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Ophthalmic Image Generation using GAN for Branch Retinal Vein Occlusions and Laser Spots

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Abstract: This research paper presents a novel methodology for generating ophthalmic images depicting Laser Spots and Branch Retinal Vein Occlusions via the application of Generative Adversarial Networks (GANs). The study's dataset includes images of both Laser Spots and Branch Retinal Vein Occlusions. Prior to GAN model training, the images undergo essential preprocessing steps, involving uniform resizing, and pixel value standardization. The GAN architecture is designed with a generator network and a discriminator network, operating collaboratively to yield images similar to the input samples and appraise their quality, respectively. After preparing the dataset of ophthalmic images, the generator and discriminator network were employed to construct the GAN model. After the model is trained, the generator network is effectively employed to synthesize new ophthalmic images of Laser Spots and Branch Retinal Vein Occlusions. The generated images were evaluated using various metrics such as visual inspection, quantitative analysis, and comparison with existing images. The experimental outcomes demonstrate that the GAN model successfully generates superior-quality ophthalmic images of Laser Spots and Branch Retinal Vein Occlusions, closely resembling the attributes of the input images. The evaluation of Fréchet Inception Distance (FID) scores demonstrates the promising quality of GAN-generated images. The generated images can potentially be used for diagnostic, educational, and research purposes.

Keywords: *Adversarial networks, Branch Retinal Vein Occlusions, Laser Spots, GANs, Generative Adversarial Networks, Ophthalmic images*

1. Introduction

Medical image generation is an emerging field that has received considerable recognition recently. High-quality medical images are critical in the analysis, treatment, and monitoring of a varied array of medical problems. To tackle this difficulty, researchers have investigated the engagement of Generative Adversarial Networks (GANs) [1], for medical image generation.

GANs entail two distinctive elements: a generator network and a discriminator network, making them a unique type of deep learning model. The generator network is tasked with learning how to produce images that closely resemble the input images, while the discriminator network examines the authenticity of the produced images. They have displayed promising results in creating high-quality medical images using techniques including magnetic resonance imaging (MRI) [2], computed tomography (CT), and ophthalmic imaging.

Ophthalmic images are a crucial part of detecting, treating, and observing the progression of various eye conditions. However, the availability of high-quality ophthalmic images is often limited due to various reasons such as privacy of patients, availability of equipment and higher costs [3]. The field of generating these images is gaining interest and researchers are investigating the use of artificial intelligence tools, notably GANs, to attain this goal. In this study, the methodology for generating ophthalmic images of two eye conditions, Laser Spots [4] and Branch Retinal Vein Occlusions [5], using GANs is presented. Branch Retinal Vein Occlusion (BRVO) is characterized by the obstruction of a retinal vein, leading to localized swelling and impaired blood flow in the retina. Laser Spots (LS) occur due to retinal laser treatment, resulting in scars and marks on the retina, affecting visual assessment and diagnosis.

Regarding synthetic imaging, GANs have the ability to learn from a collection of images related to a specific eye disorder and produce novel images that are highly similar to the original ones [6]. For instance, generated images can be used to train medical professionals, develop new diagnostic tools, and assess the performance of existing tools. This study demonstrates the effectiveness of GANs in generating ophthalmic images of specific eye conditions and gives an avenue for generating new images that can assist medical professionals in improving their skills and knowledge.

Section 2 of the document prepares a summary of the relevant studies that have been performed in this domain, while section 3 explains the approach utilized. The research

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results and ensuing discussions are described in section 4. Ultimately, section 5 summarizes the findings and suggests potential areas for future research in this field.

2. Related Work

In modern years, GANs have emerged as a powerful tool in various domains, especially where acquiring large amounts of labeled data is challenging and costly. This is particularly apparent in fields like medical imaging and art generation. The versatility and potential of GANs have led to numerous modifications and variations of the original GAN framework. These advancements have significantly expanded the capabilities of GANs, making them even more promising for various practical applications.

