AUTOMATIC DETECTION OF MACULAR EDEMA WITH ITS SEVERITY ANALYSIS

Abstract

The Macula is an important part of our human visual system that is primarily responsible for sharp and colour vision. Diabetes affects many different parts of the body, including the retina of the eye. Edema and other abnormalities near the macula are caused by retinal damage. Diabetes-related macular edema (DME) is a group of disorders that affect the macula. It has an effect on patients' vision, which can lead to vision loss. The information regarding the severity of the disease and the localization of pathologies is extremely useful to the ophthalmologist in detecting the disease and selecting the best treatment plan for the patients in order to avoid the formation of lesions and prevent vision loss. It can be avoided if the reasons for edema are identified in advance. The enlargement is caused by neovascularization and other irregularities in the blood vessels around the macula. The objective of this work focuses on preventing vision loss by recognizing abnormalities in the macula in advance. The goal of this work is to use digital OCT (Optical Coherence Tomography) pictures to construct an automated detection of edema. Using Fuzzy k- means Machine Learning algorithms to extract and detect the afflicted region, for early discovery of edema to prevent or postpone sight loss.

Keywords: Clinically Significant Macular Edema (CSME), Central retinal vein occlusion (CRVO) Exudates, Fovea, Haemorrhage, Maculopathy, Optical Coherence Tomography

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I. INTRODUCTION

Macular edema is the leading cause of vision loss in the working-age population of most developed countries. DME affects almost 560,000 Americans. Around 55% are unaware that they have the condition, and 70% of people with the most severe form of diabetic retinopathy, proliferative retinopathy, will acquire DME. Macular edema is an expansion or thickening of the macula, the part of the eye responsible for detailed, central vision. Macular edema occurs when fluid and protein deposits form on or under the macula of the eye (the yellow centre area of the retina) and cause it to thicken and expand (edema). Because the macula is in the middle of the retina at the back of the eyeball, swelling may impair central vision. This area includes tightly packed cones that provide crisp, clear central vision, letting a person perceive detail, form, and colour that is directly in the direction of gaze.

Diabetic Macular Edema (DME) is a frequent diabetes illness that can cause severe vision impairment. Manual diagnosis and assessment of DME by ophthalmologists can be time-consuming and varied. Methods that are automated have the potential to improve accuracy, efficiency, and early intervention. Diabetes causes vision loss due to the destruction of retinal blood vessels in the eye. These injured blood arteries bleed blood into the macula region, resulting in visual loss. Diabetic macular edema refers to this impairment in the macula caused by diabetes. The most common cause of diabetic macular edema is neovascularization, which is the growth of small and aberrant blood vessels inside the macular region. These blood vessels form in the wrong places, causing damage to the macula and haemorrhage. Blood vessel abnormalities in the macula are another cause of macular edema. The leakage of fluid from the vessels can be halted if this is identified in advance. The immediate amplitude and frequency properties of a picture. Ophthalmologists currently use dilated retinal imaging to detect neovascularization and other abnormalities in blood vessels. The dilating drops may produce ocular discomfort and giddiness. This course requires a minimum of 30 minutes of effort. The investigation time and impact on the patient may be minimized if the system could function on photos where the patient's pupil is not dilated. Diabetes retinopathy (DR) is an important cause of preventable vision loss worldwide. The macula is the darkest area on the focus point of a retinal fundus image Fig 1(a). When the fovea (the focal point of the macula region) is harmed in diabetic patients, it causes diabetic macular edema (DME) [1]. DME pathogenesis begins with decreased retinal oxygen strain, which manifests as retinal vessel hyperpenetrability and increased intravascular pressure [2]. Exudates are brilliant lesions characterized by the leakage of proteins and lipids from the circulatory system into the retina via damaged veins [3]. Non-Clinically Significant Macular Edema (non-CSME) is an early stage of edema in which exudates are located far from the fovea and focused vision is unaffected Fig 1(b) Yet, in Clinically Significant Macular Edema (CSME) the exudates kept near or on the fovea and influencing the focal vision of the eye Fig. 1(c) [4].

