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A Quality Initiative of the Program in Evidence-Based Care (PEBC), Ontario Health (Cancer Care Ontario)

Comparison of PET/CT and PET/MR Imaging in Oncology

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Evidence Summary

THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-Based Care (PEBC) is an initiative of the Ontario provincial cancer system, Ontario Health (Cancer Care Ontario). The PEBC mandate is to improve the lives of Ontarians affected by cancer through the development, dissemination, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer control.

The PEBC is a provincial initiative of OH (CCO) supported by the Ontario Ministry of Health (OMH). All work produced by the PEBC is editorially independent from the OMH.

INTRODUCTION

Positron emission tomography/computed tomography (PET/CT) with glucose analogue, 2-deoxy-2-[^{18}F]fluoro-D-glucose (FDG) is now an established diagnostic modality for many oncologic applications [1]. PET/CT provides combined anatomical and functional imaging information that may reveal more extensive disease than CT or magnetic resonance imaging (MRI) alone. Despite its accomplishment, PET/CT offers low soft tissue contrast and increases the radiation exposure from the CT component. These disadvantages may be overcome by substituting the CT component with MRI, given its superior soft tissue contrast with better differentiation of fat, water, and soft tissue masses [2]. Furthermore, MRI affords the ability to evaluate tissue function with dedicated sequences, such as diffusion-weighted imaging (DWI), that can lead to better lesion detection and characterization [3]. However, detailed characterization with MRI may prolong study acquisition time.

Over the past several years, the evidence on the use of integrated simultaneous PET/MRI in cancer has grown substantially. As a result, the purpose of this report was to provide an updated summary of the literature regarding the diagnostic comparability of PET/CT and PET/MRI that would permit the potential expansion of the use of PET/MRI for approved indications through the PET Scans Ontario Program. This review has been registered at International prospective register of systematic reviews (PROSPERO) as CRD42023433857.

OBJECTIVES

To evaluate the comparability of diagnostic performance between PET/CT and PET/MR imaging in patients with oncologic diseases.

RESEARCH QUESTION

Is the accuracy of the PET data obtained with PET/MRI comparable to that of PET/CT, regarding the diagnosis and staging, assessment of treatment response, detection and restaging of recurrence, or evaluation of metastasis?

TARGET POPULATION

Patients with suspected or diagnosed cancers.

INTENDED PURPOSE

To update the original document to help inform the best indications where PET/MRI may be better than PET/CT.

INTENDED USERS

This evidence summary is intended to guide the Ontario PET Steering Committee in their decision-making with respect to expanding the use of PET/MRI for approved indications. This document may also be useful to inform clinicians who are seeking information about the clinical value of PET/MRI for oncologic applications.

METHODS

This evidence summary was developed by a Working Group consisting of nuclear medicine physician (AS), a health research methodologist (RP), and a radiologist (UM) at the request of the Ontario PET Steering Committee.

The Working Group was responsible for reviewing the identified evidence and drafting the summary. Conflict of interest declarations for all authors are summarized in Appendix 1, and were managed in accordance with the *PEBC Conflict of Interest Policy*.

This evidence review was conducted in two planned stages, including a search for systematic reviews followed by a search for primary literature. These stages are described in subsequent sections.

Search for Systematic Reviews

A search for systematic reviews from July 2015 to January 25, 2023, was carried out using the electronic databases Medline, Embase, and Cochrane Database of Systematic reviews. Systematic reviews published as a component of practice guidelines were also considered eligible for inclusion. The reference lists from relevant review articles were searched for additional studies. See Appendix 2 for literature search strategy.

Search for Primary Literature

The primary literature was searched using Medline and Embase online databases from July 2015 to January 25, 2023. See Appendix 2 for literature search strategy.

Study Selection Criteria and Process

Inclusion Criteria

1. Published as a full-text article in the English language.
2. Evaluated the use of PET/CT and PET/MRI with tracer ^{18}F-FDG.
3. Performed on an integrated PET/MRI scanner.
4. A suitable reference standard such as histopathology, clinical or imaging follow-up, when appropriate.
5. Reported on diagnostic test parameters such as sensitivity, specificity, positive predictive value, negative predictive value, and accuracy, or metrics representing impact on clinical management decisions and/or survival outcomes as well as time to initiation of therapy.

Exclusion Criteria

1. Literature or narrative reviews, letters, editorials, historical articles, or commentaries.
2. Single case reports, case series or studies with <12 patients.

A review of the titles and abstracts that resulted from the search was conducted by one reviewer (RP), as were the items that warranted full-text review.

Data Extraction and Assessment of Risk of Bias

All included primary studies underwent data extraction by one reviewer (RP), with all extracted data and information audited subsequently by an independent auditor for accuracy and completeness. For each study, the principal author, publication year, country of origin, study design, number of patients, tumour subtypes, clinical indication, type of imaging modality, time of image acquisition, tracer/contrast injection protocol, name of PET/MRI device, area of image acquisition, MRI sequences, reference standard criteria, age, sex, test parameter, unit of analysis, and impact on management were recorded. The Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool [4] was used to evaluate the risk of bias and applicability concerns of each eligible study.

Synthesizing the Evidence

Data were summarized in an evidence table and described in the text. When clinically and methodologically homogenous results from four or more studies and sufficient data were available, a bivariate, random-effect model was used to produce summary estimates of sensitivity and specificity with 95% confidence intervals (CIs) and to plot summary receiver operating characteristic (SROC) curves with 95% confidence regions. This model incorporates any correlation that might exist between sensitivity and specificity and accounts for the estimated variability among the studies [5]. The I^2 index was used to quantify the percentage of the variability in the effect estimates that was due to heterogeneity. A p-value of <0.05 was considered significant. Statistical analyses were performed with STATA version 18.0 using the "midas" command.

