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Роль магнитно-резонансной томографии в выявлении злокачественных лёгочных узлов: систематический обзор и метаанализ

Ю.А. Васильев^{1, 2}, О.Ю. Панина^{1, 2, 3}, Е.А. Грик³, Е.С. Ахмад¹, Ю.Н. Васильева³¹ Научно-практический клинический центр диагностики и телемедицинских технологий, Москва, Российская Федерация² Городская клиническая онкологическая больница № 1, Москва, Российская Федерация³ Московский государственный медико-стоматологический университет имени А.И. Евдокимова, Москва, Российская Федерация

АННОТАЦИЯ

Цель — оценка возможности метода магнитно-резонансной томографии (МРТ) органов грудной клетки для выявления лёгочных узлов, подозрительных в отношении злокачественности, в сравнении с компьютерной томографией (КТ).

Материалы и методы. Проведён поиск в базах данных PubMed и Google Scholar за период до 7 апреля 2021 г. включительно. В соответствии с критериями соответствия были отобраны исследования, в которых проводилась оценка способности МРТ и КТ к выявлению лёгочных узлов, подозрительных в отношении злокачественности. Выбор метода анализа и группировки данных о чувствительности и специфичности выполняли по результатам оценки гетерогенности исследований. Для оценки статистической гетерогенности исследований, включённых в метаанализ, применяли критерий согласия Пирсона χ^2 и индекс гетерогенности I^2 .

Результаты. По результатам поиска было отобрано 168 работ, в метаанализ вошло 21 исследование. Отобранные работы включали 1188 пациентов. По результатам метаанализа выявлено наличие статистически значимой гетерогенности $p < 0,00001$ по критерию χ^2 и индекс гетерогенности $I^2=99\%$ для чувствительности и специфичности. В связи с этим для анализа данных использовали метод случайных эффектов. Значения чувствительности для МРТ находились в диапазоне от 70,4 до 100%, специфичности — от 60,6 до 100%.

Заключение. МРТ обладает достаточной чувствительностью и специфичностью для определения злокачественности лёгочных узлов, обнаруженных при КТ-диагностике.

Ключевые слова: магнитно-резонансная томография; лёгочные узлы; рак лёгкого; чувствительность; специфичность.

Как цитировать

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Role of chest MRI for the diagnosis of malignant pulmonary nodules: a systematic review and a meta-analysis

Yuriy A. Vasilev^{1, 2}, Olga Yu. Panina^{1, 2, 3}, Evgeniia A. Grik³, Kate A. Akhmad¹, Yulia N. Vasileva³

¹ Research and Practical Clinical Center for Diagnostics and Telemedicine Technologies of Moscow Health Care, Moscow, Russian Federation

² City Clinical Oncological Hospital No. 1, Moscow, Russian Federation

³ Moscow State University of Medicine and Dentistry named after A.I. Evdokimov, Moscow, Russian Federation

ABSTRACT

AIM: To evaluate the ability of magnetic resonance imaging (MRI) of the chest to detect malignant pulmonary nodules compared to compute tomography (CT).

MATERIALS AND METHODS: We searched the following databases with the final date of search on April 7th, 2021: PubMed, Google Scholar. We selected studies according to the inclusion and exclusion criteria that assessed the detection of malignant lung nodules by MRI and CT and included information about sensitivity and specificity. Method of the analysis and data grouping was chosen with regard to statistical heterogeneity of the studies included in the analysis. We used the χ^2 test and I^2 statistic to evaluate the heterogeneity.

RESULTS: We selected 168 articles for the systematic review from the PubMed and Google Scholar databases. We included 21 studies on 1,188 patients in the meta-analysis and revealed statistically significant heterogeneity ($p < 0,00001$ for χ^2 test; $I^2 = 99\%$) for sensitivity and specificity. Hence, we used a random-effect model for further analysis. As a result, values of sensitivity for detection of pulmonary nodules with MRI of 70.4%–100%, specificity — from 60.6% to 100%.

CONCLUSIONS: Thus, MRI has sufficient sensitivity and specificity for detecting malignant pulmonary nodules primarily discovered with CT.

Keywords: MRI; solitary pulmonary nodule; lung cancer; benign; malignant.