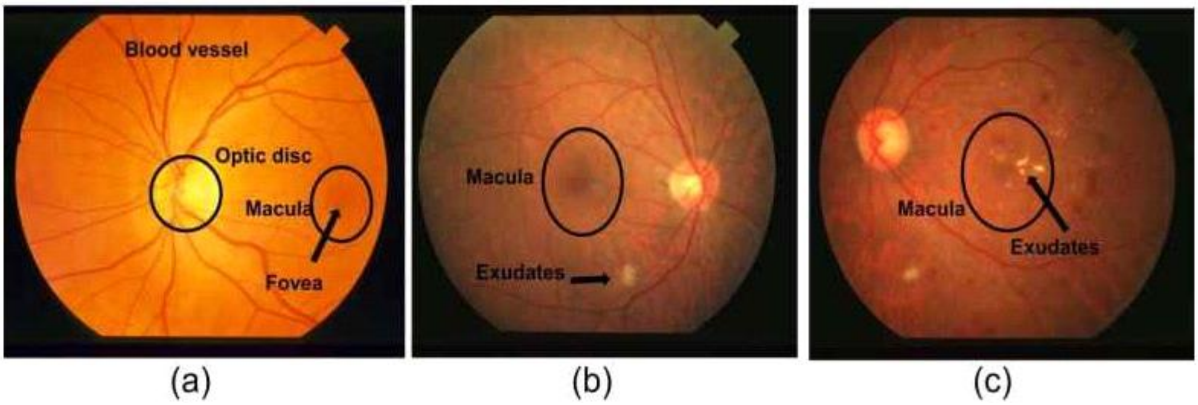

Figure 1: Images of the retinal fundus with varied properties.

II. ANATOMY OF EYE

The eyes are vision organs. In neurons, light is recognised and transformed into electrochemical impulses. In conscious vision, the most basic photoreceptor cells correlate light with movement. The eye in higher organisms is a complex optical system that collects light from its surroundings, regulates its intensity with a diaphragm, focuses it through an adjustable assembly of lenses to form an image, converts this image into a set of electrical signals, and transmits these signals to the brain via complex neural pathways that connect the eye to the visual cortex and other areas of the brain via the optic nerve. The eye is a hollow spherical organ with a diameter of 2.5cm. It has a three-layer wall, and its internal voids are filled with fluids that sustain the walls and keep the eye forming Fig 2. Depicts the cross-sectional anatomy of the eye. The eyes are so crucial that they account for one-fifth of all information received by the brain.

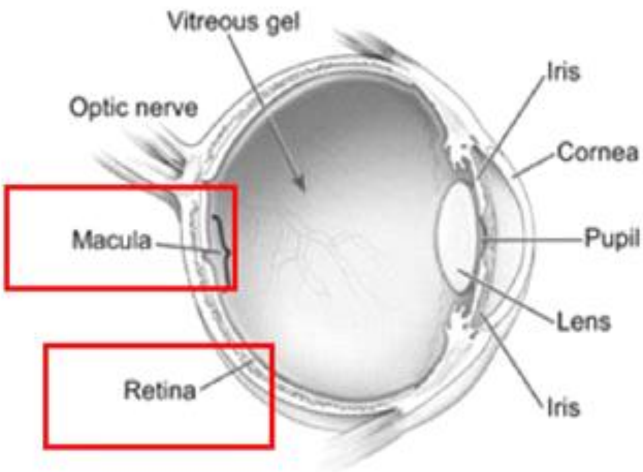

Figure 2: Structure of eye

1. **Cornea:** The cornea is a transparent covering in front of the eye that covers the iris, pupil, and anterior chamber and serves to concentrate incoming light, with a water content of 78%. The cornea is elliptical, with vertical and horizontal dimensions of 11 and 12mm, respectively. It is devoid of blood vessels. The cornea's function is to refract and transmit light.

2. **Aqueous Humour:** The aqueous humour is the aqueous fluid found between the lens and the cornea in the front of the eye. The fundamental function of aqueous fluid is to provide nutrients and oxygen to the cornea and lens [5].

3. **Iris:** The iris is a thin, pigmented circular structure in the eye that regulates the amount of light that enters the eye. The iris's role is to regulate the size of the pupil by responding to the intensity of the lighting conditions. When focusing on distant objects or in complete darkness, the Accommodation Reflex dilates the pupil to allow light to enter.

4. **Pupil:** A pupil is a hole in the centre of the iris. The pupil size is determined by the iris's dilator and sphincter muscles. Because the tissues within the eye absorb the majority of the light entering the pupil, it appears dark.

5. **Lens:** The lens is a transparent, biconvex component of the eye that, along with the cornea, serves to refract light so that it can be focused on the retina. The lens may change the focal distance of the eye, allowing it to focus on objects at different distances and form sharp images on the retina.

6. **Vitreous Humour:** The vitreous humour is a clear fluid found in the eye that fills the gap between the lens and the retina. It is the vastest domain of the human eye. Water accounts for more than 95% of the fluid.

7. **Sclera:** The sclera is the white, opaque tissue that serves as the eye's protective outer covering. Six tiny muscles join to it and control the movement of the eye. The optic nerve is linked to the sclera at the very rear of the eye.

