

Deep Learning in Age-Related Macular Degeneration Diagnosis

Manas Joshi¹, Atishay Tibrewal¹

¹Full Vision AI

Abstract - *The diagnosis of Age-Related Macular Degeneration (AMD), a leading cause of vision loss in older adults, is undergoing a transformative shift with the advent of deep learning technologies. This paper aims to provide a comprehensive overview of the current state and future potential of applying deep learning algorithms, particularly Convolutional Neural Networks (CNNs), in AMD diagnosis. The paper explores the technological advancements in deep learning algorithms and their significant impact on clinical practices, including the potential for faster, more accurate, and more accessible diagnoses. It also delves into the ethical and legal challenges that accompany these advancements, such as data privacy concerns, the interpretability of deep learning models, and issues related to healthcare equity. Furthermore, the paper discusses existing challenges like data scarcity, computational resource limitations, and the complexities of integrating these technologies into existing healthcare systems. Recommendations are provided for researchers, clinicians, and policymakers to navigate the multifaceted challenges and ethical considerations in this burgeoning field. The paper concludes that while deep learning technologies offer immense promise for revolutionizing AMD diagnosis, careful and responsible implementation is crucial for maximizing benefits and minimizing risks.*

Key Words: Age-Related Macular Degeneration (AMD), Deep Learning, Convolutional Neural Networks (CNNs), Medical Imaging, Healthcare Equity

1. INTRODUCTION

Age-Related Macular Degeneration (AMD) is a leading cause of vision loss among people aged 50 and older, affecting millions worldwide. This degenerative condition primarily impacts the macula, the central part of the retina responsible for sharp, central vision. The disease manifests in various forms, including dry and wet AMD, each with its unique set of challenges for diagnosis and treatment. Early diagnosis is crucial for managing AMD effectively. Traditional diagnostic methods often rely on clinical examinations, including fundus photography and optical coherence tomography (OCT). While these methods are valuable, they are not without limitations. For instance, they require specialized equipment and trained professionals, making them less accessible in remote or under-resourced settings.

Enter deep learning, a subset of machine learning that has shown remarkable promise in various fields, including healthcare. Deep learning algorithms, particularly

Convolutional Neural Networks (CNNs), have been successfully applied to image recognition tasks, making them well-suited for analysing medical images. In the context of AMD, deep learning models have demonstrated the ability to identify subtle patterns in retinal images that may be overlooked by human experts. The application of deep learning in AMD diagnosis is not merely a technological advancement but a paradigm shift. Traditional methods often involve manual feature extraction, which is both time-consuming and subject to human error. In contrast, deep learning models can automatically learn features from raw data, thereby improving the accuracy and efficiency of the diagnostic process.

This paper aims to provide a comprehensive overview of the current state of deep learning applications in AMD diagnosis. We will delve into the methodologies employed, compare them with traditional diagnostic methods, and discuss the challenges and limitations of integrating deep learning into existing healthcare systems. Furthermore, we will explore case studies that highlight successful implementations and suggest future directions for this burgeoning field. The significance of this review lies in its timing. As healthcare systems worldwide grapple with an aging population, the prevalence of age-related diseases like AMD is expected to rise. Concurrently, advancements in deep learning are accelerating, offering new avenues for early and accurate diagnosis. By synthesizing the existing literature, this review aims to bridge the gap between technology and healthcare, providing insights that could inform both policy and practice.

2. BACKGROUND

The medical diagnostics environment is experiencing tremendous change, inspired by breakthroughs in computer technology and artificial intelligence. One of the most promising advancements in this field is the use of deep learning algorithms to diagnose various medical disorders, including age-related macular degeneration (AMD). This section seeks to offer a thorough understanding of deep learning basics and their application in AMD diagnosis. It will also investigate the prevalence and social consequences of AMD, laying the groundwork for a full discussion on the incorporation of deep learning technology in healthcare systems for AMD diagnosis.

