Original Article

Diagnostic performance of diffusion-weighted magnetic resonance imaging in pulmonary malignant lesions: a meta-analysis

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Background: Overuse or misuse of positron emission tomography/computed tomography (PET/CT) should be avoided for its ionizing-radiation. Diffusion-weighted magnetic resonance imaging (DW-MRI), characterized by no radiation, may be regarded as an alternative in differentiating pulmonary nodules. We aim to estimate the diagnostic accuracy of DW-MRI in diagnosing of pulmonary lesions.

Methods: Relevant studies were searched through PubMed and Embase with no language restriction from inception to March 8, 2019. We selected studies reporting sensitivity and specificity of DW-MRI for differentiating pulmonary nodules. A summary estimates of sensitivity, specificity and area under curve (AUC) of receiver operating characteristic (ROC) of DW-MRI were analyzed with a random effects model.

Results: We included data from 37 studies, which altogether included 2,311 pulmonary lesions. The pooled sensitivity and specificity were 0.86 (95% CI, 0.82–0.89) and 0.79 (95% CI, 0.72–0.85), and AUC was 0.90 (95% CI, 0.87–0.92). Subsequent subgroup analysis showed the higher sensitivity of DW-MRI in pulmonary lesion >2 cm in comparison to lesions ≤2 cm, however, higher specificity was observed in smaller lesions.

Conclusions: Radiation-free DW-MRI showed a favorable balance between sensitivity and specificity in diagnosing pulmonary malignancies especially in lesion size ≤2 cm. Existing evidence indicated that DW-MRI may be considered as an independent substitute in diagnosis of lung lesions, which might help to prevent long-term side-effects from radiographic diagnosing and evaluating procedures.

Keywords: Pulmonary malignant lesions; pulmonary nodules; diffusion-weighted magnetic resonance imaging; diagnostic; meta-analysis

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Introduction

Although ^{18}F-fludeoxyglucose (FDG) positron emission tomography (PET) is recommended to evaluate suspicious lesions by diagnostic guidelines (1-3), the American Society of Clinical Oncology (ASCO) and European Society for Medical Oncology (ESMO) have all claimed that PET or PET/computed tomography (PET/CT) had been overused or misused and declined to include surveillance PET or PET/CT in disease-specific guidelines (4). For instance, US annual per capita radiation dose increased from 0.1 mSv in 1980 to 0.77 mSv in 2006 from the source of nuclear medicine (5).

However, there have not been radiation-free and noninvasive test recommended by guideline used for diagnosis and evaluation in cancer patients so far. With consideration of this condition, magnetic resonance imaging (MRI) has been gaining increasing attention due to its radiation-free characteristic. There are several well controlled and rigorously conducted investigations showing that diffusion-weighted MRI (DW-MRI) could achieve a comparable even better performance in cancer diagnosis and metastasis staging as compared to PET/CT (6-11). In clinical practice, however, clinicians generally only consider PET or PET/CT as the method used for cancer staging and follow-up examination, but ignore the potential utilization of DW-MRI in cancer patients. As for DW-MRI, it is cost- and time-efficient, and no contrast agent is involved during screening, but if it could be regarded as an alternative selection to diagnose pulmonary lesions is still to be confirmed.

A recent meta-analysis by Deepen *et al*. have found PET combined with CT or not with reduced specificity of 61% in regions where infectious lung disease is endemic (12). MRI yields information, such as integrity, about microscopic structures. When analyzing quantitatively in DW-MRI, there is a significant difference in apparent diffusion coefficient (ADC) values between malignant and benign lesions. Most recently, Shen *et al.* reported ADC value was helpful for distinguishing malignant and benign lung lesions (13). In the only known meta-analysis about accuracy of DW-MRI in lung lesions, this modality was reported to be useful for differentiation between malignant and benign pulmonary lesions with pooled sensitivity of 84% and specificity of 84% (14). However, no standardization of quality assurance protocols for DW-MRI was included in their study, which was critical to repeatability of this imaging modality in cancer screening. ADC was merely focused on as an imaging measure for lung lesion diagnosis in the previous meta-analysis by Shen *et al.*, lesion size was not considered and only 10 studies were included in the study (13). In view of this, no sufficient evidence has been available to firmly establish the advantages of DW-MRI test performance to diagnose pulmonary malignancies so far.

Our aim was to estimate the sensitivity, specificity, diagnostic odds ratio (DOR) and area under receiver-operator characteristics curve (AUC) of DW-MRI for discrimination between malignant and benign pulmonary lesions. Moreover, we intended to clarify the lesion size and other indispensable parameters of DW-MRI which may affect the accuracy of DW-MRI and drawing attention of researchers in the future.

Methods

We did a meta-analysis in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines and the guidelines described in the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (15).

