

<sup>23</sup>Tibshirani R., Hastie T. and Friedman J. (2001), 'The Elements of Statistical Learning- Data Mining, Inference and Prediction', Springer.

intelligent data analysis and data mining (Berthold and Hand 2006)<sup>24</sup>, pattern recognition and classification (Duda et al 2001)<sup>25</sup>, control systems (Dorf and Bishop 2004)<sup>26</sup>, team learning in robotic soccer (GeethaRamani 2009)<sup>27</sup> and operations research (Hillier and Lieberman 2005)<sup>28</sup>.

Computer Vision Techniques and Image analysis are growing in prominence in almost every field of medical sciences. These are particularly relatable to modern ophthalmology ever since it is heavily dependent on visually oriented signs. Reliance on manual observations may result into inappropriate conclusions which eventually may influence the planning of the treatment. Exhilarating improvements in image processing pertinent to ophthalmology over the past one and half decade includes the developments being made towards emerging automated diagnostic systems for conditions such as diabetic retinopathy, age-related macular degeneration, retinopathy of prematurity etc. The growth accomplished in this field over recent years has considerably enhanced the type of medical care that is accessible to patients. The foremost focus of this research is to investigate and explore a range of automated computational techniques that can be developed to organize the retinal pathologies and carry out disease classification. These techniques can support the physicians to appraise their patients with sophisticated diagnostic tools in order supervise the progress more competently than before. In this chapter, the implications of retinal image processing, anatomical structure detection and various

---

<sup>24</sup> Berthold M. and Hand D.J. (2006), Intelligent Data Analysis - An Introduction, 2 nd Ed., Springer - Verlag Berlin Heidelberg.

<sup>25</sup>Duda R.O., Hart P.E. and Stork D.G. (2001), 'Pattern Classification', 2nd Ed, Wiley Interscience, New York, NY.

<sup>26</sup>Dorf R.C. and Bishop R.H. (2004), 'Modern Control Systems', 10th Ed., Pearson Prentice Hall, Upper Saddle River, NJ.

<sup>27</sup>GeethaRamani R. (2009), 'Genetic Programming based team learning in robotic soccer' Ph.D. dissertation, Pondicherry University, India.

<sup>28</sup> Hillier F.S. and Lieberman G.J. (2005), 'Introduction to Operations Research', 8th Ed., McGraw Hill, Boston, MA.

computational techniques are examined in details to comprehend the objective of this research work.

In the majority developing countries inadequate number of availability of medical specialists has augmented the mortality rate of patients suffering from a variety of diseases. This deficiency of number of medical specialists does not seem to be getting unraveled in the immediate short period of time. The institutions of higher learning could nonetheless, take some immediate action to roll out as many specialist doctors as possible. Conversely though, while awaiting students to become doctors and these doctors to further turn into specialists, many patients may already start losing their lives or their conditions worsening. The existing practice for medical treatment necessitates patients to consult specialist doctors for further diagnosis and treatments. Moreover, various other medical practitioners may not be fully equipped with sufficient amount expertise or experience to deal with certain high-risk diseases. On the other hand, the waiting time for treatments by and large takes a few days, weeks or even months. By the time the patients see the specialist, the diseases may have already spread out or advanced to a different stage. Since a good number of high-risk diseases should be cured only at their premature stages, the patients may have to endure for the rest of their lives.

Computer technology can be resourcefully utilized to shrink the number of mortality and lessen the waiting time of the patients to consult the specialist. Computer program or software developed by emulating human intelligence could be used to assist the non-specialist doctors in making astute judgments in the initial stages without consulting the respective domain specialists directly. Although the software is not meant to substitute the specialist doctors completely, nevertheless, software are

designed to assist general practitioners and specialists in diagnosing and envisaging patient's condition by interpreting data based on certain rules or "experiences". Patients with high-risk factors and diagnosed with certain high level diseases or illnesses could be selectively advised to see the specialists for further timely treatments. Making use of the technology especially Artificial Intelligence (AI) techniques in medical applications could reduce the cost, time and medical error and enhance the human expertise by manifolds.

Numerous Intelligent Systems have been built with an objective of enhancing health-care diagnosis and treatments and offering better health care facilities and reduce cost etc. As articulated in many studies (Mahabala et al., 1992)<sup>29</sup>(Manickam and Abidi, 1999)<sup>30</sup>(Alexopoulos et al., 1999)<sup>31</sup>(Zelic et al.,1999)<sup>32</sup>(Ruseckaite, 1999)<sup>33</sup>(Bourlas et al., 1999)<sup>34</sup>, intelligent systems were developed to help users (specifically doctors and patients) and endow with early diagnosis and forecasts to avert certain serious illnesses. Although the system is outfitted with "human" knowledge, the system will by no means be able to override the human expertise as humans would always be obligatory for frequently monitoring

---

<sup>29</sup>Mahabala, H. N., Chandrasekhara, M. K., Baskar, S., Ramesh, S., and Somasundaram, M. S. (1992), "ICHT: An Intelligent Referral System for Primary Child Health Care", Proceedings SEARCC'92: XI Conference of the South East Asia Regional Computer Confederation. Kuala Lumpur.

<sup>30</sup>Manickam, S., and Abidi, S. S. R. (1999), " Experienced Based Medical Diagnostics System Over The World Wide Web (WWW)", Proceedings of The First National Conference on Artificial Intelligence Application In Industry, Kuala Lumpur, pp. 47 – 56.

<sup>31</sup>Alexopoulos, E., Dounias, G. D., and Vemmos, K. (1999), "Medical Diagnosis of Stroke Using Inductive Machine Learning. Machine Learning and Applications: Machine Learning in Medical Applications", Chania, Greece, pp. 20-23.

<sup>32</sup>Zelic, I., Lavrac, N., Najdenov, P., Rener-Primec, Z. (1999), "Impact of machine learning of the Diagnosis and Prognosis of First Cerebral Paroxysm. Machine Learning and Applications: Machine Learning in Medical Applications", Chania, Greece, pp. 24-26.

<sup>33</sup>Ruseckaite, R. (1999), "Computer Interactive System for Ascertainment of Visual Perception Disorders", Machine Learning and Applications: Machine Learning in Medical Applications, Chania, Greece, pp. 27-29.

<sup>34</sup>Bourlas, P., Giakoumakis, E., and Papakonstantinou, G. (1999), "A Knowledge Acquisition and management System for ECG Diagnosis. Machine Learning and Applications: Machine Learning in Medical Applications", Chania, Greece, pp. 27-29.

and updating the system's internal knowledge base. Consequently, the role of medical specialists and doctors (or medical practitioner) would perpetually remain important to ensure system validity and fortitude.

Earlier studies on the intelligent medical systems such as MYCIN, CASNET, PIP and Internist-I have revealed results that outperform manual practices of diagnosis in several disease domain (Shortliffe, 1987)<sup>35</sup>. MYCIN was developed in the early 1970s to identify some specific antimicrobial infections and suggesting relevant drug treatments. It was endowed with several features such as explanation, knowledge acquisition, teaching and system building facilities. On the other hand, CASNET (Causal ASsociational NETworks) developed in early 1960s is a general tool for building expert systems for the diagnosis and treatment of various diseases.

CASNET's key application was the diagnosis and recommendation of treatment for Glaucoma. PIP, an abbreviated term for Present Illness Program was developed in 1970s to simulate the behaviour of an expert nephrologist by considering the historical records of the illness of a patient with underlying renal disease. The efforts on Internist-I in early 1982 was focused more on the examination of heuristic methods for arresting differential diagnostic task structures on clinical decision making. It was applied in diagnoses of internal medicine.

In 1990s, the research studies on intelligent system were improvised to employ the system based on the present needs. In quite a few studies, more than two techniques were fused and the function of the system was

---

<sup>35</sup>Shortliffe, E. H. (1987), "Computer Programs to Support Clinical Decision Making. Journal of the American Medical Association", Vol. 258, No. 1.

utilized to ensure improved system performance. ICHT (An Intelligent Referral System for Primary Child Health Care) was devised to mitigate the child mortality rates, especially in rural areas (Mahabala et al., 1992)<sup>29</sup>. The system succeeded in dealing with common pediatric complaints taking into concern the imperative processes and risk factors such as weight monitoring, immunization, developmental milestones and nutrition. ICHT employed expert systems to enable the collection of the patient's historical data. Furthermore, other expert systems have been developed such as HERMES (HEpathology Rule-based Medical Expert System) an expert system for prognosis of chronic liver related diseases (Bonfa et al., 1993)<sup>36</sup>, Neo-Dat an expert system for clinical trials (Theodorou and Ketikidis, 1995)<sup>37</sup>, SETH an expert system for the management on acute drug poisoning (Droy et al., 1993)<sup>38</sup>, PROVANES a hybrid expert system for critical patients in Anesthesiology (Passold et al., 1996)<sup>39</sup> and ISS (Interactive STD Station) for diagnosis of sexually transmitted diseases (Walker and Kwon, 1997)<sup>40</sup>.

Experienced Based Medical Diagnostics System, an online interactive medical diagnostic system is accessible through the Internet for many (Manickam and Abidi, 1999)<sup>30</sup>. Case Based Reasoning (CBR) was also engaged to operate on the specific knowledge of previously experienced and concrete problems or cases. The system can be utilized by patients to diagnose themselves without being required to make frequent

---

<sup>36</sup>Bonfa, I., Maioli, C., Sarti, F., Milandri, G. L., and Monte, P. R. D. (1993), "HERMES: An Expert System for the Prognosis of Hepatic Diseases", Technical Report UBLCS-93- 19, Universiti of Bologna.

<sup>37</sup>Theodorou, T., and Ketikidis, P. (1995), "Neo-Dat An Expert System to Support the Designers of Clinical Trials", 5th Hellenic Conference on Informatics.

<sup>38</sup>Droy, J. M., Darmoni, S. J., Massari, P., Blanc, T., Moritz, F., and Leroy, J. (1993), "SETH: An Expert System for the Management on Acute Drug Poisoning", <http://www.churousen.fr/dsii/publi/seth.htm>

<sup>39</sup>Passold, F., Ojeda, R. G., and Mur, J. (1996), "Hybrid Expert System in Anesthesiology for Critical Patients", Proceedings of the 8 th IEEE Mediterranean Electrotechnical Conference - MELECON'96 (ITALIA), Vol. III, pp. 1486-1489.

<sup>40</sup>Walker, N. J., and Kwon, O. (1997), "ISS: An Expert System for the Diagnosis of Sexually Transmitted Diseases", 11th Annual Midwest Computer Conference (MCC'97) March 21, Springfield, Illinois.

visits to doctors and also at the same time, extend their knowledge in their own domain cases (for e.g. breast cancer). Data mining being an AI technique for discovery of knowledge in large databases, it could very well be used to amass hidden information for medical purposes (SitiNurul Huda and Miswan, 1999)<sup>41</sup>(SitiFatimah and Rogayah, 1999)<sup>42</sup>(Neves et al., 1999)<sup>43</sup>. It can also be used jointly with neural networks for classification of fuzzy patterns in HIV and AIDS using unsupervised learning (Siti Nurul Huda and Miswan, 1999)<sup>41</sup>. Data mining has also been used to produce scatter diagrams and a rule statement models to augment current rule base systems (Siti Fatimah and Rogayah, 1999)<sup>42</sup>. (Neves et al 1999)<sup>43</sup> developed information system that supports knowledge discovery and mining in medical imaging.

Fuzzy logic is yet an additional branch of artificial intelligence techniques. It entails uncertainty of knowledge that simulates human reasoning abilities to deal with incomplete or fuzzy data sets. (Meng 1996)<sup>44</sup> applied fuzzy relational deduction in medical diagnosis. It was utilized along within the medical knowledge based system, referred to as the Clinaid. It takes cares of functions viz. diagnostic activity, treatment recommendations and patient's administration. Neural Network (NN) is one of the powerful AI techniques that has an immense potential ability to learn from varied data sets and construct weight matrices to characterize the learning patterns. NN is a single or multi layered arrangement of

---

<sup>41</sup>SitiNurul Huda Sheikh Abdulah and MiswanSurip (1999), "SatuMetodologiPerlombongan Data UntukPesakit AIDS", Proceedings of the First National Conference on Artificial Intelligence Application in Industry. Kuala Lumpur, pp. 57-71.

<sup>42</sup>Siti Fatimah MdSaad and RogayahGhazali (1999), "Data Mining for Medical Database. Proceedings of the First National Conference on Artificial Intelligence Application in Industry", Kuala Lumpur, pp. 72-79.

<sup>43</sup>Neves, J., Alves, V., Nelas, L., Romeu, A., and Basto, S. (1999), "An Information System That Supports Knowledge Discovery and Data Mining in Medical Imaging, Machine Learning and Applications: Machine Learning in Medical Applications", Chania, Greece, pp. 37-42.

<sup>44</sup>Meng, Y. K. (1996), "Interval-Based Reasoning in Medical Diagnosis", Proceedings of National Conference on Research and Development in Computer Science and Its Applications (REDECS'96), UniversitiPertanian, Malaysia: Kuala Lumpur, pp. 220 - 224.

several simple processors or units (Sarle, 1999)<sup>45</sup>. It mimics the function of human brain to perform tasks that are human doable. For example, a research study based on approximation and classification in medicine with the use of incremental neural network shows much greater generalization performance compared with other classification models (Jankowski, 1999)<sup>46</sup>. NN has been deployed in several medical and its allied applications related to medical conditions such as Coronary Artery (Lippmann, 1995)<sup>47</sup>, Myocardial Infarction (Heden et al., 1996)<sup>48</sup>, Cancer (Street et al., 1996)<sup>49</sup> (Karkanis et al., 1999)<sup>50</sup>, Pneumonia (Caruana et al., 1996)<sup>51</sup> and Brain Disorders (Pranckeviciene, 1999)<sup>52</sup>. In Karkanis et al (1999)<sup>50</sup> NN was implemented in a hybrid form with textual description method to discover aberrations contained in the same images with high precision.

---

<sup>45</sup><sup>44</sup>Sarle, W. S. (1999), "Neural Network FAQ, part 1 of 7: Introduction", Periodic posting to the Usenet Newsgroup comp.ai.neural-nets, <ftp://ftp.sas.com/pub/neurl/FAQ.html>

<sup>46</sup> Jankowski, N. (1999), "Approximation and Classification in Medicine with IncNet Neural Networks", Machine Learning and Applications: Machine Learning in Medical Applications. Chania, Greece, pp. 53-58.

<sup>47</sup> Lippmann, R. P., Kulkolich, L., Shahian, D. (1995), "Predicting the Risk of Complications in Coronary Artery Bypass Operations Using Neural Networks", Advances in Neural Information Processing Systems 7, The MIT Press, Cambridge, pp. 1053-1062.

<sup>48</sup>Heden, B., Ohlsson, M., Rittner, R., Pahlm, O., Haisty, W. K., Peterson, C., and Edenbrandt, L. (1996), "Agreement Between Artificial Neural Networks and Human Expert for the Electrocardiographic Diagnosis of Healed Myocardial Infarction", Journal of the American College of Cardiology, Vol. 28, pp. 1012-10s16.

<sup>49</sup> Street, W. N., Mangasarian, O. L., and Wolberg, W. H. (1996), "Individual and Collective Prognostic Prediction", Thirteenth International Conference on Machine Learning.

<sup>50</sup>Karkanis, S. A., Magoulas, G. D., Grigoriadou, M., and Schurr, M. (1999), "Detecting Abnormalities in Colonoscopic Images by Textual Description and Neural Networks", Machine Learning and Applications: Machine Learning in Medical Applications. Chania, Greece, pp. 59-62.

<sup>51</sup>Caruana, R., Baluja, S., and Mitchell, T. (1996), "Using the Future to "Sort Out" the Present: Rankrop and Multitask Learning for Medical Risk Evaluation", Advances in Neural Information Processing Systems 8, The MIT Press, Cambridge, pp. 959-965.

<sup>52</sup>Pranckeviciene, E. (1999), "Finding Similarities Between An Activity of the Different EEG's by means of a Single layer Perceptron", Machine Learning and Applications: Machine Learning in Medical Applications. Chania, Greece, pp. 49-52.

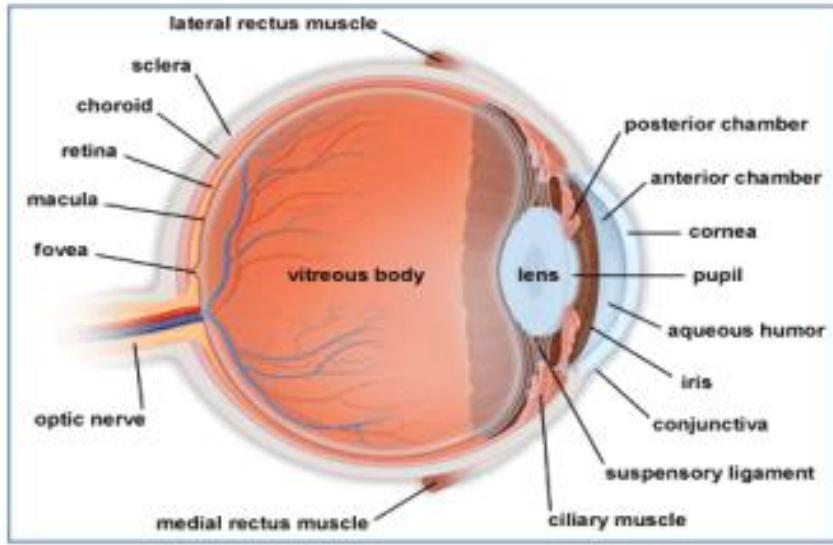
## **1.2 An Ophthalmic Condition-Glaucoma**

### **1.2.1 Human Eye**

Within the realms of the optical sciences, the human eye is time and again compared to a camera (Wade 2007)<sup>53</sup>. The light that gets reflected from an object is focused momentarily on the retina after transiting through the cornea, pupil and lens, which is quite analogous to the light passing through the camera optics onto the film or a sensor. The photoreceptor cells, which are dedicated for sensing light receive the incoming data. The impression of sight is formed when the information is conveyed to the brain via optic nerves from the retina. Throughout the transmission, the information is processed in the layers of the retina. The Figure 1.3 below depicts the cross-section of the eye and various structures involved in the formation of image. There are three essential features inside the camera which can be viewed as analogous or corresponding to the functions of the human eye: aperture, camera lens, and the camera sensor. Inside the eye, there resides the coloured Iris behind the transparent cornea and regulates the amount of light entering the eye by altering the dimensions of the pupil.

---

<sup>53</sup>Wade, N.J. "Image, eye, and retina (invited review)", Journal of the Optical Society of America A, Vol. 24, No. 5, pp. 1229-1249, 2007.



**Figure 1. 3 Anatomy of Human Eye<sup>53</sup>**

In the absence of light, the pupil widens, allowing the highest amount of light to pass through, and in the well illuminated surroundings the pupil narrows down preventing the eye from obtaining any excess amount of light. This is quite comparable to the way the camera controls the amount of light entering the camera with the aperture. With the relaxation of the Ciliary muscles, the Zonular fibers elongate the lens into a thin shape, and the distant objects are in focus. This can be equated with the function of focal length, i.e. the distance between the lens and sensor when focusing the camera. If the eye is accurately focused, the light transits through the vitreous gel onto the camera like sensor of the eye, known as the retina.

The retinal surface is practically one such place in the human body where blood vessels are visible directly and hence can be examined for any pathological changes occurring due to hypertension, diabetes mellitus, cataracts, and age-related macular diseases. The optic disc is the spot where the optic nerves exit the eyeball. The central retinal artery branch of the ophthalmic artery and the central retinal vein also reside alongside the optic

nerve. Branches of the central artery are connected to the anterior surface of the retina for its nourishment and the central retinal vein supplies blood from the retina through the optic disc.

The retina comprises of transparent tissue of multiple cellular layers designated to soak up and transform light into neural signals. Accordingly, the light has to pass through all the way through the retinal layers prior to it reaching the photoreceptor cells (Taylor 2007)<sup>54</sup>. The electric impulses are further processed inside the inner layers of the retina, throughout transmission from the photoreceptor cells to the optic nerve. The complete central vision is produced in the macula which is an extremely light sensitive region, with a size of about 5 to 6 mm in diameter in the central region of the retina (Forrester and Dick 2001)<sup>55</sup>. In the middle of the macula is a round shaped area known as fovea, where the cones are more or less found exclusively.

The cones are photoreceptor cells that are discerningly receptive towards various wavelengths of light. Adjacent to the macula is the opening of the optic nerve, from where the main artery and vein appear within the retina. There aren't any normal retinal layers in this region, and hence, the lack of photoreceptor cells falls out into a blind spot on the retinal surface. The two primary capillary networks: the nerve fiber layer network and the connecting neuron layer network provide the nutritional support to the retina (Taylor 2007)<sup>54</sup>. Moving towards the central area of the Retina, the capillary thickness increases, and the densest network is seen in the macula, but the capillaries are nonexistent in the fovea itself.

---

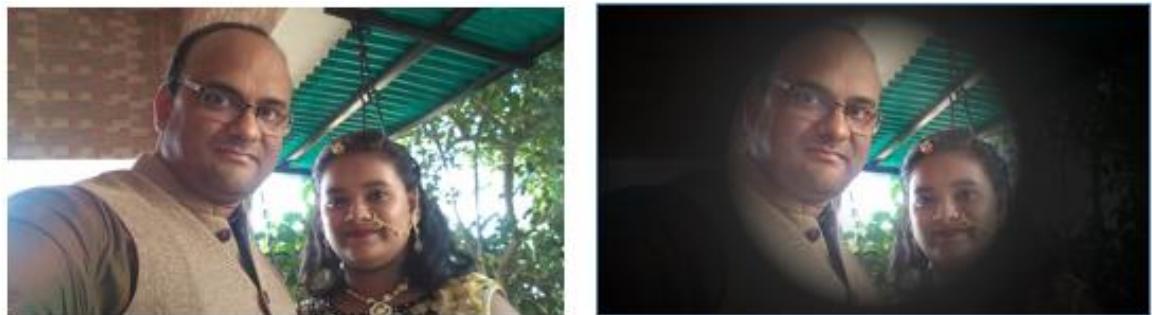
<sup>54</sup>Taylor, R. "Handbook of Retinal Screening in Diabetes", John Wiley & Sons Ltd, England, 2007.

<sup>55</sup>Forrester, J.V., Dick, A.D., William, R. and Lee, P.G.M. "The Eye, Basis sciences in practice", Saunders Ltd, 2nd edition, 2001.

For this reason, the fovea relies heavily on the choroidal blood supply from within the vascular layer at the back of the retina.

### 1.2.2 Glaucoma

Glaucoma is an eye ailment distinguished by the loss of retinal ganglion cells and their axons. Medically, this loss becomes evident by cupping, also known as excavation of the OD and concomitant visual field loss. Glaucoma has several subgroups, differentiated by causes, genetics, or morphology, and inside each group, there could be tens of different Glaucoma subtypes. Amid these all, the two major types are open-angle and angle-closure Glaucoma. These are characterized by the increase in the Intra Ocular Pressure (IOP) or pressure within the eye. Figure 1.4(a) and Figure 1.4(b) depict the vision with a normal and Glaucomatous eye, respectively.



**Figure 1. 4(a) Vision with normal eye (b)Vision with abnormal eye**

Glaucoma is a condition that causes damage to optic nerve of the eye. If untreated, over a period of time it gets worse. There are various factors associated with Glaucoma. Building up of pressure inside the eye (IOP-Intra Ocular Pressure) is the primary one. Glaucoma tends to be inherited and may not show up until later stages in life.

The increase in intraocular pressure, can damage the optic nerve severely. Optic Nerve transmits images to the brain. If high eye pressure continues to prevail, then the optic nerve continues to get damaged, that finally results into Glaucoma. Glaucoma may lead to permanent loss of vision. Glaucoma can cause total permanent blindness within few years, if not treated in its early stage.

It is imperative to regularly consult an eye specialist doctor or an ophthalmologist, as most of the people with Glaucoma have no early symptoms or pain from this increased pressure. Regular consultation is important to diagnose and treat Glaucoma before long-term visual loss occurs.

A person with age over 40 years and a family history of Glaucoma, should invariably get a complete eye checkup done from an ophthalmologist every one to two years. If the person has health problems such as diabetes or a family history of Glaucoma or are at risk for other eye diseases, he/she may need to visit the ophthalmologist more frequently.

Glaucoma usually occurs when pressure in the eye increases. This can happen when eye fluid isn't circulating normally in the front portion of the eye. Normally, this fluid, called the Aqueous Humor, flows out of the eye through a mesh-like channel. If this channel gets blocked, fluid levels builds up within, causing Glaucoma. The direct cause of this blockage is still unknown, but medical practitioners do know that it can be inherited, meaning it can get passed from parents to children.

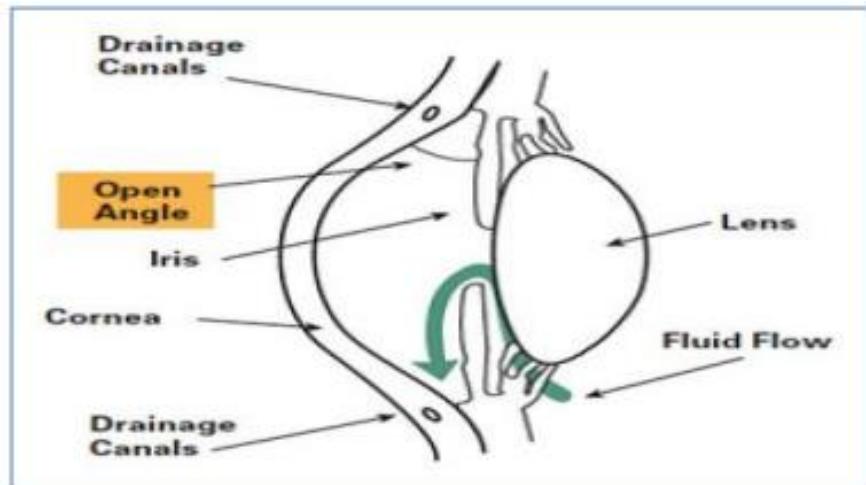
Less common causes of Glaucoma include a blunt or chemical injury to the eye, severe eye infection, blockage of blood vessels in the eye, inflammatory conditions of the eye and occasional eye surgeries to correct other conditions. Glaucoma usually occurs in both eyes, but it may get elevated at different levels in each eye.

For most people, there are usually few or no symptoms of Glaucoma. The first sign of Glaucoma is often the loss of peripheral or side vision, which can, a lot of times go unnoticed until the later stages of the disease. Detecting Glaucoma early is one reason a patient should have a complete examination done from an eye specialist every one to two years. Sporadically, intraocular pressure can rise to severe levels. In these cases, sudden eye pain, headache, blurred vision or even appearance of halos around lights may occur as symptoms.

### **1.2.2.1 Types of Glaucoma**

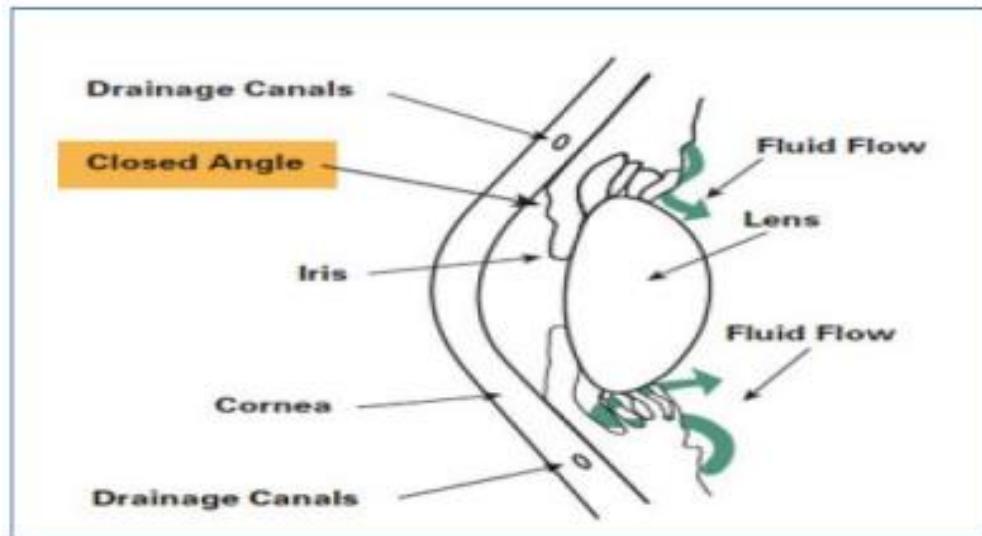
**There are two main types of Glaucoma:**

**1. Open-angle Glaucoma.** Also known as wide-angle Glaucoma, is the most common type of Glaucoma. The structures of the eye appear normal, but fluid in the eye does not flow properly through the drainage canals of the eye, called the Trabecular Meshwork.



**Figure 1. 5 Open-angle Glaucoma**

**2. Angle-closure Glaucoma.** Also called Acute or Chronic Angle-Closure or Narrow-Angle Glaucoma. This type of Glaucoma is less common but can cause a sudden buildup of pressure in the eye. Drainage may be poor because the angle between the Iris and the Cornea (where a drainage channel for the eye is located) is extremely narrow.



**Figure 1. 6 Angle-closure Glaucoma**

Other types of Glaucoma include:

1. Primary Angle-closure Glaucoma.
2. Secondary Glaucoma.

3. Primary Normal Tension Glaucoma.
4. Primary Ocular Hypertension Glaucoma.

### **1.2.2.2 Symptoms of Glaucoma**

A person likely to develop Glaucoma may exhibit any or all of the following symptoms:

- i. Seeing halos around lights
- ii. Vision loss
- iii. Redness in the eye
- iv. Eye that looks hazy (particularly in infants)
- v. Nausea or vomiting
- vi. Pain in the eye
- vii. Narrowing of vision (tunnel vision)

Glaucoma cannot be prevented completely, but if it is diagnosed and treated at an early stage, the disease can be fairly controlled. At its later stages, the loss of vision caused by Glaucoma becomes irreversible and cannot be restored. However, successfully lowering eye pressure can help prevent further visual loss due to Glaucoma. Most people with Glaucoma conditions do not go blind as long as they follow their treatment plan and have regular eye examinations.

### **1.2.2.3 Glaucoma Statistics**

Physiological or neurological factors lead to the condition of lacking visual perception known as blindness. Amongst several reasons for blindness, Glaucoma is one of the foremost reasons leading to irreversible

blindness, worldwide, which is affecting roughly 70 million people following cataract (Thylefors et al., 1995)<sup>56</sup>. Furthermore, it is the second most leading cause of global blindness (Resnikoff et al., 2004)<sup>57</sup> after cataract, principally due to Primary Open Angle Glaucoma (POAG). A statistics reported in the year 2002, projected that around 161 million people worldwide had the visual impairment, and 37 million were sightless. About 12.3% global blindness was caused due to Glaucoma whereas 47.8% was due to Cataract.

In some of the most backward regions, the visual mutilation from Glaucoma weighs a profound load, whereby adults are found more affected than children and women more affected than men (Resnikoff et al., 2004)<sup>57</sup>. By the year 2010, it was approximated that about 60.5 million people worldwide would be suffering from Open Angle Glaucoma (OAG) and Angle-Closure Glaucoma (ACG). By the year 2020, this number is estimated to rise upto a whopping 79.6 million. The mainstream (74%) of these individuals are likely to suffer from OAG. Two-sided blindness due to Glaucoma is estimated to over 11 million people by 2020. Globally, Glaucoma is a considerable basis of loss of vision that inexplicably affects women and Asians (Quigley 2006)<sup>58</sup>. The World Health Organization (WHO) has lately taken on a further methodical assessment of all population-based surveys on blindness and squat vision from about 55 countries for the year 2002 and applied it to the 17 WHO Epidemiological Sub-regions (Resnikoff et al., 2004)<sup>57</sup>. The numbers of blind and with visual impairment by WHO region are being illustrated below in Tables 1.1

---

<sup>56</sup>Thylefors, B., Negrel, A.D., Pararajasegaram, R. and Dadzie, K.Y., "Global data on blindness", Bulletin of the World Health Organization, Vol.73, No.1, pp.115-121, 1995.

<sup>57</sup>Resnikoff, S., Pascolini, D., Etyaale, D., Kocur, I., Pararajasegaram, R., Pokharel, G.P. and Mariotti, S.P. "Global data on visual impairment in the year 2002", Bulletin of the world health organization, Vol.82, No.11, pp.844-851, 2004.

<sup>58</sup> Quigley H.A. and Broman A.T. "The number of people with Glaucoma worldwide in 2010 and 2020", British Journal of Ophthalmology, Vol.90, pp. 262-267, 2006.

and 1.2 (Resnikoff et al., 2004)<sup>57</sup>.

From the Tables 1.1 and 1.2, it can be implied that roughly 39 million people are totally blind, and 246 million people have a low vision worldwide. Thus the estimated number of people blighted visually across the globe is 285 million which includes 39 million blind and 246 million possessing low vision; it can also be noticed that 65 % of visually impaired people and 82% of all blind are 50 years and older. The distribution of visually impaired people across the six WHO Regions with India and China separately is depicted in Table 1.1 with the percentage of the global impairment.

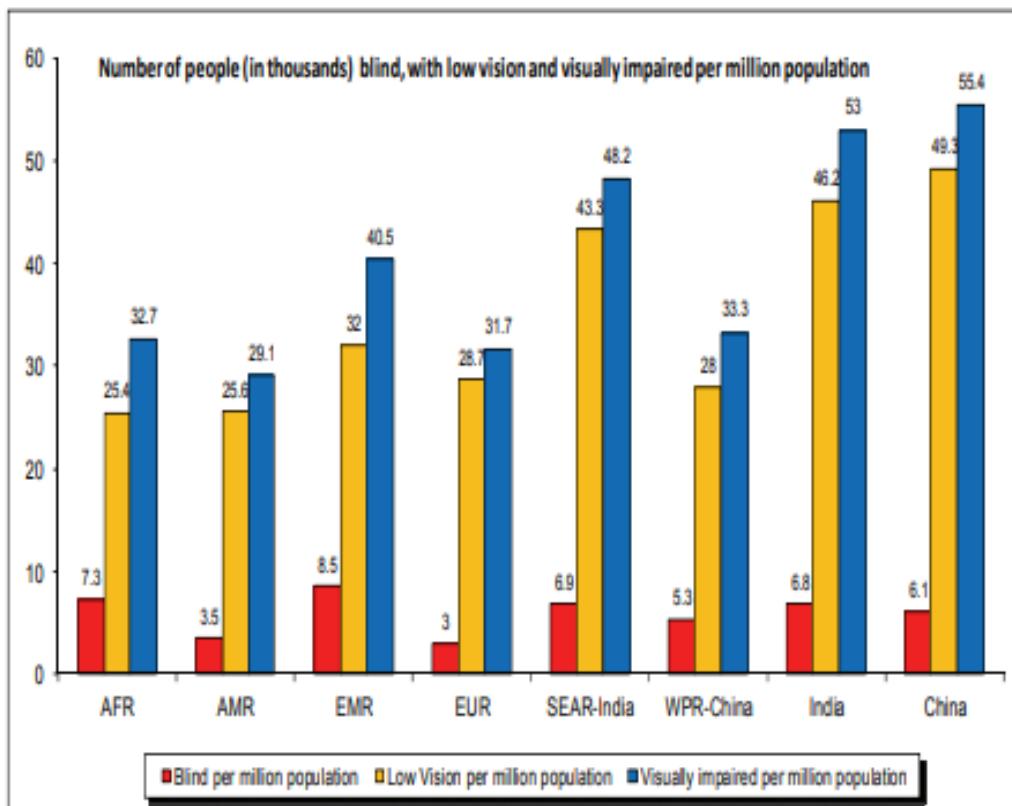
**Table 1. 1Global Estimates by WHO of Visual Impairments, 2010<sup>57</sup>**

WHO region	Total Population (million s)	Total Population%	Blindness %	Low Vision %	Visual Impairment%
Africa	804.9	11.9	15	8.3	9.2
America	915.4	13.6	8	9.5	9.3
Eastern Mediterranean	580.2	8.6	12.5	7.6	8.2
Europe	889.2	13.2	7	10.4	9.9
South-East Asia	579.1	8.6	10.1	9.7	9.8
Western Pacific	442.3	6.6	6	5	5.2
<b>India</b>	<b>1181.4</b>	<b>17.5</b>	<b>20.5</b>	<b>22.2</b>	<b>21.9</b>
China	1344.9	20	20.9	27.3	26.5
World	6737.5	100	100	100	100

**Table 1. 2Global Estimates of Visual Impairment in people by Age,  
2010<sup>57</sup>**

<b>Age (yrs.)</b>	<b>Population (millions)</b>	<b>Blind (millions)</b>	<b>Low Vision (millions)</b>	<b>Visually Impaired (millions)</b>
0-14	1848.5	1.42	17.52	18.93
15-49	3548.2	5.78	74.46	80.24
50 and older	1340.8	32.16	154.04	186.20
All Ages	6737.5	39.36	246.02	285.38

The pervasiveness of blindness differs from 1% in Europe and America to 7.0% in Africa. Amongst 37 million blind people, 1.4 million are aged in the range of 0–14 years, 5.2 million are of about 15–49 years, and 30.3 million are above 50 years, with women being affected more than men. The female to male blindness ratio ranges between 1.5 to 2.2. The chief causes of blindness across the world are Cataract, Glaucoma, Corneal Scarring including Trachoma, Age-related Macular Degeneration, and Diabetic Retinopathy. Figure 1.7 summarizes the causes of global blindness in 2010.



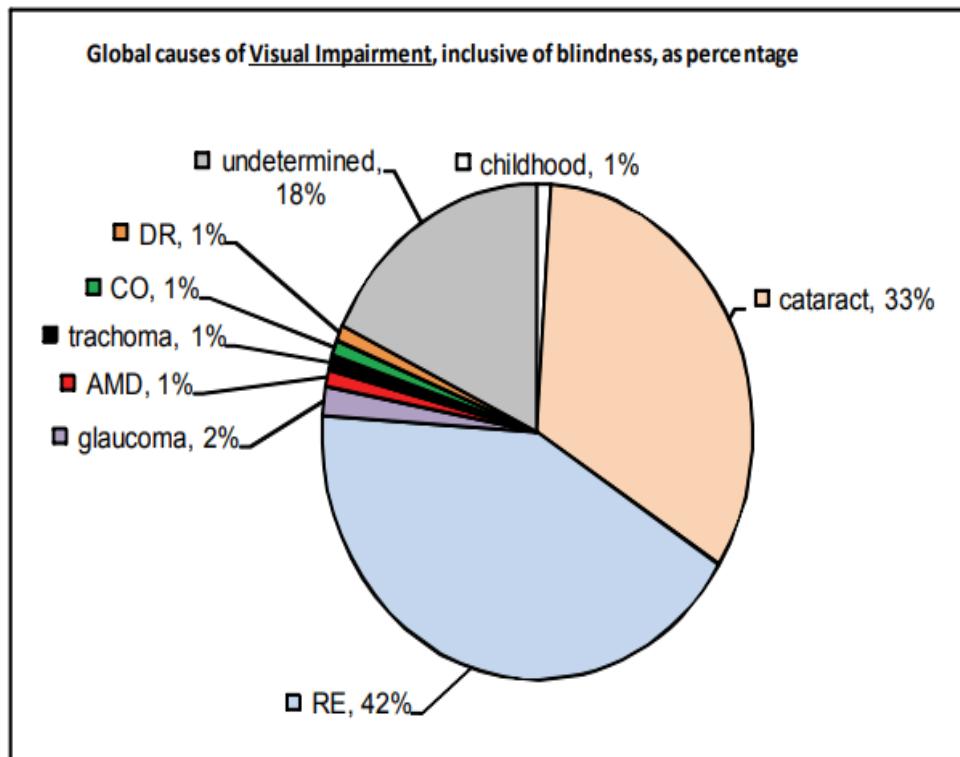
**Figure 1. 7 Causes of blindness in millions of people<sup>59</sup>**

The occurrence of visual impairment and blindness were found out for six different WHO regions across three age groups viz. 0-14 years, 15-49 years, and 50 years and older. Figure 1.8 and 1.9 indicates the worldwide estimates of visual impairment and blindness in 2010 (Mariotti2010)<sup>59</sup>.

