

综 述

磁共振成像在乳腺良恶性疾病中的研究进展*

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【摘要】乳腺癌是一项重大的全球健康挑战，已经超越肺癌成为全球发病率最高的恶性肿瘤。早期发现病变并及时干预能有效降低治疗成本，提高患者的生存质量。乳腺磁共振成像(magnetic resonance imaging, MRI)作为一种先进的成像技术，它有着最高的灵敏度和较高的软组织对比度。近年来，多模态MRI技术，如弥散加权成像、简化磁共振成像、磁共振指纹成像、超快动态对比增强成像、多核磁共振波谱成像以及基于MRI的人工智能(artificial intelligence, AI)，在乳腺良恶性疾病的筛查与诊断中的应用越来越广泛。这些技术大大提高了诊断的准确性，同时也有助于评估新辅助化疗后的效果。本文综述了多模态MRI技术及基于MRI的人工智能在乳腺良恶性疾病中的临床应用和研究进展，旨在降低乳腺疾病的发病率和个人死亡风险，提升医生对乳腺疾病的认知，并为制定个性化治疗方案提供依据。

【关键词】乳腺癌；筛查；诊断；磁共振成像；磁共振波谱成像；弥散加权成像；人工智能；综述
【中图分类号】R737.9
【文献标识码】A
【基金项目】科技部国家重点研发项目
(2022YFB4702700)
DOI:10.3969/j.issn.1672-5131.2025.02.061

The Research Progress of Magnetic Resonance Imaging in Benign and Malignant Breast Diseases*

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ABSTRACT

Breast cancer is a significant global health challenge, having surpassed lung cancer as the most common malignant tumor worldwide. Early detection and intervention can reduce treatment costs and slow disease progression. Magnetic resonance imaging (MRI) of the breast, as an advanced imaging technique, offers the highest sensitivity and relatively high soft tissue contrast. In recent years, multimodal MRI technologies, such as diffusion-weighted imaging, simplified magnetic resonance imaging, magnetic resonance fingerprint imaging, ultrafast dynamic contrast-enhanced imaging, multi-nuclear magnetic resonance spectroscopy imaging, and MRI-based artificial intelligence have been used in the screening of benign and malignant breast diseases. It is more and more widely used in diagnosis and treatment, which greatly improves the accuracy of diagnosis and can also evaluate the effect of neoadjuvant chemotherapy. This article provides an overview of the clinical applications and research progress of multimodal MRI techniques and AI based on MRI in the diagnosis of benign and malignant breast diseases, aiming to reduce the incidence and individual mortality risk of breast diseases, deepen physicians' understanding of breast diseases, and provide possibilities for personalized treatment plans.

Keywords: Magnetic Resonance Imaging; Breast Cancer; Magnetic Resonance Fingerprinting; Diffusion-Weighted Imaging; Artificial Intelligence; Review

乳腺癌严重威胁了全球女性的健康，它是世界上最常见的癌症之一^[1]。根据2020年的数据，乳腺疾病的筛查和诊断目前主要依赖数字X线摄影和超声^[2]。然而，数字X线摄影存在较大的辐射风险，并且对致密型乳腺的敏感度较低^[3]。超声诊断则过度依赖操作者的经验，且常规磁共振成像(magnetic resonance imaging, MRI)检查时间较长，可行性较差。多模态MRI技术因其无创性、可重复性以及较短的扫描时间，已被广泛应用于乳腺疾病的辅助筛查、诊疗及预后评估^[4]。此外，基于MRI的人工智能(artificial intelligence, AI)技术有助于提高乳腺癌的检出率和准确性^[5]。本文就多模态MRI及AI在乳腺良恶性疾病中的临床应用及研究进展进行综述，有助于早期发现和治疗乳腺癌，降低死亡率，改善患者的生存质量。

