·综述·

胶质母细胞瘤复发与假性进展功能磁共振成像研究进展

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【摘要】 胶质母细胞瘤术后复发与假性进展的治疗方法和预后完全不同，故二者的鉴别诊断成为临床焦点。常规MRI均表现为新的或原有病灶扩大的异常强化伴周围水肿，临床表现为颅内压增高、局灶性神经功能缺损等非特异性症状，故常规MRI和临床表现无法区分二者。随着影像学技术的发展，多种fMRI技术展现出鉴别诊断的较大潜能。本文综述功能成像技术在胶质母细胞瘤复发与假性进展鉴别诊断方面的进展。

【关键词】 胶质母细胞瘤； 肿瘤复发，局部； 磁共振成像； 综述

Progress of fMRI on the recurrence and pseudoprogression in glioblastoma

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【Abstract】 The treatment and prognosis of recurrence and pseudoprogression of glioblastoma are completely different. Therefore, distinguishing the two has become a clinical focus. However, both can be manifested as new or increasing enhancing lesions with peripheral edema on conventional MRI, and their clinical manifestations lack specificity, such as increased intracranial pressure (ICP), local neurological deficits and so on. Therefore, it is impossible to distinguish the two from clinical and conventional MRI. In recent years, with the increasing development of imaging technology, a variety of functional imaging technologies have shown great potential to distinguish the two. This article summarized the application progress of functional imaging technologies on differential diagnosis of recurrence and pseudoprogression in glioblastoma.

【Key words】 Glioblastoma; Neoplasm recurrence, local; Magnetic resonance imaging; Review

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胶质母细胞瘤是成人颅内最常见的原发性恶性肿瘤，标准治疗方式为手术切除并同步放化疗[1]，其疗效的评估采用神经肿瘤反应评价（RANO）[2]。但放化疗后6个月内临床症状的进展如生活质量下降、颅内压增高、局灶性神经功能缺损等，以及MRI的异常强化信号影，给临床医师和影像科医师提出挑战，可能提示肿瘤进展即复发（图1），也可能是治疗后反应即假性进展[3]（图2）。胶质母细胞瘤复发的病理表现为肿瘤细胞密度异常增加，肿瘤组织内不成熟新生血管增多，血-脑屏障破坏、通透性增加，新生血管迂曲、粗细不均、血流缓慢；假性进展的病理生理学机制尚不明确，目前认为主要是血管内皮、血-脑屏障和少突胶质细胞损害导致局部炎症，血-脑屏障通透性增加和血管源性水肿，形成影像学上新的或原有病变扩大的异常强化灶[4]。约1/3的胶质母细胞瘤患者病程中可见假性进展[5]，通常随时间的推移而自发消退或稳定，无需进一步治疗。因此，临床正确区分胶质母细胞瘤复发与假性进展

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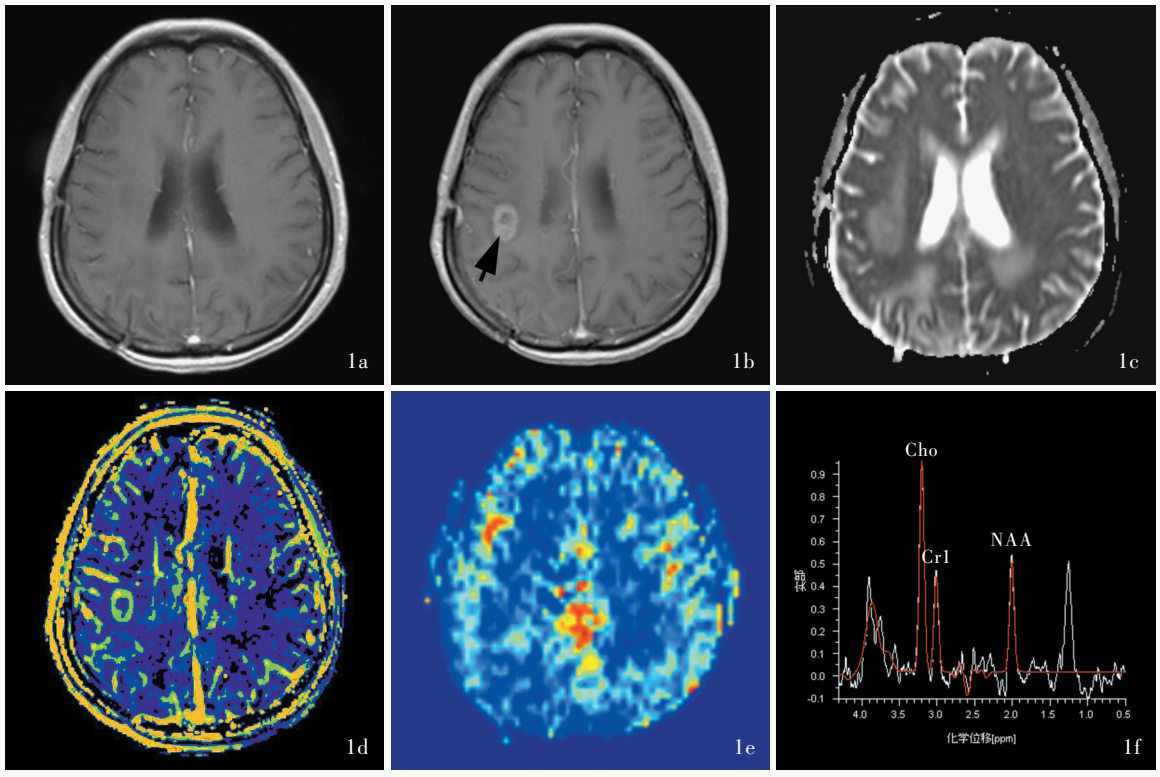