Internationally the prime causes of visual impairment are uncorrected refractive errors and cataracts amounting to roughly 43% and 33 % correspondingly. Further causes are Glaucoma upto 2%, whereas Age related Macular Degeneration (AMD), Diabetic Retinopathy, Trachoma and Corneal Opacities, all amounting to about 1%. A huge percentage of causes i.e. 18%, are undetermined, (Figure 1.8). The reasons for blindness

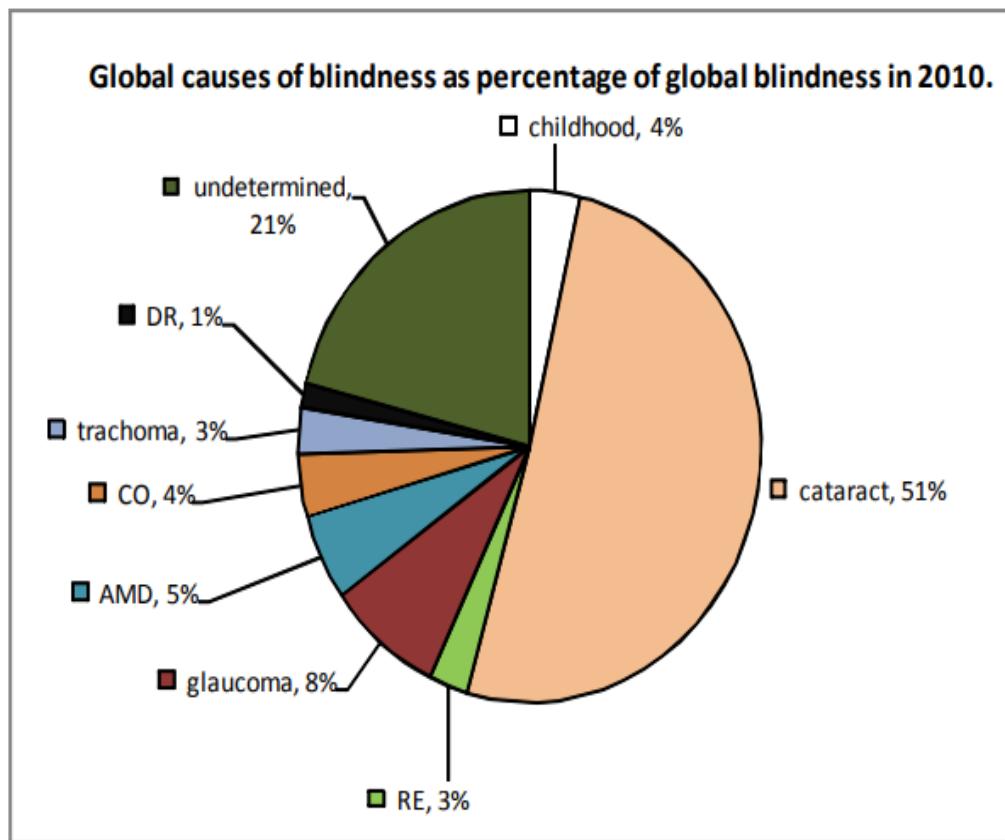
<sup>59</sup> Correspondence to: Silvio P. Mariottio, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

are Cataract - 51%, Glaucoma - 8%, AMD - 5%, Childhood Blindness and Corneal Opacities - 4%, Uncorrected Refractive Errors and Trachoma - 3%, and Diabetic Retinopathy - 1%, the uncertain causes are up to 21% (Figure 1.9)



**Figure 1. 8 Global Estimates of Visual Impairment by WHO, 2010**

<http://www.who.int/blindness/GLOBALDATAFINALforweb.pdf>



**Figure 1. 9 Global estimates of Blindness by WHO, 2010**

<http://www.who.int/blindness/GLOBALDATAFINALforweb.pdf>

The National Programme for Control of Blindness and Visual Impairment (NPCB&VI), was launched in 1976 as a 100% centrally funded scheme (presently 60:40 in all states and 90:10 in North-Eastern States) with the objective of dropping the occurrences of blindness to 0.3% by 2020. The Rapid Survey on Avoidable Blindness carried out under NPCB during 2006-07 indicated reduction in the occurrence of blindness from 1.1% (2001-02) to 1.0% (2006-07).

### **Prevalence rate of Blindness and Targets**

- Prevalence of Blindness - 1.1%. (Survey 2001-02).
- Prevalence of Blindness - 1.0 %. (Survey 2006-07).
- Current Survey (2015-18) is in progress. The estimated rate

of prevalence of blindness is close to 0.45%.

- Prevalence of Blindness target - 0.3% (by the year 2020).

## **Main Causes of Blindness**

Cataract (62.6%) Refractive Error (19.70%) Corneal Blindness (0.90%), Glaucoma (5.80%), Surgical Complication (1.20%) Posterior Capsular Opacification (0.90%) Posterior Segment Disorder (4.70%), Others (4.19%) Estimated National Prevalence of Childhood Blindness /Low Vision is 0.80 per thousand.

### **1.2.4Reviews on Primary Risk Factors for Glaucoma**

There are several risk factors linked with the development of Glaucoma disease in individual with a healthy eye. Most noteworthy risk factors for the commencement of Glaucoma are IOP, age, family history, ethnicity, and myopia. Simply by determining risk factors causing Glaucoma inception would not assure the certainty of an individual not developing Glaucoma in the future. Nevertheless, it may help to estimate the likelihood.

#### **1.2.4.1 Increased IOP**

As discussed earlier, one of the most critical and manifesting risk factor for Glaucoma development is the high IOP. In the past 10-15 years, two studies have presented insights into risk factors for developing Glaucoma among patients with Ocular Hypertension (OHT), these are the Ocular Hypertension Treatment Study (OHTS) and the European Glaucoma Prevention Study (EGPS). They surveyed and studied a

considerable population of individuals with increased levels of IOP but with normal visual fields and normal OD. The OHTS reported that the succession of Glaucoma was reduced from 9.4% to almost 4.4% over five years if the IOP was reduced by at least 20%.

The EGPS discovered that at the time of follow-up, an elevated IOP was directly related with an increased risk of developing OAG (9% per mm Hg over a five year period) (Miglior et al., 2007)<sup>60</sup>. Both EGPS and OHTS reported that among the OHT patients, thin central cornea thickness was a risk factor for the development of Glaucoma. Nonetheless, the etiology for this augmented risk is unsure (Miglior et al., 2007)<sup>60</sup>(Gordon et al., 2002)<sup>61</sup>. They furthermore reported that older baseline age, increased vertical CDR, and greater pattern standard deviations on the Humphrey Automated Perimeter were prognostic factors for OAG (Coleman et al., 2004)<sup>62</sup> (Gordon et al., 2002)<sup>61</sup>(Miglior et al., 2007)<sup>60</sup>. The early visible Glaucoma treatment trials and the EGPS revealed that that long-term IOP variations were not connected to the progression of Glaucoma (Miglior et al., 2007)<sup>60</sup>, while the AGIS study established a bigger risk of Glaucoma progression with increased long-standing IOP fluctuation, particularly in patients with low IOP (Caprioli and Coleman 2008)<sup>63</sup>(Nouri-Mahdavi et al.2004)<sup>64</sup>.

---

<sup>60</sup>Miglior, S., Pfeiffer, N., Torri, V., Zeyen, T., Cunha-Vaz, J. and Adamsons, I. "Predictive factors for open-angle Glaucoma among patients with ocular hypertension in the European Glaucoma Prevention Study", *Ophthalmology*, 114(1), pp.3–9, 2007.

<sup>61</sup>Gordon, M.O., Beiser, J.A., Brandt, J.D., Heuer, D.K., Higginbotham, E. J., Johnson, C.A. and Kass, M.A. "The ocular hypertension treatment study. Baseline factors that predict the onset of primary open-angle Glaucoma", *Archives of ophthalmology*, Vol.120, No.6, pp.714-720, 2002.

<sup>62</sup>Coleman, A.L., Gordon, M.O., Beiser, J.A., Kass, M.A. and Study, O.H.T. "Baseline risk factors for the development of primary open-angle Glaucoma in the Ocular Hypertension Treatment Study", *American Journal of Ophthalmology*, Vol.138, pp.684–685, 2004.

<sup>63</sup>Caprioli, J. and Coleman, A.L. "Intraocular pressure fluctuation: a risk factor for visual field progression at low intraocular pressures in the Advanced Glaucoma Intervention Study", *Ophthalmology*, Vol.115, No.7, pp.1123-1129, 2008.

<sup>64</sup>Nouri-Mahdavi, K., Hoffman, D., Coleman, A.L., Liu, G., Li, G., Gaasterland, D. and Caprioli, J. "Predictive factors for Glaucomatous visual field progression in the Advanced Glaucoma Intervention Study", *Ophthalmology*, Vol.111, No.,9, pp.1627–1635,2004.

Whereas an elevated level of IOP is a prominent risk factor for the advancement of Glaucoma, it should be kept in mind that a lot of people with Glaucoma have untreated IOPs of 21 mm Hg or lower. More commonly, it is expected that just about 50% of POAG is of the regular tension variety. On the other hand, studies have established a broad range in the frequency of normal tension Glaucoma amongst individuals with OAG.

#### **1.2.4.2 Age**

Studies time and again concur that an increasing age is a threat factor for the development of Glaucoma in common and patients having OHT. One of the studies revealed that in a population of white people in the state of Wisconsin (USA), the occurrence of OAG in the age group of 43–54 years was found to be 0.9%, whereas it was considerably larger at about 4.7% in individuals aged 75 years or more (Klein et al., 1992)<sup>65</sup>. The Barbados Eye Studies revealed that the frequency of POAG among people aged 40-49 was 2.2% for those aged 40–49 years at baseline and about 7.9% for those above 70 years of age, with a relative risk of emerging Glaucoma for the older age group (Leske et al., 2007)<sup>66</sup>.

#### **1.2.4.3 Family History**

Family history has been continuously suggested to be a risk factor for Glaucoma (Klein et al., 2004)<sup>65</sup>. In the Barbados Family Study of OAG,

---

<sup>65</sup>Klein, B.E., Klein, R., Sponsel, W.E., Franke, T., Cantor, L.B., Martone, J. and Menage, M.J. "Prevalence of Glaucoma. The Beaver Dam Eye Study", *Ophthalmology*, Vol.99, No.10, pp.1499–1504, 1992.

<sup>66</sup>Leske, M.C., Nemesure, B., He, Q., Wu, S.Y., Heitmancik, J.F., Hennis, A. and Barbados Family Study Group. "Patterns of open-angle Glaucoma in the Barbados Family Study", *Ophthalmology*, Vol.108. No.6, pp.1015- 1022, 2001.

40% of probands had minimum one family member who was found to be affected, one among five siblings was found to have OAG, and about 25% of the family members had distinct or suspected Glaucoma condition (Leske et al., 2001)<sup>66</sup>. Moreover, in the Baltimore Eye Survey and the Rotterdam Glaucoma Study, the risk of OAG was fairly higher for first-degree family relatives (Tielsch et al., 1994). Family history may reflect resemblance in genes straight way related to the Glaucoma development, or may indicate genetic resemblance in relation to IOP or optic nerve anatomy that may affect the Glaucoma development. Instead, the family history may be the consequence of improved access to healthcare and eye examinations and hence linked with an augmented possibility of being identified or a shared exposure to an environment.

If an individual is found to have a family history of Glaucoma, then he / she is most likely to have an enhanced risk of developing it. Glaucoma could have genetic associations, in the sense that a one or more defective genes may cause some specific individuals to be more susceptible to the disease.

#### **1.2.4.4 Myopia**

Though myopia is rarely considered as a typical risk factor for Glaucoma due to the apprehensions over selection biases, preceding clinic-based studies have certainly recognized myopia as a supporting risk factor. A population-based survey known as the Blue Mountains Eye Study that of the white Australian population, indicated that modest to high myopia was related with a two to threefold increased risk of developing Glaucoma.

The risk was higher for moderate to high myopia as compared to that

for low myopia, comparable relationship was discovered in a European-originated population in the US (Wong et al., 2003)<sup>67</sup>. The myopic Chinese population also showed an elevated risk of Glaucoma. In a different population-based research, the Chinese people having myopia greater than 6 D refractive error which is said to be high, were at bigger risk of being diagnosed with Glaucoma in contrast with the group comprising of all other refractive errors (Xu et al., 2007)<sup>68</sup>. The increase in risk rendered by myopic conditions doesn't appear to be associated with IOP. Processes for associations amongst myopia and Glaucoma have incorporated increased susceptibility of myopic nerves to Glaucomatous damage, shearing forces across the lamina cribrosa by the sclera, other connective tissue changes or a genetic link (Xu et al., 2007)<sup>68</sup>.

#### 1.2.4.5 Gender

The relationship of gender with a high risk of Glaucoma is a contentious matter. In the Beaver Dam and the Barbados eye studies, there was no statistically noteworthy greater than before risk with gender (Klein et al., 1992)<sup>65</sup>(Leske et al., 2007)<sup>66</sup>. The Rotterdam and Melbourne studies showed that there was a inclination towards increased risk for OAG in males; nevertheless, this disparity did not arrive at a statistical significance, probably due to small sample sizes (de Voogd et al., 2005)<sup>69</sup>(Mukesh et al., 2002)<sup>70</sup>. The Eye Disease Prevalence Research Group revealed that there is

---

<sup>67</sup>Wong, T.Y., Klein, B.E., Klein, R., Knudtson, M. and Lee, K.E. "Refractive errors, intraocular pressure, and Glaucoma in a white population", *Ophthalmology*, Vol.110, No.1, pp. 211–217, 2003.

<sup>68</sup>Xu, J., Chutatape, O., Sung, E., Zheng, C. and Kuan, P.C.T. "Optic disk feature extraction via modified deformable model technique for Glaucoma analysis", *Pattern Recognition*, Vol. 40, No.7, pp.2063-2076, 2007.

<sup>69</sup><sup>70</sup>De Voogd, S., Ikram, M.K. and Wolfs, R.C. "Incidence of open-angle Glaucoma in a general elderly population", *The Rotterdam Study. Ophthalmology*, Vol.112, No.9, pp. 1487–1493, 2005.

<sup>70</sup>Mukesh, B.N., McCarty, C.A., Rait, J. L. and Taylor, H.R. "Five-year incidence of open-angle Glaucoma: the Vision Impairment Project", *Ophthalmology*, Vol.109, No.6, pp.1047–1051, 2002.

no difference amongst the occurrence of Glaucoma between women and men for the black, white or Hispanic populations (Friedman et al., 2004)<sup>71</sup>.

#### **1.2.4.6 Inheritance**

Inheritance is improperly defined, given the incoherent application of variables which are at times used to define ethnicity, together with language, skin color, and geographical origin, along with the unevenness that subsists within populations that are characteristically defined as a single ethnicity (i.e., variability exists among “the Chinese”). However, ethnicity is used as a vague representation of genetic or other unidentified dissimilarities amongst populations, and trends concerning the associations among ethnicity and Glaucoma have been well recognized.

It is apparent that African descent is related to a superior risk of developing Glaucoma as against the individuals of European lineages (Friedman et al., 2004)<sup>71</sup>(Leske et al., 1994)<sup>66</sup> (Quigley and Broman 2006)<sup>72</sup>(Tielsch et al., 1994)<sup>73</sup>. The anticipated prevalence of OAG is 2 to 5 times greater for people of African descent compared to their European-originated equivalents. Of late, the results from nine years of follow-up from the Barbados Eye Studies indicated that the nine-year occurrence of POAG was 4.4% in this population of individuals primarily of African descent. These occurrences further went upto 9.4% when the cases of probable and definite POAG were included (Leske et al., 2007)<sup>66</sup>.

---

<sup>71</sup>Friedman, D.S., Wolfs, R.C.O., Colmain, B.J., Klein, B.E., Taylor, H.R., West, S., Leske M.C., Mitchell, P., Congdon, N., Kempen, J. and Eye Diseases Prevalence Research Group. “Prevalence of open-angle Glaucoma among adults in the United States”, Archives of ophthalmology, Vol.122, pp.532–538, 2004.

<sup>72</sup>Quigley H.A. and Broman A.T. “The number of people with Glaucoma worldwide in 2010 and 2020”, British Journal of Ophthalmology, Vol.90, pp. 262-267, 2006.

<sup>73</sup>Tielsch, J.M., Katz, J., Sommer, A., Quigley, H.A. and Javitt, J.C. “Family history and risk of primary open angle Glaucoma”, The Baltimore eye survey, Archives of ophthalmology, Vol. 112, No.1, pp.69-73, 1994.

Studies of European-originated populations demonstrate the five-year occurrence of distinct Glaucoma to be 0.5 to 0.6% and 1.1 to 1.8% of specific and probable cases of OAG (de Voogd et al., 2005)<sup>69</sup>(Mukesh et al., 2002)<sup>70</sup>. The Eye Disease Prevalence Research Group (Friedman et al., 2004)<sup>71</sup> carried out a partial-analysis of various studies on the occurrence of OAG globally and extrapolated and applied that data to the census population of the United States to approximate the occurrences in the United States. They estimated that around 1.57 million whites and 398,000 people of African origin have Glaucoma in the United States, and by 2020 roughly 3.36 million American citizens will develop Glaucoma, because of the swiftly aging population. The overall occurrence of OAG is found to be 1.86%.

In all age groups under the study, there was a greater occurrence of OAG in people of African origin as compared with those of the European-origin. It is unknown as to why is there a high risk of developing Glaucoma among people of African origin, even though genetic (Duggal et al., 2007)<sup>74</sup> or environmental factors have been recommended. The frequency of OAG in the Africans of the Barbados Eye Study was found to be 7% while in that of the African American people in the Baltimore Eye Survey, it was 4.2%. Further for individuals with a mixed lineage was found to be 3.3%, suggesting an influence of inheritable factors. Between the subpopulations of people of African descent, the occurrence is also a bit variable: maximum to be found in St. Lucia and Ghana (8.8% and 7.7%, respectively) whereas lesser in Tanzania and South Africa (4.2% and 2.9%,

---

<sup>74</sup>Duggal, P., Klein, A.P. and Lee, K.E. "Identification of novel genetic loci for intraocular pressure: a genomewide scan of the Beaver Dam Eye Study", Archives of ophthalmology, Vol.125, pp.74–79, 2007.

respectively) (Buhrmann et al 2000)<sup>75</sup>(Mason et al 1989)<sup>76</sup>(Ntim-Amponsah et al 2004)<sup>77</sup>(Rotchford and Johnson 2002)<sup>78</sup>. Numerous factors could have been influencing the greater risk rendered to the Africans. Physiologic disparities in the optic disc or thinner corneas compared with their peers may be influential parameters. Social discrepancies together with a lower access to health care could also be deterrent (Boland and Quigley 2007)<sup>79</sup>.

The Asian populations are found to have a lower risk of OAG as compared to the African origin people and it also depicts the occurrence which is comparable to those of people of European origin. The prevalence of POAG in the Chinese Singaporean individuals was found to be 2.1% which was quite similar to that of the Chinese population in the Liwan District (Foster et al., 2000)<sup>80</sup>(He et al., 2006)<sup>81</sup>. The frequency of OAG in the Latino ethnic group becomes evident to be higher than in the people of European-origin. The frequency of Glaucoma in largely Mexican-derived Latinos was found to be 4.74% in the Los Angeles Latino Eye Study (LALES). This occurrence increased with age, with those in 40–49 years of age group having these occurrence proportions of 1.32%, while for those above 80 years old, it was 21.76%. An astonishing 75% of individuals with

---

<sup>75</sup>Buhrmann, R.R., Quigley, H.A. and Barroy. "Prevalence of Glaucoma in a rural East African population", *Investigative Ophthalmology & Visual Science*, Vol. 41, pp.40–48, 2000.

<sup>76</sup>Mason, R.P., Kosoko, O. and Wilson, M.R. "National survey of the prevalence and risk factors of Glaucoma in St. Lucia, West Indies. Part I. Prevalence findings", *Ophthalmology*, Vol.96, pp.1363–1368, 1989.

<sup>77</sup>Ntim-Amponsah, C.T., Amoaku, W.M. and Ofosu-Amaah, S. "Prevalence of Glaucoma in an African population", *Eye*, Vol.18, No.5, pp.491497, 2004.

<sup>78</sup>Rotchford, A.P. and Johnson, G.J. "Glaucoma in Zulus: a populationbased cross-sectional survey in a rural district in South Africa", *Achieves of Ophthalmology*, Vol.120, No.4, pp.471–478, 2002.

<sup>79</sup>Boland, M.V. and Quigley, H.A. "Risk factors and open angle Glaucoma: classification and application", *Journal of Glaucoma*, Vol. 16, No. 4, pp.406–418, 2007.

<sup>80</sup>Foster, P.J., Oen, F.T. and Machin, D. "The prevalence of Glaucoma in Chinese residents of Singapore: a cross-sectional population survey of the TanjongPagar district", *Achieves of Ophthalmology*, Vol.118, No.8, pp.1105–1111, 2000.

<sup>81</sup>He, M., Foster, P.J. and Ge, J. "Prevalence and clinical characteristics of Glaucoma in adult Chinese: a population based study in Liwan District, Guangzhou", *Investigative Ophthalmology & Visual Science*, Vol.47, No.7, pp:2782–2788, 2006

OAG or OHT were formerly undiagnosed (Varma et al., 2004)<sup>82</sup>.

Yet another Latinos study revealed the general prevalence of OAG at 1.97%, with a higher occurrence as age increases (from 0.50% for the ones between 41–49 years old to 12.63% for the 80 years old). Besides, in this study, like in the LALES, about 62% of people were earlier not detected with OAG (Quigley et al., 2001)<sup>72</sup>. The native American population has not been studied that comprehensively as compared to the other US populations, but a study on the Northwest American Indians indicated some astounding outcomes. People belonging to the three native American tribes of Oregon, Washington and Idaho had an occurrence of Glaucoma of about 6.2%, and all the affected individuals were found to have Normal Tension Glaucoma (Mansberger et al., 2005)<sup>83</sup>.

There were no statistical dissimilarities in occurrences among males and females within the Black, European-origin or Hispanic ethnicities. The rate of occurrence among Hispanic people was not much significantly different from those in the adults of European-origin, but had lesser occurrence as compared to the blacks, with an odds ratio of 0.41.

On the whole, the black subjects have approximately thrice the prevalence rates than those of the individuals of European-origin.

---

<sup>82</sup>Varma, R., Ying-Lai, M. and Francis B.A. "Prevalence of open-angle Glaucoma and ocular hypertension in Latinos: the Los Angeles Latino Eye Study. Ophthalmology, Vol.111, No.8, pp.1439–144, 2004.

<sup>83</sup>Mansberger, S.L., Romero, F.C. and Smith, N.H. "Causes of visual impairment and common eye problems in Northwest American Indians and Alaska Natives", American journal of public health, Vol.95, No.5, pp. 881–886, 2005.

## **1.3 Diagnosis of Glaucoma**

The earlier the Glaucoma is detected, the better are the chances to protect the vision from getting damaged which can be accomplished by regular and complete eye examinations. A through eye examination to determine Glaucoma involves five common tests such as Tonometry, Ophthalmoscopy, Perimetry, Gonioscopy, and Pachymetry.

### **1.3.1 Tonometry**

A Tonometer is used to measure the IOP within the eye. During the Tonometry process, eye drops are used to anesthetize the eye. Subsequently, a medical practitioner or a technician uses a device known as a Tonometer to determine the internal pressure of the eye. A tiny amount of pressure is exerted on the eye by a little device or by a warm puff of air flow. 12 to 22 mm Hg is the suggested range of normal pressure. Nearly every Glaucoma case gets diagnosed with pressure beyond 20 mm Hg. However though, Glaucoma can still persist in some people at pressures between 12 to 22 mm Hg. It should be noted that the characteristic of eye pressure is unique to each person.

### **1.3.2 Ophthalmoscopy**

The optic nerve for Glaucoma damage is examined by the medical practitioner using the procedure known as Ophthalmoscopy. The pupils are dilated using Eye drops to enable the medical practitioner or the doctor to see through the eye to study the color and shape of the optic nerve. The doctor then uses a small device with a light at the end to enlarge the optic nerve. In case the intraocular pressure is not found to be within the normal

range or if the optic nerve seems to be abnormal, in that case two more Glaucoma exams viz. Perimetry and Gonioscopy are conducted.

### **1.3.3 Perimetry**

Perimetry is a visual field of investigation that constructs a map of the entire field of vision. This investigation test assists doctors to decide whether or not, an individual's vision is been affected by Glaucoma. At the time of this test, the patient is asked to stare straight ahead and then point out when a moving light passes his/her peripheral vision. This is how the test aids to depict a "map" of the vision.

### **1.3.4 Gonioscopy**

This investigative test facilitates in determining whether the angle, where the iris and the cornea meet, is open and wide or narrow and closed. All through the test, eye drops are used to anesthetize the eye. Further, a portable contact lens is softly positioned on the eye. This contact lens consists of a mirror that indicates the doctor whether the angle between the iris and cornea is wide and open or closed and blocked.

### **1.3.5 Pachymetry**

Pachymetry is an easy and painless examination to determine the corneal thickness which is a clear window in the front of the eye. A probe known as the Pachymeter is gently placed on the front of the eye to

measure its thickness. It helps in diagnosing as the corneal thickness has the likelihood to affect the eye pressure readings.

### **1.3.6 Imaging Technique**

The Retinal Imaging technique is critically used for diagnosing retinal diseases. The two most important retinal imaging techniques are Fundus Imaging and Optical Coherence Tomography (OCT) Imaging. Fundus Imaging is commonly used in population based large-scale discovery of Diabetic Retinopathy, Glaucoma, and Age-related Macular Degeneration. OCT is extensively applied in the diagnosis and supervision of patients suffering from Diabetic Retinopathy, Macular Degeneration, and Inflammatory Retinal Diseases. The Fundus image depicts the morphological variations in Optic Disc, Optic Cup, and the Macula within a Retina. Fundus Imaging is the procedure wherein the reflected light is used to acquire a two-dimensional depiction of the three-dimensional, semitransparent, retinal tissues projected on the imaging plane. Fundus Image is also utilized in diagnosing Glaucoma as well as Diabetic Retinopathy.

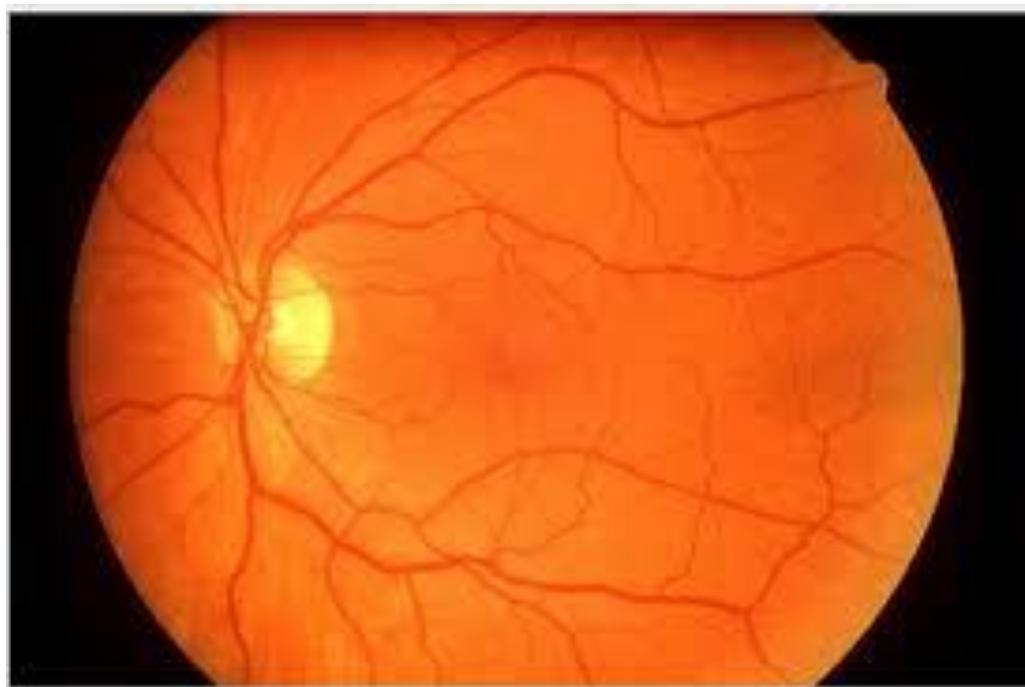


**Figure 1. 10 Fundus Camera**

A Fundus camera is a device used specifically for capturing the images of the retina. The indirect ophthalmoscope principle is the bases of such a device, where the observer's eye is substituted with a camera. A Fundus camera is a dedicated low power microscope consisting of a connected camera intended to take pictures of the internal surface of the eye, together with the Retina, Optic Disc, Macula, and Posterior Pole. A Fundus camera is depicted in the Figure 1.10.

A typical camera analysis 30 to 50 degrees of retinal region, with a magnification power upto 2.5x and permits a little adjustment of this relationship through zoom or auxiliary lenses ranging from 15 degrees which offers 5x enlargement upto 140 degrees with a wide angle lens that diminishes the image by half. The optics of a Fundus camera and that of the indirect ophthalmoscope are very similar in nature, wherein the observation and illumination systems pursue divergent paths. The observation light is focused by means of a sequence of lenses through a

doughnut shaped aperture. In turn, it goes through a central aperture to form an Annulus, prior to passing through the camera objective lens and the cornea, finally onto the retina. The illumination system forms a doughnut shape having an un-illuminated hole through which the light reflected from the retina passes through. As the light pathways of the two systems are independent, there are negligible reflections of the light source arrested in the formed image. The image forming rays go on towards the low powered telescopic eyepiece. When the button is pressed to take a picture, a mirror cuts short the path of the illumination system that permits the light from the flash bulb to enter into the eye. At the same time, a mirror cascades in front of the observation telescope, which forwards the light onto the incarcerating medium, irrelevantly of the film or a digital charge-coupled device. Because of the eye's propensity for accommodation while seeing through a telescope, it is necessary that the exiting threshold is parallel for an in-focus image to be created on the capturing medium. Figure 1.11 shows a typical Fundus image.



**Figure 1. 11 Fundus image**

The CDR value is determined by the diameters or regions of the optic cup and optic disc. Glaucoma is said to be present, if the CDR exceeds 0.3. The ophthalmologist further investigates the condition and arrangement of blood vessels in the optic disc region to enhance the diagnosis. If the blood vessels are found to have been shifted from the normal condition, then the condition is concluded as Glaucoma.

### **1.3.7 Computer Aided Diagnosis**

Computer Aided Diagnosis (CAD) may be described as the diagnosis made by the clinicians who considered the results of the computer outcome as a “second opinion”. The computer output is resultant from the quantitative analysis of diagnostic imagery. It is significant to note that the computer is used only as a tool to render some supplementary information to clinicians, who finally take the conclusive decisions. Hence the concept of CAD is undoubtedly fundamentally different from that of “Automated Diagnosis”. The objective of CAD based Glaucoma diagnosis is to improvise the diagnostic precision and also the reliability of clinician's image elucidation by using the computer output as a viewpoint or a perspective. Clinicians can make some astute subjective judgments with the use of computer outputs.

The CAD schemes involve three principal elements which are based on three diverse technologies. The first element is image pre-processing; second one is the quantification of image features. The third one is data processing for the characterizing between normal and abnormal patterns, based on the features obtained from the second element.

## **1.4 Organization of the Thesis**

**Chapter 1: INTRODUCTION.** This chapter describes the Introduction to Intelligent Systems, different techniques used in development of Intelligent Systems. This chapter also introduce the anatomy of an eye, a pathological condition of an eye-Glaucoma, along with different types of Glaucoma and factors involved in diagnosis of Glaucoma.

**Chapter 2: LITERATURE REVIEW.** This chapter discusses the work carried out by several researchers using intelligent system for disease diagnosis. The chapter also describes state of the art computational techniques for detection of Glaucoma.

**Chapter 3: RESEARCH METHODOLOGY.** This chapter presents research methodology used for the research. This chapter lists down the objectives of the research. The techniques used for data pre-processing to prepare the data for further processing in order to diagnose different stages of Glaucoma are explained in detail. This chapter also explains the proposed ensemble algorithm for classification of data, which provide diagnosis of Glaucoma and also specifies the condition of Glaucoma out of 6 different conditions.

**Chapter 4: RESULTS AND DISCUSSIONS.** This chapter shows the experimental results and performance analysis for Glaucoma diagnosis using ANN, Naïve Bayes, Decision Tree and Proposed Ensemble FGLAUC-99.

**Chapter 5: CONCLUSION, MAJOR CONTRIBUTIONS AND FUTURE WORK:** This chapter states the conclusion, major contributions of the research and future scope of this research work.

---

# **CHAPTER – 2 Literature Review**

## **2.1 Intelligent Systems in Disease Diagnosis**

Regardless of all efforts for standardization, the field of Medical diagnosis is still considered an art. It is an art of gauging the pathological status of a patient from an existing set of symptoms. It is described as an art, because it is a complex process with multiple and manifold factors, and its solution consists literally all of a human capabilities including intuitive and the subconscious thinking (Zhang et. al., 2007)<sup>84</sup>.

The procedure of medical diagnosis comprises of assessment of a given set of symptoms, carrying out related pathological tests (based on patient's test data), and eventually categorizing the diseases validating the specific findings.

The human body functioning is distinctly identified by the intricate and extremely interactive and rigorous chemistry of its organs and the overall psyche. This intensive effort yields homeostasis and the balancing and synchronization of all physiological measures. This equilibrium is upheld at a level within physiological limits that vary from person to person. Because of the exterior or interior causes, divergences from it are indicative of some kind of mental anxiety. The early recognition of the reason of these mental anxieties is the goal of medical diagnosis. Attaining an infallible diagnosis has never been a straightforward job for doctors. At the moment in medical diagnosis it is often impractical to take a glance inside a patient to figure out the major cause that led to the succession of

---

<sup>84</sup> D. Zhang, Y. Wang, H. Huang, 2007, Fuzzy-rough membership function neural network and its application to pattern recognition, Proc. SPIE 6788, MIPPR 2007: Pattern Recognition and Computer Vision, 67882N.

effects and reactions complained by the patients. Thus the diagnosis is premised on oblique evidence, symptoms and the knowledge of the medical process that narrate alleged causes to the observed effects.

The diagnosis related predicaments occur not only due to the incompleteness of knowledge, but in addition most immediate restrictions of the theoretical and practical knowledge insinuations lead from a preliminary cause to its discernible effects. There are some other predicaments, also found in medical diagnosis which may be as below:

- The associations between medical diagnosis and their symptoms, cause-effect relationships, are barely ever one-on-one. Demarcation of diagnoses that share an overlying array of symptoms is thus innately difficult.
- More or less, all observations are subject to errors. The procedures for error correction are stochastic in nature that necessitates strong postulations that do not for all time hold in practice.

(Sudha et. al., 2012)<sup>85</sup> proposed the classification algorithms viz. Naive Bayes, decision tree and neural network for envisaging the stroke diseases. Parameters consisting of patient's medical history and symptoms were utilized for classification. The records with inappropriate data were eliminated from the data warehouse prior to the mining process. Training data sets were employed for the purpose of building a classification predictive model. The testing data set was also employed for assessing the efficiency of classification. Whilst evaluating these classification algorithms, the scrutiny illustrates that the performance of the neural network was found to be better than the other two algorithms.

---

<sup>85</sup>Sudha, A., Gayathiri, P. and Jaisankar, N. "Effective Analysis and Predictive Model of Stroke Disease using Classification Methods", International Journal of Computer Applications Volume 43(14), pp.0975 – 8887, 2012.

(Sellappan Palaniappan et. al., 2008)<sup>86</sup> proposed the construction of an intelligent heart disease prediction system developed with the help of data mining techniques viz. decision trees, Naïve Bayes and Neural Networks. The result demonstrated the typical strength of each of the methods in realizing the objectives of the specified mining techniques. The complex what-if questions which the conventional decision support systems are unable to answer are easily responded by the intelligent heart disease prediction system. The system that was developed was Internet-based, user-friendly, reliable and scalable.

(LathaParthiban and Subramanian, 2007)<sup>87</sup> developed the aforementioned intelligent heart disease prediction system using CANFIS and Genetic Algorithms. Adaptable fuzzy inputs were tailored with a modular neural network to quickly and correctly estimate complex functions. The CANFIS model coalesced the neural network adaptive competencies and the fuzzy logic quantitative approach and was then incorporated with genetic algorithm to diagnose the occurrence of the disease. The heart disease related data set was procured from the UCI machine learning repository.

(Chaitrali et. al., 2012)<sup>88</sup> proposed an enhanced research on the heart disease prediction system employing the data mining classification techniques. The Prediction systems employed for the heart disease contains

---

<sup>86</sup>Sellappan Palaniappan, Rafiah Awang. "Intelligent Heart Disease Predictionsystem using data mining techniques". International Journal of ComputerScience and Network Security, Vol. 8(8), pp. 108–115, 2008.

<sup>87</sup>Latha Parthiban and Subramanian, R. "Intelligent Heart Disease Prediction System using CANFIS and Genetic Algorithm", International Journal of Biological and Life Science, Vol.15,pp. 157-160, 2007.

<sup>88</sup>Chaitrali, S. Dangare, Sulabha S. Apte,. "Improved Study of Heart DiseasePrediction System using Data Mining Classification Techniques"*International Journal of Computer Applications*, Vol. 47(10), pp. 0975 – 888,2012.

huge amount of data, used to dig out concealed information for making intelligent medical diagnosis. The primary intention of the research was to construct an Intelligent Heart Disease Prediction System that offers diagnosis of the heart disease using historical database of the heart conditions. To devise such a system, clinical parameters such as gender, blood pressure, cholesterol levels and 13 other similar vital characteristics were used.

(Resuldas et. al., 2009)<sup>89</sup> proposed neural network collectively works to predict the heart disease. The ensemble-based methods generate original models by amalgamating the posterior probabilities or the predicted measures from multiple precursor models. There were three different neural network models that were employed to build the ensemble model. The quantity of neural network nodes inside the ensemble model was also augmented, but no performance enhancement was observed.

(Olatubosun Olabode et. al., 2012)<sup>90</sup> proposed the multilayer feed forward artificial neural network with back propagation error that is used in Cerebro-vascular accident attack classification. The back-propagation error method based multilayer perceptron's artificial neural networks were feed forward nets comprising of more than one layers of nodes connecting the input and the output nodes. The entire neural network was trained by means of back propagation algorithm along with sigmoid function on a single hidden layer. There was random initiation of the weights of the neural network. The series of the weights in this work was found to be

---

<sup>89</sup>Resul Das, Ibrahim Turkoglu and Abdulkadir Sengur. "Effective diagnosis of heart disease through neural networks ensembles" *International Journal of expert systems with applications*, Vol. 36, pp. 7675-7680, 2009.

<sup>90</sup>Olatubosun Olabode and Bola Titilayo Olabode. "Cerebrovascular Accident Attack Classification Using Multilayer Feed Forward Artificial Neural Network with Back Propagation Error", *Journal of Computer Science*, pp.18-25, 2012.

between [-0.5 and 0.5], whereas the learning rate was set between 0.1 to 0.9.

(Patil and Kumaraswamy, 2009)<sup>91</sup> built an intelligent and efficient system for heart attack prediction employing the neural networks. With an intention to extract significant patterns from the heart disease warehouse for accurate heart attack estimation, a skillful frequent pattern mining methodology has been proposed. The neural network was trained using back propagation training algorithm utilized for prediction.

(Fidele et. al., 2009)<sup>92</sup> came out with a study to make use of artificial intelligence tools for clinical decision support in evaluating the cardiovascular risk in patients. In the proposed artificial neural network, a bi-layered neural network using the Levenberg–Marquardt algorithm and the flexible back propagation have been employed. At an isolated level, the application of the neural network seems to be a superior deal with the estimation of cardiovascular disease.

A variety of medical applications have widely employed the computer aided detection systems with applied optimization techniques (Pei Chann Chang et. al., 2012)<sup>93</sup>(Sultan and Siti, 2011)<sup>94</sup>(Huy and

---

<sup>91</sup>Patil, S.B.and Kumaraswamy, Y.S. "Intelligent and effective heart attackprediction system using data mining and artificial neural network," *EuropeanJournal of Scientific Research*, Vol. 31(4), pp. 642–656, 2009.

<sup>92</sup>Fidele, B., Cheeneebash, J., Gopaul, A.and Goorah, S.S.D. "Artificial neuralnetwork as a clinical decision-supporting tool to predict cardiovasculardisease", *Trends in Applied Sciences Research* Vol. 4(1), pp. 36–46, 2009.

<sup>93</sup>Pei Chann Chang, Jyun-Jie Lin and Chen-Hao Liu. "An attributeweight assignment and particle swarm optimization algorithm formmedical database classifications", *Computer methods and programs inBiomedicine*, Vol. 107, pp. 382-392, 2012.

<sup>94</sup>Sultan Noman Qasem and Siti Mariyam Shamsuddin. "Radial basisfunction network based on time variant multi-objective particle swarmoptimization for medical diseases diagnosis", *Journal of Applied SoftComputing*, Vol. 11(1), pp. 1427-1438, 2011.

Evangelos, 2009)<sup>95</sup>. CAD becomes an extremely intelligent classification job when computational intelligence is incorporated with process of medical diagnosis. The task of crafting optimal neural network architecture has always been the endeavor of a human expert and needs an exasperating trial and error process to accomplish classification precision. In recent times, the optimization techniques have been extensively applied in a variety of applications together with medical diagnosis, pattern recognition, tuning of intelligent classifiers, etc.

(Goldberg and Richardson, 1987)<sup>96</sup> pioneered the genetic algorithm with sharing for multimodal function optimization.

(Nikunj Chauhan et. al., 2009)<sup>97</sup> integrated the differential evolutionary methods along with wavelet neural network for accurately estimating bankruptcy in banks.

(Chakravarty and Dash, 2011)<sup>98</sup> utilized the differential evolution with an active filter weight neural network model for making predictions in the energy market.

(Bidyadhar and Debashinsha, 2011)<sup>99</sup> introduced differential evolution based neural network for identification of the linear systems. In

---

<sup>95</sup>Huy NguyenAnh Pham and EvangelosTriantaphyllou. "An application of anew meta-heuristic for optimizing the classification accuracy whenanalyzing some medical data sets", *Expert Systems with Applications*, Vol.36(5), pp. 9240-9249, 2009.

<sup>96</sup>Goldberg E, and Richardson J. "Genetic algorithm with sharing formultimodal function optimization", *Proceedings of the second internationalconference on genetic algorithm and their applications*, pp. 41-49, 1987.

<sup>97</sup>Nikunj Chauhan V. Ravi andKarhik Chandra, D. "Differential Evolutiontrained wavelet neural network application to bankruptcy prediction inbanks," *Expert systems with Applications*, Vol. 36(4), pp. 7659-7665, 2009.

<sup>98</sup>Chakravathy, S. and Dash, P.K. "Dynamic filter weights neural networkmodel integrated with differential evolution for day-ahead priceforecasting in energy market", *Expert systems with Applications*, Vol. 38(9),pp. 10974-10982, 2011.

the field of medicine, Genetic Algorithm (GA) is primarily utilized for optimization of weight, symptoms and other peculiar disease characteristics. The GA can be deployed to enhance the performance of ANN in many diverse ways.

(Yu et. al., 1997)<sup>100</sup> utilized GA in treatment optimization for stereotactic radiosurgery and radiotherapy and established that GA was an all-powerful and an adaptable as a computationally intelligent equivalent to human-guided strategies. The introduction of GAANN in the field of medicine, improved accuracy and performance (Dybowski et. al., 1998)<sup>101</sup>, rate of prediction (Handels et. al., 1999)<sup>102</sup> and maximized the number of neurons in the hidden layer (Heckerling et. al., 2004)<sup>103</sup>.

The medical literature such as Diagnosis of the Critically Ill have reported an agile integration of ANN with GA (Montani et. al., 2000)<sup>104</sup>, and an enhanced classification performance. GA is a stochastic general search method competent of measuring the optimal number of hidden layers and nodes, selecting appropriate feature subsets, the rate of learning

---

<sup>99</sup>Bidyadhar Subudhi and Debashinsha Jena. "A Differential Evolution basedneural network approach to non-linear system identification", *Applied SoftComputing*, Vol. 11(1), pp. 861-871, 2011.