1 多模态磁共振成像

1.1 弥散加权成像(diffusion-weighted imaging, DWI) DWI是一种在体内可视化和量化细胞外空间布朗分子运动的MRI技术。表观扩散系数(apparent diffusion coefficient, ADC)是DWI的一种指标，较低的ADC值通常说明是恶性肿瘤。通过ADC值，DWI可以有效提高乳腺良恶性病变的诊断。当ADC值低于 $1.0 \times 10^{-3} \text{ mm}^2/\text{s}$ 时，通常为恶性肿瘤，但若ADC值高于该阈值，也不能完全排除恶性病变，仍需进一步判断^[6-8]。此外，b值在DWI中也起着至关重要的作用。目前，关于乳腺检查中最佳b值的选择仍存在争议。较大的b值($b > 1000 \text{ s/mm}^2$)能更好反映弥散加权的作用，抑制良性和正常组织的信号，从而有助于癌症的检测^[9]。然而使用较高的b值会使图像信噪比下降以及延长采集时间。与传统弥散加权成像(conventional diffusion-weighted imaging, CDWI)相比，合成弥散加权成像(synthetic diffusion-weighted imaging, SDWI)通过数学方法，从至少两个不同b值的直接获取DWI数据中推导出来^[10]。这种方法可以克服CDWI的局限性，实现对非常高b值DWI的背景抑制，而无需额外的采集扫描时间。根据Choi^[11]的研究，使用CDWI，b值为800和1500s/mm²以及SDWI，b值为1000和1500 s/mm²评估50例乳腺癌患者。研究结果表明，无论成像类型(合成或传统)如何，癌实质对比度(contrast)和癌组织回声比(cancer detection rate, CDR)都随着B值的增加而增加。此外，SDWI1500的病变显著性优于CDWI1500。SDWI1500在乳腺癌临床评价中是可行的。与CDWI1500相比，它具有更高的肿瘤显著性，更好的癌实质对比，以及相当的CDR。尽管与CMRI相比，DWI能够提供更多诊断信息，但较高的b值可能会影响图像质量，同时ADC的测量也可能存在误差，从而影响最终的诊断结果。

1.2 简化磁共振成像(abbreviated breast magnetic resonance imaging, AB-MRI) AB-MRI概念的提出是为了通过减少图像采集和解释时间来降低MRI的复杂性和成本，从而提高乳房MRI的可行性^[12]。在一项开创性研究中，Kuhl等人^[13]在2014年首次报

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道了简化乳腺MRI方案用于乳腺癌筛查的可行性,该方案由未增强T1加权序列和首次增强T1加权序列、减影成像和单个最大密度投影图像组成。Moraes^[14]等人的研究,纳入了419例患者,研究表明,增强磁共振成像(AB-MRI)与全诊断磁共振成像方案(full diagnostic magnetic resonance imaging, FD-MRI)在整体上具有良好的诊断一致性。此外,考虑到他们的研究结果以及简化MRI的获取时间较短,简化MRI可能比FD-MRI更适合于乳腺癌筛查^[15]。其他研究表明AB-MRI可以替代FD-MRI,与Moraes^[14]的研究一致^[16-17]。

目前关于AB-MRI还没有正式的定义,AB-MRI方案也存在差异^[18]。在EA1141试验中,扫描方案是灵活的,只要总扫描时间小于10分钟,即可获得未增强T1加权序列、对比增强的T1加权序列和T2加权序列^[18]。尽管简化方案,扫描仪,人口和方法存在差异,但AB-MRI表现出与标准或FD-MRI相当的性能^[19-23]。此外,AB-MRI遗漏的癌症主要是低级别浸润性癌和/或原位导管癌。因此,除了筛查外,AB-MRI已被认为可用于许多诊断应用^[14]。在Kim等人^[24]的研究中,结果表明,在有乳腺癌家族史的女性中,AB-MRI在乳腺癌检测方面表现出与FD-MRI相当的敏感性,同时具有更高的特异性。在Fonseca^[25]的研究中,与单独使用MG相比,AB-MRI在PHBC中具有更高的增量癌症检出率。尽管活检率较高,但AB-MRI对焦虑、担忧和感知健康状况没有明显影响。最近,AB-MRI已经用于乳腺致密女性的筛查,与DBT相比CDR更高^[18,26]。因此,AB-MRI有可能在筛查中得到广泛应用,但在实施过程中,必须解决其在临床工作流程中所面临的挑战。

