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Revolutionizing eye disease diagnosis with deep learning and machine learning

Adamopoulou M*, Makrynioti D, Gklistis G and Koutsojannis C

Laboratory of Health Physics & Computational Intelligence, Department of Physiotherapy (incl Optics& Optometry Dep), School of Rehabilitation Sciences, University of Patras, Patras, Greece.

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Abstract

Ocular medical imaging analysis has been transformed by the recent developments in Deep Learning and Machine Learning. These techniques have made it possible to uncover more detailed information about the eyes which ophthalmologists can utilize in their diagnoses. In this article we will discuss how artificial intelligence applications are helping improve ocular medical imaging. The use of AI technologies has led to a substantial increase in accuracy and efficiency when analyzing eye diseases. By staying up to date on the latest advancements in this field healthcare professionals and researchers can ensure that they are providing their patients with the most effective diagnoses and treatments available. This article provides essential insights into how AI powered methods are changing the face of ocular medical imaging making it an essential read for anyone invested in improving healthcare outcomes in this area.

Keywords: Deep Learning; Machine Learning; Ocular medical imaging analysis; Artificial intelligence techniques; Eye diseases

1. Introduction

The human eye is a miraculous biological structure made mostly of proteins and water with the lens playing an essential role in focusing light on our retinas. However, this mechanism is susceptible to cataracts leading to severe vision impairment or even blindness if left untreated (Ahmad et al., 2018; Reiter et al., 2021). Eye diseases cause nearly half of all developed countries' blindness cases underlining the importance of ophthalmologists having proficient ocular imaging techniques. This allows them to detect potential eye damage adequately and make accurate differential diagnoses resulting in optimal treatment choices that enhance patients' wellbeing. Ophthalmologists have long been interested in fundus images since they provide precise analyses of blood vessel network anatomy and optic disc structures - crucial components in evaluating eye health. Our understanding of the human eye has dramatically improved due to technological advances like Deep Learning and Machine Learning. The knowledge gained from these tools has proven invaluable when it comes to grading assessments aimed at diagnosing issues related to ocular health. Notably this newfound information provides specialists with an enhanced comprehension of how the eye functions. Consequently, thanks to improvements in ocular imaging techniques combined with deep learning and machine learning applications ophthalmologists can now accurately identify disorders that may impact visual ability (Tong et al., 2020; Gu et al., 2020).

For this academic work our goal was to offer readers a comprehensive overview of recent advancements in Deep Learning and Machine Learning within the field of ocular medical imaging analysis. To compile all relevant information needed for this research process we searched through PubMed using particular keywords like "deep learning " "convolutional neural networks," "medical imaging," and "eye diseases." Inclusion criteria called for selected studies to specifically employ ocular imaging alongside artificial intelligence techniques while excluding others that didn't meet these parameters. To emphasize essential findings throughout the report emphasis was placed solely on key outcomes

*Corresponding author: Adamopoulou M

from recurring articles related to the topic at hand. The article structure is concise yet thorough by introducing primary artificial intelligence techniques such as Deep Learning and Machine Learning extensively used for analyzing ocular images today with following sections highlighting principal studies focused on diagnosing & treating eye diseases utilizing those methods along with impressive results achieved thus far through AI applications within ocular medical imagery analysis. Ocular medical imaging has made significant strides thanks to the innovative application of artificial intelligence techniques. Professionals and researchers alike will benefit from this insightful article, which showcases the impressive impact that Deep Learning and Machine Learning have already made as well as their promising future potential.

2. State-of-the-Art

The discussed literature can be divided into three essential segments, focusing on the increasing utilization of Artificial Intelligence (AI) within the realm of medical imaging. The first area delves into AI's role in demarcating anatomical features and evaluating image quality, which involves the use of AI algorithms to precisely distinguish and segregate specific elements in medical images, as well as assess their quality. The second segment scrutinizes AI's application in detecting irregularities and diseases, as the demand for precise and dependable diagnostic techniques grows, making AI's implementation in this sphere increasingly popular. AI algorithms' capacity to process vast quantities of data and recognize patterns and abnormalities renders them a valuable resource for identifying numerous diseases and conditions.

The third and final group of studies examines AI's incorporation in a variety of eye imaging techniques, including retinal imaging and optic nerve head analysis. These investigations demonstrate AI's versatility and potential in medical imaging, highlighting its ability to be integrated across a broad spectrum of imaging methods and modalities. Early applications of AI in medical imaging focused on image classification, which entailed providing one or multiple images and obtaining a single diagnostic result, such as the presence or absence of a particular disease. Due to the limited size of medical image datasets in comparison to computer vision data, transfer learning has become a widespread method for image classification. This approach involves using pre-trained AI networks, eliminating the need for extensive datasets in deep network training.

Employing a trained network as a feature extractor and fine-tuning a trained network on medical data have been identified as the two main transfer learning methodologies. The first method enables feature extraction from trained networks, which can subsequently be easily included into already-in-use image processing procedures. The second method involves optimizing a network that has already been trained using medical data in order to improve its performance for certain applications. Both approaches are often used and have shown good outcomes in the field of medical imaging.

In summary, the research highlighted in this paper underscores the escalating significance and potential of AI within the medical imaging sphere. AI's ability to segment anatomical structures, identify abnormalities and diseases, and adapt to a multitude of imaging modalities indicates that it has the potential to revolutionize medical imaging practices, ultimately leading to more precise and efficient diagnoses.

The detection of specific elements within medical images, such as anatomical structures or landmarks, is crucial for a wide range of medical applications. Accurately pinpointing the location of these components is essential for tasks like segmentation, therapy planning, and intervention. In the field of medical imaging, this often requires the analysis of three-dimensional (3D) data, which presents complexities not found in two-dimensional (2D) data.

In response to these challenges, researchers have explored deep learning algorithms designed for the analysis of 3D data. These techniques typically approach 3D space as a collection of 2D orthogonal slices. For example, Yang et al. (2015) leveraged traditional Convolutional Neural Networks (CNNs) to identify landmarks on the distal femur's surface using three sets of 2D MRI scans. The three-dimensional position of the landmark was then determined by combining the three scans with the most outstanding classification results.

Similarly, De Vos et al. (2016) utilized 2D analysis of a 3D CT volume to establish a rectangular 3D boundary box around anatomical regions, such as the heart, aortic arch, and descending aorta. To improve the precision of feature representation in these tasks, investigators have turned to pre-trained CNN models and Restricted Boltzmann Machines (RBMs). These models, having been trained on extensive and varied datasets, can be applied to transfer knowledge to the challenge of deciphering 3D data in the realm of medical imaging.

The continued advancement of deep learning algorithms for 3D data analysis holds great promise for the future of medical imaging. By leveraging the power of pre-trained models and innovative techniques, researchers are better equipped to tackle the complexities of 3D data analysis, leading to more accurate and efficient detection and treatment of medical conditions. As the field continues to evolve, it is likely that even more sophisticated approaches will emerge, further pushing the boundaries of what is possible in medical imaging and patient care.

Despite the difficulties posed by 3D data analysis, these studies emphasize that treating localization as a classification task holds significant potential. By using generic deep learning models and learning methods, this approach has proven to be both accurate and efficient for parsing 3D data in medical imaging.

It is essential to note that these studies represent only the beginning of the possibilities of deep learning in medical imaging. As the field continues to advance and more research is conducted, it is likely that even more innovative and effective solutions will be developed for tasks such as object localization, segmentation, and disease detection.

Identifying objects of interest or abnormalities in images is a crucial part of diagnosis and can be time-consuming for healthcare professionals. These tasks often involve localizing and identifying small lesions within the entire image space. Over the years, researchers have focused on developing computer-aided detection systems that automate lesion detection, thereby improving accuracy and reducing human experts' reading time.

It's hard to believe that back in 1995 Lo et al.'s four-layer Convolutional Neural Networks (CNNs) were already being used to detect nodules in x ray images! Since then, technology and artificial intelligence have helped push this field forward leading us to the advanced machine learning algorithms, deep learning models, and neural networks we see today. These modern detection systems can even learn from vast amounts of image data - identifying patterns and abnormalities with remarkable accuracy. This is essential when detecting objects such as lesions within medical images as it can be labor intensive work for clinicians.

Thankfully computer aided detection systems have been developed over the years to help automate lesion detection - freeing up time for professionals who have many other demands on their time. Lo et al.'s pioneering work serves as an excellent testament to ongoing innovation in this field! In addition, organ segmentation has become an intense area of interest within medical imaging research. This opens up countless possibilities for detecting internal structures and other related discoveries that could benefit both practitioners and patients alike! Medical imaging depends heavily on accurately quantifying volume and shape parameters as these can impact patient diagnoses immensely. A key component of this process involves segmentation - identifying which voxels compose objects within an image - precisely to generate meaningful results for diagnosis or treatment administration purposes. Thanks to advancements made possible by deep learning innovations - such as incorporating both CNNs and RNNs - considerable progress has been made regarding new cutting-edge models for segmenting images.

One such model that stands out is the U net created by Ronneberger et al. (2015) featuring an inventive approach equipping it with an equal number of upsampling/downsampling layers. Countless attempts have been made at solving the problem of image segmentation with varying levels of success. However, one approach stands out from all others - the ingenious design behind the U-Net architecture. Previously, other methods had learned how to upsample images in separate parts through various algorithms; however, with "skip connections" as part of their solution set up between contracting & expanding pathways - built into their architectural design - this allowed them unify these traditionally separated steps more effectively & enabled it to process complete medical images with one full pass; resulting in a more professional grade segmented output compared to other versions utilizing patch-based CNNs.

What sets the U net architecture apart is its ability to achieve complete 3D segmentation using just a few annotated 2D slices from the same volume - an impressive feat as demonstrated by Cicek et al. (2016). And it doesn't stop there - derivative designs like Milletari et al.'s (2016) V net have further expanded on this adaptability by incorporating advanced techniques such as 3D convolutional layers and a Dice coefficient based objective function for even more accurate results. Yet another innovation comes from Drozdzal et al.'s (2016) exploration of short ResNet like skip connections combined with traditional ones, providing deeper insight into what makes this architecture so effective at image segmentation. The ability to perform comprehensive 3D segmentation with just a handful of 2D annotated slices emphasizes its versatility. Additionally, the study of different skip connection styles has enhanced our comprehension of the architecture's capabilities.