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磁共振成像在恶性肺结节检测中的作用：系统回顾和荟萃分析

Yuriy A. Vasilev^{1,2}, Olga Yu. Panina^{1,2,3}, Evgeniia A. Grik³, Kate A. Akhmad¹, Yulia N. Vasileva³

¹ Research and Practical Clinical Center for Diagnostics and Telemedicine Technologies of Moscow Health Care, Moscow, Russian Federation

² City Clinical Oncological Hospital No. 1, Moscow, Russian Federation

³ Moscow State University of Medicine and Dentistry named after A.I. Evdokimov, Moscow, Russian Federation

简评

目的是评估胸部MRT与CT检测肺结节的可能性，怀疑有恶性肿瘤。

材料与方法。截至 2021 年 4 月 7 日（含）进行了 PubMed 和 Google Scholar 数据库根据资格标准，选择了评估 MRI 和 CT 识别可疑恶性肺淋巴结能力的研究。分析方法的选择和敏感性和特异性数据的分组是根据评估研究异质性的结果进行的。为了评估荟萃分析中包括的研究的统计异质性，使用了 Pearson χ^2 拟合检验和 I² 异质性指数。

结果。根据检索结果，筛选出 168 项研究，21 项研究纳入荟萃分析。入选作品包括 1188 名患者。根据 χ^2 标准和异质性指数 I² = 99% 的敏感性和特异性，荟萃分析显示存在统计学上显著的异质性 $p < 0.00001$ 。对此，采用随机效应的方法对数据进行分析。MRT 的灵敏度值范围从 70.4 到 100%，特异性 - 从 60.6 到 100%。

结论。因此，MRI 具有足够的敏感性和特异性来确定 CT 诊断中发现的肺淋巴结的恶性程度。

关键词：磁共振成像；肺结节；肺癌；灵敏度；特异性。

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绪论

光节点 (solitary pulmonary nodule, SPN) 单一的圆形聚焦, 直径尺寸小于3厘米[1, 2]。肺总被一块未改变的轻布完全包围, 与肺不张无关, 肺不张是轻微或纵隔的根部。这种形成可能是良性过程, 如错构瘤、各种感染性病变、肉芽肿性炎症, 以及恶性过程 (如原发性肺癌、转移性疾病或淋巴瘤)。直到相反的情况被证实, 淋巴结才被认为是恶性的[2]。

目前, 计算机断层扫描 (CT) 是一种金标准, 用于评估和动态控制可疑恶性肿瘤的沼泽地质量[3]。CT在存在大量优点的情况下有一个主要缺点——高辐射负荷, 这在动态控制过程中肯定会增加。随着技术和软件的发展和完善, 寻找新的可视化方法变得越来越明显。过去的20年中, 研究磁共振成像 (MRI) 在诊断胸部器官疾病中的潜在应用, 使得有可能分配一个单独的科学研究领域, 通过MRI识别轻结节。MRI的优点是不暴露于电离辐射, 并且即使在没有引入对比剂制剂的情况下, 也可以对确定的变化进行可选的定量评估。

研究的目的是评估胸部MRI与标准CT相比检测恶性肺淋巴结的可能性。

研究方法

这项工作是根据 PRISMA 标准制定的, 用于报告系统评价和荟萃分析的结果 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [4]。

研究的类型。

选标准:

- (I) 前瞻性病例对照研究、回顾性病例对照研究、前瞻性队列研究、回顾性队列研究;
- (II) 包括描述使用 MRI 检测恶性肺结节的研究;
- (III) 标准方法为 CT;
- (IV) 具有敏感性和特异性。

排除标准:

- (I) 工作全文不可用;
- (II) 研究不是以人为对象;
- (III) 这项研究是在儿童的参与下进行的;
- (IV) 临床病例描述、系列病例研究、系统回顾、元分析;
- (V) 正电子发射断层扫描 (PET) 和CT (PET/CT) 的结合以及正电子发射断层扫描和MRI (PET/MRI) 的结合; 对比强化研究;
- (VI) 将肺结核和其他炎症性肺病患者纳入研究。

参与者的类型。

年龄大于18岁;