Assessment of the Certainty of the Evidence

The certainty of the evidence per outcome for each comparison, taking into account risk of bias, inconsistency, indirectness, imprecision, and publication bias was assessed using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) approach [6].

RESULTS

Search for Systematic Reviews

The search for existing systematic reviews identified several publications that were deemed relevant after title and abstract screening. However, upon full-text review, none focused solely on comparing ^{18}F-FDG PET/CT with simultaneous ^{18}F-FDG PET/MRI and therefore are not discussed further.

Search for Primary Literature

A search for primary literature yielded a total of 8145 unique citations, of which 8061 were excluded after a review of titles and abstracts. Eighty-four were considered candidates, but on full-text review, 55 did not meet the inclusion criteria. The remaining 29 studies were included in this systematic review. See Appendix 3 for the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram.

Study Design and Certainty of the Evidence

Seventeen studies enrolled patients prospectively [8-12,17,19-22,26,27,29,31,32,34,35], while 12 studies collected and analyzed data retrospectively [7,13-16,18,23-25,28,30,33]. Of the 29 studies, the following disease sites were examined: breasts (n=3) [7-9], esophagus (n=1) [10], digestive tract (n=3) [11-13], female reproductive system (n=6) [14-19], head and neck region (n=6) [21-25], hematologic malignancies (n=2) [26,27], melanoma (n=2) [28,29], lungs (n=4) [30-33], and various primary sites (n=2) [34,35]. The

number of patients included in these studies ranged from 18 to 198. Details of the study characteristics are reported in Table 1 and Appendix 4. Quality assessment of each study was conducted according to the four QUADAS-2 domains (Appendix 5). All studies were judged to have low concerns regarding applicability, except for one study where the MRI portion of PET/MRI only included sequences that covered the abdominopelvic cavity, whereas PET/CT was performed as a whole-body procedure [19]. For the domains assessed in terms of risk of bias, one study was judged to have high risk with respect to patient selection where cases with too many liver lesions were excluded while at the same time, lesions that were difficult to diagnose on PET/CT were selected [34]. Such constraints may undermine the true accuracy of PET/CT in comparison to PET/MRI and threaten the generalizability of the findings to real-world practice. Moreover, due to incomplete reporting in six studies [14,17,18,24,25,28], readings for PET/CT and PET/MRI were unclear as to whether they were interpreted without the knowledge of the reference standard results. By the same token, a large majority of the studies conducted reference standard interpretations that were either not blinded [14] or unclear as to whether they were blinded to the index test results [7-13,15-20,22-31,33-35]. Lastly, no studies were judged as being at risk for the domain relating to flow and timing. Unclear risk of bias is often due to missing information that would otherwise permit a judgement; however, it is uncertain if this would have a notable effect on diagnostic test accuracy. With respect to the GRADE domains, the overall evidence is direct and precise and there is no suspicion of selective publication. However, there are issues with inconsistency owing to significant variability in the imaging acquisition protocols, particularly the dedicated MRI sequences of PET/MRI. Taken as a whole, the quality of the evidence was graded as low to moderate.

Table 1. Characteristics of included studies.

Study, year	Country	Study design	Tumour type (number of patients)	Mean age	Sex (M/F)	Reference standard	Clinical indication (number of patients)
Breast Cancer							
Catalano et al, 2017 [7]	US	R	Breast cancer (51)	53	0/51	Pathology, F-U (≥24.0 months)	Staging (51)
Melsaether et al, 2016 [8]	US	P	Breast cancer (51)	56	1/50	Pathology, F-U (mean, 19.2 months)	Staging (6), treatment response (26), restaging (6), surveillance (13)
Sawicki et al, 2016 [9]	Germany	P	Breast cancer (21)	59.4	1/20	Pathology, prior imaging, F-U (mean, 21.4 months),	Restaging (21)
Esophageal Cancer							
Wang et al, 2022 [10]	China	P	Esophageal cancer (35)	62	28/7	Pathology	Staging (35)
Gastrointestinal Cancer							
Akkus Gunduz et al, 2023 [11]	Turkey	P	Colorectal cancer (78)	58.8	49/29	Pathology, F-U (median, 7 months)	Staging (23), restaging (55)
Liu et al, 2019 [12]	China	P	Gastric cancer (30)	58	24/6	Pathology, F-U (>6 months)	Staging (30)
Catalano et al, 2017 [13]	US	R	Colorectal cancer (26)	61.2	15/11	Pathology, prior imaging, F-U (>12 months)	Staging (14), restaging (12)
Gynecologic Cancer							
Grueneisen et al, 2015 [14]	Germany	R	Cervical cancer (7), endometrial cancer (4), ovarian cancer (13)	57	0/24	Pathology, F-U (mean, 8.9 months)	Restaging (24)
Kirchner et al, 2017 [15]	Germany	P	Cervical cancer (12), endometrial cancer (4), ovarian cancer (23), vaginal cancer (1), vulva cancer (3)	55	0/43	Pathology, F-U (mean, 12.5 months)	Restaging (43)
Bian et al, 2019 [16]	China	R	Endometrial cancer (81)	53.7	0/81	Pathology	Staging (81)
Yu et al, 2022 [17]	China	R	Endometrial cancer (57)	57	0/57	Pathology, F-U (≥12 months)	Staging (57)
Gong et al, 2021 [18]	China	R	Cervical cancer (124)	58.3	0/124	Pathology	Staging (124)

