INVESTIGATION OF RETINAL BIOMARKERS FOR EARLY DETECTION OF VISUAL IMPAIRMENT

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by

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Dedicated to

My Family

Department of Electrical Engineering

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Hauz Khas, New Delhi, India-110016

CERTIFICATE

This is to certify that the thesis entitled **"INVESTIGATION OF RETINAL BIOMARKERS FOR EARLY DETECTION OF VISUAL IMPAIRMENT"**, submitted by **Ms. Geetha Pavani (2020EEZ8644)** to the Indian Institute of Technology Delhi, for the award of the degree of **Doctor of Philosophy** in Department of Electrical Engineering, is a record of the original, Bonafide research work carried out by him under our supervision and guidance. The thesis has reached the standards fulfilling the requirements of the regulations related to the award of the degree.

The results contained in this thesis have not been submitted in part or in full to any other University or Institute for the award of any degree or diploma to the best of our knowledge.

Prof. Tapan Kumar Gandhi
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Place:

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Geetha Pavani Pappu

Abstract

This thesis focuses on the comprehensive investigation of retinal disorders, emphasizing early detection to prevent irreversible damage and vision loss. Diagnosing retinal diseases such as Glaucoma, Macular Edema (ME), Hypertensive Retinopathy (HR), Diabetic Retinopathy (DR), and Age-related Macular Degeneration (AMD) remains a significant challenge, particularly because early-stage manifestations are often subtle and difficult to detect. The growing prevalence of diabetes and hypertension has led to a rapid increase in retinal disorders, further straining healthcare systems already facing a shortage of expert ophthalmologists. In this context, recent advancements in automated medical image processing have emerged as promising solutions, reducing diagnostic time and minimizing human errors while supporting clinical decision-making.

The primary objective of this research is to develop deep learning–based frameworks capable of detecting both structural alterations and clinical indicators in retinal images to enable accurate and timely diagnosis. The study investigates multiple retinal components, including retinal vessel maps, Optic Disc (OD), Optic Cup (OC), and pathological features such as retinal fluids and drusen from Optical Coherence Tomography (OCT) scans. By integrating structural and pathological analysis, the proposed system aims to improve early-stage detection and patient outcomes.

Despite numerous existing studies, substantial research gaps remain in enhancing the robustness and decision-making capability of automated systems. The first major contribution of this work is the development of a novel multistage dual-decoder deep learning architecture named "Multistage DPIRef-Net." This model performs precise segmentation of retinal blood vessels and further classifies them into arteries and veins to support accurate diagnosis. The architecture addresses limitations associated with pooling and striding operations by enhancing low-level feature representation, thereby preserving fine vascular details and reducing blurred boundaries. Extensive evaluations on publicly available benchmark datasets demonstrate the robustness and generalization ability of the proposed vessel segmentation framework.

To further enhance diagnostic performance, this research incorporates multimodal image analysis using both fundus photographs and OCT scans. Retinal abnormalities such as microaneurysms, haemorrhages, and soft exudates are detected from fundus images using a dual-encoder, single-decoder architecture termed "Residual Inception Local Binary Pattern–based Y-Net (RILBP-YNet)." This model combines convolutional feature extraction with

textural analysis through Local Binary Patterns (LBP) computed at multiple radii (1, 3, 5, and 7). The integration of texture-based and deep convolutional features strengthens feature learning and improves the detection accuracy of pathological signs, along with optic disc segmentation.

The second major contribution involves depth-wise retinal analysis using OCT imaging to detect fluid accumulation between retinal layers. A U-Net-inspired model, "FAM-U-Net," is proposed to identify retinal fluid regions. The architecture integrates multiscale feature representations using feature pyramid channels and dilated convolutions to enhance inter-pixel dependencies. Additionally, Convolutional Block Attention Modules (CBAM) and a Deep Aggregation Pyramid Pooling Module (DAPPM) are incorporated to refine salient feature maps and improve localization of fluid regions.

As a third contribution, clinically significant biomarkers such as the Artery-to-Vein Ratio (AVR) and Cup-to-Disc Ratio (CDR) are computed from segmented retinal structures to assist in detecting Hypertensive Retinopathy, Diabetic Retinopathy, and Glaucoma. Furthermore, a transformer-based multimodal deep learning network is developed to generate a unified diagnostic report by jointly analyzing fundus and OCT images through self-attention mechanisms.

