

• 综述 •

MRI定量技术在前列腺癌中的研究进展

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[摘要] 多参数磁共振(multiple parameter MRI, mpMRI)是目前前列腺癌无创性检出、定位和分期的首选影像学方法。然而, mpMRI图像解读基于阅片者的经验和主观判断, 往往会造成诊断偏差。MRI定量技术能够对前列腺病灶的病理生理学特性进行更加客观、精准地分析, 传统的定量技术包括扩散张量成像、扩散峰度成像、体内非相干运动成像及T2 mapping等, 但它们各自的局限性使之不能广泛应用于临床。合成磁共振序列是一种新型定量扫描方法, 单次扫描后可获得多组基于组织病理生理学特性的绝对测量值, 具有高效率和高容错率, 在前列腺癌的诊断中有良好的临床前景。本文对传统及新型MRI定量扫描方法在前列腺癌中的临床应用展开综述。

[关键词] 前列腺癌; 磁共振定量技术; 扩散张量成像; 扩散峰度成像; 体内非相干运动成像; 合成磁共振成像

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Research progress of quantitative MRI technologies in prostate cancer

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[Abstract] Currently, multiple parameter MRI(mpMRI) is the preferred imaging modality for the non-invasive detection, localization, and staging of prostate cancer. However, the interpretation of mpMRI images relies on the experience and subjective judgment of the reader, leading to potential diagnostic bias. Quantitative MRI techniques can provide a more objective and precise interpretation for the pathophysiological characteristics of prostate lesions. Traditional quantitative techniques include DTI, DKI, IVIM and T2 mapping, but their limitations restrict their widespread clinical utility. Nevertheless, synthetic MRI has emerged as a novel quantitative technique that enables the acquisition of multiple sets of absolute measurements based on histopathophysiological properties in a single scan. With its high scanning efficiency and error tolerance rate, synthetic MRI holds promising clinical prospects in prostate cancer. This review discusses the clinical applications of both traditional and novel quantitative MRI techniques in prostate cancer.

[Key words] prostate cancer; quantitative MRI technology; DTI; DKI; IVIM; synthetic MRI

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前列腺癌(prostate cancer, PCA)是男性常见的恶性肿瘤, 随着血清前列腺特异性抗原(prostate specific antigen, PSA)筛查在人群中的广泛开展及MRI技术的不断进步, PCA的检出率大幅度提高。多参数磁共振(multiple parameter MRI, mpMRI)的引入使得医生能更准确地评估和取检可疑病灶, 被

各种国际指南推荐为临床可疑PCA患者的一线检查方法^[1]。前列腺成像-报告和评分系统(prostate imaging reporting and data system, PI-RADS)依据T2加权成像(T2 weighted imaging, T2WI)、扩散加权成像(diffusion weighted imaging, DWI)和动态对比增强扫描(dynamic contrast enhancement, DCE)序列将病灶可能为PCA的概率进行1~5分的评分, 并建议3~5分的病灶接受靶向活检^[2]。但是前列腺mpMRI评估病灶的结果可能会因放射科医生的经验、检查

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执行因素等而有所差异,在缺乏无偏倚的客观定量参数的情况下,不同经验水平的医生对病灶的判读缺乏一致性^[3]。近年来,MRI定量技术在PCA中研究颇多,其中包括传统定量技术如扩散张量成像(diffusion tensor imaging, DTI)、扩散峰度成像(diffusion kurtosis imaging, DKI)、体素内不相干运动(intravoxel incoherent motion, IVIM)成像、T2 mapping等,以及新型定量技术如合成磁共振成像(synthetic MRI, SyMRI),本文将对以上各MRI定量技术在PCA中的临床研究进行综合评述。