Schwartz et al, 2018 [19]	US	P	Cervical cancer (11), endometrial cancer (7)	62.7	0/18	Pathology	Staging (18)
Head and Neck Cancer							
Chan et al, 2018 [20]	Taiwan	P	Nasopharyngeal cancer (113)	51	86/27	Pathology, F-U (≥6 months)	Staging (113)
Huang et al, 2020 [21]	China	P	Hypopharyngeal cancer (20)	55.5	20/0	Pathology	Staging (20)
Yeh et al, 2020 [22]	Taiwan	P	Hypopharyngeal cancer (96), oropharyngeal cancer (102)	56	187/11	Pathology, F-U (≥12 months)	Staging (198)
Vrachimis et al, 2016 [23]	Germany	R	Differentiated thyroid cancer (31)	61	20/11	Pathology, prior imaging, F-U (mean, 4.2 months)	Restaging (31)
Song et al, 2021 [24]	China	R	Differentiated thyroid cancer (37)	39	12/25	Pathology, F-U (>6 months)	Restaging (37)
Slouka et al, 2020 [25]	Czech Republic	R	Hypopharyngeal cancer (4), Laryngeal cancer (24), oral cancer (4), oropharyngeal cancer (35), salivary gland cancer (13), skin cancer (4), thyroid cancer (2), cancer of unknown primary (4)	61.5*	66/24	Pathology	Staging (90)
Hematologic Cancer							
Picardi et al, 2021 [26]	Italy	P	Hodgkin lymphoma (60)	40*	29/31	Pathology, F-U (median, 19 months)	Staging (60)
Giraudo et al, 2016 [27]	Austria	P	Hodgkin lymphoma (4), non-Hodgkin lymphoma (30)	56	19/15	Pathology, prior imaging	Staging (16), restaging (18)
Melanoma							
Schaarschmidt et al, 2018 [28]	Germany	R	Melanoma (52)	50.5	22/30	Pathology	Staging (52)
Berzaczy et al, 2020 [29]	Austria	P	Melanoma (22)	55.3	15/7	Pathology, prior imaging, F-U (mean, 3.4 months)	Staging (11), restaging (11)
Non-Small Cell Lung Cancer							

Wang et al, 2023 [30]	China	R	Non-small cell lung cancer (52)	61.9	34/18	Pathology	Staging (52)
Kirchner et al, 2019 [31]	Germany	P	Non-small cell lung cancer (84)	62.5	51/33	Pathology	Staging (84)
Schaarschmidt et al, 2017 [32]	Germany	R	Non-small cell lung cancer (77)	61	43/34	Pathology, MDTB	Staging (61), restaging (16)
Lee et al, 2016 [33]	South Korea	P	Non-small cell lung cancer (45)	62.9	26/19	Pathology, MDTB, F-U (mean, 13.0 months)	Staging (45)
Various Sites							
Zhou et al, 2021 [34]	China	P	Breast cancer (2), cholangiocarcinoma (4), colon cancer (16), esophageal cancer (2), gastric cancer (9), hepatocellular carcinoma (2), lung cancer (10), melanoma (3), pancreatic cancer (9), rectal cancer (12), testicular germ cell cancer (1)	62*	38/32	Pathology, F-U (mean, 5.4 months)	Staging (37), restaging (33)
Beiderwellen et al, 2015 [35]	Germany	P	Breast cancer (7), colorectal cancer (4), melanoma (7), others (14)	57	12/20	Pathology, F-U (mean, 6.1 months)	Staging (32)

Abbreviations: F, female; F-U, clinical/imaging follow-up; M, male; MDTB, multidisciplinary tumour board; P, prospective; R, retrospective; US, United States
*Median age