2.1 Deep Learning Fundamentals

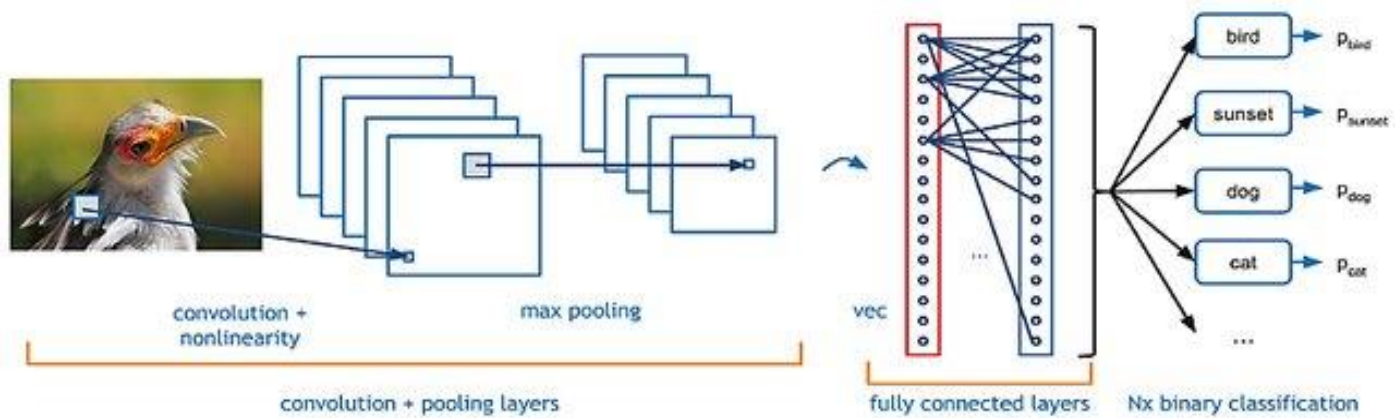


Fig 1. Deep CNN for classification [2]

Deep learning is a specialized subset of machine learning, which itself falls under the broader umbrella of artificial intelligence (AI). The term "deep" in deep learning refers to the architecture of the algorithms, which consist of multiple layers of interconnected nodes or neurons. These layers are organized in a hierarchical fashion, allowing the model to learn from data in a layered manner.

In the initial layers, the model identifies basic features in the data. For example, in image recognition tasks, the first layer might detect edges or corners. As the data progresses through the layers, the features extracted become increasingly complex. By the time the data reaches the final layers, the model is capable of recognizing intricate patterns, such as facial features in images or specific markers of diseases in medical scans.

Convolutional Neural Networks (CNNs) are a particular type of deep learning model that has gained widespread popularity, especially in tasks related to image recognition. A CNN is composed of three primary types of layers: convolutional layers, pooling layers, and fully connected layers. The convolutional layers apply a variety of filters to the input data to produce feature maps. These feature maps are simplified versions of the input data, highlighting specific features that the model considers important for the task at hand. Pooling layers follow the convolutional layers and serve to reduce the dimensions of the feature maps. This reduction makes the model more computationally efficient and helps to prevent overfitting, a common problem in machine learning where the model becomes too tailored to the training data and performs poorly on new data. The fully connected layers come after the pooling layers and serve to interpret the features extracted by the previous layers. These layers are "fully connected" because each neuron in a fully connected layer is connected to every neuron in the previous layer. This architecture allows for a high degree of interpretability and is often where the final decision or prediction is made.

Training deep learning models is a complex task that requires a large amount of labeled data. In the context of diagnosing Age-Related Macular Degeneration (AMD), this would mean having a dataset of retinal images where each image is labeled as either indicative of AMD or not. The model learns by adjusting its internal parameters to minimize the error between its predictions and the actual labels of the training data. Once the model is adequately trained, it can be used to analyze new, unlabeled data and make accurate predictions.

2.2 Age-Related Macular Degeneration Overview

Age-Related Macular Degeneration (AMD) is a degenerative eye condition that primarily affects individuals over the age of 50. It is a leading cause of vision loss in older adults and has a significant impact on the quality of life for those affected. The disease targets the macula, a small area in the center of the retina that is responsible for sharp, central vision. The macula allows us to see fine details and is crucial for tasks such as reading, driving, and recognizing faces.

AMD can manifest in two main forms: dry AMD and wet AMD. Dry AMD is the more common of the two and is characterized by the gradual thinning of the macula. As the macula thins, small yellow deposits known as drusen begin to form under the retina. Over time, these deposits can accumulate and lead to a gradual loss of central vision.

