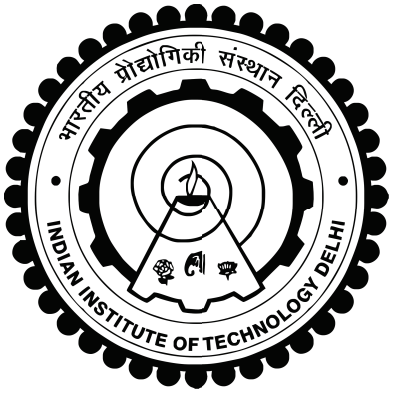
# GLAUCOMA DIAGNOSIS IN A DIGITAL RETINAL IMAGE USING MULTI CLINICAL FEATURES EXTRACTED AND FUSED BY DEEP CONVOLUTIONAL NEURAL NETWORKS

AMBIKA SHARMA




BHARTI SCHOOL OF TELECOMMUNICATION
TECHNOLOGY AND MANAGEMENT
INDIAN INSTITUTE OF TECHNOLOGY DELHI

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by

AMBIKA SHARMA
BHARTI SCHOOL OF TELECOMMUNICATION TECHNOLOGY AND MANAGEMENT

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# CERTIFICATE

This is to certify that the thesis entitled, **"GLAUCOMA DIAGNOSIS IN A DIGITAL RETINAL IMAGE USING MULTI CLINICAL FEATURES EXTRACTED AND FUSED BY DEEP CONVOLUTIONAL NEURAL NETWORKS"** being submitted by **Ms. Ambika Sharma** for the award of the degree of **Doctor of Philosophy** is a record of bonafide research work carried out by him in the Bharti School of Telecommunication Technology and Management of Indian Institute of Technology Delhi.

**Ms. Ambika Sharma** has worked under my guidance and supervision and has fulfilled the requirements for the submission of this thesis, which to my knowledge has reached the requisite standard. The results obtained here in have not been submitted to any other University or Institute for the award of any degree.

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monika

**Prof. Monika Aggarwal**
**Center of Applied Research in Electronics**
**Indian Institute of Technology Delhi**
**New Delhi-110016, India**

Sumantra Dutta Roy

**Prof. Sumantra Dutta Roy**
**Electrical Engineering**
**Indian Institute of Technology Delhi**
**New Delhi-110016, India**

Vivek Gupta

**Dr. Vivek Gupta**
**Community Ophthalmology**
**All India Institute of Medical Sciences (AIIMS)**
**New Delhi-110029, India**

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# ABSTRACT

The advancement in computerized medical imaging has pushed the boundaries of many researchers to develop automated algorithms for disease diagnosis without human intervention. Glaucoma diagnosis among various eye diseases has remained a major challenge in the medical field. The lack of trained specialists and large patient to ophthalmologist ratio, have motivated us to develop cost-effective computer-based diagnostic systems that can assist medical experts in early diagnosis and aid in reducing their time and effort on healthy scenarios. In the glaucoma prediction procedure, ophthalmologists analyze the retinal image for various eye pathologies such as increased cup-to-disc ratio (CDR), neuro-retinal rim (NRR) loss, peripapillary atrophy (PPA), retinal nerve fiber layer (RNFL) loss, disc asymmetry, etc. Through this thesis, we exploit many clinical indicators along with the recent deep convolutional neural networks for better feature learning.

Regarding the methodology, the first contribution proposes an automatic detection and segmentation of one of the major retinal landmarks i.e., optic disc. Using the location and intensity profile of the optic disc, a DI map is predicted using a U-net architecture and OD is located with the LoG operator. Following this, a Generative adversarial network is proposed to segment the disc boundary. A well-defined study is performed among retinal datasets to validate the model performance. The second contribution of this thesis is to use a multi-encoder U-net framework for optic cup segmentation which significantly outperforms the state-of-the-art. The third contribution detects the two major clinical indicators i.e., PPA and RNFL, of glaucoma using two breakthrough techniques (Transfer and Active Learning) of deep learning. We formulate a novel PPA detection algorithm using a fusion of statistical features and high-level features from a pre-trained deep CNN. Further, we propose an Active transfer learning framework for patch-level classification of RNFL loss. We show encouraging results in comparison to state of art and are able to handle well low dataset scenarios. The fourth contribution of the thesis proposes an automatic glaucoma detection algorithm using ensemble learning of various clinical signs (PPA, RNFL), an SVM-based prediction model using cup and disc extracted features like CDR, ISNT ratio, and finally deep pre-trained CNN-based prediction model. We perform a robust set of experiments to validate the algorithm under all pathological conditions.