<sup>100</sup>Yu, Y., Schell, M.C. and Zhang, J.B.Y. "Decision theoretic steering andgenetic algorithm optimization: application to stereotactic radiosurgerytreatment planning", *Medical Physics*, Vol. 24(11), pp. 1742–1750., 1997.

<sup>101</sup>Dybowski, R., Weller, P., Chang, R.and Gant, V. "Prediction of outcome inthe critically ill using an artificial neural network synthesized by a geneticalgorithm", *The Lancet Oncology*, Vol. 52(4), pp. 281–286, 1999.

<sup>102</sup>Handels, H., Th, R.O., Kreusch, J., Wolff, H.H.and Poppl, S.J. "Featureselection for optimized skin tumor recognition using genetic algorithms",*Artificial Intelligence in Medicine*,Vol. 16, pp. 283–297, 1999.

<sup>103</sup>Heckerling, P.S., Gerber, B.S., Tape, T.G.and Wigton, R.S. "Use of geneticalgorithms for neural networks to predict community-acquired pneumonia",*Artificial Intelligence in Medicine*, Vol. 30, pp. 71–84, 2004.

<sup>104</sup>Montani, S., Bellazzi, R., Porinale, L.and Stefanelli, M. "A multi-modalreasoning methodology for managing IDDM patients," *International Journalof Medical Informatics*, Vol. 58–59, pp. 243–256, 2000.

along and the momentum coefficient (Sexton et. al., 1998)<sup>105</sup> (Brill et. al., 1992)<sup>106</sup>(JihoonYang et. al., 1998)<sup>107</sup>. In the past, the hybrid GAANN has been employed in varied applications. GA has been widely utilized to discover optimal hidden-layer architectures, connectivity and training parameters (rate of learning and momentum factor) for ANN for estimating community-acquired pneumonia amongst patients with respiratory ailments (Paul et. al., 2004)<sup>108</sup>. GA has been extensively utilized to initialize and optimize the relational weight of ANN. To enhance the performance, ANN was applied onto a medical predicament for predicting stroke disease (Shanti et. al., 2009)<sup>109</sup>.

(Yao and Liu 1998)<sup>110</sup> proposed evolutionary feed forward neural network consisting of neuro-genetic approach for optimization of a trading agent. It is established that by utilizing this technique it is feasible to extract meaningful and consistent models from a collection of popular scientific indicators with the help of evolutionary algorithms together with artificial neural networks.

(Shahrilet al.2012)<sup>111</sup> proposed a hybrid multilayer feed forward neural network technique for estimating the results from a grid-connected

<sup>105</sup>Sexton, R.S., Dorsey, R.E. and Johnson, J.D. "Toward globaloptimization of neural networks: A comparison of the genetic algorithm andback propagation", *Decision Support Syst.* Vol. 22,pp. 171–185, 1998.

<sup>106</sup>Brill, F. Brown, D.and Martin, W. "Fast Genetic Selection of Features forNeural Network Classifiers", *IEEE Transactions on Neural Networks*,Vol.3(2), pp. 324-328, 1992.

<sup>107</sup>Jihoon Yang, Vasant, G. Honavar, "Feature Subset Selection Using aGenetic Algorithm", *Trans on IEEE Intelligent Systems*, Vol. 13(2), 1998.

<sup>108</sup>H. Paul S.G., Ben, S.T., Thomas, G.W. and Robert, S. "Use of geneticalgorithms for neural networks to predict community-acquiredpneumonia", *Artificial Intelligence in Medicine*, Vol. 30(1), pp.71-84,2004.

<sup>109</sup>Shanti, D., Sahoo, G.and Saravanan, N. "Evolving Connection Weights ofANN using GA with application to the Prediction of Stroke Disease",*International Journal of Soft Computing*, Vol. 4(2):pp. 95-102, 2009.

<sup>110</sup>Xin Yao and Yong Liu. "A New Evolutionary System for EvolvingArtificial Neural Network", *IEEE Transactions on Neural Networks*,Vol.8(3), pp. 694-713, 1997.

<sup>111</sup>Shahril Irwan Sulaiman,Titik Khawa Abdul Rahman and Ismail Musirin. "AGenetic Algorithm-Based Hybrid Multilayer Feed forward Neural Networkfor Predicting Grid-Connected Photovoltaic System

photovoltaic system. The quantity of neurons in the hidden layer, the rate of learning rate, the momentum rate, the type of activation function and the learning algorithm can all be optimized using the Genetic algorithm.

(Jan Karwowski et al. 2013)<sup>112</sup> deployed the Particle Swarm Optimization algorithm to the training process of an ANN on the problem of localizing a mobile GSM network terminal inside a building. They demonstrated that the PSO algorithm could be successfully applied as a preliminary training algorithm for multilayer perceptron for both problems related to regression and classification.

(Kuok King Kuok et al. 2009)<sup>113</sup> visualized and designed the ANN equipped with back propagation algorithm to standardize the rainfall runoff relationship precisely, exclusively using just the rainfall and runoff data. Nevertheless, ANN rate of convergence was found to be reasonably slow and being trapped at the local minima. This PSO-optimized FFNN was deployed onto mock-up the hourly rainfall-runoff association for Bed up Basin. The optimal configuration of PSONN could successfully simulate the current runoff accurately with the relevant and adequate input data of the current rainfall, antecedent rainfall and antecedent runoff.

---

Output", *Proceedings of 4th International Conference on Machine Learning and Computing*, Vol.25,pp. 147-150, 2012.

<sup>112</sup>Jan Karwowski, Michał Okulewicz, Jarosław Legierski,"Application ofParticle Swarm Optimization Algorithm to Neural Network Training Processin the Localization of the Mobile Terminal", *Engineering Applications of Neural Networks Communications in Computer and Information Science*,Vol. 383, pp. 122-131, 2013.

<sup>113</sup>Kuok King Kuok, Sobri Harun and Siti Mariyam Shamsuddin," ParticleSwarm Optimization Feed forward Neural Network for Hourly RainfallrunoffModeling in Bedup Basin, Malaysia" *International Journal of Civil & Environmental Engineering*, Vol. 9(10), pp. 9-14, 2009.

(Avci et. al., 2009)<sup>114</sup> have devised an expert diagnostic system for analysis of the Doppler signals produced during the heart valve diseases based on the pattern recognition. Their study entails the extraction of features from deliberate Doppler signal waveforms near the heart valve utilizing the Doppler Ultrasound Technique. The Short Term Fourier Transform and the Wavelet Transform techniques are utilized to feature extract from within the Doppler signals on the time–frequency domain and Wavelet entropy technique is deployed to these extracted features. For categorization of extracted features the authors have made use of the back-propagation neural network.

(Kukar et. al., 1999)<sup>115</sup> have put efforts on the enhancement of the diagnosis of Ischaemic heart disease employing machine learning. Ischaemic heart disease is for the most part, the foremost cause of mortality worldwide; as such enhancements and rationalization of diagnostic procedures would be very helpful.

(Rao et. al., 2007)<sup>116</sup> have anticipated an artificial intelligent system (LungCAD) that assists in the Lung cancer identification. They have employed a classification algorithm for identifying solid pulmonary nodules from the studies of CT thorax.

---

<sup>114</sup> Avci, Engin and Ibrahim Turkoglu, "An Intelligent Diagnosis System Based On Principle Component Analysis And ANFIS For The Heart Valve Diseases", Expert Systems With Applications, 36 (2009), 2873-2878 <https://doi.org/10.1016/j.eswa.2008.01.030>

<sup>115</sup> Kukar, Matjaž, et al. "Analysing and improving the diagnosis of ischaemic heart disease with machine learning." Artificial intelligence in medicine 16.1 (1999): 25-50.

<sup>116</sup> Rao, R. B., Bi, J., Fung, G., Salganicoff, M., Obuchowski, N., & Naidich, D. (2007, August). LungCAD: a clinically approved, machine learning system for lung cancer detection. In Proceedings of the 13th ACM SIGKDD international conference on Knowledge discovery and data mining (pp. 1033-1037). ACM.

(Kodaz et. al., 2009)<sup>117</sup> have suggested a medical application of a novel artificial immune system which reduces the spending of considering all attributes for computing Euclidean distance in shape-space representation used by several artificial immune systems. This application is known as the Information Gain Based Artificial Immune Recognition System (IGAIRS).

(Polat et. al., 2007)<sup>118</sup> have suggested yet another hybrid machine learning technique for diagnosis of thyroid disease making use of classification technique that involves fuzzy weighted pre-processing.

(Vander Gaag et. al., 1992)<sup>119</sup> devised a decision-support system for patient specific selection of therapies pertaining to oesophageal cancer. This system forecasts the accurate stage of cancer, which assists the oncologist to begin with the precise treatment plan for the patient.

(Ye HQ et. al., 2003)<sup>120</sup> have assessed the manifested profiles of Hepatocellular Carcinoma (HCC) samples having or without intra-hepatic metastases. With the help of a well administered machine-learning algorithm, the authors produced a molecular signature, for the first time ever, that could categorize and classify metastatic HCC patients and

---

<sup>117</sup> Kodaz, Halife, et al. "Medical application of information gain based artificial immune recognition system (AIRS): Diagnosis of thyroid disease." *Expert Systems with Applications* 36.2 (2009): 3086-3092.

<sup>118</sup> Polat, Kemal, Seral Şahan, and Salih Güneş. "A novel hybrid method based on artificial immune recognition system (AIRS) with fuzzy weighted pre-processing for thyroid disease diagnosis." *Expert systems with Applications* 32.4 (2007): 1141- 1147.

<sup>119</sup><sup>119</sup> Van der Gaag, Linda C., et al. "Probabilities for a probabilistic network: a case study in esophageal cancer." *Artificial Intelligence in medicine* 25.2 (2002): 123-148.

<sup>120</sup> Ye, Q. H., Qin, L. X., Forques, M., He, P., Kim, J. W., Peng, A. C., ... & Ma, Z. C. (2003). Predicting hepatitis B virus-positive metastatic hepatocellular carcinomas using gene expression profiling and supervised machine learning. *Nature medicine*, 9(4), 416-423.

recognized genes that were relevant to metastasis and patient's life endurance.

(Elif et. al., 2010)<sup>121</sup> proposed an automatic diagnostic system for diabetes, making use of systems with adaptive neuro-fuzzy inference that had a new approach based on the Adaptive Neuro-Fuzzy Inference System (ANFIS).

(Sarwar et. al., 2015)<sup>122</sup> demonstrated a new hybrid ensemble technique i.e. the cumulative ensemble of all ensemble methods for enhancing the predictive outputs from the Artificial intelligence based system for screening of cervical cancer by categorization and classification of Pap smear images. With the help of such a method, the classification power of individual algorithms are combined together to achieve superior classification accuracy. Additionally, they also offered a comparative analysis of a variety of artificial intelligence based algorithms for screening of cervical cancer.

(Sharpe PK et. al., 2009)<sup>123</sup> studied two different classes of artificial neural network architectures and assessed their strength in identifying the thyroid disease. The authors developed a back propagation algorithm and learning vector quantization through the multilayer perceptron.

---

<sup>121</sup> Elif Derya Ubeyli, "Automatic diagnosis of diabetes using adaptive neuro-fuzzy inference systems", Expert systems, Vol. 27; Issue 4; Sept 2010; pages: 259-266, doi: 10.1111/j.1468-0394.2010.00527.x

<sup>122</sup> Sarwar, Abid, Vinod Sharma, and Rajeev Gupta. "Hybrid ensemble learning technique for screening of cervical cancer using Papanicolaou smear image analysis." Personalized Medicine Universe 4 (2015): 54-62.

<sup>123</sup> Sharpe PK, Solberg HE, Rootwelt K, Yearworth M. Artificial neural networks in diagnosis of thyroid function from in vitro laboratory tests. Clinical Chemistry. 2009; 39:2248-53.

(Quintana et al., 2012)<sup>124</sup> suggested substantiation that Artificial Neural Networks could be a helpful tool for the investigation of Neuropsychological profiles associated with the clinical syndromes.

(Hachesu et al., 2013)<sup>125</sup> have deployed the Decision Tree, Neural Networks, and SVM to identify and predict the length of stay of cardiac patients.

(Williams et. al., 2013)<sup>126</sup> investigated the differentiation of MCI from AD, Naïve Bayes, SVM, NN, and furthermore the Decision Tree (DT) have been employed for feature selection and Naïve Bayes has been utilized as the base classifier. In their investigations, Naïve Bayes and DT have given superior results as compared to SVM.

(Gupta Anamika et. al., 2005)<sup>127</sup> analysed the medical diagnostic data with the help of classification rules in data mining and context reduction in formal concept analysis. The redundancies can be found among the different medical examination tests used in diagnosis of a disease, using this method.

---

<sup>124</sup> Quintana. M., Guàrdia. J., Sánchez-Benavides. G., Aguilar.M., Molinuevo. J.L., Robles. A., Barquero. M.S., Antúnez. C., Martínez-Parra. C., FrankGarcía. A.and Fernández. M. (2012) —Using artificial neural networks in clinical neuropsychology: High performance in mild cognitive impairment and Alzheimer's disease, Journal of clinical and experimental neuropsychology 34(2), 195-208.

<sup>125</sup> Hachesu. P.R., Ahmadi. M., Alizadeh. S.and Sadoughi. F. (2013) —Use of data mining techniques to determine and predict length of stay of cardiac patients||, Healthcare informatics research 19(2), 121-129.

<sup>126</sup> Williams. J.A., Weakley. A., Cook. D.J. and Schmitter-Edgecombe. M. (2013) —Machine learning techniques for diagnostic differentiation of mild cognitive impairment and Dementia||, Workshops at the Twenty-Seventh AAAI Conference on Artificial Intelligence.

<sup>127</sup> Anamika Gupta and Naveen Kumar,"Analysis of Medical Data using Data Mining and Formal Concept Analysis", World Academy of Science, Engineering and Technology 11 2005

(Saraee, M., and J. Keane, 2007)<sup>128</sup> suggested a method called T3 which was a decision tree classifier for constructing accurate descriptive and predictive models based on categorization of past medical data.

(Yadav Geeta et. al., 2011)<sup>129</sup> conferred about the application of Data Mining Classifier techniques viz. statistical classifier, tree classifier and support vector machine classifier applied on the symptoms of the speech articulation difficulty during the Parkinson's disease to determine and predict the Parkinson's disease.

(Maroco et. al., 2011)<sup>130</sup> evaluated the effectiveness of machine learning techniques with the sophisticated statistical methods in the diagnosis of Dementia using Neuropsychological data. The machine learning classifiers employed in the study are Random Forest, Support Vector Machine, Artificial Neural Networks and statistical methods such as Linear Discriminant Analysis, Neural Networks, Support Vector Machine, Random Forest and Decision Tree Classifiers.

(Hanirex D K et. al., 2013)<sup>131</sup> conceived a multi-classification approach for diagnosing the thyroid disease. It comprises of tracking and step grading. It had given way to an innovative multilayer thyroid detection system for higher competence and correctly predicting the disease.

---

<sup>128</sup> Saraee, M., and J. Keane, 2007, "Using T3, an improved decision tree classifier, for mining stroke-related medical data", Methods of information in medicine vol. 46, no. 5, pp. 523-529.

<sup>129</sup> Yadav, Geeta, Yugal Kumar, and Gadadhar Sahoo, 2011, "Predication of Parkinson's disease using data mining methods: A comparative analysis of tree, statistical, and support vector machine classifiers", Indian journal of medical sciences 65, no. 6, pp. 231-242.

<sup>130</sup> Maroco. D., Silva. A., Rodrigues. M., Guerreiro. I., Santana, and de Mendonça. A. (2011) —Data mining methods in the prediction of Dementia: a real-data comparison of the accuracy, sensitivity and specificity of linear discriminant analysis, logistic regression, neural networks, support vector machines, classification trees and random forests, BMC Research Notes 4(1), 299.

<sup>131</sup> Hanirex DK, Kaliyamurthie KP. Multi-classification approach for detecting thyroid attacks. 2013.

(Kalle et. al., 2006)<sup>132</sup> The Logical Similarity Measure was used for the diagnosis of liver, thyroid, diabetes and cancer. Evaluation between neural network and evaluation of support vector machine and artificial neural network algorithms have been used for the thyroid disease diagnosis.

(D Kerana et. al., 2013)<sup>133</sup> examined a multi-layer thyroid detection system that comprised of two stages for attacked detection and classification. The experimental outcomes depicted that the developed model can result in superior prediction than other models.

(E. Zoulias et. al.)<sup>134</sup> suggested a novel classifier technique premised on Decision Trees and thyroid malignancy diagnosis. The objective of the study was in two phases (a) to establish a classification scheme for medical applications and (b) to corroborate the FNA assessment. Previously the comparative analysis using several options of splitting criteria showed the marginal superiority of the proposed algorithm. Later on it was established through its by and large classification precision compared with the FNA precision in discerning malignant cases from the non-malignant ones with respect to the established diagnosis.

---

<sup>132</sup> Kalle Saastamoinen and Jaakko Ketola, Medical Data Classification using Logical Similarity Based Measures. In Proceedings of IEEE 2006.

<sup>133</sup> D.Kerana Hanirex and DR.K.P.Kaliyamurthie, —Multi-classification approach for detecting Thyroid attacks”, Int J Pharm Bio Sci, pp. - 4(3): 1246 – 1251, July 2013.

<sup>134</sup> E. Zoulias,P.A. Asvestas, G.K. Matsopoulos, N. Uzunoglu, S. TseleniBalafouta, H. Gakiopoulou, “A data mining approach for classifying FNA thyroid data||, School of Electrical and Computer Engineering, National Technical University of Athens, Greece. Department of Pathology, Medical School, University of Athens, Greece.

(Alfonso Bastias et. al.,)<sup>135</sup> formulated a machine learning classifier based on AIS for medical diagnosis and scrutinizing the proposed classifier potential. The proposed classifier has a better performance for thyroid gland disease diagnosis.

(Markus Brameier and Wolfgang Banzhaf)<sup>136</sup> Applied the tool of linear genetic programming to various medical diagnostic problems. A proficient algorithm was presented that removed the intron code amongst the linear genetic programs. The outcome of this is a considerable speedup which is particularly fascinating when operating with intricate datasets as they are been encountered in the real-world applications like medical science. Genetic programming (GP) has been formerly devised as an evolutionary technique for procreating programs using expressions from within the functional programming language like LISP<sup>136</sup>. A variation of GP has been proposed, known as linear GP, that uses series of instructions of a crucial programming language. (Markus Brameier and Wolfgang Banzhaf)<sup>136</sup> has demonstrated an efficient algorithm for the discovery of introns within the linear genetic programs. The purging of introns before each fitness assessment results into a noteworthy decrease in runtime. (T.T.Nguyen and D.N. Davis)<sup>137</sup> Neural Networks are widely employed onto a number of domains such as cognitive science, diagnosis and prediction. The decision support system in Medicine has been an extremely growing area of research interest worldwide. Enduring collaborations amongst cardiovascular physicians and computer scientists are probing into

---

<sup>135</sup> Alfonso Bastias, Ph.D., Eleonora Horvath, M.D., Felipe Baesler, Ph.D., and Claudio Silva, M.D., —Predictive model based on neural networks to assist the diagnosis of malignancy of thyroid nodules, Proceedings of the 41st International Conference on Computers & Industrial Engineering.

<sup>136</sup> Markus Brameier, Wolfgang Banzhaf, "A Comparison of Linear Genetic Programming and Neural Networks in Medical Data Mining" Fachbereich Informatik University at Dortmund 44221, Dortmund, GERMANY.

<sup>137</sup> T.T.Nguyen and D.N. Davis, "Predicting Cardio Vascular Risk Using Neural Net Techniques" University of Hull.

some new application areas of neural networks applied in the field of individual patient diagnosis, based on clinical records retrieved from Hull University and Dundee University. (T.T.Nguyen and D.N. Davis)<sup>137</sup> has testified the use of confusion matrix for every classifier to observe the types of errors being committed. A side-by-side evaluation of supervised (MLP/RBF) against unsupervised (SOM) classifiers may facilitate in determining more suitable classifications of patients. There is no golden standard existing in cardiovascular medicine for evaluating the risk of individual patients. At any individual clinical site, there is a lot of inconsistency in the medical data utilized for such purposes for analyzing the history of patients and such data may not always be immediately useable. (Frank Lemke and Johann-Adolf Mueller, 2003)<sup>138</sup> extensively described the clustering of data using Self Organizing Maps (SOM). This technique is an unsupervised neural network that was being devised (T.T. Nguyen et. al.)<sup>139</sup>. Another well accepted feature selection is being utilized in this study. ReliefF algorithms are generic in nature and successful attribute estimators. They are capable of detecting provisional dependency amongst attributes and offer an integrated view on attribute estimation through regression analysis and classification. Additionally, there is a natural interpretation of their attribute estimates. The ReliefF algorithm employed is an element of the WEKA software package.

In the domain of retinal image analysis, the identification of disease is one of the most significant applications. Much stress has been given to this domain since the entire treatment planning is premised on the results of the techniques used in this disease identification. The precision of these

---

<sup>138</sup> Frank Lemke and Johann-Adolf Mueller, "Medical data analysis using selforganizing data miningtechnologies," Systems Analysis Modeling Simulation, Vol. 43 , no. 10 , pp: 1399 - 1408, 2003.

<sup>139</sup> T.T.T.Nguyen and D.N. Davis," Feature Selection and Predicting CardioVascular Risk", University of Hull.

techniques of disease identification should also be considerably high as incorrect identification may lead to serious results. The concision time for the results should also be adequately good in addition to being cost effective. For instance, diseases like Diabetic Retinopathy (DR) are the primary cause of loss of vision and their pervasiveness is set to continuously increase. The abrasions caused due to diabetic retinopathy are similar to the bright lesions caused due to age related macular degeneration. Hence, it is extremely necessary that the lesion types should be classified as they have diverse diagnostic significance and management implications. The pre-scanning of diabetic patients for the advancements of diabetic retinopathy can potentially minimize the risk of blindness in such patients. Presently, premature detection has facilitated laser therapy to be carried out to avert or postpone visual loss and may be used to persuade progress in diabetic control. Therefore, existing techniques of detection and estimation of diabetic retinopathy are non-automated, pricey and involve trained ophthalmologists.

Thus, contemporary techniques with the above stated attributes are extremely necessary for the efficient classification of the retinal pathologies. This research work entails four diverse and closely related eye pathologies such as Central Serous Retinopathy (CSR), Central Retinal Vein Occlusion (CRVO), Choroidal Neo-Vascular Membrane (CNVM) and Non-Proliferative Diabetic Retinopathy (NPDR). These four types are automatically recognized and classified using techniques of Artificial Intelligence (AI). A concise account on these diseases is also being specified. CNVM is the growth of new, abnormal vessels below the retina, the light-sensitive multi-layered tissue that engulfs the eyeball from behind. It can harm the vital retinal layers, trading off its ability to act as an obstruction to the vascular layer known as the choroid, present beneath the

retinal surface. Once diseases like the macular degeneration cause enough damage to the retinal layers, the choroid becomes capable of producing new blood vessels (neo-vascularization) that grow up through these damaged layers and seep out or bleed inside the retina. Once this occurs, the vision can become fuzzy, murky or distorted. One of the major cause of visual loss is found to be Choroidal Neovascularization.

CSR is a visual mutilation, often momentary, typically in one eye. The disarray is distinguished by outflow of leakage of fluid in the central macular region, which results in blurred or distorted vision. A blind or hazy spot in the mid vision is common, along with frequent light flashes. People who require glasses may presume that the haziness caused by CSR is merely a change in their prescription, and are unable to have the condition evaluated by a retinal ophthalmologist. CRVO is expected to be the second most common form of medical condition affecting retinal blood vessels. At present, there is no treatment for CRVO, in which a blood clot decelerates or prevents circulation in a large vein inside the eye's light-sensitive retinal tissue. Decreased retinal circulation may cause the growth of new blood vessels and their leakage, resulting in the swelling of retinal tissues, a frequent reason of vision loss due to CRVO.

NPDR is a progressive type of pathology. Its severity is gauged by the types and number of lesions occurring on the retina. Hence there is a necessity to identify those lesions either for screening DR or for appraising its development. At present, lesion detection is a manual process. Automating this job would largely be in terms of reproducibility and objectivity. Furthermore, if the follow up becomes more widely accepted,

automated methods will be required to substitute physicians in the tedious process of lesion detection.

The 1970s decade saw the development of one of the pioneering research works on Clinical Decision Support Systems (CDSS), to help in the glaucoma diagnosis. The system is popularly known as CASNET (Causal-ASociational NETwork). (Weiss S, Kulikowski C, Amarel S, Safir A, 1978)<sup>140</sup> CASNET uses clinical data for diagnostic purposes. This data includes symptoms informed by the patient, viz. ‘decreased visual acuity’ and ‘ocular pain’. It also involves results of a variety of eye examinations such as, visual acuity, anterior chamber depth, IOP, angle closure, corneal edema and pupil abnormality. (Zhang Z et. al., 2013)<sup>141</sup> An eloquent model of the disease process is employed in logical interpretations of clinical findings for diagnosis of glaucoma by CASNET. The model comprised of a semantic net with weighted links depicting patho-physiological means. It represented some primitive expert systems in the field of medicine. The CASNET framework portrays the wisdom of expert consultants and simulates a range of facets of the clinician’s cognitive processes, close to reality. (Chan et al., 2002)<sup>142</sup> the earliest accomplishment of Support Vector Machines (SVM) for glaucoma diagnosis was reported. (Perumalsamy N et. al., 2007)<sup>143</sup> The Standard Automated Perimetry (SAP), a universal programmed visual field test generated the Clinical data output used in the research study. The authors associated the output of several machine learning algorithms with the output of SAP. Linear and

---

<sup>140</sup> Weiss S, Kulikowski C, Amarel S, Safir A: A model-based method for computer-aided medical decision making. *Artif Intell* 1978, 11:145–72.

<sup>141</sup> Zhang Z, Xu Y, Liu J, Wong DWK, Kwoh CK, Shaw SM, Wong TY: Automatic diagnosis of pathological myopia from heterogeneous biomedical data. *PLoS ONE* 2013, 8(6):e65736.

<sup>142</sup> Chan K, Lee TW, Sample PA, Goldbaum MH, Weinreb RN, Sejnowski TJ: Comparison of machine learning and traditional classifiers in glaucoma diagnosis. *IEEE Trans Biomed Eng* 2002, 49(9):963–974

<sup>143</sup> Perumalsamy N, Prasad N, Sathya S, Ramasamy K: Software for reading and grading diabetic retinopathy: Aravind diabetic retinopathy screening 3.0. *Diabetes Care* 2007, 30(9):2302–2306.

Quadratic Discriminant Analysis (LDA and QDA), Multilayer Perceptron (MLP), SVM, Mixture of Gaussian (MOG), Parzen Window, and Mixture of Generalized Gaussian (MGG) were the primary machine learning algorithms that were incorporated in the study. It was observed that machine-learning-type classifiers demonstrated some superior performance even over the best indices from SAP. In addition the authors also premeditated upon the advantages of using feature selection to further enhance the astuteness of classification with an outlook to reduce testing time by significantly dropping the number of visual field location measurements. (Bizios et al., 2011)<sup>144</sup>undertook a study scrutinizing the data fusion methods and techniques for simple permutations of attributes retrieved from SAP and measures of the Retina Nerve Fibre Layer Thickness (RNFLT) acquired from Optical Coherence Tomography (OCT) for diagnosis of glaucoma by means of Artificial Neural Networks. (Fujita H et. al.)<sup>145</sup> The outcomes depicted that the diagnostic accuracy from a combination of fused SAP and OCT data was much higher than with either of them separately. This was the very initial confirmed study that used fused data for glaucoma diagnosis. A novel study investigated the relationship between the central corneal thickness (CCT), Heidelberg Retina Tomography II (HRTII) structural measurements and IOP with the use of a pioneering non-linear multivariable regression technique, with an intention of outlining the risk variables in future glaucoma progressions. (Barella et al.)<sup>146</sup>have examined the diagnostic efficiency of machine learning classifiers (MLCs) along with random forest (RF) using RNFL

---

<sup>144</sup> Bizios D, Heijl A, Bengtsson B: Integration and fusion of standard automated perimetry and optical coherence tomography data for improved automated glaucoma diagnostics. BMC Ophthalmology 2011, 11(1):20

<sup>145</sup> Fujita H, Uchiyama Y, Nakagawa T, Fukuoka D, Hatanaka Y, Hara T, Lee G, Hayashi Y, Ikeda Y, Gao X, Zhou X: Computer-aided diagnosis: The emerging of three CAD systems induced by Japanese health care needs, Comput Methods Prog Biomed 2008, 92:238–248

<sup>146</sup> World Health Organization: Blinding trachoma fact sheet. 2014

and optic nerve data. It yielded an outcome as 0.877 of area under the ROC value using RF.

(J. B. Siddharth et. al.)<sup>147</sup> Medical Diagnosis using Artificial Neural Networks is currently a very active research area in medicine and it is believed that it will be more widely used in biomedical systems in the next few years. This is primarily because the solution is not restricted to linear form. Neural Networks are ideal in recognizing diseases using scans since there is no need to provide a specific algorithm on how to identify the disease. Neural networks learn by example so the details of how to recognize the disease is not needed.

## **2.2 Artificial Intelligent Techniques in Glaucoma Diagnosis**

Glaucoma-one of the leading cause of non-curable blindness in India, is prevalent in the aged population. (George et. al., 2010)<sup>148</sup> found from a study the population in India above 40 years were affected by glaucoma and the number of such population reported was 11.2 million. The gravity of Glaucoma disease is that the blindness roused by glaucoma is incurable. According to (Mallikarjun et. al., 2013)<sup>149</sup>, the major factors that play an important role as causes of the disease are high intra ocular pressure (IOP), family history, and high blood pressure.

---

<sup>147</sup>J. B. Siddharth Jonathan and K.N. Shruthi, "A Two Tier Neural Inter-Network Based Approach to Medical Diagnosis Using K-Nearest NeighborClassification for Diagnosis Pruning", web page available at <http://infolab.stanford.edu/~jonsid/nimd.pdf>.

<sup>148</sup>George, R& Ve Ramesh, S 2010, 'Glaucoma in India: Estimated Burden of Disease', Journal of Glaucoma, vol.19, no. 6, pp. 391-397.

<sup>149</sup>Mallikarjun, Y, 2013, 'Two molecular mechanisms causing glaucoma found', [Online], <http://www.thehindu.com/scitech/health/two-molecularmechanisms-causing-glaucoma-found/article4902049>.

(Pooja Sharma et. al., 2008)<sup>150</sup> Diagnosis of glaucoma in early stage is essential to prevent perpetual structural damage and permanent vision loss.

(Rajendra et. al., 2011)<sup>151</sup> used superior order texture and spectra attributes for the purpose of diagnosis and detection of glaucoma in patients with diabetes. Sequential Minimal Optimization, Support vector machine, Random-Forest Classifiers and Native Bayesian were employed as supervised classifier. Additionally, Bayesian and random forest classifiers were engaged in this work to discriminate the images of normal state and glaucoma. The authors accomplished a classification accuracy of 91% for the glaucoma detection.

The fractal features were considered for earlier detection of glaucoma in retinal images (Paul et al 2013)<sup>152</sup>. The fractal analysis features were extracted using a box-counting method and a multi fractional Brownian motion method from the retinal image. The fractal analysis metrics were obtained using Wavelet-Fourier Analysis (WFA) and Fast-Fourier Analysis (FFA). Support Vector Machine (SVM) classifier was employed in this task of classifying the developmental stages of glaucoma in diabetic patients. The authors accomplished 88% classification rate for detection of the disease progression.

---

<sup>150</sup>Pooja Sharma, Pamela, A, Sample, Linda, M, Zangwill & Joel S Schuman 2008, ‘Diagnostic Tools for Glaucoma Detection and Management’, Survey Of Ophthalmology, vol.53, no.1, pp.S17- S32.

<sup>151</sup> U. Rajendra Acharya, Sumeet Dua, Xian Du, Vinitha Sree S, and Chua Kuang Chua, “Automated Diagnosis of Glaucoma Using Texture and Higher Order Spectra Features,” IEEE Transactions On InformationTechnology In Biomedicine, Vol. 15, No. 3, May 2011 449-455.

<sup>152</sup>Paul Y. Kim et. Al, “Novel Fractal Feature-Based Multiclass Glaucoma Detection and Progression Prediction”, IEEE Journal of Biomedical and Health Informatics, vol. 17, no. 2, March 2013.

(Stefano et. al., 2014)<sup>153</sup> developed an algorithm for detection of glaucoma in the very initial stages based on Bayesian classifier. The classification of premature glaucoma and cluster data into various stages of disease were determined with the use of Bayesian networks. These clusters were well weighed against k-means and methods of direct knowledge. The authors accomplished sensitivity upto 85% and specificity upto 90%. Clusters were categorized with the help of learning of its structure and metric-independent clustering.

(Kwokleung et. al., 2002)<sup>154</sup> employed machine learning algorithm for diagnosis of the glaucoma disease. The SVM Classifier and the Multilayer Perceptron (MLP) were deployed for determining the decision boundary. The authors assessed the system performance by deploying various classifiers for diagnosis of glaucoma. The algorithm was applied on 25 diverse data sets to demonstrate the high performance as applied by the authors.

(Vermeer et. al., 2006)<sup>155</sup> Laser Polarimetry was used for detecting glaucoma. The authors tested their algorithm on 23 healthy eyes which included conditions like colored noise, incomplete cornea compensation and masked by the blood vessels from the retina. The detection of Glaucoma was done using Morphological operations and an anisotropic filtering technique on the retinal images. The classification results were validated using the probability tests. The proposed

---

<sup>153</sup>Ceccon, Stefano & Garway-Heath, David & Crabb, David & Tucker, Allan. (2014). Exploring Early Glaucoma and the Visual Field Test: Classification and Clustering Using Bayesian Networks. IEEE journal of biomedical and health informatics. 18. 1008-14. 10.1109/JBHI.2013.2289367.

<sup>154</sup> Kwokleung Chan, Pamela A. Sample, Michael H. Goldbaum et al, Using Machine Learning Classifiers to Identify Glaucomatous Change Earlier in Standard Visual Fields, IOVS, August 2002, Vol. 43, No. 8

<sup>155</sup>Vermeer, Koenraad & Vos, F.M. & Lo, Barrick & Zhou, Qienyuan & Lemij, Hans & Vossepoel, Albert & Van Vliet, Lucas. (2006). Modeling of scanning laser polarimetry images of the human retina for progression detection of glaucoma. Medical Imaging, IEEE Transactions on. 25. 517 - 528. 10.1109/TMI.2006.871433.

technique in their research work detected the development of glaucoma which enhanced the specificity and sensitivity.

(Kaur et. al., 2014)<sup>156</sup> could detect glaucoma in diabetic patients by measuring the cup-to-disc ratio of their images of the retina. The initial mathematical morphological operations were used in this task to sense the optic disc and optic cup from the retinal images. The primary contribution of this work was to establish the severity level of glaucoma. The authors noted that CDR value for severe glaucoma was nearly 0.3 and above.

(Foracchia et. al., 2004)<sup>157</sup> proposed a geometrical parametric model, in which the coordinates of the OD center were two of the model parameters. The simulated annealing optimization technique was used to gauge the centerline points in the vessel and consequent vessel directions, presented by any vessel identification procedure. The coordinates of the pixel axial of the center of OD was measured by estimated values. This algorithm was deployed onto 81 retinal images to identify the OD region. By identifying about 79 images, the authors could achieve around 98% classification accuracy.

The component analysis method used by (Goldbaum et.al., 2005)<sup>158</sup> to categorize the area of the cup was more precise as compared to manual threshold analysis method. The Variational Bayesian Independent Component Analysis Mixture Model partitioned the Standard Automated Perimetry (SAP) fields into the most revealing

---

<sup>156</sup>Kaur, H & Kaur, A 2014, Early Stage Glaucoma Detection in Diabetic Patients: A Review,' International Journal of Advanced Research in Computer Science and Software Engineering, vol. 4, pp. 271-274.

<sup>157</sup>Foracchia, M, Grisan, E & Ruggeri, A 2004,Detection of optic disc inretinal images by means of a geometrical model of vessel structure,IEEE Transactions on Medical Imaging, vol. 23, pp. 1189-1195.

<sup>158</sup> Goldbaum, MD 1975, 'STARE Dataset Website', Clemson, SC,Clemson Univ. Available from: <<http://www.ces.clemson.edu>> [25February 2014].

number of clusters. At the same time, the model learnt an optimal number of maximally independent axes for each cluster. The image acquired through morphological processing was then transformed into a binary image. The exact optic cup could be obtained only from the binary image data. The number of white pixels captured from the binary image, determine the actual area of optic cup.

(Cheng et. al., 2013)<sup>159</sup> made use of super pixel classification techniques to detect the optic disc and optic cup for glaucoma diagnosis amongst diabetic patients. The status of the disc, whether optic or non-optic for each super pixel in the retinal image was made possible using the histograms and center surround statistics. The location information integrated with center surround statistics features was also utilized as a feature vector to measure the optic cup. The authors accomplished an average overlapping error of 9.5% in the optic disc and 24.1% in the optic cup segmentation, for the purpose of which, the trained professional manually demarcated the boundaries of the optic disc and optic cup using 650 images.

(Yousefi et. al., 2014)<sup>160</sup> proposed classifier based on machine learning for the categorization of glaucomatous progression with the help of longitudinal series of structural data. The extracted longitudinal data was used to create the longitudinal feature vector. These features were then trained and classified using machine learning classifier into two type viz. progressed or non- progressed retina. Bayesian, Lazy, Meta, and Tree classifiers were used as individual classifiers on the

---

<sup>159</sup> Cheng, J, Jiang Liu, Yanwu Xu & Fengshou Yin 2013, SuperpixelClassification Based Optic Disc and Optic Cup Segmentation forGlaucoma Screening', IEEE Transactions on Medical Imaging, vol. 32, no. 6, pp. 1019-1032.

<sup>160</sup> Yousefi, S, Goldbaum, MH, Balasubramanian, M & Tzyy-Ping Jung 2014, Glaucoma Progression Detection Using Structural Retinal Nerve Fiber Layer Measurements and Functional Visual Field Points', IEEE Transactions on Biomedical Engineering, vol. 61, no. 4, pp. 1143-1154.

retinal image for the classification of glaucoma. Table 2.1 represents few literature review on the studies that involve Glaucoma detection techniques.

**Table 2.1 Literature survey on Glaucoma Detection**

Reference	Method	Advantages	Dis-advantages
Stefano et al (2014)	Bayesian classifier	High segmentation accuracy	Low Sensitivity (85%)
Paul et al (2013)	Support Vector Machine (SVM) classifier	Low computational time	Low classification accuracy (88%)
Cheng et al (2013)	Statistics features	OD and OC boundaries were clearly segmented	High average overlapping error of 9.5%
Rajendra et al (2011)	Bayesian random classifiers and forest	High segmentation accuracy	Low classification accuracy (91%)
Foracchia et al (2004)	Simulated annealing optimization technique	High classification accuracy (98%)	High computational time
Mendonca & Campilho (2006)	Multi-scalemorphological enhancement technique	Vessel center lines were clearly enhanced	Not suitable for low resolution retinal images
Palomera-Perez et al (2010)	Regiongrowing algorithm	Partitioning based parallelism	Low accuracy (92.5 %)

		and low latency	
Marin et al (2011)	Gray level and moment feature based supervised classifier	High contrast difference between vessel and Background	Low sensitivity (70.67%)
Fraz et al (2012)	Ensemble classifier	Suitable for both low and high resolution retinal images	Outputs were not mutually orthogonal
Xiao et al (2013)	Bayesian classifier	Clearly segments vessels from the background pixels	Low sensitivity (75.13%)
Manoj et al (2013)	Feed forward back propagation neural network classifier	Segments vessel lines clearly	High segmentation time
Bansal & Dutta (2013)	Fuzzy algorithm	Fuzzy rules were constructed and high accuracy	Requires high number of fuzzy rules ( $2^n$ rules for n-pixels)
Budai et al (2013)	Frangi algorithm	Low vessel detection computational time	Low accuracy

(Mendonca & Campilho, 2006)<sup>161</sup> suggested an algorithm for vessels segmentation that made use of the vessel center lines followed by the process of vessel filtering. To enhance the contrast of the blood vessels, the Multi Scale Morphological Enhancement Technique was employed. The authors accomplished an accuracy of about 96.33 % in the DRIVE dataset and an accuracy of about 95.79% in the STARE dataset.

(Palomera-Perez et. al., 2010)<sup>162</sup> made use of a region growing algorithm based on feature extraction for blood vessels segmentation. A concept known as the domain partitioning based parallelism was used to cluster the vessels. The authors achieved an accuracy of 92.5 % in the DRIVE dataset and an accuracy of 92.6% in STARE dataset.

(Fraz et. al., 2012)<sup>163</sup> made use of ensemble classifier to stratify the vessels. The ensemble classifier also made use of a feature that used the Gradient Vector Field and Gabor Transform constructed specially for this purpose. The authors could accomplish a sensitivity of about 72.62% along with specificity of 97.64% and accuracy of 95.11% on STARE dataset whereas a sensitivity of 74.06%, specificity of 98.07% and an accuracy of 94.8% on the DRIVE dataset.

---

<sup>161</sup>Mendonca, AM & Campilho, A 2006, 'Segmentation of Retinal bloodvessels by combining the detection of centre lines and morphologicalreconstruction', IEEE Transactions on Medical Imaging, vol. 25, no. 9,pp. 1200-1213.

<sup>162</sup>Palomera-Perez, MA, Martinez-Perez, ME, Benitez-Perez, H & Ortega-Arjona, JL 2010, 'Parallel multiscale feature extraction andregion growing: Application in retinal blood vessel detection', IEEE Transactions on Information Technology in Biomedicine, vol. 14,no. 2, pp. 500-506.

<sup>163</sup> Fraz, MM, Remagnino, P, Hoppe, A, Uyyanonvara, B, Rudnicka, AR, Owen, CG & Barman, SA 2012, 'An ensemble classification-based approach applied to retinal blood vessel segmentation', IEEE Transactions on Biomedical Engineering, vol. 59, pp. 2538-2548.