Search strategy and selection criteria

We searched Embase and PubMed to identify the relevant studies. Under the supervision of a librarian at the Fourth Military Medical University, we searched these databases from their inception through March 8 2019. No language restriction was placed on these searches. We checked reference lists of all retrieved articles to identify additional suitable studies. A radiologist and an oncologist were asked to look through these literatures and assess their eligibility for analysis. The inclusion criteria included studies that assessed the diagnostic accuracy of DW-MRI in lung lesions. The inclusion criteria included: (I) studies that assessed the diagnostic accuracy of DW-MRI, among which systematic reviews and meta-analyses were used only as a source of references, (II) studies that assessed pulmonary lesions, (III) studies that validated the performance of DW-MRI in lung lesion diagnosis and should state that all participants had the index and reference tests, and (IV) studies which was possible to allow calculation of sensitivity and specificity. Conference abstracts were included when they contained relevant data or relevant unpublished data could be obtained from the authors. We excluded all studies that could be classified as (I) narrative reviews, letters,

editorials, comments, and case reports; (II) surveillance of the tumor response to therapy and survival in patients with cancers treated with chemoradiotherapy. A total of 37 studies were finalized. Any disagreement between them was resolved by discussing with a third investigator. The information, including author list, journals, affiliation, and the publication date, remained blinded to the above reviewers. All studies were selected in two rounds, first on title and abstract and second on full text, against the following criteria.

Quality assessment

The quality of the selected studies and the potential bias were assessed using the pre-specified STARD and the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) instrument (16), including additional items as recommended by the Cochrane Collaboration. This quality assessment procedure was independently performed by two pairs of reviewers and was checked by a fifth reviewer. Any disagreements were resolved by discussion involving all researchers when necessary. The reference of standard (ROS) was validated by a clinical review committee consisting of three researchers.

Data extraction

Two reviewers independently extracted relevant data from the selected studies in a standard form, a third investigator checked the extracted data, and a fourth investigator arbitrated on discrepancies between the first two investigators. Any identified discrepancies were discussed and corrected. 2×2 contingency tables were constructed, summarizing true positives (TP), false positives (FP), true negatives (TN), and false negatives (FN). Moreover, if various kinds of research type (per-patient *vs.* per-lesion and DW-MRI only *vs.* DW-MRI with other sequence) were available in individual study, we incorporated them into our study separately and made a subgroup analysis of each type. In some investigations, either the number of patients or the number of lesions was used for the statistical analyses. In order to avoid this inconsistence, we also conducted separate analyses for each category.

Statistical analysis

A random effects model was performed for the primary meta-analysis using a non-linear mixed model approach. The objective is to estimate the sensitivity and the specificity with 95% confidential intervals (CIs) of DW-MRI. We also computed the distribution of individual studies on summary receiver-operator characteristic (sROC) plots. Positive and negative likelihood ratios (LR^+ and LR^-) are metrics that combine sensitivity and specificity in their calculation for the discriminating ability of each imaging modality (17,18). If the LR^+ is >5.0 and the LR^- is <0.2, then the test can both rule in and rule out the disease.

The heterogeneity was assessed using the Cochrane Q and I^2 statistics (19). I^2 over 50% indicates heterogeneous, while $P<0.05$ was considered having heterogeneity in likelihood ratio χ^2 test. We assessed publication bias by Deeks' plots (20). Subgroup analyses by statistical modeling were planned for pre-specified items. Allowing for variation in result of three signaling questions in QUADAS-2, we put them into subgroup analysis (consecutive enrollment, reference standard and operation interval) to seek potential impact. To assess the impact of covariates (i.e., subgroup factors) on test performance of DW-MRI for cancer diagnosing, we considered a meta-regression with various covariates, and it is a tool used in meta-analysis to examine the impact of moderator variables on study effect size using regression-based techniques. It is more effective at this task than standard meta-analytic techniques (21).

We reported the average adjusted estimates of sensitivity and specificity because of the validity of their interpretation and general applicability. All tests were 2-sided with a type I error of .05. All analyses were performed using the software StataSE version 12 (StataCorp).

Results

A total of 748 articles were reviewed. Among them, 711 were excluded after primary and subsequent reviewing. The remaining 37 articles involved 2,311 pulmonary lesions (*Figure 1*, *Table S1*).

The quality of the included studies was assessed by the QUADAS-2 tool. Discriminations were primarily found in domain of "consecutive enrollment, reference standard and operation interval" for all studies. Consequently, we selected these signaling questions as covariates in subgroup analysis, to explore if they could affect the accuracy of our research.

For the assessment of efficacy of DW-MRI in lung cancer (with a 95% CI reported in the included individual studies), the detailed sensitivity and specificity values were illustrated by forest plot (*Figure 2*). Pooled sensitivity and specificity of 37 studies for DW-MRI were 0.86 (95% CI,