Table 1 Key Articles Referenced in the State-of-the-Art Section

Authors	Year	Title	Methods	Results
Konstantinos Kamnitsas et al.	2017	*Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation*	• DR-Net: novel CNN-based architecture • Two main components: feature extraction and classification • Feature extraction: fine-tuned pre-trained CNN • Classification: fully connected layers for DR stages • Evaluation on Messidor and Kaggle datasets	• State-of-the-art performance on Messidor and Kaggle datasets • Significant improvement in DR detection from color fundus photographs • Effective feature extraction and classification for DR stages
Mohsen Ghafoorian et al.	2017	*Transfer Learning for Domain Adaptation in MRI: Application in Brain Lesion Segmentation*	• Longitudinal study of small vessel disease patients (RUN DMC) • Baseline scans (2006): FLAIR images • Follow-up scans (2011): higher contrast acquisition • 3D T1 MPRAGE images for each subject • Semi-automatic reference WMH annotations • 280 baseline scans (source domain) • 159 follow-up scans (target domain) • Data split: training, validation, and test sets	• Model performance on source domain: Dice score of 0.76 • Model performance on target domain without fine-tuning: Dice score of 0.005 • Comparison of domain-adapted models and network trained from scratch • Test set Dice scores as a function of target domain training set size and fine-tuned layers • Qualitative results of WMH segmentation for different models
Olaf Ronneberger et al.	2015	*U-Net: Convolutional Networks for Biomedical Image Segmentation*	• U-Net: network and training strategy for biomedical image segmentation • Contracting path for context capture • Symmetric expanding path for precise localization • End-to-end training from few images • Outperforms prior best method on ISBI challenge • Fast network with full implementation available online • Data augmentation for efficient use of annotated samples • Applicable to various biomedical segmentation problems	• Very good performance on diverse biomedical segmentation applications • Data augmentation with elastic deformations requires few annotated images • Reasonable training time: 10 hours on NVidia Titan GPU (6 GB) • Full Caffe-based implementation and trained networks provided • U-Net architecture easily applicable to various tasks

Identifying and separating lesions in medical images, known as lesion segmentation, is crucial in medical diagnosis and treatment planning. Lately, deep learning algorithms have proven to be a potential solution for object detection and organ segmentation, offering improved accuracy in lesion segmentation.

The precision of lesion segmentation depends on considering both the global and local context of the image, as shown in the works of Kamnitsas et al. (2017) and Ghafoorian et al. (2017). In response, algorithms like U-net and its derivatives have been used for lesion segmentation, taking advantage of the unique architecture of U-net with its downsampling and upsampling paths and essential skip connections.

Wang et al. (2015) developed a deep learning architecture akin to U-net but lacking the essential skip connections. In a separate study, Brosch et al. (2016) utilized a U-net-inspired architecture for white matter lesion segmentation in brain MRI, integrating three-dimensional convolutions and a single skip connection to take advantage of both the global and local context of the image.

Lesion segmentation and object detection often encounter class imbalance obstacles, as the majority of the image is generally comprised of the non-diseased class. Various approaches have been adopted to address this issue. Brosch et al. (2016) tackled it by employing a modified loss function that blended sensitivity and specificity, assigning a greater weight to specificity. Meanwhile, researchers like Kamnitsas et al. (2017), Litjens et al. (2017), and Pereira et al. (2016) sought to balance the dataset by incorporating positive samples.

In conclusion, lesion segmentation is an essential aspect of medical imaging, and deep learning algorithms have great potential in addressing its challenges. U-net and its derivatives have proven effective in considering both global and local context, and various methods have been employed to tackle class imbalance, as demonstrated in the works of Kamnitsas et al. (2017), Litjens et al. (2017), Brosch et al. (2016), and Pereira et al. (2016).

Lesion segmentation, a field within medical image analysis, has been significantly influenced by advancements in object detection and organ segmentation, as they often face similar challenges, leading to the sharing of methods and techniques. Image registration, another crucial aspect of medical image analysis, involves aligning two medical images by determining the coordinate transformation between them. This process requires iteratively optimizing a specific transformation assumption and a predefined metric, such as the L2-norm. Recently, deep learning has also gained attention in image registration, with two main approaches for integration.

One approach involves using deep networks to calculate the similarity measure between images, guiding the iterative optimization process. The other approach utilizes deep regression networks to predict transformation parameters directly. Both of these strategies have demonstrated improvements in the accuracy and efficiency of image registration in medical image analysis.

In conclusion, the domain of lesion segmentation is swiftly progressing, reaping the advantages of advancements in object detection and organ segmentation. Furthermore, the deployment of deep learning in image registration has demonstrated its worth in augmenting the precision and efficacy of medical image analysis.

Conversely, Mahapatra et al. (2016) focused their efforts on creating algorithms tailored to evaluate the quality of retinal images. Addressing the shortcomings of earlier IQA algorithms, which were dependent on manually-engineered features, the team incorporated elements of the human visual system into their approach. This led to the development of an innovative algorithm that merged unsupervised data derived from local saliency maps with supervised data obtained from expertly trained convolutional neural networks (CNNs).

Mahapatra's research underscores the growing importance of deep learning methodologies in the analysis of ocular imagery. The algorithms they formulated provide answers to essential issues surrounding blood vessel segmentation and retinal image quality assessment, possibly resulting in considerable advancements in diagnosing and treating a range of eye-related disorders and ailments. As the fusion of deep learning techniques and human visual system principles continues, it holds the promise of transforming the ocular imaging field and ultimately enhancing patient outcomes.

Xu Zhang et al. (2019) aimed to create a streamlined, high-performance framework for optic disc segmentation. They introduced a novel approach that incorporated a lightweight cascade framework consisting of two essential components: a parsimonious segmentation network and a shape-refinement network cascade. The segmentation network was designed to minimize computational resources, while the shape-refinement network was implemented to counteract any potential performance decline resulting from the streamlined design of the segmentation network.

The researchers evaluated the framework's efficiency by conducting experiments on three different databases, including DRIVE, DIARETDB1, and DRIONS-DB. The results demonstrated that the framework exhibited slightly better segmentation performance compared to the widely-used U-net method, while also requiring significantly fewer trainable parameters. Memory usage during both training and testing phases was also considerably reduced, making the framework a more resource-friendly and efficient option for researchers and practitioners.

In summary, the lightweight cascade framework proposed by Xu Zhang and his team presents a highly promising solution for optic disc segmentation. Its emphasis on improved performance and reduced computational resource consumption makes it an attractive alternative to existing methods. The streamlined design of the framework is ideal for those looking to segment optic discs with minimal computational resources while still achieving significant performance results. This framework represents a major advancement in the field of optic disc segmentation and has the potential to greatly enhance the accuracy and speed of this critical task.

Veena et al. (2022) achieved a significant advancement in glaucoma detection by devising a cutting-edge method for segmenting the optic disc and optic cup within retinal fundus images. Their objective involved precisely calculating the Cup-to-Disc Ratio (CDR) and diagnosing glaucoma through the integration of a deep learning convolutional neural network (CNN). This approach entails employing two distinct CNN architectures for the individual segmentation of the Optic Cup (OC) and Optic Disc (OD).

The innovative system was trained and evaluated on the publicly available DRISHTI – GS database, achieving an accuracy rate of 98% for optic disc segmentation and 97% for optic cup segmentation. This demonstrates the immense potential of deep learning in medical imaging. However, while deep learning has significantly improved vessel detection in color fundus (CF) images, the same cannot be said for fluorescein angiography (FA) images. The lack of labeled ground truth datasets hampers the training and evaluation of machine learning models for FA image analysis. This highlights the crucial importance of data availability in the development of deep learning algorithms for medical imaging and the need for increased investment in this area.

In conclusion, H.N Veena and the team's work has opened new avenues for glaucoma diagnosis using retinal fundus images and deep learning. Their proposed system offers an efficient and accurate approach for segmenting the optic cup and disc, which is vital in determining the Cup-to-Disc Ratio (CDR) and diagnosing glaucoma. This contribution to the field of medical imaging represents a significant step forward in the fight against glaucoma.

Zilly et al. (2017) introduce a revolutionary technique for retinal image segmentation, skillfully merging convolutional neural networks (CNNs) with ensemble learning. This inventive method leverages entropy sampling to identify the most critical points, reducing computational requirements while simultaneously enhancing performance compared to uniform sampling approaches.

An entropy-driven sampling method underlies the training of a boosting-based learning framework, in which convolutional filters are trained across multiple layers, with each layer's output feeding into the next. The final step involves training a SoftMax logistic classifier on the combined output of all filters, which is then utilized on test images. The classifier's output is further processed through an unsupervised graph cut algorithm and a convex hull transformation to achieve the ultimate segmentation.

When applied to the DRISHTI-GS dataset, the suggested algorithm demonstrated remarkable results, outperforming existing techniques across various evaluation metrics. These outcomes validate the efficacy of the proposed method and its readiness for deployment in clinical settings.

In summary, Zilly et al. present an innovative approach for retinal image segmentation that combines CNNs with ensemble learning. The use of entropy sampling, boosting-based learning, and SoftMax logistic classifier leads to accurate and efficient segmentations, rendering the proposed method a significant advancement in the field and its potential for clinical application.

3. The following is the presentation of the studies that dealt with the detection of abnormalities and diseases using AI.

The assessment of retinal images is of utmost importance in the detection of retinal disorders. This evaluation process is crucial in identifying images that display anatomical structures and lesions with high precision and excluding images that could lead to misdiagnosis, which is a critical aspect of retinal diagnosis. In an innovative effort to address this challenge, Ziwen Xu et al. (2023) have proposed an advanced technique known as Sal StructuI QA.

The authors initiate their approach by defining two key structures that are essential for the automated assessment of retinal quality. These structures encompass large-scale salient structures, such as the optic disc and exudates, and small-scale salient structures primarily composed of vessels. By integrating these two salient structure priors, the authors then utilize a deep convolutional neural network (CNN) to concentrate on salient structures, resulting in the development of two CNN architectures: the Dual-branch Sal StructI QA and the Single-branch Sal StructI QA.

The Dual-branch Sal StructI QA comprises two separate CNN branches, each guided by either large-scale or small-scale salient structures. The Single-branch Sal StructI QA, conversely, is a lighter-weight CNN, guided by a combination of both large and small salient structures. The empirical results obtained from the Eye-Quality dataset demonstrate that the Dual-branch Sal StructI QA method surpasses existing state-of-the-art methods in retinal image quality assessment. Additionally, the Single-branch Sal StructI QA method offers a lighter-weight option that still achieves competitive performance while being significantly lighter compared to other deep retinal image quality assessment methods.

The Sal StructuI QA method presents a unique and innovative solution to retinal image quality assessment by employing two salient structure priors and a deep CNN. With its ability to evaluate retinal images accurately and efficiently, it holds immense potential for clinical applications, and its implementation could revolutionize the diagnosis of retinal disorders and improve patient outcomes. The Dual-branch Sal StructI QA provides a comprehensive assessment of retinal images, while the Single-branch Sal StructI QA offers a lighter-weight option with competitive performance.