For deep learning applications that require larger datasets, GAN based data extension gain importance, predominantly for images. A. Creswell et al. [7] explore the training and applications of GANs, then discuss some of the challenges and future directions in this field. Different architectures including Convolutional GANs, Conditional GANs and GANs with inference models are also discussed as covered in previous work. The paper also provides a comprehensive overview, starting with the GAN training process and the motivation to generate realistic data samples for various applications. S. Kumar et al. [8] cover the basic architecture of GANs, and how they are trained concurrently in a game-like setting in their paper. Modifications to the basic architecture, loss functions used in GANs, challenges associated with training GANs, and techniques for overcoming them are also analyzed. They specifically discuss Vanilla GAN, DCGAN, Wasserstein GAN, Least Square GAN etc. Beyond image generation, GANs excel in various CV applications, including image transformation to image, super-resolution, and inpainting of images. In [9], two datasets, MNIST and Fashion-MNIST are used for generating multiple images using different GAN models. Qualitative and quantitative evaluations are done, and FID indicators are calculated. Methods for generating better GAN are also explored. By leveraging the power of GANs in countless tasks, researchers have been able to overcome challenges that previously hindered conventional machine learning approaches.

C. Li et al. [10] present a novel technique, TT-GAN, which addresses the issue of using GANs in Natural Language Processing. TT-GAN generates authentic text, paraphrases, and semantic summaries by utilizing the semantic information of the source text. GAN-based methods can be used to contribute to port container handling by identifying container codes using deep learning networks [11]. This method can generate synthetic container code images that closely resemble real images for creating a new training set. C-Self Attention GAN (C-SAGAN) models are trained for 100,000 iterations to generate these codes. The future scope of this paper includes the differentiation of similar characters. Several typical GAN improvement models, including their theoretical advances, features, disadvantages, application areas, and implementation costs are discussed in [12].

The MI-GAN model proposed in [13] can learn from a small training set and produce an unlimited quantity of synthetic images, with explicit focus on retinal images. The model offers advantages such as a reduced number of false positives and shorter training time, based on limited training data from the STARE and DRIVE datasets. This version had an F1-score of 0.832 on DRIVE and 0.837 on STARE. W. Ahmed et al. [14] discuss the need for high-resolution medical images for accurate diagnoses but acknowledges the cost and difficulty of acquiring such images. The paper presents a novel architecture based on GAN which utilizes a multi-path approach for extracting shallow features, a ResNet34 architecture for deep feature extraction, and a mini-CNN with residual connections for extracting features of the upscaled image version.

Deep learning-based GAN models were also used to fabricate artificial data for brain tumor imaging [15]. Noise or image-based image generation GANs can also be developed for brain MRI increase [16] to improve tumor recognition. Mohamed et al. [17] introduce a novel GAN architecture for augmenting chest X-rays. to increase pneumonia and COVID-19 classification accuracy. In [18], the practicality of utilizing GAN for synthetic data augmentation is exhibited through the application of Radiographs capturing Waters' view in individuals diagnosed with chronic sinusitis. The suggested method achieves notably improved diagnostic performance metrics compared to models trained through conventional data augmentation.

GANs are also applied in generating ophthalmic image datasets. A. You et al. [19] conducted a survey of peer-reviewed papers published before 2021 that used GAN and presented a comprehensive overview of the different relevance of GAN in ophthalmology image domains, covering 48 studies. They provide detailed descriptions of the numerous GAN architectures used for each task and summarize the results achieved in recent studies. Optical coherence tomography (OCT) image generation can possibly enhance the identification of age-related macular degeneration (AMD) as well [20]. An unsupervised GAN was trained to create high-resolution OCT images from images with low resolution that can be employed to improve the visibility of retinal features and the accuracy of diagnosis.