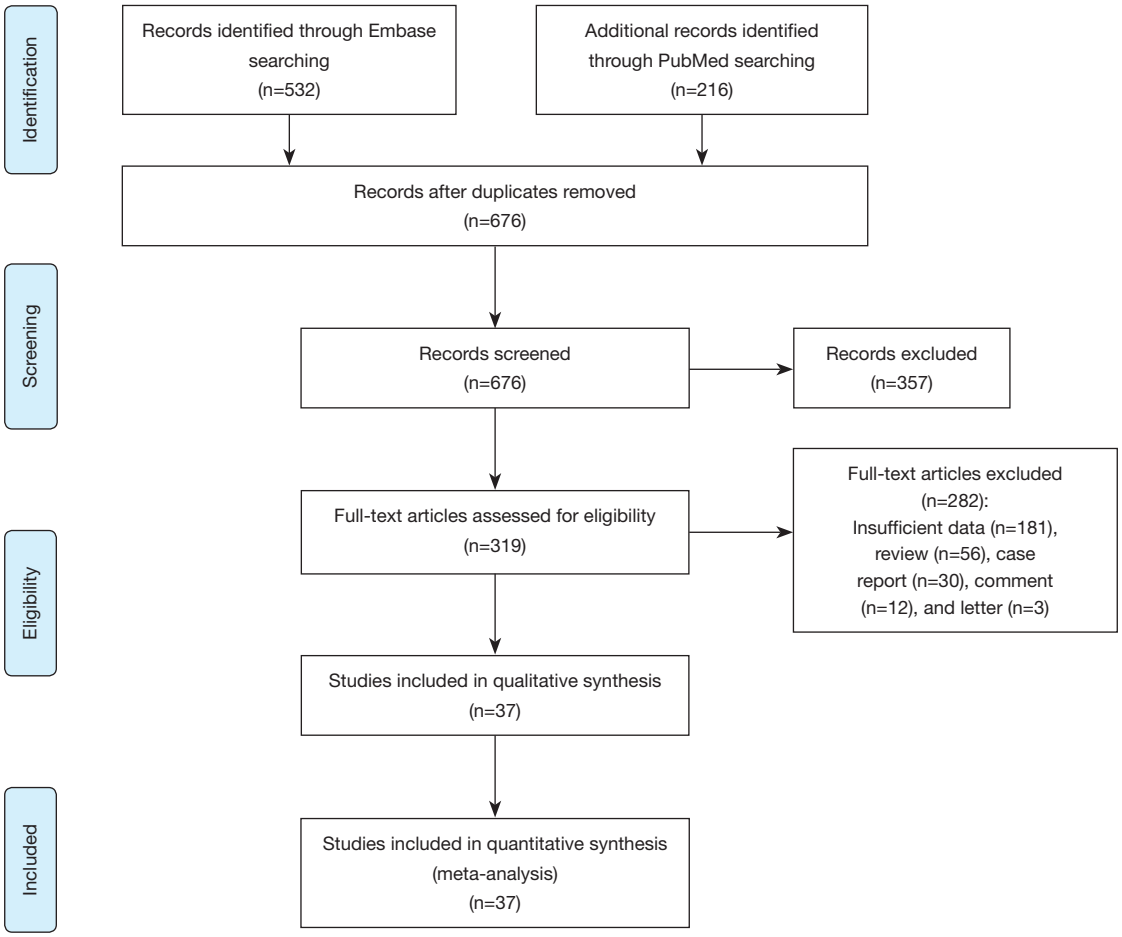

Figure 1 Flowchart for the selection procedure for studies.

0.82–0.89) and 0.79 (95% CI, 0.72–0.85). The value of diagnostic odds ratio (DOR) was 23 (95% CI, 15–36), while summary estimates were 4.1 (95% CI, 3.1–5.6) for positive likelihood ratio (LR^+) and 0.18 (95% CI, 0.14–0.23) for negative likelihood ratio (LR^-). All these results indicated DW-MRI's excellent ability to both confirm and exclude presence of lung cancer.

Meta-regression showed heterogeneity from DW-MRI examinations were found in subgroups of b value (I^2=0, P=0.48). There was also a trend for the subgroup of lesion size to show heterogeneity (I^2=98, P<0.01). Allow for lesion size is a heterogeneous factor which may affect the diagnostic accuracy of screening modality, a new histopathological classification for pulmonary nodule was proposed measuring ≤2 cm and >2 cm in maximum dimension. Among the included studies, 14 reported average or median lesion size of less than 2 cm, and 16 larger than 2 cm. Average adjusted sensitivity of DW-MRI to diagnose lung cancer was significantly influenced by lesion size (0.83, (95% CI, 0.80–0.85) for studies with mean lesions ≤2 cm and 0.86 (95% CI, 0.83–0.88) for lesion size >2 cm P<0.01), however, results indicated that average adjusted specificity of lesion size ≤2 cm (0.85; 95% CI, 0.80–0.89) significantly higher than lesion size >2 cm (0.77; 95% CI, 0.71–0.82) (P<0.01).

The sROC curves reported the predictive value of DW-MRI for all studies, the AUC value was 0.90 (95% CI, 0.87–0.92) (*Figure 3*). The ROC space did not illustrate a curvilinear trend of points and no threshold effect in diagnostic accuracy was observed. Since we tried to gather all evidence in the published works, potential biases were unavoidable. The Deeks' funnel plot showed the evidence of publication bias towards studies (P<0.05) (*Figure 4*). In view of this, we performed the subgroup analysis without this study and estimated the publication bias for each subgroup of different lesion size, asymmetric test did not

