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Identification of Memory Loss disease by Ocular Biomarkers using Deep Learning Models

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***Abstract*—This paper explores the application of deep learning techniques to analyze retinal images obtained through Optical Coherence Tomography Angiography (OCTA) for detecting Alzheimer's disease (AD). By examining alterations in retinal blood vessel characteristics, such as flow and density, the approach identifies patterns associated with AD. The research builds on existing methodologies and incorporates clinical per- spectives to develop a cost-effective, non-invasive solution for early diagnosis. It also highlights the relevance of specific retinal regions in the detection process, providing valuable information for clinicians and contributing to the understanding of retinal biomarkers related to AD. The findings underscore the potential of this method to enhance both the accuracy and accessibility of diagnosing neurodegenerative conditions.**

***Index Terms*—OCTA, Alzheimer's Disease, Polar Transformation**

I. Introduction

Alzheimer's disease (AD) is a progressive neurological disorder that leads to cognitive and functional impairments, affecting millions globally. Early detection is essential for effective management and improving patient quality of life. Traditional diagnostic methods like MRI and PET scans, while effective, are often expensive, time-intensive, and not readily available in resource-limited regions. These limitations highlight the importance of developing non-invasive, cost-effective alternatives.

Emerging research has identified significant connections between the structural and functional features of the eyes and the brain, with notable findings showing reduced blood vessel density in specific retinal regions, such as the superficial parafoveal and choriocapillaris layers, in individuals with AD. This has spurred interest in Optical Coherence Tomography Angiography (OCTA), a high-resolution imaging technology capable of capturing detailed views of retinal microvasculature, including the superficial vascular complex (SVC), deep vascular complex (DVC), and choriocapillaris (CC).

Clinical analysis methods, such as the use of the early treatment diabetic retinopathy study (ETDRS) grid, provide valuable insights by dividing retinal areas into specific regions for localized assessment of vascular metrics. Studies have shown a significant reduction in metrics like vascular area density and vascular length density in sub-regions such as the nasal-outer, superior-inner, and inferior-inner regions in individuals with AD.

Deep learning has gained prominence in medical image analysis, particularly in detecting AD. However, many existing models do not integrate region-specific clinical insights, limiting their ability to align results with established medical findings or provide interpretable outcomes.

This study introduces a novel deep-learning framework that incorporates clinical region-based analysis for detecting AD using OCTA images. By transforming OCTA images from a Cartesian to a radial coordinate system, the framework replicates clinical sector-based analysis, enabling precise feature extraction. Additionally, a weighted matrix is employed during training to emphasize the importance of specific regions, ensuring the model aligns with clinical observations. Explainability analyses validate the model's consistency with clinical findings, demonstrating its potential to reveal the relationship between retinal biomarkers and AD.

This approach represents a significant step forward in early AD detection, offering an efficient, interpretable, and non-invasive diagnostic solution that bridges advanced deep learning techniques with established clinical practices.

II. RESEARCH OBJECTIVES

- Utilizing Advanced Techniques: Employ state-of-the-art deep learning methods, particularly Convolutional Neural Networks (CNNs), to process and analyze Optical Coherence Tomography Angiography (OCTA) images for detecting Alzheimer's disease (AD).
- Feature Extraction and Analysis: Focus on identifying critical retinal vascular features, such as density and flow patterns, through deep learning models. These features help establish a connection between retinal changes and AD. .

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- Optimized Resource Utilization: Design computationally efficient deep learning models to minimize resource consumption, ensuring compatibility with environments that have limited computational capacity.
- Improving Model Performance: Train and fine-tune the models to enhance accuracy, sensitivity, and specificity in detecting AD. The goal is to ensure consistent performance across diverse datasets.
- Framework Validation: Test the proposed methodology using multiple retinal OCTA datasets to confirm its reliability and applicability in clinical scenarios, ensuring the system meets practical diagnostic requirements.

III. LITERATURE SURVEY

[1] This paper presents a deep-learning model called Polar-Net for detecting Alzheimer's Disease using Optical Coherence Tomography Angiography (OCTA) images. This model aims to enhance interpretability and clinical relevance with region-based analysis, utilizing a dataset of 199 OCTA images from 114 AD patients and 566 images from 291 healthy subjects, with additional validation from the OCTA- 500 dataset. However, it notes the minimal improvement from prior knowledge matrices and the potential issue with high-dimensional features.

[2] Which focuses on developing a machine learning model for early diagnosis of Alzheimer's Disease. It employs an ensemble-based approach using classifiers such as GaussianNB, Decision Tree, Random Forest, XGBoost, and Voting Classifier. The researchers utilized the OASIS dataset, which includes MRI data from 150 individuals aged 60-96, with 64 subjects diagnosed with dementia and 72 non-demented. The study highlights the importance of data preprocessing, including feature selection, outlier detection, and data augmentation, to improve model performance. Despite the promising results, the paper notes the need for further optimization in removing redundant features and extracting more relevant ones to enhance the model's accuracy.