8. **Optic Disc:** The optic disc, commonly known as the optic nerve head or the blind spot, is where the optic nerve meets the eye. This causes a visual gap known as "the blind spot" or "physiological blind spot."

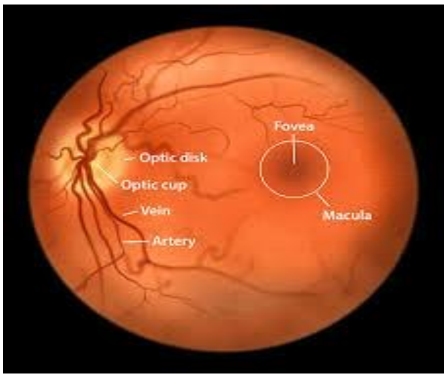

Figure 3: location of the macula

9. **Retina:** The retina is a thin layer of nerve cells that lines the inside of the eye. It is sensitive to light and absorbs it. Rods and cones are the two types of light receptors found in the retina. The rods absorb both black and white light. The rods are in charge of night vision. Cones are more colour-sensitive and absorb light. Colour vision is controlled by the cones.

10. **Macula:** The macula is the region around the fovea. Fig 3 depicts an oval-shaped highly pigmented yellow area towards the centre of the retina [6] is a tiny but very sensitive area of the retina.

11. **Fovea:** The fovea is the most central component of the macula. The visual cells in the fovea are the most densely packed, resulting in the sharpest vision. Unlike the retina, it lacks blood veins that may obstruct light from hitting the foveal cone mosaic.

III. MACULAR EDEMA

Macular edema develops when fluid and protein deposits build on or under the macula of the eye (a yellow centre portion of the retina) and cause it to thicken and enlarge (edema). Because the macula is towards the centre of the retina at the rear of the eyeball, swelling may impair central vision [7] is region contains densely packed cones that give crisp, clear centre vision, allowing a person to discern detail, shape, and colour that is immediately in the direction of gaze.

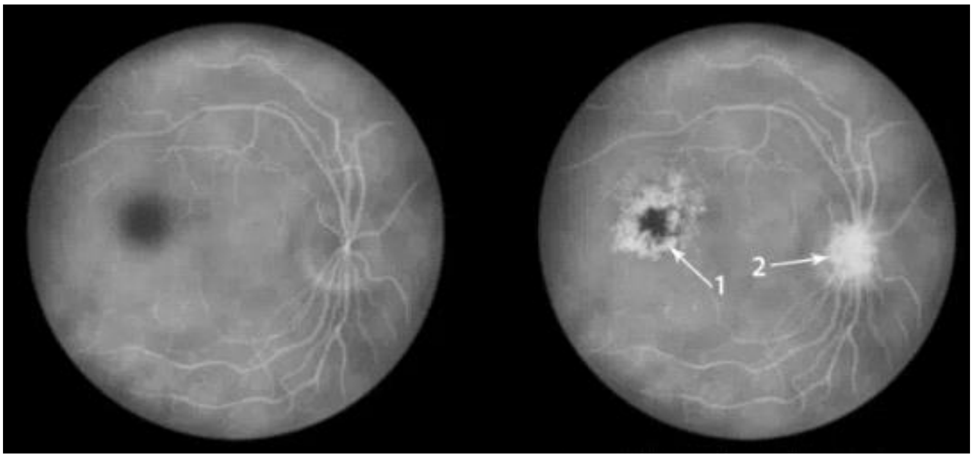

Figure 4: Normal Retina ,cystoid macula edema l and optic disk edema

Macular edema can arise a few days or weeks following cataract surgery, but most instances can be adequately treated with NSAID or corticosteroid eye drops. There were no effective treatments available for macular edema induced by central retinal vein occlusion (CRVO) until recently. [8]Macular edema induced by branch retinal vein occlusion (BRVO) has been treated with laser photocoagulation.[9]

1. **Causes of Macular Edema:** Macular edema can be caused by a variety of factors. It is usually linked with diabetes, in which damaged blood vessels in the retina begin to leak fluids into the retina, including tiny quantities of blood. Fat deposits can sometimes seep within the retina. The macula swells because of the leaking. Because blood vessels

become inflamed and leak fluids, eye surgery, particularly cataract surgery, can raise your chance of developing macular edema.

2. **Macular Edema Symptoms:** Macular edema is a disorder that affects the macula, the core region of the retina that is responsible for delivering crisp central vision for tasks such as reading, recognizing people, and driving. When fluid collects within the macula, it can cause macular edema. This syndrome frequently coexists with other eye conditions such as diabetic retinopathy and age-related macular degeneration. Macular edema symptoms include:

   - **Blurry or Distorted Central Vision:** The predominant symptom of macular edema is the distortion or blurriness of central vision. This makes objects appear unclear or fuzzy, particularly when attempting to discern fine details.