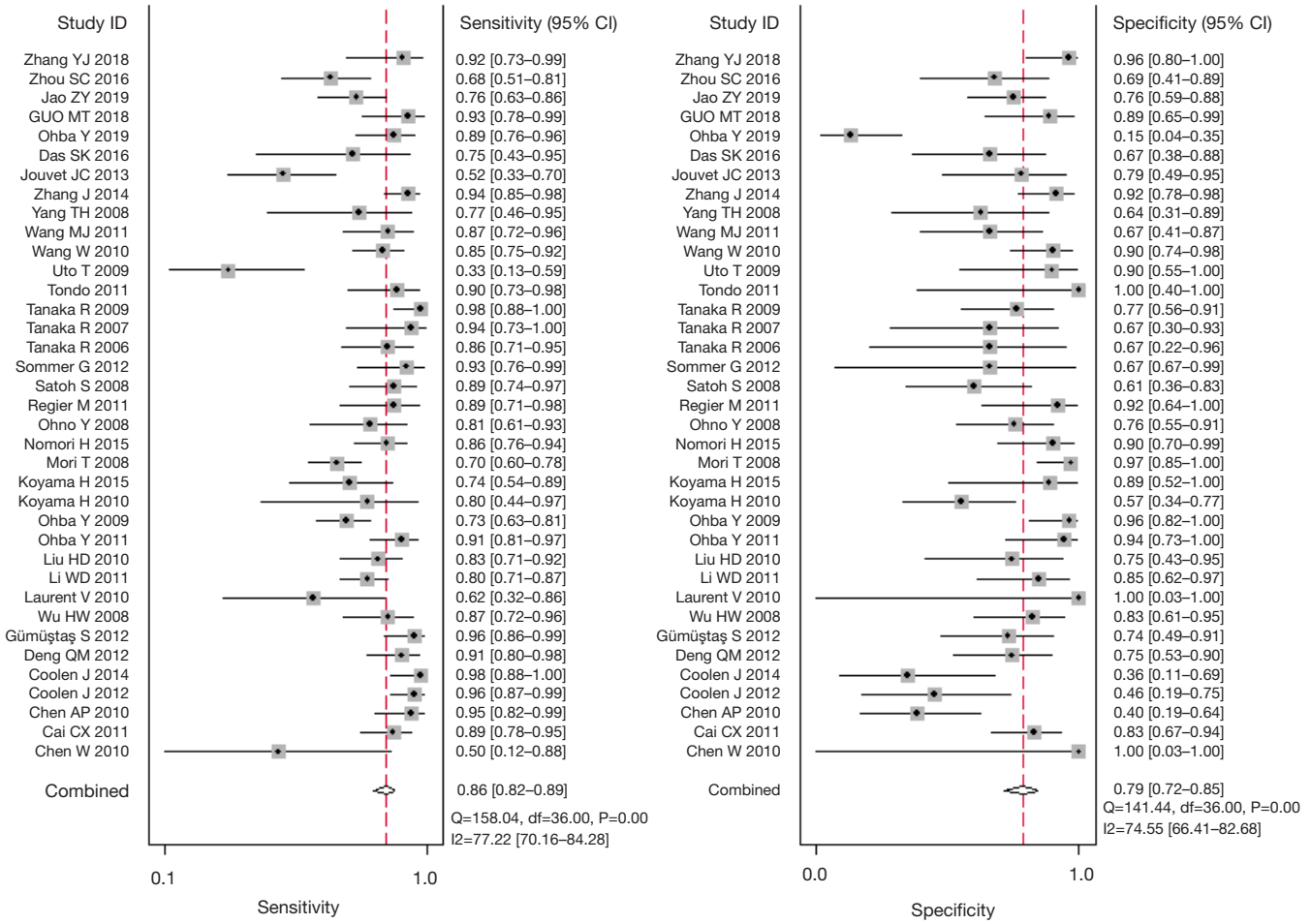

Figure 2 Forest plots of sensitivity and specificity for DW-MRI in 37 studies.

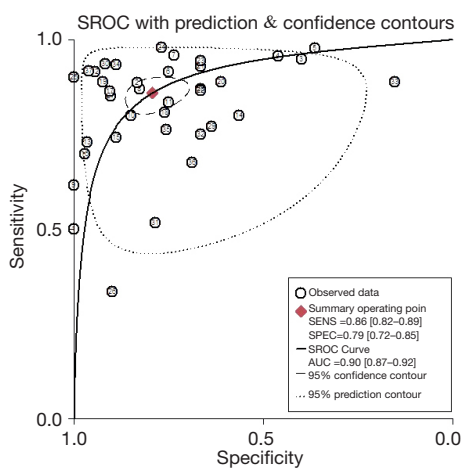

Figure 3 Summary receiver-operator characteristic (sROC) curves for DW-MRI in 37 studies.

show any evidence in lesion size >2 cm (P=0.09) and ≤2 cm (P=0.14) (*Figures 5*,*6*).

Table 1 illustrated average adjusted sensitivity and specificity in subgroup analysis to estimate the magnitude of the effect by classifying studies in each covariate. As for critical parameter, DW-sequences are now almost routinely used as an adjunct to conventional MRI images. However, if it requires any other morphologic sequences to improve accuracy? The adjusted sensitivity and specificity for the imaging modality with DWI sequence only was 0.84 (95% CI, 0.78–0.90) and 0.75 (95% CI, 0.67–0.82), while those for DWI combined with other sequence was 0.84 (95% CI, 0.79–0.89) and 0.77 (95% CI, 0.69–0.86), the pooled AUC was 0.87 and 0.91 for DWI sequence only and DWI with other sequence. Our results indicated that accuracy of DWI sequence only was lower than that of DWI combined with

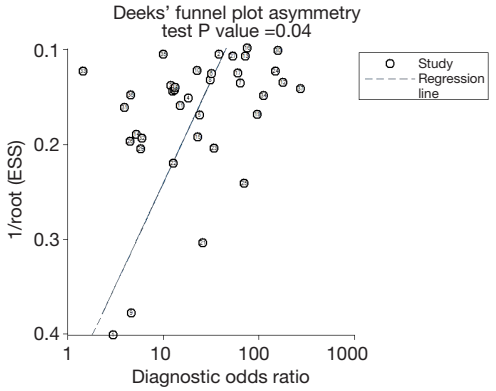

Figure 4 The Deeks' funnel plot showed publication bias towards studies.