图1　女性患者，57岁，临床诊断为胶质母细胞瘤，手术切除并辅以放化疗后肿瘤复发。头部影像学检查所见　1a　复发前横断面增强T_1WI未见明显异常　1b　放化疗后2个月横断面增强T_1WI显示，右侧顶叶异常强化影（箭头所示）　1c　横断面ADC图显示，右侧顶叶病灶区ADC值为1.11×10^{-3} mm²/s　1d　横断面DCE-MRI显示，右侧顶叶病灶区呈高灌注（环形黄绿色区域所示），Ktrans值为0.07/min　1e　横断面ASL显示，右侧顶叶病灶区呈高灌注（黄色和亮蓝色区域所示）　1f　MRS显示，异常强化脑组织Cho值升高，NAA值降低

Figure 1　A 57-year-old female patient was clinically diagnosed with glioblastoma, and the tumor recurrence after surgical resection and adjuvant chemoradiotherapy. Head imaging findings　Axial enhanced T_1WI showed no abnormal enhancement (Panel 1a). Axial enhanced T_1WI at 2 months after chemoradiotherapy showed abnormal enhancement in the right parietal lobe (arrow indicates, Panel 1b). Axial ADC map showed the ADC value of the right parietal lesion was 1.11×10^{-3} mm²/s (Panel 1c). Axial DCE-MRI showed hyperperfusion in the right parietal lobe with a Ktrans value of 0.07/min (circular yellow and green areas indicate, Panel 1d). Axial ASL showed hyperperfusion lesion in the right parietal lobe (yellow and bright blue areas indicate, Panel 1e). MRS showed Cho value increased and NAA value decreased at abnormally enhanced brain tissue (Panel 1f).

至关重要，可以避免不必要的再次手术，以及替莫唑胺或其二线替代药物、其他治疗手段的过早停用。组织病理学是鉴别肿瘤复发与假性进展的“金标准”，但其为创伤性检查方法，加重患者及其家庭心理和经济负担；但是由于二者可能同时存在，且对手术标本取材精准性的要求较高，有时临床难以区分，因此，采用可靠的非侵入性影像学方法区分肿瘤复发与治疗相关假性进展具有重要意义。胶质母细胞瘤复发与假性进展在细胞结构、血流动力学、代谢和生物学功能等方面均存有差异，本文综述fMRI在上述方面的表现和研究进展。

一、扩散加权成像及其衍生技术

扩散加权成像（DWI）是通过检测组织中水分子扩散状态以反映组织细胞密度的功能成像技术。组织细胞密度增加，水分子扩散受限，表观扩散系数（ADC）可以量化这种扩散受限程度。胶质瘤病理分级越高，肿瘤细胞密度越大，水分子扩散受限程度越严重，即ADC值越低[6]，因此，胶质母细胞瘤复发的ADC值较低（图1a～1c），假性进展因表现为血管源性水肿而具有较高的ADC值[7]（图2a～2c），ADC值＞1.31×10^{-3} mm²/s提示假性进展的可能性较大，其鉴别肿瘤复发与假性进展的灵敏度和特异度分别达98.30%和100%[8]。亦有研究显示，ADC值鉴别胶质母细胞瘤复发与假性进展的能力有限，ADC截断值为1.30×10^{-3} mm²/s时，受试者工作特征（ROC）曲线下面积（AUC）为0.61[9]。上述研究表明，ADC值鉴别胶质母细胞瘤复发与假性进展的能力相对较差，可能与胶质母细胞瘤的高异质性相