(Manoj et. al., 2013)<sup>164</sup> employed the Feed Forward Back Propagation Neural Network Classifier for the segmentation of the blood vessels. The attributes such as the line strength vectors, gradient vector regions and morphological transformation vectors were extracted from the images of the retina.

(Marin et. al., 2011)<sup>165</sup> employed the Gray Level and Moment feature based supervised classifier for segmentation of the blood vessels.

(Xiao et. al., 2013)<sup>166</sup> elucidated a spatial Bayesian classifier based on constraint for blood vessel segmentation. The customized level set approach was utilized to outline the boundaries of the vessels from within the retinal images.

(Budai et. al., 2013)<sup>167</sup> designed the extended edition of the Frangi Algorithm that was employed in the segmentation of blood vessel tree from the retina.

(Joel Koh et. al., 2013)<sup>168</sup> devised a highly automated system for glaucoma detection using features based on Discrete Wavelet Transform (DWT). The effort depends on the information

---

<sup>164</sup> Manoj, S, Muralidharan & Sandeep, PM 2013, 'Neural network based classifier for retinal blood vessel segmentation', International Journal of Recent Trends in Electrical & Electronics Engineering, vol. 3, no. 1, pp. 44-53.

<sup>165</sup> Marin, D , Aquino, A, Emilio Gegundez-Arias, M & Bravo, JM 2011,'A new supervised method for blood vessel segmentation in retinal images by using gray-level and moment invariants-based features', IEEE Transactions on Medical Imaging, vol. 30, pp. 146-158.

<sup>166</sup> Xiao, Z, Adel, M & Bourennane, S 2013, 'Bayesian method with spatial constraint for retinal vessel segmentation', Computational and Mathematical Methods in Medicine, vol. 13, no. 401413, pp. 1-9.

<sup>167</sup> Budai, A, Bock, R, Maier, A, Hornegger, J & Michelson, G 2013, 'Robust vessel segmentation in fundus images', International Journal of Biomedical Imaging, vol. 20, pp. 1-11.

<sup>168</sup> Joel EW Koh, Muthu Rama Krishnan Mookiah & Nahrizul Adib Kadri 2013, 'Application of Multiresolution Analysis for the Detection of Glaucoma.' Journal of Medical Imaging and Health Informatics, vol. 3, no. 1, pp.1-8.

content in the relative entropy and energy based features.

(Jian Wang et. al., 2011)<sup>169</sup> deliberate upon Feed Forward Neural Networks with Back Propagation (BP) training methods that have been extensively applied in various areas of scientific investigation and technological applications. The Back Propagation Algorithm tries to mitigate the least squared error of the objective part, described by the inconsistency amongst the actual network results and the preferred outputs.

(Yuji Hatanaka et. al., 2012)<sup>170</sup> examined Gaussian, linear, polynomial, and sigmoid functions as forms of kernel functions of SVM for glaucoma diagnosis.

(Katarzyna Stapor et. al., 2006)<sup>171</sup> has devised based glaucoma diagnosis based on segmentation and the classification is implemented using SVM.

(Vidotti et. al.)<sup>172</sup> from the research, proved that MLCs using RNFL thickness measurements captured with SD-OCT show superior diagnostic accuracy.

---

<sup>169</sup>Jian Wang, Wei Wu & Jacek M Zurada 2011, 'Deterministic convergence of conjugate gradient method for feedforward neural networks', Neurocomputing, vol.74 , no14-15 , pp.2368-2376

<sup>170</sup>Yuji Hatanaka, Chisako Muramatsu, Akira Sawada Takeshi Hara, Tetsuya Yamamoto & Hiroshi Fujita2012, 'Glaucoma Risk Assessment Based on Clinical Data and Automated Nerve Fiber Layer Defects Detection', 34th Annual International Conference of the IEEE EMBS,San Diego, California USA, pp.5963-5966.

<sup>171</sup>Katarzyna Stapor, Adrian Brueckner & Adam Switonski 2006, 'Mathematical Morphology and Support Vector Machines for Diagnosis of Glaucoma on Fundus Eye Images', Computer Vision and Graphics, vol.32, pp.888–893.

<sup>172</sup>Vidotti VG, Costa VP, Silva FR, et al. Sensitivity and specificity of machine learning classifiers and spectral domain OCT for the diagnosis of glaucoma. European Journal of Ophthalmology. 2012

(Huang et. al., 1991)<sup>173</sup> examined three different MLCs with the purpose of improving the accuracy of glaucoma diagnosis based on RNFL and ONH data captured with TD-OCT.

(Townsend et. al., 2008)<sup>174</sup> intended to review the performance of seven different classifiers trained on HRTIII attributes. They inferred that MLC can offer a considerable enhancement in HRTIII diagnostic supremacy over single parameters and GPS.

(Brigatti et. al., 1996)<sup>175</sup> and (Uchida et. al., 1996)<sup>176</sup> the different Optic Nerve Head Imaging Analyzer Parameters were used to train the Artificial Neural Networks for classifying the eyes as either glaucomatous or healthy in the context of the Confocal Scanning Laser Ophthalmoscopy.

(Lietman et. al., 1999)<sup>177</sup> has formulated a Feed-Forward Neural Network with a single layer that was hidden and was trained to identify visual field defects earlier collected in a glaucoma study with longitudinal follow-up, and subsequently tested on fields taken from the same study but not utilized during the training.

---

<sup>173</sup> Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science*. 1991;254(5035):1178–1181.

<sup>174</sup>Townsend KA, Wollstein G, Danks D, et al. Heidelberg Retina Tomograph 3 machine learning classifiers for glaucoma detection. *British Journal of Ophthalmology*. 2008;92(6):814–818.

<sup>175</sup>Brigatti, L., Hoffman, D. & Caprioli, J. (1996). Neural networks to identify glaucoma with structural and functional measurements, *Am J Ophthalmol* 121(5): 511–21.

<sup>176</sup>Uchida, H., Brigatti, L. & Caprioli, J. (1996). Detection of structural damage from glaucoma with confocal laser image analysis, *Invest Ophthalmol Vis Sci* 37(12): 2393–401.

<sup>177</sup>Lietman, T., Eng, J., Katz, J. & Quigley, H. A. (1999). Neural networks for visual field analysis: how do they compare with other algorithms?, *J Glaucoma* 8(1): 77–80.

(Bowd et. al., 2004)<sup>178</sup> made use of the parameters from the Optic Disc Topography of the Heidelberg Retina Tomograph. The parameters were used for neural network methods to enhance the distinction between eyes with glaucoma and without it. They trained neural networks, with international and regional parameters Heidelberg Retina Tomograph that were used as input, indicated improvement on earlier proposed attributes of Glaucoma. The use of Artificial Neural Networks was to determine the Glaucoma Stages discerning between glaucomatous and non-glaucomatous eyes.

(Rumelhart & McClelland, 1986)<sup>179</sup> demonstrated the Back Propagation Learning algorithm that can be considered the keystone of the ANNs contemporary history. ANN models have been exhaustively studied and deployed in recent times in the look forward to of reaching human performance in different areas.

(Asaoka et. al., 2018)<sup>180</sup> in addition, researched on the Fundus photography-based Deep Learning algorithm for the identification of Glaucoma, notwithstanding the smaller number of images. The researchers revealed that the algorithm could detect Glaucoma from the images as precisely as or better than the ones that can be diagnosed by an ophthalmologist, with 0.954 of AUC, 95.0% of sensitivity, and 70.3% of specificity. The fact that the algorithm gave excellent reasons even in high myopia settings was quite

---

<sup>178</sup>Bowd, C., Zangwill, L. M., Medeiros, F. A., Hao, J., Chan, K., Lee, T. W., Sejnowski, T. J., Goldbaum, M. H., Sample, P. A., Crowston, J. G. & Weinreb, R. N. (2004). Confocal scanning laser ophthalmoscopy classifiers and stereophotograph evaluation for prediction of visual field abnormalities in glaucoma-suspect eyes, *Invest Ophthalmol Vis Sci* 45(7): 2255–62.

<sup>179</sup>Rumelhart, D. & McClelland, J. (1986). Parallel distributed processing, MIT Press, Cambridge, MA.

<sup>180</sup>Asaoka R, Shibata N, Murata H, Tanito M. Construction of a deep learning algorithm to automatically diagnose glaucoma using a fundus photograph. Presented at: Association for Research in Vision and Ophthalmology (ARVO) 2018 Annual Conference; April 29 – May 3, 2018; Honolulu, HI. <http://www.arvo.org/annual-meeting/program/online-planner>. Accessed June 17, 2018.

encouraging.

(Seo et. al., 2018)<sup>181</sup> demonstrated the outcomes of a study assessing the diagnostic precision of optic disc image assessment by Glaucoma specialist as against an automated, deep learning-based decision support tool.

(Zangwill et. al., )<sup>182</sup> could train a deep learning model premised on Scanning Laser Ophthalmoscopy (SLO) images and RNFL thickness maps extorted from spectral-domain OCT cube acquisitions from among a group of 375 subjects (538 eyes) having glaucomatous visual field damage as against 254 subjects (444 eyes) not having any damage of the visual field. The researchers discovered that for sensing a confirmed visual field damage from OCT images, an integrated SLO and RNFL thickness deep-learning model could accomplish the utmost AUC (0.92) from the 3 models analyzed and tested (SLO only model with AUC=0.81, and RNFL Thickness only model with AUC=0.85).

(Wen et. al., )<sup>183</sup> The authors, to know whether a future 24-2 HVF finding can be forecasted by using successive Humphrey 24-2 visual fields (HVF) between 1998 and 2018 from an organizational

---

<sup>181</sup>Seo E, Jaccard N, Trikha S, Pasquale LR, Song BJ. Automated evaluation of optic disc images for manifest glaucoma detection using a deep-learning, neural network-based algorithm. Presented at: Association for Research in Vision and Ophthalmology (ARVO) 2018 Annual Conference; April 29 – May 3, 2018; Honolulu, HI. <http://www.arvo.org/annual-meeting/program/online-planner>. Accessed June 17, 2018.

<sup>182</sup>Zangwill LM, Christopher M, Belghith A, Bowd C, Goldbaum MH, Weinreb RN. Deep learning approaches can detect glaucomatous functional loss better than standard SD-OCT retinal nerve fiber layer thickness. Presented at: Association for Research in Vision and Ophthalmology (ARVO) 2018 Annual Conference; April 29 – May 3, 2018; Honolulu, HI. <http://www.arvo.org/annual-meeting/program/online-planner>. Accessed June 17, 2018.

<sup>183</sup>Wen JC, Lee CS, Keane PA, et al. Forecasting future Humphrey visual fields using deep learning. Preprint. <https://www.biorxiv.org/content/early/2018/04/02/293621.article-info>. Accessed June 17, 2018.

database, these researchers trained a deep-learning Artificial Neural Network. A total number of 32,443 visual fields of type 24-2 HVFs were extracted, yielding more than 1.7 million perimetry points with hundredth-decimal correctness. The study group discovered that the deep-learning models effectively envisaged progressive loss of visual-field in Glaucomatous eyes by about 5.5 years earlier than the occurrence of the actual condition, with a positive correlation of 0.92 between the mean derivations based on model predictions as against and actual mean deviations on prospective and futuristic HVFs.

## 2.3 Research Gap

Glaucoma, an eye illnesses is prevailing in growing old populace. It causes an irreversible lack of vision. (Mdahulika J. et. al., 2015)<sup>184</sup> There is a distinct need of computer aided answers for analysis functions. The growing situation for the remedy of this disease is increasing looking at the propagation of glaucoma cases in past few recent years. Its miles majorly massive in urban ageing populace. (R. Bock et. al., 2010)<sup>185</sup> (G. Joshi et. al., 2011)<sup>186</sup> according to an estimation, seventy nine million individuals all around the international could be laid low with glaucoma via 12 months 2020. (R. Saxena et. al., 2013)<sup>187</sup> within a decade, the estimation shows a 33% boom in the number of humans affected by glaucoma. As a result, screening for

---

<sup>184</sup>Madhulika Jain, "A Hierarchical System Design for detection of Glaucoma from Color Fundus Images", Thesis for MS by Research in Electronics & Communication, International Institute of Information Technology Hyderabad - 500 032, July 2015.

<sup>185</sup>R. Bock, J. Meier, L. G. Nyl, and G. Michelson. Glaucoma risk index: automated glaucoma detection from color fundus images. *Medical Image Analysis*, 14(3):471–481, 2010.

<sup>186</sup>G. Joshi, J.Sivaswamy, and S. Krishnadas. Optic disk and cup segmentation from monocular colour retinal images for glaucoma assessment. *IEEE Transactions on Medical Imaging*, 30(6):1192–1205, 2011.

<sup>187</sup>R. Saxena, D. Singh, and P. Vashist. Glaucoma: An emerging peril. *Indian Journal of Community Medicine*, 38(3):135–137, 2013.

glaucoma is essential, because of the nature, for the early detection and allowing powerful remedy in early stages to save from everlasting blindness.

(High Eye Pressure and Glaucoma [online])<sup>188</sup> prognosis of glaucoma is dependent on numerous findings which includes IOP (if IOP > 21 mm Hg [17], it is considered as a suspicious case for glaucoma), optical nerve cupping and visual view loss. (Diagnosis of Glaucoma, [online])<sup>189</sup> Detection and analysis of Glaucoma is done thru numerous exams inclusive of Tonometry, Ophthalmoscopy, Perimetry, OCT, Gonioscopy and Pachymetry.

The logical taking into consideration clinical practitioner involves quite a few subjective selection making and its complexity makes conventional quantitative strategies of evaluation beside the point. The PC based diagnostic equipment and information base certainly enables for early prognosis of illnesses. (Smita S. et. al., 2012)<sup>190</sup> and (high Eye stress and Glaucoma [online])<sup>189</sup> one zero five the clever choice making systems can correctly cope with each the uncertainty and imprecision. (Jiang F. et. al., 2017)<sup>191</sup> AI can honestly help clinicians to make better medical decisions or it may update human judgment in positive useful regions of healthcare. (Murdoch TB., Detsky AS., 2013)<sup>192</sup> (Kolker E et. al.,

---

<sup>188</sup>"High Eye Pressure and Glaucoma", accessed on, <http://www.glaucoma.org/gleams/high-eye-pressure-andglaucoma.php6>

<sup>189</sup>DIAGNOSING GLAUCOMA. [Online]. Available:  
[https://www.glaucomafoundation.org/diagnosing\\_and\\_treating\\_glaucoma.htm](https://www.glaucomafoundation.org/diagnosing_and_treating_glaucoma.htm).

<sup>190</sup>Smita Sushil Sikchi, Sushil Sikchi, M. S. Ali, "Artificial Intelligence in Medical Diagnosis", International Journal of Applied Engineering Research, ISSN 0973-4562 Vol.7 No.11 (2012).

<sup>191</sup>Jiang F, Jiang Y, Zhi H, et al. Artificial intelligence in healthcare: past, present and future. Stroke and Vascular Neurology 2017; 0: e000101.doi:10.1136/svn-2017-000101.

<sup>192</sup>Murdoch TB, Detsky AS. The inevitable application of big data to health care. JAMA 2013;309:1351–2.doi:10.1001/jama.2013.393.

2016)<sup>193</sup>(Dilsizian SE, Siegel EL. et. al., 2014)<sup>194</sup> Guided via relevant questions referring to various medical parameters, powerful AI techniques can monitor hidden records from the big quantity of statistics, which performs a key function in helping clinical selection making.

The last few decades, a long time have seen a proliferation of shrewd structures for prognosis, advising and associated programs. Shrewd systems for analysis have been used in an expansion of domain names: plant disease prognosis, crop control hassle diagnosis, credit score assessment and authorization, monetary assessment, identification of software program and hardware issues and integrated circuit screw ups, troubleshooting of electrical, mechanical and digital gadget, scientific prognosis, fault-detection in nuclear electricity structures, oil exploration, prospecting, seismic research, etc. in spite of the notable kind of tactics and technology used inside the design of such structures, they all deal with the identical pattern type hassle: the undertaking of assigning a given enter (e.g., a pattern, picture, set of observations, etc.) to some category (or magnificence). (Dean T. et. al., 1995)<sup>195</sup> (Durkin J. et. al., 1994)<sup>196</sup> (Ginsberg M., 1993)<sup>197</sup> (Russell S. et. al., 1995)<sup>198</sup> prognosis structures classify the found signs as being caused by some precise problem

---

<sup>193</sup>Kolker E, Özdemir V, Kolker E. How Healthcare can refocus on its Super-Customers (Patients, n =1) and Customers (Doctors and Nurses) by Leveraging Lessons from Amazon, Uber, and Watson. OMICS 2016;20:329–33.doi:10.1089/omi.2016.0077.

<sup>194</sup>Dilsizian SE, Siegel EL. Artificial intelligence in medicine and cardiac imaging: harnessing big data and advanced computing to provide personalized medical diagnosis and treatment. Curr Cardiol Rep 2014;16:441.doi:10.1007/s11886-013-0441-8.

<sup>195</sup>Dean T., Allen J., & Aloimonos, Y. "Artificial Intelligence - Theory and Practice", Redwood City, CA: Benjamin/Cummings, 1995.

<sup>196</sup>Durkin J., Expert Systems - Design and Development, New York, NY: Macmillan Publishing Company, 1994.

<sup>197</sup>Ginsberg M., Essentials of Artificial Intelligence, San Mateo, CA: Morgan Kaufmann Publishers Inc., 1993.

<sup>198</sup>Russell S., Norvig P., Artificial Intelligence - A Modern Approach, Englewood Cliffs, NJ: Prentice-Hall, 1995

(prognosis elegance) whilst advising structures perform such a type and endorse corrective remedies.

The identified issues in research from literature study are:

1. The prognosis in medicine is extra complex than in different areas due to scientific terms, semantic members of the family and quantity of statistics worried in procedure of analysis. It deals with good sized quantity of analysis even though advanced investigating system, producing minute examination records in addition to evaluation of such data in the shape of numeric, bar charts, line charts and many others. This requires especially designed intelligent system for complex analysis in order to provide accurate diagnosis.
2. In India, maximum of the healthcare transport structures are primarily based on manual report maintaining or electronic fitness record systems (EHRs) which allows in upkeep of affected person records. Currently, accuracy of analysis depends on the human attributes which include, past experience and domain precise information, the usage of which, practitioners are concluding their prognosis. Sufferers are required to seek advice from a couple of doctor for second opinion, that's costly in economic phrases as well as time intake. A wise system can thoroughly address such problems and reduce dependency on human attributes for accurate diagnosis.

The studies were performed inside the place of synthetic Intelligence-machine learning, more mainly almost about the correct type and Prediction Algorithms of artificial Intelligence-system gaining knowledge of. The studies also encompasses the development of latest

algorithms/techniques and testing them within the domain of Ophthalmology for diagnosing various degrees of Glaucoma-an eye ailment.

The proposed research is supposed to guide clinicians at various stages in the eye care process, from preventive care via prognosis, observed by means of right remedy and medical advice. The machine might be used to searching for 2nd opinion for the practitioner and could be capable of facilitate far flung analysis at decrease prices, advanced performance & pace, and decreased physician's bodily intervention at the patient's exam web site.

---

# **CHAPTER – 3 Research Methodology**

## **3.1 Objectives**

The primary focus of this research was to develop an intelligent diagnostic system for Glaucoma- an eye related disease, from the data obtained through clinician by various examination devices or equipment used in ophthalmology. This was used as training set to multi-classifier, developed using ensemble of various techniques of Artificial Intelligence. The classification was done by a ensemble approach using Artificial Neural Network, Naïve Bayes Algorithms and Decision Tree Algorithms. A design/development of a technique is required for such diagnosis and it is tested for its efficacy. Using the algorithms and techniques of Neural Network, Naïve Bayes Algorithm and Decision Tree based classifiers, the proposed ensemble is anticipated to intelligently analyze and perform diagnosis for patient's visionary predicaments, thus lessening the intervention of medical practitioners in terms of decision making.

The Objectives of this research were:

1. To determine the patient wise classification of glaucoma conditions (types).
2. To study and analyze various techniques for detection of glaucoma conditions (types) in patients.
3. To identify the most appropriate detection technique for different conditions (types) of glaucoma.
4. To explore and analyze techniques / algorithms for diagnosing various conditions (types) of glaucoma in patients.
5. Devising appropriate techniques / algorithms for testing diagnosis of various conditions (types) of glaucoma and studying the efficacy of these techniques.

### **3.2 Obtaining and pre-processing Data**

The data set with details of various clinical examinations for diagnosis of Glaucoma was obtained from a practicing ophthalmologist Dr. Hemant Patel, Care Sight Eye Clinic, Vadodara. Initially, the dataset classified into 2 classes namely, Glaucomatous-Glaucoma and Non Glaucomatous-No Glaucoma. A total of 163 patients form the data. Later the dataset was classified into more specific 4 classes, and then 7 classes. Out of these classes, 1 class was ‘No Glaucoma’ Class.

The details of the classes at various stages of classification and the variable categories used for diagnosis are as follows :

**Table 3. 1 Glaucoma Diagnosis with 2 classes**

<b>Diagnosis Class</b>	<b>History (optional)</b>	<b>IOP</b>	<b>Gonioscopy</b>	<b>Disc</b>	<b>Visual Fields</b>	<b>OCT-RNFL</b>
<b>No Glaucoma</b>	Normal	Normal	Normal	Normal	Normal	Normal
<b>Glaucoma</b>	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal

**Table 3. 2 Glaucoma Diagnosis with 4 classes**

<b>Diagnosis Class</b>	<b>History (optional)</b>	<b>IOP</b>	<b>Gonioscopy</b>	<b>Disc</b>	<b>Visual Fields</b>	<b>OCT-RNFL</b>
<b>No Glaucoma</b>	Normal	Normal	Normal	Normal	Normal	Normal
<b>Glaucoma Suspect (closed angle suspect)</b>	Abnormal (Normal)	Abnormal (Normal)	Normal (Abnormal)	Normal/ Suspicious (Normal)	Normal (Normal)	Abnormal (Normal)
<b>Glaucoma Suspect (open angle suspect)</b>	Abnormal	Abnormal	Normal	Normal/ Suspicious/ Abnormal	Normal (Abnormal)	Abnormal
<b>Glaucoma</b>	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal

**Table 3. 3 Glaucoma Diagnosis with 7 classes**

<b>Diagnosis Class</b>	<b>History (optional)</b>	<b>IOP</b>	<b>Gonioscopy</b>	<b>Disc</b>	<b>Visual Fields</b>	<b>OCT-RNFL</b>
<b>No Glaucoma</b>	Normal	Normal	Normal	Normal	Normal	Normal
<b>Primary Open Angle Glaucoma</b>	Abnormal	Abnormal	Normal	Abnormal	Abnormal	Abnormal
<b>Primary Normal Tension Glaucoma</b>	Normal	Normal	Normal	Abnormal	Abnormal	Abnormal
<b>Primary Ocular Hypertension</b>	Normal	Abnormal	Normal	Normal	Normal	Abnormal
<b>Primary Angle closure</b>	Normal	Abnormal	Abnormal	Normal	Normal	Normal
<b>Angle closure Glaucoma</b>	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal

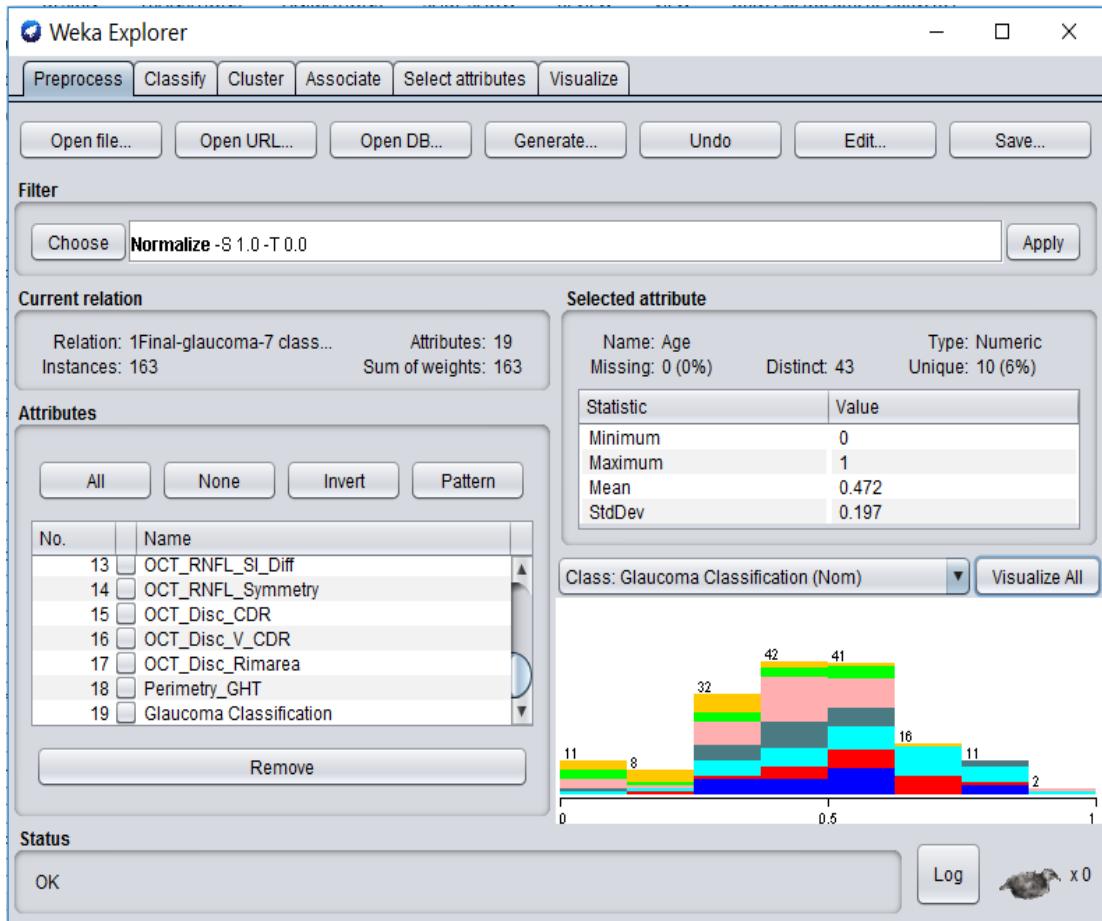
There were 18 variables selected for study, which included details related to patients' individual and clinical data as follows:

- Patient's Age
- Patient's Gender
- Symptoms(Complaints)
- Past History of Symptoms
- Family History

- Clinical Findings
  - Posterior Segment CDR
  - IOP
  - Pachymetry
  - Gonioscopy
  - OCT-RNFL
  - OCT-Disc
  - Perimetry

The above dataset was pre-processed before applying different classification techniques. Few modifications were done manually throughout the dataset. The nominal values of attributes, such as, IOP (Intra Ocular Pressure) Bilateral Difference, Perimetry GTH, Complaints etc. were converted to ordinal values. The binominal values of attributes, such as, Gender, Past History, Family History, CDR Bilateral Symmetry etc. were converted to binary numerical values. In Gender attribute, Male was assigned 1 and Female was assigned 0. Other attribute assigned 1 for presence of the characteristic of the attribute, while 0 was assigned to absent of the characteristic.

Rest of the attributes having numeric values, such as, CDR Value, IOP Variations, Pachymetry, RNFL, OCT Disc Rimarea etc. were pre-processed to normalize the values in WEKA. Figure 3.1 and 3.2 Shows the pre-processing stage.



**Figure 3. 1 Normalizing Data**



**Figure 3. 2 Attributes after applying normalize**

The dataset then used for classification using various classifiers, such as, ANN (MLP-Multi Layer Perceptron), Decision Tree(DT)-J48 and Naïve Bayes.

### **3.3 Artificial Neural Network**

An Artificial Neural Network (ANN) is an information processing prototype which is inspired by the way biological nervous systems, such as the brain, to process information. The key element of this prototype is the novel structure of the information processing system. It is composed of a large number of highly interconnected processing elements (neurons) working in union to solve specific problems. Like people, ANNs also learn by example. An ANN is configured for a specific application, such as pattern recognition or data classification, through a learning process. Learning in biological systems involves adjustments to the synaptic connections that exist between the neurons. This is true in case of ANNs as well.

Artificial Neural Networks have remarkable ability to derive meaning from complicated or imprecise data and can be used to extract patterns and detect trends that are too complex to be noticed by either humans or other computer techniques. A trained neural network can be thought of as an "expert" in the category of information it has been given to analyze. This expert can then be used to provide projections given new situations of interest and answer "what if" questions.

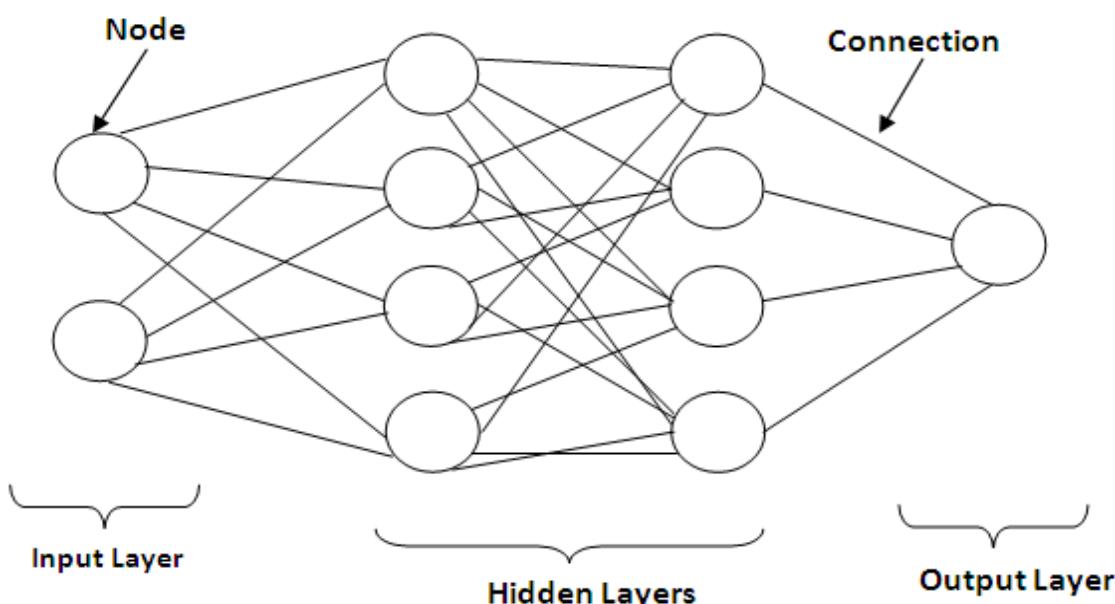
Other advantages include:

1. Adaptive learning: An ability to learn how to do tasks based on the data given for training or initial experience.

2. Self-Organization: An ANN can create its own organization or representation of the information it receives during learning time.
3. Real Time Operation: ANN computations may be carried out in parallel, and special hardware devices are being designed and manufactured which take advantage of this capability.

**Fault Tolerance via Redundant Information Coding:** Partial destruction of a network leads to the corresponding degradation of performance. However, some network capabilities may be retained even with major network damage.

Artificial Neural networks are typically organized in layers. Layers are made up of a number of interconnected 'nodes' which contain an 'activation function'. Patterns are presented to the network via the 'input layer', which communicates to one or more 'hidden layers' where the actual processing is done via a system of weighted 'connections'. The hidden layers then link to an 'output layer' where the answer is output as shown in Figure 3.3.



**Figure 3.3 Structure of Artificial Neural Network**

Most ANNs contain some form of 'learning rule' which modifies the weights of the connections according to the input patterns that it is presented with. In a sense, ANNs learn by example as do their biological counterparts; a child learns to recognize dogs from examples of dogs.

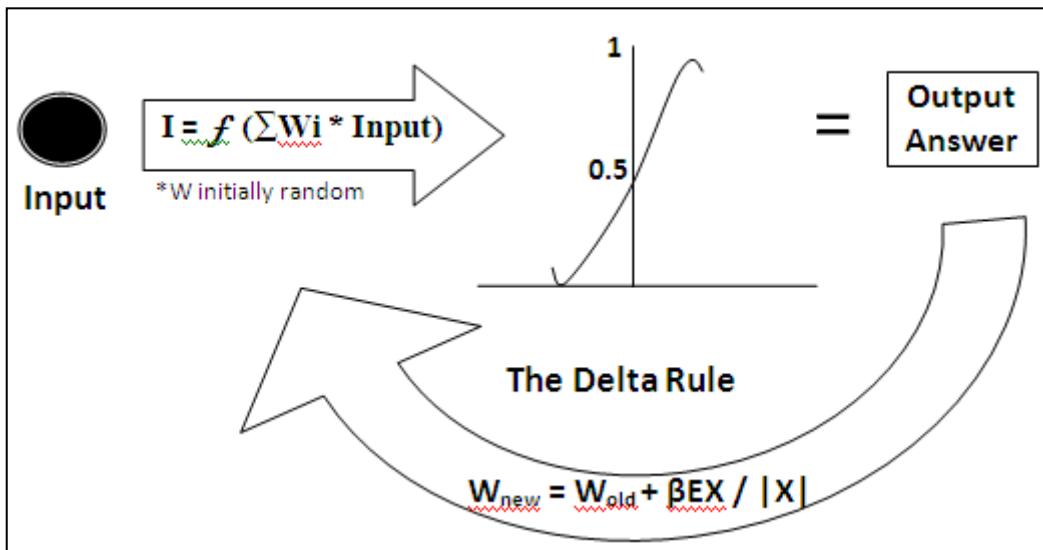
Although there are many different kinds of learning rules used by neural networks, this demonstration is concerned only with one; the delta rule. The delta rule is often utilized by the most common class of ANNs called 'backpropagational neural networks' (BPNNs). Backpropagation is an abbreviation for the backwards propagation of error.

With the delta rule, as with other types of backpropagation, 'learning' is a supervised process that occurs with each cycle or 'epoch' (i.e. each time the network is presented with a new input pattern) through a forward activation flow of outputs, and the backwards error propagation of weight adjustments. More simply, when a neural network is initially presented with a pattern it makes a random 'guess' as to what it might be. It then sees how far its answer was from the actual one and makes an appropriate adjustment to its connection weights. More graphically, the process looks something like Figure 3.4.

Within each hidden layer node is a sigmoid activation function which polarizes network activity and helps it to stabilize.

Backpropagation performs a gradient descent within the solution's vector space towards a 'global minimum' along the steepest vector of the error surface. The global minimum is that theoretical solution with the lowest possible error. The error surface itself is a hyperparaboloid but is seldom 'smooth' as is depicted in the graphic below. Indeed, in most problems, the solution space is quite irregular with numerous 'pits' and

'hills' which may cause the network to settle down in a 'local minum' which is not the best overall solution.

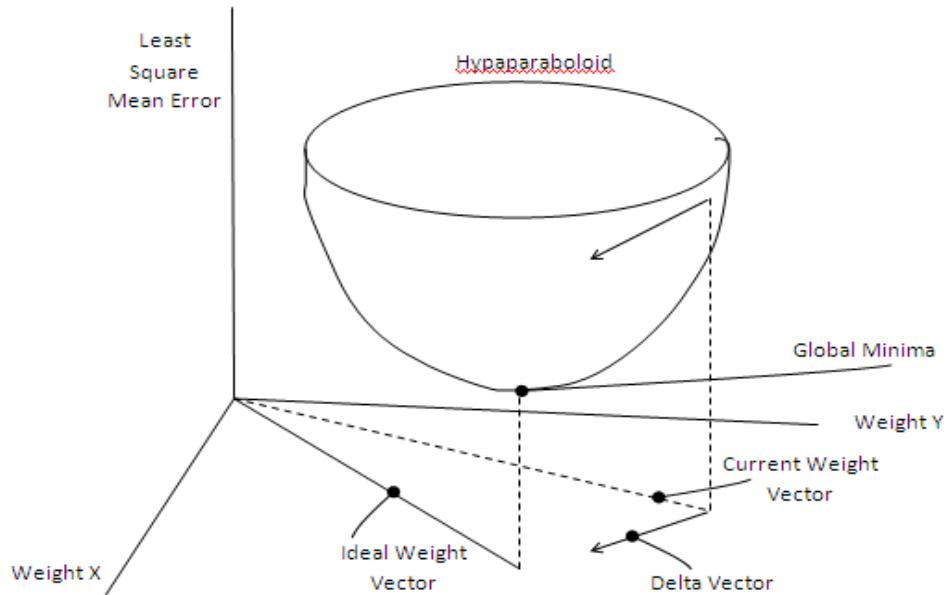


**Figure 3.4 The delta rule of Backpropagation Network**

Since the nature of the error space cannot be known a priori, neural network analysis often requires a large number of individual runs to determine the best solution. Most learning rules have built-in mathematical terms to assist in this process which control the 'speed' (Beta-coefficient) and the 'momentum' of the learning. The speed of learning is actually the rate of convergence between the current solution and the global minimum. Momentum helps the network to overcome obstacles (local minima) in the error surface and settle down at or near the global minimum.

Once a neural network is 'trained' to a satisfactory level it may be used as an analytical tool on other data. To do this, the user no longer specifies any training runs and instead allows the network to work in forward propagation mode only. New inputs are presented to the input pattern where they filter into and are processed by the middle layers as though training were taking place, however, at this point the output is retained and no backpropagation occurs. The output of a forward

propagation run is the predicted model for the data which can then be used for further analysis and interpretation.



**Figure 3.5 Backpropagation**

It is also possible to over-train a neural network, which means that the network has been trained exactly to respond to only one type of input; which is much like rote memorization. If this should happen then learning can no longer occur and the network is referred to as having been "grandmothered" in neural network jargon. In real-world applications this situation is not very useful since one would need a separate grandmothered network for each new kind of input.

### 3.3.1 Applications of Artificial Neural Networks

From the applications perspective, the strength of the artificial neural networks is in the management of the non linear, adaptive, and parallel processes. The ANN have found diverse successful applications in computers vision, images/signal processing, speech/characters recognition,

expert systems, medical images analysis, remote sensing, industrial inspection and scientific exploration. In a superficial way, the domain of the applications of the artificial neural networks can be divided into the following categories:

1. **Pattern recognition:** or supervised classification, an entry given represented by a vector, it assigns a class label existing in the predefined structure of classes.
2. **Grouping:** Also denominated non supervised classification, because there is no predefined structure of classes. The networks explore the objects presented and generate the groups of elements that follow certain similarity criteria.
3. **Approximation of functions:** with base in a group of pairs (ordered pairs of entry/exit) generated by an unknown function of the network adjusts its internal parameters to produce exits that implicitly correspond to the approximation of the function.
4. **Prediction:** Predicting the behavior of an event which depends from the time, with base in a group of values that are obtained from different moments.
5. **Optimization:** A great variety of problems in Math, Science, Medicine and Engineering can be focused as problems where is required to determine a solution that accomplishes with a group of restrictions and diminishes or maximizes an objective function.
6. **Association:** There are made two kinds of associative formulations: the self-association and the hetero-association. In the problems of self-association problems from partial information complete information is recovered. The hetero-association consists in recovering an element from a group B, given an element from a group A.

7. **Control:** From a defined system by the pair  $(u(t), y(t))$ , where  $u(t)$  is the control entrance and  $y(t)$  is the exit of the system to time  $t$ , in a model of adaptive control. The objective is to generate a control entrance  $u(t)$  so that the system keeps the expected behavior, which is determined by the reference model.

For such applications are successful solution form a classics perspective, however in most of the cases they are only valid in restricted environments and present little flexibility out of its domain. The ANN give alternatives which give flexible solutions in a great domain.

### 3.3.2 Limitations

There are many advantages and limitations to artificial neural network analysis. In reference to backpropagational networks, there are some specific issues potential users should be aware of.

- Backpropagational neural networks (and many other types of networks) are in a sense the ultimate 'black boxes'. Apart from defining the general architecture of a network and perhaps initially seeding it with a random numbers, the user has no other role than to feed it input and watch it train and await the output. In fact, it has been said that with backpropagation, "you almost don't know what you're doing". Some freely available software packages (NevProp, bp, Mactivation) do allow the user to sample the networks 'progress' at regular time intervals, but the learning itself progresses on its own. The final product of this activity is a trained network that provides no equations or coefficients defining a relationship (as in regression)

beyond it's own internal mathematics. The network 'IS' the final equation of the relationship.

- Backpropagational networks also tend to be slower to train than other types of networks and sometimes require thousands of epochs. If run on a truly parallel computer system this issue is not really a problem, but if the BPNN is being simulated on a standard serial machine (i.e. a single SPARC, Mac or PC) training can take some time. This is because the machines CPU must compute the function of each node and connection separately, which can be problematic in very large networks with a large amount of data. However, the speed of most current machines is such that this is typically not much of an issue.

### **3.3.3 Advantages**

Depending on the nature of the application and the strength of the internal data patterns you can generally expect a network to train quite well. This applies to problems where the relationships may be quite dynamic or non-linear. ANNs provide an analytical alternative to conventional techniques which are often limited by strict assumptions of normality, linearity, variable independence etc. Because an ANN can capture many kinds of relationships it allows the user to quickly and relatively easily model phenomena which otherwise may have been very difficult or impossible to explain otherwise.

## **3.4 Decision Tree**

Decision Tree (DT) is a common technique used for classification of data. It is created by examining a set of training samples, the class labels for these data is known. These characteristics of such samples with known

class labels are then applied to decide the properties of unknown samples. Decision Trees is considered a powerful and popular tool for classification and prediction. Attribute value description are the key requirements for building a decision tree, which means that its objects should be expressible in terms of a fixed collection of points called attributes, predefined classes also called target classes with discrete output values and principles and finally sufficient data to fully understand the model.

Decision Tree is a classifier which has the form similar to that of a tree and has the structure elements as follows:

1. Root node – It is the left-most in a tree
2. Decision node – It is test node on single attribute
3. Leaf node - Value of target attribute
4. Edge: Split of an attribute
5. End-point: Right most node representing final outcome

Decision Tree is built using divide and conquer approaches (D&C). Each DT path lays down a decision rule. It usually follows a greedy approach from top to bottom, i.e. repetitively from the root node to the end node to determine the final outcome and can therefore deal with uncertainties. In the following way, D&C strategy addresses a problem:

- a. Breaking the problem into various sub-problems that are the cases of problem
- b. Resolve each of these problems repeatedly
- c. Finally, each response to these sub-problems can be considered more interpretable than neural networks and vector support machines, since they combine more data in an easily understandable format.