In summary, the Sal StructuI QA method is a groundbreaking advancement in retinal image quality assessment and has the potential to reshape the landscape of retinal diagnosis.

Table 2 Key Articles on the Use of AI in Detecting Abnormalities and Diseases

Authors	Year	Title	Methods	Results
Julien Jomier et al.	2003	*Quantification of Retinopathy of Prematurity via Vessel Segmentation*	• Lens and digital video acquisition system • Speech recognition and image processing software • Vessel segmentation method for automatic disease estimation • Scale space technique with sub-voxel accuracy for vessel extraction • Width estimation via maximizing medialness function • Tortuosity defined as ratio of straight distance to geodesic distance of segmented model	• Tested on 20 premature infants (10 normal, 10 with various degrees of dilation and tortuosity) • 20 posterior pole images analyzed by the algorithm and two masked ROP-experienced examiners • Examiners agreed on presence or absence of plus disease in 17 of 20 cases • Algorithm correctly identified 4 of 5 images with plus disease (80% sensitivity) • Algorithm correctly identified 11 of 12 images without plus disease (92% specificity) • In 3 images where examiners disagreed, algorithm calculated greater than normal dilation and tortuosity, but insufficient for plus disease
Varun Gulshan et al.	2016	*Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs*	• Deep convolutional neural network for image classification • Trained on 128,175 retinal images graded 3-7 times • Graded by 54 US licensed ophthalmologists and senior residents (May-Dec 2015) • Algorithm validated with 2 separate data sets (Jan-Feb 2016) • Validation sets graded by 7+ US board-certified ophthalmologists with high intragrader consistency	• EyePACS-1 dataset: 9963 images, 4997 patients, RDR prevalence 7.8% • Messidor-2 dataset: 1748 images, 874 patients, RDR prevalence 14.6% • Algorithm's area under the receiver operating curve: 0.991 (EyePACS-1), 0.990 (Messidor-2) • High specificity operating point: ▪ EyePACS-1: sensitivity 90.3%, specificity 98.1% ▪ Messidor-2: sensitivity 87.0%, specificity 98.5% • High sensitivity operating point: ▪ EyePACS-1: sensitivity 97.5%, specificity 93.4% ▪ Messidor-2: sensitivity 96.1%, specificity 93.9%
Ling Dai et al.	2021	*A deep learning system for detecting diabetic retinopathy across the disease spectrum*	• Deep learning-based Diabetic Retinopathy screening system: DeepDR • Developed using 666,383 fundus images from 173,346 patients • Three deep-learning sub-networks: image quality assessment, lesion-aware, and DR grading • High sensitivity and accuracy in whole-process DR detection • Improves image collection quality, provides clinical reference, and facilitates DR screening • Further studies needed for evaluating DR progression detection and prediction	• DeepDR system achieved high sensitivity and specificity in DR grading • System provides visual hints to help users identify lesion types • Image quality and lesion-aware sub-networks improved diagnostic performance • DeepDR can run on standard personal computers with average-performance processors • Tested using two independent real-world cohorts and EyePACS dataset for external validation • Achieved satisfactory sensitivity and specificity in external validation

Daniel E. Worrall et al.	2016	Automated Retinopathy of Prematurity Case Detection with Convolutional Neural Networks	• Two methods for aiding ROP detection using CNNs • Method 1: Fine-tuning pre-trained GoogLeNet as ROP detector (per image and per examination) • Method 2: Training second CNN for novel feature map visualizations of pathologies • Feature maps highlight discriminative information • Aids clinicians in screening alongside classifier	• First fully automated ROP detection system presented • System handles single images or multiple images from a single examination • Augmented pathology visualizations returned from CNNs with large feature maps • Good agreement exhibited with some expert labelers • To surpass human performance, less human-dependent training data needed, potentially using unsupervised and semi-supervised learning
José E. Valdez-Rodríguez et al.	2021	Optic Disc Preprocessing for Reliable Glaucoma Detection in Small Datasets	• Detecting glaucoma using CNN model in digital retinal fundus color images • Preprocessing to extract optic disc for glaucoma information • CNN model based on AlexNet, trained on small dataset (366 examples) • Experiment with RGB channels, combinations, and depth information • Accuracy: 0.945 for GB and full RGB, 0.934 for grayscale transformation • Depth information didn't improve accuracy • Accurate glaucoma classification under low data conditions	• CNN model based on AlexNet accurately classifies glaucoma in digital retinal fundus color images under low data conditions • Experimented with different RGB channels and combinations to improve accuracy • Accuracy of 0.945 using GB and full RGB combination, and 0.934 for grayscale transformation • Depth information did not improve accuracy • Conclusion: simple CNN model accurately classifies glaucoma in digital retinal fundus color images under low data conditions
Noushin Eftekhari et al.	2019	Microaneurysm detection in fundus images using a two-step convolutional neural network	• Two-step method for detecting microaneurysms in fundus images using CNN • Step 1: Preprocessing for image quality improvement and removal of anatomical components • Step 2: Two-stage CNN for microaneurysm detection • First stage: Selecting microaneurysm candidates from informative part of image • Second stage: Classifying each pixel as microaneurysm or non-microaneurysm • Addresses imbalanced dataset problem and reduces training time • Evaluated on two standard publicly available datasets with promising results	• Proposed two-stage CNN method addresses imbalanced dataset problem and decreases training time compared to previous studies • Evaluated on two standard publicly available datasets: Retinopathy Online Challenge and E-Ophtha-MA • Achieved sensitivity value of about 0.8 for an average of >6 false positives per image, competitive with state-of-the-art approaches • Authors conclude the method represents a significant improvement in microaneurysm detection using retinal fundus images for monitoring diabetic retinopathy
Varun Gulshan et al.	2019	Performance of a Deep-Learning Algorithm vs Manual Grading for Detecting Diabetic Retinopathy in India	• Prospective observational study at two eye care centers in India • Included 3049 patients with diabetes • Aim: Validate automated DR system performance across sites • Comparison: Automated DR grading system vs manual grading by trained grader and retina specialist • Adjudication by panel of three retinal specialists in case of disagreement	• Proposed automated DR grading system performed equal to or exceeded manual grading by trained graders and retinal specialists • For moderate or worse DR, sensitivity and specificity for manual grading ranged from 73.4% to 89.8% and 83.5% to 98.7%, respectively • Automated DR system's performance: ▪ 88.9% sensitivity, 92.2% specificity, and AUC of

			• Main outcomes: Sensitivity and specificity for moderate or worse DR or referable diabetic macula edema	0.963 on data set from Aravind Eye Hospital ▪ 92.1% sensitivity, 95.2% specificity, and AUC of 0.980 on data set from Sankara Nethralaya • Authors conclude that the automated DR system generalizes well to the population of Indian patients and demonstrates the feasibility of using it to expand screening programs
Chaoxi Xu et al.	2019	*Fully Deep Learning for Slit-lamp Photo based Nuclear Cataract Grading*	• Fully deep learning-based solution for nuclear cataract grading using slit-lamp photos • Step 1: Localize nuclear region using Faster R-CNN, a state-of-the-art object detection network • Step 2: Grade cataract with ResNet-101-based grading model • Batch balancing strategy to address imbalanced data and improve training • Tested on 157 slit-lamp photos from 70 patients (39 female, 31 male) • Outperforms state-of-the-art, reducing mean absolute error from 0.357 to 0.313	• Proposed fully deep learning-based solution for grading nuclear cataracts outperforms state-of-the-art • Reduces mean absolute error from 0.357 to 0.313 • Method involves localizing nuclear region using Faster R-CNN and grading cataract using ResNet-101-based grading model • Authors introduce a simple batch balancing strategy to improve training of the grading network • Tested on clinical dataset of 157 slit-lamp photos from 70 patients • Shown to be effective and efficient, processing a slit-lamp photo in approximately 0.1 second
Ziwen Xu et al.	2023	*A Deep Retinal Image Quality Assessment Network with Salient Structure Priors*	• Method for retinal image quality assessment using deep CNN with salient structure priors • Proposed SalStructuIQA focuses on two salient structures: large-size structures (optic disc region, exudates) and tiny-size structures (vessels) • Two CNN architectures developed: Dual-branch SalStructIQA and Single-branch SalStructIQA • Dual-branch SalStructIQA: Two CNN branches guided by large-size and tiny-size salient structures • Single-branch SalStructIQA: One CNN branch guided by concatenation of both salient structures • Evaluated on Eye-Quality dataset; Dual-branch SalStructIQA outperforms state-of-the-art methods	• Proposed method, SalStructuIQA, incorporates salient structure priors into a deep CNN for retinal image quality assessment • Outperforms state-of-the-art methods • Dual-branch SalStructIQA demonstrates superior performance in retinal image quality assessment • Single-branch SalStructIQA is lighter in terms of computational resources but still achieves competitive performance • Authors conclude that their method represents a significant improvement in retinal image quality assessment by incorporating salient structure priors into a deep CNN
Julian Zilly et al.	2017	*Glaucoma detection using entropy sampling and ensemble learning for automatic optic cup and disc segmentation*	• Novel method for segmenting retinal images using ensemble learning based CNN architectures • Entropy sampling technique to select informative points, reducing computational complexity • Novel learning framework for convolutional filters based on boosting	• Proposed method uses ensemble learning based CNN architectures for retinal image segmentation • Outperforms existing methods on the public DRISHTI-GS dataset on several metrics • Uses entropy sampling technique to select informative points, reducing computational complexity

			• Filters learned in several layers, with output of previous layers serving as input to the next layer • Softmax logistic classifier trained on output of learned filters and applied on test images • Classifier output subject to unsupervised graph cut algorithm and convex hull transformation for final segmentation • Algorithm outperforms existing methods on DRISHTI-GS data set on several metrics for optic cup and disc segmentation	• Novel learning framework for convolutional filters based on boosting is designed • Softmax logistic classifier trained on the output of all learned filters and applied to test images • Classifier output subject to unsupervised graph cut algorithm and convex hull transformation for final segmentation • Authors conclude that their algorithm represents a significant improvement in retinal image segmentation

Identifying glaucoma is crucial, as this debilitating condition can substantially affect the optic nerve, with the highest accuracy value for diagnosis being 0.934. Norah Asiri et al. (2019) discovered that untreated diabetic retinopathy (DR) may result in vision impairment. A computer-assisted diagnostic (CAD) tool that utilizes retinal fundus images has demonstrated its efficiency and effectiveness in diagnosing DR and supporting healthcare professionals in early detection. Employing a computer-assisted diagnostic system can help prevent blindness caused by DR through timely detection, consistent monitoring, and appropriate treatment, which can stop the disease from progressing and ward off vision loss.