Wet AMD is less common but tends to be more severe. It is characterized by the growth of abnormal blood vessels under the retina. These new vessels are often fragile and prone to leaking, which can lead to a rapid and significant loss of central vision. The leaking can cause scarring, further exacerbating vision loss and making treatment more challenging.

Risk factors for developing AMD include age, family history, smoking, and certain lifestyle choices such as diet and exercise. While there is currently no cure for AMD, various treatments exist that can slow the progression of the disease if it is caught early. These treatments can include medications, laser therapy, and lifestyle changes.

2.3 Prevalence and Societal Impact

The increasing prevalence of AMD worldwide is a significant public health concern. Current estimates suggest that nearly 200 million people will be affected by AMD by the end of 2020, and this number is expected to rise to almost 300 million by 2040. This growing prevalence places a considerable burden on healthcare systems around the world, both in terms of the direct costs associated with treating the disease and the indirect costs related to loss of productivity and the need for caregiving.

The economic impact of AMD is substantial. The direct costs include the price of medications, surgical procedures, and ongoing medical care. The indirect costs can be even more significant, encompassing loss of productivity for those affected and their caregivers, as well as the costs associated with modifying homes and lifestyles to accommodate vision loss.

Beyond the economic factors, the psychological impact of AMD is profound. Vision loss can lead to a decreased quality of life, increased rates of depression, and other mental health issues. The loss of independence that often accompanies severe vision loss can be particularly devastating, affecting not only the individual but also their family and community.

In summary, the intersection of deep learning and AMD diagnosis represents a frontier of medical technology fraught with both opportunities and challenges. Through this review, we seek to navigate this complex landscape, offering a balanced perspective that could guide future research and implementation.

3. LITERATURE REVIEW

The integration of deep learning into the medical field, particularly in the diagnosis of Age-Related Macular Degeneration (AMD), has been the subject of numerous studies and research projects. This section aims to provide a comprehensive review of the existing literature on this subject. We will explore early attempts at automated AMD diagnosis, delve into the application of various deep learning models, and compare these advanced techniques with traditional diagnostic methods. This review will serve as a foundation for understanding the current state of the art and identifying gaps that future research could address.

3.1 Early Attempts at Automated AMD Diagnosis

Before the advent of deep learning, automated diagnosis of AMD relied on traditional machine learning algorithms and hand-crafted features. Researchers used techniques like Support Vector Machines (SVMs) and Random Forests to classify retinal images. These methods required extensive feature engineering, where experts had to manually identify and extract relevant features from retinal images. While these approaches showed promise, they were often limited by the quality and quantity of the hand-crafted features, leading to less accurate and less reliable diagnostic models.

3.2 Introduction of Deep Learning Models

The introduction of deep learning algorithms, particularly Convolutional Neural Networks (CNNs), marked a significant turning point in automated AMD diagnosis. Unlike traditional machine learning models, CNNs could automatically learn relevant features from raw image data, eliminating the need for manual feature engineering. This capability led to more accurate and reliable diagnostic models.

Several studies have explored the use of CNNs in AMD diagnosis. These studies often employed various architectures and training techniques to optimize the performance of the CNN models. For example, some studies used transfer learning, where a CNN pre-trained on a large dataset, like ImageNet, was fine-tuned on a smaller AMD-specific dataset. This approach leveraged the feature-learning capabilities of CNNs while overcoming the limitations posed by smaller medical datasets.

3.3 Comparison with Traditional Methods

One of the critical aspects of evaluating the effectiveness of deep learning models in AMD diagnosis is comparing their performance with traditional diagnostic methods. Traditional methods often involve the use of specialized imaging techniques like Optical Coherence Tomography (OCT) and fundus photography, interpreted by experienced ophthalmologists.

Several studies have conducted comparative analyses to evaluate the diagnostic accuracy, sensitivity, and specificity of deep learning models against traditional methods. The results have been promising, with deep learning models often outperforming or matching the diagnostic accuracy of expert ophthalmologists. These findings suggest that deep learning models could serve as valuable diagnostic aids, potentially speeding up the diagnostic process and even identifying cases that might be overlooked by human experts.

3.4 Challenges and Limitations

While the application of deep learning in AMD diagnosis has shown significant promise, it is not without challenges and limitations. One of the primary challenges is the need for large, labeled datasets for training the models. Medical data is often challenging to acquire due to privacy concerns and the need for expert labeling.

