



· 综述 ·

磁共振成像在肺结节检出和诊断中的研究进展

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[摘要] 功能性磁共振成像 (functional magnetic resonance imaging, fMRI) 对肿瘤的定位、定性诊断具有十分重要的应用价值。以往受磁敏感伪影、呼吸运动伪影等影响, 磁共振成像 (magnetic resonance imaging, MRI) 在肺部疾病诊断中应用较少。随着快速采集技术和去伪影技术的发展, MRI检出肺小结节、判断结节良恶性、评估肺结节治疗效果成为可能。本文就MRI在肺结节中的应用进行综述, 探究MRI在肺结节检出、诊断及疗效评估中的应用价值。

[关键词] 功能性磁共振成像; 肺结节; 诊断; 评估; 预后

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[Abstract] Functional magnetic resonance imaging (fMRI) is valuable to the location and qualitative diagnosis of the tumor. In the past, there was less for pulmonary lesions because of the limitation of magnetic resonance imaging (MRI) technology. With the rapid development of MRI technology, it is allowable for fMRI to diagnose, evaluate and predict the pulmonary lesions. This article reviewed the application of MRI in pulmonary nodules and explored the value of MRI in detecting, diagnosing and evaluating the efficacy of pulmonary nodules.

[Key words] Functional magnetic resonance imaging; Pulmonary lesions; Diagnosis; Evaluation; Prognosis

肺癌是威胁人们生命健康最常见的肿瘤, 肺癌的发病率和死亡率居中国首位。相关研究^[1]发现, I 期肺癌患者术后10年生存率可达92%。肺癌的早期发现、诊断和治疗能极大程度地提高患者的生存率, 改善其生活质量。目前, 低剂量CT (low-dose computer tomography, LDCT) 是肺结节筛查、随访最常用的检查方法。但高危人群长期随访的累积辐射损害以及敏感器官, 如乳腺、甲状腺等部位射线暴露可能诱发新的肿瘤^[2-4]; 并且, LDCT诊断依赖形态学特征, 如分叶、毛刺等, 对病变良恶性判断的能力有限。因此, 具有无放射损害、多序列多参数成像等优势的功能磁共振成像 (magnetic resonance imaging, MRI) 技术成为关注的焦点。以往受磁敏感伪

影、呼吸运动伪影等影响, MRI使用较少。近年来, 随着快速采集技术和去伪影技术等发展, 如快速弛豫增强序列 (rapid acquisition with relaxation enhancement, RARE)、鸡尾酒技术 (controlled aliasing in parallel imaging results in higher acceleration, CAIPIRINHA) 等, 信号采集时间显著缩短, 伪影减少, 对比度和图像信噪比显著提高, 小病灶的检出率增加, MRI检出、诊断肺结节成为可能。研究发现, 扩散加权成像 (diffusion-weighted imaging, DWI)、动态增强磁共振成像 (dynamic contrast-enhanced MRI, DCE-MRI) 等功能成像方法, 对病变良恶性判断和疗效评估具有重要的临床意义。随着放射组学和放射基因组学研究的深入, 可以通过对图像的

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获取和分割, 图像特征的提取和量化, 预测模型的构建和统计学分析, 建立将影像图像特征与临床、病理及基因组信息相结合的预测模型, 从而在分子水平和基因水平反映肿瘤的异质性, 为精准医疗提供新的方法。

