

SCALABLE, LOW-COST, FAST SCREENING OF RETINOPATHY OF PREMATURITY (ROP)

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SCALABLE, LOW-COST, FAST SCREENING OF RETINOPATHY OF PREMATURITY (ROP)

by

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Submitted

in fulfillment of the requirements of the degree of **Doctor of Philosophy**

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*In loving memory of my dear mother and father, who
always wished for my happiness. This thesis is a
tribute to you, Mom! and Dad!*

Certificate

This is to certify that the thesis titled **SCALABLE, LOW-COST, FAST SCREENING OF RETINOPATHY OF PREMATURITY (ROP)** being submitted by **Mr. VIJAY KUMAR** for the award of **Doctor of Philosophy in Amar Nath and Shashi Khosla School of Information Technology** is a record of bona fide work carried out by her under my guidance and supervision at the **Amar Nath and Shashi Khosla School of Information Technology, Indian Institute of Technology Delhi**. The work presented in this thesis has not been submitted elsewhere, either in part or full, for the award of any other degree or diploma.

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Abstract

Retinopathy of prematurity (ROP) is a significant cause of blindness in preterm infants globally. Early diagnosis and treatment can reduce its impact. However, the decreasing number of neonatal ophthalmologists, particularly in low- and middle-income countries (LMICs) like India, poses challenges in addressing the rising cases of ROP among high-risk infants. The unbalanced distribution of resources and time constraints further complicate the situation. Traditional ROP screening methods struggle to cope, especially in present circumstances.

Therefore, this thesis proposes an affordable, scalable ROP screening and eye health monitoring solution. Utilizing mHealth, eHealth, Internet of Medical Things (IoMT), and telemedicine, we aim to provide cost-effective ROP screening, diagnosis, and monitoring using digital imaging devices. However, challenges arise from the quality of retinal images in premature infants, affected by various noises and artifacts, including motion blur and uneven illumination. Additionally, underdeveloped retinal landmarks in premature infants complicate the detection and quantification of ROP through retinal scans.

Despite challenges, recent advances in data-driven machine learning (ML) and deep learning (DL) techniques show promise in imaging-based diagnosis and monitoring of diseases, particularly retinal conditions. These methods excel in medical image segmentation, classification, diagnosis, and monitoring of eye diseases. However, developing disease-specific ML/DL models requires sufficient labelled image datasets and addresses the explainability issue. Moreover, sharing health data, particularly images, gives rise to integrity and provenance issues, notably in LMICs.

Thus, this thesis proposes solutions for early ROP detection and treatment, aiming to reduce healthcare costs and enhance care accessibility in LMICs. Key contributions include:

- **IIRIR dataset:** To facilitate the development and fine-tuning of deep learning models, the thesis introduces a labelled retinal image dataset, the Indian Infant Retinal Image of ROP (IIRIR) collected from AIIMS Delhi.

- **DL-assisted ROP Screening Technique:** This approach utilizes a deep convolutional neural network (DCNN) and computer vision to automatically recognize optical disc (OD) and retinal blood vessels in ROP patients. The system categorizes the severity of ROP (Zone-1), providing a scalable solution for areas lacking large historical datasets.
- **Plus Disease Classification:** Extending the DL-assisted screening technique, the study introduces an analysis of Plus disease, a severe form of ROP. The research explores various methods to compute and locate blood vessel map features, offering insights into tortuosity and vascular features for better treatment decisions.
- **Device Fingerprint and Image Watermarking-Based Data Provenance Framework:** The thesis also explores a Device Fingerprint (DFP) and image watermarking-based medical image data provenance and integrity framework for interconnected healthcare systems. This framework ensures the integrity and provenance of medical image data by embedding device attributes into raw images before sharing them with remote experts. Additionally, the study introduces a DevFing-based daughterboard for DFP generation, utilizing the concept of Physical Unclonable Function (PUF) to generate unique device identifications based on electrical characteristics. This ensures the use of legitimate healthcare devices within the proposed framework.