Another limitation is the "black box" nature of deep learning models. While these models can make accurate predictions, their decision-making process is often not transparent, making it difficult for medical professionals to trust the model's diagnosis fully. This lack of interpretability is a significant hurdle in the adoption of deep learning models in clinical settings.

3.5 Future Directions

The field of deep learning in AMD diagnosis is still evolving, with new research continually emerging. Future directions could involve the development of more interpretable models that provide insights into their decision-making process. Another avenue could be the integration of deep learning models into existing healthcare systems, allowing for real-time analysis of medical images.

Moreover, future research could explore the use of other types of deep learning models, such as Recurrent Neural Networks (RNNs) and Generative Adversarial Networks (GANs), in AMD diagnosis. These models offer different capabilities and could provide new perspectives on automated diagnosis.

4. METHODOLOGIES

The methodologies employed in the application of deep learning for diagnosing Age-Related Macular Degeneration (AMD) are as diverse as they are innovative. This section aims to dissect these methodologies in detail, focusing on data collection techniques, the types of deep learning algorithms used, and the evaluation metrics commonly applied. Understanding these methodologies is crucial for both replicating existing studies and developing new approaches that could advance the field.

4.1 Data Collection Techniques

Data serves as the backbone of any deep learning model, and its quality and quantity directly influence the model's performance. In the context of AMD diagnosis, the primary types of data used are retinal images, obtained through various imaging techniques.

4.1.1 Imaging Methods

Optical Coherence Tomography (OCT) and fundus photography are the most commonly used imaging methods for capturing retinal images. OCT provides cross-sectional

images of the retina, offering a detailed view of its layers, while fundus photography captures a more general, top-down view of the retina. Both imaging techniques have their advantages and disadvantages. OCT offers higher resolution but is more expensive and less widely available than fundus photography.

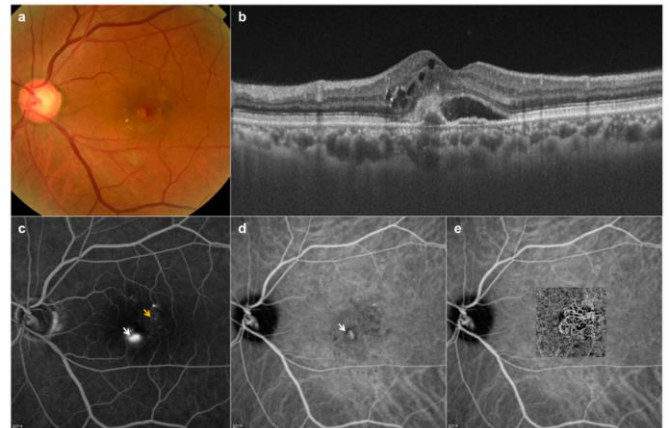


Fig -1: Multimodal images of neovascular age-related macular degeneration in a 61-year-old man[3]

4.1.2 Data Preprocessing

Before feeding the retinal images into a deep learning model, they often undergo preprocessing to enhance their quality and make them more suitable for analysis. Common preprocessing steps include image resizing, normalization, and augmentation. Image augmentation techniques such as rotation, flipping, and zooming are used to artificially increase the size of the dataset, thereby improving the model's ability to generalize to new data.

4.2 Deep Learning Algorithms

The choice of deep learning algorithm is a critical factor in the development of automated AMD diagnosis systems. While Convolutional Neural Networks (CNNs) are the most commonly used, other types of deep learning algorithms have also been explored.

Table -1: Summary of Key Deep Learning Algorithms

Algorithm Type	Common Architectures	Advantages
CNNs	AlexNet, VGG, ResNet	High accuracy in image classification, automatic feature extraction
RNNs	LSTM, GRU	Good for sequence data, can model time-series changes in AMD progression

GANs	DCGAN, CycleGAN	Can generate new data for training, useful for data augmentation
------	--------------------	--

4.2.1 Convolutional Neural Networks (CNNs)

CNNs are especially effective for image recognition tasks, making them the go-to choice for most studies in AMD diagnosis. Various architectures, such as AlexNet, VGG, and ResNet, have been employed, each with its unique configuration of layers and neurons. Some studies have also developed custom CNN architectures tailored to the specific challenges posed by AMD diagnosis.