   - **Loss of Central Vision:** As the condition advances, individuals might experience a progressive loss of central vision [10] is impairs activities requiring distinct vision, including reading, watching television, and recognizing faces.

   - **Alterations in Colour Perception:** Some individuals affected by macular edema might notice changes in their ability to accurately perceive colors.

   - **Presence of Dark Spots:** Dark patches or gaps in the central vision could manifest, creating the sensation of viewing objects through a cloudy or smudged area.

   - **Visual Distortions:** Straight lines might take on a wavy or bent appearance, a phenomenon referred to as metamorphosis, which is a common manifestation of macular edema.

   - **Difficulty in Low-Light Settings:** Macular edema can result in difficulties when trying to see clearly under conditions of low light or darkness.

IV. MACULAR EDEMA DIAGNOSIS

During an eye exam, our ophthalmologist will dilate our pupils and inspect our retina. Because macular edema originates inside the layers of retina tissue, we may employ fluorescein angiography or optical coherence tomography (OCT) [11] aid make an accurate diagnosis. Fluorescein angiography photos reveal our Eye M.D. whether blood vessels are bleeding and how much leakage there is OCT uses a unique camera to image our retina. It assesses the thickness of the retina and is extremely sensitive to edema and fluid.

Classification of Macular Edema

- Cystoid macular edema
- Diabetic macular edema

- **Cystoid macular edema (CME)** is characterized by fluid buildup in the outer plexiform layer because of aberrant peritoneal retinal capillary permeability. The edema is called "cystoid" because it seems cystic yet, because it lacks an epithelial layer, it is not genuinely cystic. The healthy retina is a thin, semi-transparent tissue that borders the back of the eye. When the core section of the retina (the macula) gets dilated and filled with fluid, it swells like a sponge. This swelling appears in grape-like clusters and resembles cysts, therefore the term cystoids macular edema [12]

- **Symptoms of Cystoid Macular Edema:** Patients with cystoid macular edema typically have impaired reading vision. The peripheral vision, or side vision, stays unaffected. Object distortion and poor eyesight are common symptoms [13].addition, eyes with cystoid edema may seem inflamed and red, leak profusely, and be delicate to the touch.

- **Diabetic macular edema (DME)** is also caused by leaky macular capillaries. DME is the most prevalent cause of vision loss in both proliferative and non-proliferative diabetic retinopathy. Diabetes-related macular edema (DME) is a dangerous eye disorder that affects persons with type 1 or type 2 diabetes. The term "macular" refers to the macula, [14] Centre section of the retina and the component of the eye that provides clear central vision.2 Edema is the swelling of tissues caused by fluid. DME occurs when damaged blood vessels leak fluid, causing swelling and blurring of vision. As retinopathy progresses, the eye may begin to produce new, aberrant blood vessels over the retina, which can easily burst and bleed, resulting in significant vision loss and perhaps blindness. DME can occur at any stage of diabetic retinopathy, [15] though it is more probable as the illness advances.

  - **Symptoms and Diagnosis of DME:** The mac la is a black structure in the middle of the retina. If there is no, (roughly) rotational symmetry. seen in fig 5 the circular zone around the macula Approximately twice the size of an optical disc.

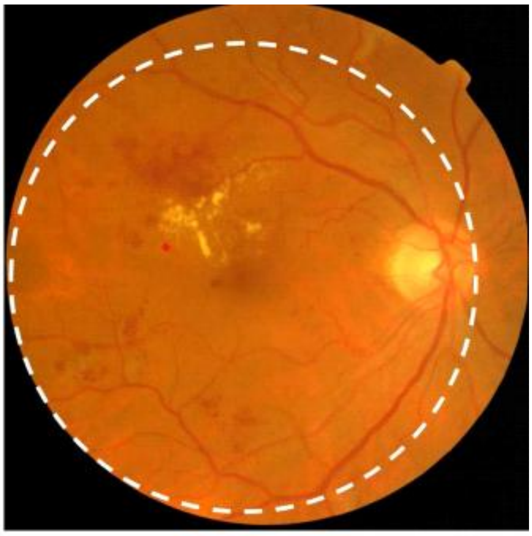

Figure 5: Sample fundus image and the circular region of interest centres on macula

The image used for evaluation is first presumed to be normal. Any divergence from normal traits is considered abnormal. It is viewed as a warning indication of anything awry. DME severity is determined for each imaging anomaly by determining HE's position about the macula that detects the fovea. Which can be easily detected in locations where blood vessels do not exist. Exist. Fovea is centralized. Where the specific macula region is present.