The proposed approach was empirically validated using preterm infant retinal images from IIRIR image dataset. Experimental results demonstrate robust ROP screening with 96.69% vessel segmentation accuracy and an overall OD detection accuracy of 98.94%. Our system can accurately diagnose ROP in Zone-1 with 88.23% accuracy. For Plus disease screening, various blood vessel map features are computed and analyzed, and the algorithm achieves notable precision in parameter recognition. The study reveals tortuosity indices for Plus, pre-Plus, Healthy infants, and the percentage of severely infected vessels. Finally, the effectiveness of the medical image data provenance framework is evaluated regarding computational time, image quality, security, and trustworthiness. The proposed DFP-based watermarking method significantly improves matching percentage accuracy, strengthening data integrity in the system.

सार

रेटिनोपैथी ऑफ प्रीमैच्योरिटी (आरओपी) वैश्विक स्तर पर समय से पहले जन्मे शिशुओं में अंधेपन का एक महत्वपूर्ण कारण है। समय पर निदान और उपचार से इसके प्रभाव को कम किया जा सकता है। हालाँकि, नवजात नेत्र रोग विशेषज्ञों की घटती संख्या, विशेष रूप से भारत जैसे निम्न और मध्यम आय वाले देशों (एलएमआईसी) में, उच्च जोखिम वाले शिशुओं में आरओपी के बढ़ते मामलों को संबोधित करने में चुनौतियाँ पैदा करती हैं। संसाधनों के असंतुलित वितरण और समय की कमी स्थिति को और जटिल बना देती है। पारंपरिक आरओपी स्क्रीनिंग विधियाँ, विशेष रूप से वर्तमान परिस्थितियों में, इस समस्या का समाधान करने में संघर्ष कर रही हैं।

इसलिए, यह शोध एक सस्ती, विस्तार योग्य आरओपी स्क्रीनिंग और नेत्र स्वास्थ्य निगरानी समाधान प्रस्तावित करता है। एम-हेल्थ, इ-हेल्थ, इंटरनेट ऑफ़ मेडिकल थिंग्स (आईओएमटी), और टेलीमेडिसिन का उपयोग करके, हम डिजिटल इमेजिंग उपकरणों का उपयोग करके सस्ती आरओपी स्क्रीनिंग, निदान और निगरानी प्रदान करना चाहते हैं। हालाँकि, समय से पहले जन्मे शिशुओं में रेटिना की छवियों की गुणवत्ता विभिन्न शोरोँ और कलाकृतियों से प्रभावित होती है, जिसमें गति धुंधलापन और असमान रोशनी शामिल है। इसके अतिरिक्त, समय से पहले जन्मे शिशुओं में अविकसित रेटिना स्थलचिह्न रेटिना स्कैन के माध्यम से आरओपी का पता लगाने और मात्रा निर्धारित करने को जटिल बनाते हैं।

चुनौतियों के बावजूद, डेटा-संचालित मशीन लर्निंग (एमएल) और डीप लर्निंग (डीएल) तकनीकों में हाल ही में हुई प्रगति इमेजिंग-आधारित निदान और बीमारियों, विशेष रूप से रेटिना संबंधी स्थितियों की निगरानी में आशाजनक है। ये विधियाँ चिकित्सा छवि विभाजन, वर्गीकरण, निदान और नेत्र रोगों की निगरानी में उत्कृष्ट हैं। हालाँकि, रोग-विशिष्ट एमएल/डीएल मॉडल विकसित करने के लिए पर्याप्त लेबल वाली छवि डेटासेट की आवश्यकता होती है और व्याख्यात्मकता की समस्या का समाधान करना होता है। इसके अलावा, स्वास्थ्य डेटा, विशेष रूप से छवियों को साझा करना, विशेष रूप से एलएमआईसी में, अखंडता और उत्पत्ति के मुद्दों को जन्म देता है।