Table 2. Diagnostic performance of PET/CT and PET/MRI

Study, year	Unit of analysis	Imaging modality	Prev	TP	FP	FN	TN
Regional lymph node metastases							
Liu et al, 2019 [12]	Patient-based	PET/CT	57.7%	11	3	4	8
		PET/MRI	57.7%	14	3	1	8
Bian et al, 2019 [16]	Patient-based	PET/CT	8.1%	1	3	2	31
		PET/MRI	9.1%	2	0	2	40
Yu et al, 2022 [17]	Patient-based	PET/CT	14.0%	7	2	1	47
		PET/MRI	14.0%	7	2	1	47
Gong et al, 2021 [18]	Patient-based	PET/CT*	44.6%	27	3	2	33
		PET/MRI*	44.1%	25	4	1	29
		PET/CT**	9.2%	2	15	4	44
		PET/MRI**	6.8%	4	9	0	46
Slouka et al, 2020 [25]	Patient-based	PET/CT	71.7%	36	8	2	7
		PET/MRI	70.3%	23	4	3	7
Wang et al, 2022 [10]	Station-based	PET/CT	10.8%	12	6	11	183
		PET/MRI	10.8%	18	3	5	186
Chan et al, 2018 [20]	Level-based	PET/CT	26.4%	379	21	38	1144
		PET/MRI	26.4%	415	9	2	1156
Huang et al, 2020 [21]	Level-based	PET/CT	31.5%	13	1	4	36
		PET/MRI	31.5%	15	1	2	36
Schaarschmidt et al, 2018 [28]	Node-based	PET/CT	20.0%	3	3	14	65
		PET/MRI	20.7%	4	2	13	63
Liver metastases							
Akkus Gunduz et al, 2023 [11]	Lesion-based	PET/CT	64.9%	143	2	114	137
		PET/MRI	64.9%	250	0	7	139
Zhou et al, 2021 [34]	Lesion-based	PET/CT	94.2%	83	2	113	10
		PET/MRI	94.2%	192	0	4	12
Beiderwellen et al, 2015 [35]	Lesion-based	PET/CT†	39.8%	32	2	13	66
		PET/MRI†	39.8%	42	0	3	68
		PET/CT‡	39.8%	29	2	16	66
		PET/MRI‡	39.8%	41	0	4	68
Recurrence and/or metastases							
Sawicki et al, 2016 [9]	Patient-based	PET/CT	81.0%	17	0	0	4
		PET/MRI	81.0%	17	0	0	4
	Lesion-based	PET/CT	86.6%	111	2	5	16
		PET/MRI	86.6%	116	2	0	16
Grueneisen et al, 2015 [14]	Patient-based	PET/CT	87.5%	20	0	1	3
		PET/MRI	87.5%	20	1	1	2
	Lesion-based	PET/CT	77.9%	66	2	15	21
		PET/MRI	77.9%	69	3	12	20
Kirchner et al, 2017 [15]	Patient-based	PET/CT	88.4%	37	1	1	4
		PET/MRI	88.4%	36	1	2	4
	Lesion-based	PET/CT	73.4%	110	7	3	34
		PET/MRI	73.4%	111	7	2	34
Vrachimis et al, 2016 [23]	Patient-based	PET/CT	83.9%	25	0	1	5
		PET/MRI	83.9%	25	0	1	5
	Lesion-based	PET/CT	70.7%	109	16	7	32
		PET/MRI	70.7%	95	13	21	35
Song et al, 2021 [24]	Patient-based	PET/CT	73.0%	21	0	6	10
		PET/MRI	73.0%	26	0	1	10
	Lesion-based	PET/CT	59.2%	47	10	30	43
		PET/MRI	59.2%	62	8	15	45

Abbreviations: CT, computed tomography; FN, false-negative; FP, false-positive; MRI, magnetic resonance imaging; PET, positron emission tomography; Prev, prevalence; TN, true-negative; TP, true-positive

*Diagnostic measures for detecting pelvic lymph node metastases.

**Diagnostic measures for detecting para-aortic lymph node metastases.

†Diagnostic measures for reader 1.

‡Diagnostic measures for reader 2.

Tumour, Node, Metastasis (TNM) Staging

The overall staging accuracy of PET/MRI was determined to be superior to that of PET/CT in breast cancer (98.0% versus 74.5%, p=0.005) [7] and colorectal cancer (92.2% versus 69.2%, p=0.02) [13], or on par with PET/CT in gastric cancer (T staging, 76.9% [PET/MRI] versus 57.7% [PET/CT], p=0.18; N staging, 54.9% [PET/MRI] versus 38.5% [PET/CT], p=0.29, although a significant difference was found in the area under the ROC curve for N1 staging, 0.63 [PET/MRI] versus 0.53 [PET/CT], p=0.03) [12], endometrial cancer (International Federation of Gynecology and Obstetrics staging system, 86.0% [PET/MRI] versus 77.2% [PET/CT], p=0.18) [17], hypopharyngeal cancer (T staging, 81.8% [PET/MRI] versus 63.6% [PET/CT], p=0.5) [21], Hodgkin or non-Hodgkin lymphoma (revised Ann Arbor staging system, 90.0% [PET/MRI] versus 90.0% [PET/CT], p=0.034 for the equivalence test; κ coefficient, 0.92) [26,27], and non-small cell lung cancer (T staging, 80.0% to 89.7% [PET/MRI] versus 80.0% to 92.3% [PET/CT]; N staging, 57.1% to 91.7% [PET/MRI] versus 52.4% to 92.9% [PET/CT], p>0.5 for all comparisons) [30,31,33].

Detection of Primary Tumour

PET/MRI was demonstrated to be more sensitive than PET/CT in the patient-level depiction of primary tumours of the breast (100% versus 58.8%/64.7%, p<0.001) [8] and cervix (93.2% versus 66.2%, p<0.05) [18]. Meanwhile, PET/MRI and PET/CT showed similar lesion-level sensitivity for primary tumours of the endometrium (100% [PET/MRI] versus 100% [PET/CT], p-value not reported) [16] and hypopharynx (100% [PET/MRI] versus 95.2% [PET/CT], p-value not reported) [21].

Detection of Regional Lymph Node Metastases

Of the nine studies that provided sufficient data for meta-analysis, two investigated endometrial cancer [16,17], and one each examined gastric cancer [12], cervical cancer [18], head and neck cancer [25], esophageal cancer [10], nasopharyngeal cancer [20], hypopharyngeal cancer [21], and melanoma [28] (Table 2).