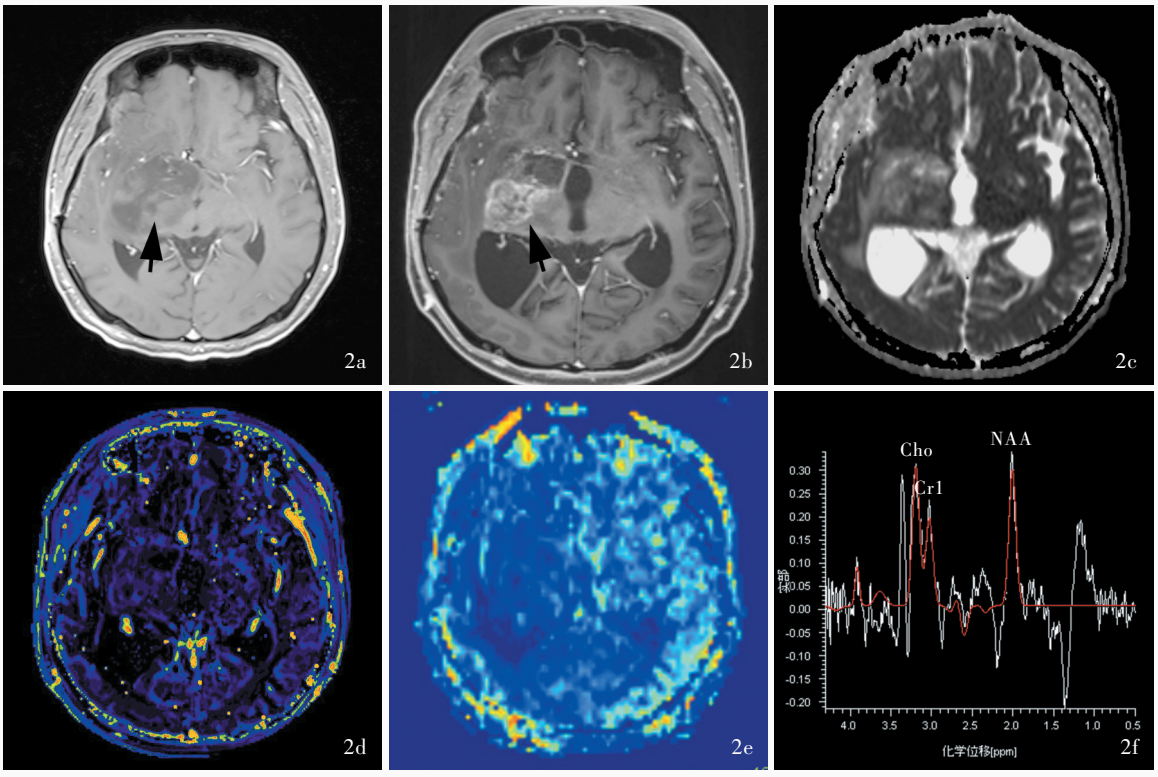

图2　男性患者，21岁，临床诊断为胶质母细胞瘤，手术切除并辅以放化疗后肿瘤假性进展。头部影像学检查所见　2a　假性进展前横断面增强T_1WI显示，右侧基底节区低信号影（箭头所示）　2b　放化疗后4个月横断面增强T_1WI显示，右侧基底节区异常强化影（箭头所示）　2c　横断面ADC图显示右侧基底节区病灶ADC值为1.41×10^{-3} mm²/s　2d　横断面DCE-MRI显示，右侧基底节区病灶区域呈低灌注（紫色和黑色区域所示），Ktrans值为0.02/min　2e　横断面ASL显示，右侧基底节区病灶区域呈低灌注（深蓝色区域所示）　2f　MRS显示，异常强化脑组织Cho值略降低，NAA值降低

Figure 2　A 21-year-old male patient was clinically diagnosed with glioblastoma, and the tumor pseudoprogression after surgical resection and adjuvant chemoradiotherapy. Head imaging findings　Axial enhanced T_1WI before pseudoprogression showed hypointensity in the right basal ganglia region (arrow indicates, Panel 2a). Axial enhanced T_1WI at 4 months after chemoradiotherapy showed abnormal enhancement in the right basal ganglia (arrow indicates, Panel 2b). Axial ADC map showed the ADC value of the right basal ganglia lesion was 1.41×10^{-3} mm²/s (Panel 2c). Axial DCE-MRI showed hypoperfusion in the right basal ganglia lesion with a Ktrans value of 0.02/min (purple and black areas indicate, Panel 2d). Axial ASL showed hypoperfusion in the right basal ganglia lesion (dark blue areas indicate, Panel 2e). MRS showed Cho value slightly decreased and NAA value decreased at abnormally enhanced brain tissue (Panel 2f).

关，肿瘤复发时若肿瘤细胞同时伴坏死或水肿，可导致ADC值的测量出现偏差。随着影像学技术的发展，多种DWI衍生技术被开发并应用于胶质母细胞瘤复发与假性进展的鉴别诊断。(1)扩散张量成像(DTI)：根据水分子扩散运动的各向异性以反映正常组织与病变组织内水分子各向异性扩散程度的差异。与胶质母细胞瘤假性进展相比，复发的各向异性分数(FA)、线性各向异性分数(CL)和平面各向异性分数(CP)显著增加[10]，可能与肿瘤细胞过度产生的特异性细胞外基质的方向有关。亦有研究显示，上述参数鉴别胶质母细胞瘤复发与假性进展的能力有限[11]。目前，国内外针对DTI鉴别胶质母细胞瘤复发与假性进展的研究较少、样本量较小且研究结论不尽一致，尚待设计更合理、纳入指标更多的大样本临床研究的验证。(2)限制波谱成像(RSI)：系多b值、多扩散时间的DWI技术，b值>3000 s/mm²可区分受胞膜限制的细胞内水分子扩散与细胞外间隙水分子扩散，且细胞内扩散信号与区域细胞结构相关[12]。胶质母细胞瘤复发时细胞内水分子扩散受到限制，RSI呈阳性即肿瘤呈高信号；而假性进展时RSI呈阴性。一项采用RSI鉴别胶质母细胞瘤复发与假性进展的试验性研究显示，RSI阳性诊断胶质母细胞瘤复发的灵敏度和特异度分别为84%和86%[13]。(3)体素内不相干运动成像(IVIM)：由Le Bihan等[14]于20世纪80年代开发，采用双指数模型(扩散和灌注)自组织扩散参数中分离灌注参数，主要包括真扩散系数D(代表单纯水分子扩散)、伪扩散系数D*(代表微循环引起的血液扩