本综述不包括缺乏标准参考方法 (标准胸部器

官CT) 诊断数据的患者。

干预类型。

对MRI和标准CT检测疑似恶性肺结节的能力进行了评估的研究。

结果类型。

初期的效果: 肺MRI敏感性和特异性数值评价恶性肺结节的鉴别诊断。

二次结果: 确定最佳MR脉冲序列。

信息来源

2021年4月7日前搜索 PubMed和Google Scholar 数据库。

探索

PubMed数据库使用了两种类型的搜索查询, 使用Mesh库术语和关键字搜索最近的文章, 由于PubMed大约需要一个月的时间才能将Mesh一词分配给已出版的作品:

«Magnetic Resonance imaging» [Mesh] or «MRI» and «Computed tomography» or «CT» and «Lung neoplasms» [Mesh] or «Solitary Pulmonary Nodule» [Mesh] and «Sensitivity» and «Specificity»;

«Lung MRI» or «chest MRI» and «Computed tomography» or «CT» and «lung cancer» or «Solitary Pulmonary Nodule».

Google Scholar使用“MRI、CT、Lung Cancer、Specificity、Sensitivity”查询进行搜索。

数据收集过程和数据元素

使用Google服务, Spreadsheet开发了一个数据提取表。作者可以同时和不受限制地访问该文件。两位研究人员 (O.Yu. Panina 和 E.A. Grik) 从所选作品中提取了以下数据: 文章标题、期刊 (或发布预印本的服务)、发表日期、DOI、MRI 协议、MRI 的磁感应值、类型MRI 和 CT 识别的病变、敏感性、特异性、标准偏差。分别为每个脉冲序列 (PT) 计算灵敏度和特异性指标的情况下, 元分析包括最有效的指标。

其他三名研究人员 (E.S. Akhmad, Yu.N. Vasileva 和 Yu.A. Vasiliev) 验证了提取的数据。在作者之间的讨论中, 所有的分歧都得到了解决。

研究中出现系统错误的风险。

为了评估与诊断准确性研究相关的方法论困难, 作者使用了美国卫生保健研究和质量机构 ([5] Agency for Healthcare Research and Quality, Cochrane Collaboration) 推荐的系统评审的QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) 检查表[15]。

每一篇被选中的论文都在四个方面进行了评估：患者选择、研究测试、参考测试和患者流量。

《Cochrane干预措施系统评价手册》(Cochrane Handbook) 提供了每个方向的完整描述和使用的判断标准[16][6]。

统计分析

根据评估研究异质性的结果，选择分析方法和敏感性和特异性数据分组（随机效应模型或固定效应模型）。 χ^2 检验和 I^2 异质性指数用于评估纳入荟萃分析的研究的统计异质性。研究中具有统计学意义的异质性在 χ^2 和 $I^2 > 40\%$ 的标准中为 $p < 0.10$ 。元分析是使用Revman 5.4.1软件包进行的。

结果

基于在PubMed和Google Scholar数据库的搜索结果，我们选择了168项研究，这些研究通过Mendeley链接管理软件导入到图书馆。经过对纳入排除标准的补充验证和研究文本的研究，剩下33件作品（图1）。

对剩余33篇论[7 - 38]文文本的研究中发现，两项研究进行了对比增强CT检查，[23, 24]这也是一种不相关的干预类型。此外，10篇论[20 - 22, 25 - 29, 31, 32]文完全缺乏对CT的敏感性和特异性值，因此决定排除研究数据。荟萃分析包括对照研究为低剂量 CT[9, 10, 16] 的文章，这不是排除标准。因此，21 项研究被直接纳入荟萃分析（图 1）。

入选作品包括 1188 名患者。所有的研究都包含了有关MRI和肺CT程序的信息。所有论文都提供了MRI和CT的敏感性数据，但三篇论文没有给出特异性指标[8, 16, 30]。大多数研究是在磁场感应为 1.5 T 的断层扫描仪上进行的（表 1）。

偏倚风险

11 项研究充分报告了研究和参考测试信息[7, 8, 10 - 13, 15 - 18, 33]。错误的主要来源是指数测试 (MRI) 及其解释（图 2）。一些研究没有充分的数据来判断偏见的风险：例如，是否在不知道基准测试结果的情况下对指标测试结果进行了解释，反之亦然，在不知道指标测试结果的情况下对基准测试进行了解释。如果发现效果的研究比没有效果的研究更容易发表，那么也存在系统错误的风险。然而，在所有的研究中，参与者都符合本综述的方案标准。