4.2.2 Other Deep Learning Models

While CNNs dominate the field, other deep learning models like Recurrent Neural Networks (RNNs) and Generative Adversarial Networks (GANs) have also been explored. RNNs are particularly useful for analyzing sequences and could be applied to time-series data, such as tracking the progression of AMD over time. GANs, on the other hand, are adept at generating new data and could be used for data augmentation or even for simulating how AMD might progress in a particular patient.

4.3 Evaluation Metrics

Evaluating the performance of a deep learning model in AMD diagnosis involves several metrics, each providing different insights into the model's capabilities.

4.3.1 Accuracy

Accuracy is the most straightforward metric, representing the proportion of correctly classified images. While a useful starting point, accuracy alone is often insufficient for medical applications where both false positives and false negatives can have serious consequences.

4.3.2 Sensitivity and Specificity

Sensitivity (or True Positive Rate) measures the model's ability to correctly identify positive cases, while Specificity (or True Negative Rate) measures the ability to correctly identify negative cases. In the context of AMD diagnosis, high sensitivity is crucial to ensure that patients with AMD are not missed, while high specificity is essential to avoid unnecessary treatments or further tests.

4.3.3 Area Under the ROC Curve (AUC-ROC)

The AUC-ROC is a comprehensive metric that considers both the sensitivity and specificity of the model. A model with an AUC-ROC close to 1 is considered excellent, while an AUC-ROC close to 0.5 indicates no discriminative power.

5. DISCUSSION AND IMPLICATIONS

The burgeoning field of deep learning in healthcare has opened up new vistas for diagnosing and treating a variety of medical conditions. One of the most promising applications lies in the diagnosis of Age-Related Macular Degeneration (AMD), a leading cause of vision loss in older adults. While the potential benefits are enormous, the integration of deep learning into the medical diagnostic process also presents a host of challenges and ethical considerations. This section aims to delve into these aspects, offering a nuanced discussion on the broader implications, challenges, and future directions.

5.1 Clinical Implications

The clinical implications of applying deep learning to AMD diagnosis are both profound and transformative.

5.1.1 Speed and Efficiency

Firstly, the speed and efficiency offered by deep learning models are unparalleled. Traditional diagnostic methods often involve a series of tests and evaluations that can be both time-consuming and subject to human error. Deep learning models can analyze complex retinal images in seconds, providing immediate results. This rapid diagnosis is not just a matter of convenience; it could be life-changing in scenarios where early detection and treatment are crucial for preventing severe vision loss.

5.1.2 Accessibility

Secondly, the accessibility of diagnostic services could be significantly improved. Specialized ophthalmological services are often centralized in urban centers, making them less accessible to rural populations. Deep learning models can be deployed in remote healthcare centers, enabling more widespread screening for AMD. This democratization of healthcare services could be a game-changer for global public health, particularly in low-income countries where healthcare resources are scarce.

5.1.3 Precision Medicine

Lastly, the advent of deep learning in AMD diagnosis could herald a new era of precision medicine. The granularity of data that these models can analyze allows for a more nuanced understanding of the disease. This could lead to more personalized treatment plans, optimized for individual patient characteristics, thereby improving the efficacy of treatments and potentially reducing healthcare costs.

5.2 Ethical and Legal Considerations

The ethical and legal landscape surrounding the use of AI in healthcare is still evolving, and several critical issues must be addressed.

5.2.1 Data Privacy

The collection and storage of medical data for training deep learning models present significant data privacy challenges. Medical data is sensitive by nature, and the risk of data breaches or unauthorized access is a constant concern. Strict protocols for data encryption and anonymization must be in place, and compliance with regulations such as the Health Insurance Portability and Accountability Act (HIPAA) in the United States or the General Data Protection Regulation (GDPR) in Europe is essential.

5.2.2 Interpretability

Another ethical quandary is the interpretability, or lack thereof, of deep learning models. The so-called "black box" nature of these models makes it difficult to understand how they arrive at a particular diagnosis. This opacity can be a significant barrier to clinical adoption, as medical professionals may be hesitant to rely on a system whose workings they do not fully understand. Efforts are underway in the field of explainable AI to make these models more transparent, but much work remains to be done.