Comprehensive qualitative and quantitative evaluations are conducted on multiple public datasets, including INSPIRE-AVR, DRIVE, ORIGA, DRISHTI, UCSD, RETOUCH, OPTIMA, and DUKE, along with real-time clinical datasets collected from eye hospitals. The experimental results demonstrate that the proposed frameworks outperform existing state-of-the-art methods, offering a robust, efficient, and clinically relevant solution for automated retinal disease detection.

सारांश

यह शोध-प्रबंध रेटिना से संबंधित रोगों के व्यापक अध्ययन पर केंद्रित है, जिसमें अपरिवर्तनीय क्षति और दृष्टि हानि को रोकने हेतु प्रारंभिक पहचान पर विशेष बल दिया गया है। ग्लूकोमा, मैक्यूलर एडेमा (ME), हाइपरटेंसिव रेटिनोपैथी (HR), डायबिटिक रेटिनोपैथी (DR) तथा आयु-संबंधी मैक्यूलर डिजनरेशन (AMD) जैसे रेटिनल रोगों का निदान एक महत्वपूर्ण चुनौती बना हुआ है, विशेष रूप से इसलिए क्योंकि प्रारंभिक अवस्था में इनके लक्षण अत्यंत सूक्ष्म होते हैं और पहचानना कठिन होता है। मधुमेह और उच्च रक्तचाप की बढ़ती व्यापकता के कारण रेटिनल रोगों में तीव्र वृद्धि हो रही है, जिससे पहले से ही विशेषज्ञ नेत्र चिकित्सकों की कमी से जूझ रही स्वास्थ्य प्रणालियों पर अतिरिक्त दबाव पड़ रहा है। इस संदर्भ में, स्वचालित चिकित्सा छवि प्रसंस्करण में हालिया प्रगति आशाजनक समाधान के रूप में उभरी है, जो निदान समय को कम करने, मानवीय त्रुटियों को न्यूनतम करने तथा नैदानिक निर्णय प्रक्रिया को समर्थन प्रदान करती है।

इस शोध का मुख्य उद्देश्य गहन अधिगम (डीप लर्निंग) आधारित ऐसे ढांचे विकसित करना है जो रेटिनल छवियों में संरचनात्मक परिवर्तनों और नैदानिक संकेतकों दोनों का पता लगाकर सटीक एवं समयोचित निदान संभव बना सकें। इस अध्ययन में रेटिना के विभिन्न घटकों का विश्लेषण किया गया है, जिनमें रेटिनल रक्त वाहिका मानचित्र, ऑप्टिक डिस्क (OD), ऑप्टिक कप (OC) तथा ऑप्टिकल कोहेरेंस टोमोग्राफी (OCT) स्कैन से प्राप्त रेटिनल द्रव एवं ड्रूज़न जैसी रोगात्मक विशेषताएँ सम्मिलित हैं। संरचनात्मक एवं रोगात्मक विश्लेषण को एकीकृत करके प्रस्तावित प्रणाली प्रारंभिक अवस्था में रोग पहचान की क्षमता तथा रोगी परिणामों में सुधार लाने का लक्ष्य रखती है। यद्यपि इस क्षेत्र में अनेक अध्ययन उपलब्ध हैं, फिर भी स्वचालित प्रणालियों की मजबूती और निर्णय क्षमता को बढ़ाने के संदर्भ में कई शोध अंतराल विद्यमान हैं। इस कार्य का प्रथम प्रमुख योगदान “मल्टीस्टेज DPIRef-Net” नामक एक नवीन बहु-चरणीय द्वि-डिकोडर गहन अधिगम संरचना का विकास है। यह मॉडल रेटिनल रक्त वाहिकाओं का सटीक सेगमेंटेशन करता है तथा उन्हें धमनियों और शिराओं में वर्गीकृत करता है, जिससे निदान में सहायता मिलती है। यह संरचना पूलिंग और स्ट्राइडिंग से जुड़ी सीमाओं को दूर करते हुए निम्न-स्तरीय विशेषताओं के प्रतिनिधित्व को सुदृढ़ बनाती है, जिससे सूक्ष्म रक्तवाहिका विवरण सुरक्षित रहते हैं और धुंधली सीमाओं में कमी आती है। सार्वजनिक रूप से उपलब्ध मानक डेटासेट पर किए गए व्यापक मूल्यांकन प्रस्तावित रक्तवाहिका सेगमेंटेशन ढांचे की मजबूती और सामान्यीकरण क्षमता को दर्शाते हैं। निदान क्षमता को और अधिक बढ़ाने हेतु इस शोध में फंडस फोटोग्राफ तथा OCT स्कैन दोनों का उपयोग करते हुए मल्टीमोडल छवि विश्लेषण को सम्मिलित किया गया है। फंडस छवियों से माइक्रोएन्यूरिज़्म, रक्तस्राव तथा सॉफ्ट एक्सूडेट्स जैसी रेटिनल असामान्यताओं का पता “रेज़िडुअल इनसेप्शन लोकल बाइनरी पैटर्न आधारित वाई-नेट (RILBP-YNet)” नामक द्वि-एन्कोडर, एकल-डिकोडर संरचना द्वारा लगाया जाता है। यह मॉडल कन्वोल्यूशनल विशेषता निष्कर्षण को बहु-त्रिज्या (1, 3, 5 और 7) पर गणना किए गए लोकल बाइनरी पैटर्न (LBP) आधारित टेक्सचर विश्लेषण के साथ संयोजित करता है। टेक्सचर-आधारित तथा गहन कन्वोल्यूशनल विशेषताओं का संयोजन विशेषता अधिगम को सुदृढ़ बनाता है और रोगात्मक लक्षणों की पहचान के साथ-साथ ऑप्टिक डिस्क सेगमेंटेशन की सटीकता में सुधार करता है।