Glaucoma is typically detected through various examinations, including tonometry, gonioscopy, and pachymetry. José E. Valdez-Rodriguez et al. (2021) have developed a method for detecting glaucoma using images captured with retinal cameras, which enable visualization of the optic nerve's condition. The primary objective of their work is to create a precise diagnostic methodology for classifying these optical images using Convolutional Neural Networks (CNNs). Most existing studies necessitate a large volume of images to train their CNN architectures and perform classification on the entire image.

On the other hand, Valdez-Rodriguez and his colleagues trained their suggested CNN architecture on a comparatively small dataset composed of merely 366 samples. Their research was solely dedicated to analyzing the optic disc by isolating it from the entire image, as it contains the most crucial information related to glaucoma. They experimented with various RGB channels and combinations derived from the optic disc, as well as depth data. They attained an accuracy of 0.945 with the GB and complete RGB combinations, and 0.934 when employing the grayscale conversion. The depth data did not produce the anticipated accuracy.

The computer-aided diagnosis (CAD) system encompasses multiple stages, including lesion detection, segmentation, and classification within fundus images. Historically, a multitude of conventional machine learning (ML) methods relying on manually crafted features have been put forward. Nevertheless, the burgeoning prominence of deep learning (DL) and its notable triumphs over traditional machine learning techniques in a wide spectrum of applications have inspired researchers to employ DL methodologies for DR diagnosis. As a result, several deep learning-centric strategies have been proposed to achieve this goal.

Deep learning (DL) techniques present a range of benefits and drawbacks, which the investigators meticulously examine. Furthermore, they delve into the complexities associated with the creation and cultivation of efficient, effective, and resilient deep learning algorithms for tackling diverse issues in diagnosing diabetic retinopathy (DR). The researchers also offer valuable perspectives on possible future avenues of exploration within this domain.

In conclusion, the early detection of glaucoma and diabetic retinopathy is crucial for preventing vision loss and blindness. Computer-aided diagnosis systems that utilize retinal fundus images and Convolutional Neural Networks have proven to be efficient and effective tools for diagnosing these conditions and assisting medical professionals in their early detection. By focusing on the optic disc and experimenting with various RGB channels and their combinations, researchers have achieved promising accuracy rates in glaucoma detection. Additionally, deep learning-based methods have been introduced for DR diagnosis, offering a range of advantages and disadvantages, as well as presenting challenges and future research opportunities in the development of efficient, effective, and robust algorithms.

Diabetic retinopathy (DR) is a prevalent condition and the leading cause of blindness across the globe. Early detection of DR is crucial in preventing eye injuries associated with the disease. In their research, NoushinEftekhari et al. (2019) investigate DR and the use of fundus images for its diagnosis. Microaneurysms (MA), one of the primary symptoms of

DR, play a vital role in early detection. Identifying this complication within fundus images enables timely intervention and treatment of DR.

The objective of the study by Eftekhari and colleagues is to introduce an automated analysis method for retinal images, leveraging the power of convolutional neural networks (CNNs). Their innovative approach incorporates a two-stage process using two online datasets, which significantly reduces training time compared to previous studies. The method also addresses the challenge of imbalanced data, resulting in accurate detection of DR.

The suggested CNNs were developed utilizing the Keras library, a well-known deep learning framework. To evaluate the efficacy of their approach, the investigators carried out an experiment employing two readily accessible public datasets: the Retinopathy Online Challenge dataset and the E-Ophtha-MA dataset. The outcomes of their experiment revealed an encouraging sensitivity value of roughly 0.8, accompanied by an average of more than six false positives per image. This performance aligns with the most advanced methods in DR detection currently available.

In summary, early detection of diabetic retinopathy is critical for preventing blindness and other eye injuries related to the disease. Eftekhari and colleagues have presented an automated analysis method for retinal images, utilizing a convolutional neural network to detect DR with high accuracy. Their innovative two-stage process, which employs two online datasets, not only significantly reduces training time but also effectively addresses the issue of imbalanced data. The implementation of the proposed CNNs using the Keras library has yielded promising results, with a sensitivity value of approximately 0.8 and a performance comparable to state-of-the-art approaches. This method has the potential to greatly assist in early detection and diagnosis of DR, ultimately leading to better patient outcomes and improved eye health.

India has over 60 million individuals living with diabetes, a demographic that faces a heightened risk of developing diabetic retinopathy (DR), a condition that can significantly impair vision. To ensure a robust DR screening program is sustainable and scalable, automating the interpretation of retinal fundus photographs can prove invaluable. The goal of this research was to prospectively validate an automated DR system's performance across two sites in India.

Varun Gulshan et al. (2019) carried out a progressive observational study at a pair of eye care facilities in India, involving a total of 3,049 diabetic individuals. The process of data collection and participant enrollment occurred at Aravind between April and July of 2016, while at Sankara Nethralaya, it took place from May 2016 to April 2017. The DR model's development and fine-tuning were completed in March 2016. The researchers juxtaposed the automated DR grading mechanism with manual grading performed by a skilled grader and a retina expert at each site. In cases where discrepancies emerged, a group of three retinal specialists acted as the reference standard for resolving the differences. The sensitivity and specificity for moderate or more severe DR or referable diabetic macula edema were ascertained in the cohort of 3,049 patients.

Of the participants, 1,091 (35.8%) were female. The average age (± SD) of patients at Aravind and Sankara Nethralaya was 56.6 (± 9.0) and 56.0 (± 10.0) years, respectively. Sensitivity and specificity for manual grading by non-adjudicator graders for moderate or worse DR ranged between 73.4% and 89.8% and between 83.5% and 98.7%, respectively. The automated DR system performed similarly to or surpassed manual grading when assessed on the dataset from Aravind Eye Hospital. It achieved an 88.9% sensitivity (95% confidence interval [CI]), a 92.2% specificity (95% CI, 90.3-93.8), and an area under the curve (AUC) of 0.963. The system exhibited a 92.1% sensitivity (95% CI), a 95.2% specificity (95% CI), and an AUC of 0.975 when evaluated on the dataset from Sankara Nethralaya.

This study highlights the automated DR system's generalizability to the Indian patient population in a prospective setting. Furthermore, it underscores the feasibility of expanding DR screening programs by employing an automated DR grading system. By automating the grading process, healthcare providers can reach a larger patient population, while streamlining the diagnostic process and reducing the burden on eye care specialists. This, in turn, can lead to more efficient and effective screening programs, ensuring timely detection and treatment of DR, ultimately reducing the risk of vision loss for millions of diabetic patients in India and beyond. By leveraging cutting-edge technology and innovative approaches, the research paves the way for more accessible and efficient eye care solutions, particularly in regions with high diabetic populations and limited access to specialized care.

Chaoxi Xu et al. (2019) present a groundbreaking approach to grading nuclear cataracts, the most common form of cataract associated with aging, in their recent paper. They propose a novel automated grading system based on slit-lamp photographs, which diverges from conventional methods utilizing feature extraction and grade modeling techniques. Instead, the authors employ deep learning to provide a comprehensive solution. The authors use Faster R-CNN to localize the nuclear area in the slit-lamp image, followed by the implementation of a grading model based on

Res Net. They address the problem of imbalanced data by introducing a batch balancing strategy that optimizes the training of the grading network.

The suggested system underwent testing on a clinical dataset consisting of 157 slit-lamp images from 39 female and 31 male patients, yielding remarkable results that surpassed the current state-of-the-art. The mean absolute error experienced a reduction from 0.357 to 0.313, and the system was able to process a slit-lamp image in a mere 0.1 second, making it two orders of magnitude quicker than existing approaches. This groundbreaking automated solution has the potential to revolutionize nuclear cataract grading. Given its efficiency and effectiveness, it stands as an exemplary candidate for automating the diagnosis of this prevalent type of cataract.

With the aging demographic and increasing burden of eye diseases, the creation of automated grading systems is vital in enhancing the delivery of eye care and ensuring prompt and accurate diagnoses for patients. This solution marks a pivotal step towards this goal and could have a significant impact on the future of nuclear cataract diagnosis and treatment.

Within the realm of medical imaging, creating dependable computational models necessitates a substantial quantity of annotated training data. Yet, annotating voxel-level specifics for these datasets frequently proves unfeasible due to the enormous amount of data involved. Consequently, employing a combination of imaging data and reports produced during standard clinical procedures presents an attractive option. To address this issue, weakly supervised learning techniques can connect volume-level labels to image content. However, such methods grapple with the imbalance commonly found in medical imaging datasets, where only a small portion of the labels pertain to clinically relevant structures.

To address this issue, alternative approaches that leverage the rich information present in medical imaging data are essential. Advancing computational models from medical imaging data holds the potential to revolutionize medical care by providing accurate diagnoses and improving patient outcomes. The ongoing search for alternatives to manual annotation and overcoming the limitations of weakly supervised learning is a paramount area of research, paving the way for the future of medical imaging.

Diagnostic precision is paramount in medical imaging, as categorizing and distinguishing various structures within an image is crucial. Thomas Schlegl et al. (2015) presents an innovative strategy for predicting semantic representation in clinical reports, harnessing the power of Convolutional Neural Networks (CNNs). The study aims to demonstrate the importance of incorporating semantic information in image classification and its potential impact on accuracy.

This study concentrates on 157 Optical Coherence Tomography (OCT) volumes with the objective of training voxel-level classifiers to precisely detect three structures: Intraretinal Cystoid Fluid (IRC), Subretinal Cystoid Fluid (SRF), and Normal Retinal Tissue. The authors assess three strategies, encompassing a rudimentary weakly supervised learning method, a weakly supervised learning technique enhanced with semantic descriptions, and supervised learning.

The elementary weakly supervised learning approach serves as a reference point, achieving an overall classification accuracy of 66.30%. Nonetheless, it demonstrates low accuracy in detecting IRC, with only 21.94% of samples being accurately identified. In contrast, the SRF category is classified with remarkable precision, reaching 90.30%. The authors then put forth a more sophisticated weakly supervised learning technique that integrates semantic descriptions, resulting in an overall accuracy of 81.73% across all three categories. A marginally lower accuracy for the healthy group (78.72%) is observed in comparison to SRF (92.09% accuracy).

The results indicate that incorporating semantic information into the training process leads to considerable improvement in classification accuracy. Finally, the authors showcase that supervised learning outperforms the other two approaches, with an overall classification accuracy of 95.98%. Supervised learning is most effective in classifying the healthy class, with an accuracy of 97.70%, while it encounters challenges in identifying IRC, with 89.61% accuracy. Despite the challenges, the results still exhibit a substantial improvement compared to the benchmark.

In conclusion, the study by Thomas Schlegl and his team highlights the importance of incorporating semantic information in image classification and its potential to enhance accuracy. The findings hold immense potential for advancing the field of medical imaging and improving patient care.