根据 χ^2 标准和异质性指数 $I^2 = 99\%$ 的敏感性和特异性，荟萃分析显示存在统计学上显著的异质性 $p < 0.00001$ 。对此，采用随机效应的方法对数据进行分析。

胸部MRI诊断准确性

在 21 篇论文中，每篇论文都将 MRI 与参考方法进行了比较。MRI 的灵敏度值范围从 70.4

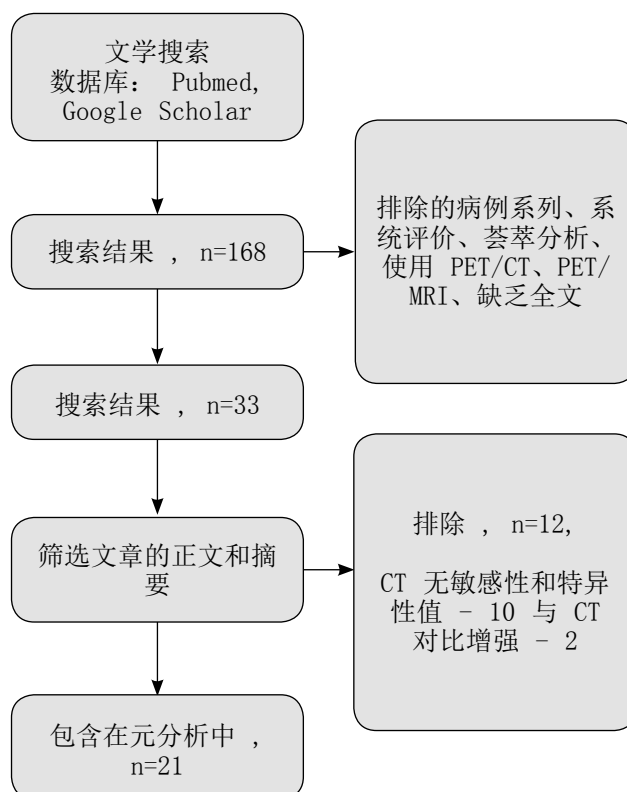


图 1 研究选择过程概述 (flow diagram)。

到 100%，特异性 - 从 60.6 到 100%（图 3）。MRI 敏感性的平均值为 88.3%，特异性为 - 71.3。未标明敏感性和特异性标准差 SD 参数的作品中，通过评估指标值进行计算[40]。

置信区间表 2 显示了荟萃分析中包含的研究的特征，MRI 的敏感性和特异性值最高可与CT相媲美。图3中研究数据被标记为在 MRI 和 CT 的敏感性和特异性方面具有最小差异。

讨论

与CT相比，本元分析结果显示MRI方法的特异性和灵敏度平均值较低。大多数包括元分析在内的研究中，胸部CT对肺结节的敏感性和特异性为100%。只有三件作品的表现较低。这是因为在包括的研究中，CT起到了参考试验的作用。对于MRI，21项研究中有5项具有100%的灵敏度，2项研究具有100%的灵敏度和特异性。

分析荟萃分析的结果时，发现在研究中观察到高敏感性指标，其中敏感性和特异性的一般指标是针对整个MR协议计算的，而不是针对每个PT单独计算的（表 2）。这种现象显示了 MRI 荟萃分析的特殊性，因为它是一种结合扫描协议执行信号特征评估的方法。这些例子可能表明对 MRI 在肺结节鉴别诊断中的能力了解不足，需要研究现代 PT，以及在断层扫描仪上仔细调整常规 PT。这种方法将有助于提高MRI检测肺淋巴结并研究其特征的效率，这在肺癌的诊断中尤为重要。