At the patient level (prevalence, 6.8% to 71.7%), the pooled sensitivity of PET/CT was 80% (95% CI, 55% to 93%) and the pooled specificity was 84% (95% CI, 68% to 93%) across five studies [12,16-18,25] (Figure 1). Significant heterogeneity was observed among the studies for both sensitivity (I^2=80.9%, p<0.001) and specificity (I^2=83.1%, p<0.001). Positive likelihood ratio (LR), negative LR, and diagnostic odds ratio (DOR) were 5.0 (95% CI, 2.3 to 10.9), 0.24 (95% CI, 0.09 to 0.62), and 21 (95% CI, 5 to 88), respectively. The area under the SROC curve was 0.89 (95% CI, 0.86 to 0.92) (Figure 2). For PET/MRI, the pooled sensitivity was 89% (95% CI, 77% to 95%) and the pooled specificity was 90% (95% CI, 75% to 96%) (Figure 3). Significant heterogeneity was only detected for specificity (I^2=73.6%, p<0.001). Positive LR, negative LR, and DOR were 8.9 (95% CI, 3.5 to 22.7), 0.12 (95% CI, 0.06 to 0.26), and 75 (95% CI, 27 to 210), respectively. The area under the SROC curve was 0.95 (95% CI, 0.92 to 0.96) (Figure 4).

Figure 1. Forest plots of the combined sensitivity and specificity of PET/CT for the detection of regional lymph node metastases at the patient level.

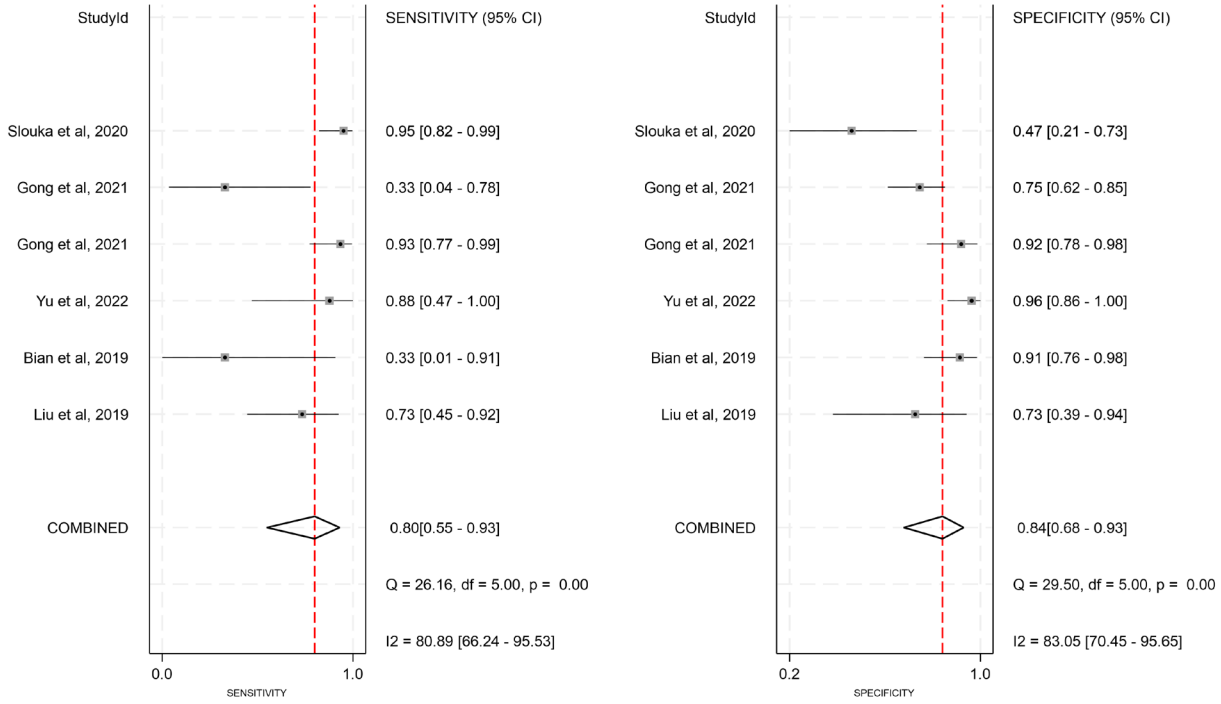


Figure 2. Summary receiver operating characteristic curve for PET/CT in the detection of regional lymph node metastases at the patient level.

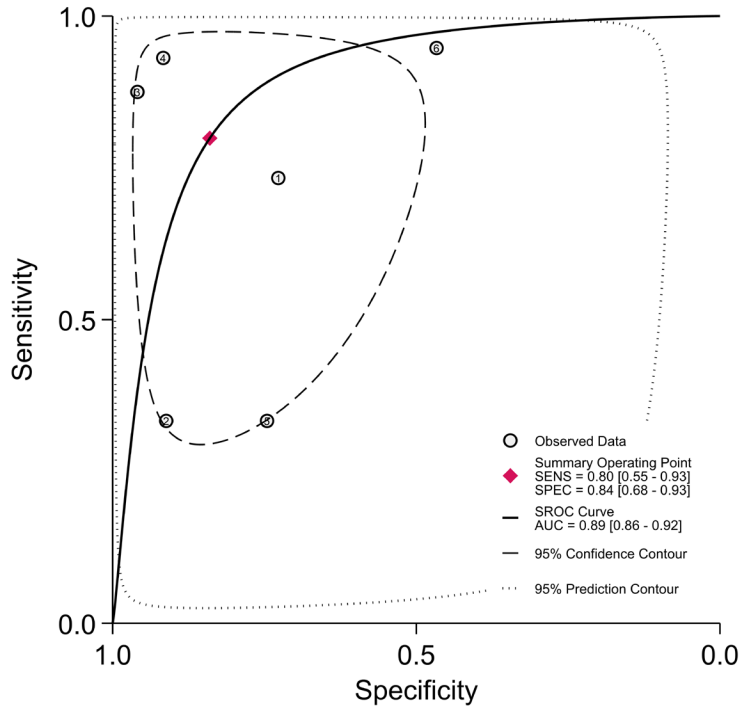


Figure 3. Forest plots of the combined sensitivity and specificity of PET/MRI for the detection of regional lymph node metastases at the patient level.