Even small changes in the input data can lead to large variations in the DT structure. It has to deal with uncertainties in some cases. This can be resolved through DT's sequential decision making. The process to determine the expected values from the end node back to the root node is referred to as the decision tree roll-back. DT is usually a top - down approach. This can be used to determine if the climate is good for tennis. Therefore, it is easy to determine the current climate and what will be followed in the future and to decide whether or not the match can be held. This can also be used for prediction analysis in various other applications, such as rolling a die, product decision, etc.

The algorithm for J48 is as follows:

INPUT : Tr // Tr: Training set

OUTPUT : Ts //Ts: Testing set

DTJ\_BUILD(\*Tr)

{ Ts=NULL;

Ts = Create ROOT node and label with splitting attribute;

Ts= Add BRANCH to ROOT node for each split predicate and label;

For each BRANCH do

Tr= Dataset created by applying splitting predicate to Tr;

If stopping criteria reached

Ts' = Create leaf node and label with appropriate class;

Else

Ts' = DTJ\_BUILD(Tr);

```
Ts= Add Ts' to BRANCH;  
}  
  
}
```

J48 (C4.5) is an algorithm used for the development of a decision tree developed by Ross Quinlan. C4.5 is an extension of the earlier ID3 algorithm of Quinlan. The C4.5 decision trees can be used for classification, which is why C4.5 is often referred to as a statistical classifier.

### **3.4.1 Advantages**

Some of DT's advantages are computer-efficient, easy to use and simple to implement. It also provides objective analysis, flexibility and efficiency in decision - making.

DT is very fast to classify unknown records. It is easy for interpretation up to medium sized trees. DT is capable of handling attributes with continuous values as well as attributes with discrete. It also works well in case of attribute having redundant values. In cases where methods to avoid overfitting are provided, DT is very robust even in the presence of noise in data.

### **3.4.2 Disadvantages**

The main disadvantage of DT is that the entire process depends on the accuracy of the input data used and requires qualitative data to determine the accuracy of the output.

The DT construction can be badly affected by the irrelevant attributes. Structure of DT depends on the data supplied as training set. Small change in the data can lead to generation of a very different structure of DT. A sub-tree can be replicated several times in construction of a DT. Accuracy reduces as the number of classes increase.

### **3.5 Naïve Bayes Algorithm**

The Bayesian classifier is based on the Bayes decision theory principle, which provides a basic methodology for solving the problem of statistical classification when the probability of pattern distribution is known. Bayesian classification uses a probabilistic approach to assign a sample to the class label. Let C describe m classes[ c1, c2, c3... cm] and Xd is a sample described by the d-feature vector, i.e.  $X_d = [x_1, x_2, \dots, x_d]^t$ . The Bayesian classifier calculates the conditional probability posterior  $p(c_i|X_d)$  using the Bayes rule and is given as:

$$p(c_i|X_d) = \frac{p(X_d|c_i)p(c_i)}{p(X_d)} \quad \text{for } i=1,2,\dots,m$$

Using training data  $p(X_d|c_i)p(c_i)$  and  $p(X_d)$  are calculated. According to Bayesian theory, a class label for which the subsequent probability is maximum is predicted for a given Xd observation and returns class probability Ci if,

$$p(c_i|X_d) > p(c_j|X_d) \quad \text{for all } j \neq i$$

The denominator term is common in posterior probability of each class. Therefore, efficient representation of the above equation can be represented as:

$$g_i(X_d) > g_j(X_d) \quad \text{for all } j \neq i$$

Where,  $g_i(X_d) = p(X_d|c_i)p(c_i)$

$$p(X_d|c_i) = \frac{1}{(2\pi)^{d/2} |\Sigma_d|^{1/2}} \exp(-\frac{1}{2} (X_d - \mu_d)^t \Sigma_d^{-1} (X_d - \mu_d))$$

Mostly, the distribution of the probabilities of given training data set is generally unknown. The probability distribution, in such cases, is estimated using parametric or non-parametric methods. In parametric approach, some form of underlying distribution is supposed and estimation of its parameters is carried out with the help of the maximum probability or Bayesian estimate. The distribution of probabilities, either Gaussian or normal is amongst the most frequently found probability density functions (PDF) out of the most frequent PDFs. The main reason for its popularity is its computer traceability. It models a large number of cases appropriately. One of the most famous statistical theorems is the central theorem of limitation. It states that if a random variable is the result of a summary of the number of independent random variables, its pdf approaches the function of Gaussian as the number of terms tends to infinity. In practice, the most common assumption taken is, distribution of the sum of random variables is in Gaussian or normal PDF for a sufficiently large number of summary terms.

The general multivariate normal probability density of d-dimensional sample  $X_d$  for a given class label  $C_i$  is given by :

$$g_i(X_d) = \ln p(X_d|c_i) + \ln p(c_i)$$

Where,

$$g_i(X_d) = -\frac{1}{2} (X_d - \mu_d)^t \Sigma_j^{-1} (X_d - \mu_i) + \ln p(c_i) + b_i$$

$$\text{where } b_i = -d/2 \ln(2\pi) - \frac{1}{2} \ln |\Sigma_i|$$

$$g_i(X_d) = -\frac{1}{2} X_d^t \sum_i^{-1} X_d + \frac{1}{2} X_d^t \sum_i^{-1} \mu_i - \frac{1}{2} \mu_i^t \sum_i^{-1} \mu_i + \frac{1}{2} \mu_i^t \sum_i^{-1} X_d + \ln p(c_i) + b_i$$

$$g_i(X_d) = w_i^t X_d + w_{i0}$$

Here  $g_i(X_d)$  is a linear function of  $X_d$ . This classifier is known as linear discriminant classifier (LDC). When the distribution of the data is characterized by  $I = I_{::}$ , then LDC is simple to understand and computationally more efficient.

### 3.5.1 Advantages

Naïve Bayes Classifier is fast to converge even with less training data. It is not sensitive to irrelevant features, unlike DTs. It can handle real data as well as discrete data very well. It works well with classification of datasets.

### 3.5.2 Disadvantages

The major disadvantage of Naïve Bayes Classifier is that it takes a very strong assumption that the attributes are independent. Performance of this classifier can be poor in case of datasets where attributes are dependent.

## 3.6 Ensemble Method for Classification

Ensemble methods help in improvement of classification results. It combines several models. This method can produce better predictive performance in comparison to single classifiers.

In predictive modelling, a single model based on one data sample can have biases, high variability or inaccuracies that affect the reliability of the results. By combining different models this limitation effect can be reduced.

Ensemble methods are techniques that create multiple models and then combine them to produce improved results. Two or more models that are combined in ensemble methods, are known as base models.

Ensemble methods are meta-algorithms that combine several machine learning techniques into one predictive model in order to decrease variance (bagging), bias (boosting), or improve predictions (stacking).

Ensemble methods can be divided into two groups:

1. Sequential Ensemble Methods: In these methods, the base learners are generated sequentially (e.g. AdaBoost). The basic motivation of sequential methods is to exploit the dependence between the base learners. The overall performance can be boosted by weighing previously mislabeled examples with higher weight.
2. Parallel Ensemble Methods: In these methods, the base learners are generated in parallel (e.g. Random Forest). The basic

motivation of parallel methods is to exploit independence between the base learners since the error can be reduced dramatically by averaging.

Most ensemble methods use a single base learning algorithm to produce homogeneous base learners, i.e. learners of the same type, leading to homogeneous ensembles.

There are also some methods that use heterogeneous learners, i.e. learners of different types, leading to heterogeneous ensembles. In order for ensemble methods to be more accurate than any of its individual members, the base learners have to be as accurate as possible and as diverse as possible.

Voting is the ensemble method used for classification of dataset. Voting method uses different approaches for prediction:

### 1. Majority Voting

Every model makes a prediction (votes) for each test instance and the final output prediction is the one that receives more than half of the votes. If none of the predictions get more than half of the votes, we may say that the ensemble method could not make a stable prediction for this instance. Although this is a widely used technique, you may try the most voted prediction (even if that is less than half of the votes) as the final prediction. In some articles, you may see this method being called “plurality voting”.

## 2. Average of Probabilities

In average of probabilities method, the base classifiers calculate probabilities for the outcomes. The method arrive at the best result by averaging out the probabilities calculated by individual algorithms.

## 3. Maximum Probability

In maximum probability method, the base classifiers calculate probabilities for the outcomes. The method arrive at the best result by taking out the maximum probability calculated by individual algorithms.

## 4. Minimum Probability

In minimum probability method, the base classifiers calculate probabilities for the outcomes. The method arrive at the best result by taking out the minimum probability calculated by individual algorithms.

## 5. Product of Probability

In product probability method, the base classifiers calculate probabilities for the outcomes. The method arrive at the best result by taking out the product of probability calculated by individual algorithms.

## 6. Median

In median method, the base classifiers calculate probabilities for the outcomes. The method arrive at the best result by taking out the median of probability calculated by individual algorithms.

### **3.7 Ensemble FGLAUC-99**

The research is multidisciplinary and diagnostic in nature, involving computer science as well as medicine domain. It is multidisciplinary since it maps some domains of Computer Science and Ophthalmology which is a branch of medicine. It is also diagnostic as it follows case-based method using in depth approaches of various classification techniques of computer science to reach basic causal relations. The sample size is also small and require deep probing data gathering devices used in ophthalmology.

Information was gathered on various fields of medicine where automated diagnosis was required such as, radiology, cardiology and ophthalmology. (Ranadive F. et. al., 2014)<sup>199</sup> The Ophthalmic diseases lack fatality, but have tendency to progress overtime leaving permanent disability-morbidity, that have more impact on daily life of the patients. In this context, the Indian population is more vulnerable to these diseases due to their genetic predisposition, changing lifestyle and timely diagnosis of the disease. As the diseases are chronic and non-treatable at later stage, they impose heavy economic and social burden to over developing economy in the form of loss of working hours and treatment cost.

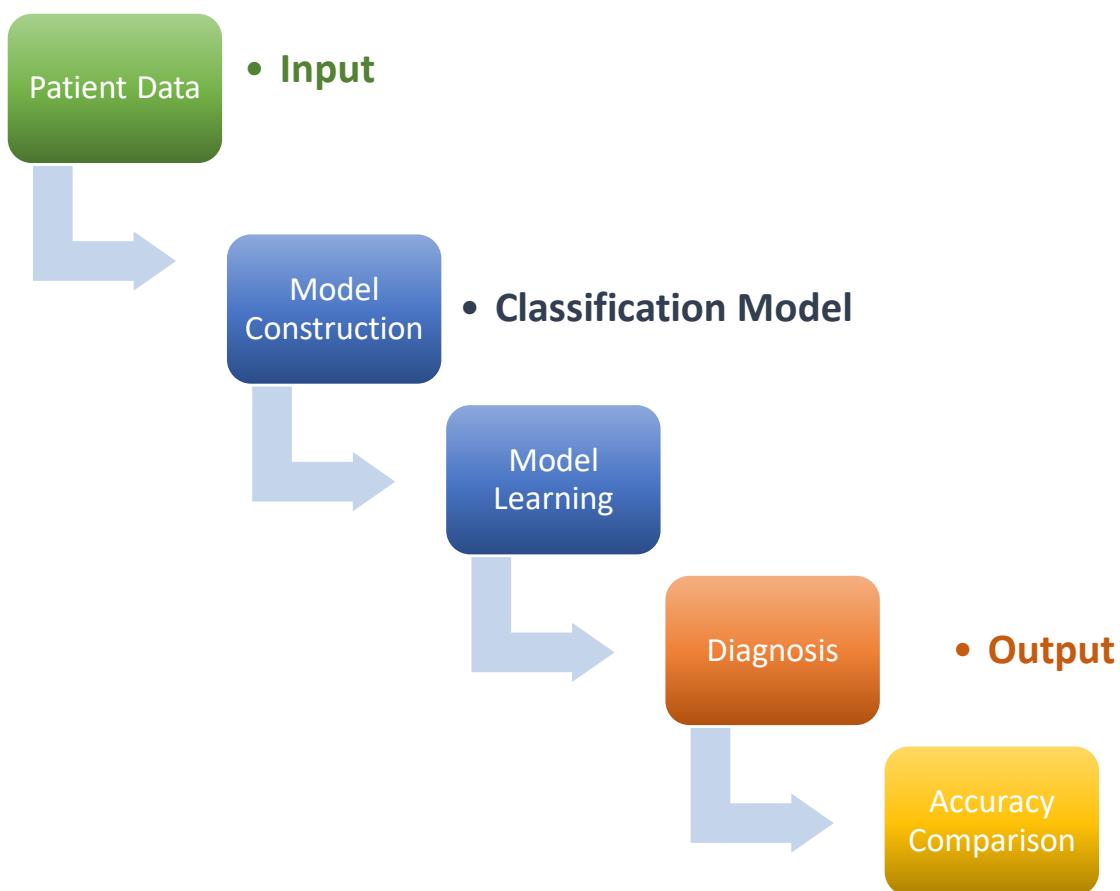
The trade-off between prediction power and interpretability is one of the well-known issues in machine learning. The black box models such as Support Vector Machine (SVM) and deep learning algorithm show good prediction power. However, it is difficult to understand how the model gives the prediction result. Therefore, they are not entirely suitable for medical diagnosis because clinicians want to know both the prediction and

---

<sup>199</sup>Falguni Ranadive, Prof. Priyanka Sharma, "OphtoABM-An Intelligent Agent Based Model for Diagnosis of Ophthalmic Diseases", International Journal of Engineering and Computer Science ISSN: 2319-7242 Volume 3 Issue 12 December 2014, Page No. 9667-9670.

the reason for the prediction. (Seong et. al., 2017)<sup>200</sup> Decision tree models such as C5.0 (Quinlan JR, 1986)<sup>201</sup> (Quinlan JR, 1993)<sup>202</sup> show good interpretability and poor prediction power. Logistic Regression and Naïve Bayes are algorithms used for probabilistic classification (Caruana R., 2006)<sup>203</sup>.

The sample size is 163. Out of these 163 samples 107 were used for training set and 56 were used for testing set.



**Figure 3. 6 Flow of Research**

<sup>200</sup>Seong Jae Kim, Kyong Jin Cho, Sejong Oh, “Development of machine learning models for diagnosis of glaucoma”, <https://doi.org/10.1371/journal.pone.0177726>, 2017.

<sup>201</sup>Quinlan JR, Induction of decision trees, *Mach. Learn* 1986, 1(1):81–106.

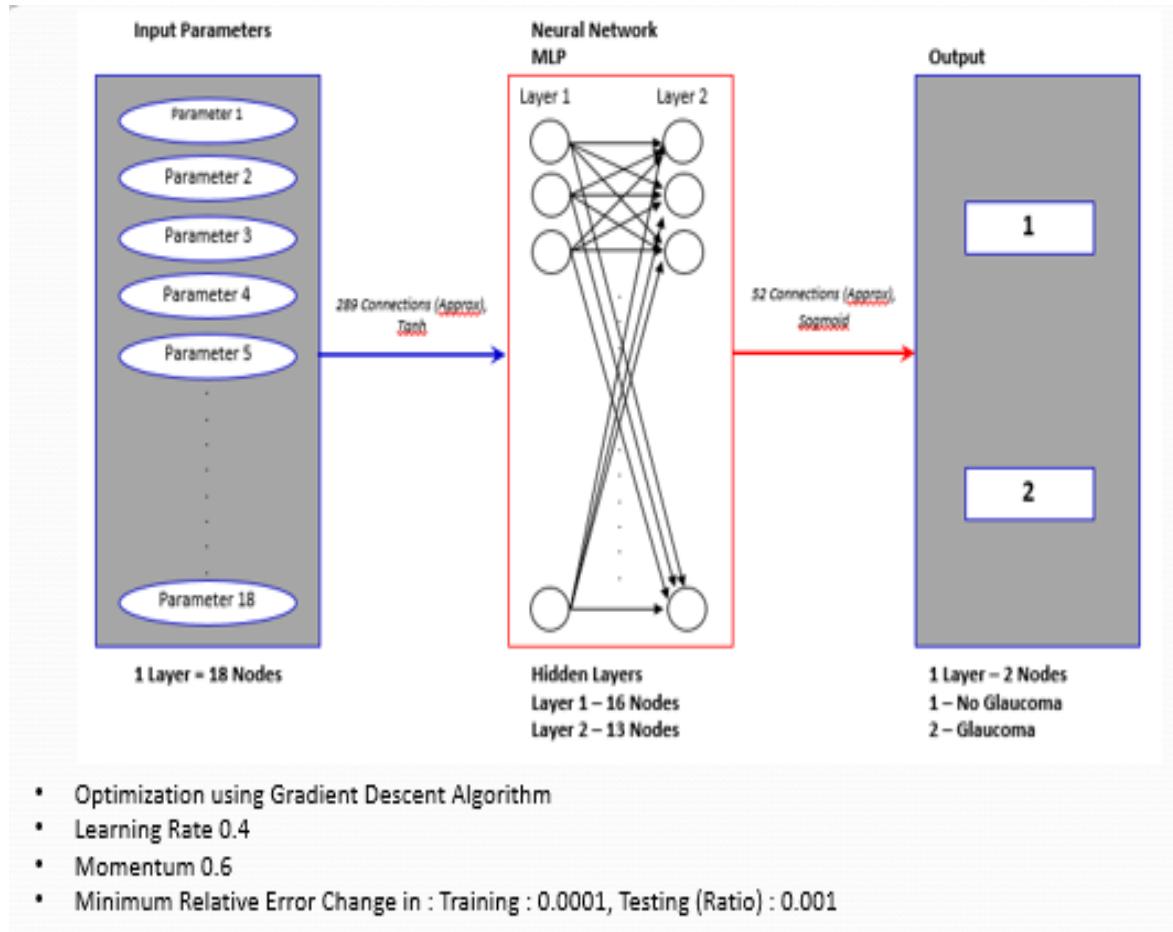
<sup>202</sup>Quinlan J. R., C4.5: Programs for Machine Learning, Morgan Kaufmann Publishers, 1993.

<sup>203</sup>Caruana R. An Empirical Comparison of Supervised Learning Algorithms. Proceedings of the 23rd international conference on Machine learning. 2006 June 25–29; Pittsburgh USA; ACM; 2006. p.161-168.

The Glaucoma dataset used in this research was obtained from practitioner. The data was validated by the practitioner. It was normalized and standardized. The training set was used for construction of a classification model. The model was constructed using 10-fold cross validation. The model learning was carried out using training set. It was used for classification of the testing set. The model provided diagnosis of various conditions (types) of glaucoma disease. The accuracy obtained by the model was compared with other models found in the literature review.

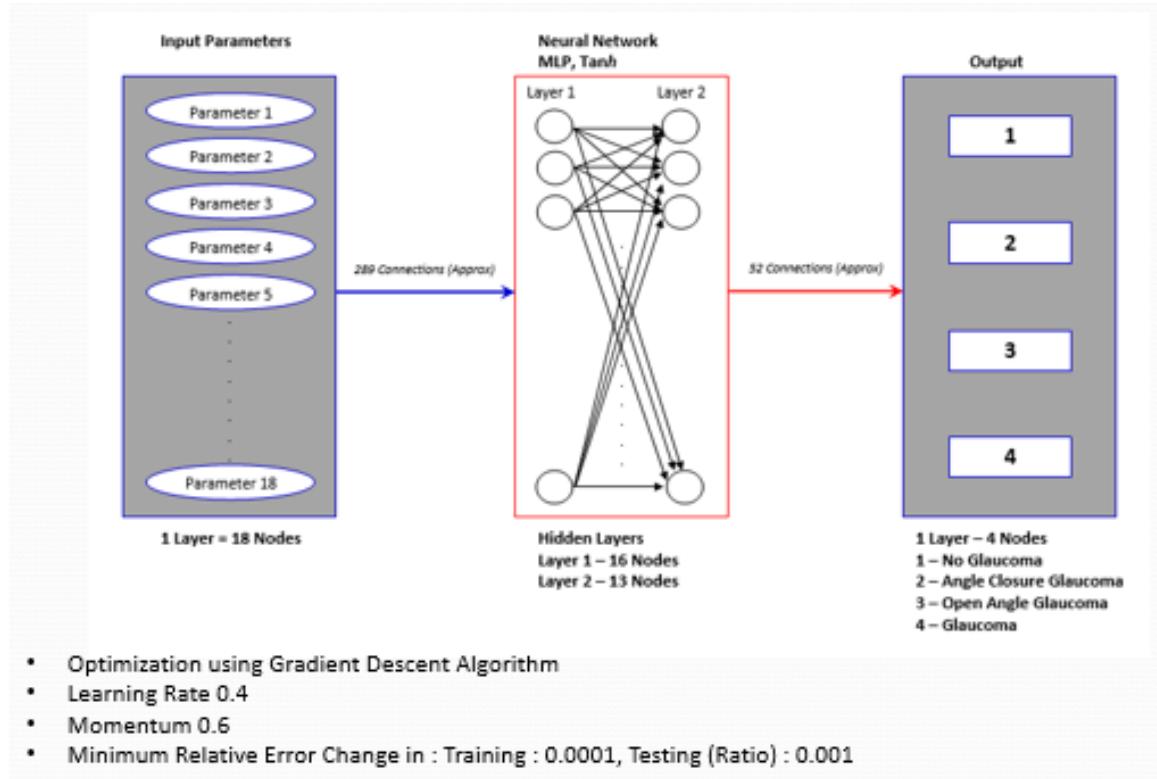
The goal of this research was to develop an Intelligent System that has strong prediction power and an equally good results' interpretability for diagnosis of various stages of glaucoma.

To achieve the goal, the glaucoma dataset was classified in three stages. In the first stage the glaucoma dataset was classified using supervised classifier-Artificial Neural Network for diagnosis. The glaucoma dataset had 2 classes, ‘Glaucoma’ and ‘No Glaucoma’. 3.7 shows the configuration of ANN classifier with 2 classes.



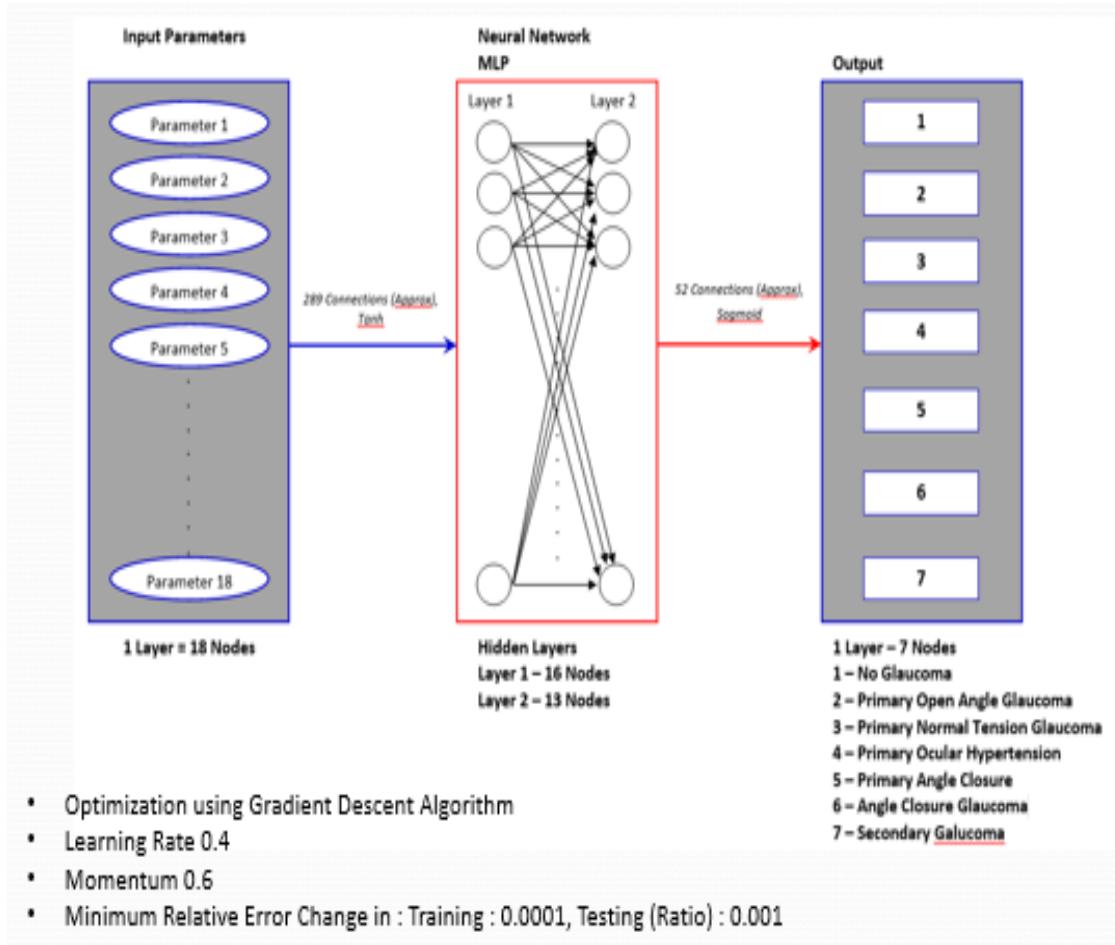
**Figure 3.7 Configuration of ANN for classification with 2 classes**

The classifier was then updated to include 4 classes, ‘Glaucoma’, ‘No Glaucoma’, ‘Angle Closure Glaucoma’ (Suspect for closed angle glaucoma) and ‘Open Angle Glaucoma’ (Suspect for open angle glaucoma) to diagnose more specific condition of glaucoma from the glaucoma dataset. Figure 3.8 shows the configuration of ANN classifier with 4 classes.



**Figure 3.8 Configuration of ANN for classification with 4 classes**

The classes further specified as 7 classes, ‘No Glaucoma’, ‘Primary Open Angle Glaucoma’, ‘Primary Normal Tension Glaucoma’, ‘Primary Ocular Hypertension’, ‘Primary Angle closure’, ‘Angle closure Glaucoma’, ‘Secondary Glaucoma’ for detailed diagnosis of various conditions of glaucoma. Figure 3.9 shows configuration of ANN classifier with 7 classes.

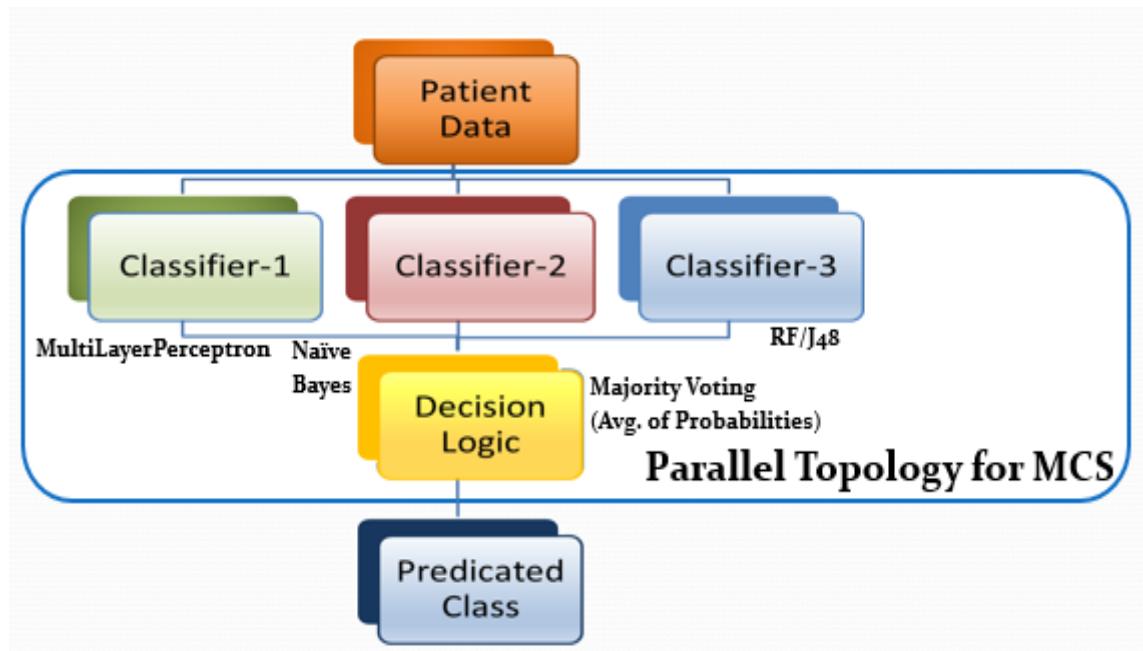


**Figure 3.9 Configuration of ANN for classification with 7 classes**

Later, the glaucoma dataset was also used for classification using single classifier, such as, Decision Tree (J48 in WEKA), Naïve Bays Classifier, Random Forest and SVM (SMO in WEKA).

To improve the classification accuracy and in order to provide more accurate diagnosis, an ensemble FGLAUC-99 was developed for classification and prediction from glaucoma dataset-clinical eye examination data.

There are different combinations of algorithms used for ensemble. Figure 3.10 and Figure 3.11 shows the configuration of these ensemble classifiers.

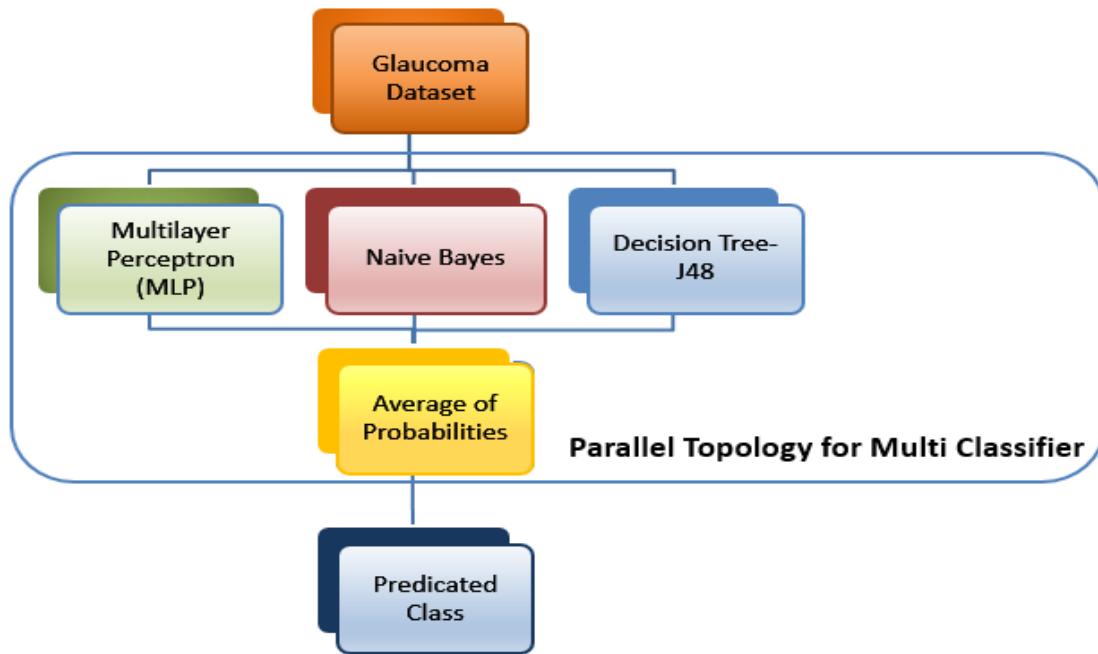


**Figure 3.10 Configuration of Initial Ensemble Classifier**

The Classifier for diagnosis of various conditions of Glaucoma, was using ensemble of more than one classifiers. The configuration of Multi-classifier (Ensemble) was Parallel Configuration for combining classifiers. The classifiers used for Multi-classifier (MCS) were Neural Network classifier, Decision Tree classifier and Naïve Bayes classifier. These classifiers were further optimized to improve accuracy. The decision logic, which provides final classification from different classifiers was also optimized to nullify the bias of individual classifiers.

The ensemble method used was Vote, which is a meta classifier in WEKA 3.8.1.

The Average of Probabilities was used as an evaluation operator in Vote ensemble classifier. This ensemble is a heterogeneous classifier. It can combine classifiers from different group of classifiers and give the prediction result.



**Figure 3.11 Configuration of Ensemble Classifier**

The ensemble designed with MLP, Naïve Bayes and J48 hence forth termed as FGLAUC-99 exploits the benefit of different group of classifiers and complement their disadvantages to improve prediction accuracy of the model. The ensemble model utilize the accuracy of MLP and overcomes the poor interpretability being disadvantage of ANN. Decision Trees are sensitive towards data values, slight change in data may also lead to construction of different decision tree. But decision trees provide good interpretability. While, Naïve Bayes works on probability calculations, it works well in almost all cases, where attributes are independent. The accuracy of Naïve Bayes does not get affected even in case of major changes in data.

# **CHAPTER – 4 Results and Discussions**

## **4.1 Experimental Setup**

This research has used three types of Glaucoma datasets and developed the learning models:

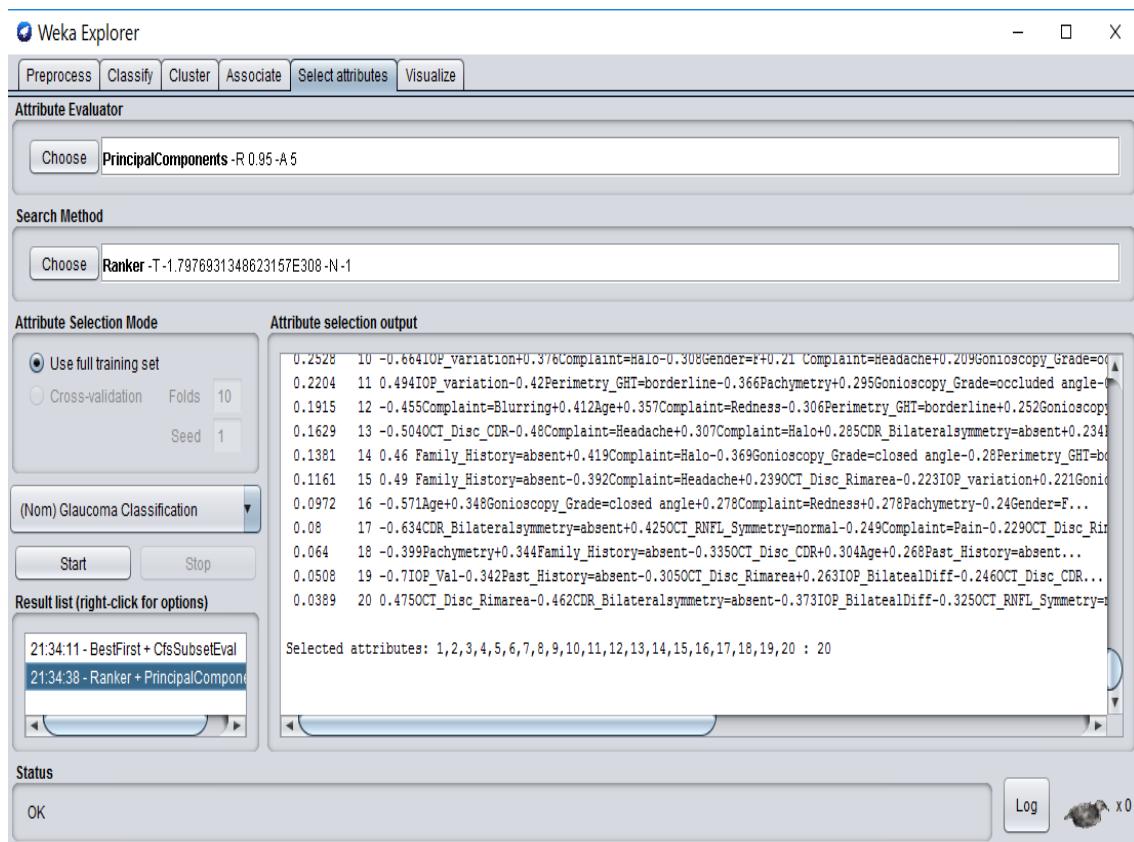
1. Dataset with 2 Classes-‘Glaucoma’(Glaucomatous) and ‘No Glaucoma’(Normal)
2. Dataset with 4 Classes-‘Glaucoma’, ‘No Glaucoma’, ‘Angle Closure Glaucoma’ (Suspect for closed angle glaucoma) and ‘Open Angle Glaucoma’ (Suspect for open angle glaucoma)
3. Dataset with 7 Classes-‘No Glaucoma’, ‘Primary Open Angle Glaucoma’, ‘Primary Normal Tension Glaucoma’, ‘Primary Ocular Hypertension’, ‘Primary Angle closure’, ‘Angle closure Glaucoma’, ‘Secondary Glaucoma’

The glaucoma dataset was obtained from ophthalmology practitioner. It had glaucomatous cases and non-glaucomatous cases that formed our diseased and healthy controls respectively. The important features were extracted from patients’ clinical examinations and arranged as a data table. The records with missing values were removed.

The glaucoma dataset with 2 classes, 4 classes and 7 classes were supplied to an ANN classifier to build a model for glaucoma diagnosis. The dataset was also used for classification and prediction using different classifiers.

Principal Component Analysis (PCA) was performed to select

suitable features from glaucoma dataset for classifying healthy controls and glaucoma. There were total 163 patients' data in glaucoma dataset. The split percentage of the dataset was 66%. The dataset was divided into a test dataset (56 cases) and training dataset (107 cases). Training dataset was used to develop and train the model. After developing the best learning model, it was evaluated using the test dataset. The machine learning algorithms used to develop the learning model for glaucoma prediction were: J48, Naïve Bayes, MLP, RF, KNN and SVM. Figure 4.1 Shows PCA for glaucoma dataset. All attributes are selected as principal components. There are total 18 attributes and 2 glaucoma class attributes. PCA selected 20 attribute as principal attributes. This validates that all attributes are independent and glaucoma class attribute depends on these 18 attributes. Therefore the study carried out with 18 attributes for further processing and classification.



**Figure 4. 1 PCA applied to glaucoma dataset**

The models, after construction of the best learning models of these algorithms, were evaluated in various ways. The models were validated with 10 fold cross validation method. The classification accuracy were compared. Receiver operating characteristics, (ROC) curves and areas under the curve (AUC) value were also analyzed. All the classification algorithms were implemented in java using WEKA APIs. Figure. 4.2 Shows the input screen and diagnosis of glaucoma diagnosis system.

**Figure 4. 2 Glaucoma Diagnosis System**

Further to improve the accuracy of glaucoma diagnosis, an ensemble of classifiers FGLAUC-99 was used. The ensemble used here was heterogeneous ensemble of multiple classifiers. The ensemble Vote method uses combination of classifiers, such as, Naïve Bayes, Decision Tree, Artificial Neural Network, Support Vector Machine, K-Nearest neighbor. Figure. 4.3 shows the java implementation of glaucoma diagnosis.

The screenshot shows the NetBeans IDE interface with the title "WekaTest1 - NetBeans IDE 8.2". The menu bar includes File, Edit, View, Navigate, Source, Refactor, Run, Debug, Profile, Team, Tools, Window, Help. The search bar at the top right says "Search (Ctrl+I)". The Projects tab shows a hierarchy: CDRAPPLICATION, HTMLApplication, WekaTest1, Source Packages (containing wekatest1 with files 3.jpg, CC data.txt, CC data1.txt, NewFrame.java, WekaTest1.java, eye for phd.jpg, glaucomascreening.txt, weather.txt, weather1.txt), Test Packages, Libraries, and Test Libraries. The main editor window displays Java code for "WekaTest1.java" with line numbers 58 to 84. The code implements cross-validation and uses J48 decision trees:

```

public static Instances[][] crossValidationSplit(Instances data, int numberOfFolds) {
    Instances[][] split = new Instances[2][numberOfFolds];
    for (int i = 0; i < numberOfFolds; i++) {
        split[0][i] = data.trainCV(numberOfFolds, i);
        split[1][i] = data.testCV(numberOfFolds, i);
    }
    return split;
}

public static void main(String[] args) throws Exception {
    BufferedReader datafile = readDataFile("C:\\\\Users\\\\FalguniRanadive\\\\Documents\\\\NetBeansProject\\\\wekatest1\\\\glaucomascreening.txt");
    Instances data = new Instances(datafile);
    data.setClassIndex(data.numAttributes() - 1);

    // Do 10-split cross validation
    Instances[][] split = crossValidationSplit(data, 10);

    // Separate split into training and testing arrays
    Instances[] trainingSplits = split[0];
    Instances[] testingSplits = split[1];

    // Use a set of classifiers
    Classifier[] models = {
        new J48(), // a decision tree
    };
}

```

The Navigator pane shows the members of the "main" package, including "classify(Classifier model, Instances trainingSet, In", "crossValidationSplit(Instances data, int numberO", and "main(String[] args)". The status bar at the bottom right shows "78:64 INS".

**Figure 4. 3 Java Implementation of Glaucoma Diagnosis**

## 4.2 Results and Discussion

### 4.2.1 Demographic Profile of Patients

The data gathered in this research was of the patients showing symptoms related to diverse eye ailments. The data of the ophthalmic patients was collected from one of the practitioner's clinic in the city of Vadodara, Gujarat. The probability of eye patients likely to suffer from eye disease such as Glaucoma is also influenced by demographic factors such as Age and Gender. In this type of a research work, there is a requisite to underscore the demographic characteristics of the sample.

Taking into account this sample as a representative sample, one can surely develop or can extrapolate and judge the demographic characteristics of the patients at large. The analysis of Demographic profiles especially – Age and Gender of patient would definitely reveal relationships among examination data and such demographic factors of the patients. The success of any good intelligent system would be strongly determined by its ability to analyze and predict results of patients from diverse demographic make ups. A cross sectional sample of patients would undeniably give a snapshot at a point of time but nonetheless it is always more gratifying and informative to any clinician or practitioner.