इस प्रकार, यह शोध आरओपी का शीघ्र पता लगाने और उपचार के लिए समाधान प्रस्तावित करती है, जिसका उद्देश्य स्वास्थ्य सेवा लागत को कम करना और एलएमआईसी में देखभाल की सुलभता को बढ़ाना है। मुख्य योगदानों में शामिल हैं:

1. **आईआईआरआईपी डेटासेट:** डीप लर्निंग मॉडल के विकास और परिशोधन की सुविधा के लिए, इस शोध में एम्स दिल्ली से एकत्रित “इंडियन इन्फैंट रेटिनल इमेज ऑफ़ आरओपी (आईआईआरआईपी) नामक लेबल वाली रेटिनल इमेज डेटासेट को पेश किया गया है।
2. **डीएल-सहायता प्राप्त आरओपी स्क्रीनिंग तकनीक:** यह दृष्टिकोण डीप कॉन्वोल्यूशनल न्यूरल नेटवर्क (डीसीएनएन) और कंप्यूटर विज्ञान का उपयोग करके आरओपी रोगियों में ऑप्टिकल डिस्क (ओडी) और रेटिनल रक्त वाहिकाओं को स्वचालित रूप से पहचानता है। यह प्रणाली आरओपी की

गंभीरता (जोन-1) को वर्गीकृत करती है, जो उन क्षेत्रों के लिए एक स्केलेबल समाधान प्रदान करती है जहाँ बड़े ऐतिहासिक डेटासेट की कमी है।

3. **प्लस रोग वर्गीकरण:** डीएल सहायता प्राप्त स्क्रीनिंग तकनीक का विस्तार करते हुए, यह अध्ययन प्लस रोग, आरओपी के एक गंभीर रूप के विश्लेषण को पेश करता है। अनुसंधान विभिन्न विधियों का पता लगाता है ताकि रक्त वाहिका मानचित्र विशेषताओं की गणना और पहचान की जा सके, जिससे बेहतर उपचार निर्णयों के लिए टेढ़ेपन और संवहनी विशेषताओं में अंतर्दृष्टि मिल सके।
4. **डिवाइस फिंगरप्रिंट और इमेज वॉटरमार्किंग-आधारित डेटा प्रोवेंस फ्रेमवर्क:** यह शोध चिकित्सा छवि डेटा प्रोवेंस और अखंडता के लिए डिवाइस फिंगरप्रिंट (डीएफपी) और इमेज वॉटरमार्किंग-आधारित फ्रेमवर्क का भी पता लगाता है। यह फ्रेमवर्क दूरस्थ विशेषज्ञों के साथ साझा करने से पहले कच्ची छवियों में डिवाइस विशेषताओं को एम्बेड करके चिकित्सा छवि डेटा की अखंडता और उत्पत्ति सुनिश्चित करता है। इसके अतिरिक्त, अध्ययन डीएफपी निर्माण के लिए डेवफिंग (DevFing)-आधारित डॉटरबोर्ड को पेश करता है, जो फिजिकल उंक्लोनाब्ले फंक्शन (पीयूएफ) की अवधारणा का उपयोग करके विद्युत विशेषताओं के आधार पर अद्वितीय डिवाइस पहचान उत्पन्न करता है। यह प्रस्तावित फ्रेमवर्क के भीतर वैध स्वास्थ्य देखभाल उपकरणों के उपयोग को सुनिश्चित करता है।