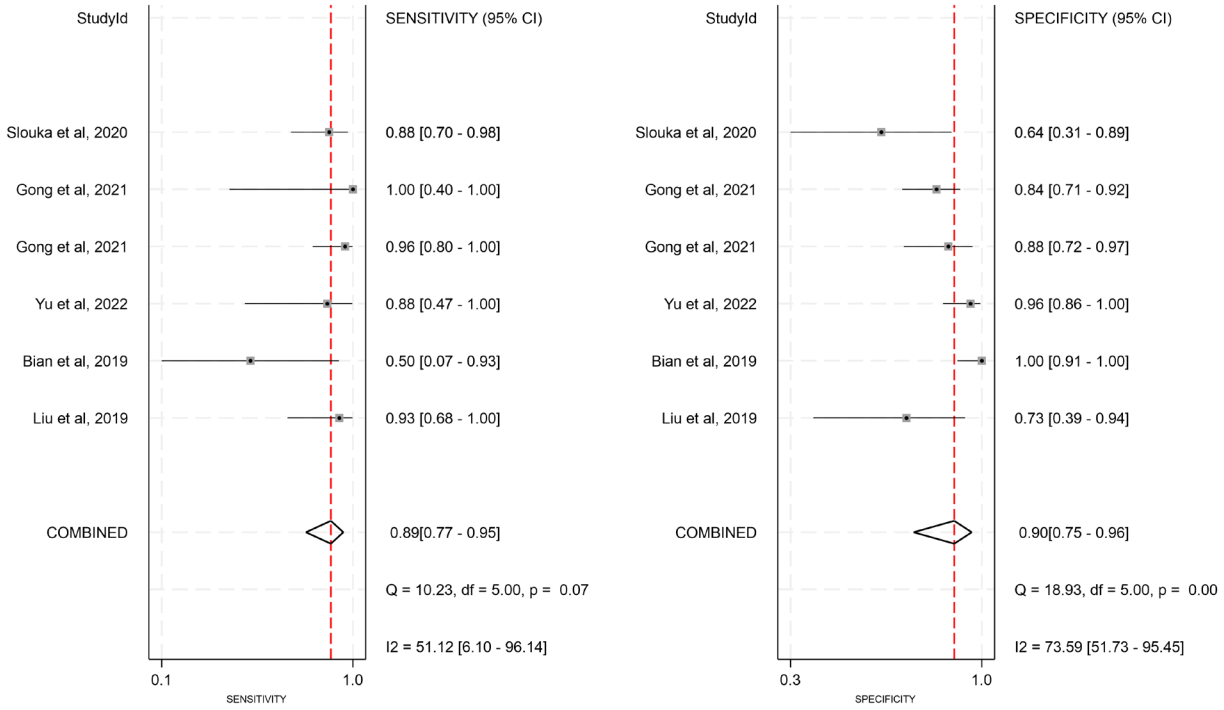
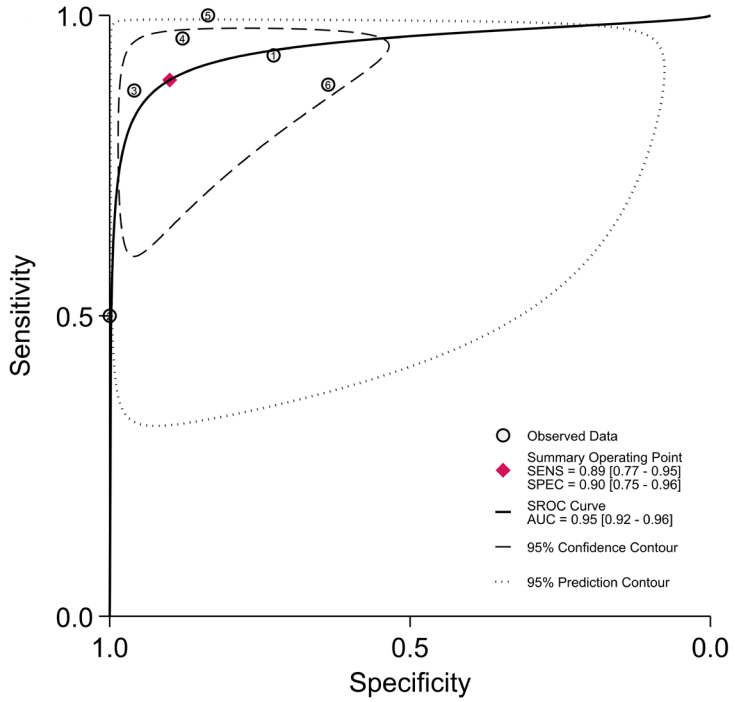


Figure 4. Summary receiver operating characteristic curve for PET/MRI in the detection of regional lymph node metastases at the patient level.