दूसरा प्रमुख योगदान OCT इमेजिंग का उपयोग करते हुए रेटिना की गहराई-आधारित विश्लेषण से संबंधित है, जिसके अंतर्गत रेटिनल परतों के बीच द्रव संचय का पता लगाया जाता है। इस हेतु “FAM-U-Net” नामक U-Net से प्रेरित एक मॉडल प्रस्तावित किया गया है, जो रेटिनल द्रव क्षेत्रों की पहचान करता है। यह संरचना फीचर पिरामिड चैनलों और डाइलेटेड कन्वोल्यूशनों के माध्यम से बहु-पैमाना विशेषताओं को एकीकृत करती है, जिससे पिक्सल-स्तरीय निर्भरताओं में सुधार होता है। इसके अतिरिक्त, कन्वोल्यूशनल ब्लॉक अटेंशन मॉड्यूल (CBAM) तथा डीप एग्रीगेशन पिरामिड पूलिंग मॉड्यूल (DAPPM) को सम्मिलित किया गया है, जिससे महत्वपूर्ण फीचर मैप्स को परिष्कृत किया जा सके और द्रव क्षेत्रों का सटीक स्थानीयकरण संभव हो सके। तीसरे योगदान के रूप में, धमनियों-शिराओं का अनुपात (AVR) तथा कप-टू-डिस्क अनुपात (CDR) जैसे चिकित्सकीय रूप से महत्वपूर्ण बायोमार्कर्स को सेगमेंटेड रेटिनल संरचनाओं से गणना किया गया है, जिससे हाइपरटेंसिव रेटिनोपैथी, डायबिटिक रेटिनोपैथी और ग्लूकोमा की पहचान में सहायता मिलती है। इसके अतिरिक्त, एक ट्रांसफॉर्मर-आधारित मल्टीमोडल डीप लर्निंग नेटवर्क विकसित किया गया है, जो सेल्फ-अटेंशन तंत्र के माध्यम से फंडस और OCT छवियों का संयुक्त विश्लेषण कर एक एकीकृत नैदानिक रिपोर्ट तैयार करता है।

INSPIRE-AVR, DRIVE, ORIGA, DRISHTI, UCSD, RETOUCH, OPTIMA और DUKE सहित अनेक सार्वजनिक डेटासेट्स के साथ-साथ नेत्र चिकित्सालयों से प्राप्त वास्तविक नैदानिक डेटासेट्स पर व्यापक गुणात्मक एवं मात्रात्मक मूल्यांकन किए गए हैं। प्रायोगिक

परिणाम यह दर्शाते हैं कि प्रस्तावित ढांचे वर्तमान अत्याधुनिक विधियों की तुलना में बेहतर प्रदर्शन करते हैं और स्वचालित रेटिनल रोग पहचान के लिए एक सुदृढ़, प्रभावी एवं चिकित्सकीय रूप से उपयोगी समाधान प्रदान करते हैं।