[3] explores the use of deep learning methods for diagnosing Alzheimer's disease (AD). It delves into the application of AD-related biomarkers, feature extraction techniques, and evaluates the performance of deep learning models in detecting AD from medical images. The study utilizes several publicly available datasets commonly used in AD detection research, such as ADNI, OASIS, and AIBL. However, the study acknowledges challenges such as a lack of sufficient data samples, which can hinder generalization, and the time-consuming manual annotation

[4] aims to distinguish between AD patients and healthy subjects by analyzing brain MRI images. The method employed evaluates brain structural changes over time by assessing the existence probabilities of different brain tissue types, including gray matter, white matter, and cerebrospinal fluid. The dataset used for this study was obtained from the Japanese Alzheimer's Disease Neuroimaging Initiative (J-ADNI). However, limitations include the uncertainty surrounding the onset of Alzheimer's disease in the studied samples, which could potentially impact the classification accuracy, and the study's lack of consideration for the disease's progression during the initial measurement period.

[5] To develop a deep learning (DL) model that integrates multiple data types (MRI imaging, clinical data, and genetic information) to classify patients into different stages of Alzheimer's disease (AD), including healthy controls (CN), mild cognitive impairment (MCI), and AD. The fusion of data is expected to improve accuracy compared to single- modality models. The study utilizes the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, which includes imaging (MRI), clinical, and genetic (SNP) data from over 2,200 patients across various ADNI studies. However, the small sample size of the ADNI dataset limits the potential of the models, especially in the multi-modality integration scenarios. There is also a challenge in effectively interpreting the complex deep-learning models for clinical decision-making.

[6] Recent progress in understanding the early stages of Alzheimer's disease (AD), with a focus on the pre-dementia stage known as mild cognitive impairment (MCI). It emphasizes the early cognitive profile and associated neuroimaging studies. The paper does not refer to a specific dataset but discusses various studies and findings from neuropsychological and neuroimaging research focused on MCI and early AD detection. The paper highlights the difficulty in developing robust criteria for diagnosing MCI and differentiating it from normal aging and other cognitive conditions. Additionally, it points out the challenges in finding early diagnostic markers that are both sensitive and specific.

[7] To investigate retinal alterations in Alzheimer's disease (AD) patients, explore the associations between retinal changes and AD biomarkers, and develop an optimal machine learning model for diagnosing AD based on retinal thickness measurements. The study included 159 AD patients and 299 healthy controls with data collected through Optical Coherence Tomography (OCT) imaging. The study acknowledges certain limitations, such as the inability to include patients with advanced-stage AD due to the need for cooperation during OCT examinations. Additionally, being a cross-sectional study, it cannot track changes in retinal thickness over time.

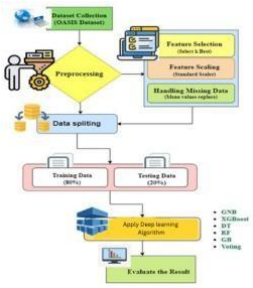
[8] To develop a convolutional neural network (CNN) model to identify Alzheimer's disease (AD) by analyzing multimodal retinal images, including OCT, OCTA, and ultra-widefield (UWF) images, combined with patient data. The dataset included 284 eyes from 159 subjects with 222 eyes from 123 cognitively healthy controls and 62 eyes from 36 subjects with AD. Limitations include the small dataset size, potential overfitting issues, exclusion of patients with ocular diseases, and limited generalizability. Additionally, UWF im- ages contributed minimally to predictive accuracy, partly due to image quality issues such as eyelid artifacts.

IV. METHODOLOGY

The methodology focuses on analyzing Optical Coher- ence Tomography Angiography (OCTA) images to derive key vascular metrics, including Vascular Area Density, Vascular

Length Density, and Choriocapillaris Flow Density, within regions outlined by the ETDAR framework (FAZ, Perifoveal, and Parafoveal). The preprocessing stage involves image normalization, noise reduction, thresholding, and segmentation to improve image clarity and define anatomical areas of interest. Following preprocessing, the images are transformed from Cartesian to polar coordinates, enabling a radial analysis centered on the FAZ.

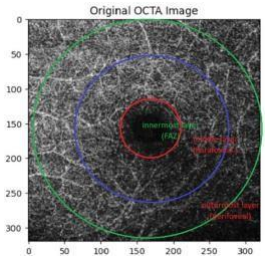
Feature extraction leverages binary masks, skeletonization, and flow area measurements to calculate the desired metrics. These metrics are represented visually in a concentric ET- DAR graph, which provides insights into regional vascular health through bar charts or heatmaps. Tools such as Python libraries (e.g., OpenCV and Scikit-Image) facilitate the image processing steps, while Matplotlib supports the visualization process. Cross-validation against ground truth data ensures the reliability and accuracy of the results.



A. *Input and Dataset Description*

• Input Data: The input consists of OCTA images, which provide detailed visualizations of the retinal microvascular structures. These images are essential for analyzing both vascular and structural properties.

• Objective: The goal is to process these images to compute three key metrics: Vascular Area Density, Vascular Length Density, and Choriocapillaris Flow Density. These metrics are evaluated within specific regions defined by the ETDRS grid, including the FAZ, perifoveal, and parafoveal regions.