1.3 磁共振指纹成像(magnetic resonance fingerprinting, MRF) MRF是一种快速序列,它提供了一种新的机制来定量检测和分析复杂的变化,这些变化可以代表物质的物理改变或疾病的早期指标^[27]。MRF还可用于特异性识别目标物质或组织的存在,这将提高MRI研究的灵敏度、特异性和速度,并有可能引入新的诊断检查方法^[27]。在Zanderigo^[28]的研究中,探讨乳腺癌的定量特征是否与正常纤维腺组织(fibroglandular tissue, FGT)的定量特征不同,并评估在重建的MRF参数图上是否可以检测到癌症。结果表明MRF有望用于区分乳腺癌和FGT以及分析对比前/后T1变化。目前MRF还在处于研究探索阶段,还未广泛的用于乳腺检查,在未来MRF有可能作为一种额外的序列,用于开发无需使用造影剂的MRI诊断方案。

1.4 乳腺超快动态对比增强MRI(ultrafast dynamic contrast-enhanced, UF-DCE) UF-DCE是动态对比增强扫描(dynamic contrast-enhanced, DCE)的快速扫描方案,UF-DCE-MRI通常的时间分辨率小于每帧10秒,比传统DCE-MRI的每帧60秒快^[29]。近年来UF-DCE MRI与加速技术的发展密不可分,主要有视图共享、或压缩感知(compressed sensing, CS)技术等^[30-34],这些技术有助于在几秒钟内实现高时间分辨率。视图共享方法通过对密度不均匀的k空间进行采样来加速采集,低频采样的频率远高于高空间频率。在UF-DCE MRI的第一项研究中,Mann^[35]等人将时间分辨血管造影采集引入临床实践,并证明使用如此快速的方案可以保留重要的诊断信息。而且它在涉及UF-DCE MRI的报告中最为常见。CS允许从随机和高度欠采样的频域数据中重建图像^[36],CS已应用于乳房的UF-DCE MRI,以减少扫描时间,同时保持足够高的时间和空间分辨率^[33,37-40]。

UF-DCE-MRI有几个重要的动力学参数,包括最大斜率;增强时间;和推注到达时间^[41]。较高最大斜率、较短增强时间和短推注到达时间往往提示恶性病变^[42]。几项研究结果表明UF-DCE-MRI提取的动力学参数在鉴别乳腺良恶性病变时,诊断性能与常规DCE-MRI相当或更高^[36-45]。在ohashi^[43]的研究中比较了UF-DCE MRI和常规DCE MRI在191例浸润性癌中的形态学描述符表明:大约70%的病变中,UF-DCE MRI和常规DCE MRI的形态学评估相同,但UF-DCE MRI上出现了簇状环增强(提示导管原位癌的发现)的频率较低,这一结果可能归因于当前UF-DCE MRI协议的空间分辨率不足。也有研究报道了UF-DCE MRI在新辅助治疗中的诊断价值^[39-40]。UF-DCE对肿瘤相关血管的描述可能是肿瘤侵袭性的标志,并为理解癌症发展和治疗反应中的肿瘤微环境提供线索

^[41-42]。但也有其局限性,使用增强扫描时,需要注射对比剂,对于肾功能不全的人无法进行扫描,且会有造影剂的残留^[46]。因此不使用对比剂的DWI成像在未来可能成为增强成像的替代诊断方法,但是需要大量的实验证明。