Y. Zhou et al. [21] introduce a GAN model that can create diverse DR data with varying scoring levels. The resulting synthetic images can aid in training a grading model. EyePACS and FGADR datasets are utilized for this objective. Examining the retina with a fundus camera through cataracts can be a fault-prone operation due to the reduced image quality. An algorithm to clarify images to aid in identification by specialists or machines is suggested in [22]. W. Fuhl et al. [23] have successfully applied GANs for pupil and eyelid segmentation, data generation, achieving advanced results and improving the results of existing algorithms. The study by Yoo et al. [24] aimed to develop a GAN approach to predict post-operative development after orbital decompression surgery for thyroid eye disease (TED). The authors collected pre- and postoperative computed tomography (CT) images from 72 patients who underwent surgery for TED. A. Diaz-Pinto et al. [25] utilize retinal image synthesis and semi-supervised learning for the evaluation of glaucoma. The classification was done on a dataset augmented with new images generated by GANs. There is a need to focus on careful validation and ethical considerations when utilizing synthetic retinal images in ophthalmology. J. Chen et al. [26] suggest that the potential benefits of using synthetic images may outweigh the risks but further study is required to fully evaluate the validity of this approach. They employed Pix2Pix HD, a high-resolution GAN to generate eight hundred eighty images of fundus images. Evaluation of these images was performed using a Fisher exact test. Examining the difficulties encountered by GANs and envisioning the prospective pathways for their development are important in the current scenario. [27] provides a comprehensive overview of GAN models, covering key areas. It starts by explaining the fundamental principles and training processes of GANs. Furthermore, the paper explores the benefits and applications of GAN models in medical image fusion, highlighting advantages in three key aspects. It also delves into the primary challenges faced by GANs and their specific challenges within the medical image fusion domain.

While the use of GANs for medical image generation has shown promising results there is a notable research gap concerning the evaluation of the generated images. There is a lack of comprehensive studies that rigorously assess the accuracy and authenticity of the generated images. The existing literature predominantly focuses on the technical aspects of GAN-based image generation demonstrating their competence to produce images that resemble real medical images. However, most studies fall short in providing robust validation metrics and comparative analyses involving the created images and original patient data. The absence of such thorough validation can hinder the clinical application and adoption of these generated images in real-world situations. AI autonomy in medical image analysis is an important field for consideration [28]. One major challenge faced is the absence of well-balanced annotated medical image data along with the presence of noisy image data from patients affecting deep neural networks. This paper through the creation of better quality, annotated ophthalmic images aims to contribute to the resolution of these issues.

Research specifically addressing the distinctive challenges posed by BRVO and Laser Spots is currently limited. These conditions are clinically significant and can have severe implications on a patient's vision and overall eye health. Addressing this research gap is crucial as BRVO and LS require timely and accurate diagnosis. The development of a GAN-based methodology to generate realistic and diverse ophthalmic images of these conditions could significantly contribute to the advancement of medical imaging technologies.

3. Methodology

The methodology for creating a GAN involves a series of vital steps as depicted in Fig. 1. The initial step is the gathering of data, where representative dataset of the target images is gathered. Next comes data preprocessing, where the collected images are standardized, resized, and converted into a suitable format to facilitate model training.

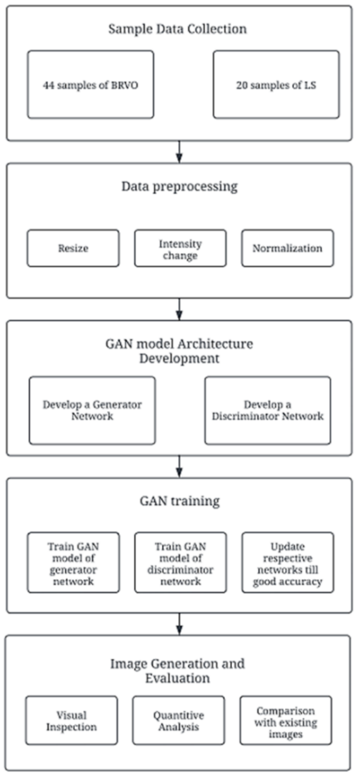


Fig. 1. Block Schematic for Generative Adversarial Networks

The third step involves the development of the GAN model architecture. This involves designing the generator network responsible for generating synthetic images and the discriminator network tasked with distinguishing between real and generated images. Careful consideration is given to the model's hyperparameters and architecture to optimize its performance.

Following the architecture development, the GAN training phase commences. The two networks engage in an adversarial learning process, where the generator attempts to yield increasingly truthful images, and the discriminator continually refines its capability to differentiate between real and synthetic images. The training process involves iterative updates to the model's parameters to enhance its performance.

After the GAN model is trained, the succeeding step is image generation. The generator network is employed to generate new synthetic images, which closely resemble the characteristics of the original dataset. Lastly, the evaluation stage assesses the quality and fidelity of the generated images. Various metrics are used, such as visual inspection, quantitative analysis, and comparison with real images. The evaluation process helps to gauge the success of the GAN model in generating authentic and high-quality images.

