Review of Image Processing Techniques for Detection of Age-related Macoular Degeneration (ARMD)

Literature Review

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Abstract

Detection of retinal drusen is important in the diagnosis of Age-related Macular Degeneration (ARMD). Automated image processing has the potential to assist in the early detection of ARMD, by changing in blood vessels and pattern in retina. Age- related macular degeneration cause gradual loss of vision by oxidation of macula and can cause irreversible vision loss. The main goal of the proposed system is twofold at first it is used to diagnose the type of age-related macular degeneration either it is dry macular degeneration or wet macular degeneration, and then further helps to classify the stage of dry macular degeneration into early, intermediate, or advanced dry ARMD and to automatically detect and segment ARMD without human supervision.

Detection of ARMD is done by using Auto Associative Neural Network (AANN) method and the two classes of Age-related macular degeneration (dry or wet ARMD), one of which dry macular can be further classify into three classes, will be classify and diagnose successfully as future work.

Keywords: *Fundus Images, OCT Images, Drusen, Macular Degeneration, ARMD.*

INTRODUCTION

Age-related macular degeneration (ARMD) the leading cause of worldwide blindness in the elderly age is a bilateral ocular condition that affects the central area of retina known as the macula. Although the macula comprises only four percent of retinal area, it is responsible for the majority of useful photonic vision [1]. ARMD is the main cause of the elderly blindness in developed countries e.g. Australia, United Kingdom, and America. According to a survey approximately 17% of the participants were diagnosed with ARMD; further, more than 95% of these were aged 60 years and above [2]. In United States ARMD is also a growing public health problem, almost 11 million, or 7.6% of all Americans are estimated to have ARMD, and it is the cause of blindness for 54% of all legally blind Americans. ARMD is a major societal problem in terms of disability and health care costs. For example, severe ARMD reduces the likelihood of employment by 61% and salary by 39%, while mild ARMD reduces these by 44% and 32% respectively. The estimated annual cost burden from ARMD in the U.S. is $30 billion (USD) or about 0.3% of gross domestic product [3]. The occurrence of ARMD is expected to double over the next 25 years.

ARMD caused due to deposits of bright lesions called drusen. Drusen are formed at retinal level and could affect eyesight. Many researches have been done in the field of medical care. The diagnosis of ARMD is typically undertaken through the inspection of the macula (see Figure:1). Manual recognition and detection of drusen from retinal images is time consuming and expensive. Moreover, it is subjective and its reproducibility is a concern. To save workload and facilitate large-scale clinical use, it is important to have a precise, cost effective and efficient system to detect drusen automatically for ARMD diagnosis [4]. ARMD

Figure: 1 Fundus Image: showing normal retina (left) and intermediate ARMD affected retina (right)

is characterized by the appearance of sub retinal deposits termed drusen, as well as abnormalities of the retinal pigment epithelium (RPE) consisting of depigmentation and/or increased retinal pigment [5, 6, 7] see Figure: 2. Identifying and segmenting drusen on a retinal image is central in the classification of ARMD. Therefore, their measurements and quantification are important in research and various clinical studies. The size, density, and other characteristics of the drusen will determine the classification of the stage of the disease of serve as a basis for establishing more refined phenotype of ARMD [8]. Several algorithms have been proposed for detection and classification of ARMD from retinal images. Fundus and optical coherence topology (OCT) images with image processing techniques are used for automated detection of ARMD. Theme of this paper is to review different image processing techniques used in automated ARMD detection systems.

Automated or computer-assisted analysis of ARMD affected patients retina can help eye care specialists to screen larger populations of patients. ARMD can be classifies into two types; Dry macular degeneration can be characterized by thinning of the retina and drusen; small yellowish white deposits that form with in the retina (see Figure: 2 (left)). It results in slow, gradual progressive “dimming” of the central vision. Dry ARMD can be sub divided into further three categories e.g. early, intermediate, and advanced. Dry ARMD can change into wet ARMD at any stage and can be characterized by abnormal growth of new blood vessel under the retina called “neovascularisation” (see Figure: 3 (right)). Blood vessels are usually weak in their structure and prone to leak and be easily broken and bleed [19]. Even though a lots of work have been done in the field of automated Age-Related Macular Degeneration detection systems but ARMD prediction at an early stage still remains an open problem.