This thesis presents localization, segmentation, and classification techniques for medical images and can be applied to other applications. The proposed algorithms have been validated on public standard datasets, such as Drishti-GS, Origa, Refugee, and a private community camp-based challenging dataset collected from the All India Institute of Medical Sciences (AIIMS), Delhi. In conclusion, we have shown encouraging results for disease identification. Ensemble learning with clinically significant features and a deep CNN is a novel approach for glaucoma.

# सार

कम्प्यूटरीकृत चिकित्सा इमेजिंग में प्रगति ने मानव हस्तक्षेप के बिना रोग निदान के लिए स्वचालित एल्गोरिदम विकसित करने के लिए कई शोधकर्ताओं की सीमाओं को प्रोत्साहित किया है। विभिन्न नेत्र रोगों में ग्लूकोमा का निदान चिकित्सा क्षेत्र में एक बड़ी चुनौती बना हुआ है। प्रशिक्षित विशेषज्ञों की कमी और नेत्र रोग विशेषज्ञ अनुपात के लिए बड़े रोगी ने हमें लागत प्रभावी कंप्यूटर-आधारित निदान प्रणाली विकसित करने के लिए प्रेरित किया है जो चिकित्सा विशेषज्ञों को प्रारंभिक निदान में सहायता कर सकता है और स्वस्थ परिदृश्यों पर उनके समय और प्रयास को कम करने में सहायता कर सकता है। ग्लूकोमा भविष्यवाणी प्रक्रिया में, नेत्र रोग विशेषज्ञ विभिन्न नेत्र विकृति के लिए रेटिना छवि का विश्लेषण करते हैं जैसे कि कप-टू-डिस्क अनुपात (सीडीआर), न्यूरो-रेटिनल रिम (एनआरआर) हानि, पेरिपैपिलरी एट्रोफी (पीपीए), रेटिना तंत्रिका फाइबर परत (आरएनएफएल) हानि, डिस्क विषमता, आदि। इस शोध प्रबंध के अंतर्गत, हम बेहतर विशेषताएँ सीखने के लिए नवीनतम गहरे दृढ़ तंत्रिका संजाल के साथ-साथ कई नैदानिक संकेतकों का फायदा उठाते हैं।

कार्यप्रणाली के संबंध में, पहला योगदान प्रमुख रेटिनल लैंडमार्क यानी ऑप्टिक डिस्क में से एक का स्वचालित पता लगाने और विभाजन का प्रस्ताव करता है।ऑप्टिक डिस्क के स्थान और तीव्रता प्रोफ़ाइल का उपयोग करते हुए, यू-नेट आर्किटेक्चर का उपयोग करके एक DI मानचित्र की भविष्यवाणी की जाती है और OD LoG ऑपरेटर के साथ स्थित होता है। इसके बाद, डिस्क सीमा को खंडित करने के लिए एक जनरेटिव प्रतिकूल संजाल का प्रस्ताव है। मॉडल प्रदर्शन को मान्य करने के लिए रेटिना डेटासेट के बीच एक अच्छी तरह से परिभाषित अध्ययन किया जाता है। इस शोध प्रबंध का दूसरा योगदान ऑप्टिक कप सेगमेंटेशन के लिए एक मल्टी-एनकोडर यू-नेट फ्रेमवर्क का उपयोग करना है जो अत्याधुनिक रूप से बेहतर प्रदर्शन करता है। तीसरा योगदान दो प्रमुख नैदानिक संकेतकों यानी पीपीए और आरएनएफएल का पता लगाता है, गहन शिक्षा की दो सफलता तकनीकों (ट्रांसफर और एक्टिव लर्निंग) का उपयोग करके ग्लूकोमा के। हम एक पूर्व-प्रशिक्षित गहरे सीएनएन से सांख्यिकीय विशेषताओं और उच्च-स्तरीय सुविधाओं के संलयन का उपयोग करके