3.1. Dataset Collection

The study's dataset encompasses 20 samples of Laser Spots and 44 samples of Branch Retinal Vein Occlusions. Original dataset images of Branch Retinal Vein Occlusion (BRVO) are displayed in Fig. 2, while images of Laser Spots (LS) are showcased in Fig. 3.

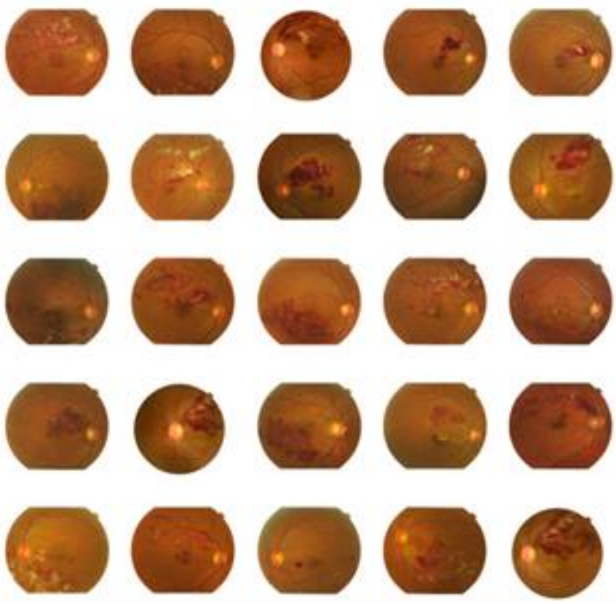


Fig. 2. Branch Retinal Veins Occlusion sample images

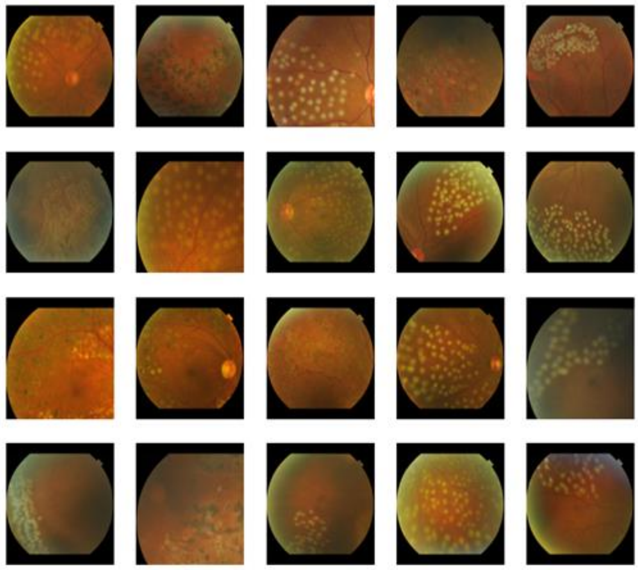


Fig. 3. Laser Spots sample images

3.2. Data pre-processing

Initially, the Branch Retinal Vein Occlusions dataset has a total of 44 images and the Laser Spots dataset has 20 images. However, these images, even those belonging to the same class differ in dimensions. The images in the original dataset had an approximate width of 3046 pixels and a height of 2572 pixels. These dimensions were adjusted by cropping to a width of 128 pixels and a height of 128 pixels. The cropping of rectangles from the images was performed using the (0, difference, original width, original height - diff) coordinates. Here, the difference was calculated using (1).

$$Difference = (original\ height - original\ width) // 2 \quad (1)$$

Therefore, the images were first cropped to a common dimension. The program iterates over the image files in the original directory. For each image, it crops and resizes it to the desired output dimensions. Finally, the processed images are normalized to scale the pixel values between 0 and 1.

3.3. GAN model architecture development

The GAN model architecture consists of two main components: a generator network and a discriminator network, engaged in an adversarial training process; refer to Fig. 4 for visualization.