1 病灶检出

MRI检出肺结节常用的扫描序列包括快速自旋回波 (turbo spin echo, TSE) 序列、半傅里叶采集单次激发快速自旋回波 (half-Fourier acquisition single-shot turbo spin-echo, HASTE) 序列、平衡稳态式自由进动 (balanced steady-state free precession, bSSFP) 序列、三维容积内插屏气检查 (three-dimensional volume interpolated breath-hold examination, 3D-VIBE) 等。采用以上扫描序列能检出3~4 mm的实性小结节^[5]。不同MRI序列检出实性结节的灵敏度和特异度各不相同。1.5T MRI TSE序列检出直径 ≥ 6 mm实性结节的灵敏度和特异度分别为80%~87%、93%~96%^[6]。HASTE序列检出直径 < 3 、3~5、6~10和 > 10 mm结节的灵敏度分别为73.0%、86.3%、95.7%和100.0%, 检出直径 > 3 mm结节总灵敏度为92.1%, 直径 > 5 mm为97.6%^[7]。HASTE序列容易区分结节和流空的肺外周小血管, 而由于T2衰减快, 容易导致图像模糊。bSSFP对直径4~6 mm的实性结节检出率达75%^[8]。另1项研究^[6]发现, 1.5T bSSFP检出直径 ≥ 6 mm实性结节的灵敏度和特异度分别为65%~70%、96%~98%, 其中, 检出恶性结节的灵敏度、特异度、阳性预测值和阴性预测值分别为100.0%、98.0%、88.9%、100.0%。3D-VIBE检出直径4~8、 ≥ 8 mm的实性结节灵敏度分别为64.1%、100.0%^[9]。3.0T MRI VIBE采用CAIPIRINHA快速采集技术, 可将直径 ≥ 5 mm结节的灵敏度提高至93.1%。压脂方法能明显减少运动、化学位移伪影, 增加图像对比度^[10]。有研究^[6]表明1.5T短时反转恢复序列 (short-time inversion recovery, STIR) 检出 ≥ 6 mm实性结节的灵敏度为85.9%。其中, 检出恶性结节的灵敏度、特异度、阳性预测值和阴性预测值分别为100.0%、98.0%~100.0%、

88.9%~100.0%和100.0%。但STIR压脂重复时间 (repetition time, TR) 长, 信号选择性较低, 某些T1值与脂肪相近的信号也会被抑制。频谱衰减反转恢复序列 (spectral attenuated inversion recovery, SPAIR) 结合了化学饱和法和STIR的优点, 能选择性地抑制脂肪信号, 提高病变的对比度。Yan等^[11]研究发现, SPAIR (3.0T MRI) 检出结节总灵敏度为88.6%, 明显优于STIR (68.2%), 其中检出直径为1~5、 > 6 mm结节的灵敏度分别为61.5%、100.0%。

MRI对检出实性小结节有较高的灵敏度和特异度, 但对部分亚实性结节和纯磨玻璃结节, MRI显示能力有限, 其检出率与实性成分百分比密切相关^[12]。相关研究^[13]发现, 超短回波时间 (ultrashort echo time, UTE) 序列可以清晰地显示亚实性结节及纯磨玻璃结节, 检出结节的灵敏度分别为57.7%、90.9%, 特异度分别为97.6%、98.0%。但是, 显示结节边缘较CT更加平滑, 最大长径与CT测量值变异较大。

不同序列的联合应用可进一步提高结节的检出率和特异度。1.5T MRI T2W MultiVane XD、bSSFP和T1高分辨各向同性容积激发序列 (enhanced-T1 high resolution isotropic volume examination, THRIVE), 检出直径为4~5、6~7、8~14、 ≥ 15 mm实性结节的灵敏度分别为69.3%、95.2%、100.0%、100.0%, 特异度分别为96.4%、99.6%、99.6%、100.0%。对于直径 < 20 mm的亚实性结节, 其灵敏度和特异度分别为72.7%、99.2%。并且, MRI显示结节的最大直径与LDCT一致^[14]。3.0T MRI联合T2W FSE FS和3D T1WI VIBE, 总灵敏度为93.2%, 直径 > 5 mm的结节灵敏度增加至97.9%^[15]。不同序列检出结节的灵敏度和特异度见表1。综上, MRI检出直径 > 5 mm的结节, 灵敏度较高。根据美国放射学会 (American College of Radiology, ACR) 2017年版肺癌指南, 只有直径 ≥ 6 mm的结节存在超过1%的恶性风险, 需要短期随访。因而, 无放射损害的MRI可以作为CT的可替代检查方法, 用于肺结节的检出。