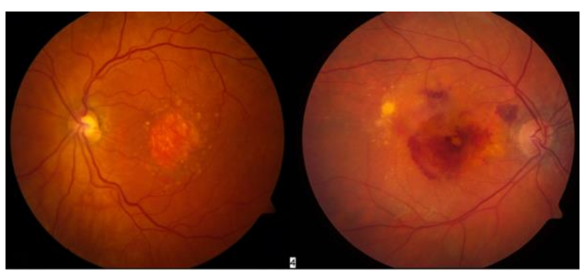


Figure: 2 Fundus Image: showing dry age-related macular degeneration (left) and neovascular age-related macular degeneration (right)

The rest of the paper is organized as follow: Section II consists on literature review of related work with an endeavor to analyze different image processing techniques used in computerized/automated ARMD detection system briefly, with the purpose of investigate their strengths, weaknesses and suitability according to detect different types of ARMD. Section III is comprised on illustration of generic automated ARMD detection process. In section IV an overview of proposed system has discussed. In last section V concluded remarks are discussed.

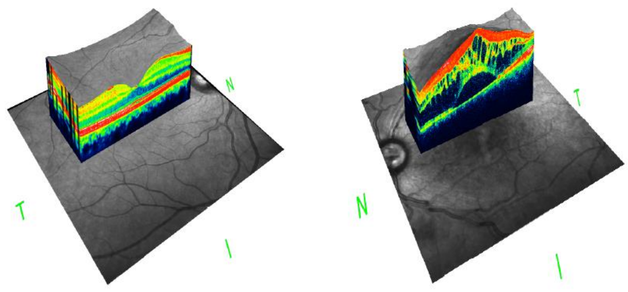
RELATED WORK

In [10] a drusen detection algorithm has been used on fundus images from 349 participants in the age-related eye disease study trial to quantitate drusen on digitized images and determined its precision and accuracy. The size, number, and area of the drusen in two macular regions were computed by readers using an interactive approach. Measurements were then compared with the data generated by reading center method. Comparison has shown similar results as generated by more labor intensive reading center technique but proposed algorithm is more sensitive and precise. To detect early causes of diabetic retinopathy, lesions like cotton wool spot, drusen and exudates must be detected and separated. Early diabetic retinopathy lesions may be classified as red lesions like hemorrhages and intra-retinal micro-vascular abnormalities and white lesions like exudates, lipoproteins which are caused due to fats in blood vessels. These lesions must be separated by distinctively from lesions related to ARMD called drusen. Neimeijer et al [11] in their studies found that drusen and exudates are similar in size whereas cotton wool spots are different. Moreover, exudates have sharper edges and drusen have comparatively soft edges. In spite of that separating drusen from rest of the objects in candidate region is a difficult task. A KNN classifier was used to detect and differentiate between lesions by selecting a threshold to segment classify them further. The method achieved an area under curve of 0.95. The specificity/sensitivity 0.88/0.95 for any kind of bright lesions present in the macula was also detected, whereas specificity/sensitivity 0.86/0.95 was for the detection of exudates, same 0.93/.70 was for cotton wool spots and 0.88/0.77 was for the drusen