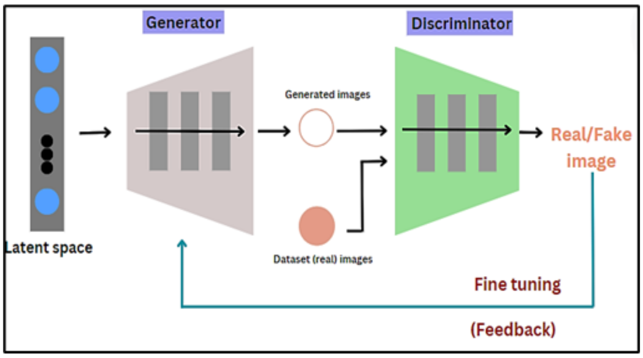


Fig. 4. GAN architecture block diagram

3.3.1. Generator Network

The program defines a generator network using the Keras API. The generator network architecture consists of several layers to transform a random input noise vector into a realistic image. The first layer of the network is therefore a Input layer which considers a random noise vector as input. The generator takes a latent dimension vector as input, and then the vector is fed into a dense layer to increase its dimensions. A LeakyReLU activation function is applied to the dense layer output to introduce nonlinearity and prevent the function from becoming saturated at zero. Subsequently, the tensor is passed through a series of convolutional and transpose convolutional layers to up sample the input and produce higher resolution images. Finally, a convolutional layer with a Tanh activation function is applied to the output to generate an image with values between -1 and 1.

3.3.2. Discriminator Network

The discriminator is specifically designed to differentiate between authentic and synthetic images. The input to the discriminator is an image tensor of size (height, width, channels). The discriminator starts with a series of convolutional layers with a LeakyReLU activation function, which introduces non-linearity into the model. After the convolutional layers, the output is flattened and passed through a dropout layer. This is followed by a fully connected dense layer and a sigmoid activation function. Finally, the discriminator is compiled using the RMSprop optimizer. The loss function used is binary cross-entropy.

3.4. GAN training

Algorithm 1 describes the steps for training the GAN network and saving the images generated. The training is done in a manner where a balance point can be reached between the two constituent networks. The utility of the generator is to produce an image from the noise vector that is as close to the real dataset image as possible. The utility of the discriminator is to closely identify the variation between the real and generated image. The final objective is to tune both the generator and discriminator to give the most optimum results.

Algorithm 1: GAN Training and Image Saving

Input: Random latent vectors

Output: Images similar to original dataset

```
1. Start
2. start = 0, d_losses = [], a_losses = [], images_saved = 0
3. For training step □ (iters) do
4.      Generate random latent vectors.
5.      Generate fake images
6.      Select batch of real images from dataset.
7.      Combine generated and real images
8.      Create labels for the combined images
9.      Train the discriminator.
10.            d_losses.append(d_loss)
11.            Generate new latent vectors
12.                   Create misleading targets for generator.
13.            Train GAN
14.            a_losses. append(a_loss)
15.            If real images == used begin
16.               start = 0
17.            end if
18.            If current_step%500==0 begin:
19.               save(weights)
20.            end if
21.            Generate control_generated images
22.        End For
23.        End of Algorithm
```

The latent vector which served as input had dimensions (16, 32) where 16 was the batch size and 32 was the latent dimension, the channel size was set to 3.

4. Results

Eye diseases represent a diverse group of conditions affecting the visual system including glaucoma, cataracts, and macular degeneration. An example of such a medical condition is BRVO, which stands for Branch Retinal Vein Occlusion. BRVO is a disorder characterized by the blockage of one of the retinal veins. The occlusion results in the disturbance of regular blood flow causing fluid to accumulate in the affected retinal region. As a result, the retina experiences localized swelling, leading to impaired vision. Risk factors for BRVO include age, hypertension, diabetes, and a history of vascular diseases. Timely diagnosis and appropriate management of BRVO are essential to prevent potential complications and preserve visual function.

Laser spots form on the retina due to retinal laser treatment used to manage diabetic retinopathy (DR). Photocoagulation or laser treatment is employed to slow down the progression of the disease by sealing leaky blood vessels.

Throughout the laser treatment, minor burns are induced in the region of the retina with anomalous blood vessels, effectively arresting the flow of blood and fluids. As a result, the retina bears scars and markings, manifesting as either compact, circular spots or extensive, asymmetrical marks in retinal images. The presence of laser marks on retinal images can pose challenges to the assessment and diagnosis of diabetic retinopathy.