散)和灌注分数f(代表快速扩散占总体扩散效应的百分比)。因此,采用IVIM成像可以同时获得组织灌注和细胞密度信息,且无需注射外源性对比剂。廖旦等[15]采用IVIM成像鉴别胶质母细胞瘤复发与假性进展,发现复发组真扩散系数D低于假性进展组(曲线下面积为0.925),而伪扩散系数D*(曲线下面积为0.804)和灌注分数f(曲线下面积为0.743)高于假性进展组。真扩散系数D值降低还是判断贝伐单抗治疗后胶质瘤复发的有效指标[16]。然而,IVIM成像亦存在一定的局限性,如影像采集时间长、分离扩散参数与灌注参数需较高的信噪比(SNR)、数据后处理过程较复杂、b值的选取等[17]。

二、灌注成像

灌注成像(PWI)可以反映组织中微循环血流动力学信息,间接评估组织活性和功能状态,在胶质瘤病理分级、鉴别诊断和胶质母细胞瘤预后判断等方面具有重要价值[18-19]。根据是否需要外源性对比剂分为两种技术,一种是利用对比剂的动态增强灌注,即动态磁敏感对比增强灌注成像(DSC-MRI)和动态对比增强磁共振成像(DCE-MRI);另一种是利用自身动脉血标记的动脉自旋标记(ASL)。

胶质母细胞瘤复发与假性进展的病理学差异是二者得以在PWI上进行区分的基础。肿瘤复发时,新生血管表现为高灌注(图1d,1e),而放化疗引起血管内皮细胞损伤导致的假性进展则表现为低灌注[20-24](图2d,2e)。Meta分析显示,DSC-MRI鉴别胶质母细胞瘤复发与假性进展的灵敏度和特异度分别为87%和86%,DCE-MRI为92%和85%,ASL为52%~79%和64%~82%[25],故认为DCE-MRI的鉴别诊断灵敏度最高。与DSC-MRI相比,DCE-MRI虽然时间分辨率较低,但空间分辨率较高,使其在肿瘤复发与假性进展并存的混合性病变中更准确地区分二者[25]。但是受到药物代谢动力学模型不统一、参数量化复杂等的限制,DCE-MRI并未广泛应用于临床。目前关于ASL区分胶质母细胞瘤复发与假性进展的研究较少,尽管ASL是一种无创和定量的检查方法,又可避免DSC-MRI对比剂外渗造成的结果低估或高估现象,但受限于信噪比较低、参数较单一且自旋标志物丢失伪影[26]等,尚无法普遍应用于临床。DSC-MRI、DCE-MRI和ASL这3种技术可能受抗血管生成药物的影响较大,如贝伐单抗可以使肿瘤血管通透性降低,血-脑屏障正常化,病变强化范围缩小。

三、磁共振波谱

磁共振波谱(MRS)是无创性评估活体组织代谢的功能成像技术,胆碱(Cho)、N-乙酰天冬氨酸(NAA)和肌酸(Cr)是评估胶质瘤代谢的重要指标。胶质母细胞瘤复发时,肿瘤细胞代谢活跃,正常神经元破坏,Cho值异常升高、NAA值和Cr值降低,故Cho/NAA和Cho/Cr比值显著升高(图1f);假性进展表现为神经细胞损害和炎症反应,不存在代谢活跃的肿瘤细胞,故Cho/NAA和Cho/Cr比值无变化或降低(图2f)。Verma等[27]采用MRS鉴别胶质母细胞瘤复发与假性进展,复发组Cho/NAA比值(P = 0.003)和Cho/Cr比值(P = 0.023)均高于假性进展组,Cho/NAA和Cho/Cr比值的灵敏度和特异度分别为94%和87%。亦有研究显示,Cho/NAA比值(曲线下面积为0.68,95%CI:0.460~0.910,P = 0.160)和Cho/Cr比值(曲线下面积为0.70,95%CI:0.480~0.930,P = 0.250)在胶质瘤(WHOⅢ级)和胶质母细胞瘤(WHOⅣ级)复发与假性进展、放射性坏死之间差异无统计学意义[9]。上述研究结果不一致的原因可能与MRS采集标准不同、兴趣区(ROI)组织差异等相关。应注意的是,对无强化病灶(排除出血和坏死)进行肿瘤复发与假性进展的区分时,MRS较PWI是更好的影像学方法,Cho/NAA比值>2.70鉴别高级别胶质瘤复发与假性进展的灵敏度和特异度分别为61%和81%[23]。

四、酰胺质子转移成像

酰胺质子转移(APT)成像是一种蛋白水平的MRI分子成像,旨在检测内源性移动蛋白和多肽骨架中可交换酰胺质子,并与水分子中氢质子交换,从而转化为MRI图像[28]。目前已应用于胶质瘤的病理分级、分子分型预测、放化疗早期反应评估、复发和治疗相关改变评估等[29-32]。蛋白质组学研究显示,活跃的肿瘤组织表达的蛋白种类更多且蛋白水平更高[33]。胶质母细胞瘤假性进展由于肿瘤细胞密度较低以及胞质破坏,脑组织移动蛋白和多肽较少[34],其APT成像信号强度与正常脑组织相似;胶质母细胞瘤复发则相反,故呈APT成像高信号。Ma等[35]的研究显示,胶质瘤复发的APT成像信号强度明显高于假性进展(P < 0.001),且APT成像平均信号强度为2.42%时,其鉴别肿瘤复发与假性进展的灵敏度和特异度分别为85%和100%。然而,APT成像亦存在不足,如成像时间较长、易受核奥佛豪泽(nuclear Overhauser)增强信号的影响等。