A fuzzy logic approach in [12] for the segmentation of the drusen image has been used. In the presence of noise, regions' heterogeneity and low contrast, it is difficult to segment drusen images from candidate region. To accommodate this problem, a two step approach was used in this study. Proposed approach was applied to several angiographic retinal images. In first step optimal partitioning performed in which image was sub divided into three classes like image background, ambiguous regions (fuzzy regions), and already detected drusen classes. This was done to get the desired region where actual analysis has been performed to extract drusen from image. In second step application of fuzzy logic method to the intermediate (ambiguous) regions has been performed. After that an iterative process to analyze either the pixel belonged to drusen or background class. Histograms have been widely used to represent color distribution of an image, and can be effective representation for identifying objects in an image [13]. A histogram based approach in [14] has been used for drusen detection. At first image enhancement was done using multi-level equalization method. Different color bands were used to analyze the image during image enhancement process, since drusen can be extracted from background on the basis of morphology, yellowish color and brightness; it was observed that green band consist on more information about bright lesions than the other two bands (red and blue). Process of normalization has been performed then to remove irregular objects from the candidate region. For segmentation of drusen from background a histogram based local thresholding (HALT operator) have been used. Experimental results of 23 samples used; show specificity and sensitivity for all samples was more than 0.96 except one which had 0.86 because of presence of noise. For automated screening of retinal images three phases have been used in [15]: (1) image processing to filter unnecessary information presented in image, (II) histogram generation was used to translate retinal image into histogram representation, two suits then have been generated, first suit comprises histogram per image for all three colors (RGB) and second suit comprises histogram describing Hue, Saturation and Intensity (HSI) components for each retinal image. It has been noted that green and red channels have given a better visual contrast of drusen as compared to the blue channel. (III) Classification; a case-base, based on this histogram approach of pre-labeled (ARMD +ve and –ve) histograms has been used. A new retinal image has then classified to a histogram that has the best wrapping path. To analyze the effectiveness of using colored channel histogram and HSI histogram an experiment has been performed on144 hand labeled images, 86 of these images were AMD affected and the rest were normal images. HSI did better in term of classification accuracy with 74% recorded by the saturation component that shows the ability of HSI in identifying patterns through the colors of the image. Representative patterns of retinal images with and without drusen were extracted in the form of histogram. Labeled exemplar histograms were then stored in a case-base. Unseen examples were then classified by comparing with this case-base and analyzed for drusen using dynamic time wrapping comparison process.

D. Jayanthi et al [16], proposed a framework that help in diagnosing human retinal diseases using auto-associative neural network based classifier. The level of disease spread in the retina can be identified by extracting the texture based features of the retina. Different methods have been discussed with the purpose that these methods can be used to detect features, classify and diagnosing the type of retinal disease at an early stage. In [17] Independent Component Analysis (ICA) was used to extract features at different spatial scales to be used as input to a classifier. ICA minimizes the redundancy in the samples and obtains unique independent features, that represents the fundus image.ICA methodology founds to be used extensively for the purpose of extracting statistically independent features from audio and video signals and clinical electrophysiology [18]. For the identification and classification of two different types of ARMD (Dry and Wet ARMD) an automated approach using probabilistic neural network (PNN) classifier has been proposed in [19]. In [20] Y. Zheng et al have proposed a system to automatically assess the risk of the development of ARMD that incorporates learning based drusen detection and includes fundus image analysis techniques for image denoising, illumination correction, and color transfer. Validation of the system has been performed by comparing result produced by the proposed system with those obtained via manual drusen segmentation.

Fundus imaging is intricate by the fact that resulting imaging setup is technically challenging and historically involved comparatively expensive equipment and highly trained ophthalmic photographer. Many automated system have been proposed to make fundus imaging more accessible, resulting in less dependence on such experience and expertise. One of the advanced three dimensional imaging technologies called Optical Coherence Tomography introduced by Huang et al [9] makes use of low coherence light and ultra short laser pulses in order to perceive the spatial positions of tissues and resolve depth information. Acquisition of images (volumes) with very high resolution that can expose precise details of internal structures can be possible with the use of light waves. In the diagnosis of ARMD use of OCT technology is really helpful. ARMD damages the retina causing retinal pigment epithelium atrophy, detachment and other abnormalities e.g. drusen and fluid inside the retina [21]. OCT is so for the only imaging technique that has makes possible the cross-sectional details of the retina and choroid, where most of the ARMD signs can be clearly seen as shown in Figure: 3. there have been lots of researches performed with respect to macular diseases diagnosis using OCT images, but mainly focused on 2D image analysis. In [22] a method for automatically identify-



(a) A 3D OCT for a normal eye (b) A 3D OCT for an AMD eye

Figure:3 OCT images showing the difference between normal and ARMD retina.

-ing ARMD in 3D OCT images of the form shown in Figure: 3 have been proposed for ARMD detection. The novel element of the proposed method in the context of the image volume has to combine oriented gradient and local binary pattern histogram with a decomposition based method in order to generate an effective volumetric representation. All of the researches carried out to diagnose ARMD presence in retina; some of the automated systems further diagnose and classify ARMD into either dry macular degeneration or wet macular degeneration. Dry macular can be further classified into early, intermediate, and advanced stages. Dry ARMD can change into wet ARMD at any stage and can be characterized by abnormal growth of new blood vessel under the retina called "neovascularisation" also called wet macular that is more severe form of ARMD and can end up in complete loss of vision which is irreversible. Therefore, there is need of an automated system to further detect/classify different stages of dry ARMD to protect patients of dry ARMD from being more severe form of wet ARMD.