It is critical to determine the macula region. The fovea area, where blood vessels do not pass through it. Once found, the optic disc is easy to find. The favela area, which is located at one dia.

V. OPTICAL COHERENCE TOMOGRAPHY (OCT)

Optical Coherence Tomography (OCT) is a non-invasive medical imaging technology used to see and collect high-resolution cross-sectional pictures of biological tissues. It is frequently utilized in different medical domains, notably ophthalmology and cardiology, for diagnostic and research reasons. OCT gives precise information about tissue structure and can aid in the diagnosis of many illnesses by allowing physicians to examine the layers of tissue and spot irregularities.

Figure 6: Optical Coherence Tomography (OCT)

1. **OCT Principle:** The optical setup commonly consists of an interferometer with a low coherence, broad bandwidth light source, where light is divided into and recombined from the reference and sample arms, respectively. The underlying concept of OCT is white light or low coherence interferometry. In time domain OCT, the route length of the reference arm is translated longitudinally in time [16], and the reference of two partially coherent light beams can be described as

$$\mathbf{I = 11 + 12 + 2\tilde{A}Gcos \quad where\ Ai = —\phi_2}$$

Broadband interference is obtained in frequency domain OCT using spectrally separated detectors (either by recording the optical frequency in time with a spectrally scanning source or with a dispersive detector, such as a grating and a linear detector array).

2. **OCT Advantages**

- High Resolution: OCT provides micro meter-level resolution, enabling visualization of fine tissue structures that might not be visible with other imaging methods.
- Non-invasiveness: OCT is non-invasive and uses light waves, making it safer than techniques like X-rays.

- Real-time Imaging: OCT can provide real-time images during a procedure, allowing doctors to make immediate decisions.
- Depth Information: Unlike traditional two-dimensional imaging, OCT provides depth information, enabling accurate assessment of layered structures.
- Various Applications: OCT is extensively used in ophthalmology for imaging the retina and diagnosing conditions like macular degeneration, diabetic retinopathy, and glaucoma. It's also used in cardiology for imaging blood vessels, aiding in the diagnosis and monitoring of heart diseases.
- Research and Development: OCT is valuable for research, as it helps scientists and clinicians understand tissue behaviour, disease progression, and treatment effectiveness.
- Minimal Patient Discomfort: The procedure is generally well-tolerated by patients and doesn't require contact with the body, making it more comfortable.

3. **OCT Image:** Optical Coherence Tomography (OCT) is a non-contact, non-invasive 3-1) imaging technology that conducts optical sectioning at microscopic resolution, as seen in Fig 7 . It was commercially introduced into ophthalmology for detecting the existence and development of certain ocular diseases. This method monitors the optical back scattering of tissues, allowing visualization of intraocular structures such as the retina and optic nerve head. The capacity to see the interior components of the retina allows for objective and quantitative diagnosis of disorders such as glaucoma and macular holes, among others. OCT detects macular edema, which is found in the inner region of the eye.

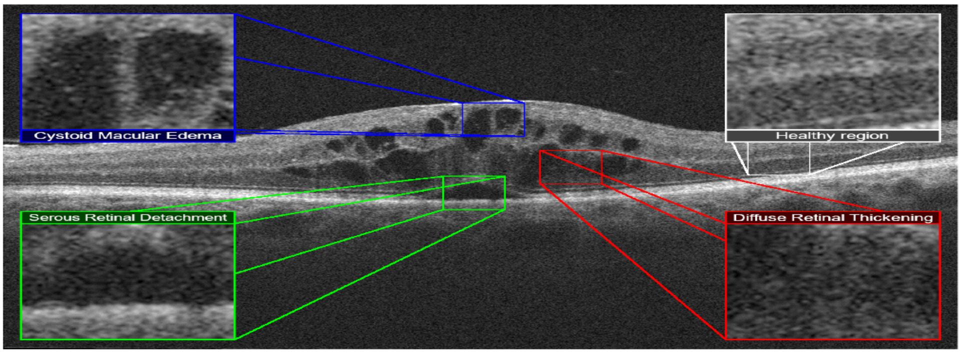

Figure 7: Macular edema OCT images

Although OCT imaging technology continues to evolve, the development of tools to aid in the interpretation of OCT images has lagged. With increasing volumes of OCT data being generated and collected at increasing sample rates, there is a pressing need for computer aided analysis to better disease diagnosis. This requirement is worsened by the fact that, in most clinical scenarios, an ophthalmologist making a diagnosis does not have the assistance of a specialist in interpreting OCT data. In contrast, a radiologist is usually present in other medical imaging settings.

VI. ALGORITHM DESIGN

The following edema macular severity algorithm have been depicted with an aid of block diagram shown in the fig 8 below.