Sample image

B. *Preprocessing*

• Image Normalization: The brightness and contrast of the OCTA images are normalized to improve the visibility of vascular structures, ensuring uniformity across the dataset.

• Noise Reduction: Techniques such as Gaussian blur or median filtering are applied to minimize noise while preserving the intricate details of the vascular network.

• Binarization: Adaptive or global thresholding methods are used to convert the images into binary form, isolating the vascular structures from the background.

• Segmentation: The Foveal Avascular Zone (FAZ) is identified through morphological operations to delineate the central non-vascular region. Perifoveal and parafoveal areas are then defined based on anatomical distances surrounding the FAZ.

C. *Polar Transformation*

• Polar Coordinate Conversion: OCTA images are transformed from Cartesian to polar coordinates, centering the FAZ as the origin. This transformation supports radial or circular analysis, allowing for simplified and targeted evaluation of vascular metrics in perifoveal and parafoveal regions.

D. *Feature Extraction*

Vascular Area Density: • The proportion of the vascular area (in pixels) within each region is calculated.

$$\text{VAD} = \frac{\text{Vascular Pixels}}{\text{Total Pixels in Region}} \times 100\% \quad (1)$$

Vascular Length Density: • The total length of vessels in each region is calculated by skeletonizing the vascular structures. • Skeletonization converts the binary vascular mask into 1-pixel-wide representations of the vessels.

$$\text{VLD} = \frac{\text{Total Vascular Length}}{\text{Total Area of Region}} \quad (2)$$

Lower Choriocapillaris Flow Density: • The choriocapillaris layer is isolated by analyzing the lower layers of the OCTA image. • The flow density is computed as the percentage of the area exhibiting blood flow signals.

$$\text{LCFD} = \frac{\text{Flow Area}}{\text{Total Area of Region}} \times 100\% \quad (3)$$

E. *Generation of ETDAR Graph*

•Definition of ETDRS Graph:

The ETDRS (Early Treatment Diabetic Retinopathy Study) grid is used to segment the macular region into three distinct areas:

FAZ (Foveal Avascular Zone)

Perifoveal Region

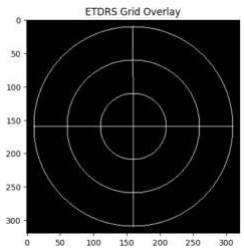
Parafoveal Region

These regions are represented as concentric circles, with the FAZ at the center, allowing for structured analysis.

• Metric Visualization:

Key metrics—Vascular Area Density, Vascular Length Density, and Choriocapillaris Flow Density—are computed for each defined region (FAZ, perifoveal, and parafoveal).

The results are presented visually using techniques like bar charts, heatmaps, or color-coded gradients, expressed as percentages to facilitate comparison within the ETDRS framework.



ETDAR Grid

F. Output

• Generated Output:

• ETDRS Graph: A concentric visualization that segments the macular region into FAZ, perifoveal, and parafoveal areas, with clear labels and distinct color coding for each region.

• Computed Metrics:

Vascular Area Density for each region.

Vascular Length Density for each region.

Choriocapillaris Flow Density (lower values) for each region.

G. Tools and Technologies

• Libraries and Frameworks:

Python with libraries such as OpenCV, Scikit-Image, and NumPy for image preprocessing and feature extraction.

Visualization tools like Matplotlib or Seaborn for creating the ETDRS graph. Image Processing Methods:

• Segmentation using morphological operations.

Radial analysis facilitated by polar coordinate transformations.

• Validation Process:

Outputs are validated by comparing results with manual annotations or established ground truth data to ensure reliability and accuracy.

V. Conclusion

This study presents a detailed methodology for processing and analyzing Optical Coherence Tomography Angiography (OCTA) images to extract vital vascular metrics from retinal regions defined by the ETDAR graph. The approach incorporates advanced image preprocessing, polar transformations, and the calculation of key metrics such as Vascular Area Density (VAD), Vascular Length Density (VLD), and Lower Choriocapillaris Flow Density (LCFD). These metrics are essential for evaluating microvascular health and diagnosing conditions like diabetic retinopathy, macular degeneration, and other retinal disorders.

Each stage of the process, from data acquisition to feature extraction and visualization, is systematically addressed. Preprocessing steps, including normalization, noise reduction, and segmentation, ensured the OCTA images were optimized for analysis. Polar transformations enabled radial examination of retinal areas surrounding the Foveal Avascular Zone (FAZ). Clear mathematical formulations for vascular metrics provided precise and reliable insights into the health of the FAZ, perifoveal, and parafoveal regions.

The integration of deep learning techniques further enhanced the framework, enabling automated feature extraction, classification, and prediction. Advanced models, such as convolutional neural networks (CNNs) and transformer-based architectures, can uncover intricate vascular patterns often missed by traditional approaches. These models also improve scalability and ensure accuracy across larger datasets.

The ETDAR graph, generated during the analysis, serves as an effective visualization tool. By providing a clear representation of vascular metrics across different regions, it aids clinicians and researchers in interpreting data and making evidence-based decisions for diagnosis and treatment. This approach demonstrates significant potential for advancing diagnostic accuracy and clinical efficiency in retinal and neurovascular health assessments.

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