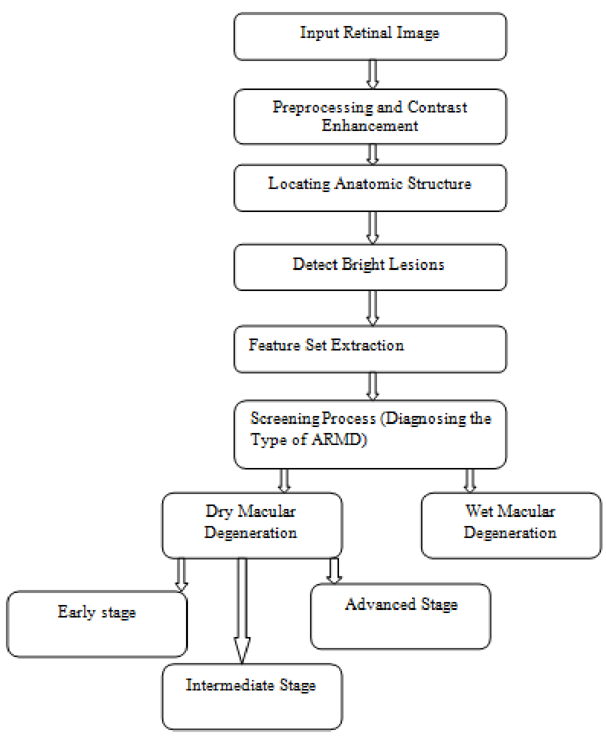


Figure: 4 Block diagram of the proposed system

Table 1: Comparative Analysis of Image Processing Techniques Used For Detection of ARMD

No.	Author	Year	Method	Features	Dataset	Performance
1	Thomas R. Friberg et al	2007	Histogram Based Adaptive Local Thresholding	Morphological Features (size, area, and number) of macular region	349 (IRIDEX Corporation, Mountain View, CA) fundus images	Precision/accuracy
2	Niemeijer et al.	2007	Machine Learning Algorithm (KNN Classifier)	Size	300 participants fundus images	Specificity (0.88%) /Sensitivity (0.77%)
3	P. Soliz et al	2008	Independent Component Analysis	Spatially and statistically Independent Components (ICs), pixel based features (intensity & color)	2500 fundus images	ICA replicated the ophthalmologist's visual classification by correctly assigning all images from two of the classes.
4	E.S. Barriga et al	2009	Amplitude Modulation Frequency Modulation (AM-FM Histogram) and partial least square., principle component analysis	Retinal Background, Vessels, Hard and Soft drusen	Wisconsin Fundus Photo Reading Center's website	100% Sensitivity/Specificity
5	M. Hanafi et al	2010	Histogram Based Approach (Dynamic Time Wrapping)	RGB channels and HSI	144 hand labeled images	Specificity of 62% (on the green channels) /Sensitivity 83% (on the blue channels) /Accuracy 69% (for blue channels)
6	D. Jayanthi et al	2010	Texture Features and Auto Associative Neural Network Based Classifier	Texture based shape analysis namely statistical and structural.	100 fundus images	True positive, true negative, false positive, false negative
7	R. Priya and Dr. P. Aruna	2011	Probabilistic Neural Network (PNN), Discrete Wavelet Transform (reversed biorthogonal wavelet), kirsch edge detection algorithm	Area, mean, standard deviation, Radius, perimeter, variance, entropy of preprocessed image	300 fundus images	Sensitivity/Specificity (94.0% / 95.0)
8	Y. Zheng et al	2013	Image denoising (with mom-linear means filter), retina mask generation (by image thresholding and hole filling with certain morphological operations), illumination correction, color transfer, Ada-Ls-SVM classifier (for pixel wise classification), LS-SVM (region wise classification)	Pixel wise classification (hue histogram and color histogram), region wise classification (region area, region average values of green and red channels, regional maximum brightness, border average, maximum, and minimum brightness values, border average brightness gradient, and border gradient's standard deviation)	CAPT study consisting of 50 stereoscopic color fundus images, and Amish study consisting 88 color fundus Photographs (CFP's)	Accuracy/ Specificity/Sensitivity :for CAPT CFP's 0.82,0.75,0.82), for Amish CFP's (0.86,0.71,0.85)
9	A. Albarrak et al	2013	Bayesian Network Classifier	Local histogram based feature vectors	140 volumetric OCT images(68 normal, 72 ARMD effected)	Area Under the Receiver Operating Curve (AUC) 94.4%, accuracy, sensitivity, specificity.

