

人工智能辅助青光眼眼底照相筛查技术的进展

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摘 要

青光眼是全球不可逆性失明的主要原因, 其特征是视神经乳头凹陷和视野损伤。慢性青光眼通常无痛, 典型的视野缺损多出现在晚期。该疾病主要影响视神经, 如不及时干预, 可能会导致失明。因此, 早期检测和治疗对于保护患者视力至关重要。随着数字成像技术的进步, 如眼底照相机和扫描激光检眼镜 (Scanning Laser Ophthalmoscopes, SLO), 眼科专业人员能够更有效地识别青光眼。近年来, 人工智能 (Artificial Intelligence, AI) 在医学领域迅速发展, 在提升青光眼筛查效率和降低成本方面展现了巨大潜力。本文回顾了基于人工智能的彩色眼底照相技术在青光眼筛查中的最新技术进展, 探讨了当前临床实施中的挑战与发展方向。

关键词

青光眼, 人工智能, 深度学习, 彩色眼底照相, 筛查

Progress in Artificial Intelligence-Assisted Fundus Photography Screening Technology for Glaucoma

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Abstract

Glaucoma is the leading cause of irreversible blindness worldwide, characterized by optic nerve

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head cupping and visual field damage. Chronic forms of glaucoma are often painless, with symptomatic visual field defects appearing only in later stages. The disease primarily affects the optic disc, and without timely intervention, it can progressively lead to blindness. Therefore, early detection and treatment are critical to preserving patients' vision. Advances in digital imaging technologies, such as fundus cameras and Scanning Laser Ophthalmoscopes (SLO), have enabled eye care professionals to identify glaucoma more effectively. In recent years, Artificial Intelligence (AI) has rapidly evolved in the medical field, offering significant potential to enhance glaucoma screening efficiency and reduce costs. This article reviews the latest technological advancements in AI-driven color fundus photography for glaucoma screening, discusses current challenges and future directions in clinical implementation.

Keywords

Glaucoma, Artificial Intelligence, Deep Learning, Color Fundus Photography, Screening

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1. 引言

青光眼是全球首位不可逆性致盲眼病, 2013 年全球患者总数已突破 6430 万例, 根据人口老龄化趋势预测, 2040 年患病人群将增至 1.118 亿例, 增幅达 73.8% [1]。另有研究显示, 我国青光眼病例占全球 1/6。全球所有原发性闭角型青光眼患者中, 近一半为中国人[2]。尽管在过去的 20 年中, 青光眼的诊断和治疗条件有很大进步[3], 青光眼仍是世界不可逆转失明的主要原因[4] [5]。

早期青光眼是无症状的, 因此诊断十分困难[6]。研究显示, 即使是在发达国家, 也有 50 %的青光眼患者不知道自己的病情, 这一比例在我们发展中国家更高[7]。因此, 青光眼的早期诊断和干预治疗至关重要[8] [9]。唐建团队[10]通过马尔可夫模型模拟青光眼 10 年进展轨迹发现, 对中国 50 岁及以上人群进行青光眼筛查, 无论是在农村还是在城市, 都具有显著的成本效益优势。

临床诊断青光眼时, 主要依赖于眼压测量(Intraocular Pressure, IOP)、视野检查(Visual Field Test, VF)、光学相干断层扫描(Optical Coherence Tomography, OCT)对视网膜神经纤维层厚度的分析以及彩色眼底照相(Color Fundus Photography, CFP)中视盘的形态[11]。这些检查中, 眼压检查虽然快速, 但用于筛查容易漏诊, 例如一些正常眼压性青光眼的病人, 即使眼压不高也已经出现了视神经损害[12]。相比于其他检查, CFP 更容易获得且相对便宜, 获取的眼底图像不仅可用于青光眼筛查, 还能同步检测其他眼底病变, 避免了额外检查的需求, 加之随着技术进步, 还出现了可以不用散瞳的便携式相机。然而, CFP 的阅片通常存在主观性, Almazroa 对比了 6 名眼科医生对 750 幅眼底图像中视盘、视杯范围和垂直杯盘比的标注, 垂直杯盘比的一致性只有不到 45% [13]。传统的阅片方式用于筛查, 时间成本高且主观差异大, 不仅对资源依赖性强, 对检查医生的专业性要求也很高[14]。因此, 需要开发一类客观、标准化且快速的诊断工具来实现青光眼筛查的普及。