Utilizing deep learning algorithms in medical image analysis introduces a series of unique challenges. The scarcity of extensive training datasets is frequently mentioned as a substantial hurdle. However, this concept is only partially true. For more than ten years, Picture Archiving and Communication System (PACS) has been widely used in radiology departments in the majority of Western hospitals, preserving millions of images in well-organized repositories. Few other fields have access to this amount of specialized imaging data that is digitally available. Although some medical disciplines, such as ophthalmology and pathology, have not extensively embraced PACS-like systems, this circumstance is evolving as imaging becomes increasingly widespread across various specialties.

This shift has led to an increase in the availability of extensive public datasets. For example, Esteva et al. (2017) utilized 18 public datasets and over 105 training images, while a similar number of retinal images were released during the Kaggle diabetic retinopathy competition, and several chest X-ray studies included more than 104 images. Consequently, the primary challenge lies not in gathering image data but in obtaining relevant annotations or labels for these images. Historically, PACS systems have stored free-text reports authored by radiologists detailing their observations. Automating the transformation of these reports into precise annotations or structured labels demands advanced text-mining techniques, a substantial field of research where deep learning is now widely applied. As structured reporting is adopted across various medical specialties, it is expected that the extraction of labels from data will become increasingly uncomplicated in the future.

For example, several studies have already leveraged radiologist-generated Breast Imaging-Reporting and Data System (BI-RADS) categories to educate deep networks (Mohamedet al., 2018) or incorporated semantic descriptions in optical coherence tomography image examination (Schlegl et al., 2015). The optimal use of free-text and structured reports for network training is expected to become a growing area of research focus in the near future.

In summary, the implementation of deep learning algorithms in medical image analysis presents distinct challenges, mainly linked to obtaining pertinent annotations or labels rather than the accessibility of image data. As PACS systems are embraced across multiple medical disciplines, the quantity of available digital images has expanded significantly. However, automating the conversion of radiologists' free-text reports into precise annotations or structured labels remains a considerable challenge that necessitates sophisticated text-mining techniques.

As structured reporting gains traction across various medical fields, label extraction from data is anticipated to become more streamlined. The direct application of radiologist-created BI-RADS classifications or semantic descriptions in image analysis exemplifies the potential of this methodology. As a result, research efforts concentrating on the best utilization of free-text and structured reports for network training are likely to intensify in the coming years, further advancing the proficiency of deep learning algorithms in medical image analysis and enhancing patient outcomes.

The utilization of deep learning algorithms in medical image analysis brings about numerous intricacies that need to be addressed for achieving optimal outcomes. Despite these obstacles, significant progress has been made by experts, as evidenced by the work of Esteva et al. (2017) in dermatology and Gulshan et al. (2016) in ophthalmology. These instances illustrate that deep learning can outperform human medical professionals in specific tasks. Nevertheless, it is essential to understand that these accomplishments should be considered in their appropriate context, as many tasks in medical image analysis remain far from being fully solved.

The achievements of Esteva et al. (2017) and Gulshan et al. (2016) can be attributed to their concentration on small-scale 2D color image classification, which closely aligns with computer vision tasks, such as ImageNet. This approach allowed them to employ well-established network frameworks like ResNet and VGG-Net, which have demonstrated exceptional performance in similar tasks. Furthermore, they had access to pre-trained networks based on an extensive and accurately labeled dataset of natural images, which aided them in overcoming the lack of comparably large, labeled medical datasets.

However, these successes may not be replicable for other tasks in medical image analysis that require 3D grayscale or multi-channel images, which present unique challenges, such as non-uniform voxel sizes, minimal registration errors between different channels, or varying intensity ranges. Addressing these challenges demands the development of specialized architectures and techniques that surpass the limitations of current computer vision.

Additionally, while some tasks in medical image analysis can be modeled as classification problems, this approach may not always be ideal. This is because it often requires subsequent processing using non-deep learning techniques, such as counting, segmentation, or regression tasks, which can introduce additional complexities and biases into the analysis, making it difficult to achieve accurate results.

In conclusion, while deep learning has demonstrated immense potential in medical image analysis, much work remains before this technology can be fully utilized in the medical industry. Researchers must continue to develop specialized architectures and techniques that can address the distinct challenges posed by medical images and overcome the limitations of current deep learning algorithms.

Ling Dai et al. (2021) developed a comprehensive deep learning system for detecting diabetic retinopathy (DR) across various stages of the disease. The Deep DR system was composed of three sub-networks: image quality assessment, lesion identification, and DR grading. ResNet41 and Mask-RCNN57 were used as the foundation for creating these sub-networks. Both ResNet and Mask-RCNN can be split into two main components: a feature extractor that takes images as input and generates features as output, and a task-specific header that receives the features as input to generate task-specific outputs, such as classification or segmentation.

The researchers intentionally chose Mask-RCNN and ResNet with the same feature extractor architecture to enable the effortless transfer of the feature extractor between sub-networks. During this research, 5176 retinal images were gathered from 1294 patients. Among these images, 1487 (28.7%) were deemed low-quality due to artifacts, lack of sharpness, and/or field definition issues. Based on feedback, a second photograph of these patients was taken. Out of the initial 1487 low-quality images, 1065 (71.6%) were recaptured at an acceptable quality level.

Ling Dai and his team improved the diagnostic accuracy of each DR grade by replacing low-quality images with recaptured ones. The area under the curve (AUC) rose from 0.880 (0.859–0.895) to 0.933 (0.918–0.950) (P 0.001) for mild non-proliferative diabetic retinopathy (NPDR), and sensitivity increased from 78.5% (72.7–83.4%) to 87.6%. In cross-validation, the trained network's accuracy percentage varied between 80% and 83%. These outcomes suggest that the machine-based segmentation was on par with manual segmentation performed by a human evaluator.

In conclusion, Ling Dai and his team developed a cutting-edge deep learning system to detect diabetic retinopathy across different stages of the condition. Employing ResNet41 and Mask-RCNN57, they established three interconnected sub-networks: image quality assessment, lesion identification, and DR grading. They deliberately selected the same feature extractor architecture for both Mask-RCNN and ResNet, enabling the seamless transfer of the feature extractor between sub-networks.

During the assessment of both intra- and interrater comparisons, the study discovered comparable levels of agreement between the repeated segmentations performed by a single individual and those executed by two separate raters. This demonstrated significant variability in manual segmentation for both intra- and interrater evaluations. The findings imply that the trained neural network might be as effective as a newly introduced human rater.

Considering the substantial time difference between manual segmentation by a human rater, which takes approximately 20 to 25 minutes, and the automated method, which only requires 2 minutes, this tool could prove highly beneficial in clinical settings. By saving precious human resources and providing results to medical professionals more swiftly, this technology has the potential to enhance the overall efficiency in diagnosing and managing mild non-proliferative diabetic retinopathy (NPDR) with an accuracy rate ranging from 83.2% to 92.3%.

Daniel E. Worrall et al. (2016) conducted research on the automatic detection of retinopathy of prematurity (ROP) using convolutional neural networks (CNNs). Their investigation focused on two distinct methods for employing CNNs to enhance ROP identification. They claim to have developed the first-ever fully automated ROP detection system, which can independently classify images and examinations. This innovative system blends traditional deep learning approaches with contemporary variational Bayesian methods.

Throughout their research, the team documented the practical adjustments that proved effective or ineffective in achieving their goal. Furthermore, they demonstrated how the feature maps of deep CNNs could be employed to visualize disease indicators learned directly from the data, thus providing valuable insights into the underlying pathologies.

As expected, the average results are typically higher than the per-image results since averaging across exams helps to mitigate incorrect per-image labels. The Bayesian model boosts class-normalized accuracy by around 5% for both per-image and per-exam classification, while also significantly improving per-exam sensitivity. When compared to other methods, their approach is competitive, though it doesn't quite achieve the per-image sensitivity of Wallace et al. Nonetheless, direct comparison of their results is challenging due to differences in test set sizes (20 images) and the distinct methodology employed by Jomier et al. (2003), which only tests non-borderline images. Assessing the Fleiss' Kappa (FK) scores, they find that their model's agreement ranges from 0.54 to 0.72, considered "moderate" to "substantial."

Since no ground truth exists for the London dataset, they report only the FK score. They combine the outputs of the nine cross-validation trained CNNs for a single prediction by calculating the mean and thresholding at 50%. The FK score among experts is 0.427, but it drops to 0.366/0.372 with their system. Interestingly, the system strongly agrees with one expert while strongly disagreeing with another, and the agreement with the nearest expert is more stable than the agreement with the most distant expert (0.194). For comparison, they report an FK of 0.32 for interclinician agreement on a separate dataset.

In summary, the researchers observed that their Bayesian model improves class-normalized accuracy and sensitivity for both per-image and per-exam classifications. Although their approach is competitive, it does not outperform Wallace et al.'s per-image sensitivity, and comparing the results is challenging due to differences in test set size and methodology. Evaluating the Fleiss' Kappa scores, they found their model's agreement to be "moderate" to "substantial." For the London dataset, where there is no ground truth, they reported an FK score that showed a varying degree of agreement with different experts. Despite these variations, their approach demonstrates potential for advancing the field of medical image analysis.

4. The following is the presentation of the studies that dealt with other imaging modalities on the eye.

Xinting Gao et al. (2015) led an initiative that demonstrated the capability of deep learning to extract essential, semantically rich features for evaluating nuclear cataracts. They employed the unsupervised Convolutional-Recursive Neural Network (CRNN) approach, initially introduced by Socher et al. (2012). The CRNN process consists of three stages: pre-training CNN filters on randomly selected patches, generating local representations of each image by inputting pre-trained filters into a CNN layer, and utilizing multiple RNNs with random weights to derive hierarchical feature representations. Prior to implementing the CRNN method for cataract assessment, the lens anatomy and structure were identified. CRNNs were subsequently used to learn a representation for each lens segment, and Support Vector Regression (SVR) estimated the cataract grade by merging the features. The test results on the ACHIKO-NC dataset were remarkable, with the system achieving a 68.6% exact agreement ratio (R0) compared to clinical integral grading, an 86.5% decimal grading error of 0.5 (Re0.5), a 99.1% decimal grading error of 1.0 (Re1.0), and a 0.322 mean absolute error. These outcomes surpassed the performance of the existing state-of-the-art technique.

In another study, Thomas Schlegl et al. (2015) investigated the possibility of predicting semantic descriptions from medical images using Convolutional Neural Networks (CNNs). Developed in 1980 by Fukushima, CNNs have become a standard in solving classification problems by automatically learning translation-invariant visual input representations. This adaptability allows visual feature extractors to adjust to data rather than being manually engineered, showcasing the efficacy of deep learning in managing complex medical imaging tasks.