5.2.3 Equity and Inclusion

The issue of equity and inclusion cannot be overlooked. Deep learning models are only as good as the data they are trained on. If the training data lacks diversity, the model may perform poorly on underrepresented groups, exacerbating existing healthcare disparities. Ensuring that training datasets are diverse and representative is crucial for the equitable delivery of healthcare services.

5.3 Challenges and Limitations

While the promise of deep learning in AMD diagnosis is tantalizing, the path to its widespread clinical adoption is fraught with challenges.

5.3.1 Data Scarcity and Quality

One of the most pressing challenges is the scarcity of high-quality, labeled data. Deep learning models require large datasets for training, and in the medical field, such datasets are often difficult to come by. Even when data is available, it may be imbalanced, with far more examples of one class than another, leading to biased models.

5.3.2 Computational Resources

The computational intensity of training and deploying deep learning models is another significant hurdle. These models require specialized hardware, such as Graphics Processing Units (GPUs), which may not be readily available in all healthcare settings. This limitation is particularly relevant for low-resource environments where the need for advanced diagnostic tools is often the greatest.

5.3.3 Clinical Integration

The integration of deep learning models into existing clinical workflows is a complex undertaking. It's not just a matter of plugging in a new piece of software; it involves a complete rethinking of diagnostic protocols, staff training, and patient engagement. The human element of this integration cannot be underestimated; healthcare professionals must be comfortable with these new tools for them to be effectively utilized.

6. CONCLUSION AND RECOMMENDATIONS

The application of deep learning in the diagnosis of Age-Related Macular Degeneration (AMD) represents a transformative shift in healthcare, offering the potential for rapid, accurate, and accessible diagnostic services. However, as we have discussed in the preceding sections, this promising landscape is not without its complexities. From technical challenges to ethical considerations, the path to widespread clinical adoption is fraught with obstacles that require thoughtful navigation. This concluding section aims to synthesize the key points discussed in this paper and offer recommendations for future research, clinical practice, and policy-making.

6.1 Summary of Key Points

Before delving into the recommendations, it's essential to summarize the key points that have emerged from this review.

6.1.1 Technological Advancements

The technological advancements in deep learning algorithms, particularly Convolutional Neural Networks (CNNs), have revolutionized the field of medical imaging. These algorithms can automatically learn features from raw image data, eliminating the need for manual feature engineering and significantly improving diagnostic accuracy.

6.1.2 Clinical Implications

The clinical implications are profound, with the potential for faster diagnoses, greater accessibility of services, and the advent of more personalized treatment plans. These benefits could significantly improve patient outcomes and make healthcare more efficient and cost-effective.

6.1.3 Ethical and Legal Challenges

However, the ethical and legal challenges are equally significant. Issues surrounding data privacy, model interpretability, and healthcare equity must be carefully considered to ensure responsible and fair implementation.

6.1.4 Existing Challenges

The existing challenges, such as data scarcity, computational resource requirements, and the complexities of clinical integration, are substantial but not insurmountable. Ongoing research and technological advancements are continually providing new solutions to these challenges.

6.2 Recommendations

Based on the insights gained from this review, several recommendations can be made for different stakeholders involved in this field.

6.2.1 For Researchers

Interdisciplinary Collaboration: Researchers in computer science, ophthalmology, ethics, and law should collaborate to address the multifaceted challenges in this field.

Focus on Explainable AI: Research should be directed towards making deep learning models more interpretable to gain the trust of medical professionals and patients alike.

Diverse Data Collection: Efforts should be made to collect diverse and representative datasets to train models that are equitable and unbiased.

6.2.2 For Clinicians

Continued Education: Clinicians should stay updated on the latest advancements in AI and medical imaging to effectively integrate these technologies into their practice.

Patient Engagement: Clear communication with patients about the role of AI in their diagnosis and treatment is essential for gaining patient trust and informed consent.

Ethical Vigilance: Clinicians should be vigilant about the ethical implications of using AI, particularly concerning data privacy and healthcare equity.

6.2.3 For Policy Makers

Regulatory Frameworks: Comprehensive regulatory frameworks should be developed to govern the use of AI in healthcare, focusing on data privacy, model transparency, and healthcare equity.

Funding and Resources: Adequate funding should be allocated for research and implementation of AI in healthcare, with a focus on making these technologies accessible to underserved populations.