1.5 多核磁共振波谱成像(multinuclear magnetic resonance spectroscopic imaging, Multi-NMRS) 磁共振波谱(magnetic resonance spectroscopic imaging, MRS)成像是一种无辐射的无创技术,应用最广泛的是¹H。体内氢质子MRS通过检测乳腺组织样本中含胆碱化合物3.2 ppm的水平来区分乳腺恶性和良性病变,胆碱化合物水平较高,表明恶性肿瘤迅速繁殖^[47]。一有研究表明,¹H-MRS的敏感性和特异性分别为87.9%和88.9%,其阳性预测值和阴性预测值分别为93.5%和80%^[48]。然而,由于¹H-MRS仅能反映胆碱、肌酸等少数分子,因此限制了其应用范围。随着氟、钠、磷等探针和成像技术的发展,超极化增强信号强度,使得²H、¹³C、¹⁵N、¹⁸F、²³Na、³¹P、¹²⁹Xe等其他核成像光谱得以实现^[49-51]。这些Multi-NMRS提供了多种代谢活动和体内真实代谢的能力,目前已经在神经系统,脑瘤,肝脏疾病,肺部疾病,乳腺,泌尿系统等疾病中应用^[52-59]。在乳腺成像中,同时使用¹H和²³Na MRI在3T上扫描,采集时间将缩短一半^[60]Bitencourt等人^[61]研究了乳腺癌是否表现出与正常FGT不同的基于MRS的脂质组成,结果表明:基于MRS的脂质测量可以作为多变量方法中的自变量,以提高乳腺癌表征的特异性。由于受场强,磁共振扫描仪及成像气体等各种技术的限制,Multi-NMRS在乳腺疾病中还未广泛应用,在未来将会更多的应用于乳腺疾病。

2 基于MRI的影像组学与AI技术

2.1 基于MRI的影像组学及AI理论 最近,人们一直关注AI增强的预测建模方法的实施,使用影像组学,各种经典机器学习(machine learning, ML)与深度学习(deep learning)相结合。

影像组学是一种新兴的方法,通过对医学影像数据进行定量分析和特征提取,以提供更深入的诊断信息^[62]。影像组学的应用领域包括肿瘤诊断、治疗反应评估、疾病进展监测等。ML的目标是让计算机系统能够从数据中学习模式和规律,并利用这些学到的知识来做出预测、决策或者行为,而无需明确地进行编程。深度学习(DL)是机器学习(ML)的一种形式,它能够构建复杂的模型,自动从数据中学习特征并进行分类,从而实现机器的自主学习^[62]。在未来,乳腺成像将与AI一起运作,简化流程,辅助决策,改善监管^[63]。同时也可以提供更多的诊断信息,有助于病灶的识别与检出和良恶性疾病鉴别。

2.2 对乳腺良恶性疾病的诊断 提高乳腺良恶性疾病诊断的准确性可以减轻病人痛苦,精准治疗疾病,提高生存率^[64]。ZHANG等^[64]开发和验证基于MRI的多模态影像组学模型,用于乳腺良恶性病变的鉴别诊断,最优模型受试者工作特征曲线下面积(area under the curve, AUC)为0.921,准确率为0.83,表明影像组学能很好的鉴别乳腺良恶性疾病,Stogiannos^[65]等基于第一个对比后动态序列,ADC图谱和ML算法在区分乳腺良恶性疾病方面具有70%的敏感性、66%的特异性、82%的阴性预测值和67%的总体准确性。这可为乳腺疾病的诊断分析提供一种很有前途的新工具。Gao等^[66]开发了一种基于DL的级联特征金字塔网络系统,用于DCE-MRI中乳腺病变的检测和分类。结果表明级联特征金字塔网络系统优于其他系统,平均精度和最高灵敏度分别为 0.826 ± 0.051 和 0.970 ± 0.014 (误报率为0.375)。级联特征金字塔网络在检测大病灶和小病灶时的平均精度值分别达到 0.779 ± 0.152 和 0.790 ± 0.080 。特别是对于小病灶,级联特征金字塔网络在切片和患者水平上检测良性和恶性乳腺病变的性能最佳。因此,基于MRI的影像组学能够提升乳腺良恶性疾病诊断的准确性。