प्रस्तावित दृष्टिकोण को आईआईआरआईपी इमेज डेटासेट से प्रारंभिक शिशुओं की रेटिनल छवियों का उपयोग करके अनुभवजन्य रूप से मान्य किया गया था। प्रयोगात्मक परिणाम मजबूत आरओपी स्क्रीनिंग को 96.69% जहाज विभाजन सटीकता और 98.94% की समग्र ओडी पहचान सटीकता के साथ प्रदर्शित करते हैं। हमारा सिस्टम जोन-1 में आरओपी का 88.23% सटीकता के साथ सटीक निदान कर सकता है। प्लस रोग स्क्रीनिंग के लिए, विभिन्न रक्त वाहिका मानचित्र विशेषताओं की गणना और विश्लेषण किया जाता है, और एल्गोरिथम पैरामीटर पहचान में उल्लेखनीय सटीकता प्राप्त करता है। अध्ययन प्लस, प्री-प्लस, स्वस्थ शिशुओं के लिए टॉरचोसिटी इंडेक्स और गंभीर रूप से संक्रमित वाहिकाओं के प्रतिशत को प्रकट करता है। अंत में, चिकित्सा छवि डेटा प्रोवेंस फ्रेमवर्क की प्रभावशीलता को कम्प्यूटेशनल समय, छवि गुणवत्ता, सुरक्षा और विश्वासनीयता के संदर्भ में मूल्यांकन किया जाता है। प्रस्तावित डीएफपी -आधारित वॉटरमार्किंग विधि मिलान प्रतिशत सटीकता में काफी सुधार करती है, जो प्रणाली में डेटा अखंडता को मजबूत करती है।

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List of Abbreviations

AMBE	Absolute Mean Brightness Error.
AMD	Age-related Macular Degredation.
AO	Adaptive Optics.
API	Application Programming Interface.
AUROC	Area Under the Receiver Operating Curve.
BIO	Binocular Indirect Ophthalmoscopy.
BV	Blood Vessels.
CAD	Computer-aided Diagnosis.
CDR	Cup to Disc Ratio.
cGAN	conditional GAN.
CII	Contrast Improvement Index.
CLAHE	Contrast-Limited Adaptive Histogram Equalization.
CNS	Central Nervous System.
COVID-19	Coronavirus Disease 2019.
CPCU	Central Processing and Control Unit.
CPS	Cyber-Physical Systems.
CPU	Central Processing Unit.
CT	Computed Tomography.
CVD	Cardiovascular Disease.
DCNN	Deep Convolutional Neural Network.
DDoS	Distributed Denial of Service.
DFP	Device Fingerprint.
DL	Deep Learning.
DR	Diabetic Retinopathy.
DWT	Discrete Wavelet Transform.

EMI	Electromagnetic Interference.
FAF	Fundus Autofluorescence.
FN	False Negative.
FOV	Field of View.
FP	False Positive.
GAN	Generative Adversarial Network.
HBP	High Blood Pressure.
HIS	Hardware Intrinsic Security.
ICROP	International Classification of Retinopathy of Prematurity.
ICT	Information and Communications Technology.
IIRIR	Indian Infant Retinal Image of ROP.
IoMT	Internet of Medical Things.
IoT	Internet of Things.
IoU	Intersection over Union.
JPG/JPEG	Joint Photographic Experts Group.
LMIC	Low and Middle-income Countries.
MAP	Mean Average Precision.
MHEALTH	Mobile Health.
MI	Molecular Imaging.
ML	Machine Learning.
MRI	Magnetic Resonance Imaging.
NICU	Neonatal Care Unit.
OC	Optical Cup.
OCT	Optical Coherence Tomography.
OCTA	OCT angiography.
OD	Optical Disk.
ONH	Optical Nerve Head.

OS	Operating System.
PAM	Photoacoustic Microscopy.
PC	Personal Computer.
PCB	Printed Circuit Board.
PNG	Portable Network Graphics.
PPM	Portable Pixmap.
PR	Retinitis Pigmentosa.
PUF	Physical Unclonable Function.
RAM	Random-access Memory.
RAO	Retinal Artery Occlusion.
RD	Retinal Detachment.
RL	Reinforcement Learning.
ROI	Regions of Interest.
ROM	Read Only Memory.
ROP	Retinopathy of Prematurity.
RVO	Retinal Vein Occlusion.
SBFI	Smartphone Based Fundus Imaging.
SHA	Secure Hash Algorithm.
SLO	Scanning Laser Ophthalmoscopy.
SSIM	Structural Similarity Index.
TIFF	Tag Image File Format.
TN	True Negative.
TP	True Positive.
WHO	World Health Organization.
YOLO	You Only Live Once.