In this study, the data of total 163 patients has been collected and used for further analysis. All the required information pertaining to relevant aspects of the ophthalmic disease–Glaucoma under the study was extensively covered. The information collected from the practitioner was about the patients' examination data on different parameters such as, symptoms (complaints), past history of symptoms, family history, posterior segment CDR, CDR asymmetry, IOP, IOP Bilateral Difference, IOP min max difference, pachymetry, gonioscopy grades, OCT-RNFL superior inferior value difference, OCT-RNFL Avg, OCT-RNFL symmetry, OCT-disc vertical CDR, OCT-Disc Rimarea and Perimetry Glaucoma Hemifield Test. In addition, the two demographic factors viz. patient's age, patient's gender were also recorded for the purpose of this research, the characteristics of which have been detailed below.

The final aim of this research is to develop an intelligent system for diagnosis of various conditions of glaucoma disease. For this reason, data for some of the parameters listed above have been formatted, transformed, normalized and conditioned wherever required so as to give a more

consequential analytical perspective.

### a. AGE

**Table 4. 1 Demographic profile of patients' age groups**

Age Groups	No. of Patients	% Patients
25-44	21	12.88
45-64	92	56.44
65-79	43	26.38
Above 80	7	4.29

Since the proliferation of Glaucoma and related eye disorders are more prominently observed in specific age groups such as Adults in the age groups of 40 years and above, the major age groups of population are middle aged to old aged individuals. The age group to which an individual belongs is likely to have an impact on his probability of being diagnosed with Glaucoma. Since a scant idea about the specific age groups being affected by Glaucoma and related disorders could be predetermined by the researcher during his interaction with the medical practitioner, a brief description of this age characteristic is given below:

- The data collected of the patient's sample was categorized into 4 classes based on the Age structure suggested by the Census 2011 of India.
- In the patient's data 12.88% patients were found to be in the ages between 25 years and 44 years. 56.44% patients were found to be in the ages between 45 years and 64 years. 26.38% patients were found to be in the ages between 65 years and 79 years whereas 4.29% patients were

above the age of 80 years.

### b. GENDER

**Table 4. 2 Demographic profile of patients gender groups**

Gender	Nos.	%
Male	106	65.03
Female	57	34.97

- The data collected of the patient's sample was categorized into 2 classes based on the Age structure suggested by the Census 2011 of India.
- In the patient's data 65.03% patients were found to be Males and 34.97% were found to be Females.
- 79.33% patients in totality were males and 20.67% were females.

**Table 4. 3 Demographic profile of patients' age group wise gender groups**

Age Groups	No. of Patients	% Patients	Male Patients	% Male Patients	Female Patients	% Female Patients
25-44	21	12.88	15	9.20	6	3.68
45-64	92	56.44	61	37.42	31	19.02
65-79	43	26.38	28	17.18	15	9.20
Above 80	7	4.29	2	1.23	5	3.07

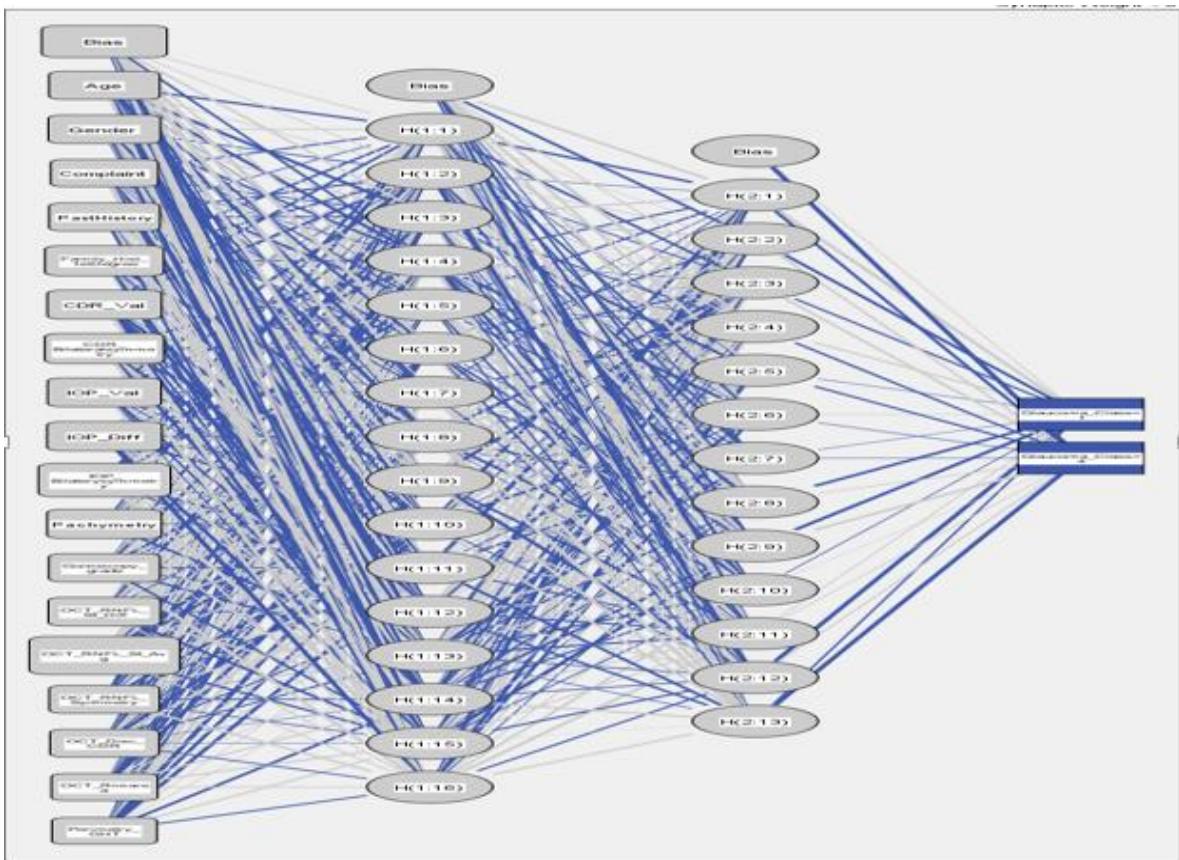
The above Table 4.3 shows the distribution of the two genders of patient sample population across four age groups.

- As depicted in the Table 4.3 above, it was observed that 9.20% male and 3.68% females were found to be in the ages between 25 years and 44 years. Also 37.42% males and 19.02% female patients were found to be in the ages between 45 years and 64 years. Further, 17.18% males and 9.20% female patients were found to be in the ages between 65 years and 79 years whereas 1.23% male and 3.07% female patients were found to be in the ages above 80 years.

#### **4.2.2 Result from Artificial Neural Network Classifier**

An Artificial Neural Network Classifier model is developed to predict the glaucoma diagnosis for new data supplied to the model. The model was implemented in SPSS software. The model had 1 input layer with 18 nodes to input 18 attribute values, 2 hidden layers with 16 and 13 nodes respectively and 1 output layer. The learning rate of the model was set to 0.4 and momentum was set to 0.6. Sigmoid function was used as activation function for this model.

A structure of ANN (Multilayer Perceptron) with 2 classes- ‘Glaucoma’ and ‘No Glaucoma’ is shown in Figure 4.4:



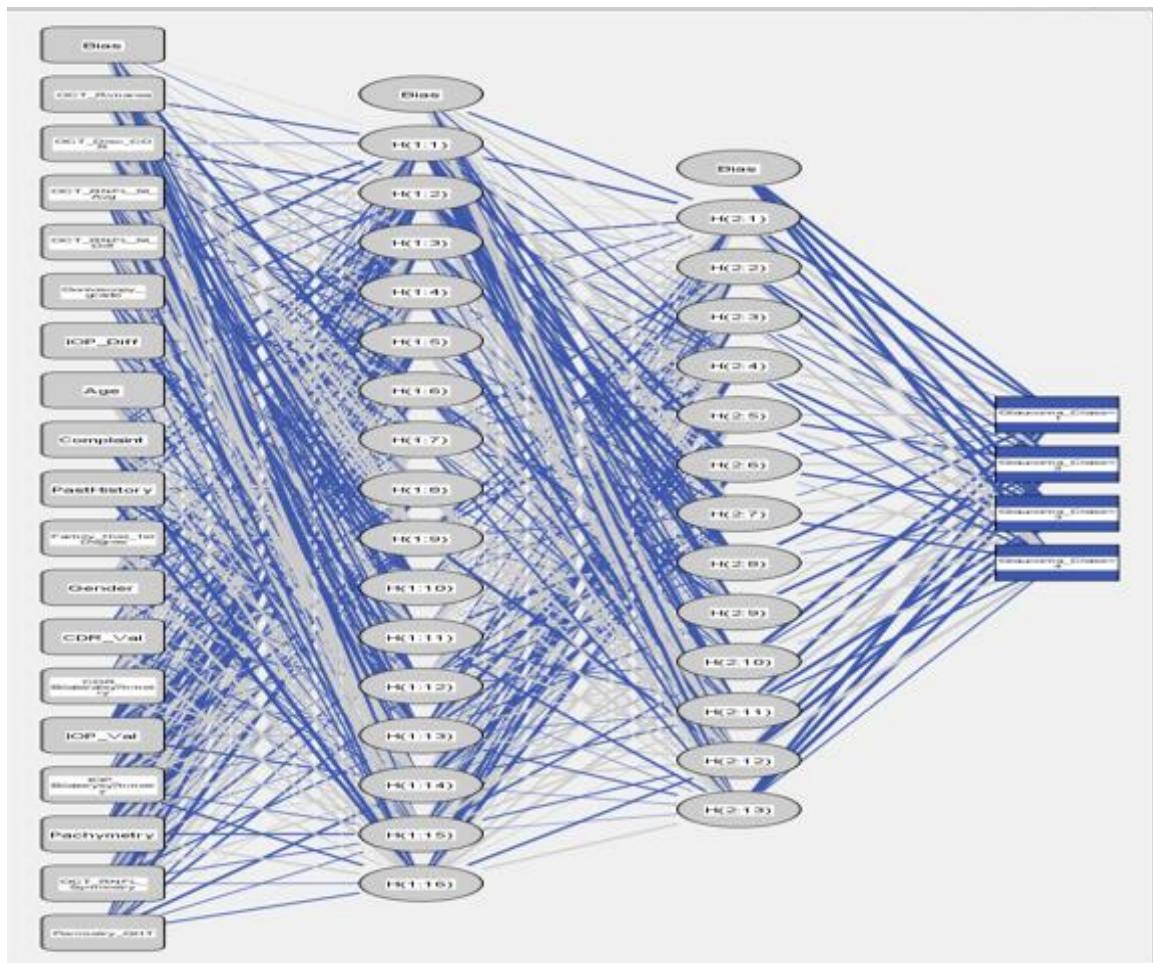
**Figure 4.4 Structure of ANN (Multilayer Perceptron) with 2 classes**

The model accuracy was 79%. The Area Under the Curve (AUC) of ROC Curve are as shown in Table 4.4. The AUC were approximately 0.8, which shows that the classifier is excellent classifier.

**Table 4.4 Area Under the Curve for 2-classes**

Glucoma class	AUC
1-No Glaucoma	0.83
2-Glaucoma	0.83

A structure of ANN (Multilayer Perceptron) with 4 classes- ‘Glucoma’, ‘Angle Closure Glaucoma’ (Suspect for closed angle glaucoma), ‘Open Angle Glaucoma’ (Suspect for open angle glaucoma) and ‘No Glaucoma’ is shown in Figure 4.5:

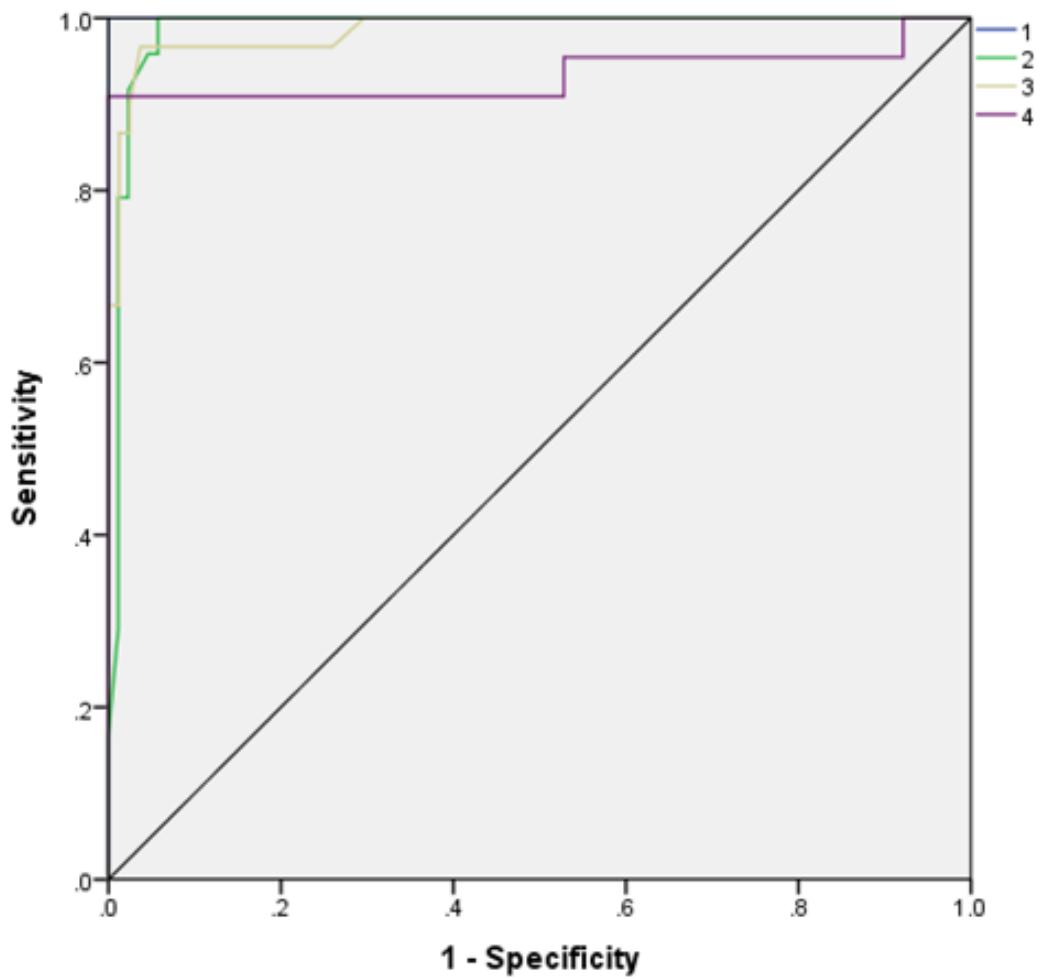


**Figure 4. 5 Structure of ANN (Multilayer Perceptron) with 4 classes**

The model accuracy was 89.9%. The Area Under the Curve (AUC) of ROC Curve are as shown in Table 4.5. The AUC were  $> 0.9$ , which shows that the classifier is excellent classifier.

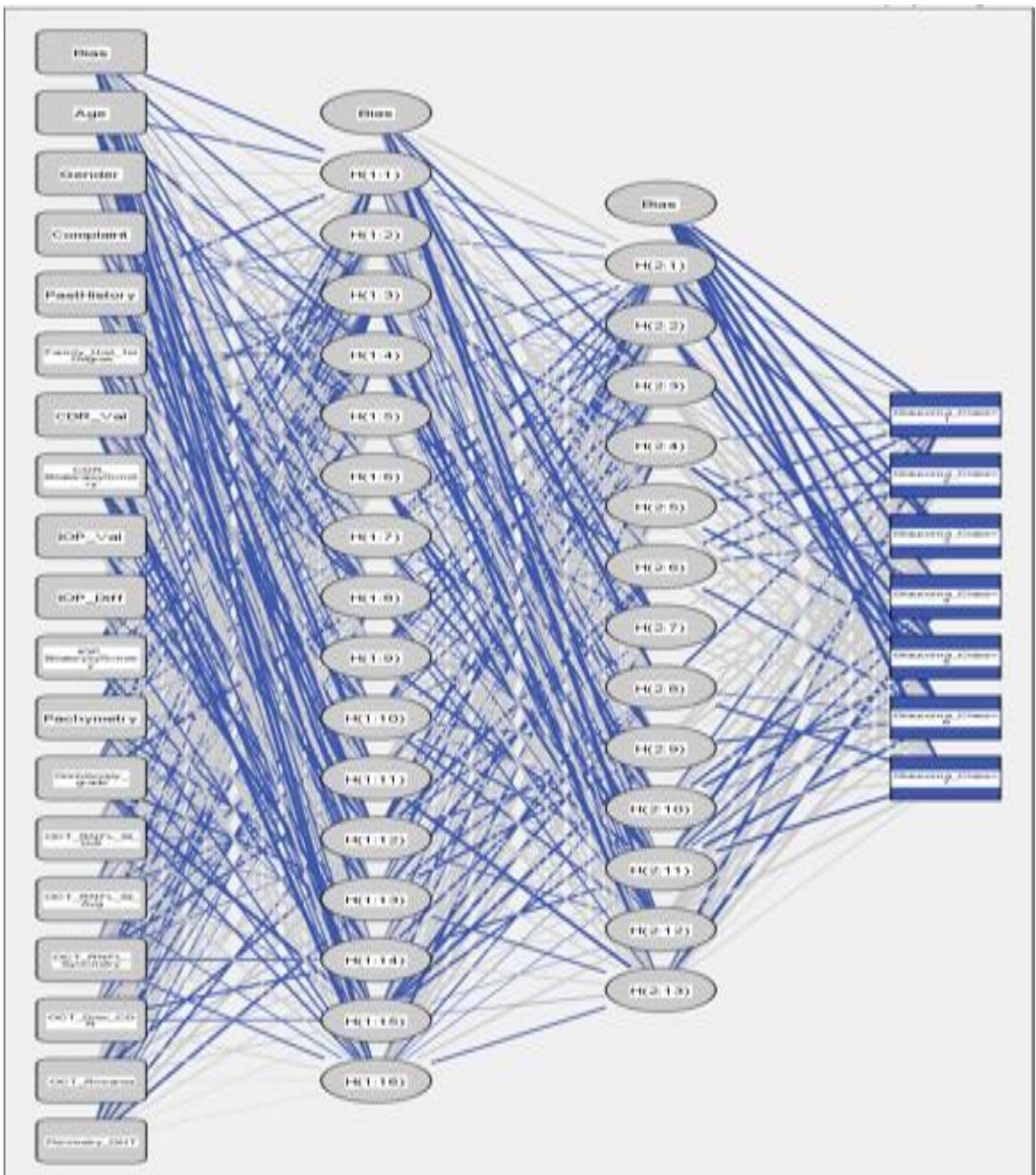
**Table 4. 5 Area Under the Curve for 4-classes**

Glucoma class	AUC
1-No Glaucoma	1.000
2-Angle Closure Glaucoma	.987
3-Open Angle Glaucoma	.985
4-Glaucoma	.934



**Figure 4. 6 ROC Curve for 4-classes**

A structure of ANN (Multilayer Perceptron) with 7 classes--‘No Glaucoma’, ‘Primary Open Angle Glaucoma’, ‘Primary Normal Tension Glaucoma’, ‘Primary Ocular Hypertension’, ‘Primary Angle closure’, ‘Angle closure Glaucoma’, ‘Secondary Glaucoma’ is shown in Figure 4.7:

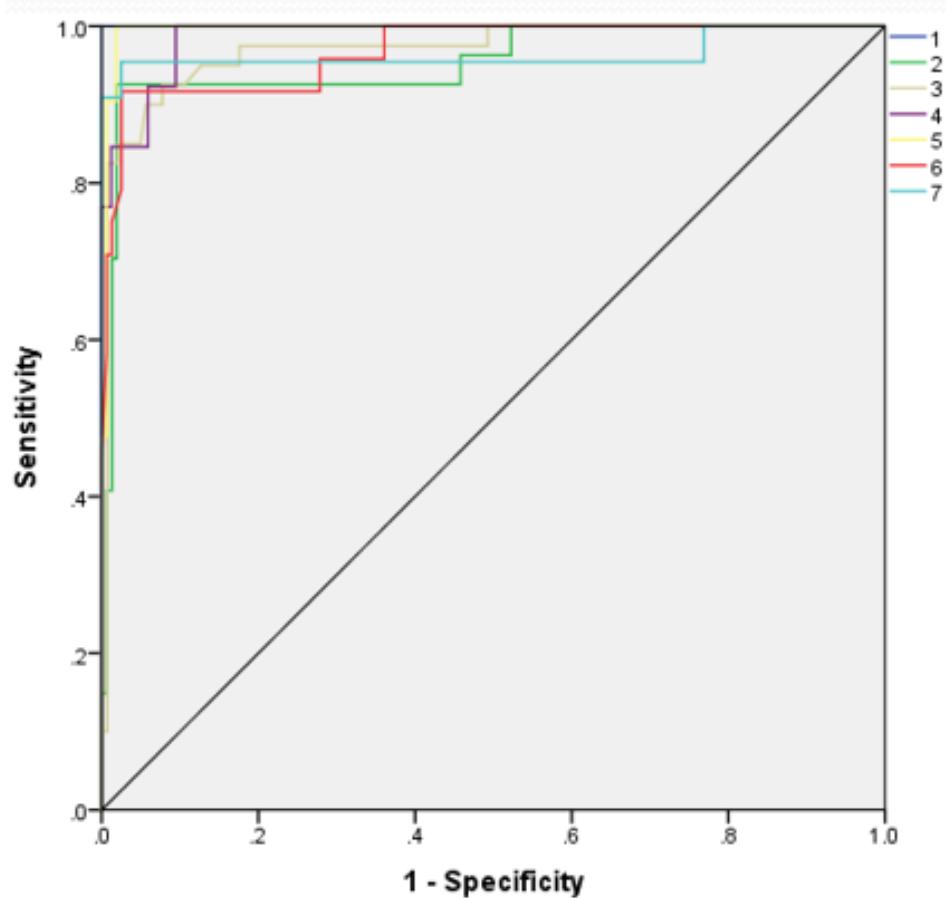


**Figure 4. 7 Structure of ANN (Multilayer Perceptron) with 7 classes**

The model accuracy was 92.6%. The Area Under the Curve (AUC) of ROC Curve are as shown in Table 4.6. The AUC were  $> 0.9$ , which shows that the classifier is excellent classifier.

**Table 4. 6 Area Under the Curve for 7-classes**

<b>Glaucoma class</b>	<b>AUC</b>
1-No Glaucoma	1.000
2-Primary Open Angle Glaucoma	.954
3-Primary Normal Tension Glaucoma	.970
4-Primary Ocular Hypertension	.987
5-Primary Angle Closure	.996
6-Angle Closure Glaucoma	.968
7-Secondary Glaucoma	.964



**Figure 4. 8 ROC Curve for 7-classes**

### 4.2.3 Principal Component Analysis for feature selection

The primary idea of the Principal Component Analysis (PCA) is to reduce the size of a data set that has number of interrelated variables while maintaining as much variation as possible in the data set. This is achieved by converting the main components (PCs) into a new set of variables that are not correlated and ordered so that the first few keep most variations in all the original variables and fewer variables in the following components. PCA is widely used in multivariate statistical analysis technique to reduce dependent variables to a smaller set of underlying variables (called components) based on patterns of correlation between the original variables. The pulse transit time attributes and other parameters in the data set can correlate multiple dependent variables. PCA identifies patterns for correlation between dependent variables and substitutes a new (component) variable for the original attribute group.

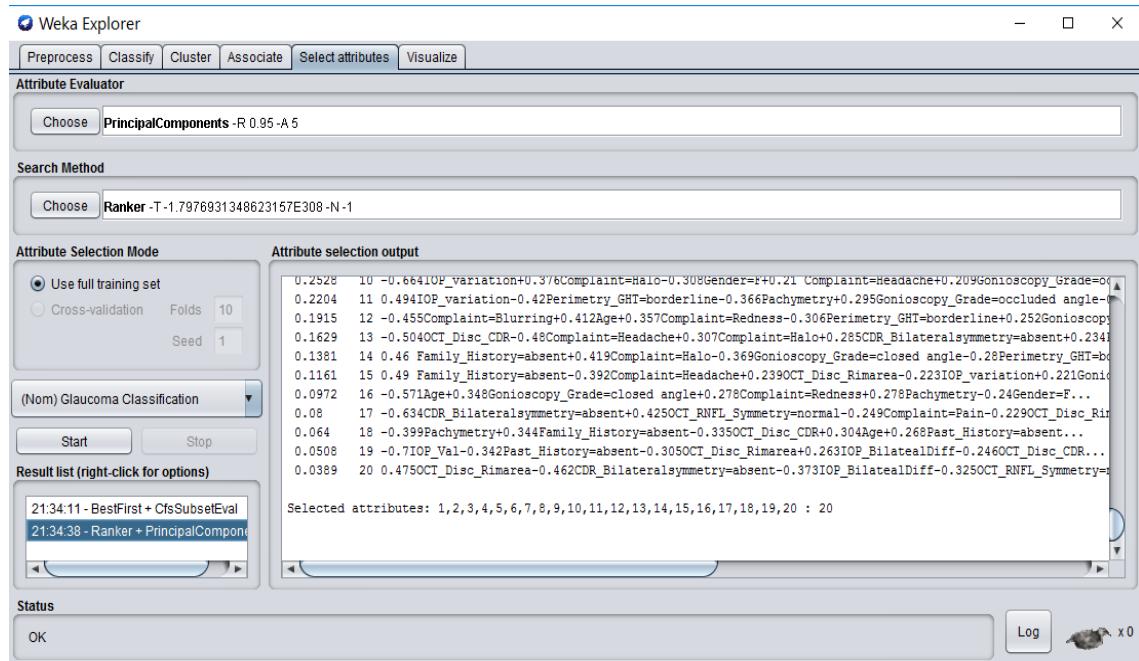


Figure 4. 9 PCA for glaucoma dataset

Here, PCA was performed on glaucoma dataset. PCA selected all 18 attributes as principal components. The reason being all the 18 attributes in glaucoma dataset are independent attributes. So, all 18 attributes were used for input to different classification algorithms for classification and prediction of glaucoma diagnosis.

#### 4.2.4 Result from Artificial Neural Network Classifier using WEKA

The implementation of ANN using WEKA for 7 classes was done with the help of MLP (Multilayer Perceptron) function available in WEKA. The MLP configuration had learning rate 0.4 and momentum 0.6. The accuracy of MLP in WEKA was 90%. Figure 4.10 shows the implementation of MLP.

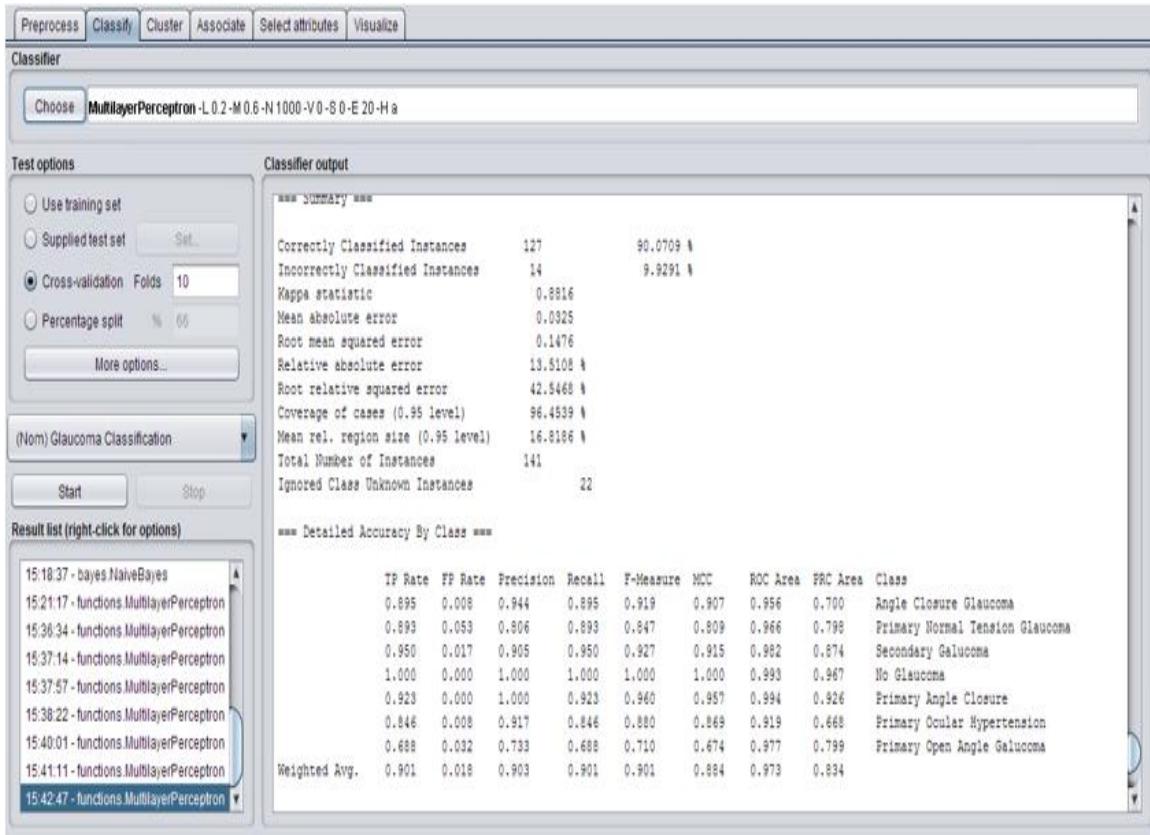


Figure 4. 10 MLP in WEKA

#### 4.2.5 Result from J48-Decision Tree Classifier(C 4.5) using WEKA

The implementation of J48, which is a decision tree classifier that implements C 4.5 classifier in WEKA was done in WEKA. The J48 configuration had confidence factor 0.25 and minimum number of objects was 2. The accuracy of J48 in WEKA was 86.50%. Figure 4.11 shows the implementation of J48.

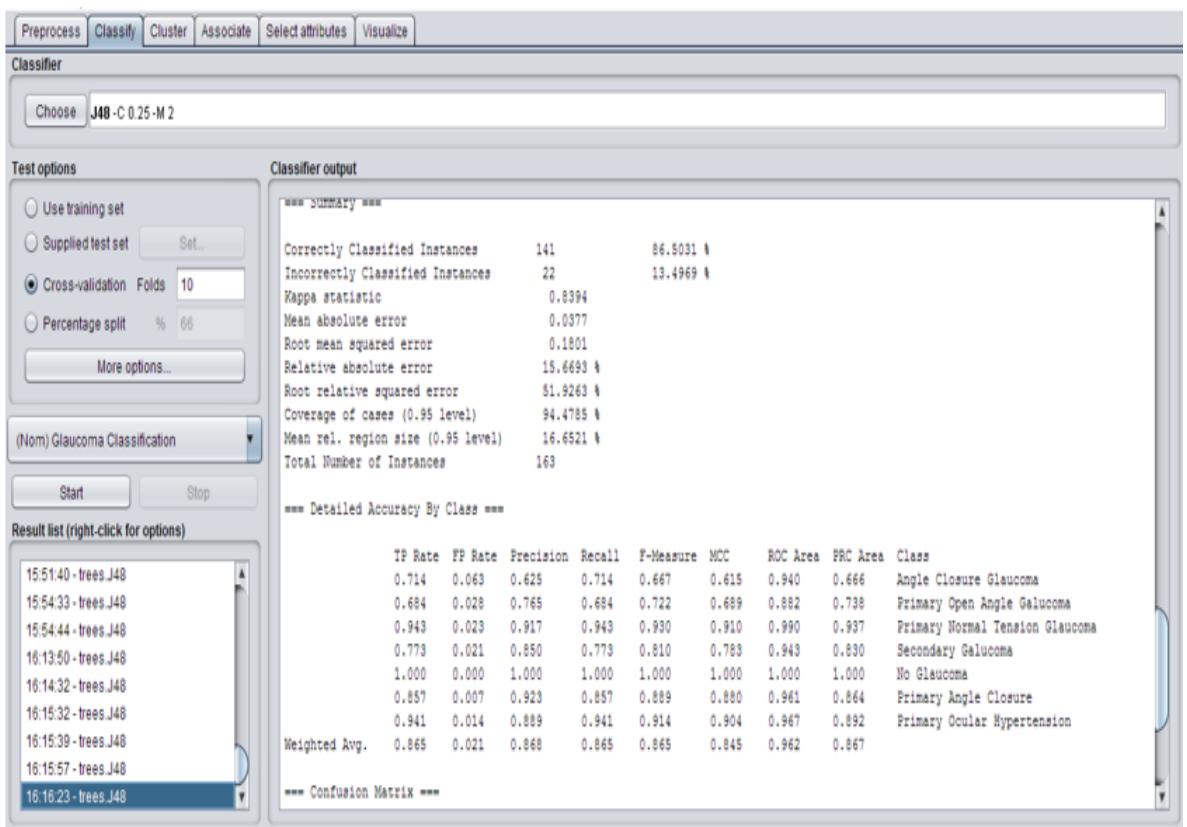


Figure 4.11 J48 in WEKA

#### 4.2.6 Result from Naïve Bayes Classifier using WEKA

Naïve Bayes is a probability based classifier. It takes a strong assumption of attribute independence. The implementation of Naïve Bayes classifier was done in WEKA using configuration with kernel estimator and with supervised discretization. The accuracy of Naïve Bayes with kernel estimator was 94.32%, while with supervised discretization the accuracy improved to 98.58%. Figure 4.12 shows the implementation of Naïve Bayes with kernel estimator Figure 4.13 shows the implementation with supervised discretization.

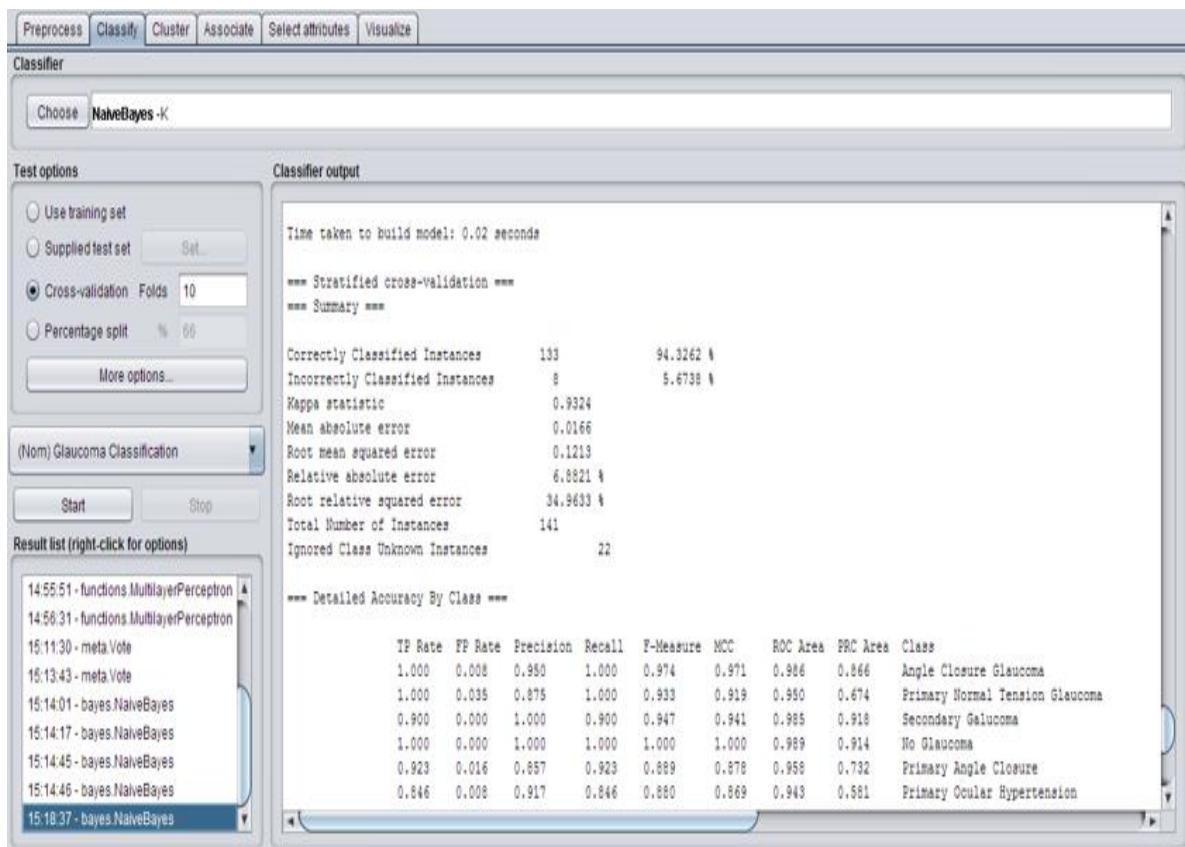
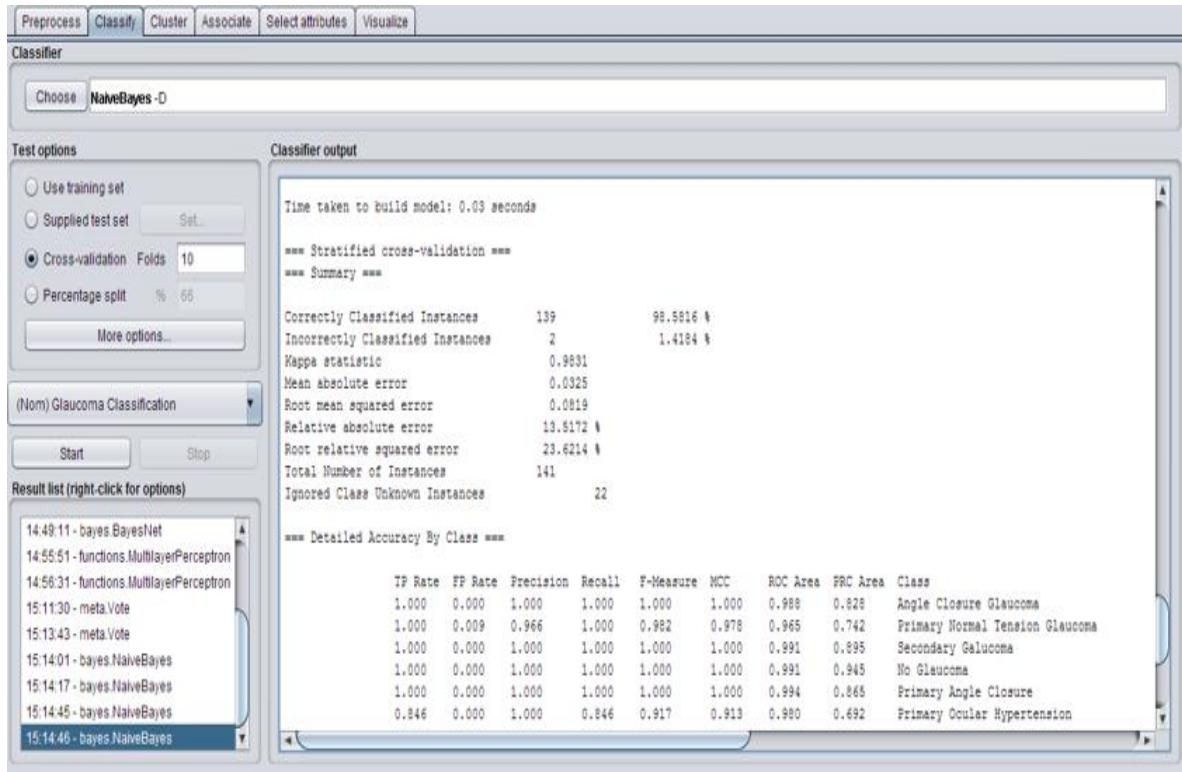


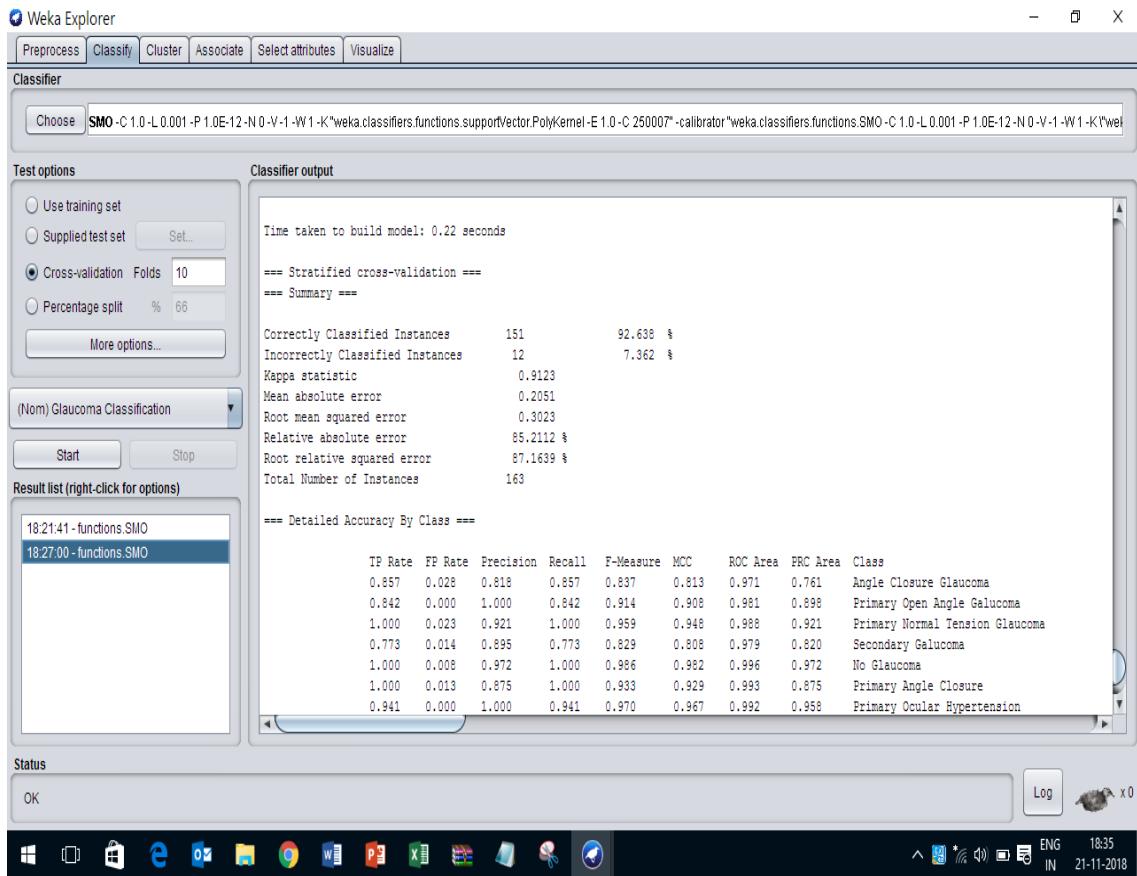
Figure 4. 12 Naïve Bayes with kernel estimator



**Figure 4. 13 Naïve Bayes with supervised discretization**

#### 4.2.7 Result from SMO Classifier using WEKA

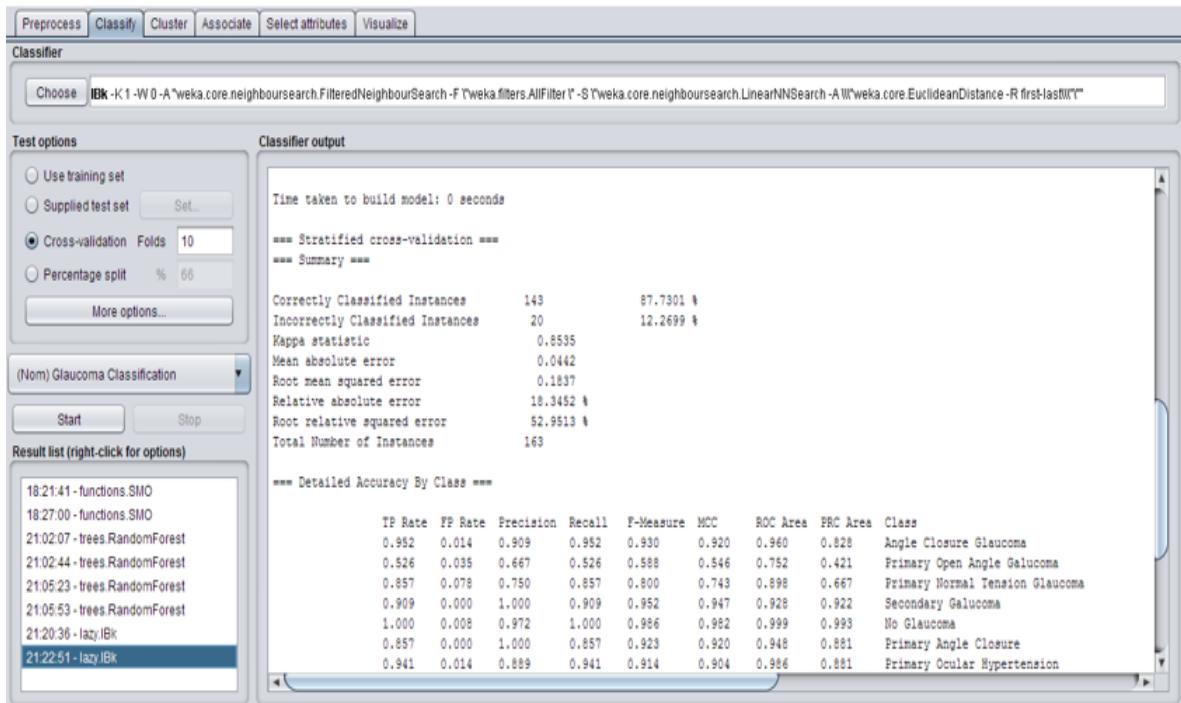
The implementation of Sequential Minimal Optimization (SMO), which is a Support Vector Machine (SVM) classifier implementation in WEKA was done using poly-kernel by normalizing the data. The accuracy of SMO in WEKA was 92.63%. Figure 4.14 shows the implementation of SMO.