The first stage in the algorithm creation process is to retrieve OCT image database picture samples and convert them from colour to grey scale. The thresholding procedure depicted produces a binary picture from a grayscale image.

Figure 8: Algorithm Design diagram

The preliminary step in the algorithm design is to retrieve the data base image samples of OCT Images and convert them from colour to grey scale. New map = rgb2gray (map) returns a grayscale colour map equivalent to map.

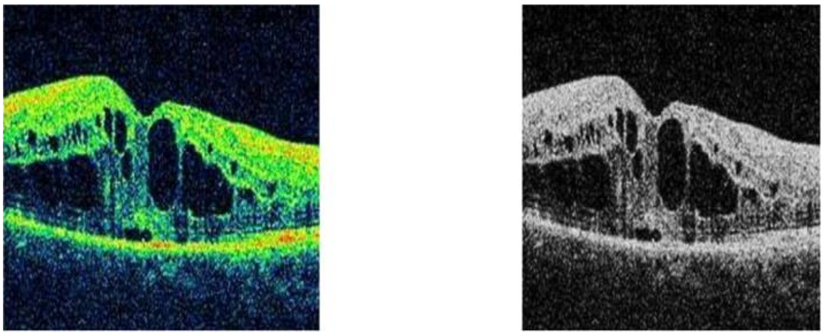

Figure 9: RGB to grey colour conversion of OCT Images

Consideration of the picture as grayscale can simplify the segmentation question and result in straightforward calumniation, but some image information will be lost. Changing the image to a colour one will assist to Denise it, but it will result in extra computations. As a result, if we have a clean image with no noise, we can presumably consider it as a grey image. The programme is designed to recover data by using picture samples from OCT images and converting them from colour to grey scale. A binary picture is created from a grayscale image using a proper thresholding procedure. The pixels in the equalized picture have an intensity range of O to 255. Because the method involves extracting the damaged or accumulated region, a 2-level picture representation would suffice for faster processing. BW = im2bw (1, level) converts the grayscale image into a binary image.[17]

Figure 10: Grey to black and white conversion of OCT Images

VII. FUZZY K- MEANS

Fuzzy k-means is a clustering technique that expands on the classic k-means algorithm by enabling data points to belong to numerous clusters with various degrees of membership, as opposed to a hard assignment in k-means. This is especially beneficial when data points do not clearly belong to a single cluster, but instead have unclear or fuzzy membership[18].Macular edoema is a medical disorder characterised by enlargement of the macula, the central portion of the retina of the eye. It can be caused by a variety of underlying illnesses, including diabetic retinopathy, age-related macular degeneration, and vascular diseases. When it comes to medical data analysis, particularly photographs of the macula, clustering techniques like as fuzzy k-means can be used to understand patterns and correlations within datasets.

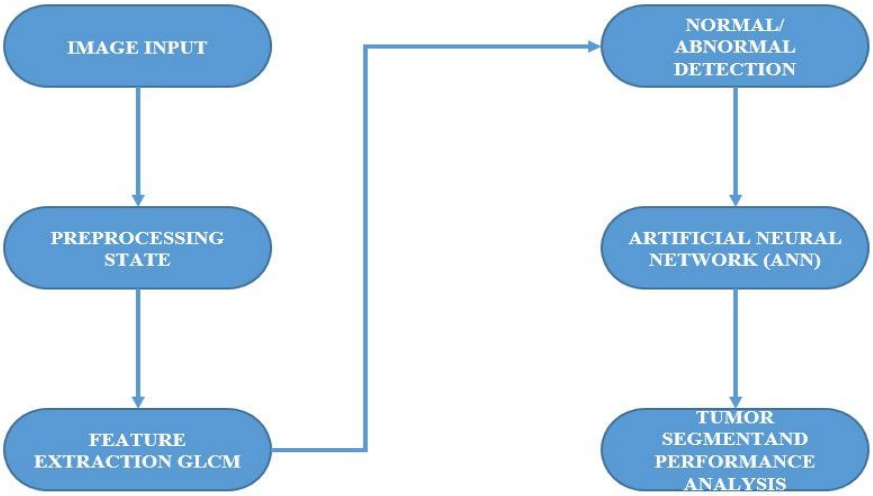

Figure 11: segmentation with the fuzzy k-means

1. **Data Representation:** In the case of macular edoema, data could be represented as information taken from medical pictures of the macula, such as pixel intensities, texture features, or other relevant attributes.

2. **Fuzzy Membership:** Instead of assigning each data point to a single cluster as in traditional k-means, fuzzy k-means assigns each data point a degree of membership to

each cluster [19].In the instance of macular edoema, this could indicate the possibility of a specific feature vector pertaining to distinct types or stages of edoema.