2.3 对乳腺新辅助化疗效的预测 新辅助化疗可以减轻肿瘤负荷,甚至完全病理缓解。在2023年,Liu等人^[67]对420名接受新辅助化疗的患者进行了研究,比较了logistic回归、决策树和其他ML技术,用于预测肿瘤消退模式。研究结合了治疗前MRI形态学和动力学特征以及临床变量,获得了0.68的AUC值。ElAdoui等人^[68]基于42名乳腺癌患者在第一个周期新辅助化疗前后的多输入

DCE-MRI数据,构建了卷积神经网络,成功预测完全病理缓解,AUC达到了0.91。类似地,Zhou等人^[69]在2023年探索了使用多通道3D卷积神经网络来预测完全病理缓解,并在开发集、独立测试集和前瞻性测试集中分别获得了0.82、0.86和0.83的AUC值。Li^[70]使用影像组学模型,调查了448例非转移性浸润性导管乳腺癌患者,训练组和验证组AUC分别为0.98和0.92。结果表明了肿瘤和肿瘤周围影像组学模型在癌症管理中的潜在价值。

但AI也存在缺点,在calabres^[71]研究表明DL方法目前在使用CNN预测乳腺癌患者远处转移状态方面的能力不足。该模型的灵敏度、特异性、准确度和AUC分别为52.50%、80.51%、73.42%和68.56%。总体来看,尽管各项研究的AUC值和准确性有所差异,但这些结果仍然凸显了AI增强MRI在个性化乳腺癌治疗方案制定与治疗反应评估中的潜力^[72]。

3 小结与展望

综上所述,近年来MRI的应用无疑在癌症的诊断、监测、术前乳腺癌预后预测以及新辅助化疗方面带来了显著变化。即使其广泛应用仍然存在一些限制,例如检查的时间。为了增加乳腺MRI的可及性,AB-MRI和UF-DCE MRI在准确率相当的情况下大大缩短了图像的采集时间^[6-8]。特别是在筛查领域,MRI已被广泛应用于高危人群以外的女性^[72]。此外,MRI技术仍在不断发展,新的方法正在被探索,以改进肿瘤的检测、表征和治疗反应预测。DWI作为一种非增强影像检查方法,可避免造影剂的不良反应。MRF能够定量评估疾病特征,未来有望成为一种新的诊断手段。Multi-NMRS则提供了多种代谢活动的检测能力,并能真实反映体内的代谢过程,进而提高乳腺癌的敏感性。然而,这些多模态MRI的应用受到扫描仪差异、成像参数不同、图像处理方法及图像质量等多方面因素的影响。基于MRI的影像组学与AI的结合能够将数据处理并融合到多个分析模型中,为医生提供更好的肿瘤检测和表征工具^[73-74]。此外,它们也有助于指导预后评估、复发监测及转移评估等^[75]。然而,由于特征提取软件的缺乏和数据处理方法的多样性,这些技术尚难广泛应用于临床实践^[76]。未来也需要额外的生物标志物来为BC的患者提供个体化的治疗^[77]。目前的研究多为回顾性、单中心、小样本研究。因此,未来应继续优化多模态MRI和多参数MRI的使用,探索新的方法;同时,亟需进行大规模前瞻性实验以验证研究结果;最后,需要使用大样本数据以提升特征模型的准确性和一致性。今后开发更先进的多模态MRI成像技术以及更精准的人工智能将可能成为一大研究热点。MRI有其较高的软组织分辨率,在乳腺疾病的诊断中取得了良好效果^[78]。随着技术的不断发展,乳腺MRI在临床上的应用将变得更加广泛,同时其诊断准确性也将不断提升。

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(收稿日期: 2024-02-26)

(校对编辑: 赵望淇)