**Figure 4. 14 SMO in WEKA**

#### 4.2.8 Result from IBk-KNN Classifier using WEKA

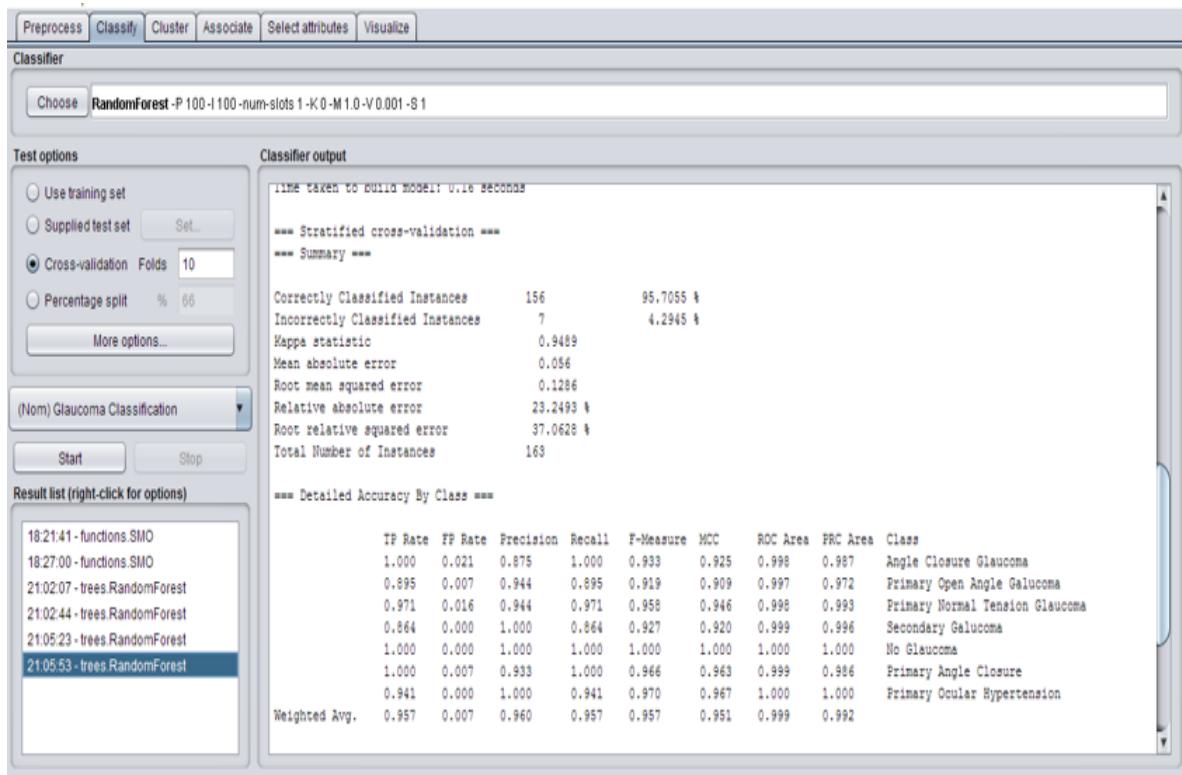
The implementation of Instance Based Learner (IBk), which is a K-Nearest Neighbor (KNN) classifier implementation in WEKA. The implementation of IBk was done using Euclidian distance to calculate nearest neighbors. The accuracy of IBk in WEKA was 87.73%. Figure 4.15 shows the implementation of IBk.



**Figure 4. 15 IBk in WEKA**

#### 4.2.9 Result from RF Classifier using WEKA

The classifier Random Forest (RF) is a combination of different decision trees used as classifier. The implementation of Random Forest was done using 100 as batch size in single execution slot. The accuracy of Random Forest in WEKA was 95.70%. Figure 4.16 shows the implementation of RF.



**Figure 4. 16 Random Forest(RF) in WEKA**

Table 4.7 represent the comparison of accuracies from single classifiers from different group of classifiers. It can be seen from the table that single classifiers such as, J48 and IBk has less accuracy compared to probability based Naïve Bayes classifier and Multilayer Perceptron and SMO function based classifier. Random Forest being a multi classifier works well with good accuracy.

**Table 4. 7 Comparison of different group of classifiers**

<b>Classifier group</b>	<b>Classifier</b>	<b>Accuracy</b>
Decision Trees	J48	86.50%
	Random Forest	95.70%
Bayes	Naïve Bayes	94.32%, 98.58%
Functions	Multilayer Perceptron	90%
	SMO	92.63%
Lazy	IBk	87.73%

#### **4.2.10 Result from Vote-Ensemble Classifier using WEKA**

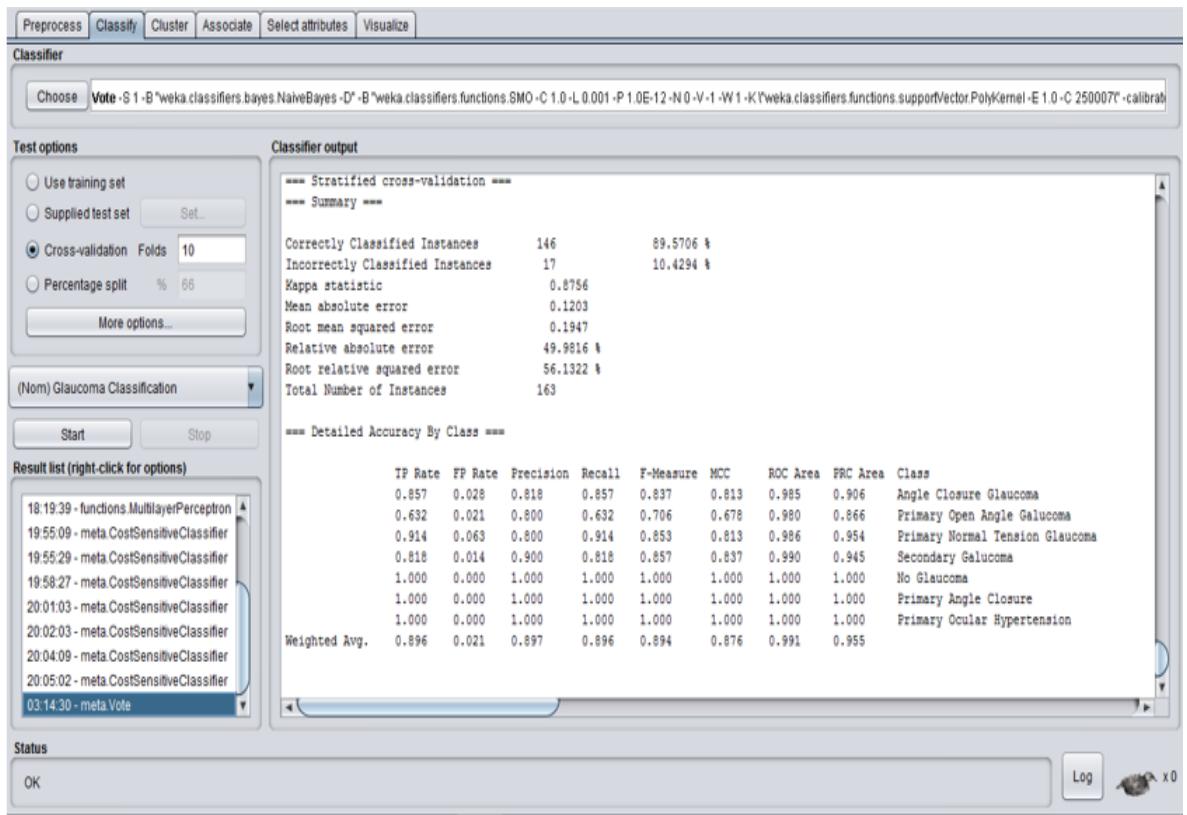
To improve the classification accuracy in order to get accurate diagnosis of glaucoma, an ensemble method approach was used. In this ensemble of classifiers, strengths of each classifier is utilized to overcome weaknesses of the classifiers participating in the ensemble. Here, the ensemble methods used is Vote method. Here, Vote ensemble collects the probability of classification from the base classifier participating in the ensemble and calculates the average of these probabilities to determine the class label for the data supplied to the ensemble. It assigns a class label with highest probability to the test data.

The Vote ensemble in this research had 3 base classifiers or base learners. The combination of J48, MLP and Naïve Bayes was used as one ensemble. The other ensemble used RF, MLP and Naïve Bayes. So, The MLP was combined with different Decision Tree Classifiers and with Naïve Bayes classifier using re-sampling of dataset.

Optimization of MLP is done by tuning Learning Rate and momentum parameters. While, Optimization of Naïve Bayes algorithm is done by kernel estimator for estimating numeric values. The Multi-classifier combiner-Vote ensemble is optimized to use average of probabilities produced by each base classifier. Average of probabilities help in reducing over fitting by the base learners.

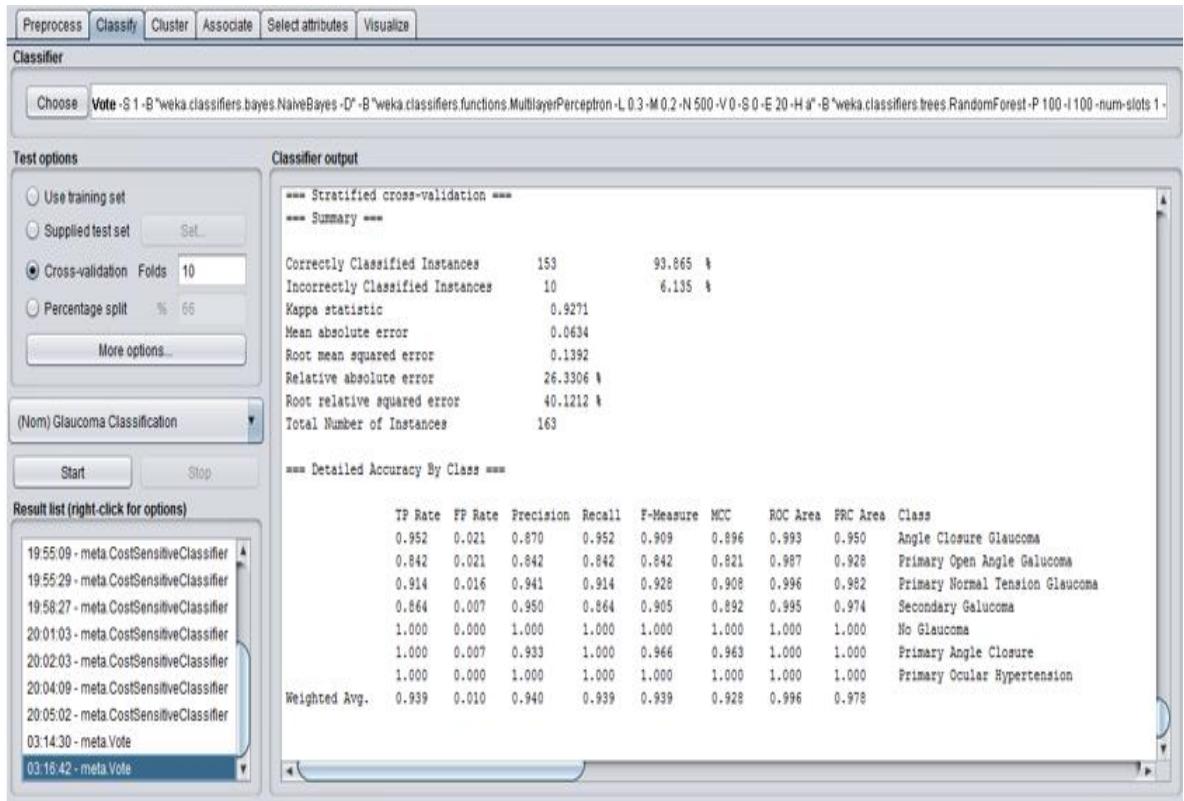
The Vote ensemble is used because it is a heterogeneous ensemble, which enables combination of classifiers from different group of classifiers, thus resulting in improvement of accuracy of the results.

Figure 4.17 shows the implementation of Vote ensemble method with base learners, Naïve Bayes, SMO and RF. The accuracy was 89.57%.



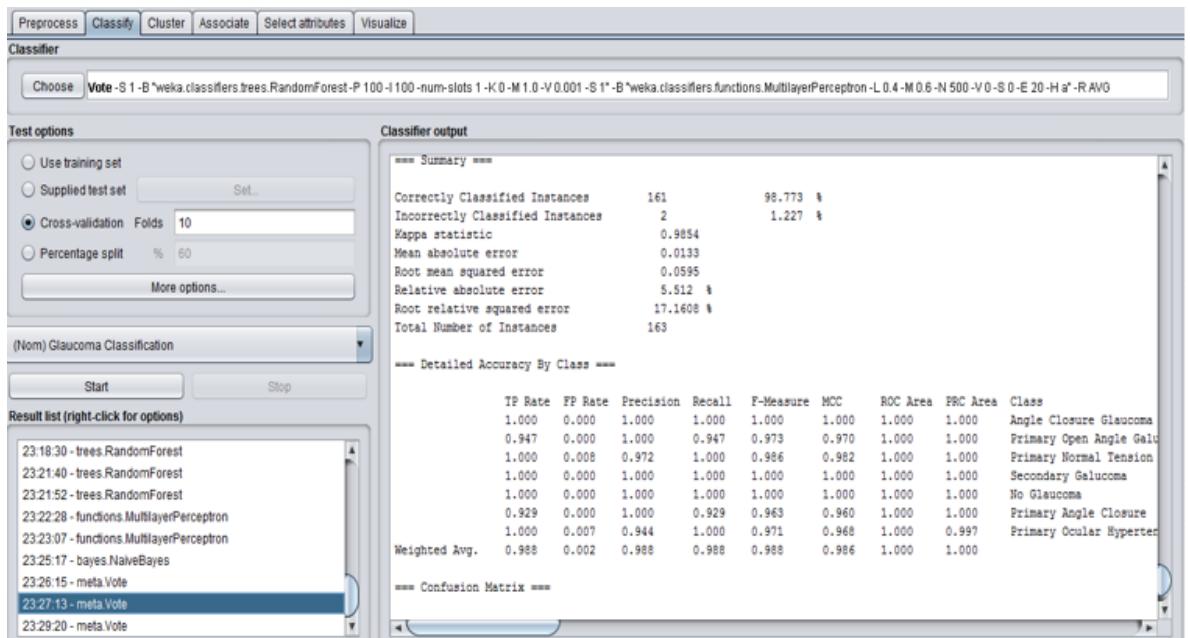
**Figure 4. 17 Ensemble of Naïve Bayes, SMO and Random Forest**

Figure 4.18 shows the implementation of Vote ensemble method with base learners, Naïve Bayes, MLP and RF. The accuracy was 93.86%.



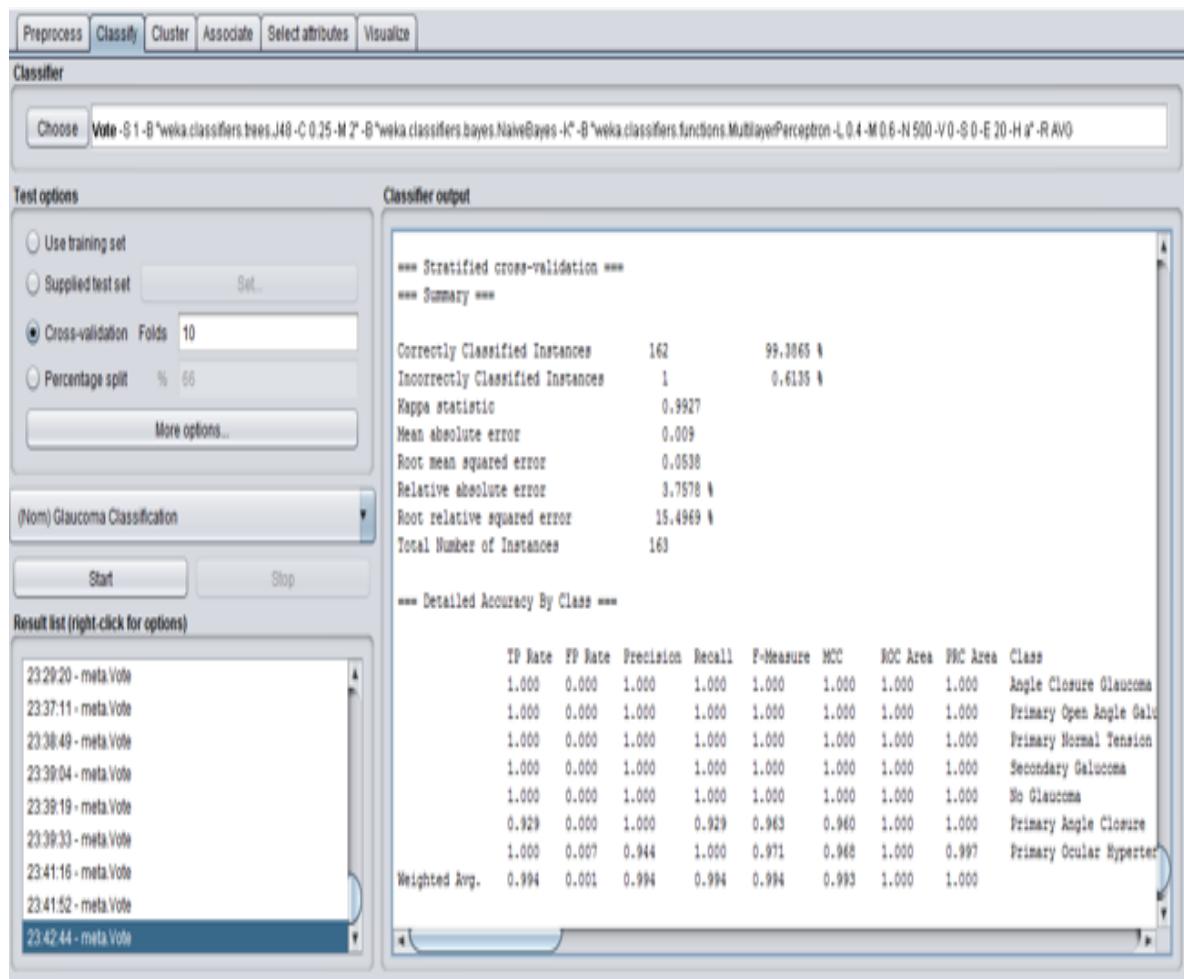
**Figure 4. 18 Ensemble of Naïve Bayes, MLP and RF**

Figure 4.19 shows the implementation of Vote ensemble method with base learners, MLP and RF. The accuracy was 98.77%.



**Figure 4. 19 Ensemble of MLP and RF**

Figure 4.20 shows the implementation of Vote ensemble method with base learners, MLP, Naïve Bayes and J48. The accuracy was 99.38%.



**Figure 4. 20 Ensemble of MLP, Naïve Bayes and J48**

Table 4.8, present comparison of different ensemble classifiers. The ensemble of MLP, Naïve Bayes and J48 performs with maximum accuracy of results. This ensemble has been used in classification and prediction of various conditions of glaucoma using glaucoma dataset having 7 different classes. Out of which 1 class is a normal control class and other 6 represent various conditions in glaucoma. As glaucoma is an eye disease leads to permanent loss of vision, thus to blindness, it is very crucial to diagnose this disease in early stage of occurrence. This disease is not reversible, but

its progression can be prevented, if it is detected in early stage. Thus, preventing permanent loss of vision.

**Table 4. 8 Comparison of different ensembles**

<b>Classifier group</b>	<b>Vote Ensemble- Base Classifiers</b>	<b>Accuracy</b>
Decision Trees, Bayes, Functions	RF, Naïve Bayes, SMO	89.57%
Bayes, Functions, Decision Trees	Naïve Bayes, MLP, RF	93.86%
Functions, Decision Trees	MLP, RF	98.77%
Bayes, Functions, Decision Trees,	Naïve Bayes, MLP, J48	99.38%

Figure 4.21 shows the result as diagnosis of a condition of glaucoma. Here, the diagnosis of the values provided is ‘Angle Closure Glaucoma’.

Care Sight Glaucoma Diagnosis System - Input Screen

**CARE SIGHT GLAUCOMA DIAGNOSIS**



**Age:**

**Gender:**  Male  Female

**Complaint :**

**Past Occurance of Complaint :**  Absent  Present

**Family History of Glaucoma :**  Absent  Present

**CDR Value:**

**CDR Bilateral Symmetry:**  Absent  Present

**IOP Value:**

**IOP Variation:**

**IOP Bilateral Difference:**

**Pachymetry :**

**Gonioscopy Grade :**

**OCT - RNFL SI Difference :**

**OCT RNFL Symmetry :**

**OCT - Disc CDR :**  Absent  Present

**OCT - Disc VCDR :**

**OCT - Disc Rimarea :**

**Perimetry GTH :**

**Diagnose Glaucoma...**

**Your Diagnosis :**

**Figure 4. 21 Diagnosis of Condition of Glaucoma**

Table 4.9, present the AUC Curve for ensemble of MLP and RF. The accuracy of this ensemble is 98.77%. The Area Under the Curve shows 1.000, which represents most accurate classifier.

**Table 4. 9 AUC for ensemble of MLP and RF**

Area Under the Curve (ROC)		
Glaucoma Class		Area
	Angle Closure Glaucoma	1.000
	Primary Open Angle Galucoma	1.000
	Primary Normal Tension Glaucoma	1.000
	Secondary Galucoma	1.000
	No Glaucoma	1.000
	Primary Angle Closure	1.000
	Primary Ocular Hypertension	1.000

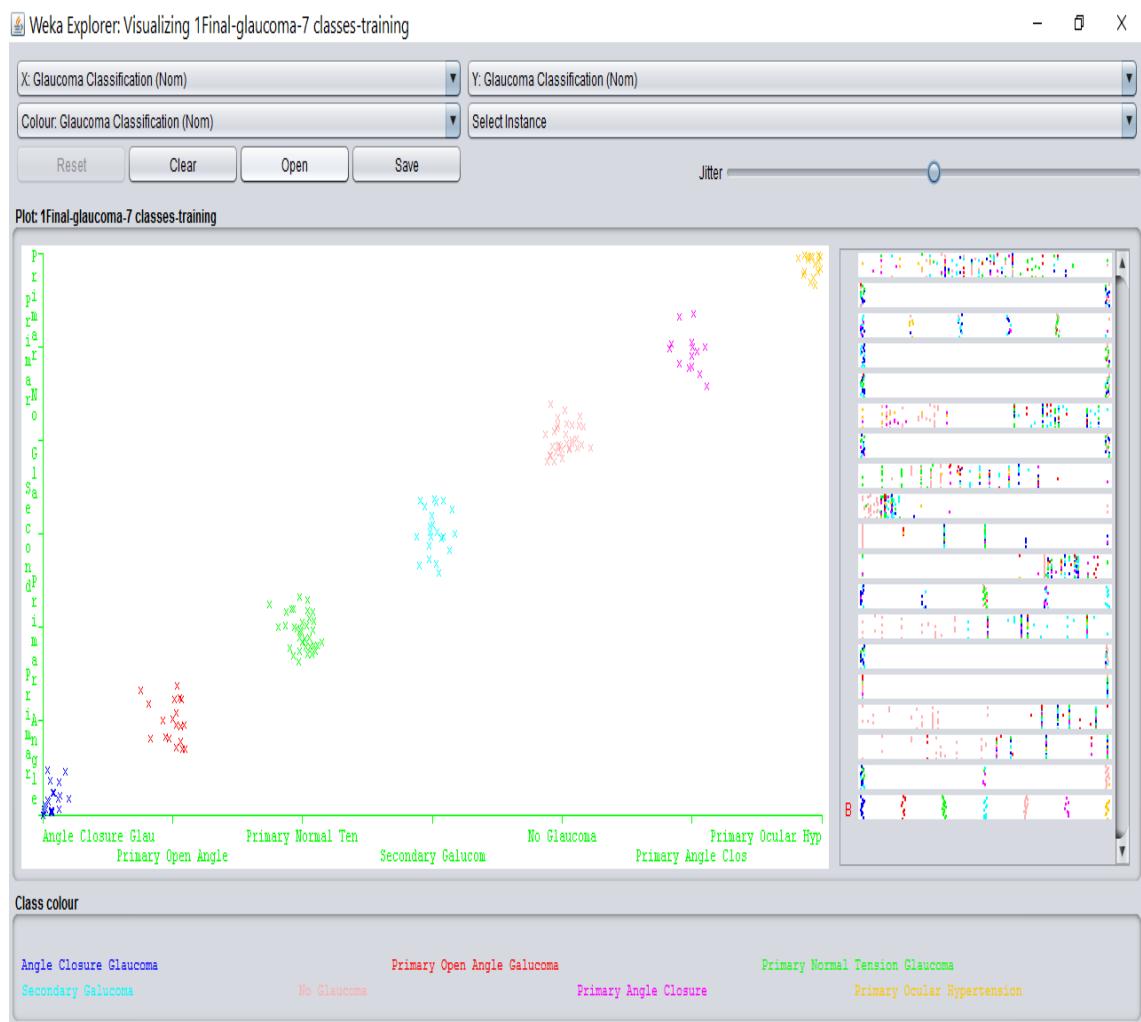
Table 4.10, present the AUC Curve for ensemble FGLAUC-99 of MLP, Naïve Bayes and J48. The accuracy of this ensemble is 99.38%. The Area Under the Curve shows 1.000, which represents most accurate classifier.

**Table 4. 10 AUC for ensemble of MLP, Naïve Bayes and J48**

Area Under the Curve (ROC)		
Glaucoma Class		Area
	Angle Closure Glaucoma	1.000
	Primary Open Angle Galucoma	1.000
	Primary Normal Tension Glaucoma	1.000
	Secondary Galucoma	1.000
	No Glaucoma	1.000
	Primary Angle Closure	1.000
	Primary Ocular Hypertension	1.000

Table 4.11, present comparison of performance achieved by proposed Vote ensemble classifier that uses Naïve Bayes, MLP and J48 algorithms with the performance of other algorithms or techniques available in literature.

Figure 4.22 shows classification plot of data after applying ensemble method.



**Figure 4. 22 Classification plot by ensemble method with MLP, J48 and Naïve Bayes**

**Table 4. 11 Comparison of performance of algorithms for glaucoma diagnosis**

Sr. No.	Author	Parameters	Classifier	Measuring Parameter
1	Nagaraj et al <sup>204</sup>	Visual Disc	ANN	Sensitivity-95% Specificity-94% Accuracy-94%
2	Biizioz et al <sup>205</sup>	Optic Nerve Head	ANN	Sensitivity-93% Specificity-94%
3	Nayak et al <sup>206</sup>	Optic Disc, Blood Vessel	ANN	Sensitivity-100% Specificity-80%
4	Huang et al <sup>207</sup>	RNFL Thickness	ANN	Area ROC-0.97

<sup>204</sup>Nagarajan et al, Neural network model for early detection of glaucoma using multi-focal visual evoked potential (M-Vep), *Investigative Ophthalmology & Visual Science* 42 (2002)

<sup>205</sup>Bizios D, Heijl A, Bengtsson B, "Integration and fusion of standard automated perimetry and optical coherence tomography data for improved automated glaucoma diagnostics", *BMC Ophthalmology*. 2011, 11 (1): 20.

<sup>206</sup>JagadishNayak et al, Automated Diagnosis of Glaucoma Using Digital Fundus Images, *Journal of Medical Systems*, Vol. 33, Issue 5, pp-337-346, October 2009.

<sup>207</sup>Mei-LingHuang,Hsin-YiChen,Jian-JunHuang,Glaucoma Detection using Adaptive Neuro-Fuzzy Inference System, *Expert Systems with Applications* Vol.32458–468,2007.

5	Chauhan et al <sup>208</sup>	CDR, Perimetry, OCT	SVM	Sensitivity- 84.1%  Specificity- 96.3%  Accuracy- 92.6%
6	Nacer Eddine Benzebouchi et al <sup>209</sup>	Fundus Image	Convolutional Neural Network	96.9%
7	Seong Jae Kim et al <sup>210</sup>	RNFL, OCT, Visual Field	Random Forest	98%
8	Huazhu Fu et al <sup>211</sup>	CDR, Optic Disc from Fundus Image	Ensemble Network	77%
9	Kleyton Arlindo Barella et al <sup>212</sup>	RNFL, OCT	CTREE	87.77%

<sup>208</sup>Chauhan et al, "Data Mining Techniques for Diagnostic Support of Glaucoma using Stratus OCT and Perimetric Data", International Journal of Computer Applications (0975 – 8887), Volume 151 – No.8, October 2016

<sup>209</sup>Eddine Benzebouchi, Nacer & Azizi, Nabiha & Bouziane, Seif Eddine. (2018). GLAUCOMA DIAGNOSIS USING COOPERATIVE CONVOLUTIONAL NEURAL NETWORKS. International Journal of Advances in Electronics and Computer Science (ijaeics).

<sup>210</sup>Kim, S. J., Cho, K. J., & Oh, S. (2017). Development of machine learning models for diagnosis of glaucoma. PloS one, 12(5), e0177726. doi:10.1371/journal.pone.0177726.

<sup>211</sup> Huazhu Fu et al, "Disc-aware Ensemble Network for Glaucoma Screening from Fundus Image", arXiv:1805.07549v1 [cs.CV]

<sup>212</sup>Kleyton Arlindo Barella et al, "Glaucoma Diagnostic Accuracy of Machine Learning Classifiers Using Retinal Nerve Fiber Layer and Optic Nerve Data from SD-OCT", Journal of Ophthalmology, Volume 2013, Article ID-789129, 7 pages, <http://dx.doi.org/10.1155/2013/789129>

From the above Table 4.11, it can be derived that the performance accuracy obtained by the proposed ensemble classifier FGLAUC-99 is better than the classifiers used in literature. The results so far seems promising and shows improvement in accuracy of classification, in turn, improvement in automated diagnosis of various conditions of glaucoma.

The ensemble classifier FGLAUC-99, developed in this research, use machine learning classifiers and intelligently provide accurate diagnosis of various conditions of glaucoma.

---

# **CHAPTER – 5 Conclusions, Major Contributions and Scope of Future Work**

## **5.1 Conclusions**

The research encompasses study of different classification algorithm, finding out the most suitable and accurate algorithm by applying these algorithm to the glaucoma dataset, developing an ensemble algorithm to improve the accuracy of classification for glaucoma diagnosis.

The data obtained from practitioner shows that patients with age group 45-64 formed the major part of the data, which was 56.44%. From the total data, 63.05% patients were male, representing the eye ailment. The ensemble classifier FGLAUC-99 shows accuracy 99.38%, which is higher than accuracy of other techniques found in literature review.

Amongst the list of algorithms used for classification, C5.0, RF, SVM, KNN, Naïve Bayes and ANN, probability based algorithm Naïve Bayes and decision tree based algorithm Random Forest gave better accuracy than the other algorithms. The accuracy for Naïve Bayes algorithm was 94.32% and accuracy for Random Forest was 95.70%, which is better than the accuracy of following algorithms considered for the study :

<b>Classifier</b>	<b>Accuracy</b>
J48	86.50%
Multilayer Perceptron	90%
SMO	92.63%
IBk	87.73%
Naïve Bayes	94.32%
Random Forest	95.70%

Ensemble of classifiers gives improved accuracy compared to single individual classifiers. Different ensembles of classification algorithm were developed. Ensemble FGLAUC-99 of J48, Naïve Bayes and MLP gave the best result with 99.38% accuracy. Accuracies of other ensembles studied are:

<b>Vote Ensemble- Base Classifiers</b>	<b>Accuracy</b>
RF, Naïve Bayes, SMO	89.57%
Naïve Bayes, MLP, RF	93.86%
MLP, RF	98.77%
Naïve Bayes, MLP, J48	99.38%

## **5.2 Major Contribution**

The contribution of the thesis, aligned to the research objective are as follows:

1. The data was obtained from a practicing ophthalmologist.
2. The patients with age group 45-64 formed the major part of the data which was 56.44%. 26.38% patients were found to be in the age group 65-79 years. From the total data, 63.05% patients were male and 34.97% patients were female, representing the eye ailment.
3. Various classification techniques based on experiments, such as, C5.0 (J48 in WEKA), RF, SVM (SMO in WEKA), and k-nearest neighbour (KNN) (IBk in WEKA) algorithms, Naïve Bayes,

Multilayer Perceptron (ANN) were studied for diagnosis of various conditions (types) of glaucoma in patients.

4. Out of all the classification algorithms, such as, C5.0 (J48 in WEKA), Random Forest, Support Vector Machine (SMO in WEKA), and k-nearest neighbor (KNN) (IBk in WEKA) algorithms, Naïve Bayes, Multilayer Perceptron (ANN), Naïve Bayes algorithm and Random Forest (RF) gives good accuracy which is 94.32% and 95.70% respectively.
5. The Ensemble Classifier technique gives improved classification accuracy compared to individual classifiers, such as, C5.0, RF, SVM, and k-nearest neighbour (KNN) algorithms, Naïve Bayes, Multilayer Perceptron, J48. It complements the strengths and weaknesses of individual classifiers and gives better results.
6. Ensemble Classifier were developed using different heterogeneous base classifier algorithms. The improved accuracies obtained by the ensemble classifiers on the data obtained from practicing ophthalmologist are as follows :
  1. Random Forest, Naïve Bayes, SMO : Accuracy-89.57%
  2. Naïve Bayes, MLP, RF : Accuracy-93.86%
  3. MLP, RF : Accuracy-98.77%
  4. Naïve Bayes, MLP, J48 : Accuracy-99.38%

An Ensemble classifier FGLAUC-99 designed using Naïve Bays, MLP and J48 has shows maximum accuracy of 99.38%, that

helps in more accurate diagnosis of various conditions of glaucoma.

### **5.3 Scope of future work**

With the further advancements in the field of computer science, this research can be extended to link the proposed system with the patient's electronic records for diagnosis support. This system can be extended to include monitoring and follow-up procedures. It can be employed with telemedicine to support diagnosis process, to the areas where doctors are out of reach.

---

## List of References

1. Teach, R.L. and Shortliffe, E.H. (1981), “An analysis of physician attitudes regarding computer-based clinical consultation systems”, *Comput. Biomed. Res.* 14, pp. 542-558.
2. Wallis, J.W. and Shortliffe, E.H. (1982), “Explanatory power for medical expert systems: studies in the representation or causal relationships for clinical consultations”, *Meth. Info. Med.* 21, pp.127-136.
3. Park S.C., Pu J. and Zheng B. (2009), “Improving performance of computer-aided detection scheme by combining results from two machine learning classifiers”, *Academic Radiology*, No. 16, No.3, pp 266-274.
4. Mangasarian O.L., Street W.N. and Wolberg W.H. (1995), “Breast cancer diagnosis and prognosis via linear programming”, *Operations Research*, Vol. 43, No.4, pp. 570-577.
5. Xin Yao and Yong Liu (1996), “Neural networks for breast cancer diagnosis”, *Proceedings of the 1999 Congress on Evolutionary Computation*, IEEE Press, Vol. 3, pp. 1760-1767.
6. Abbass H.A. (2002), “An evolutionary artificial neural networks approach for Breast Cancer Diagnosis”, *Artificial Intelligence in Medicine*, Vol.25, No.3, pp.265-281.
7. Duch W. (2007), “What is computational intelligence and Where it is going”, W.Duch and J.Mandziuk (Eds.), *Challenges for Computational Intelligence*, pp. 1 -13, Springer Verlag, Heidelberg.
8. Hong X. and Mitchell R.J. (2007), ‘Backward elimination model construction for regression and classification using leave-one-out criteria’ *International Journal of Systems Science*, Vol. 38 , No.2, pp. 101 – 113.
9. Mahabala, H. N., Chandrasekhara, M. K., Baskar, S., Ramesh, S., and Somasundaram, M. S. (1992), “ICHT: An Intelligent Referral System for Primary Child Health Care”, *Proceedings SEARCC’92: XI Conference of the South East Asia Regional Computer Confederation*. Kuala Lumpur.

10. Manickam, S., and Abidi, S. S. R. (1999), “Experienced Based Medical Diagnostics System Over The World Wide Web (WWW)”, Proceedings of The First National Conference on Artificial Intelligence Application In Industry, Kuala Lumpur, pp. 47 – 56.
11. Alexopoulos, E., Dounias, G. D., and Vemmos, K. (1999), “Medical Diagnosis of Stroke Using Inductive Machine Learning. Machine Learning and Applications: Machine Learning in Medical Applications”, Chania, Greece, pp. 20-23.
12. Zelic, I., Lavrac, N., Najdenov, P., Rener-Primec, Z. (1999), “Impact of machine learning of the Diagnosis and Prognosis of First Cerebral Paroxysm. Machine Learning and Applications: Machine Learning in Medical Applications”, Chania, Greece, pp. 24-26.
13. Ruseckaite, R. (1999), “Computer Interactive System for Ascertainment of Visual Perception Disorders”, Machine Learning and Applications: Machine Learning in Medical Applications, Chania, Greece, pp. 27-29.
14. Bourlas, P., Giakoumakis, E., and Papakonstantinou, G. (1999), “A Knowledge Acquisition and management System for ECG Diagnosis. Machine Learning and Applications: Machine Learning in Medical Applications”, Chania, Greece, pp. 27-29.
15. Shortliffe, E. H. (1987), “Computer Programs to Support Clinical Decision Making. Journal of the American Medical Association”, Vol. 258, No. 1.
16. Neves, J., Alves, V., Nelas, L., Romeu, A., and Basto, S. (1999), “An Information System That Supports Knowledge Discovery and Data Mining in Medical Imaging, Machine Learning and Applications: Machine Learning in Medical Applications”, Chania, Greece, pp. 37-42.
17. Jankowski, N. (1999), “Approximation and Classification in Medicine with IncNet Neural Networks”, Machine Learning and Applications: Machine Learning in Medical Applications. Chania, Greece, pp. 53-58.
18. Lippmann, R. P., Kulkolich, L., Shahian, D. (1995), “Predicting the Risk of Complications in Coronary Artery Bypass Operations Using Neural Networks”, Advances in Neural Information Processing Systems 7, The MIT Press, Cambridge, pp. 1053-1062.
19. Heden, B., Ohlsson, M., Rittner, R., Pahlm, O., Haisty, W. K., Peterson, C., and Edenbrandt, L. (1996), “Agreement Between Artificial Neural Networks and Human Expert for the Electrocardiographic Diagnosis of

Healed Myocardial Infarction”, Journal of the American College of Cardiology, Vol. 28, pp. 1012-10s16.