एक उपन्यास पीपीए डिटेक्शन एल्गोरिदम तैयार करते हैं। इसके अलावा, हम आरएनएफएल नुकसान के पैच-स्तरीय वर्गीकरण के लिए एक सक्रिय हस्तांतरण सीखने की रूपरेखा का प्रस्ताव करते हैं। हम अत्याधुनिक की तुलना में उत्साहजनक परिणाम दिखाते हैं और कम डेटासेट परिदृश्यों को संभालने में सक्षम हैं। शोध प्रबंध का चौथा योगदान विभिन्न नैदानिक संकेतों (पीपीए, आरएनएफएल) के पहनावा सीखने का उपयोग करते हुए एक स्वचालित ग्लूकोमा डिटेक्शन एल्गोरिदम का प्रस्ताव करता है, एक एसवीएम-आधारित भविष्यवाणी मॉडल जिसमें सीडीआर, आईएसएनटी अनुपात और अंत में गहन पूर्व-प्रशिक्षित सीएनएन जैसे कप और डिस्क निकाले गए सुविधाओं का उपयोग किया जाता है। आधारित भविष्यवाणी मॉडल। हम सभी रोग स्थितियों के तहत एल्गोरिथ्म को मान्य करने के लिए प्रयोगों का एक मजबूत सेट करते हैं।

यह शोध प्रबंध चिकित्सा छवियों के लिए स्थानीयकरण, विभाजन और वर्गीकरण तकनीकों को प्रस्तुत करता है और अन्य अनुप्रयोगों पर लागू किया जा सकता है। प्रस्तावित एल्गोरिदम को सार्वजनिक मानक डेटासेट, जैसे दृष्टि-जीएस, ओरिगा, रिफ्यूजी, और अखिल भारतीय आयुर्विज्ञान संस्थान (एम्स), दिल्ली से एकत्र किए गए एक निजी समुदाय शिविर-आधारित चुनौतीपूर्ण डेटासेट पर मान्य किया गया है। अंत में, हमने रोग की पहचान के लिए उत्साहजनक परिणाम दिखाए हैं। नैदानिक रूप से महत्वपूर्ण विशेषताओं के साथ सीखना और गहन सीएनएन ग्लूकोमा के लिए एक नया दृष्टिकोण है।

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| | |
|---|---|
| OD | Optic Disc |
| RNFL | Retinal Nerve Fiber layer |
| WHO | World Health Organization |
| VHI | Vision Health Initiative |
| CDC | Center for Disease Control and Prevention |
| AMD | Age related Macular Degeneration |
| DR | Diabetic Retinopathy |
| IAPB | International Agency for the Prevention of Blindness |
| CAD | Computer Aided Diagnosis |
| OCT | Optical Coherence Tomography |
| ONH | Optic Nerve Head |
| FOV | Field of View |
| IOP | Intra Ocular Pressure |
| VFT | Visual Field Test |
| CFP | Colored Fundus Photographs |
| NTG | Normal Tension Glaucoma |
| NEI | National Eye Institute |
| HRT | Heidelberg Retinal Tomography |
| CDR | Cup-to-Disc Ratio |
| PPA | Peripapillary Atrophy |
| NRR | Neuro Retinal Rim |
| ISNT | Inferior Superior Nasal Temporal |
| ML | Machine Learning |
| GT | Ground Truth |
| PCA | Principal Component Analysis |
| SVM | Support Vector Machine |
| KNN | K-Nearest Neighbor |
| ROI | Region of Interest |
| CNN | Convolutional Neural Network |
| CHT | Circular Hough Transform |

| | |
|---|---|
| LIF | Local Image Fitting |
| DCNN | Deep Convolutional Neural Network |
| BN | Batch Normalization |
| CCE | Categorical Cross-Entropy |
| CRF | Conditional Random Field |
| CFI | Colored Fundus Image |
| CSD | Coupled Sparse Dictionary |
| CCA | Canonical Correlation Analysis |
| CV | Chan-Vese |
| FCM | Fuzzy c-Means |
| SWFCM | Spatially Weighted Fuzzy c-Means |
| LS | Least Square |
| MSE | Mean Square Error |
| MAE | Mean Absolute Error |
| SLIC | Simple Linear Iterative Clustering |
| GAN | Generative Adversarial Networks |
| SGD | Stochastic Gradient Descent |
| RBF | Radial Basis Function |
| LDA | Linear Discriminant Analysis |
| LBP | Local Binary Pattern |
| GLCM | Gray Level Co-occurrence Matrix |
| HOG | Histogram of Gaussian |
| BIF | Biologically Inspired Features |
| LOG | Laplacian of Gaussian |
| CLACHE | Contrast Limited Adaptive Histogram Equalization |
| ACC | Accuracy |
| ROC | Receiver Operating Characteristic |
| AUC | Area Under Curve |
| DRIVE | Digital Retinal Images for Vessel Extractions |
| DRIU | Deep Retinal Image Understanding |
| DDLS | Disc Damage Likelihood Scale |