表 1元分析研究的特点

序号	研究	年纪	磁场感应, T (特斯拉)	型号, MRI 制造商	PT MRI
1	Both [7]	2005	1,5	Magnetom Vision, Siemens	VIBE, HASTE, T2TSE
2	Bruegel [8]	2007	1,5	Magnetom Sonata, Siemens	STIR
3	Chang [19]	2015	1,5	Intera Achieva, Philips	SS-TSE-HF
4	Cieszanowski [30]	2016	1,5	Magnetom Avanto, Siemens	T2TSE, T2-STIR, T2-HASTE
5	Dewes [33]	2016	3,0	Magnetom Prisma, Siemens	CAIPIRINHA-VIBE
6	Fatihoglu [34]	2019	1,5	Magnetom Aera, Siemens	DWI (ADC)
7	Heye [35]	2012	1,5	Avanto, Siemens	VIBE, HASTE
8	Huang [39]	2020	1,5	Magnetom Aera, Siemens	UTE free-breathing
9	Koo [36]	2019	3,0	Magnetom Skyra, Siemens	T2FSE
10	Koyama [37]	2008	1,5	Intera, Philips	STIR
11	Koyama [38]	2015	1,5	Achieva, Philips	DWI (ADC)
12	Meier-Schroers [9]	2016	1,5	Ingenia, Philips	T2FSE
13	Meier-Schroers [10]	2019	1,5	Ingenia, Philips	T2STIR
14	Ohno [11]	2017	3,0	Vantage Titan, Canon Medical Systeme	UTE
15	Regier [12]	2011	1,5	Achieva, Philips	DWI (ADC)
16	Satoh [13]	2008	1,5	Intera NovoDual, Philips	DWI (ADC)
17	Schaefer [14]	2006	1,0	Magnetom Expert, Siemens	PDWI
18	Schroeder [15]	2005	1,5	Magnetom Sonata, Siemens	HASTE
19	Sommer [16]	2014	1,5	Magnetom Avanto, Siemens	HASTE
20	Vogt [17]	2004	1,5	Magnetom Sonata, Siemens	HASTE
21	Yi [18]	2007	3,0	Achieva, Philips	T1WI 3D TFE*

注意: PT MRI - 磁共振成像的脉冲序列。

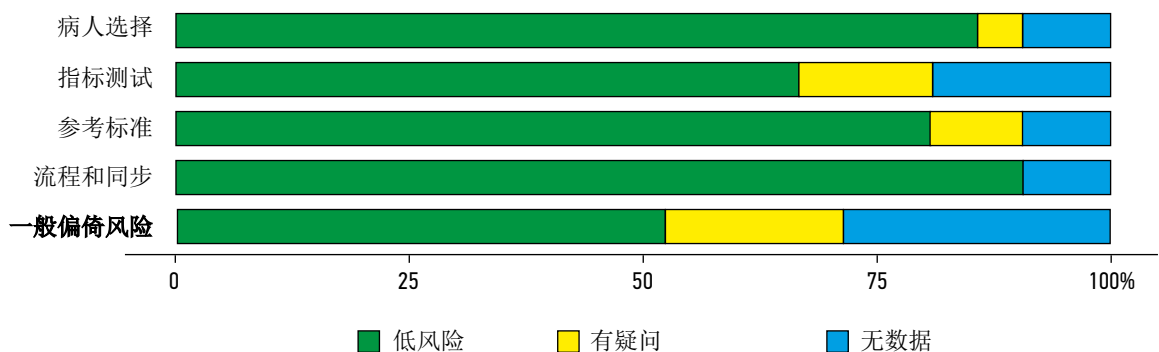


图 2 偏差风险直方图

肺癌继续在世界范围内的死亡率中占据主导地位, 包括在俄罗斯联邦, 这是一个严重的社会经济问题[41, 42]。已识别的肺结节中, 癌症的存在范围为 10% 至 70%[2]。一些国家, 低剂量 CT 扫描是在高危人群中进行的, 作为筛查的一部分。但目前, 筛查计划的人群覆盖率仍然较低, 患者的纳入标准有限, 以确保其经济可行性。因此, 许多患者在出现症状后仍会被诊断出来, 即不是在疾病发展的早期阶段, 并且在

错误诊断的情况下会导致高昂的错误成本[41]。监测和管理不明确的肺结节对于放射线技师和临床医生来说仍然是一个挑战, 因此, 只有综合方法总是用于进行诊断、患者路由和选择最佳管理和治疗策略[43]。