Public Awareness: Public awareness campaigns should be conducted to educate people about the benefits and limitations of AI in healthcare, thereby fostering a more informed public discourse.

6.3 Future Outlook

The future of deep learning in AMD diagnosis is incredibly promising but requires a concerted effort from all stakeholders to realize its full potential. As technology continues to advance, the focus should shift towards creating more robust, interpretable, and equitable models. Long-term studies are needed to assess the real-world impact of these technologies on patient outcomes and healthcare systems.

Moreover, as the global population continues to age, the prevalence of AMD is expected to rise, making the need for effective diagnostic tools more urgent than ever. Deep learning models offer a viable solution to this growing challenge, but their responsible and equitable implementation is crucial.

6.4 Final Thoughts

In conclusion, the application of deep learning in the diagnosis of Age-Related Macular Degeneration represents a significant leap forward in medical technology. The potential benefits are enormous, from improving the speed and accuracy of diagnoses to making healthcare more accessible and personalized. However, these advancements come with their own set of challenges and ethical considerations that must be carefully navigated. Through interdisciplinary collaboration, continued research, and thoughtful policy-making, we can overcome these challenges and usher in a new era of healthcare that is more efficient, equitable, and patient-centered.

REFERENCES

- [1] Saritha, R., Paul, V., & Kumar, P. G. (2018). Content based image retrieval using deep learning process. *Cluster Computing*, 22(S2), 4187–4200. <https://doi.org/10.1007/s10586-018-1731-0>
- [2] Kaplanoglou, Pantelis. (2017). Content-Based Image Retrieval using Deep Learning. 10.13140/RG.2.2.29510.16967.
- [3] Heo, T. Y., Kim, K. M., Min, H. K., Gu, S. M., Kim, J. H., Yun, J., & Min, J. K. (2020). Development of a Deep-Learning-Based Artificial Intelligence Tool for Differential Diagnosis between Dry and Neovascular Age-Related Macular Degeneration. *Diagnostics (Basel, Switzerland)*, 10(5), 261. <https://doi.org/10.3390/diagnostics10050261>
- [4] Burlina, P., Joshi, N., Pacheco, K. D., Freund, D., Kong, J., & Bressler, N. M. (2018). Use of deep learning for detailed severity characterization and estimation of 5-Year risk among patients with Age-Related Macular degeneration. *JAMA Ophthalmology*, 136(12), 1359. <https://doi.org/10.1001/jamaophthmol.2018.4118>