五、脑血管反应性成像

脑血管反应性(CVR)成像基于血氧水平依赖性功能磁共振成像(BOLD-fMRI),即BOLD-fMRI扫描期间同时予二氧化碳刺激,经后处理获得CVR图,定量测定病灶内部和周围CVR值可以反映脑血流自动调节(CA)能力[36]。由于弥漫性胶质瘤新生血管结构异常,不具有改变管径以调节血流的能力,因此予以血管活性刺激时,异常的肿瘤血管反应不充分,使脑血流分流至脑血管反应性良好的区域,从而导致受影响的脑组织血氧水平依赖(BOLD)信号降低。研究显示,弥漫性胶质瘤患者肿瘤内部和周围CVR值显著低于正常脑组织[37-38]。放射性坏死与胶质母细胞瘤的生物学特性不同,前者是一种局灶性炎症反应,后者则是一种弥漫性浸润性疾病,具有向周围组织不规则浸润的生长模式,因此,两种疾病病灶内部和周围CVR值亦不同:放射性坏死的CVR值在病灶内部明显低于新诊断的胶质母细胞瘤,在病灶周围则有所增加;而新诊断的胶质母细胞瘤CVR值仍持续降低[39]。目前尚无关于胶质母细胞瘤复发与假性进展或放射性坏死的基于血氧水平依赖的CVR成像模式的研究,但是由于其病理学和生物学行为存在差异,推测其基于血氧水平依赖的CVR成像模式亦可能存在差异。

六、放射组学

放射组学(radiomics)是一种新的自动化、高通量研究方法,通过直方图和纹理分析获得数千个基于图像的特征,可在微观级别(体素/像素水平)量化肿瘤表型[40-41]。目前已广泛应用于胶质瘤的各方面[42-46],如诊断与鉴别诊断、分子分型预测、疗效评估等,在胶质母细胞瘤复发与假性进展的鉴别中也有较高的潜能。Kim等[47]将DWI和DSC-MRI数据导入放射组学模型,发现多参数放射组学模型的ROC曲线下面积为0.90(95%CI:0.820~0.980),且内部验证(曲线下面积为0.96,95%CI:0.880~1.000)和外部验证(曲线下面积为0.85,95%CI:0.710~0.990)均表现出较高的准确性。Elshafeey等[48]将DCE-MRI和DSC-MRI数据导入放射组学模型,其ROC曲线下面积为0.89(P=0.017)。上述研究表明基于扩散和灌注的多参数放射组学模型可以提高胶质母细胞瘤复发与假性进展的鉴别诊断效能。

上述功能成像技术从不同角度对胶质母细胞瘤复发与假性进展进行区分,均显示出较高的敏感性和特异性,但是由于各项技术的自身限制以及病变的异质性,单一影像学方法无法有效区分二者,多种成像技术结合可以提高二者鉴别诊断的准确性。此外,目前尚缺少验证上述各种功能影像技术的大样本循证医学证据。放射组学高通量影像学特征的提取和对数据的深层次挖掘,使得基于各种功能成像技术的放射组学与人工智能(AI)相结合,有望为鉴别胶质母细胞瘤复发与假性进展提供更大的帮助。

利益冲突 无

参 考 文 献

[1] Tan AC, Ashley DM, López GY, Malinzak M, Friedman HS, Khasraw M. Management of glioblastoma: state of the art and future directions[J]. CA Cancer J Clin, 2020, 70:299-312.

[2] Ellingson BM, Wen PY, Cloughesy TF. Modified criteria for radiographic response assessment in glioblastoma clinical trials [J]. Neurotherapeutics, 2017, 14:307-320.

[3] Reardon DA, Ballman KV, Buckner JC, Chang SM, Ellingson BM. Impact of imaging measurements on response assessment in glioblastoma clinical trials[J]. Neuro Oncol, 2014, 16 Suppl 7(Suppl 7):vii24-35.

[4] Brandsma D, Stalpers L, Taal W, Sminia P, van den Bent MJ. Clinical features, mechanisms, and management of pseudoprogression in malignant gliomas [J]. Lancet Oncol, 2008, 9:453-461.

[5] Le Fèvre C, Lhermitte B, Ahle G, Chambrelant I, Cebula H, Antoni D, Keller A, Schott R, Thiery A, Constans JM, Noël G. Pseudoprogression versus true progression in glioblastoma patients: a multiapproach literature review: part 1: molecular, morphological and clinical features [J]. Crit Rev Oncol Hematol, 2021, 157:103188.

[6] Darbar A, Waqas M, Enam SF, Mahmood SD. Use of preoperative apparent diffusion coefficients to predict brain tumor grade[J]. Cureus, 2018, 10:e2284.

[7] Tsakiris C, Siempis T, Alexiou GA, Zikou A, Sioka C, Voulgaris S, Argyropoulou MI. Differentiation between true tumor progression of glioblastoma and pseudoprogression using diffusion - weighted imaging and perfusion - weighted imaging: systematic review and meta - analysis [J]. World Neurosurg, 2020, 144:e100-109.

[8] Kazda T, Bulik M, Pospisil P, Lakomy R, Smrcka M, Slampa P, Jancalek R. Advanced MRI increases the diagnostic accuracy of recurrent glioblastoma: single institution thresholds and validation of MR spectroscopy and diffusion weighted MR imaging[J]. Neuroimage Clin, 2016, 11:316-321.