1 DTI

DTI依据生理条件下组织内水分子沿多个方向扩散的原理,提供各向异性的扩散信息,使水分子扩散的路径可视化^[4]。该技术以DWI为基础,于至少6个(多则上百)非线性方向上施加扩散敏感梯度,并使用较大的扩散敏感因子b值计算出各个方向上的扩散张量,以获得扩散的各向异性信息。一般来说使用更多的梯度方向可增加DTI的信噪比^[5]。大多数前列腺DTI的研究强调比较癌灶和健康组织的平均扩散率(mean diffusivity, MD)和部分各向异性指数(fractional anisotropy, FA)之间的差异^[6-7]。其中MD代表体素内水分子朝各个方向扩散幅度的平均值,一般使用平均扩散系数(average diffusion coefficient, ADC)作为指标,其值越大说明在单位时间内扩散能力越强。FA是分析扩散各向异性最常用的参数,是扩散的各向异性部分与扩散张量总值之比,取值为0~1,常用于表征纤维束的走行方向及完整性^[8]。

既往众多研究证明PCA病灶的MD值降低,而FA值变化不一致^[9-12]。Nezzo等^[10]通过分析38例PCA患者的DTI图像发现,MD值与Gleason评分呈负相关,而FA值与Gleason评分无关。另有研究认为,PCA灶的细胞膜屏障和复杂纤维结构相比于正常腺体组织增加,从而使病灶MD值降低且FA值增加^[13],并且分析认为FA值的可靠性可能与采集参数或后处理技术(梯度扩散方向数目、b值选择)有关^[14-15]。此外,Gürses等^[9]比较了60余例前列腺炎与正常腺体组织的MD和FA值,并未发现明显差异,但仍需要更大样本的研究来进一步验证。Gholizadeh等^[16]在前人对DTI研究基础上通过结合体积扩散系数和表面扩散系数等新型DTI定量参数,使图像显示出更清楚的肿瘤边缘和更多可疑信号区,其研究表明DTI衍生的纤维追踪技术具有探

索PCA细微结构的潜能,有望更为准确地指导保留神经的PCA根治手术,从而减轻患者术后阳痿及尿失禁的发生率。同时该研究观察到在DTI纤维追踪术下显示的癌区平均纤维束密度明显高于正常组织区,这也与以往研究一致^[17-18]。此外,其他DTI相关研究还观察到,PCA区域的神经纤维束中断、结构紊乱,而前列腺增生的纤维束走行连续、规则,这些都说明DTI技术具有更大的探查前列腺解剖细节的潜力^[8]。

但DTI技术也有很多限制:①纤维束追踪技术难以准确追踪交叉束;②增加扩散敏感梯度的方向虽然可提高信噪比及测量准确性,但会延长扫描时间;③DTI成像模型是基于水分子在人体内的扩散运动满足高斯分布这一理想状况,但实际情况下水分子的扩散运动呈非高斯分布,因此也衍生了DKI技术,以拟合水分子的非高斯扩散模型。

2 DKI

众所周知,组织内水分子的随机扩散运动在一定时间段内呈概率性分布,这是理想的正态分布,即高斯分布形式。然而,由于生物组织不同的生化特性及细胞膜等屏障结构的存在,水分子扩散偏移正态分布而呈非高斯分布^[19]。因此,DKI技术的产生历经了对组织内水分子扩散模式由高斯分布到非高斯分布的认知转变过程,以及将四阶张量应用于MRI的过程。DKI模型中新参数Kapp对扩散的信号强度衰减进行更精准的数学曲线拟合,可量化高斯模式与水分子真实扩散的偏差^[20]。DKI较DWI及DTI技术能够提供更丰富、真实、准确的组织微观结构信息,它主要参数有平均峰度(mean kurtosis, MK)值、经过非高斯扩散模型校正过的ADC值(D值)等。近年来,DKI逐渐应用于各种疾病的研究,尤其在中枢神经系统及前列腺中取得了初步成果,展现出良好的临床价值。Yao等^[21]的研究表明,DKI的参数MK和FA值有助于区分PCA和良性前列腺增生(benign prostatic hyperplasia, BPH),MK和FA值越高,PCA的可能性就越大。此外,据以往研究分析,不同级别PCA之间的ADC值存在很大程度的重叠^[22-24],但Rosenkrantz等^[25]的研究指出,DKI对区分外周带低/高级别PCA的敏感性明显高于ADC(68.6% vs. 51.0%, $P < 0.001$),且DKI的曲线下面积明显 $>$ ADC(0.70 vs. 0.62, $P=0.010$)。但也有研究并未赋予DKI额外的临床价值,一项纳入463例PCA患者的荟萃分析比较了单指数DWI和DKI在PCA