表1 不同研究报道的各种MRI序列肺结节检出结果分析

作者(年份)	机型	例数	病灶数/个	病变直径/mm	序列	病变检出率/%
Meier-Schroers等 ^[6] (2018)	1.5T (Ingenia, Philips Healthcare, Best, The Netherlands)	32	46	6~35	T2WI、T2WI STIR、bSSFP、3D-T1WI	灵敏度/特异度 T2-STIR: 85~89、92~94 T2WI: 80~87、93~96 bSSFP: 65~70、96~98 3D-T1WI: 63~67、96~100
Cieszanowski等 ^[9] (2016)	1.5T (Magnetom Avanto, Siemens MedicalSolutions, Erlangen, Germany)	50	113	2~28	Breath-hold T2WI TSE、T2WI SPIR、T2WI STIR、T2WI HASTE、T1WI VIBE、T1WI out-of-phase	灵敏度 T1WI VIBE: 69.0 T2WI SPIR: 54.9 T2WI TSE: 48.7 T1WI out-of-phase: 48.7 T2WI STIR: 45.1 T2WI HASTE: 25.7
Yan等 ^[11] (2015)	3.0T (Achieva TX, Philips Medical Systems, Best, The Netherlands)	34	44	1~10	RT-TSE、RT-T2WI SPAIR、RT-T2WI STIR、3D THRIVE、2D T1WI FFE	灵敏度 1~5 mm结节: TSE (23.1)、STIR (38.5)、SPAIR (61.5)、THRIVE (61.5)、T1-FFE (15.4) 6~10 mm结节: TSE (85.7)、STIR (71.4)、SPAIR (100.0)、THRIVE (85.7)、T1-FFE (42.9)
Meier-Schroers等 ^[14] (2017)	1.5T (Ingenia, Philips Healthcare, Best, The Netherlands)	224	137	≥4	T2-STIR MultiVane XD、bSSFP、3D-THRIVE、DWI	灵敏度/特异度/阳性预测值/阴性预测值/受试者工作特征曲线的曲线下面积 4~5 mm结节: 69.3、96.4、91.0、85.8、0.829 6~7 mm结节: 95.2、99.6、95.2、99.6、0.974 8~14 mm结节: 100.0、99.6、92.3、100、0.998 亚实性结节<20 mm结节: 72.7、99.2、80.0、98.8、0.860
Sommer等 ^[16] (2014)	1.5T (Magnetom Avanto, Siemens Healthcare, Erlangen, Germany)	49	54	平均: 6~38; 最大: 15	T2 HASTE、bSSFP、3D-VIBE	灵敏度/特异度/准确度/阳性预测值/阴性预测值 总体: 48、88、63、87、51 ≥10 mm结节: 50、91、-、87、- <10 mm结节: 42、95、-、77、- 恶性结节: 78、94、-、86、- 良性结节: 36、91、-、82、-
Koyama等 ^[17] (2008)	1.5T (Intera T-15, Philips Medical Systems, Best, The Netherlands)	161	200	6~38 平均直径: 15.6	T1-SE、T2-TSE、TSE STIR	检出率 总体: 82.5 恶性结节: 96.1 良性结节: 68.1

注: 呼吸触发 (respiratory-trigger, RT)

2 肺结节的诊断

肺结节见于多种良恶性病变, 如肺结核、真菌感染及肺腺癌等, 缺乏典型表现的结节鉴别诊断存在一定难度。MRI功能成像如DWI、体素内不相干运动成像 (intravoxel incoherent motion, IVIM) 和扩散峰度成像 (diffusion kurtosis imaging, DKI) 和DCE-MRI等, 通过定性、定量的评估, 能够为疾病的鉴别诊断、分期分型、疗效评估提供参考。

2.1 鉴别诊断

恶性肿瘤由于细胞密度高、增殖细胞体积大以及细胞外空间减少, 导致水分子扩散受限, DWI呈高信号, 表观扩散系数 (apparent diffusion coefficient, ADC) 降低。相关文献^[18-19] Meta分