人工智能是近年来一个发展迅速的领域, 专注于开发可以模拟人类智能思维的算法, 机器学习(Machine Learning, ML)是 AI 的一个分支, 通过统计学方法使计算机系统基于经验数据自主优化任务性能, 其理论基础可追溯至 1959 年 Samuel 提出的强化学习框架[15]; 而深度学习(Deep Learning, DL)作为 ML 的进阶形态, 依赖于多层人工神经网络架构来实现复杂特征的自适应提取, 2015 年 LeCun 团队提出

的卷积神经网络(Convolutional Neural Network, CNN)标志着该技术进入成熟应用阶段[16]。AI 在青光眼筛查中的应用,不仅可以提升筛查效率,标准化筛查降低误诊率,还能弥补基层医疗资源的缺乏,已有众多研究显示其在提高效率和节约成本上的巨大潜力[17]-[19]。本文概述了 AI 利用眼底图像筛查青光眼的研究与新进展,并讨论了该技术在临床实践中应用的挑战与机遇。

2. AI 与眼底图像

2.1. 眼底图像特征提取

AI 诊断用于图像识别的核心技术在于利用深度学习算法对大规模标注医学影像数据进行训练,使模型能够自主提取病理特征,这一技术在糖尿病视网膜病变筛查中展现出了显著的临床价值[20][21]。而 AI 与青光眼的交会始于 2015 年, Lim 等人首次提出将 DL 架构用于视神经乳头(Optic Nerve Head, ONH)的分析中,开发的 CNN 算法[22]主要通过提取眼底图像中视杯视盘区域信息,而后将视杯和视盘区域分别分割提取,计算杯盘比来进行评估。在这之后,随着 DL 模型的迭代升级,不仅能通过杯盘比大小来进行筛查,还能整合盘沿其他特征进行筛查[23]-[27]。例如 Chowdhury 等人通过双阶段生成对抗网络聚焦 ONH 区域的结构重建,增强模型对青光眼特征的敏感性,提出“Rim-aware”特征提取模块,利用时空卷积捕捉视神经纤维层厚度(Retinal Nerve Fiber Layer, RNFL)随病程的动态变化,建立起不仅是关注杯盘比大小,而是以视盘边缘为主要指标的青光眼检测框架[28]。