检测中的诊断性能,认为两种技术诊断价值相当,但由于DKI检查时间明显长于单指数DWI,暂时不建议将DKI纳入常规临床应用^[26]。因此,现阶段仍需继续优化DKI检查方法,统一标准进行大规模的前瞻性研究,以探索DKI检查的优势。

3 IVIM-DWI

IVIM-DWI是一种基于双指数模型的扩散加权成像技术,用于量化组织内水分子的微观运动,包括自由扩散和血流的微循环灌注^[27]。传统的单指数模型DWI只考虑了水分子的扩散信息,没有剔除微血管灌注对扩散的影响。而IVIM-DWI通过拟合b值和信号强度的关系图,将图像的数学模型分为两部分:低b值主要反映微血管的血流灌注情况;高b值主要反映水分子的真实扩散运动^[28]。

在IVIM-DWI模型中主要量化3个参数: D^* (快扩散/假性扩散系数),反映了血流灌注对DWI信号衰减的贡献; D (慢扩散/真性扩散系数),反映了水分子真实扩散对DWI信号衰减的贡献; F (灌注分数),反映了血流量。近年来IVIM-DWI逐渐成功应用于肝、肾、胰腺等弥漫性及肿瘤性疾病,从临床角度证实了双指数模型的原理基础^[29-31]。现研究认为,IVIM-DWI的定量参数能够准确地反映扩散及灌注的特征,从形态和功能双角度更好地评价前列腺病灶的微观结构,并反映前列腺的生理病理特征^[32]。

一项研究比较了48例BPH和48例PCA患者的IVIM-DWI定量参数,结果发现与BPH组相比,PCA组的D、ADC及F值显著降低,而 D^* 值显著升高;PCA患者中,D、ADC及F值与Gleason评分呈负相关,而 D^* 值则呈正相关^[33],这一结果与高级别肿瘤细胞排列更小更密,导致水分子扩散运动更加受限有关,与以往报道基本一致^[34-35]。另有研究指出,IVIM-DWI有望在不使用造影剂的情况下,同时评估高风险PCA患者可疑盆腔淋巴结的扩散和灌注情况^[36]。恶性淋巴结的D值较良性淋巴结显著降低($0.54 \times 10^{-3} \text{ mm}^2/\text{s}$ vs. $1.10 \times 10^{-3} \text{ mm}^2/\text{s}$, $P < 0.001$),而F值显著提高(33% vs. 27%, $P=0.02$)^[37]。此外,IVIM-DWI灌注参数具有监测PCA治疗反应的潜力,Kooreman等^[38]对接受PCA综合治疗的患者每个治疗日均行IVIM-DWI检查,发现D值在PCA灶中有所增加,而在非PCA组织中保持稳定;且随着抗雄激素治疗时长增加, D^* 值略有降低,这可能与PCA病灶接受治疗后血供中断有关^[39]。当放射治疗过程中整个前列腺都被照射时,总体的F值和 D^* 值均

增加,可能是放疗后炎症所致^[40]。IVIM-DWI的这些灌注参数值表明它具有改善PCA诊断、分级分期及监测治疗反应的潜力,且与DCE-MRI相比无需另外注射造影剂,因此更适合肾功能不全和需要反复多次评估的患者。