These conditions can arise due to genetic factors, aging, environmental influences or a combination of these factors. The impact of eye diseases on an individual's overall well-being is significant, emphasizing the importance of early detection, accurate diagnosis, and timely intervention.

GANs can provide synthetic pictures that can be utilized to supplement the training data and enhance the effectiveness of computer-aided diagnosis systems when it comes to the development of ophthalmic images. The GAN model here was trained on a dataset of ophthalmic pictures confining instances of Laser Spots and Branch Retinal Vein Occlusions. The objective was to generate ophthalmic images depicting these specific disorders. Following the training process, the GAN model successfully produced new images that closely resemble the input images of these disorders. In the beginning, the images produced by the GAN model display a degree of indistinctness and absence of sharpness when contrasted with the images present in the initial data set, as depicted in Fig. 5 and Fig. 6. The GAN was trained for a total of 15,000 epochs, and the notable enhancement in generating images was observed prominently after approximately 4000 epochs. This extended training duration allowed for a discernible transition from generating random images to producing coherent and authentic representations that closely resembled the target image distribution. However, as the GAN model continues to learn and refine its generation process through training, it progressively improves its ability to produce more precise and focused images.

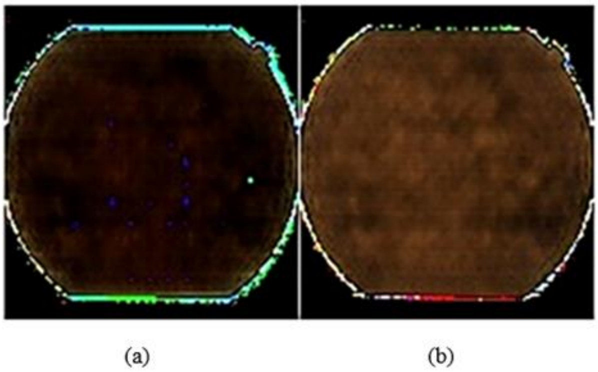


Fig. 5. Images generated Branch Retinal Veins Occlusion: (a) after 300 epochs, (b) after 1500 epochs.

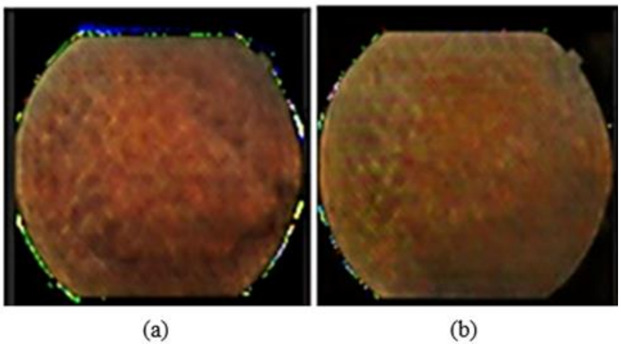


Fig. 6. Images generated Laser Spots: (a) after 300 epochs, (b) after 1500 epochs.

Over time, the GAN model refines its understanding of the features and patterns associated with the specific diseases, resulting in generated images that closely resemble the characteristics and details present in the original dataset. This iterative improvement throughout the training progression ensures that the GAN model eventually generates images that are increasingly faithful to the input images of these ophthalmic disorders as shown in Fig.7, Fig.8.