该荟萃分析显示了评估可疑肺结节癌症的替代方法的可能性。我们的研究中, 重点是不使用对比度增强的标准研究。

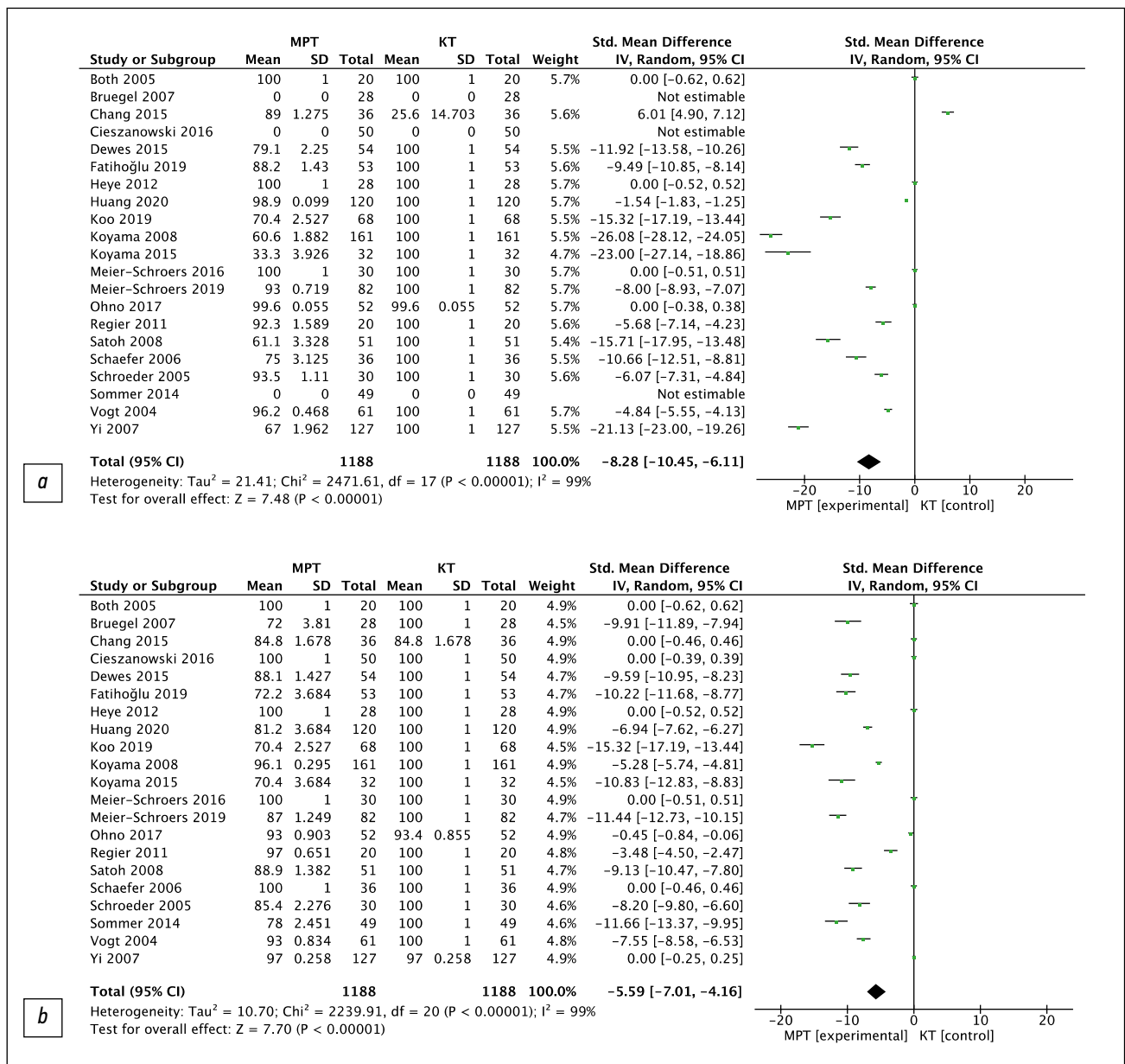


图 3 特异性 (a) 和敏感性 (b) 分组数据的森林图[40]。

注意: SMD (standardized mean difference) — 标准化平均差; CI (confidence interval) — 置信区间。