3. **Membership Estimation:** Fuzzy k-means computes membership values by utilising a weighting factor that quantifies how closely a data point is related to the centroid of a cluster. The closer a data point's features are to the centroid, the bigger its membership value in that cluster. This is especially useful when the distinction between clusters is uncertain due to volatility in the data.

4. **Cluster Centers:** Like classic k-means, fuzzy k-means will iteratively change the cluster centers based on the weighted memberships of data points. This technique seeks to identify the cluster centers that best represent the data distribution while accounting for fuzzy memberships.

5. **Interpretation:** Once the algorithm has converged, you may analyse the findings by examining the memberships of each data point across clusters. [20] This can provide insights into potential subgroups or patterns in the macular edoema data.

VIII. RESULTS

Certainly, let's discuss the potential results and implications of using Fuzzy k-means for the detection of macular edema.

- **Cluster Centres:** Fuzzy k-means would have discovered cluster centres in the data that represent various patterns or traits. In the context of macular edoema detection, these cluster centres may correlate to various types or phases of macular edoema.

- **Membership Values:** The membership values for each data point represent the degree of link with each cluster. Higher membership values for a specific cluster indicate a greater presence of the cluster's relevant features in the data point. This could disclose the variable degrees to which different regions of a retinal picture exhibit edema-related characteristics in the identification of macular edoema.

- **Cluster Assignment:** Each data point (or region of interest in the retinal picture) can be assigned to one or more clusters based on the highest membership value. This process would effectively segment the retinal picture into separate sections that could be indicative of macular edoema.

1. DISCUSSION

- **Interpretability:** The ability of Fuzzy k-means to capture the ambiguity and partial membership of data points in multiple clusters is one of its advantages. This could be useful in detecting macular edoema because the disorder does not usually have clear-cut boundaries in medical pictures.

- **Edoema Quantification:** The membership values allow you to assess the degree of macular edoema in different places. This could help ophthalmologists determine the severity of the illness and track its evolution over time.

- **Segmentation and Localization:** The segmentation of the retinal image by the algorithm into separate clusters can aid in localizing areas of possible concern. This data may help medical practitioners focus on certain areas during diagnosis and treatment planning.

- **Ambiguity Challenges:** Due to differences in image quality, illumination, and other circumstances, detecting macular edoema can be difficult. Fuzzy k-means may still struggle in circumstances when edoema is vague or poorly defined.

- **Validation and Expert Input:** Validating Fuzzy k-means results for macular edoema detection is critical. This validation could entail comparing the clustered regions to ground truth annotations supplied by skilled ophthalmologists. Their feedback would also be critical in refining the algorithm and changing the membership function to correspond with clinical knowledge of macular edoema.

- **Integration Potential:** Fuzzy k-means results might be incorporated into a wider diagnostic workflow, potentially followed by more advanced machine learning techniques or expert evaluation for confirmation and ultimate diagnosis.

- **Clinical Implications:** The successful application of Fuzzy k-means for macular edoema detection may result in improved early detection and treatment, which is critical for reducing vision loss in patients.

In conclusion, Fuzzy k-means provides a method for dealing with the complexity and unpredictability of macular edoema detection. However, in order to assure clinical relevance and accuracy, its application should be led by collaboration between data scientists and medical professionals.

IX. CONCLUSION

In this study, an effective and innovative method based on mathematical morphology is provided for the automatic detection of anatomical features such as the optic disc and macula (the centre of the fovea), as well as pathological features such as hard exudates, in digital colour retinal pictures. As a result, an automated approach for detecting and rating DM severity levels has been created. The approach can handle photos with significant differences in artefact presence and quality. Our suggested strategy uses precise exudates and segmentation of the macula along with straightforward noise removal algorithms to achieve this goal. The proposed method has been examined in comparison to state-of-the-art techniques and validated using the publicly accessible MESSIDOR database. The outcome of the experiment demonstrates that the new method performs better and requires less parameters than other methods. Only the macula region is where exudates are now found. The complete image is included in the exudates detection, leaving this task for later. The technique is directly utilized when screening for eye conditions for the ever-growing diabetic population.

REFERENCES

[1] Zhang, Jingfa, et al. "Diabetic macular edema: current understanding, molecular mechanisms and therapeutic implications." Cells 11.21 (2022): 3362.

[2] Takamura, Yoshihiro, Yutaka Yamada, and Masaru Inatani. "Role of Microaneurysms in the Pathogenesis and Therapy of Diabetic Macular Edema: A Descriptive Review." Medicina 59.3 (2023): 435.