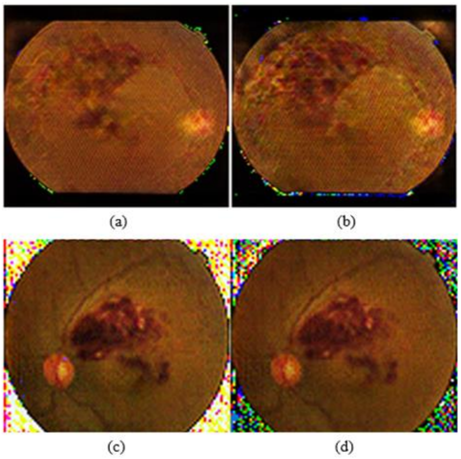
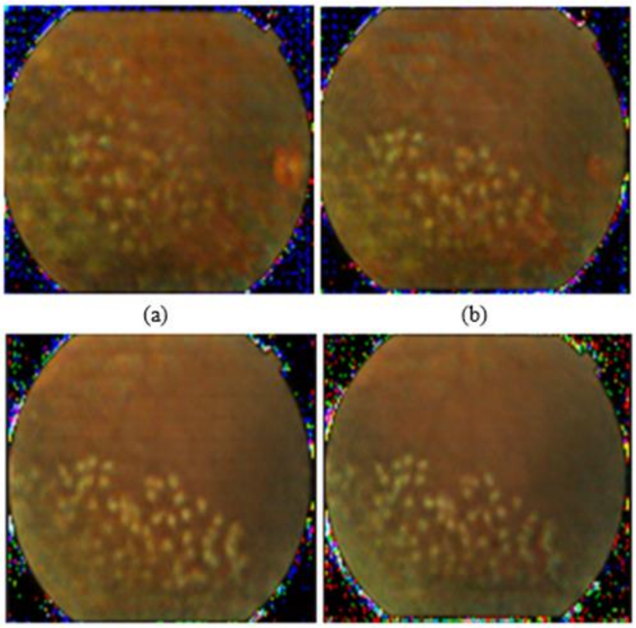


Fig. 7. Ophthalmic images generated for Branch Retinal Veins Occlusion: (a) after 4000 epochs, (b) after 5500 epochs, (c) after 7000 epochs, (d) after 8000 epochs.



(a) (b) (c) (d)

Fig. 8. Ophthalmic images generated for Laser Spots: (a) after 4000 epochs, (b) after 5500 epochs, (c) after 7000 epochs, (d) after 8000 epochs.

Validation of the generated images is the next step. Initially, visual inspection was performed, comparing images of the original dataset and those synthetically generated. Authors performed visual inspection and based on reference images the images found to exhibit the patterns of the fundus image disorders. Further, the FID score metric was calculated for the images.

The FID score or Fréchet Inception Distance is a common metric utilized to evaluate the quality of GAN generated images. It quantifies the likeness between the distributions of genuine and generated (synthetic) images by analyzing attributes extracted from an InceptionV3 model. The algorithm for calculating the Fréchet Inception Distance is mentioned in Algorithm 2.

Algorithm 2: Fréchet Inception Distance

Input: Real images, Generated images

Output: FID score

1. Start

2. Load and preprocess the InceptionV3 model, pretrained on ImageNet, for feature extraction.

3. Calculate activations for real and generated images using the InceptionV3 model.

4. Calculate the mean (mu_real, mu_generated) and covariance (sigma_real, sigma_generated) statistics for the activations of real and generated images, respectively.

5. ssdiff = sum((mu_real - mu_generated)**2.0)

6. covmean=sqrtm(sigma_real.dot(sigma_generated))

7. if iscomplexobj(covmean) begin

covmean = covmean.real

end if

8. fid = ssdiff + trace(sigma_real + sigma_generated - 2.0 * covmean)

9. End of Algorithm

A minimal FID score suggests that the generated images exhibit greater similarity to the real images in relation to their statistical characteristics. On the other hand, a higher FID score is indicative of poorer quality images being generated by the GAN. While the FID value itself does not provide specific insights into the quality or shortcomings of the generative model, it can be used as a relative measure to compare different models or training settings.

The FID score for real and generated (synthetic) images of the BRVO class is 158.625 as depicted in Table 1. The FID score for real and generated (synthetic) images of the Laser Spots class is 217.158 as depicted. The FID scores achieved align well with those from [29], where a FID score of 220.43 was reported for 3000 generated images using the LiWGAN architecture.

Table 1. Fréchet Inception Distance

FID SCORE	BRVO	LS
Real and Real images	-0.00	-1.06404e-05
Real and Generated Images	158.625	217.158

To further validate the generated images, a classification model was created, classifying images as Real or Fake (synthetically generated images). The Real class consisted of images belonging to the original dataset of BRVO or LS respectively. The Fake class consisted of synthetically generated images from the GAN training process in between 0 to 2000 epochs, with higher amounts of noise as depicted in Fig. 9., Fig. 10.