- [5] Chen, Y., Lin, Z., Zhao, X., Wang, G., & Gu, Y. (2014). Deep Learning-Based Classification of Hyperspectral data. *IEEE Journal of Selected Topics in Applied Earth Observations and Remote Sensing*, 7(6), 2094–2107. <https://doi.org/10.1109/jstars.2014.2329330>
- [6] Graßmann, F., Mengelkamp, J., Brandl, C., Harsch, S., Zimmermann, M. E., Linkohr, B., Peters, A., Heid, I. M., Palm, C., & Weber, B. H. F. (2018). A Deep Learning Algorithm for Prediction of Age-Related Eye Disease Study Severity Scale for Age-Related Macular Degeneration from Color Fundus Photography. *Ophthalmology*, 125(9), 1410–1420. <https://doi.org/10.1016/j.ophtha.2018.02.037>
- [7] Kermany, D., Goldbaum, M. H., Cai, W., Valentim, C. C. S., Liang, H., Baxter, S. L., McKeown, A., Yang, G., Wu, X., Yan, F., Dong, J., Prasadha, M. K., Pei, J., Ting, M. Y. L., Zhu, J., Li, C., Hewett, S., Dong, J., Ziyar, I., . . . Zhang, K. (2018). Identifying medical diagnoses and treatable diseases by Image-Based Deep Learning. *Cell*, 172(5), 1122–1131.e9. <https://doi.org/10.1016/j.cell.2018.02.010>
- [8] Lee, C. S., Baughman, D., & Lee, A. (2017). Deep Learning Is Effective for Classifying Normal versus Age-Related Macular Degeneration OCT Images. *Ophthalmology Retina*, 1(4), 322–327. <https://doi.org/10.1016/j.oret.2016.12.009>
- [9] Lee, C. S., Baughman, D., & Lee, A. (2017). Deep Learning Is Effective for Classifying Normal versus Age-Related Macular Degeneration OCT Images. *Ophthalmology Retina*, 1(4), 322–327. <https://doi.org/10.1016/j.oret.2016.12.009>
- [10] Lee, C. S., Baughman, D., & Lee, A. (2017). Deep Learning Is Effective for Classifying Normal versus Age-Related Macular Degeneration OCT Images. *Ophthalmology Retina*, 1(4), 322–327. <https://doi.org/10.1016/j.oret.2016.12.009>
- [11] Litjens, G., Kooi, T., Bejnordi, B. E., Setio, A. a. A., Ciompi, F., Ghafoorian, M., Van Der Laak, J., Van Ginneken, B., & Sánchez, C. I. (2017). A survey on deep learning in medical image analysis. *Medical Image Analysis*, 42, 60–88. <https://doi.org/10.1016/j.media.2017.07.005>
- [12] Motozawa, N., An, G., Takagi, S., Kitahata, S., Mandai, M., Hirami, Y., Yokota, H., Akiba, M., Tsujikawa, A., Takahashi, M., & Kurimoto, Y. (2019). Optical Coherence Tomography-Based Deep-Learning models for classifying normal and Age-Related macular degeneration and exudative and Non-Exudative Age-Related macular degeneration changes. *Ophthalmology and Therapy*, 8(4), 527–539. <https://doi.org/10.1007/s40123-019-00207-y>
- [13] Peng, Y., Dharssi, S., Chen, Q., Keenan, T. D. L., Agrón, E., Wong, W. T., Chew, E. Y., & Lu, Z. (2019). DeepSeeNet: A Deep Learning Model for Automated Classification of Patient-based Age-related Macular Degeneration Severity from Color Fundus Photographs. *Ophthalmology*, 126(4), 565–575. <https://doi.org/10.1016/j.ophtha.2018.11.015>
- [14] Schmidhuber, J. (2015). Deep learning in neural networks: An overview. *Neural Networks*, 61, 85–117. <https://doi.org/10.1016/j.neunet.2014.09.003>
- [15] Shen, D., Wu, G., & Suk, H. (2017). Deep learning in medical image analysis. *Annual Review of Biomedical Engineering*, 19(1), 221–248. <https://doi.org/10.1146/annurev-bioeng-071516-044442>
- [16] Shin, H., Roth, H. R., Gao, M., Lü, L., Xu, Z., Nogues, I., Yao, J., Mollura, D. J., & Summers, R. M. (2016). Deep Convolutional Neural Networks for Computer-Aided Detection: CNN architectures, dataset characteristics and transfer learning. *IEEE Transactions on Medical Imaging*, 35(5), 1285–1298. <https://doi.org/10.1109/tmi.2016.2528162>
- [17] Ting, D. S. W., Cheung, C. Y., Lim, G., Tan, G. S. W., Quang, N. T., Gan, A. T. L., Hamzah, H., García-Franco, R., Yeo, I., Lee, S. Y., Wong, E., Sabanayagam, C., Baskaran, M., Ibrahim, F., Tan, N. C., Finkelstein, E. A., Lamoureux, E. L., Wong, I. Y., Bressler, N. M., . . . Wong, T. Y. (2017). Development and validation of a deep learning system for diabetic retinopathy and related eye diseases using retinal images from multiethnic populations with diabetes. *JAMA*, 318(22), 2211. <https://doi.org/10.1001/jama.2017.18152>
- [18] Treder, M., Laueremann, J. L., & Eter, N. (2017). Automated detection of exudative age-related macular degeneration in spectral domain optical coherence tomography using deep learning. *Graefes Archive for Clinical and Experimental Ophthalmology*, 256(2), 259–265. <https://doi.org/10.1007/s00417-017-3850-3>
- [19] Yim, J., Chopra, R., Spitz, T., Winkens, J., Obika, A., Kelly, C., Askham, H., Lukić, M., Huemer, J., Fasler, K., Moraes, G., Meyer, C., Wilson, M., Dixon, J. M., Hughes, C., Rees, G., Khaw, P., Karthikesalingam, A., King, D., . . . De Fauw, J. (2020). Predicting conversion to wet age-related macular degeneration using deep learning. *Nature Medicine*, 26(6), 892–899. <https://doi.org/10.1038/s41591-020-0867-7>