Convolutional Neural Networks (CNNs) have gained considerable traction in medical image analysis, with uses such as manifold learning in 3D brain magnetic resonance imaging data in the frequency domain and improving lung tissue classification accuracy in computed tomography imaging through unsupervised pre-training for domain adaptation. In contrast, our research methodology deviates from these conventional techniques by eschewing any supervised (pre-)training and relying exclusively on medical images. Furthermore, our approach's classifier not only predicts global image labels that indicate the presence or absence of particular objects, but also determines their exact location information, attaining a classification accuracy of 66.30% across all three classes.

While our study's results are promising, there is still room for improvement, particularly in classifying samples displaying IRC, as only 21.94% of them were accurately classified. On the other hand, our approach demonstrated remarkable accuracy in the SRF class, with 90.30% of all patches correctly classified as SRF.

Table 3 Key Articles on Other Imaging Modalities on the Eye

Authors	Year	Title	Methods	Results
Xinting Gao et al.	2015	*Automatic Feature Learning to Grade Nuclear Cataracts Based on Deep Learning*	• Detecting lens structure and anatomical sections of the lens • Applying convolutional-recursive neural networks (CRNNs) to each section to learn a representation • Using support vector regression (SVR) to estimate the cataract grade • Pre-training CNN filters from randomly selected patches • Generating local representations of each image using a convolutional neural network (CNN) layer • Learning hierarchical feature representations using multiple recursive neural networks (RNNs) with random weights	• Mean absolute error (ε): 0.322 • Exact integral agreement ratio (R0): 68.6% • Decimal grading error ≤ 0.5 (Re0.5): 86.5% • Decimal grading error ≤ 1.0 (Re1.0): 99.1%
Thomas Schlegl et al.	2015	*Predicting Semantic Descriptions from Medical Images with Convolutional Neural Networks*	• Using weakly supervised learning to link volume-level labels to image content • Employing a semantic representation of clinical reports as a learning target predicted from imaging data by a CNN • Learning accurate voxel-level classifiers based on weak volume-level semantic descriptions on a set of 157 optical coherence tomography (OCT) volumes • Demonstrating how semantic information increases classification accuracy for intraretinal cystoid fluid (IRC), subretinal fluid (SRF), and normal retinal tissue • Showing how the learning algorithm links semantic concepts to image content and geometry	• Naïve weakly supervised learning: 66.30% classification accuracy • Learning semantic descriptions: 81.73% classification accuracy • Supervised learning: 95.98% classification accuracy
Richard Socher et al.	2012	*Convolutional-Recursive Deep Learning for 3D Object Classification*	• Unsupervised pre-training of CNN filters using k-means clustering on random patches from RGB and depth images • Generating low-level features with a single CNN layer • Feeding low-level features into multiple fixed-tree Recursive Neural Networks (RNNs) to obtain high-level features • Demonstrating that RNNs with random weights can produce high-quality features for quick exploration of various RNN architectures	• New model combines convolutional and recursive neural networks • Features: fixed tree structure, multiple vector combination, multiple RNN weights, random parameter initialization • Allows for fast parallelization and high speeds • Outperforms two-layer CNNs • Achieves state-of-the-art performance without external features • Demonstrates effectiveness in depth image domain

5. Classification Methods

Recent advancements in deep learning algorithms have significantly influenced the field of ophthalmic imaging enabling researchers to gain new insights into eye images that were not detectable before using traditional methods alone. The focus has been on utilizing Convolutional Neural Networks (CNNs) for analyzing Color Fundus Imaging (CFI) data efficiently. Deep learning techniques can be used for various applications such as detecting retinal abnormalities segmenting eye anatomy diagnosing eye diseases and evaluating image quality with remarkable success rates that surpass traditional analytical methods alone. An example demonstrating their efficacy is evident in the Kaggle competition held in 2015 where over 35k color fundus images were used to train deep learning models for estimating diabetic retinopathy severity on around 53k test images. With end-to-end CNN utilization four participating teams surpassed human expertise levels which highlights the potential of deep learning technology in ophthalmology. Another study conducted by Gulshan et al. (2016) evaluated Google Inception v3 network performance and found it comparable to seven certified ophthalmologists in identifying diabetic retinopathy. Discoveries emphasize just how powerful deep learning algorithms are when it comes to ophthalmic imaging. They have the capacity to produce speedy, streamlined and precise outcomes.

5.1. Machine Learning Methods

When it comes to machine learning we have two main techniques: supervised and unsupervised approaches. Researchers like Mookiah et al. (2021) and Srinidhi et al. (2017) have explored both in detail. Supervised methods involve using labeled data to train classification models that can recognize specific features in images. Ground truth labels are used, and there are a variety of algorithms available such as Bayesian methods, discriminant analysis, k nearest neighbor (kNN) support vector machine (SVM) artificial neural network (ANN) random forest, AdaBoost, and fuzzy computing methodologies including deep learning-based models. On the other hand, unsupervised methods don't require exact labeled information but instead operate by understanding inherent structures within unlabeled datasets. Algorithms such as Gaussian mixture models (GMM) fuzzy c means (FCM) and k means clustering are commonly utilized for vessel segmentation tasks. The best approach between the two will be dictated by your specific applications requirements as well as your access to labeled data. However supervised techniques typically result in higher accuracies due to their reliance on known labels for feature recognition. The field of medical imaging relies heavily on machine learning algorithms where there are primarily two areas that researchers focus on – supervised and unsupervised methods. Utilizing labeled data in a controlled environment makes supervised approaches such as deep learning highly accurate in classification tasks while retaining predictive capabilities based on past cases analyzed by clustered-based frameworks which come under the category of unsupervised methods although at a reduced level compared to their counterparts when working without any input labeling criteria set during model training phase.

5.2. Deep Learning

Deep learning models, particularly convolutional neural networks (CNNs), possess a remarkable capability to compute representations essential for classification and categorization tasks. CNNs have been utilized either independently or in combination with other techniques like random forests for vessel segmentation, as demonstrated by Guo et al. (2018). Other approaches include using CNNs with conditional random fields (CRFs) as reported by Fu et al. (2016), and others.

Numerous researchers have proposed modified architectures with specialized layers for combined vessel-optic disk detection, including the work by Tan et al. (2017) and Jiang et al. (2018), which utilize millions of natural images for training. CRF layers have been shown to improve lesion segmentation by simulating long-range pixel interactions (Luo et al., 2017). Models incorporating dense CRFs, such as those described by Oliveira et al. (2018), use reinforcement sample learning to shorten training time.

Dasgupta and Singh (2017) successfully segmented thin vessels, which were challenging for traditional methods. In addition, fully convolutional networks (FCNs) have demonstrated better vessel segmentation results compared to networks with only a few fully connected layers, as seen in the work of Yan et al. (2018b). To significantly reduce the number of training examples, several networks have been combined, as demonstrated by Xu et al. (2018).

Multi-scale analysis has been explored, such as merging the outputs of width-specific vessel detectors (Yan et al., 2018b) or integrating a wavelet transform into the model (Oliveira et al., 2018). Generative adversarial networks (GANs) have been utilized for training and are commonly employed to generate synthetic retinal images. These GANs have been found to enhance segmentation performance in the presence of lesions (Park et al., 2020).

In conclusion, deep learning models, particularly CNNs, have exhibited remarkable potential for vessel segmentation tasks. A variety of approaches, such as blending CNNs with other techniques, modifying architectures, and incorporating multi-scale analysis, have been explored to enhance vessel segmentation outcomes. The application of GANs has also emerged as an encouraging method for improving segmentation performance. Overall, this expanding body of research continues to advance the vessel segmentation process using deep learning techniques.

5.3. Other Machine Learning Methods

In the field of retinal vessel segmentation, various machine learning methods have been employed to improve performance and tackle challenges, such as segmenting thin vessels, enhancing visibility, and classifying arteries and veins. The methods mentioned in the text above can be broadly categorized as:

5.3.1. Supervised Methods:

- Neural Networks (NNs): Strategies to improve NN performance include incorporating features like texture, color, intensity, and moment invariants. Cross-modality learning, deep architectures, and linear discriminant analysis have also been applied to boost performance (Naghsh-Nilchi&Fathi, 2014).
- Ensemble learning algorithms: Bagging and boosting algorithms, such as AdaBoost, have proven effective in vessel segmentation by incorporating features like intensity, texture, and Gabor (Memari et al., 2017).

- Support Vector Machines (SVM): SVM has shown to improve segmentation results in computer vision tasks, especially when combined with fully connected conditional random fields (Strisciuglio et al., 2016).
- Random forest classifiers: These classifiers have been used in conjunction with visual attention modeling to tackle challenges posed by images with closely situated parallel vessels and other issues (Srinidhi et al., 2018).

5.3.2. Unsupervised Methods:

- Gaussian Mixture Model-Expectation Maximization (GMM-EM): GMM-EM has gained interest due to its use in maximum-likelihood vessel/non-vessel classification (Roychowdhury et al., 2014).
- Fuzzy C-Means (FCM) clustering: FCM has been used to amplify thin vessels and remove blobs from fundus images using a blend of filters (Hassan and Hassanien, 2018; Neto et al., 2017).

5.3.3. Matched Filtering Methods

This method involves comparing retinal images with pre-designed kernel models to imitate the intensity profiles of vessels (Farokhian et al., 2017).

5.3.4. Morphological Image Processing Methods

Mathematical morphology is used to identify boundaries, skeletons, and convex hulls, as well as improving vessel visibility (Dash and Bhoi (2017)).

5.3.5. Vessel Centerline Segmentation

Various techniques have been developed to accurately detect vessel centerlines and differentiate them from pathological lesions, such as FoDoG, adaptive thresholding, and morphology-based global thresholding (Jiang et al., 2017).

5.3.6. Artery/Vein Classification Methods

A multi-stage approach has been proposed, which includes pre-processing, defining a region of interest (ROI), feature extraction using deep convolutional neural networks (DCNN), and feature selection. The selected features are then inputted into multi-class classifiers for disease detection (Mahum et al., 2021).

These methods demonstrate the versatility and adaptability of machine learning techniques in retinal vessel segmentation. As advancements in image processing and machine learning continue, these methods are expected to improve further, leading to more accurate and robust vessel segmentation algorithms.

5.4. Comparative Results

Drawing fair comparisons between numerous reported methods in medical image validation is complex due to challenges related to public datasets, design, and evaluation criteria used in international grand challenges (Maier-Hein et al., 2018; Joskowicz et al., 2019). Retinal image analysis challenges, such as REFUGE at MICCAI and IDRiD, serve as platforms to develop and compare techniques and algorithms, leading to advancements in the field.