4 SyMRI

SyMRI在单次采集中对组织多组弛豫值进行定量测量,并生成多种对比度加权图像,是一种快速、稳健、可重复性高的新型定量技术。该技术基于多动态多回波(multidynamic multiecho, MDME)序列,采用 120° 交叉层面选择饱和脉冲及多回波采集模式,通过设置2个回波时间及4个延迟时间并采集不同TE之后的回波,计算得到组织的T1值、T2值、PD值及射频磁场的B1值。SyMRI可通过设置不同的回波时间、重复时间、反转时间和翻转角等参数来重建不同对比度的图像,比如T1WI、T2WI、PDWI等序列,医生通过调整参数得到不同的图像对比度^[41]。

已有研究表明SyMRI在PCA的诊断、分级分期及疗效评估中具有良好的临床价值。Cui等^[42]研究证明,从SyMRI中获得的多组mapping图有助于区分PCA与非癌病灶,T2值和PD值鉴别低/高级别PCA的诊断效能与ADC值相似。孟铁豹等^[43]认为SyMRI诊断PCA的灵敏度更高,该研究前瞻性地对20例外周带PCA患者和20例健康受试者行SyMRI扫描,发现PCA灶的T1和T2值均显著低于正常腺体组织,分析是由于排列疏松的腺泡结构被排列紧密的肿瘤细胞所取代,黏蛋白和液体含量减少。这些研究初步探实SyMRI不仅能提供一个无偏倚的组织弛豫值,还可以分析定量参数值与组织生理病理学特征之间的关系,为组织学活检提供一种非侵入性的替代方法。另外有研究证实PCA活动性骨转移灶的PD值明显高于非活动性骨转移灶,PD值可作为鉴别活动性骨病灶的显著指标,且诊断效能高于T1和T2值^[44]。

SyMRI相较于传统定量技术优势颇多,例如以往前列腺MRI定量技术T2 mapping耗时10 min以上,且各报道中组织T2值存在较大差异,缺乏统一的标准,因此临床上实用性和准确性都有限^[45]。而SyMRI采用的MDME序列在保证和常规序列相同分辨率的条件下,扫描时间仅需5 min左右,具有更低的运动发生率^[46],更适合日常工作。MDME序列成像过程中还计算了各个体素的射频场值以进

行射频场校正^[47],从而使T1、T2值测量更为准确。Hagiwara等^[48]研究表明,不同厂家的设备MDME序列对T1、T2、PD值的测量依然具有高准确度(变异系数<5%)。因此,采用统一参数的MDME序列成像不仅可以在不同PCA病灶间进行横向比较,还可以纵向随访同一患者,实现多中心研究并建立标准化数据库。

但SyMRI作为新型定量技术,目前还存在一些不足,譬如SyMRI使用的定量技术假设弛豫时间遵循单指数衰减模型,但活体组织中水分子存在于多种复杂微环境中,因此多指数衰减模型或许更能准确地反映前列腺组织真实的弛豫时间。且现阶段

针对PCA方面的SyMRI研究仍处于初步阶段,纳入研究的患者数有限,还需要大样本量的数据来探实SyMRI在PCA中的临床应用价值。

5 总结与展望

目前各种MRI定量技术逐渐应用于临床和科研领域中(表1),不但为精准医疗奠定技术基础,也为大数据分析、医疗人工智能、影像组学等前沿科技提供更为客观准确的数据。相信在精准医疗的时代趋势下,未来MRI定量技术势必有更广阔的发展空间,为临床诊断和治疗提供更加标准和个体化的信息。

表1 各MRI定量技术在PCA中的应用
Table 1 Application of MRI quantification technique in PCA

MRI quantification technique	Sequence	Characteristic	Disadvantage or advantage
Traditional MRI quantification technique	T2 mapping	Measures the T2 relaxation time of the tissue	These techniques require a long scanning and post-processing time, some studies suggest they are not better than ADC
	DTI	Provides anisotropic diffusion information	
	DKI	Quantifies the deviation between the real diffusion and the ideal diffusion of the water molecules	
	IVIM	Diffusion and perfusion characteristics of tissues are assessed using a bi-exponential model	
Novel MRI quantification technique	SyMRI	The absolute quantitative values of tissue T1, T2, and PD are obtained from a single scan	Objectively reflects tissue characteristics; fast scanning; high standardization and repeatability

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