[9] Liu J, Li C, Chen Y, Lv X, Lv Y, Zhou J, Xi S, Dou W, Qian L, Zheng H, Wu Y, Chen Z. Diagnostic performance of multiparametric MRI in the evaluation of treatment response in glioma patients at 3T[J]. J Magn Reson Imaging, 2020, 51:1154-1161.

[10] Wang S, Martinez-Lage M, Sakai Y, Chawla S, Kim SG, Alonso-Basanta M, Lustig RA, Brem S, Mohan S, Wolf RL, Desai A, Poptani H. Differentiating tumor progression from pseudoprogression in patients with glioblastomas using diffusion tensor imaging and dynamic susceptibility contrast MRI [J]. AJNR Am J Neuroradiol, 2016, 37:28-36.

[11] Agarwal A, Kumar S, Narang J, Schultz L, Mikkelsen T, Wang

S, Siddiqui S, Poptani H, Jain R. Morphologic MRI features, diffusion tensor imaging and radiation dosimetric analysis to differentiate pseudo-progression from early tumor progression [J]. J Neurooncol, 2013, 112:413-420.

[12] White NS, McDonald C, Farid N, Kuperman J, Karow D, Schenker-Ahmed NM, Bartsch H, Rakow-Penner R, Holland D, Shabaik A, Bjørnerud A, Hope T, Hattangadi-Gluth J, Liss M, Parsons JK, Chen CC, Raman S, Margolis D, Reiter RE, Marks L, Kesari S, Mundt AJ, Kane CJ, Carter BS, Bradley WG, Dale AM. Diffusion-weighted imaging in cancer: physical foundations and applications of restriction spectrum imaging [J]. Cancer Res, 2014, 74:4638-4652.

[13] Khan UA, Rennert RC, White NS, Bartsch H, Farid N, Dale AM, Chen CC. Diagnostic utility of restriction spectrum imaging (RSI) in glioblastoma patients after concurrent radiation-temozolomide treatment: a pilot study [J]. J Clin Neurosci, 2018, 58:136-141.

[14] Le Bihan D, Breton E, Lallemand D, Grenier P, Cabanis E, Laval-Jeantet M. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders [J]. Radiology, 1986, 161:401-407.

[15] Liao D, Liu YC, Tang B, Wang D, Li XH, Dai B, Wang RP. Comparison of DWI based on monoexponential, biexponential and stretched-exponential models in differentiating tumor recurrence and pseudoprogression of glioblastoma[J]. Zhongguo Yi Xue Ying Xiang Ji Shu, 2019, 35:1450-1455.[廖旦, 刘远成, 唐斌, 王峤, 李小海, 代斌, 王荣品. 对比单指数、双指数及拉伸指数DWI鉴别诊断胶质母细胞瘤术后复发与假性进展[J]. 中国医学影像技术, 2019, 35:1450-1455.]

[16] Miyoshi F, Shinohara Y, Kambe A, Kuya K, Murakami A, Kurosaki M, Ogawa T. Utility of intravoxel incoherent motion magnetic resonance imaging and arterial spin labeling for recurrent glioma after bevacizumab treatment[J]. Acta Radiol, 2018, 59:1372-1379.

[17] Li B, Li H, Xu D, Zhou J, Xu HB. Research progress and clinical application of IVIM in glioma[J]. Fang She Xue Shi Jian, 2021, 36:262-266.[李波, 李欢, 徐聃, 周杰, 徐海波. IVIM在胶质瘤中的研究进展及临床应用[J]. 放射学实践, 2021, 36:262-266.]

[18] Chen HY, Chen XZ, Ru XJ, Zhang YQ, Wang XP, Huang W, Ren XH, Lin S, Li Y, Wu T, Liu YO. The comparative study of multimodal MRI techniques in prognosis of glioblastoma [J]. Zhongguo Xian Dai Shen Jing Ji Bing Za Zhi, 2019, 19:850-857.[陈红燕, 陈绪珠, 茹小娟, 张月青, 汪晓鹏, 黄伟, 任晓辉, 林松, 李洋, 吴涛, 刘亚欧. 不同磁共振成像模式判断胶质母细胞瘤预后研究[J]. 中国现代神经疾病杂志, 2019, 19:850-857.]

[19] Han T, Guo J, Liu L, Liu H, Bai X, Lei J, Hao NN, Guo Y, Liu ML, Cui SM. Evaluation of clinical application in diagnosis of brain tumor with dynamic contrast-enhanced perfusion MR imaging [J]. Zhongguo Xian Dai Shen Jing Ji Bing Za Zhi, 2006, 6:211-219.[韩彤, 郭军, 刘力, 刘卉, 白旭, 雷静, 郝妮娜, 郭迎, 刘梅丽, 崔世民. 动态对比增强磁共振灌注成像在脑肿瘤诊断中的应用价值[J]. 中国现代神经疾病杂志, 2006, 6:211-219.]

[20] Zhang W, Hu WG, Song QB. Value of 3D-ASL and DCE-MRI in differential diagnosis of recurrent glioma and radiation-induced brain necrosis[J]. Guo Ji Zhong Liu Xue Za Zhi, 2021, 48:631-634.[张雯, 胡伟国, 宋启斌. 3D-ASL与DCE-MRI在脑胶质瘤复发与放射性脑坏死鉴别诊断中的价值[J]. 国际肿瘤学杂志, 2021, 48:631-634.]