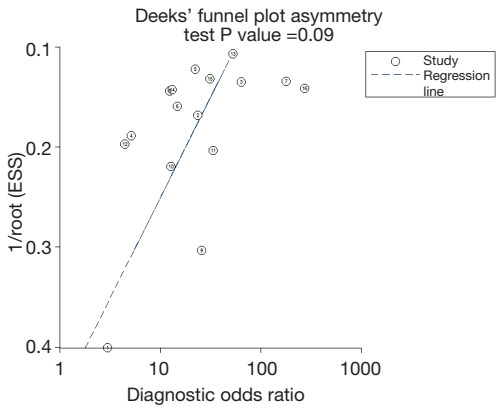

Figure 5 The Deeks' funnel plot showed the publication bias in lesion size >2 cm.

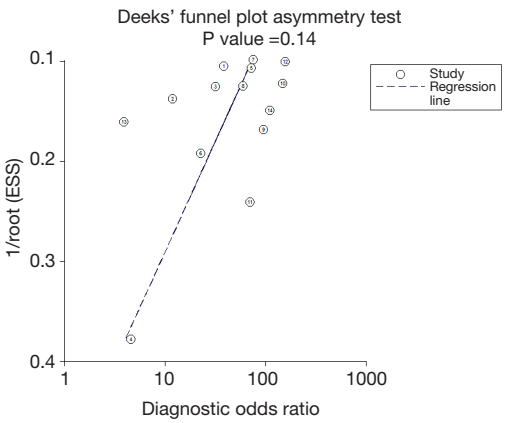

Figure 6 The Deeks' funnel plot showed the publication bias in lesion size ≤2 cm.

other sequence.

Additionally, DW-MRI should be performed with sufficient degrees by appropriate choices of b values, with considerations given for the anatomic region, tissue composition, and pathologic processes. According to previous study, we summarized b values that may be used as a guide when performing DW-MRI for qualitative assessment and 750–1,000 s/mm^2 may be served as optimal value for whole-body imaging purpose. Thus, we conducted a subgroup analysis to compare the b value of 750–1,000 s/mm^2 with other values, pooled sensitivity, specificity and AUC of b value of 750–1,000 s/mm^2 was 0.84 (95% CI, 0.79–0.88), 0.79 (95% CI, 0.72–0.86) and 0.91, while those of other b value were comparatively lower of 0.84 (95% CI, 0.78–0.91), 0.71 (95% CI, 0.58–0.85) and 0.88, respectively. Field strength is another essential parameter of MRI in predicting lung lesion. On the basis of our result, although 1.5 T was less sensitive than 3.0 T in screening pulmonary nodule [0.82 (95% CI, 0.77–0.87) *vs.* 0.88 (95% CI, 0.83–0.92)], it was more specific than 3.0 T [0.80 (95% CI, 0.74–0.86 *vs.* 0.69 (95% CI, 0.53–0.85)].

As for study method, the adjusted sensitivity and specificity for quantitative analysis was 0.84 (95% CI, 0.79–0.89) and 0.79 (95% CI, 0.71–0.87), while those for qualitative analysis was 0.84 (95% CI, 0.78–0.90) and 0.73 (95% CI, 0.63–0.83). It was significantly specific in quantitative analysis (P<0.05). What's more, prospective design and consecutive enrollment were with higher sensitivity in comparison to retrospective and inconsecutive study design.

Discussion

Use of PET/CT for routine surveillance is now clearly not recommended by Centers for Medicare and Medicaid Services (CMS) (22). In concurrence with this assessment, Cancer Care Ontario systematically reviews the literature and to date has not recommended PET/CT for surveillance (23). Available evidence from clinical studies suggests that using PET/CT to monitor for recurrence does not improve outcomes and therefore generally is not recommended, notably increased radiation from PET and PET/CT (5). Until high-level evidence demonstrates that routine surveillance with PET/CT scans help prolong life or promote well-being after treatment for a specific type of cancer, this practice should

Table 1 Quantitative subgroup analysis of all available covariate on a per-lesion basis. Data were present as accuracy data with 95% confidence interval