On a node- or station- or level-based analysis (prevalence, 10.8% to 31.5%), the pooled sensitivity and specificity of PET/CT from four studies [10,20,21,28] were 64% (95% CI, 30% to 88%; I^2=97.0%, p<0.001) and 97% (95% CI, 95% to 98%; I^2=72.4%, p=0.01), respectively, with substantial heterogeneity (Figure 5). Positive LR, negative LR, and DOR were 23.1 (95% CI, 9.0 to 59.1), 0.37 (95% CI, 0.15 to 0.93), and 62 (95% CI, 10 to 381), respectively. The area under the SROC curve was 0.97 (95% CI, 0.96 to 0.98) (Figure 6). As for PET/MRI, the pooled sensitivity, specificity, positive LR, negative LR, and DOR were 87% (95% CI, 39% to 99%), 98% (95% CI, 97% to 99%), 55.9 (95% CI, 21.1 to 148.0), 0.13 (95% CI, 0.02 to 1.04), and 432 (95% CI, 24 to 7942), respectively. Significant heterogeneity was seen in the sensitivity (I^2=97.5%, p<0.001) calculation only (Figure 7). The area under the SROC curve was 0.99 (95% CI, 0.98 to 0.99) (Figure 8).

Figure 5. Forest plots of the combined sensitivity and specificity of PET/CT for the detection of regional lymph node metastases as per node/station/level.

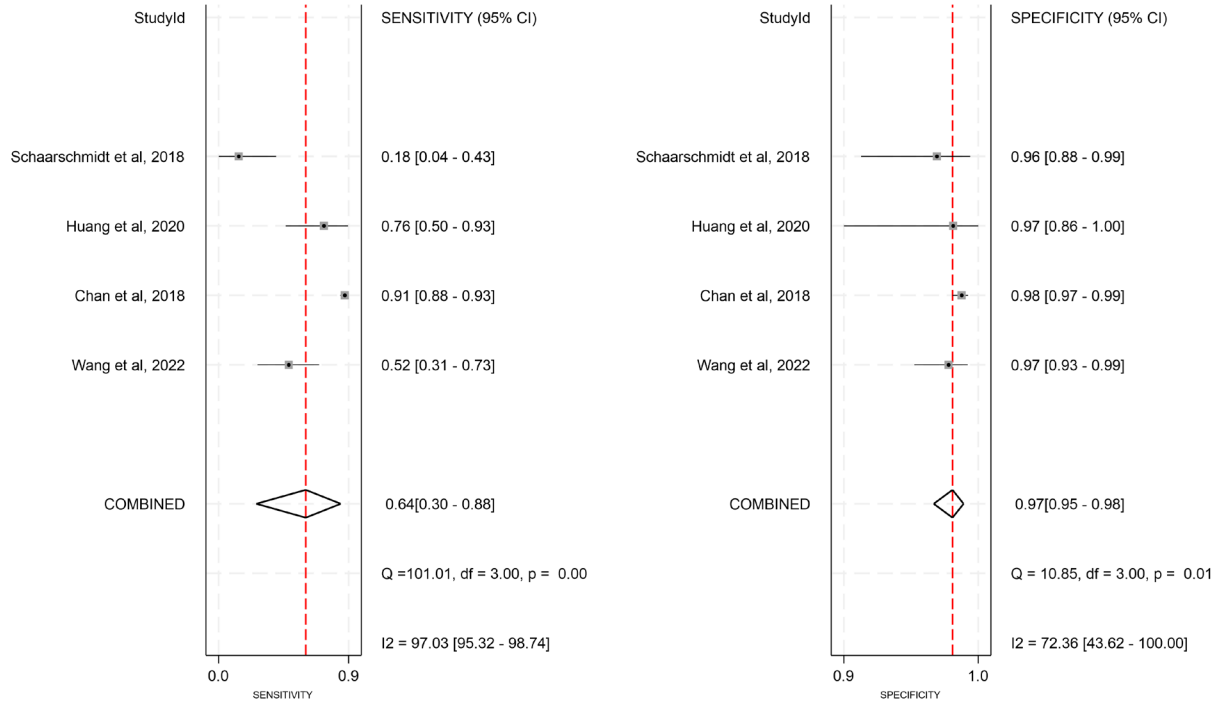


Figure 6. Summary receiver operating characteristic curve for PET/CT in the detection of regional lymph node metastases as per node/station/level.

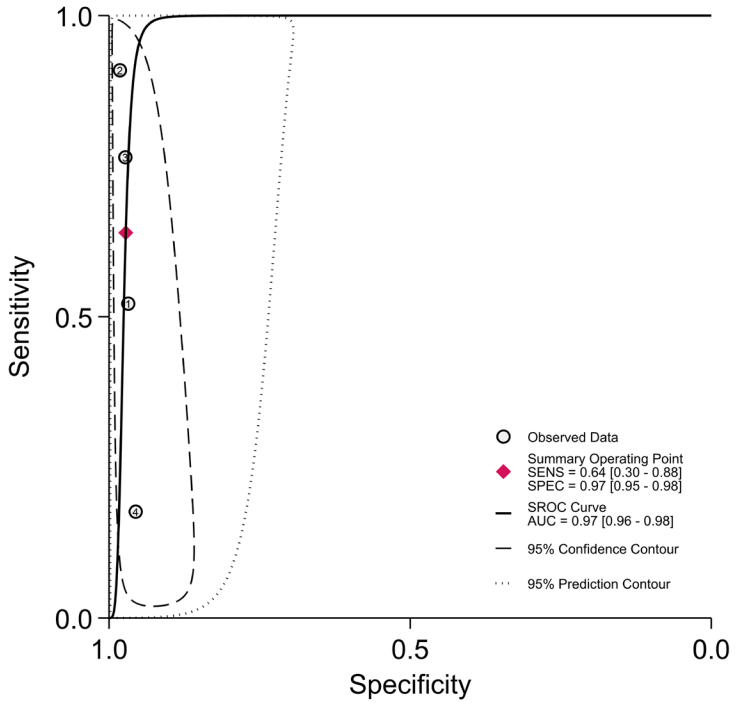


Figure 7. Forest plots of the combined sensitivity and specificity of PET/MRI for the detection of regional lymph node metastases as per node/station/level.