20. Karkanis, S. A., Magoulas, G. D., Grigoriadou, M., and Schurr, M. (1999), “Detecting Abnormalities in Colonoscopic Images by Textual Description and Neural Networks”, Machine Learning and Applications: Machine Learning in Medical Applications. Chania, Greece, pp. 59-62.
21. Caruana, R., Baluja, S., and Mitchell, T. (1996), “Using the Future to “Sort Out” the Present: Rankrop and Multitask Learning for Medical Risk Evaluation”, Advances in Neural Information Processing Systems 8, The MIT Press, Cambridge, pp. 959-965.
22. Pranckeviciene, E. (1999), “Finding Similarities Between An Activity of the Different EEG’s by means of a Single layer Perceptron”, Machine Learning and Applications: Machine Learning in Medical Applications. Chania, Greece, pp. 49-52.
23. Wade, N.J. (2007), “Image, eye, and retina (invited review)”, Journal of the Optical Society of America A, Vol. 24, No. 5, pp. 1229-1249.
24. Thylefors, B., Negrel, A.D., Pararajasegaram, R. and Dadzie, K.Y., (1995), “Global data on blindness”, Bulletin of the World Health Organization, Vol.73, No.1, pp.115-121.
25. Resnikoff, S., Pascolini, D., Etyaale, D., Kocur, I., Pararajasegaram, R., Pokharel, G.P. and Mariotti, S.P. (2004), “Global data on visual impairment in the year 2002”, Bulletin of the world health organization, Vol.82, No.11, pp.844-851.
26. Quigley H.A. and Broman A.T. (2006), “The number of people with Glaucoma worldwide in 2010 and 2020”, British Journal of Ophthalmology, Vol.90, pp. 262-267.
27. Miglior, S., Pfeiffer, N., Torri, V., Zeyen, T., Cunha-Vaz, J. and Adamsons, I. (2007), “Predictive factors for open-angle Glaucoma among patients with ocular hypertension in the European Glaucoma Prevention Study”, Ophthalmology, 114(1), pp.3-9.

28. Gordon, M.O., Beiser, J.A., Brandt, J.D., Heuer, D.K., Higginbotham, E. J., Johnson, C.A. and Kass, M.A. (2002), “The ocular hypertension treatment study. Baseline factors that predict the onset of primary open-angle Glaucoma”, *Archives of ophthalmology*, Vol.120, No.6, pp.714-720.
29. Coleman, A.L., Gordon, M.O., Beiser, J.A., Kass, M.A. and Study, O.H.T. (2004), “Baseline risk factors for the development of primary open-angle Glaucoma in the Ocular Hypertension Treatment Study”, *American Journal of Ophthalmology*, Vol.138, pp.684–685.
30. Caprioli, J. and Coleman, A.L. (2008), “Intraocular pressure fluctuation: a risk factor for visual field progression at low intraocular pressures in the Advanced Glaucoma Intervention Study”, *Ophthalmology*, Vol.115, No.7, pp.1123-1129.
31. Nouri-Mahdavi, K., Hoffman, D., Coleman, A.L., Liu, G., Li, G., Gaasterland, D. and Caprioli, J. (2004), “Predictive factors for Glaucomatous visual field progression in the Advanced Glaucoma Intervention Study”, *Ophthalmology*, Vol.111, No.,9, pp.1627–1635.
32. Klein, B.E., Klein, R., Sponsel, W.E., Franke, T., Cantor, L.B., Martone, J. and Menage, M.J. (1992), “Prevalence of Glaucoma. The Beaver Dam Eye Study”, *Ophthalmology*, Vol.99, No.10, pp.1499–1504.
33. Leske, M.C., Nemesure, B., He. Q., Wu, S.Y., Heitmancik, J.F., Hennis, A. and Barbados Family Study Group. (2001), “Patterns of open-angle Glaucoma in the Barbados Family Study”, *Ophthalmology*, Vol.108. No.6, pp.1015- 1022.
34. Wong, T.Y., Klein, B.E., Klein, R., Knudtson, M. and Lee, K.E. (2003), “Refractive errors, intraocular pressure, and Glaucoma in a white population”, *Ophthalmology*, Vol.110, No.1, pp. 211–217.

35. Xu, J., Chutatape, O., Sung, E., Zheng, C. and Kuan, P.C.T. (2007), “Optic disk feature extraction via modified deformable model technique for Glaucoma analysis”, *Pattern Recognition*, Vol. 40, No.7, pp.2063-2076.
36. De Voogd, S., Ikram, M.K. and Wolfs, R.C., (2005), “Incidence of open-angle Glaucoma in a general elderly population”, *The Rotterdam Study. Ophthalmology*, VOl.112, No.9, pp. 1487–1493.
37. Mukesh, B.N., McCarty, C.A., Rait, J. L. and Taylor, H.R. (2002),“Five-year incidence of open-angle Glaucoma: the Vision Impairment Project”, *Ophthalmology*, Vol.109, No.6, pp.1047–1051.
38. Friedman, D.S., Wolfs, R.C.O., Colmain, B.J., Klein, B.E., Taylor, H.R., West, S., Leske M.C., Mitchell, P., Congdon, N., Kempen, J. and Eye Diseases Prevalence Research Group. (2004), “Prevalence of open-angle Glaucoma among adults in the United States”, *Archives of ophthalmology*, Vol.122, pp.532–538.
39. Quigley H.A. and Broman A.T. (2006),“The number of people with Glaucoma worldwide in 2010 and 2020”, *British Journal of Ophthalmology*, Vol.90, pp. 262-267.
40. Tielsch, J.M., Katz, J., Sommer, A., Quigley, H.A. and Javitt, J.C. (1994), “Family history and risk of primary open angle Glaucoma”, *The Baltimore eye survey, Archives of ophthalmology*, Vol. 112, No.1, pp.69-73.
41. Quigley H.A. and Broman A.T. (2006), “The number of people with Glaucoma worldwide in 2010 and 2020”, *British Journal of Ophthalmology*, Vol.90, pp. 262-267.
42. Tielsch, J.M., Katz, J., Sommer, A., Quigley, H.A. and Javitt, J.C. (1994), “Family history and risk of primary open angle Glaucoma”, *The Baltimore eye survey, Archives of ophthalmology*, Vol. 112, No.1, pp.69-73.
43. Varma, R., Ying-Lai, M. and Francis B.A. (2004), “Prevalence of open-angle Glaucoma and ocular hypertension in Latinos: the Los Angeles Latino Eye Study. *Ophthalmology*, Vol.111, No.8, pp.1439–144.
44. Mansberger, S.L., Romero, F.C. and Smith, N.H. (2005), “Causes of visual impairment and common eye problems in Northwest American

- Indians and Alaska Natives”, American journal of public health, Vol.95, No.5, pp. 881–886.
45. D. Zhang, Y. Wang, H. Huang. (2007), Fuzzy-rough membership function neural network and its application to pattern recognition, Proc. SPIE 6788, MIPPR 2007: Pattern Recognition and Computer Vision, 67882N.
  46. Sudha, A., Gayathiri, P.and Jaisankar, N. (2012) “Effective Analysis and Predictive Model of Stroke Disease using Classification Methods”, International Journal of Computer Applications Volume 43(14), pp. 0975 – 8887.
  47. Sellappan Palaniappan, Rafiah Awang. “Intelligent Heart Disease Prediction system using data mining techniques”. International Journal of Computer Science and Network Security, Vol. 8(8), pp. 108–115, 2008.
  48. Latha Parthiban and Subramanian, R. “Intelligent Heart Disease Prediction System using CANFIS and Genetic Algorithm”, International Journal of Biological and Life Science, Vol.15,pp. 157-160, 2007.
  49. Chaitrali, S. Dangare, Sulabha S. Apte. (2012). “Improved Study of Heart Disease Prediction System using Data Mining Classification Techniques ”International Journal of Computer Applications, Vol. 47(10), pp. 0975 – 888.
  50. Resul Das, Ibrahim Turkoglu and Abdulkadir Sengur. (2009), “Effective diagnosis of heart disease through neural networks ensembles” International Journal of expert systems with applications, Vol. 36, pp. 7675-7680.
  51. Olatubosun Olabode and Bola Titilayo Olabode. (2012), “Cerebrovascular Accident Attack Classification Using Multilayer Feed Forward Artificial Neural Network with Back Propagation Error”, Journal of Computer Science, pp.18-25.
  52. Patil, S.B. and Kumaraswamy, Y.S. (2009) “Intelligent and effective heart attack prediction system using data mining and artificial neural network,” European Journal of Scientific Research, Vol. 31(4), pp. 642–656.
  53. Fidele, B., Cheeneebash, J., Gopaul, A.and Goorah, S.S.D. (2009) “Artificial neural network as a clinical decision-supporting tool to predict cardio vascular disease”, Trends in Applied Sciences Research Vol. 4(1), pp. 36–46.
  54. Pei Chann Chang, Jyun-Jie Lin and Chen-Hao Liu. (2012), “An attribute weight assignment and particle swarm optimization algorithm for medical

- database classifications”, Computer methods and programs in Biomedicine, Vol. 107, pp. 382-392.
55. Sultan Noman Qasem and Siti Mariyam Shamsuddin. (2011), “Radial basis function network based on time variant multi-objective particle swarm optimization for medical diseases diagnosis”, Journal of Applied Soft Computing, Vol. 11(1), pp. 1427-1438.
56. Huy Nguyen Anh Pham and Evangelos Trianaphyllou. (2009), “An application of anew meta-heuristic for optimizing the classification accuracy when analyzing some medical data sets”, Expert Systems with Applications, Vol.36(5), pp. 9240-9249.
57. Nikunj Chauhan V. Ravi and Karhik Chandra, D. (2009), “Differential Evolution trained wavelet neural network application to bankruptcy prediction in banks,” Expert systems with Applications, Vol. 36(4), pp. 7659-7665.
58. Chakravathy, S. and Dash, P.K. (2011), “Dynamic filter weights neural network model integrated with differential evolution for day-ahead price forecasting in energy market”, Expert systems with Applications, Vol. 38(9),pp. 10974-10982.
59. Bidyadhar Subudhi and Debashinsha Jena. (2011), “A Differential Evolution based neural network approach to non-linear system identification”, Applied Soft Computing, Vol. 11(1), pp. 861-871.
60. Yu, Y., Schell, M.C. and Zhang, J.B.Y. (19997), “Decision theoretic steering and genetic algorithm optimization: application to stereotactic radiosurgery treatment planning”, Medical Physics, Vol. 24(11), pp. 1742–1750.
61. Dybowski, R., Weller, P., Chang, R.and Gant, V. (1999), “Prediction of outcome inthe critically ill using an artificial neural network synthesized by a genetic algorithm”, The Lancet Oncology, Vol. 52(4), pp. 281–286.
62. Handels, H., Th, R.O., Kreusch, J., Wolff, H.H.andPoppl, S.J. (1999), “Feature selection for optimized skin tumor recognition using genetic algorithms”, Artificial Intelligence in Medicine, Vol. 16, pp. 283–297.
63. Heckerling, P.S., Gerber, B.S., Tape, T.G. and Wigton, R.S. (2004), “Use of geneticalgorithms for neural networks to predict community-acquired pneumonia”, Artificial Intelligence in Medicine, Vol. 30, pp. 71–84.

64. Montani, S., Bellazzi, R., Porinale, L. and Stefanelli, M. (2000), "A multimodal reasoning methodology for managing IDDM patients," International Journal of Medical Informatics, Vol. 58–59, pp. 243–256.
65. Sexton, R.S., Dorsey, R.E. and Johnson, J.D. (1998), "Toward global optimization of neural networks: A comparison of the genetic algorithm and back propagation", Decision Support Syst. Vol. 22,pp. 171–185.
66. Brill, F. Brown, D. and Martin, W.(1992), "Fast Genetic Selection of Features for Neural Network Classifiers", IEEE Transactions on Neural Networks, Vol.3(2), pp. 324-328.
67. Jihoon Yang, Vasant, G. Honavar, (1998), "Feature Subset Selection Using a Genetic Algorithm", Trans on IEEE Intelligent Systems, Vol. 13(2), 1998.
68. H. Paul S.G., Ben, S.T., Thomas, G.W. and Robert, S. (2004), "Use of genetic algorithms for neural networks to predict community-acquired pneumonia", Artificial Intelligence in Medicine, Vol. 30(1), pp.71-84.
69. Shanti, D., Sahoo, G. and Saravanan, N. (2009), "Evolving Connection Weights of ANN using GA with application to the Prediction of Stroke Disease", International Journal of Soft Computing, Vol. 4(2):pp. 95-1029.
70. Xin Yao and Yong Liu. (1997), "A New Evolutionary System for Evolving Artificial Neural Network", IEEE Transactions on Neural Networks, Vol.8(3), pp. 694-713.
71. Shahril Irwan Sulaiman, Titik Khawa Abdul Rahman and Ismail Musirin. (2012), "AGenetic Algorithm-Based Hybrid Multilayer Feed forward Neural Network for Predicting Grid-Connected Photovoltaic System Output", Proceedings of 4th International Conference on Machine Learning and Computing, Vol.25,pp. 147-150.
72. Jan Karwowski, Michał Okulewicz, Jarosław Legierski, (2013), "Application of Particle Swarm Optimization Algorithm to Neural Network Training Process in the Localization of the Mobile Terminal", Engineering Applications of Neural Networks Communications in Computer and Information Science, Vol. 383, pp. 122-131.
73. Kuok King Kuok, Sobri Harun and Siti Mariyam Shamsuddin, (2009), "Particle Swarm Optimization Feed forward Neural Network for Hourly Rainfall run off Modeling in Bedup Basin, Malaysia" International Journal of Civil & Environmental Engineering, Vol. 9(10), pp. 9-14.
74. Avci, Engin and Ibrahim Turkoglu, (2009), "An Intelligent Diagnosis System Based On Principle Component Analysis And ANFIS For The

Heart Valve Diseases", Expert Systems With Applications, 2873-2878  
<https://doi.org/10.1016/j.eswa.2008.01.030>

75. Kukar, Matjaž, et al. (1999), "Analysing and improving the diagnosis of ischaemic heart disease with machine learning." Artificial intelligence in medicine 16.1: 25-50.
76. Rao, R. B., Bi, J., Fung, G., Salganicoff, M., Obuchowski, N., & Naidich, D. (2007). LungCAD: a clinically approved, machine learning system for lung cancer detection. In Proceedings of the 13th ACM SIGKDD international conference on Knowledge discovery and data mining (pp. 1033-1037). ACM.
77. Kodaz, Halife, et al.(2009), "Medical application of information gain based artificial immune recognition system (AIRS): Diagnosis of thyroid disease." Expert Systems with Applications 36.2 : 3086-3092
78. Polat, Kemal, SeralŞahan, and SalihGüneş. (2007), "A novel hybrid method based on artificial immune recognition system (AIRS) with fuzzy weighted pre-processing for thyroid disease diagnosis." Expert systems with Applications 32.4: 1141- 1147.
79. Van der Gaag, Linda C., et al. (2002), "Probabilities for a probabilistic network: a case study in esophageal cancer." Artificial Intelligence in medicine 25.2 : 123-148.
80. Ye, Q. H., Qin, L. X., Forgues, M., He, P., Kim, J. W., Peng, A. C. & Ma, Z. C. (2003). "Predicting hepatitis B virus-positive metastatic hepatocellular carcinomas using gene expression profiling and supervised machine learning.", Nature medicine, 9(4), 416-423.
81. Elif Derya Ubeyli, (2010), "Automatic diagnosis of diabetes using adaptive neuro-fuzzy inference systems", Expert systems, Vol. 27; Issue 4; pages: 259-266, doi: 10.1111/j.1468-0394.2010.00527.x
82. Sarwar, Abid, Vinod Sharma, and Rajeev Gupta. "Hybrid ensemble learning technique for screening of cervical cancer using Papanicolaou smear image analysis." Personalized Medicine Universe 4 (2015): 54-62.
83. Sharpe PK, Solberg HE, Rootwelt K, Yearworth M. (2000), "Artificial neural networks in diagnosis of thyroid function from in vitro laboratory tests", Clinical Chemistry. 39:2248–53.
84. Quintana. M., Guàrdia. J., Sánchez-Benavides. G., Aguilar.M., Molinuevo. J.L., Robles. A., Barquero. M.S., Antúnez. C., Martínez-Parra. C., FrankGarcía. A.andFernández. M. (2012), "Using artificial neural networks in clinical neuropsychology: High performance in mild

- cognitive impairment and Alzheimer's disease", Journal of clinical and experimental neuropsychology 34(2), 195-208.
85. Hachesu. P.R., Ahmadi. M., Alizadeh. S.andSadoughi. F. (2013) —Use of data mining techniques to determine and predict length of stay of cardiac patientsl, Healthcare informatics research 19(2), 121-129.
  86. Anamika Gupta and Naveen Kumar, (2005), "Analysis of Medical Data using Data Mining and Formal Concept Analysis", World Academy of Science, Engineering and Technology.
  87. Saraee, M., and J. Keane, (2007), "Using T3, an improved decision tree classifier, for mining stroke-related medical data", Methods of information in medicine vol. 46, no. 5, pp. 523-529.
  88. Yadav, Geeta, Yugal Kumar, and GadadharSahoo, (2011), "Predication of Parkinson's disease using data mining methods: A comparative analysis of tree, statistical, and support vector machine classifiers", Indian journal of medical sciences 65, no. 6, pp. 231-242.
  89. Maroco. D., Silva. A., Rodrigues. M., Guerreiro. I., Santana, and de Mendonça. A. (2011) —Data mining methods in the prediction of Dementia: a real-data comparison of the accuracy, sensitivity and specificity of linear discriminant analysis, logistic regression, neural networks, support vector machines, classification trees and random forests, BMC Research Notes 4(1), 299.
  90. Hanirex DK, Kaliyamurthie KP. (2013), "Multi-classification approach for detecting thyroid attacks." 2013.
  91. D.KeranaHanirex and DR.K.P.Kaliyamurthie, (2013) —Multi-classification approach for detecting Thyroid attacks", Int J Pharm Bio Sci, pp. - 4(3): 1246 – 1251.
  92. E. Zoulias,P.A. Asvestas, G.K. Matsopoulos, N. Uzunoglu, S. TseleniBalafouta, H. Gakiopoulou, (2009) "A data mining approach for classifying FNA thyroid data", School of Electrical and Computer Engineering, National Technical University of Athens, Greece. Department of Pathology, Medical School, University of Athens, Greece.
  93. Markus Brameier, Wolfgang Banzhaf, (2008) "A Comparison of Linear Genetic Programming and Neural Networks in Medical Data Mining"

Fachbereich I Informatik University at Dortmund 44221, Dortmund, GERMANY.

94. T.T.Nguyen and D.N. Davis, "Predicting Cardio Vascular Risk Using Neural Net Techniques" University of Hull.
95. Frank Lemke and Johann-Adolf Mueller, "Medical data analysis using selforganizing data miningtechnologies," Systems Analysis Modeling Simulation, Vol. 43 , no. 10 , pp: 1399 - 1408, 2003.
96. T.T.Nguyen and D.N. Davis," Feature Selection and Predicting CardioVascular Risk", University of Hull.
97. Weiss S, Kulikowski C, Amarel S, Safir A: A model-based method for computer-aided medical decision making. *ArtifIntell* 1978, 11:145–72.
98. Zhang Z, Xu Y, Liu J, Wong DWK, Kwoh CK, Shaw SM, Wong TY: Automatic diagnosis of pathological myopia from heterogeneous biomedical data. *PLoS ONE* 2013, 8(6):e65736.
99. Chan K, Lee TW, Sample PA, Goldbaum MH, Weinreb RN, Sejnowski TJ: Comparison of machine learning and traditional classifiers in glaucoma diagnosis. *IEEE Trans Biomed Eng* 2002, 49(9):963–974
100. Perumalsamy N, Prasad N, Sathya S, Ramasamy K: Software for reading and grading diabetic retinopathy: Aravind diabetic retinopathy screening 3.0. *Diabetes Care* 2007, 30(9):2302–2306.
101. Bizios D, Heijl A, Bengtsson B: Integration and fusion of standard automated perimetry and optical coherence tomography data for improved automated glaucoma diagnostics. *BMC Ophthalmology* 2011, 11(1):20
102. Fujita H, Uchiyama Y, Nakagawa T, Fukuoka D, Hatanaka Y, Hara T, Lee G, Hayashi Y, Ikeda Y, Gao X, Zhou X: Computer-aided diagnosis: The emerging of three CAD systems induced by Japanese health care needs, *Comput Methods Prog Biomed* 2008, 92:238–248
103. George, R&Ve Ramesh, S (2010), 'Glaucoma in India: Estimated Burden of Disease', *Journal of Glaucoma*, vol.19, no. 6, pp. 391-397.
104. Pooja Sharma, Pamela, A, Sample, Linda, M, Zangwill & Joel S Schuman (2008), 'Diagnostic Tools for Glaucoma Detection and Management', *Survey Of Ophthalmology*, vol.53, no.1, pp.S17- S32.

105. U. Rajendra Acharya, SumeetDua, Xian Du, VinithaSree S, and Chua Kuang Chua, (2011), “Automated Diagnosis of Glaucoma Using Texture and Higher Order Spectra Features,” IEEE Transactions On Information Technology In Biomedicine, Vol. 15, No. 3, 449-455.
106. Paul Y. Kim et. al., (2013), “Novel Fractal Feature-Based Multiclass Glaucoma Detection and Progression Prediction”, IEEE Journal of Biomedical and Health Informatics, vol. 17, no. 2, March 2013.
107. Ceccon, Stefano & Garway-Heath, David & Crabb, David & Tucker, Allan. (2014). Exploring Early Glaucoma and the Visual Field Test: Classification and Clustering Using Bayesian Networks. IEEE journal of biomedical and health informatics. 18. 1008-14. 10.1109/JBHI.2013.2289367.
108. Kwokleung Chan, Pamela A. Sample, Michael H. Goldbaum et al, (2002), Using Machine Learning Classifiers to Identify Glaucomatous Change Earlier in Standard Visual Fields, IOVS, Vol. 43, No. 8
109. Vermeer, Koenraad&Vos, F.M. & Lo, Barrick& Zhou, Qienyuan&Lemij, Hans & Vossepoel, Albert & Van Vliet, Lucas. (2006). Modeling of scanning laser polarimetry images of the human retina for progression detection of glaucoma. Medical Imaging, IEEE Transactions on. 25. 517 - 528. 10.1109/TMI.2006.871433.
110. Kaur, H & Kaur, A (2014), “Early Stage Glaucoma Detection in Diabetic Patients: A Review,” International Journal of Advanced Research in Computer Science and Software Engineering, vol. 4, pp. 271-274.
111. Foracchia, M, Grisan, E & Ruggeri, A. (2004), “Detection of optic disc in retinal images by means of a geometrical model of vessel structure”, IEEE Transactions on Medical Imaging, vol. 23, pp. 1189-1195.
112. Cheng, J, Jiang Liu, Yanwu Xu & Fengshou Yin, (2013), “Super pixel Classification Based Optic Disc and Optic Cup Segmentation for Glaucoma Screening”, IEEE Transactions on Medical Imaging, vol. 32, no. 6, pp. 1019-1032.
113. Yousefi, S, Goldbaum, MH, Balasubramanian, M & Tzyy-Ping Jung, (2014), “Glaucoma Progression Detection Using Structural Retinal Nerve Fiber Layer Measurements and Functional Visual Field Points”, IEEE Transactions on Biomedical Engineering, vol. 61, no. 4, pp. 1143-1154.
114. Mendonca, AM & Campilho, A. (2006), “Segmentation of Retinal blood vessels by combining the detection of centre lines and morphological

- reconstruction”, IEEE Transactions on Medical Imaging, vol. 25, no. 9, pp. 1200-1213.
115. Palomera-Perez, MA, Martinez-Perez, ME, Benitez-Perez, H & Ortega-Arjona, JL (2010), “Parallel multiscale feature extraction and region growing: Application in retinal blood vessel detection”, IEEE Transactions on Information Technology in Biomedicine, vol. 14, no. 2, pp. 500-506.
116. Fraz, MM, Remagnino, P, Hoppe, A, Uyyanonvara, B, Rudnicka, AR, Owen, CG & Barman, SA. (2012), ‘An ensemble classification-based approach applied to retinal blood vessel segmentation’, IEEE Transactions on Biomedical Engineering, vol. 59, pp. 2538-2548.
117. Manoj, S, Muralidharan & Sandeep, PM. (2013), ‘Neural network based classifier for retinal blood vessel segmentation’, International Journal of Recent Trends in Electrical & Electronics Engineering, vol. 3, no. 1, pp. 44-53.
118. Marin, D , Aquino, A, Emilio Gegundez-Arias, M & Bravo, JM. (2011), ‘A new supervised method for blood vessel segmentation in retinal images by using gray-level and moment invariants-based features’, IEEE Transactions on Medical Imaging, vol. 30, pp. 146-158.
119. Xiao, Z, Adel, M & Bourennane, S., (2013), ‘Bayesian method with spatial constraint for retinal vessel segmentation’, Computational and Mathematical Methods in Medicine, vol. 13, no. 401413, pp. 1-9.
120. Budai, A, Bock, R, Maier, A, Hornegger, J & Michelson, G. (2013), ‘Robust vessel segmentation in fundus images’, International Journal of Biomedical Imaging, vol. 20, pp. 1-11.
121. Joel EW Koh, Muthu Rama Krishnan Mookiah & Nahrizul Adib Kadri. (2013), ‘Application of Multi resolution Analysis for the Detection of Glaucoma.’ Journal of Medical Imaging and Health Informatics, vol. 3, no. 1, pp.1-8.
122. Jian Wang, Wei Wu & Jacek M Zurada (2011), ‘Deterministic convergence of conjugate gradient method for feedforward neural networks’, Neurocomputing, vol.74, no14-15 , pp.2368-2376
123. Katarzyna Stapor, Adrian Brueckner& Adam Switonski. (2006), ‘Mathematical Morphology and Support Vector Machines for Diagnosis

- of Glaucoma on Fundus Eye Images’, Computer Vision and Graphics, vol.32, pp.888–893.
124. Vidotti VG, Costa VP, Silva FR, et al. (2012), “Sensitivity and specificity of machine learning classifiers and spectral domain OCT for the diagnosis of glaucoma.”, European Journal of Ophthalmology.
125. Huang D, Swanson EA, Lin CP, et al. (1991), “Optical coherence tomography”. Science. 1991;254(5035):1178–1181.
126. Brigatti, L., Hoffman, D. & Caprioli, J. (1996). “Neural networks to identify glaucoma with structural and functional measurements”, Am J Ophthalmol 121(5): 511–21.
127. Uchida, H., Brigatti, L. & Caprioli, J. (1996). Detection of structural damage from glaucoma with confocal laser image analysis, Invest Ophthalmol Vis Sci 37(12): 2393–401.
128. Lietman, T., Eng, J., Katz, J. & Quigley, H. A. (1999). Neural networks for visual field analysis: how do they compare with other algorithms?, J Glaucoma 8(1): 77–80.
129. Bowd, C., Zangwill, L. M., Medeiros, F. A., Hao, J., Chan, K., Lee, T. W., Sejnowski, T. J., Goldbaum, M. H., Sample, P. A., Crowston, J. G. & Weinreb, R. N. (2004). Confocal scanning laser ophthalmoscopy classifiers and stereophotograph evaluation for prediction of visual field abnormalities in glaucoma-suspect eyes, Invest Ophthalmol Vis Sci 45(7): 2255–62.
130. Madhulika Jain,(2015), “A Hierarchical System Design for detection of Glaucoma from Color Fundus Images”, Thesis for MS by Research in Electronics & Communication, International Institute of Information Technology Hyderabad - 500 032.
131. R. Bock, J. Meier, L. G. Nyl, and G. Michelson.(2010), “Glaucoma risk index: automated glaucoma detection from color fundus images.” Medical Image Analysis, 14(3):471–481.

132. G. Joshi, J.Sivaswamy, and S. Krishnadas.(2011), “Optic disk and cup segmentation from monocular colour retinal images for glaucoma assessment.” IEEE Transactions on Medical Imaging, 30(6):1192–1205.
133. R. Saxena, D. Singh, and P. Vashist. (2013), “Glaucoma: An emerging peril. Indian Journal of Community Medicine,” 38(3):135–137.
134. SmitaSushilSikchi, SushilSikchi, M. S. Ali, (2012), “Artificial Intelligence in Medical Diagnosis”, International Journal of Applied Engineering Research, ISSN 0973-4562 Vol.7 No.11.
135. Jiang F, Jiang Y, Zhi H, et al. (2017), Artificial intelligence in healthcare: past, present and future. *Stroke and Vascular Neurology*; 0: e000101.doi:10.1136/svn-2017-000101.
136. Murdoch TB, Detsky AS. (2013), “The inevitable application of big data to health care.”, *JAMA* 2013;309:1351–2.doi:10.1001/jama.2013.393.
137. Kolker E, Özdemir V, Kolker E. (2016), “How Healthcare can refocus on its Super-Customers (Patients, n=1) and Customers (Doctors and Nurses)”, by Leveraging Lessons from Amazon, Uber, and Watson. *OMICS* 2016;20:329–33.doi:10.1089/omi.2016.0077.
138. Dilsizian SE, Siegel EL. (2014), “Artificial intelligence in medicine and cardiac imaging: harnessing big data and advanced computing to provide personalized medical diagnosis and treatment.”, *CurrCardiol Rep* 2014;16:441.doi:10.1007/s11886-013-0441-8.
139. Bizios D, Heijl A, Bengtsson B, (2011), “Integration and fusion of standard automated perimetry and optical coherence tomography data for improved automated glaucoma diagnostics”, *BMC Ophthalmology*. 11 (1): 20.
140. Jagadish Nayak et al,(2009), “Automated Diagnosis of Glaucoma Using Digital Fundus Images, *Journal of Medical Systems*,” Vol. 33, Issue 5, pp- 337-346.
141. Mei-LingHuang, Hsin-YiChen, Jian-JunHuang, (2007), “Glaucoma Detection using Adaptive Neuro-Fuzzy Inference System, *Expert Systems with Applications*”, Vol.32458–468.
142. Chauhan et al, (2016), “Data Mining Techniques for Diagnostic Support of Glaucoma using Stratus OCT and Perimetric Data”, *International Journal of Computer Applications (0975 – 8887)*, Volume 151 – No.8.

143. Eddine Benzebouchi, Nacer & Azizi, Nabiha & Bouziane, SeifEddine. (2018). ‘Glaucoma Diagnosis Using Cooperative Convolutional Neural Networks.’, International Journal of Advances in Electronics and Computer Science (ijaecs).
144. Kim, S. J., Cho, K. J., & Oh, S. (2017). Development of machine learning models for diagnosis of glaucoma. PloS one, 12(5), e0177726. doi:10.1371/journal.pone.0177726.
145. Huazhu Fu et al, (2018), “Disc-aware Ensemble Network for Glaucoma Screening from Fundus Image”, arXiv:1805.07549v1 [cs.CV]
146. Nagarajan et al, (2002), “Neural network model for early detection of glaucoma using multi-focal visual evoked potential (M-Vep),” Investigative Ophthalmology & Visual Science 42.
147. Kleyton Arlindo Barella et al,(2013), “Glaucoma Diagnostic Accuracy of Machine Learning Classifiers Using Retinal Nerve Fiber Layer and Optic Nerve Data from SD-OCT”, Journal of Ophthalmology, Volume 2013, Article ID-789129, 7 pages, <http://dx.doi.org/10.1155/2013/789129>

## **Chapter in Books**

1. Wenzel HJ, Schwartzkroin PA (2006) Morphologic approaches to the characterization of epilepsy models. In: Pitkanen A, Schwartzkroin PA, Moshe SL (eds) Models of seizures and epilepsy, Elsevier Academic Press, San Diego, pp. 629-652.

## **Book**

1. Breiman L. (1984), “Classification and Regression Trees”, Wadsworth International group, Belmont, California.
2. M. Negnevitsky, (2005), Artificial Intelligence. Pearson Education Limited.
3. B. D. Ripley. (1996), Pattern recognition and neural networks. Cambridge university press, 1996. 403 s. ISBN 0-521-46086-7.
4. Rumelhart DE, Hinton G, Williams R, (1986), Learning representations of back-propagation errors. Nature. 1986;

323:533–536.

5. Kennedy J. and Eberhart R.C. (2001), “Swarm Intelligence”, Morgan Kaufmann Publisher, San Francisco, CA.
6. Dorigo M. and Stutzle T. (2004), ‘Ant Colony Optimization’, MIT Press, Cambridge, MA.
7. Tibshirani R., Hastie T. and Friedman J. (2001), ‘The Elements of Statistical Learning- Data Mining, Inference and Prediction’, Springer.
8. Berthold M. and Hand D.J. (2006), Intelligent Data Analysis - An Introduction, 2 nd Ed., Springer - Verlag Berlin Heidelberg.
9. Duda R.O., Hart P.E. and Stork D.G. (2001), ‘Pattern Classification’, 2nd Ed, Wiley Interscience, New York, NY.
10. Dorf R.C. and Bishop R.H. (2004), ‘Modern Control Systems’, 10th Ed., Pearson Prentice Hall, Upper Saddle River, NJ.
11. GeethaRamani R. (2009), ‘Genetic Programming based team learning in robotic soccer’ Ph.D. dissertation, Pondicherry University, India.
12. Hillier F.S. and Lieberman G.J. (2005), ‘Introduction to Operations Research’, 8th Ed., McGraw Hill, Boston, MA.
13. Castro L.N.De. and Timmis J. (2002), “Artificial Immune Systems : A New Computational Intelligence Approach”, Springer, Heidelberg.
14. Taylor, R. “Handbook of Retinal Screening in Diabetes”, John Wiley & Sons Ltd, England, 2007.
15. Forrester, J.V., Dick, A.D., William, R. and Lee, P.G.M. “The Eye, Basis sciences in practice”, Saunders Ltd, 2nd edition, 2001
16. Rumelhart, D. & McClelland, J. (1986). Parallel distributed processing, MIT Press, Cambridge, MA.

### **Book in a series**

1. R. Dybowski and V. Gant, Clinical Applications of Artificial Neural Networks, Cambridge University Press, 2007.
2. Eberhart R.C., Simpson P.K. and Dobbins R.W. (1996), “Computational Intelligence PC Tools”, Academic Press, Boston, MA
3. Pal S.K., Dillon T.S. and Yeung D.S. (2000), “Soft Computing in Case Based Reasoning”, Springer-Verlag, U.K.
4. S. Kajan. (2009), “GUI for classification using multilayer perceptron network”, Technical Computing Prague.
5. Angelov P.P. (2002), “Evolving Rule-Based Models- A tool for design of Flexible Adaptive Systems”, Physica-Verlag, Springer Verlag, Heidelberg.
6. Bonfa, I., Maioli, C., Sarti, F., Milandri, G. L., and Monte, P. R. D. (1993), “HERMES: An Expert System for the Prognosis of Hepatic Diseases”, Technical Report UBLCS-93- 19, Universiti of Bologna.
7. World Health Organization: Blinding trachoma fact sheet. 2014

### **Conference proceedings**

1. Walker, N. J., and Kwon, O. (1997), “ISS: An Expert System for the Diagnosis of Sexually Transmitted Diseases”, 11th Annual Midwest Computer Conference (MCC’97) March 21, Springfield, Illinois.
2. Passold, Fs., Ojeda, R. G., and Mur, J. (1996), “Hybrid Expert System in Anesthesiology for Critical Patients”, Proceedings of the 8 th IEEE Mediterranean Electrotechnical Conference - MELECON’96 (ITALIA), Vol. III, pp. 1486-1489.
3. SitiNurul Huda Sheikh Abdulah and MiswanSurip (1999),

“SatuMetodologiPerlombongan Data UntukPesakit AIDS”, Proceedings of the First National Conference on Artificial Intelligence Application in Industry. Kuala Lumpur, pp. 57-71.

4. Siti Fatimah MdSaad and RogayahGhazali (1999), “Data Mining for Medical Database. Proceedings of the First National Conference on Artificial Intelligence Application in Industry”, Kuala Lumpur, pp. 72-79.
5. Meng, Y. K. (1996), “Interval-Based Reasoning in Medical Diagnosis”, Proceedings of National Conference on Research and Development in Computer Science and Its Applications (REDECS’96), UniversitiPertanian, Malaysia: Kuala Lumpur, pp. 220 - 224.
6. Street, W. N., Mangasarian, O. L., and Wolberg, W. H. (1996), “Individual and Collective Prognostic Prediction”, Thirteenth International Conference on Machine Learning.
7. Goldberg E, and Richardson J. (1987), “Genetic algorithm with sharing for multimodal function optimization”, Proceedings of the second international conference on genetic algorithm and their applications, pp. 41-49.
8. KalleSaastamoinen and JaakkoKetola, (2006) Medical Data Classification using Logical Similarity Based Measures. In Proceedings of IEEE 2006.
9. Alfonso Bastias, Ph.D., Eleonora Horvath, M.D., Felipe Baesler, Ph.D., and Claudio Silva, M.D., (2009) ,Predictive model based on neural networks to assist the diagnosis of malignancy of thyroid nodules, Proceedings of the 41st International Conference on Computers & Industrial Engineering.
10. Yuji Hatanaka, Chisako Muramatsu, Akira Sawada Takeshi Hara, Tetsuya Yamamoto & Hiroshi Fujita, (2012), ‘Glaucoma Risk Assessment Based on Clinical Data and Automated Nerve Fiber Layer Defects Detection’, 34th Annual International Conference of the IEEE EMBS, San Diego, California USA, pp.5963-5966.
11. Williams. J.A., Weakley. A., Cook. D.J. and Schmitter-Edgecombe. M. (2013), Machine learning techniques for diagnostic differentiation of mild cognitive impairment and Dementia, Workshops at the Twenty-

Seventh AAAI Conference on Artificial Intelligence.

12. Asaoka R, Shibata N, Murata H, Tanito M. (2018), “Construction of a deep learning algorithm to automatically diagnose glaucoma using a fundus photograph.” Presented at: Association for Research in Vision and Ophthalmology (ARVO) 2018 Annual Conference; Honolulu, HI. <http://www.arvo.org/annual-meeting/program/online-planner>. Accessed June 17, 2018.
13. Seo E, Jaccard N, Trikha S, Pasquale LR, Song BJ. (2018), Automated evaluation of optic disc images for manifest glaucoma detection using a deep-learning, neural network-based algorithm. Presented at: Association for Research in Vision and Ophthalmology (ARVO) 2018 Annual Conference; Honolulu, HI. <http://www.arvo.org/annual-meeting/program/online-planner>, Accessed June 17, 2018.
14. Zangwill LM, Christopher M, Belghith A, Bowd C, Goldbaum MH, Weinreb RN. (2018), “Deep learning approaches can detect glaucomatous functional loss better than standard SD-OCT retinal nerve fiber layer thickness”, Presented at: Association for Research in Vision and Ophthalmology (ARVO) 2018 Annual Conference; Honolulu, HI. <http://www.arvo.org/annual-meeting/program/online-planner>. Accessed June 17, 2018.
15. Caruana R. (2006), “An Empirical Comparison of Supervised Learning Algorithms.”, Proceedings of the 23rd international conference on Machine learning. 2006 June 25–29; Pittsburgh USA; ACM; 2006. p.161-168.

### Citations from Internet

1. “High Eye Pressure and Glaucoma”, accessed on, <http://www.glaucoma.org/gleams/high-eye-pressure-andglaucoma.php6>
2. Droy, J. M., Darmoni, S. J., Massari, P., Blanc, T., Moritz, F., and Leroy, J. (1993), “SETH: An Expert System for the Management on Acute Drug Poisoning”, <http://www.churousen.fr/dsii/publi/seth.htm>

3. Theodorou, T., and Ketikidis, P. (1995), "Neo-Dat An Expert System to Support the Designers of Clinical Trails", 5th Hellenic Conference on Informatics.
  4. Sarle, W. S. (1999), "Neural Network FAQ, part 1 of 7: Introduction", Periodic posting to the Usenet Newsgroup comp.ai.neural-nets, <ftp://ftp.sas.com/pub/neurl/FAQ.html>
  5. J. B. Siddharth Jonathan and K.N. Shruthi, "A Two Tier Neural Inter-Network Based Approach to Medical Diagnosis Using K-Nearest NeighborClassification for Diagnosis Pruning", web page available at <http://infolab.stanford.edu/~jonsid/nimd.pdf>
  6. Mallikarjun, Y, 2013, 'Two molecular mechanisms causing glaucoma found', [Online], <http://www.thehindu.com/scitech/health/two-molecularmechanisms-causing-glaucoma-found/article4902049>.
  7. Goldbaum, MD (1975), 'STARE Dataset Website', Clemson, SC,Clemson Univ. Available from: <<http://www.ces.clemson.edu>> [25February 2014].
  8. Wen JC, Lee CS, Keane PA, et al. (2018), "Forecasting future Humphrey visual fields using deep learning." Preprint. <https://www.biorxiv.org/content/early/2018/04/02/293621.article-info>. Accessed June 17, 2018.
  9. "High Eye Pressure and Glaucoma", accessed on, <http://www.glaucoma.org/gleams/high-eye-pressure-andglaucoma.php6>
  10. DIAGNOSING GLAUCOMA. [Online]. Available: [https://www.glaucomafoundation.org/diagnosing\\_and\\_treating\\_glaucoma.htm](https://www.glaucomafoundation.org/diagnosing_and_treating_glaucoma.htm).
-

## **Annexure – XIX**

### **List of Publications**

#### **Paper Publication**

1. “Intelligent System using Neural Network Classifier for Glaucoma Diagnosis”, UGC Approved, International Journal For Research in Applied Science and Engineering Technology, Volume 6 Issue III, ISSN : 2321-9653, March '18.
2. “OphthoIntelli-Doc:The Future of Ophthalmic Diagnosis”, National Conference “Innovating for Development and Sustainability”, Navrachana University, Oct 2015.
3. “OphtoABM-An Intelligent Agent Based Model for Diagnosis of Ophthalmic Diseases”, International Journal of Engineering & Computer Science(IJECS), ISSN : 2319-7242, Volume 3 Issue 12, Dec 2014.

#### **Paper Acceptance**

1. “Comparative Analysis of Machine Learning Classifiers on Bioinformatics and Clinical Datasets”,6th 2019 International Conference on “Computing for Sustainable Global Development”, 13th – 15th March, 2019.
2. “Evaluation of Data Mining Classifiers for Crime Prediction”, International Conference in Police Science, Sep 2019, Raksha Shakti Universiy.