析显示DWI ADC值鉴别良恶性病变的灵敏度和特异度分别为80%~88%, 89%~93%。肺癌的ADC值显著低于良性病变^[20-22]。尽管ADC值具有一定的鉴别诊断价值, 但由于磁敏感效应、病变内部坏死等因素的影响, 测量的准确率和重复性减低。研究^[23-24]发现, 直径≤2 cm的结节, ADC值的变异系数较高, 但对于直径≥2 cm的结节, ADC值的重复性较高。并且, 病变的平均ADC值容易受b值参数的影响, 最佳的诊断b值存在诸多争议^[25-27]。DWI病灶/脊髓信号比率 (lesion-to-spinal cord ratio, LSR) 的定量评估方法几乎不受b值的影响, 重复性和准确性更好^[28], 鉴别良恶性病变的灵敏度、特异度和准确率分别为88.8%、96.7%和93.9%^[29]。

DWI获得的扩散信息并非水分子的真实扩散, 而是包括了组织的微灌注。IVIM在DWI的基础上, 采用多 b 值的检查、双指数模型分析的方法, 获得快扩散系数 D 、慢扩散系数 D^* 及比例系数 f , 其中 D 主要反映组织扩散, D^* 反映毛细血管的灌注, f 为灌注信号的比例。Deng等^[30]发现炎症反应的 f 值显著高于肺癌, 诊断灵敏度和特异度为80%和75%, 而 D 和 D^* 无明显差异。Wan等^[31]发现恶性肺结节的ADC值和 D 值明显低于良性结节, D 值较ADC值评价效果更好, 灵敏度和特异度可达92.16%和81.82%。ADC、 D 和 f 值鉴别肺癌与阻塞性肺不张具有重要意义, 而 D^* 值诊断的准确率较低^[32]。Das等^[33]研究发现, DKI图像上肺癌的平均峰度 (mean kurtosis, MK) 显著高于良性结节, 诊断效率与DWI相仿。

DCE-MRI能连续、快速地获取注射对比剂前后的图像, 将病变的形态学特征与灌注、渗透信息结合。恶性结节的最大信号强化率 (maximum enhancement, ME)、早期峰值 (early peak, EP)、初始斜率 (initial slope, SI) 及第4 min最大强化值均高于良性病变, 其中EP > 15%, ME > 40%检出恶性病变的特异度达100.0%^[34]。Zou等^[35]发现, 当第4 min最大增强率 ≤ 65%时, 鉴别活性炎症结节与肺癌的灵敏度和特异度可达93%和100%。EP、ME及廓清率对肺癌和富血供的良性结节也具有较高的鉴别诊断价值^[36]。ME (0.13) 和强化斜率 (0.016/s) 能进一步诊断高、低生物学活性的良性病变, 为选择干预治疗或随访提供临床依据^[37]。肺癌的容积转运常数 (Ktrans) 和速率常数 (Kep) 数值高于良性病变, 灵敏度分别为90.6%、87.5%, 特异度为82.4%、76.5%, 明显优于PET/CT (灵敏度75.0%, 特异度70.6%)^[38]。Mamata等^[39]发现良性病变的Kep值均小于 1.0 min^{-1} , Kep阈值设为 1.0 min^{-1} 时, 诊断灵敏度、特异度、准确率、阳性预测值和阴性预测分别为76%, 100%, 80%, 100%和45%。通过不同功能成像方法如DCE-MRI和DWI/IVIM的联合应用, 可以进一步提高良恶性病变诊断的效能^[40-41]。呼吸运动是影响

DCE-MRI的主要因素, 与屏气扫描相比, 自由呼吸扫描结果重复性更好^[42], 同时, 采用3D非刚性运动校准方法也可以大大减少呼吸运动导致的图像形变, 减少漏诊和误诊机会^[43]。