Study characteristics	No. of studies	I^2	Independent estimates [95% CI]					
			Sensitivity	Specificity	LR^+	LR^-	DOR	AUC
Total	37	N/A	0.86 [0.82–0.89]	0.79 [0.72–0.85]	4.1 [3.1–5.6]	0.18 [0.14–0.23]	23 [15–36]	0.90 [0.87–0.92]
Analytical method								
Quantitative	18	0	0.84 [0.79–0.89]	0.79 [0.71–0.87]	3.8 [2.6–5.7]	0.19 [0.15–0.25]	26 [16–43]	0.91 [0.89–0.93]
Qualitative	19		0.84 [0.78–0.90]	0.73 [0.63–0.83]	3.3 [1.9–5.8]	0.25 [0.16–0.38]	16 [8–30]	0.88 [0.84–0.90]
Consecutive enrollment								
Consecutive	18	49	0.87 [0.82–0.92]	0.69 [0.59–0.79]	2.9 [1.9–4.5]	0.22 [0.15–0.32]	16 [9–31]	0.88 [0.85–0.91]
Inconsecutive or unclear	19		0.82 [0.76–0.87]	0.83 [0.76–0.90]	4.5 [2.9–7.0]	0.20 [0.15–0.29]	27 [17–43]	0.91 [0.89–0.93]
Sequence								
DWI combined other sequence	24	0	0.84 [0.79–0.89]	0.77 [0.69–0.86]	4.1 [2.5–6.7]	0.21 [0.15–0.29]	23 [14–38]	0.91 [0.88–0.93]
DWI sequence only	13		0.84 [0.78–0.90]	0.75 [0.67–0.82]	3.0 [2.2–4.1]	0.22 [0.15–0.33]	19 [10–35]	0.87 [0.84–0.90]
Region								
Caucasian	8	0	0.88 [0.77–0.99]	0.69 [0.54–0.84]	2.4 [1.5–3.8]	0.16 [0.07–0.38]	21 [9–51]	0.88 [0.85–0.90]
Mongoloid	29		0.83 [0.79–0.87]	0.77 [0.70–0.84]	4.0 [2.6–6.0]	0.22 [0.17–0.29]	21 [13–33]	0.90 [0.87–0.92]
Field strength								
1.5T	27	53	0.82 [0.77–0.87]	0.80 [0.74–0.86]	3.7 [2.7–5.1]	0.22 [0.16–0.30]	23 [14–36]	0.90 [0.87–0.92]
3T	10		0.88 [0.83–0.92]	0.69 [0.53–0.85]	3.0 [1.6–5.9]	0.19 [0.13–0. 29]	18 [8–41]	0.90 [0.87–0.92]
Lesion size*								
Mean size ≤2 cm	14	98	0.83 [0.80–0.85]	0.85 [0.80–0.89]	5.7 [3.1–10.4]	0.19 [0.12–0.29]	40 [22–76]	0.93 [0.91–0.95]
Mean size >2 cm	16		0.86 [0.83–0.88]	0.77 [0.71–0.82]	3.3 [2.3–4.7]	0.19 [0.12–0.30]	22 [14–38]	0.90 [0.87–0.93]
Study design								
Prospective	25	35	0.85 [0.82–0.87]	0.72 [0.68–0.76]	3.2 [2.2–4.7]	0.22 [0.16–0.29]	18 [11–31]	0.89 [0.86–0.92]
Retrospective	12		0.82 [0.76–0.89]	0.85 [0.79–0.91]	4.5 [3.1–6.5]	0.20 [0.13–0.32]	30 [18–49]	0.92 [0.89–0.94]
b value (s/mm^2)								
750–1,000	24	0	0.84 [0.79–0.88]	0.79 [0.72–0.86]	3.8 [2.7–5.4]	0.20 [0.15–0.27]	26 [16–41]	0.91[0.88–0.93]
Other value or ND	13		0.84 [0.78–0.91]	0.71 [0.58–0.85]	3.2 [1.7–6.1]	0.23 [0.15–0.37]	15 [7–31]	0.88 [0.85–0.91]

*, seven studies did not report mean lesion diameters. LR^+, positive likelihood ratio; LR^-, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under curve; ND, not documented.

not be performed (4). Therefore, if radiation-free DW-MRI could be an alternative selection, this imaging test might help to prevent long-term side-effects from radiographic staging procedures.

Substantial advantage lies in the new MRI techniques nowadays. The principle of DW-MRI exploits the random motion, Brownian movement, of water protons in biologic tissue, leading to DW-MRI possessing no exposure to ionizing radiation and reflecting the diffusivity of water molecules in tissue. When ADC values are assessed with DW-MRI, there is a significant difference in ADC between malignant and benign lesions. Moreover, the use of T1-weighted sequence obviates the need for an intravenous contrast medium, so patients with poor renal function can also undergo MRI for this purpose. In addition, compared to PET or PET/CT, advantages of DW-MRI include no anaphylaxis to high spatial resolution of images, diverse information from various sequences, high efficiency, and low consumption. To some extent these might explain why DW-MRI may outperform PET/CT in the assessed contexts.

Pulmonary lesion is a common finding on chest imaging, in which lung cancer represents the most frequently diagnosed malignancy. Lung cancer is regarded as the most common cancer and leading cause of cancer death in the whole world (24,25). Radiation-free DW-MRI, which has been applied in recent years, may yields similar or even superior diagnostic value especially in lung cancer in comparison of PET/CT (10). The combination of anatomical, physiological and biological information makes multiparametric MRI an appealing tool for the diagnosis of malignant lesions, among which DW-MRI, visualizing the diffusion characteristics of tissue, is widely used and has presented promising results. Since the diagnostic performance of DW-MRI in distinguishing pulmonary lesions has been performed in many studies, we attempt to evaluate the overall diagnostic accuracy with a meta-analysis.