Many methods for retinal vessel segmentation have been analyzed using databases like DRIVE, STARE, CHASEDB1, HRF, DIARETDB1, MESSIDOR, ARIA, REVIEW, GoDARTS, IOSTAR, and RC-SLO. Artery and vein classification techniques have been evaluated through databases like VICAVR, INSPIREAVR, and WIDE. These databases feature images with lesions and address specific segmentation issues related to central venous refilling, thin vessels, and bifurcations or crossover points.

A/V segmentation has fewer studies compared to vessel segmentation due to restricted access to ground truth labels and the task's added complexity. Deep learning systems have simplified the A/V segmentation process, resulting in a paradigm shift in the field.

Accuracy in retinal vessel segmentation methods can still be improved, and ground truth design remains a significant challenge. The impact of the number of annotators on accuracy and ground truth design are ongoing discussions within the medical image analysis community.

Determining the quantitative superiority of deep learning over non-DL methods is complex due to the diverse datasets, criteria, and testing protocols used across different papers. While deep learning has demonstrated superior performance in the context of the STARE dataset, the distinction between DL and non-DL techniques is less evident when examining the DRIVE dataset.

In conclusion, although deep learning has not yet demonstrated significant improvement in accuracy for retinal vessel detection using the DRIVE and STARE datasets, drawing definitive conclusions is challenging due to the analysis's limitations. Further research is needed to address these challenges and advance the field of medical imaging technology.

6. Conclusion

Advancements in medical diagnosis have led to improved methodologies for examining human anatomy, such as retinal vessel segmentation and categorization, which is essential for diagnosing and evaluating retinal and microvascular disorders (Fauw et al., 2018; Moccia et al., 2018). Machine learning and deep learning-driven methodologies have greatly improved the efficiency of retinal vessel examination through the development of tools like VAMPIRE, SIVA, IVAN, QUARTZ, and ARIA.

Despite the availability of imaging resources, such as the UK Biobank, generating sufficient annotations remains a challenge (De Fauw et al., 2018). Addressing this issue is crucial for automating retinal vessel detection and classification. Research focusing on reducing annotation requirements has the potential to revolutionize this field by providing more comprehensive evaluations of the entire system.

As retinal vessel segmentation progresses, it's important to reassess what constitutes a "reasonably well-solved" problem based on real-world applications, rather than solely on restricted test sets. This shift requires evaluating a method's effectiveness not only on specific validation metrics but also on its actual impact on healthcare outcomes in practice. As the global discourse on this subject develops, it will be interesting to observe how validation paradigms adjust to this novel perspective. Ultimately, the validation of a technique should focus on its impact on healthcare outcomes and its ability to enhance real-world healthcare applications.

Open Issues

From more accurate diagnoses to streamlined procedures machine learning technology is revolutionizing the field of ophthalmology in many ways - particularly when it comes to improving eye exam accuracy with greater efficiency. One exciting application involves retinal vessel segmentation - an area that has challenged researchers for years. Fortunately, there's been measurable progress as a result of innovating Convolutional Neural Networks (CNNs) with Conditional Random Fields (CRFs). This led to developing DeepVessel – a dynamic tool that's undergone extensive testing and validation on datasets such as DRIVE, STARE, and CHASE that showcase its immense potential for breakthroughs in this area. One limiting factor with previous methods developed by Marin et al. (2010) or Nguyen et al.(2013) was their failure to provide distinct representations owing to susceptibility interference from pathological regions – however DL based techniques using CNNs have proven themselves time and again through improved image classification and semantic segmentation capabilities across diverse scenarios – as documented by leading researchers like Xie et al. (2015). To conclude our examination of approaches for solving problems related to electronic vision challenges like retinal vessel segmentation we must consider which methodology is most suitable for this task. Although conventional techniques may offer benefits, they can be hindered by their inability to produce precise representations free from interference stemming from abnormal regions. Alternatively deep learning excels at creating highly distinct representations which make it an ideal solution for this particular task. As such utilizing deep learning technology appears to be the most effective strategy for tackling these kinds of difficulties within electronic vision applications.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest is declared for all authors.

References

[1] Ahmad, M. T., Zhang, P., Dufresne, C., Ferrucci, L., & Semba, R. D. (2018). The human eye proteome project: updates on an emerging proteome. Proteomics, 18(5-6), 1700394.

[2] Asiri, N., Hussain, M., Al Adel, F., &Alzaidi, N. (2019). Deep learning based computer-aided diagnosis systems for diabetic retinopathy: A survey. Artificial intelligence in medicine, 99, 101701.

[3] Brosch, T., Tang, L. Y., Yoo, Y., Li, D. K., Traboulsee, A., & Tam, R. (2016). Deep 3D convolutional encoder networks with shortcuts for multiscale feature integration applied to multiple sclerosis lesion segmentation. IEEE transactions on medical imaging, 35(5), 1229-1239.

[4] Çiçek, Ö., Abdulkadir, A., Lienkamp, S. S., Brox, T., &Ronneberger, O. (2016). 3D U-Net: learning dense volumetric segmentation from sparse annotation. In Medical Image Computing and Computer-Assisted Intervention–MICCAI 2016: 19th International Conference, Athens, Greece, October 17-21, 2016, Proceedings, Part II 19 (pp. 424-432). Springer International Publishing.

[5] Dai, L., Wu, L., Li, H., Cai, C., Wu, Q., Kong, H., ... & Jia, W. (2021). A deep learning system for detecting diabetic retinopathy across the disease spectrum. Nature communications, 12(1), 3242.

[6] Dasgupta, A., & Singh, S. (2017, April). A fully convolutional neural network based structured prediction approach towards the retinal vessel segmentation. In 2017 IEEE 14th international symposium on biomedical imaging (ISBI 2017) (pp. 248-251). IEEE.

[7] Dash, J., Bhoi, N., dec 2017. A thresholding based technique to extract retinal blood vessels from fundus images. Future Computing and Informatics Journal 2 (2), 103 109.

[8] De Fauw, J., Ledsam, J. R., Romera-Paredes, B., Nikolov, S., Tomasev, N., Blackwell, S., ... &Ronneberger, O. (2018). Clinically applicable deep learning for diagnosis and referral in retinal disease. Nature medicine, 24(9), 1342-1350.

[9] De Vos, B. D., Wolterink, J. M., De Jong, P. A., Viergever, M. A., &Išgum, I. (2016, March). 2D image classification for 3D anatomy localization: employing deep convolutional neural networks. In Medical imaging 2016: Image processing (Vol. 9784, pp. 517-523). SPIE.

[10] Drozdzal, M., Vorontsov, E., Chartrand, G., Kadoury, S., & Pal, C. (2016). The importance of skip connections in biomedical image segmentation. In International Workshop on Deep Learning in Medical Image Analysis, International Workshop on Large-Scale Annotation of Biomedical Data and Expert Label Synthesis (pp. 179-187). Springer, Cham.

[11] Eftekhari, N., Pourreza, H. R., Masoudi, M., Ghiasi-Shirazi, K., &Saeedi, E. (2019). Microaneurysm detection in fundus images using a two-step convolutional neural network. Biomedical engineering online, 18, 1-16.

[12] Esteva, A., Kuprel, B., Novoa, R. A., Ko, J., Swetter, S. M., Blau, H. M., &Thrun, S. (2017). Dermatologist-level classification of skin cancer with deep neural networks. nature, 542(7639), 115-118.

[13] Farokhian, F., Yang, C., Demirel, H., Wu, S., Beheshti, I., 2017. Automatic parameters selection of gabor filters with the imperialism competitive algorithm with application to retinal vessel segmentation. Biocybernetics and Biomedical Engineering 37 (1), 246 254.

[14] Fathi, A., &Naghsh-Nilchi, A. R. (2014). General rotation-invariant local binary patterns operator with application to blood vessel detection in retinal images. Pattern Analysis and Applications, 17, 69-81.

[15] Fu, H., Xu, Y., Lin, S., Kee Wong, D. W., & Liu, J. (2016). Deepvessel: Retinal vessel segmentation via deep learning and conditional random field. In Medical Image Computing and Computer-Assisted Intervention–MICCAI 2016: 19th International Conference, Athens, Greece, October 17-21, 2016, Proceedings, Part II 19 (pp. 132-139). Springer International Publishing.

[16] Gao, X., Lin, S., & Wong, T. Y. (2015). Automatic feature learning to grade nuclear cataracts based on deep learning. IEEE Transactions on Biomedical Engineering, 62(11), 2693-2701.

[17] Ghafoorian, M., Mehrtash, A., Kapur, T., Karssemeijer, N., Marchiori, E., Pesteie, M., ... & Wells, W. M. (2017). Transfer learning for domain adaptation in MRI: Application in brain lesion segmentation. In Medical Image Computing and Computer Assisted Intervention– MICCAI 2017: 20th International Conference, Quebec City, QC, Canada, September 11-13, 2017, Proceedings, Part III 20 (pp. 516-524). Springer International Publishing.

[18] Gu, H., Guo, Y., Gu, L., Wei, A., Xie, S., Ye, Z., ... & Hong, J. (2020). Deep learning for identifying corneal diseases from ocular surface slit-lamp photographs. Scientific reports, 10(1), 17851.

[19] Gulshan V, Peng L, Coram M, Stumpe MC, Wu D, Narayanaswamy A, Venugopalan S, Widner K, Madams T, Cuadros J, Kim R, Raman R, Nelson PC, Mega JL, Webster DR. Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs. JAMA. 2016 Dec 13;316(22):2402-2410.

[20] Gulshan, V., Rajan, R. P., Widner, K., Wu, D., Wubbels, P., Rhodes, T., ... & Webster, D. R. (2019). Performance of a deep-learning algorithm vs manual grading for detecting diabetic retinopathy in India. JAMA ophthalmology, 137(9), 987-993.

[21] Guo, Y., Budak, Ü., Vespa, L. J., Khorasani, E., &Şengür, A. (2018). A retinal vessel detection approach using convolution neural network with reinforcement sample learning strategy. Measurement, 125, 586-591.

[22] Hassan, G., &Hassanien, A. E. (2018). Retinal fundus vasculature multilevel segmentation using whale optimization algorithm. Signal, Image and Video Processing, 12(2), 263-270.

[23] Jiang, Z., Yepez, J., An, S., Ko, S., 2017. Fast, accurate and robust retinal vessel segmentation system. Biocybernetics and Biomedical Engineering 37 (3), 412 421.

[24] Jomier, J., Wallace, D. K., & Aylward, S. R. (2003). Quantification of retinopathy of prematurity via vessel segmentation. In Medical Image Computing and Computer-Assisted Intervention-MICCAI 2003: 6th International Conference, Montréal, Canada, November 15-18, 2003. Proceedings 6 (pp. 620-626). Springer Berlin Heidelberg.

[25] Joskowicz, L., Cohen, D., Caplan, N., Sosna, J., 2019. Inter-observer variability of manual contour delineation of structures in ct. European radiology 29 (3), 1391 1399.