[21] Bani-Sadr A, Berner LP, Barritault M, Chamard L, Bidet CM, Eker OF, Hermier M, Guyotat J, Jouanneau E, Meyronet D, Gouttard S, D'Hombres A, Iziquierdo C, Honnorat J, Berthezène Y, Ducray F. Combined analysis of MGMT methylation and dynamic-susceptibility-contrast MRI for the distinction between early and pseudo-progression in glioblastoma patients[J]. Rev Neurol (Paris), 2019, 175:534-543.

[22] Kickingereder P, Brugnara G, Hansen MB, Nowosielski M, Pflüger I, Schell M, Isensee F, Foltyn M, Neuberger U, Kessler T, Sahm F, Wick A, Heiland S, Weller M, Platten M, von Deimling A, Maier-Hein KH, Østergaard L, van den Bent MJ, Gorlia T, Wick W, Bendszus M. Noninvasive characterization of tumor angiogenesis and oxygenation in bevacizumab-treated recurrent glioblastoma by using dynamic susceptibility MRI: secondary analysis of the European Organization for Research and Treatment of Cancer 26101 Trial[J]. Radiology, 2020, 297:164-175.

[23] Cluceru J, Nelson SJ, Wen Q, Phillips JJ, Shai A, Molinaro AM, Alcaide-Leon P, Olson MP, Nair D, LaFontaine M, Chunduru P, Villanueva-Meyer JE, Cha S, Chang SM, Berger MS, Lupo JM. Recurrent tumor and treatment-induced effects have different MR signatures in contrast enhancing and non-enhancing lesions of high-grade gliomas[J]. Neuro Oncol, 2020, 22:1516-1526.

[24] Yu XY, Ren L, Liu JJ, He Y, Liu SG, Zhu M, Han G. The value of three-dimensional arterial spin labeling in identifying recurrence and pseudo-progression of high-grade glioma[J]. Shi Yong Fang She Xue Za Zhi, 2021, 37:196-198.[于秀英, 任乐, 刘俊杰, 何勇, 刘松国, 朱明, 韩广. 三维动脉自旋标记成像在鉴别高级别胶质瘤术后复发与假性进展的价值[J]. 实用放射学杂志, 2021, 37:196-198.]

[25] van Dijken BRJ, van Laar PJ, Holtman GA, van der Hoorn A. Diagnostic accuracy of magnetic resonance imaging techniques for treatment response evaluation in patients with high-grade glioma, a systematic review and meta-analysis[J]. Eur Radiol, 2017, 27:4129-4144.

[26] Amukotuwa SA, Yu C, Zaharchuk G. 3D pseudocontinuous arterial spin labeling in routine clinical practice: a review of clinically significant artifacts[J]. J Magn Reson Imaging, 2016, 43:11-27.

[27] Verma G, Chawla S, Mohan S, Wang S, Nasrallah M, Sheriff S, Desai A, Brem S, O'Rourke DM, Wolf RL, Maudsley AA, Poptani H. Three-dimensional echo planar spectroscopic imaging for differentiation of true progression from pseudoprogression in patients with glioblastoma [J]. NMR Biomed, 2019, 32:e4042.

[28] Zhou J, Heo HY, Knutsson L, van Zijl PCM, Jiang S. APT-weighted MRI: techniques, current neuro applications, and challenging issues[J]. J Magn Reson Imaging, 2019, 50:347-364.

[29] Song Q, Zhang C, Chen X, Cheng Y. Comparing amide proton transfer imaging with dynamic susceptibility contrast-enhanced perfusion in predicting histological grades of gliomas: a meta-analysis[J]. Acta Radiol, 2020, 61:549-557.

[30] Zhang H, Cui YY, Feng J, Peng H, Zhang J, Wang Y, Wang YL, Xiao HF, Chen XJ, Ma L. Diagnostic and predictive efficacy of amide proton transfer MRI in tumor grading, isocitrate dehydrogenase status and the expression level of Ki-67 and p53 in gliomas[J]. Zhongguo Yi Xue Ying Xiang Xue Za Zhi, 2020, 28:327-332.[张浩, 崔园园, 冯杰, 彭虹, 张君, 王岩, 王玉林, 肖华锋, 陈新静, 马林. 氨基质子转移成像对脑胶质瘤分级及异柠檬酸脱氢酶、Ki-67、p53表达的诊断及预测价值[J]. 中国医学影像学杂志, 2020, 28:327-332.]

[31] Meissner JE, Korzowski A, Regnery S, Goerke S, Breitling J, Floca RO, Debus J, Schlemmer HP, Ladd ME, Bachert P, Adeberg S, Paech D. Early response assessment of glioma