III.AUTOMATED ARMD DETECTION PROCESS

The main goal of the proposed system is twofold at first it is used to diagnose the type of age-related macular degeneration either it is dry or wet (non-neovascularisation or neovascularisation) macular degeneration, and then further helps to classify the stage of dry macular degeneration into early, intermediate, or advanced dry ARMD and to automatically detect and segment ARMD without human supervision.

There are five modules in the proposed system, they are as follow:

1) *Preprocessing and contrast enhancement*

Due to the nature of image acquisition, the quality of the required image is usually not good. In order to improve quality of retinal image preprocessing is performed to remove the noisy area from the retinal image. This is required for the reliable extraction of features and abnormalities as feature extraction and abnormality detection algorithms give poor results in the presence of noisy background. First, the green component is extracted from the colored retinal image. After the green component extraction, histogram equalization is used to enhance the contrast and improve the quality of the retinal image. Finally an-isotropic diffusion is applied to remove the noise from the image.

2) *Locating anatomic structure*

Since image would contain many other structures too like blood vessels based on segmentation of vascular arcades. Detection of the anatomic structure is the characterization of the normal or affected state that exists in retina. The algorithm is based on mathematical morphology and curvature evaluation for the detection of vessel like patterns in a noisy environment.

3) *Detect bright lesions*

vessels like patterns are bright features defines by morphological properties like linearity, connectivity, width, and by a specific Gaussian like profile whose curvatures varies smoothly along the vessels. Since drusen are bright lesion, therefore other dark regions are covered up using morphological closing so that bright regions get highlighted. Outcome of this process was a smooth image which contained candidate regions.

4) *Feature set extraction*

After applying preprocessing techniques like histogram equalization we obtain a better contrast image. Feature extraction can be done in two steps:

A. *Feature detecting optic nerve*

i. Vessel Density

Vessel density is defined as the number of vessels existing in a unit area of the retina. since the vasculature that feeds the retina enters the eye, the vessels tend to be most dense in this region.

ii. Average Vessel Thickness

Vessels are also observed to be thickest near the optic nerve since most branching of both the arterial and venous structure does not take place until the tree is more distal from the optic nerve.

B. *Feature detecting disease*

Some of the features that are extracted for detecting disease are given blow:

i. Area
ii. Radius
iii. Perimeter
iv. Mean
v. Standard Deviation
vi. Variance
vii. Entropy

The entropy is a statistical measure of randomness that can be used to characterize the textural feature of the input image..

5) *Screening\classification process*

Artificial neural network (ANN) has been used in different ways in medical field. The principle advantage of ANN is to generalize, adapting to signal distortion and noise without the loss of robustness [16]. Auto associative neural network have the same number of neurons in input and output layers and less in the hidden layers. The network is trained using the input vector itself as the desired output. Each auto associative network is trained independently for each class using feature vector of the class. The squared error between an input and the output is generally minimized by the network of the class to which the input pattern belongs. This property of AANN enables us to classify an unknown input pattern. The unknown pattern is fed to all the networks and is classified to the class with minimum squared error.

IV. CONCLOSION

This paper gives a survey of the classical and up-to-date image processing techniques in the field of ophthalmology for the diagnosis of age-related macular degeneration. Automated diagnosis of the retinal diseases is one of the most important tasks when dealing with a hug population, within less time and without human supervision. The proposed system is an attempt to provide a framework for the diagnosis of ARMD and further to classify different stages of dry ARMD. This paper provides a widespread reference source for the researchers involved in automatic diagnosis of fundus retinal images.

V.REFERENCES

[1] H. Kolb, The Organization of the Retina and Visual System, Part XII: Cell biology of retinal degenerration, Age-Related Macular Degeneration (ARMD) by Gregory S. Hageman, 2012.