We observed lower sensitivity but higher specificity of DW-MRI in diagnosis of pulmonary malignancies when compared with sensitivity of 0.89 (95% CI, 0.87–0.91) and specificity of 0.75 (95% CI, 0.71–0.78) in PET/CT on basis of a recent study by Deppen *et al.* (12). Allow for heterogeneous results in different lesion size of imaging modality, we compared average adjusted sensitivity and specificity between DW-MRI and PET/CT in Deppen's study, which nodule was proposed measuring ≤2 cm and >2 cm in maximum dimension. In comparison, DW-MRI had a significantly higher average adjusted specificity in both ≤2 cm and >2 cm subgroup, although with lower sensitivity (P=0.01 for studies with lesions ≤2 cm and P<0.01 for studies with larger average lesion size) in comparison to PET/CT in both subgroup. Although adjusted specificity of DW-MRI was higher than PET/CT, we found it had a lower specificity among studies reporting larger lesions than those with smaller lesions. From the practical aspect, difficulty of defining areas where the regions of interest are made to measure ADC values due to variable signal intensity on ADC maps, leading to certain confounds, might account for lower specificity in larger lesions.

As a trend in clinical practice, parameters in examination modalities were increasingly added to analytical method. Empirically, our study showed quantitative analysis with ADC value was with similar sensitivity and higher specificity than qualitative analysis in differentiating pulmonary lesion, which may imply that ADC is an objective value that can improve the efficiency of DW-MRI in screening on pulmonary nodules. Most scanners generate identical ADC value without significant difference, regardless of the manufacture, scanner type, field strength, gradient strength, or gradient slew rate. There are agreements among all stakeholders on standards for both acquisition protocols, repeatability/reproducibility and for the post-processing procedures, to ensure that quantitative ADC values have similar meanings across institutions, because the technique is quantifiable and can be repeated easily. For instance, the measured ADC values show good reproducibility between different MR systems, a GE 1.5 T (Signa Twin-Speed HD, GE Healthcare, Milwaukee, WI), a Siemens 1.5 T (Magnetom Espree, Siemens Healthcare, Erlangen, Germany) and a Philips 3.0 T (Achieva Dual, Philips Healthcare, Best, The Netherlands) scanners (26). Thus, ADC value has the potential for clinical trials and cancer screening.

As for standardized data sets, additionally, DW-MRI should be performed with sufficient degrees by appropriate choices of b values, with considerations given for the anatomic region, tissue composition, and pathologic processes. According to a previous study, we summarized b values that may be used as a guide when performing DW-MRI for qualitative assessment and 750–1,000 s/mm^2 may be served as optimal value for whole-body imaging purpose. Thus, we conducted a subgroup analysis to compare the b value of 750–1,000 with other values, and the results confirmed that b value of 750–1,000 s/mm^2 was with comparable sensitivity and significant higher specificity in comparison to others. It may

be concluded that 750–1,000 s/mm^2 may be served as optimal value for DW-MRI in whole-body imaging purpose.

Although subgroup of prospective and consecutive enrollment only exerted higher sensitivity, it may be caused by limited sample size or other potential biases. On basis of our result, we suggest more scientific experiment design in future, which will predict the efficacy of imaging modality in a more convincing way. Despite a noninvasive test to assess the risk of cancer or benign disease recommended by diagnostic guidelines (1-3), PET or PET/CT should be limited for use of diagnosing lung cancer in regions where infectious lung disease is endemic (12). Our meta-analysis established the advantages of DW-MRI for the diagnosis of lung cancer. This strong evidence exists for health-care systems to consider the introduction of DW-MRI as a crucial evaluating examination for lung lesions.

Advances in MRI technique, providing operability to achieve whole-body DW imaging and excellent tissue contrast, have led to good diagnostic performance in clinical practice and investigation. DW-MRI, for either whole-body or regional purposes (7,8), is no more technically challenging and prone to be reliable as an examination.

Although the application of PET/CT has grown rapidly during the past several years, this modality is associated with substantial exposure to ionizing radiation equivalent to roughly 700–750 chest radiographs (27). Exposure to ionizing radiation in radiosensitive patients causes roughly an increased risk of cancer, especially leukemia and brain cancer (28). According to our result, radiation-free DW-MRI may be considered as a potential alternative by medical practitioner. This finding will contribute to balance against an increasing tendency of diagnosing cancer patient using PET/CT initially and the risk of radiation on certain population before evaluation has been done.