表 2 灵敏度和特异性指标最高的研究特点

序号	作者, 研究年	灵敏度 (一般指标)	特异性 (一般指标)	PT MRI	磁场感应, T (特斯拉)
1	Both, 2005 [7]	100	100	VIBE, HASTE, T2TSE	1, 5
2	Cieszanowski, 2016 [30]	100	-	T2TSE, T2-STIR, T2-HASTE	1, 5
3	Meier-Schroers, 2016 [9]	100	100	T2FSE	1, 5
4	Regier, 2011 [12]	97	92, 3	DWI (ADC)	1, 5
5	Heye, 2012 [35]	100	100	VIBE, HASTE	1, 5
6	Schaefer, 2006 [14]	100	75	PDWI	1, 5

注意: PT MRI - 磁共振成像的脉冲序列。

研究的局限性

这项研究有几个局限性。出于多种原因，荟萃分析纳入了病变大于6毫米的数据。首先，研究中最常见的结节尺寸大于6毫米；其次，根据 Fleischner 社区的最新数据，小于6毫米的淋巴结具有相当低的恶性风险 [3]。此外，荟萃分析没有将 MRI 方法与组织学数据进行比较，这也可能是研究的局限性。

结论

MRI 对 CT 上发现的可疑肺结节的额外诊断具有足够的敏感性和特异性。MRI 敏感性平均值为 88.3%，特异性为 71.3%。

MRI 是一种非电离辐射诊断方法，此外，在评估各种 PI 时，它可以作为解决有争议病例的附加方法。

有必要进一步研究最有效的脉冲序列、对比度增强的可行性以及高质量诊断肺淋巴结的新技术解决方案。

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附加信息

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所有作者都确认其作者符合国际 ICMJE 标准（所有作者为文章的概念，研究和准备工作做出了重大贡献，并在发表前阅读并批准了最终版本）。

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AUTHORS' INFO

* **Olga Yu. Panina**, MD;

address: 24/1 Petrovka str., 127051, Moscow, Russia;
ORCID: <https://orcid.org/0000-0002-8684-775X>;
eLibrary SPIN: 5504-8136; e-mail: o.panina@npcmr.ru

Yuriy A. Vasilev, MD, Cand. Sci. (Med.);

ORCID: <https://orcid.org/0000-0002-0208-5218>;
eLibrary SPIN: 4458-5608; e-mail: dr.vasilev@me.com

Evgeniia A. Grik, MD;

ORCID: <http://orcid.org/0000-0002-7908-3982>;
eLibrary SPIN: 5558-7307; e-mail: evgeniyagrik@gmail.com

Kate S. Akhmad;

ORCID: <http://orcid.org/0000-0002-8235-9361>;
eLibrary SPIN: 5891-4384; e-mail: e.ahmad@npcmr.ru

Yulia N. Vasileva, MD, Cand. Sci. (Med.);

ORCID: <http://orcid.org/0000-0002-1066-3989>;
eLibrary SPIN: 9777-2067; e-mail: drugya@yandex.ru

ОБ АВТОРАХ

* **Панина Ольга Юрьевна**,

адрес: Россия, 127051, Москва, ул. Петровка, д. 24, стр. 1;
ORCID: <https://orcid.org/0000-0002-8684-775X>;
eLibrary SPIN: 5504-8136; e-mail: o.panina@npcmr.ru

Васильев Юрий Александрович, к.м.н.;

ORCID: <https://orcid.org/0000-0002-0208-5218>;
eLibrary SPIN: 4458-5608; e-mail: dr.vasilev@me.com

Грик Евгения Андреевна;

ORCID: <http://orcid.org/0000-0002-7908-3982>;
eLibrary SPIN: 5558-7307; e-mail: evgeniyagrik@gmail.com

Ахмад Екатерина Сергеевна;

ORCID: <http://orcid.org/0000-0002-8235-9361>;
eLibrary SPIN: 5891-4384; e-mail: e.ahmad@npcmr.ru

Васильева Юлия Николаевна, к.м.н.;

ORCID: <http://orcid.org/0000-0002-1066-3989>;
eLibrary SPIN: 9777-2067; e-mail: drugya@yandex.ru

* Corresponding author / Автор, ответственный за переписку