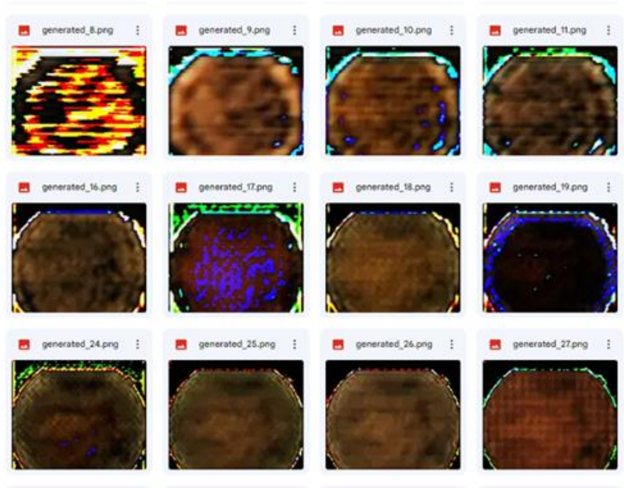


Fig. 9. Images belonging to Fake class – Branch Retinal Veins Occlusion

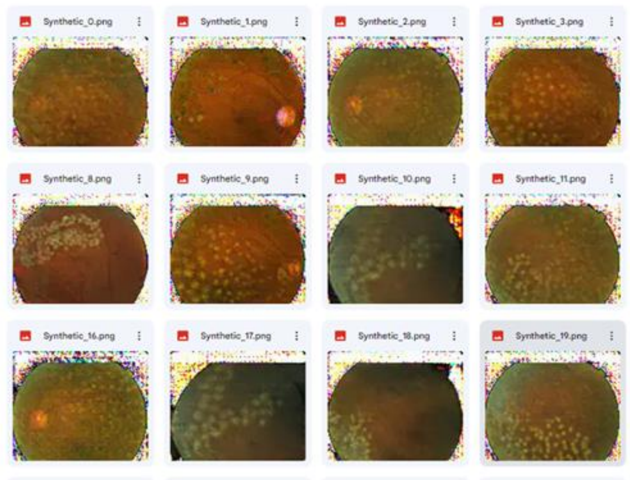


Fig. 10. Images belonging to Fake class – Laser Spots.

The classification model achieved an accuracy of 95.83% for BRVO and 91% for LS. Validation is performed by predicting the class of 10 synthetic images passed to the model. Of the 10 images passed, 8 of the synthetically generated images are classified as belonging to the "Real" class. This result indicates that the model is having difficulty distinguishing between the synthetic/generated images and the images from the authentic dataset. When the model has trouble recognizing actual and synthetic images, it indicates that the generator has produced realistic images.

5. Conclusion

In conclusion, the Generative Adversarial Network (GAN) model has emerged as a transformative tool for image generation in the context of Branch Retinal Vein Occlusion (BRVO) and Laser spots. The unique architecture of GANs, with its generator and discriminator networks, has enabled the synthesis of highly realistic ophthalmic images. Through the integration of medical image data and GAN training, the model has showcased its potential in producing novel ophthalmic images that closely resemble real-world pathology and laser-induced effects. The FID score evaluation confirms the promising quality of GAN-generated images.

The GAN's ability to address challenges associated with data scarcity and the generation of diverse image variations has been invaluable in advancing research in ophthalmology. These synthetic images can serve as valuable tools for diagnostic training, educational purposes, and even enhancing the interpretation of medical images by healthcare professionals.

The ongoing research is necessary to ensure the GAN model's stability during training and to further refine the generated images' accuracy. Ethical considerations are also vital, particularly in the medical domain, where the reliable interpretation of real and synthetic images is crucial for patient care.

Looking forward, the continuous refinement and responsible use of GAN technology hold promise for advancing medical imaging and diagnosis in ophthalmology. The performance of computer-aided diagnostic systems may be enhanced by creating ophthalmic images on a T4 GPU utilizing GANs for the mentioned diseases. Collaborative efforts between researchers, clinicians, and AI experts will drive the innovation needed to fully harness the potential of GANs. As the field progresses, it is essential to maintain a vigilant and ethical approach to ensure the safe and beneficial integration of GAN-generated images into clinical practice.

Conflicts of interest

The authors declare no conflicts of interest.

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