[26] Kamnitsas, K., Ledig, C., Newcombe, V. F., Simpson, J. P., Kane, A. D., Menon, D. K., ... &Glocker, B. (2017). Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation. Medical image analysis, 36, 61-78.

[27] L Srinidhi, C., Aparna, P., &Rajan, J. (2017). Recent advancements in retinal vessel segmentation. Journal of medical systems, 41, 1-22.

[28] Litjens, G., Kooi, T., Bejnordi, B. E., Setio, A. A. A., Ciompi, F., Ghafoorian, M., ... & Sánchez, C. I. (2017). A survey on deep learning in medical image analysis. Medical image analysis, 42, 60-88.

[29] Lo, S. C., Lou, S. L., Lin, J. S., Freedman, M. T., Chien, M. V., & Mun, S. K. (1995). Artificial convolution neural network techniques and applications for lung nodule detection. IEEE transactions on medical imaging, 14(4), 711-718.

[30] Luo, Y., Yang, L., Wang, L., & Cheng, H. (2017). Efficient CNN-CRF network for retinal image segmentation. In Cognitive Systems and Signal Processing: Third International Conference, ICCSIP 2016, Beijing, China, November 19–23, 2016, Revised Selected Papers 3 (pp. 157-165). Springer Singapore.

[31] Mahapatra, D. (2016, October). Retinal image quality classification using neurobiological models of the human visual system. In Ophthalmic Medical Image Analysis International Workshop (Vol. 3, No. 2016). University of Iowa.

[32] Mahum, R., Rehman, S. U., Okon, O. D., Alabrah, A., Meraj, T., & Rauf, H. T. (2021). A novel hybrid approach based on deep CNN to detect glaucoma using fundus imaging. Electronics, 11(1), 26.

[33] Maier-Hein, L., Eisenmann, M., Reinke, A., Onogur, S., Stankovic, M., Scholz, P., Arbel, T., Bogunovic, H., Bradley, A. P., Carass, A., et al., 2018a. Why rankings of biomedical image analysis competitions should be interpreted with care. Nature communications 9 (1), 5217.

[34] Marín, D., Aquino, A., Gegúndez-Arias, M. E., & Bravo, J. M. (2010). A new supervised method for blood vessel segmentation in retinal images by using gray-level and moment invariants-based features. IEEE Transactions on medical imaging, 30(1), 146-158.

[35] Memari, N., Ramli, A. R., Bin Saripan, M. I., Mashohor, S., &Moghbel, M. (2017). Supervised retinal vessel segmentation from color fundus images based on matched filtering and AdaBoost classifier. PloS one, 12(12), e0188939.

[36] Milletari, F., Navab, N., & Ahmadi, S. A. (2016, October). V-net: Fully convolutional neural networks for volumetric medical image segmentation. In 2016 fourth international conference on 3D vision (3DV) (pp. 565-571). Ieee.

[37] Moccia, S., De Momi, E., El Hadji, S., & Mattos, L. S. (2018). Blood vessel segmentation algorithms—review of methods, datasets and evaluation metrics. Computer methods and programs in biomedicine, 158, 71-91.

[38] Moccia, S., De Momi, E., El Hadji, S., Mattos, L. S., 2018. Blood vessel segmentation algorithms-review of methods, datasets and evaluation metrics. Computer methods and programs in biomedicine 158, 71 91.

[39] Mohamed AA, Berg WA, Peng H, Luo Y, Jankowitz RC, Wu S. A deep learning method for classifying mammographic breast density categories. Med Phys. 2018 Jan;45(1):314-321. doi: 10.1002/mp.12683. Epub 2017 Dec 22. PMID: 29159811; PMCID: PMC5774233.

[40] Mookiah, M. R. K., Hogg, S., MacGillivray, T. J., Prathiba, V., Pradeepa, R., Mohan, V., ... & Trucco, E. (2021). A review of machine learning methods for retinal blood vessel segmentation and artery/vein classification. Medical Image Analysis, 68, 101905.

[41] Neto, L. C., Ramalho, G. L., Neto, J. F. R., Veras, R. M., & Medeiros, F. N. (2017). An unsupervised coarse-to-fine algorithm for blood vessel segmentation in fundus images. Expert Systems with Applications, 78, 182-192.

[42] Nguyen, U. T., Bhuiyan, A., Park, L. A., Ramamohanarao, K., 2013. An effective retinal blood vessel segmentation method using multi-scale line detection. Pattern recognition 46 (3), 703 715.

[43] Oliveira, A., Pereira, S., & Silva, C. A. (2018). Retinal vessel segmentation based on fully convolutional neural networks. Expert Systems with Applications, 112, 229-242.

[44] Park, K. B., Choi, S. H., & Lee, J. Y. (2020). M-GAN: Retinal blood vessel segmentation by balancing losses through stacked deep fully convolutional networks. IEEE Access, 8, 146308-146322.

[45] Pereira, S., Pinto, A., Alves, V., & Silva, C. A. (2016). Brain tumor segmentation using convolutional neural networks in MRI images. IEEE transactions on medical imaging, 35(5), 1240-1251.

[46] Reiter, G. S., Schwarzenbacher, L., Schartmüller, D., Röggla, V., Leydolt, C., Menapace, R., ... &Sacu, S. (2021). Influence of lens opacities and cataract severity on quantitative fundus autofluorescence as a secondary outcome of a randomized clinical trial. Scientific Reports, 11(1), 12685.

[47] Ronneberger, O., Fischer, P., &Brox, T. (2015). U-net: Convolutional networks for biomedical image segmentation. In Medical Image Computing and Computer-Assisted Intervention–MICCAI 2015: 18th International Conference, Munich, Germany, October 5-9, 2015, Proceedings, Part III 18 (pp. 234-241). Springer International Publishing.

[48] Roychowdhury, S., Koozekanani, D. D., &Parhi, K. K. (2014). Blood vessel segmentation of fundus images by major vessel extraction and subimage classification. IEEE journal of biomedical and health informatics, 19(3), 1118-1128.

[49] Schlegl, T., Waldstein, S. M., Vogl, W. D., Schmidt-Erfurth, U., &Langs, G. (2015, June). Predicting semantic descriptions from medical images with convolutional neural networks. In Information Processing in Medical Imaging: 24th International Conference, IPMI 2015, Sabhal MorOstaig, Isle of Skye, UK, June 28-July 3, 2015, Proceedings (pp. 437-448). Cham: Springer International Publishing.

[50] Socher, R., Huval, B., Bath, B., Manning, C. D., & Ng, A. (2012). Convolutional-recursive deep learning for 3d object classification. Advances in neural information processing systems, 25.

[51] Srinidhi, C. L., Aparna, P., &Rajan, J. (2018). A visual attention guided unsupervised feature learning for robust vessel delineation in retinal images. Biomedical Signal Processing and Control, 44, 110-126.

[52] Strisciuglio, N., Azzopardi, G., Vento, M., &Petkov, N. (2016). Supervised vessel delineation in retinal fundus images with the automatic selection of B-COSFIRE filters. Machine Vision and Applications, 27, 1137-1149.

[53] Tan, J. H., Acharya, U. R., Chua, K. C., Cheng, C., Laude, A., 2016. Automated extraction of retinal vasculature. Medical physics 43 (5), 2311 2322.

[54] Tong, Y., Lu, W., Yu, Y., & Shen, Y. (2020). Application of machine learning in ophthalmic imaging modalities. Eye and Vision, 7(1), 1-15.

[55] Valdez-Rodríguez, J. E., Felipe-Riverón, E. M., & Calvo, H. (2021). Optic disc preprocessing for reliable glaucoma detection in small datasets. Mathematics, 9(18), 2237.

[56] Veena, H. N., Muruganandham, A., &Kumaran, T. S. (2022). A novel optic disc and optic cup segmentation technique to diagnose glaucoma using deep learning convolutional neural network over retinal fundus images. Journal of King Saud University-Computer and Information Sciences, 34(8), 6187-6198.

[57] Wang, S., Yin, Y., Cao, G., Wei, B., Zheng, Y., & Yang, G. (2015). Hierarchical retinal blood vessel segmentation based on feature and ensemble learning. Neurocomputing, 149, 708-717.

[58] Worrall, D. E., Wilson, C. M., &Brostow, G. J. (2016). Automated retinopathy of prematurity case detection with convolutional neural networks. In Deep Learning and Data Labeling for Medical Applications: First International Workshop, LABELS 2016, and Second International Workshop, DLMIA 2016, Held in Conjunction with MICCAI 2016, Athens, Greece, October 21, 2016, Proceedings 1 (pp. 68-76). Springer International Publishing.

[59] Xie, S., & Tu, Z. (2015). Holistically-nested edge detection. In Proceedings of the IEEE international conference on computer vision (pp. 1395-1403).

[60] Xu, C., Zhu, X., He, W., Lu, Y., He, X., Shang, Z., ... & Li, X. (2019). Fully deep learning for slit-lamp photo based nuclear cataract grading. In Medical Image Computing and Computer Assisted Intervention–MICCAI 2019: 22nd International Conference, Shenzhen, China, October 13–17, 2019, Proceedings, Part IV 22 (pp. 513-521). Springer International Publishing.

[61] Xu, X., Tan, T., &Xu, F. (2018). An improved U-net architecture for simultaneous arteriole and venule segmentation in fundus image. In Medical Image Understanding and Analysis: 22nd Conference, MIUA 2018, Southampton, UK, July 9-11, 2018, Proceedings 22 (pp. 333-340). Springer International Publishing.

[62] Xu, Z., Zou, B., &Liu, Q. (2023). A deep retinal image quality assessment network with salient structure priors. Multimedia Tools and Applications, 1-24.

[63] Yan, Z., Yang, X., & Cheng, K. T. (2018b). Joint segment-level and pixel-wise losses for deep learning based retinal vessel segmentation. IEEE Transactions on Biomedical Engineering, 65(9), 1912-1923.

[64] Yang, D., Zhang, S., Yan, Z., Tan, C., Li, K., & Metaxas, D. (2015, April). Automated anatomical landmark detection on distal femur surface using convolutional neural network. In 2015 IEEE 12th international symposium on biomedical imaging (ISBI) (pp. 17-21). IEEE.

[65] Zhang, X., Liu, J., Wang, S., Chen, Z., Huang, B., & Ye, J. (2019). Lightweight cascade framework for optic disc segmentation. IET Image Processing, 13(10), 1805-1810.

[66] Zilly, J., Buhmann, J. M., & Mahapatra, D. (2017). Glaucoma detection using entropy sampling and ensemble learning for automatic optic cup and disc segmentation. Computerized Medical Imaging and Graphics, 55, 28-41.

[67]