2.2. 算法模型和技术进展

除了传统的卷积神经网络以外,基于混合卷积神经网络和多模态学习的新型算法正逐步推动青光眼诊疗的革新。Fan 团队训练的 ResNet-50 模型在高眼压症治疗研究队列中展现出高诊断准确性,证实 DL 模型有望实现原发性开角型青光眼(Primary Open-angle Glaucoma, POAG)临床试验终点的标准化与自动化评估[29]。该团队还进一步探索了视觉变换器(Vision Transformer, ViT)在青光眼筛查中的应用——相比于传统 CNN(如 ResNet-50), ViT 有着完全不同的架构设计,在外部数据集中展现出更优的泛化性能,具有更强的跨中心数据适应能力。另一点与 CNN 不同的是, ViT 生成的显著性热图与注意力分布图将注意力聚焦于视盘边缘,而 CNN 模型则呈现弥散性特征响应模式,这一特点为模型可解释性研究提供了新视角[30]。混合卷积神经网络是通过整合不同卷积架构来提升模型性能。Akbar 等人的研究发现,融合现有的 CNN 模型(如 Dense Net、DarkNet 等)可以提高诊断准确性,该组合在高分辨率眼底图像数据集中准确性可达 99.7%,但是在 RIM1 数据库验证时,特异性只有 88.46%,证明在图像质量不稳定的情况下,模型准确性仍待提高[31]。Chaurasia 等通过整合全球 20 个公共数据库的 18,468 张眼底图像,筛选并优化了 20 种预训练模型(如基于 Fastai 与 PyTorch 的架构),性能最佳模型在青光眼和健康眼的分类中的受试者工作特征曲线下面积(Areas under the receiver operating characteristic curve, AUROC)可达 0.9920,体现了 AI 在区分青光眼视盘和健康视盘方面的高效性和可靠性,然而,该模型在对边缘病例进行分类方面表现并不是很好。其次,在纳入的 20 个公共数据集中,眼底图像的分类标准并不统一,其中还不乏有错误的眼底特征标记,这种错误标记严重影响了模型性能[32]。Wu 等人设计了一个以 ImageNet 预训练的 ResNet-152 为骨干的孪生神经网络,可通过连续复查的视盘照片和 RNFL 厚度来预测视野进展,在使用来自不同 OCT 检查仪器的 RNFL 数据时, AUROC 仍可保持 0.893 [33]。这种基于多种检查手段的多模态学习算法有望在现有基础上减少由于不同品牌仪器或不同人群特征产生的影响,增强模型的泛化性。

2.3. 模型验证和临床转化

尽管 AI 模型在内部数据集验证中都表现出良好的性能,当用外部数据集进行测试时结果却并不完全

理想。临床中应用时,由设备型号差异、屈光介质混浊及拍摄操作不规范导致的图像质量参差不齐,成为了影响模型临床落地的主要障碍。针对这一挑战,De Vente 等人通过构建涵盖 60,000 患者和 500 个筛查中心的真实世界数据集,由 grand-challenge 平台发起 AIROGS 挑战,其中最佳团队的表现与 20 名专业眼科医生和验光师相似,并且在动态检测不可分级眼底图像方面尤为突出(AUROC = 0.99, 95%CI: 0.98~0.99) [34]。美中不足的是,该挑战仅侧重于基于单个 CFP 的分类,不能结合双眼图像对比分析,无法模拟临床真实场景。除此之外,Pascal 团队研发的 MTL-IO 框架,采用了多任务学习加独立优化器的设计,能够捕捉到更全面的青光眼眼底特征,在不同眼底相机来源的数据集中也可以做到 AUROC > 0.92,有效优化了模型泛化能力的同时还提升了训练效率[35]。Lin 等研究者通过模拟临床医生识别青光眼的动态过程,利用孪生 CNN 对比不同时间眼底图像特征,所构建的模型 AUROC 可达 0.9587,明显优于单数据模型,这种纵向对比眼底图像的方法,不仅增加了 AI 模型的可解释性,还为提升模型的泛化性提供了新思路[36]。

要快速有效提高 AI 模型在跨人群应用中的泛化能力,关键在于建立覆盖不同地域、种族及影像设备的多元化数据库。Shi 等人研究发现,青光眼筛查模型在不同种族和少数民族人群中准确度并不高,随即开发了 FIN 模型来调整在不同种族中各青光眼改变特征的重要性,提高了 DL 模型在不同种族中的泛化性[37]。Ran 等人则进一步考虑到受试者隐私权益,基于联邦学习范式开发了一种隐私保护的 DL 模型,每个中心先将数据集及模型参数上传至中央服务器,中央服务器采用 FedProx 算法聚合所有中心的模型参数,并将聚合后的参数重新分发给各中心以优化其本地模型。实现无须跨中心共享即可整合数据,实现泛化性能,保护患者隐私信息和数据安全[38]。针对医疗资源匮乏地区青光眼筛查的迫切需求,基于智能手机的便携式眼底照相技术也崭露头角[39]。例如国外 Rao 等人评估了智能手机眼底照相使用离线 AI 系统筛查青光眼能力,AI 系统在可诊断青光眼检测中的灵敏度和特异性可达到 93.7%和 85.6%。且在青光眼分级中表现良好[40]。国内范国团队开发的“眼宝”应用程序,在进行临床测试时也可以达到 0.7731 的总准确度[41]。