Conclusions

Radiation-free DW-MRI shows a favorable balance between sensitivity and specificity in diagnosing pulmonary malignancies. Existing evidence may indicate that DW-MRI could be considered as an independent substitute in diagnosis of lung lesions, which might help to prevent long-term side-effects from radiographic diagnosing and evaluating procedures.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Table S1 Baseline characteristics of the included studies

Study	Country	Patient number	Lesion number	Man/women	Age	Design	Consecutive enrollment	Magnetic field strength, T	b value, s/mm^2	Modality	Analytical method	Lesion size
Chen W 2010 (29)	China	56	7	35/21	51	P	Yes	1.5	1,000	Only	Qualitative	>2 cm
Cai C 2011 (30)	China	133	97	77/56	55	R	ND	1.5	600	Combined	Quantitative	<2 cm
Chen A 2010 (31)	China	58	58	38/20	55	P	ND	1.5	300, 600, 900	Combined	Quantitative	<2 cm
Coolen J 2012 (32)	Belgium	80	80	ND	ND	P	Yes	3.0	ND	Only	Quantitative	ND
Coolen J 2014 (33)	Belgium	54	54	36/18	61	P	Yes	3.0	50, 500, 750, 1,000	Combined	Quantitative	>2 cm
Das SK 2017 (34)	China	32	27	ND	ND	P	Yes	3.0	500, 1,000	Only	Quantitative	ND
Deng QM 2012 (35)	China	71	71	46/25	52	R	ND	1.5	300, 500, 800	Only	Quantitative	<2 cm
Gümüştaş S 2012 (36)	Turkey	67	67	49/17	64	P	Yes	1.5	500, 1,000	Only	Quantitative	>2 cm
Guo MT 2018 (37)	China	46	48	33/13	ND	P	Yes	3.0	1,000	Only	Quantitative	<2 cm
Jao ZY 2019 (38)	China	96	96	43/53	ND	P	Yes	3.0	600, 800, 1,000	Combined	Quantitative	ND
Jouvet JC 2014 (39)	France	37	45	ND	ND	P	ND	1.5	600	Combined	Qualitative	<2 cm
Koyama H 2010 (40)	Japan	32	33	14/18	65	P	Yes	1.5	1,000	Only	Qualitative	>2 cm
Koyama H 2015 (41)	Japan	32	36	20/12	68	P	Yes	1.5	500, 1,000	Combined	Qualitative	<2 cm
Laurent V 2010 (42)	France	35	14	ND	ND	P	Yes	1.5	600	Combined	Qualitative	<2 cm
Li W 2011 (43)	China	116	120	69/47	58	ND	ND	3.0	200, 500, 800, 1,000	Only	Quantitative	>2 cm
Liu H 2010 (44)	China	62	66	38/24	58	P	Yes	1.5	500	Only	Quantitative	>2 cm
Mori T 2008 (45)	Japan	104	140	55/49	68	P	ND	1.5	1,000	Combined	Quantitative	<2 cm
Nomori H 2015 (46)	Japan	77	87	ND	ND	P	ND	1.5	800	Combined	Qualitative	<2 cm
Ohba Y 2011 (47)	Japan	58	76	ND	ND	P	ND	1.5 3.0	1,000	Combined	Quantitative	>2 cm
Ohba Y 2009 (48)	Japan	110	124	56/54	68	R	ND	1.5	1,000	Only	Quantitative	<2 cm
Ohno Y 2019 (49)	Japan	57	71	38/19	ND	P	Yes	3.0	ND	Combined	Qualitative	ND
Ohno Y 2008 (7)	Japan	203	51	109/94	72	P	Yes	1.5	1,000	Combined	Qualitative	ND
Regier M 2011 (50)	Germany	20	71	10/10	66	P	Yes	1.5	500	Combined	Qualitative	<2 cm
Satoh S 2008 (51)	Japan	51	54	37/14	66	P	Yes	1.5	1,000	Combined	Qualitative	>2 cm
Sommer G 2012 (52)	Switzerland	33	31	24/9	66	P	ND	1.5	800	Combined	Qualitative	>2 cm
Tanaka R 2006 (53)	Japan	43	43	22/21	66	ND	ND	1.5	1,000	Combined	Qualitative	>2 cm
Tanaka R 2007 (54)	Japan	45	45	19/26	68	ND	ND	1.5	1,000	Combined	Qualitative	>2 cm
Tanaka R 2009 (55)	Japan	46	72	18/28	67	P	Yes	1.5	1,000	Only	Qualitative	<2 cm
Tondo F 2011 (56)	Italy	34	34	25/9	59	ND	ND	1.5	500, 1,000	Combined	Quantitative	<2 cm
Uto T 2009 (57)	Japan	28	28	22/6	64	ND	ND	1.5	1,000	Combined	Qualitative	>2 cm
Wang W 2010 (58)	China	105	105	58/47	57	ND	ND	1.5	1,000	Combined	Qualitative	>2 cm
Wang MJ 2011 (59)	China	56	56	39/17	58	P	ND	3.0	300, 500, 700, 900	Combined	Qualitative	>2 cm
Wu HW 2008 (60)	China	61	61	42/19	58	ND	ND	3.0	500	Combined	Quantitative	>2 cm
Yang TH 2008 (61)	China	13	24	ND	ND	ND	ND	1.5	400, 500, 600	Only	Qualitative	ND
Zhang J 2014 (10)	China	113	113	67/46	59	P	Yes	3.0	1,000	Combined	Quantitative + qualitative	<2 cm
Zhang YJ 2018 (62)	China	50	50	28/22	61	R	ND	1.5	800	Combined	Quantitative	>2 cm
Zhou SC 2016 (63)	China	56	56	41/15	52	P	Yes	1.5	500	Only	Quantitative	ND

P, prospective; R, retrospective; ND, not documented; only, DWI; combined, DWI combined with other sequence.

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