[3] Tang, Yi, et al. "the development of risk factors and cytokines in retinal vein occlusion." Frontiers in Medicine 9 (2022): 910600.

[4] Li, Zijing, et al. "Nomogram-based prediction of clinically significant macular edema in diabetes mellitus patients." Acta Diabetologica 59.9 (2022): 1179-1188.

[5] McDowell, Colleen M., et al. "Consensus recommendation for mouse models of ocular hypertension to study aqueous humor outflow and its mechanisms." Investigative ophthalmology & visual science 63.2 (2022): 12-12

[6] Bolstad, K., & Novales Flamarique, I. (2023). Chromatic organization of retinal photoreceptors during eye migration of Atlantic halibut (Hippoglossus hippoglossus). Journal of Comparative Neurology, 531(2), 256-280.

[7] İnam, O., Kaplan, H. J., & Tezel, T. H. (2023). Retinal Hydration Assessment With Optical Coherence Tomography: Unraveling Its Significance in Retinal Fluid Dynamics, Macular Edema and Cell Viability. Translational Vision Science & Technology, 12(8), 4-4.

[8] Pinna, Antonio, Angelo Zinellu, Rita Serra, Giacomo Boscia, Lorenza Ronchi, and Stefano Dore. "Combined Branch Retinal Artery and Central Retinal Vein Occlusion: A Systematic Review." Vision 7, no. 3 (2023): 51.

[9] Afshar, Pedram, Haniyeh Zeidabadinejad, Fariba Ghassemi, Hamid Riazi-Esfahani, and Elias Khalili Pour. "Retinal astrocytic hamartoma complicated by branch retinal vein occlusion in a patient with tuberous sclerosis complex." American Journal of Ophthalmology Case Reports (2023): 101920.

[10] Ali, Saba Ghazanfar, Xiangning Wang, Ping Li, Younhyun Jung, Lei Bi, Jinman Kim, Yuting Chen et al. "A systematic review: Virtual-reality-based techniques for human exercises and health improvement." Frontiers in Public Health 11 (2023): 1143947.

[11] Mirmosayyeb, O., Zivadinov, R., Weinstock-Guttman, B., Benedict, R. H., & Jakimovski, D. (2023). Optical coherence tomography (OCT) measurements and cognitive performance in multiple sclerosis: a systematic review and meta-analysis. Journal of Neurology, 270(3), 1266-1285.

[12] Kaushik, Priyanka, and S. R. Nirmala. "Automated system for detection and classification of cystoid macular oedema using OCT images." Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization (2023): 1-15.

[13] Sztrigler-Cohen, O., Bromberger, N., Thee, Y., Lender, R., & Ben-Eli, H. (2023). Effect of Contact Lens Design on Objective Visual Acuity-Based Parameters in Pre-Presbyopic Patients in Photopic and Mesopic Lighting Conditions. Vision, 7(2), 46.

[14] Nguyen, V. S., & Nandakumar, S. (2023). Functional Ophthalmological Symptoms in Children and Adolescents. In Handbook of Mind/Body Integration in Child and Adolescent Development (pp. 205-216). Cham: Springer International Publishing.

[15] Kumar, Yogesh, and Surbhi Gupta. "Deep transfer learning approaches to predict glaucoma, cataract, choroidal neovascularization, diabetic macular edema, drusen and healthy eyes: an experimental review." Archives of Computational Methods in Engineering 30, no. 1 (2023): 521-541.

[16] Zhang, J., Zhang, J., Zhang, C., Zhang, J., Gu, L., Luo, D. and Qiu, Q., 2022. Diabetic macular edema: current understanding, molecular mechanisms and therapeutic implications. Cells, 11(21), p.3362.

[17] Dash, P., & Sigappi, A. N. (2022). Detection of DME in OCT Images Based on Histogram Descriptor. In Emerging Electronics and Automation: Select Proceedings of E2A 2021 (pp. 357-371). Singapore: Springer Nature Singapore.

[18] Srividya, K., and K. Lakshmi Joshitha. "A Survey on Detection of Diabetic Retinopathy Lesions Using Deep Learning." In 2022 International Conference on Communication, Computing and Internet of Things (IC3IoT), pp. 1-6. IEEE, 2022.

[19] Ma, Guangzhi, Jie Lu, Feng Liu, Zhen Fang, and Guangquan Zhang. "Multiclass classification with fuzzy-feature observations: Theory and algorithms." IEEE Transactions on Cybernetics (2022).

[20] Ikotun, A. M., Ezugwu, A. E., Abualigah, L., Abuhaija, B., & Heming, J. (2022). K-means clustering algorithms: A comprehensive review, variants analysis, and advances in the era of big data. Information Sciences.