patients to definitive chemoradiotherapy using chemical exchange saturation transfer imaging at 7 T[J]. J Magn Reson Imaging, 2019, 50:1268-1277.
[32] Jiang S, Eberhart CG, Lim M, Heo HY, Zhang Y, Blair L, Wen Z, Holdhoff M, Lin D, Huang P, Qin H, Quinones-Hinojosa A, Weingart JD, Barker PB, Pomper MG, Laterra J, van Zijl PCM, Blakeley JO, Zhou J. Identifying recurrent malignant glioma after treatment using amide proton transfer-weighted MR imaging: a validation study with image-guided stereotactic biopsy[J]. Clin Cancer Res, 2019, 25:552-561.
[33] Ren T, Lin S, Wang Z, Shang A. Differential proteomics analysis of low- and high-grade of astrocytoma using iTRAQ quantification[J]. Onco Targets Ther, 2016, 9:5883-5895.
[34] Gonçalves FG, Chawla S, Mohan S. Emerging MRI techniques to redefine treatment response in patients with glioblastoma[J]. J Magn Reson Imaging, 2020, 52:978-997.
[35] Ma B, Blakeley JO, Hong X, Zhang H, Jiang S, Blair L, Zhang Y, Heo HY, Zhang M, van Zijl PC, Zhou J. Applying amide proton transfer-weighted MRI to distinguish pseudoprogression from true progression in malignant gliomas[J]. J Magn Reson Imaging, 2016, 44:456-462.
[36] Fisher JA, Venkatraghavan L, Mikulis DJ. Magnetic resonance imaging-based cerebrovascular reactivity and hemodynamic reserve[J]. Stroke, 2018, 49:2011-2018.
[37] Sebök M, van Niftrik CHB, Muscas G, Pangalu A, Seystahl K, Weller M, Regli L, Fierstra J. Hypermetabolism and impaired cerebrovascular reactivity beyond the standard MRI-identified tumor border indicate diffuse glioma extended tissue infiltration[J]. Neurooncol Adv, 2021, 3:vdab048.
[38] Muscas G, van Niftrik CHB, Sebök M, Seystahl K, Piccirelli M, Stippich C, Weller M, Regli L, Fierstra J. Hemodynamic investigation of peritumoral impaired blood oxygenation-level dependent cerebrovascular reactivity in patients with diffuse glioma[J]. Magn Reson Imaging, 2020, 70:50-56.
[39] Muscas G, van Niftrik CHB, Sebök M, Della Puppa A, Seystahl K, Andratschke N, Brown M, Weller M, Regli L, Piccirelli M, Fierstra J. Distinct cerebrovascular reactivity patterns for brain radiation necrosis[J]. Cancers (Basel), 2021, 13:1840.
[40] Peng H, Huo J, Li B, Cui Y, Zhang H, Zhang L, Ma L. Predicting isocitrate dehydrogenase (IDH) mutation status in gliomas using multiparameter MRI radiomics features[J]. J Magn Reson Imaging, 2021, 53:1399-1407.
[41] Yi Z, Long L, Zeng Y, Liu Z. Current advances and challenges in radiomics of brain tumors[J]. Front Oncol, 2021, 11:732196.
[42] Sohn CK, Bisdas S. Diagnostic accuracy of machine learning-based radiomics in grading gliomas: systematic review and meta-analysis[J]. Contrast Media Mol Imaging, 2020:ID2127062.
[43] Choi YS, Bae S, Chang JH, Kang SG, Kim SH, Kim J, Rim TH, Choi SH, Jain R, Lee SK. Fully automated hybrid approach to predict the IDH mutation status of gliomas via deep learning and radiomics[J]. Neuro Oncol, 2021, 23:304-313.
[44] Wei J, Yang G, Hao X, Gu D, Tan Y, Wang X, Dong D, Zhang S, Wang L, Zhang H, Tian J. A multi-sequence and habitat-based MRI radiomics signature for preoperative prediction of MGMT promoter methylation in astrocytomas with prognostic implication[J]. Eur Radiol, 2019, 29:877-888.
[45] Su C, Jiang J, Zhang S, Shi J, Xu K, Shen N, Zhang J, Li L, Zhao L, Zhang J, Qin Y, Liu Y, Zhu W. Radiomics based on multicontrast MRI can precisely differentiate among glioma subtypes and predict tumour-proliferative behaviour[J]. Eur Radiol, 2019, 29:1986-1996.
[46] Han Y, Cui GB, Nan HY. Radiomics model based on plain MRI for distinguishing solitary brain inflammation from atypical glioma[J]. Shi Yong Fang She Xue Za Zhi, 2021, 37:1578-1582.[韩宇, 崔光彬, 南海燕. 基于平扫MRI影像组学模型鉴别单发性脑炎与不典型胶质瘤[J]. 实用放射学杂志, 2021, 37:1578-1582.]
[47] Kim JY, Park JE, Jo Y, Shim WH, Nam SJ, Kim JH, Yoo RE, Choi SH, Kim HS. Incorporating diffusion- and perfusion-weighted MRI into a radiomics model improves diagnostic performance for pseudoprogression in glioblastoma patients[J]. Neuro Oncol, 2019, 21:404-414.
[48] Elshafeey N, Kotrotsou A, Hassan A, Elshafei N, Hassan I, Ahmed S, Abrol S, Agarwal A, El Salek K, Bergamaschi S, Acharya J, Moron FE, Law M, Fuller GN, Huse JT, Zinn PO, Colen RR. Multicenter study demonstrates radiomic features derived from magnetic resonance perfusion images identify pseudoprogression in glioblastoma[J]. Nat Commun, 2019, 10:3170.

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《中国现代神经疾病杂志》关于谨防盗用编辑部名义的声明

近日，有作者举报不法分子盗用《中国现代神经疾病杂志》编辑部名义给作者发送邮件，让作者添加其微信好友，借以窃取相关信息甚至进行钱财诈骗。这种行为严重违反了国家《关于维护互联网安全的决定》等法律法规，严重损害了我刊编辑部和作者的利益。

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