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ME	Macular Edema
HR	Hypertensive Retinopathy
DR	Diabetic Retinopathy
AMD	Age-related Macular Degeneration (AMD)
OD	Optic Disc
OC	Optic Cup
OCT	Optical Coherence Tomography
CBAM	Convolutional Block Attention Modules
DAPPM	Deep Aggregation Pyramid Pooling Module
AVR	Arteries-to-Veins Ratio
CDR	Cup-to-Disc Ratio
WHO	World Health Organization
CDCP	Centers for Disease Control and Prevention
RE	Refractive Error
IAPB	International Agency for the Prevention of Blindness
CAD	Computer Aided Diagnosis
RPE	Retinal Pigment Epithelium
PL	Photoreceptor Layer

ELM	External Limiting Membrane
ONL	Outer Nuclear Layer
OPL	Outer Plexiform Layer
INL	Inner Nuclear Layer
IPL	Inner Plexiform Layer
GCL	Ganglion Cell Layer
NFL	Nerve Fiber Layer
ILM	Inter Limiting Membrane
FOV	Field of View
ONH	Optic Nerve Head
SD-OCT	Spectral Domain OCT
PED	Pigment Epithelium Detachment (PED)
SRF	Sub Retinal Fluid
IRF	Intra Retinal Fluid
NPDR	Non-Proliferative Diabetic Retinopathy
PDR	Proliferative Diabetic Retinopathy
NVD	Neovascularization on Optic Disc (NVD)
NVE	Neovascularization Elsewhere (NVE)
IDF	International Diabetes Federation
IOP	Intraocular Pressure
ARIC	Atherosclerosis Risk in Communities

OAG	Open-Angle Glaucoma (OAG)
CAG	Closed-Angle Glaucoma (CAG)
RVO	Retinal Vein Occlusion
DME	Diabetic Macular Edema
CME	Cystoid Macular Edema
MA	Microaneurysms
HE	Hemorrhages
EX	Hard Exudates
SE	Soft Exudates
LSSVM	Least Square Support Vector Machines
GMM	Gaussian Mixture Models
SVM	Support Vector Machine
LDA	Linear Discriminant Analysis
SGRIF	Structure-Preserving Guided Retinal Image Filtering
FCM	Fuzzy C-Means
CNN	Convolutional Neural Network
DCNN	Deep Convolutional Neural Network
FCNN	Fully Convolutional Neural Network
AI	Artificial Intelligence
CLAHE	Contrast Limited Adaptive Histogram Equalization
SUACE	Speed Up Adaptive Contrast Enhancement
CAM	Class Activation Maps

LBP	Local Binary Patterns
BCE	Binary Cross Entropy
ACC	Accuracy
SEN	Sensitivity
SP	Specificity
MCC	Mathew's Correlation Coefficient (MCC)
DC	Dice Coefficient
ROC	Receiver Operating Characteristics
AUC	Area Under the Curve
ISBI	International Symposium on Biomedical Imaging
PSNR	Peak Signal-to-Noise Ratio
AUPR	Area Under Precision-Recall Curve
NSR	Neuro-Sensory Retina
MFE	Multiscale Feature Extraction
LN	Layer Normalization
GeLU	Gaussian Error Linear Unit
BM3D	Block Matching and 3D Filtering
FP	Feature Pyramid
SEB	Squeeze and Excitation Block
GAP	Global Average Pooling
RoI	Region of Interest
WCE	Weighted Cross Entropy

GPU	Graphical Processing Unit
STAPLE	Simultaneous Truth and Performance Level Estimation
SLO	Scanning Laser Ophthalmoscopy
NRR	Neuro-Retinal Rim
RHAC	Residual Hybrid Atrous Convolution
RCM	Recurrent Convolution Modules
SAF	Split Attention-Fusion
MSFF	Multiscale Feature Fusion
ARL	Attention Residual Learning
CRVE	Central Retinal Venular Equivalent
CRAE	Central Retinal Artery Equivalent
DPDSF	Dual Path Dual Scale Fusion
TMRF	Transformer Encoder-based Multiscale Residual Fusion
TEEB	Transformer Embedded Encoder Block
MSRF	Multiscale Residual Fusion
GTB	Global Transformer Block
RNFL	Retinal Nerve Fiber Layer
UCSD	University of California San Diego
JL	Jaccard Loss