[2] D. Nitsch, I. Douglas, L. Smeeth, , and A. Fletcher "Age-Related macular Degeneration and Complement Activation-relatedDiseases", *Journal of Ophthalmology* **115**(11), pp 1904-1910, 2008.

[3] Brown MM, "Age-related macular degeneration: economicburden and value-based medicine analysis", Can J Ophthalmol 40, pp. 277-287. 2005.

[4] J. Cheng and et al, " Early Age-Related Macular Degenration Detection by Focal Biologically Inspired Feature", In Proceding of ICIP 2012 IEEE, pp. 2805-2808, 2012.

[5] Bressler NM and et al, "Five-year incidence anddisappearance of drusen and retinal pigment epithelial abnormalities." Waterman study Arch Ophthalmol 113, pp.301-308, 1995.

[6] Abdelsalam A, and et al, "Drusen in agerelated macular degeneration: pathogenesis, natural course, and laser photocoagulation-induced regression", Survey Ophthalmol 44,pp.1-29, 1999.

[7] Bressler NM, and et al, "Drusen characteristics in patients with exudative versus non-exudative age-related macular degeneration" Retina 8,pp.109-114, 1998.

[8] E.S. Barriga et al, " Multi-Scale AM-FM for Lesion Phenotyping on Age-Related Macular Degeneration", In Proceedings of IEEE, 2009.

[9] D. Huang et al, "Optical Cohernce Tomography", *Science,* vol.254(5035), pp. 1178-1181, 1999.

[10] R. Friberg et all, "Computerized Detection and Measurement of Drusen in Age-Related Macular Degeneration", Ophthalmic Surgery, Laser & Imaging, vol 38(2), pp. 126-134, 2007.

[11] Niemeijer et al, "Automated Detection and Differentiation of Drusen, Exudates, and Cotton-Wool Spoot in Digital Color Fundus Photgraphs for diabetic Retinopathy Diagnosis", *Investigative Opthamamology & Visual Science*, Vol. 48(5), pp. 2260-2267, 2007.

[12] A. Thaibaoui et al, " A Fuzzy Logic Approach to Drusen Detection in Retinal Angiographic Images", In proceedings of 5th IEEE International Conference on Pattern Recoginition, pp. 748-751, 2000.

[13] M. J. Swain, D. H. Ballard, " Color Indexing", *International Journal of Computer Vision,* vol. 7(1), pp. 11-32,1991.

[14] K. Rapantzikos et al, "Dtection and Segmentation of Drusen Deposits in Human Retina: A Potential in the Diagnosis of Age-Related Maccula Degeneration", Medical Image Analysis, pp. 95-108,2003.

[15] M. Hanafi et al, " A Histogram Approach for the Screening of Age-Related Macular Degeneration" , In proceeding of International Joint Conference on Neural Networks , pp. 1-7, 2010.

[16] D. Jayanthi et al, "Automatic Diagnosis of Retinal Diseases from Color Retinal Images", *Internation Journal of Computer Science and Information Security*, vol. 7(1), pp.234-238, 2010.

[17] P. Soliz et al, "Independent Component Analysis for Vision-Inspired Classification of Retinal Images with Age-Related Macular Degeneration", In Proceedings of SSIAS IEEE, 2008.

[18] E.S. Barriga et al, "Spatiotemporal Independent Component Analysis for the Detection of Functional Responses in Cat Retinal Images", IEEE Transactions on Medical Imaging, vol. 26, pp. 1035-1045, 2007.

[19] R. Priya, Dr. P. Aruna, "Automated Diagnosis of Age-Related Maculer Degeneration", IEEE, pp. 227-230.2011.

[20] Y. Zheng et al, "An Automated Drusen Detection System for Classifying Age-Related Macular Degeneration with Color Fundus Photographs", In processdings of IEEE 10th International Symposium on Miomedical Imaging, pp. 1440-1443,2013.

[21] R. D. Jager, W. F. Mieler, J. W. Miller, “ Age –Related Maculer Degeneration”, *New England Journal of Medicine*, vol.358(24), pp.2606-2617, 2008.
[22] A. Albarrak et al, “Age-Related Macular Degeneration Identification in Volmetric Optical Coherence Tomography using Decomposition and Local Feature Extraction”, AMD IDENTIFICATION IN 3D OCT, pp. 1-6, 2013

BIOGRAPHY

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