2.2 分期分型

2.2.1 组织分型

肺癌的组织学分型包括小细胞肺癌 (small cell lung cancer, SCLC) 和非小细胞肺癌 (non-small cell lung cancer, NSCLC)。其中, NSCLC包括大细胞肺癌、鳞状上皮细胞癌和肺腺癌。高分化腺癌的ADC最小值显著高于其他组织类型的肺癌 (鳞癌、低分化腺癌、SCLC)^[44-46]。NSCLC的ADC值、 D 值显著高于SCLC^[47-48]。而 D^* 和 f 值在腺癌、SCLC中无明显差异^[41]。DCE-MRI结果显示^[48], NSCLC的Ktrans、Kep和血管外细胞外容积分数 (Ve) 均高于SCLC, 并且, 腺癌上述值也显著高于鳞状细胞癌, 其灵敏度分别为73.1%、69.2%, 69.2%, 特异度分别为85.7%、84.3%、100%。Pauls等^[49]也发现NSCLC的最大强化率 (maximum contrast upslope, mCUS) 和最大强化值 (maximum contrast uptake, mCU) 明显高于SCLC, 鳞状细胞癌的达峰时间 (time to peak, TTP) 明显高于腺癌。

2.2.2 肺癌的TN分期

肺癌常合并继发性改变, 如肺不张等, 影响T分期评估, MR T2WI序列及功能成像DWI、IVIM、DCE-MRI能区分实质肿瘤和肺不张^[21, 31, 50-53]。并且, MRI高软组织分辨率能清晰反映邻近胸膜的受累情况^[50, 54]。

CT测量淋巴结短径超过10 mm及异常强化是诊断肺癌淋巴结转移的常用方法, 但早期浸润的淋巴结无明显肿大。MRI通过信号改变可早期发现受累的淋巴结^[54-55]。研究^[56]发现, STIR和DWI用于N分期的灵敏度分别为84%、69%, 特异度为91%、93%。常用的评估方法包括形态学特征 (如边缘皮质的增厚或淋巴结脂肪成分的消失^[57-58]) 肺癌和淋巴结的ADC差值^[59]、STIR淋巴结信号强度与0.9% NaCl溶液信号强度比率、淋巴结-肌肉信号比^[59]。与DWI、PET/FDG

相比, STIR评估淋巴结转移的准确率和灵敏度更高^[60]。

3 预后评估

放化疗后肿瘤细胞坏死、凋亡, 水分子扩散受限程度降低, ADC值明显增加^[61-62]。ADC值与肺癌的治疗预后有关, 在治疗后的3或6个月内, ADC值与肿瘤复发率呈显著的负相关, ADC值可以作为预测早期治疗效果的独立预测因子^[63-64]。关于DCE-MRI的研究^[65]发现, 接受化疗后肺癌的Ktrans和Ve明显降低。肿瘤组织的Ktrans值越高, 对化疗越敏感, 当Ktrans阈值为 0.032 min^{-1} 时, 灵敏度、准确率和特异度分别为84.62%、77.78%和81.82%。Tao等^[64]也发现Ve值(<0.24)可以预测NSCLC对放化疗的早期反应, 从而及时提供疗效评估结果, 指导对临床治疗方案的选择。

4 不足和展望

既往研究^[5-10, 14-15]发现, MRI检出直径 $\geq 5 \text{ mm}$ 实性结节的灵敏度和特异度较高, 对肺结节的筛查和随访具有重要意义, 可以作为CT筛查的可替代检查工具。但是, 对部分亚实性结节和纯磨玻璃结节, MRI检出能力有限。由于受运动、磁敏感伪影的影响, MRI显示小结节的大小、边缘与CT检查存在一定差异。并且, 由于MRI检查时间长、费用昂贵, 如何优化检查序列, 制定合理的筛查、随访方案仍然需要进一步探讨。

MRI诊断肺结节具有独特的优势, 其功能成像方法有助于良恶性病变的诊断、组织学分类、肿瘤治疗效果评估和预后预测, 从而指导临床治疗。随着放射组学和放射基因组学的研究和发展, MRI新技术, 如DKI、IVIM、动脉自旋标记(arterial spin labeling, ASL)等能提供更多灵敏的影像标志物, 将图像特征与基因表达、蛋白质水平等联系起来, 促进精准化医疗的进展。

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