3. 挑战与争议

3.1. 诊断标准差异性

不同研究对青光眼定义存在分歧,有的使用面积杯盘比(area cup-to-disc ratio, ACDR),有的使用垂直杯盘比(vertical cup-to-disc ratio, VCDR)或者 VCDR 与其他指标的组合,如 ONH 特征和 RNFL 厚度[42]。此外,青光眼筛查的分类标准也不相同,疑似青光眼的 VCDR 临界值在 0.6 至 0.8 间波动[43][44],而确诊病例的 VCDR 中位数虽高达 0.85,但约 17%的早期病例仍低于 0.7 [45],“疑似”与“确诊”的界限模糊。由于这种不一致的存在,严重制约了模型的泛化能力和临床适用性。因此,需要建立统一的眼底图像标注标准,持续优化算法对诊断标准演变的适应能力。

3.2. 更多外部验证

尽管大量研究已经证实 AI 算法在内部数据集中可以展现出优异的筛查性能,但其在外部验证中的可靠性仍需审慎评估。研究统计发现,目前只有 26.1%的青光眼 DL 模型有外部验证,而这些外部验证数据集普遍存在着样本量不足、异质性低等缺陷[46]。缺乏外部验证的情况可能导致性能评估出现偏倚,其报告的准确性指标往往难以反映真实筛查环境中的表现[47]。要有效提升算法应对非典型眼底特征和图像质量波动的能力,需要大规模、多样化的外部数据集来进行系统性优化训练。但是由于隐私、安全和数据所有权问题,共享数据往往具有挑战性。可以通过建立隐私保护框架来促进数据共享和外部验证,除此之外,还可以尝试使用合成数据来训练 AI 模型并保护隐私。应对那些图像质量低的眼底图像,则可以

引入注意力机制解析血管形态，模拟人工阅片时通过血管形态和走向来评估杯盘比等信息，或者通过多模态数据集成分析，提高算法性能。

3.3. 提高可解释性

人工智能技术在近几年快速迭代更新，在提升医疗效率的同时，也直接导致了外行越来越难理解算法模型的运作。例如 DL 赖以决策的特征区分机制，建立在高维空间的复杂运算之上，其抽象性对于非专业人士来说实在难以把握，甚至可能超出临床医生的常规认知范畴。研究表明[48]，提升模型可解释性和算法的透明性，能有效识别数据偏差与逻辑缺陷，这对医疗 AI 在临床实践中的安全部署具有决定性意义。尤其在眼科诊疗领域，模型解释的精确性直接关乎患者健康权益。可解释的 AI 系统不仅能清晰展示诊断依据的决策路径，更能解构出影响预后的关键特征参数，不仅能优化模型，还能帮助青年医生更好识别疾病特征。这种技术与认知的良性互动，正是实现疾病早期筛查应用于临床实践的核心支撑，也是构建医工交叉领域互信协作的重要基石。提升模型的可解释性可以通过生成包含热力图、关键参数对比的诊断报告，直观展示模型关注的病变区域，便于医生快速理解。也可以采用分层 DL，将诊断流程划分为多个模块，如图像分割模块、特征提取模块和最终决策模块，实现中间预测过程的可视化。

4. 小结

目前 AI 通过眼底图像筛查青光眼的技术已具备较高准确性，但还需解决模型泛化性，用户信任度等问题才能更好地应用于实际的临床筛查中。未来通过优化多中心数据共享机制、增强算法的可解释性以及开发低成本的筛查工具，有望重塑青光眼防治模式，让各个地区都能获得快速精准的青光眼筛查服务。

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