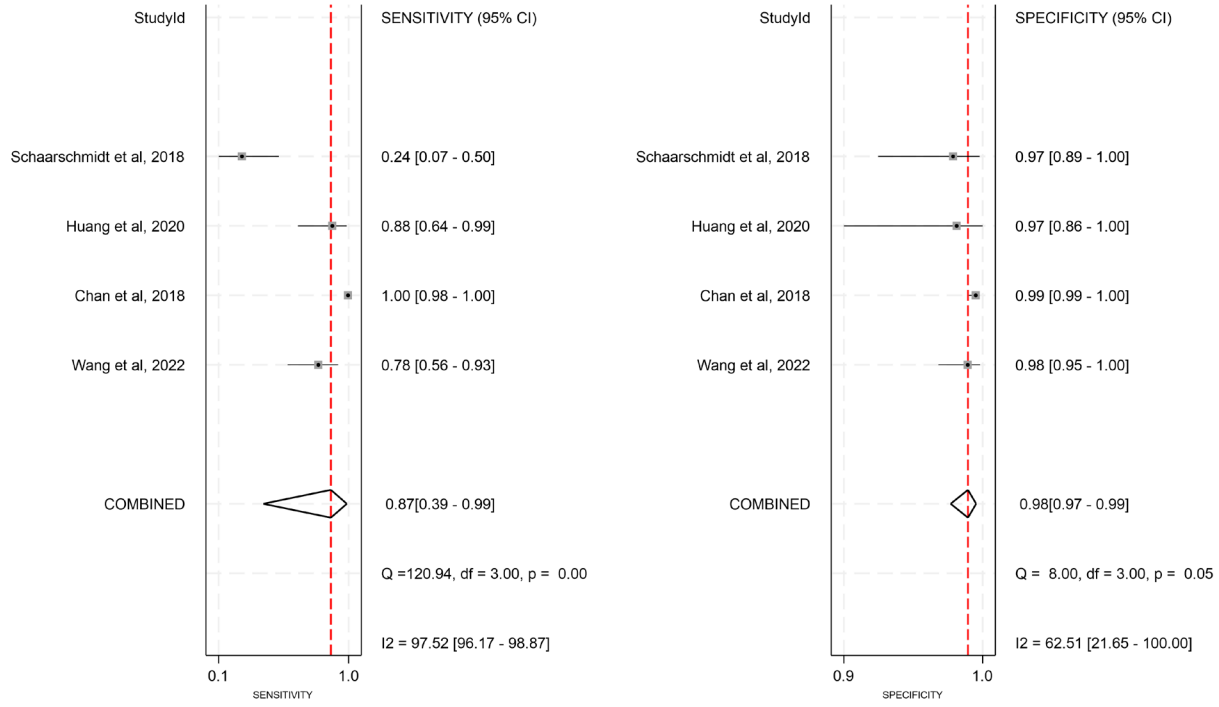
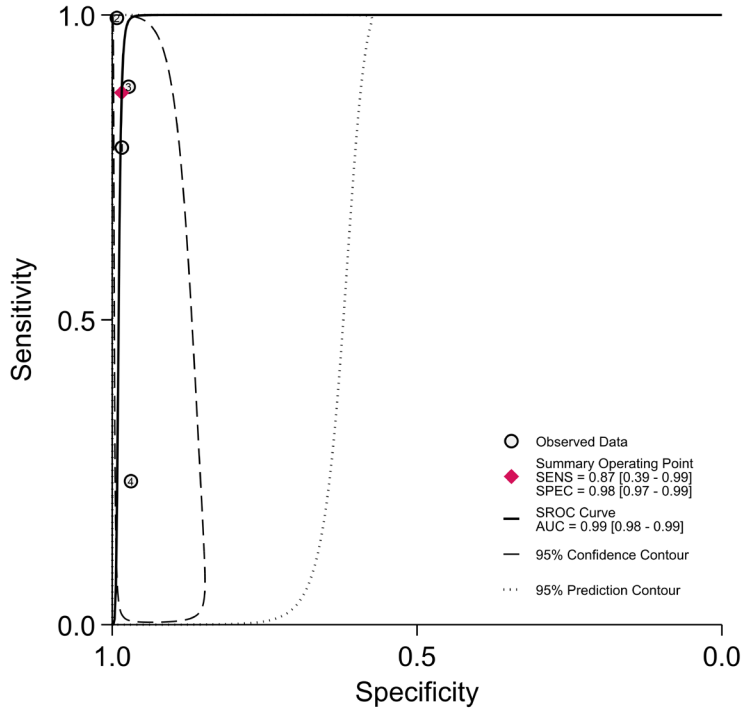


Figure 8. Summary receiver operating characteristic curve for PET/MRI in the detection of regional lymph node metastases as per node/station/level.



Detection of Distant Metastases

Region-level detection of distant metastatic disease was comparable between PET/MRI and PET/CT in nasopharyngeal cancer (accuracy, 98.9% [PET/MRI] versus 97.8% [PET/CT], p-value not reported) [20], oropharyngeal and hypopharyngeal cancer (accuracy, 98.2% [PET/MRI] versus 97.6% [PET/CT], p-value not reported) [22], and melanoma (accuracy, 96.1% [PET/MRI] versus 97.4% [PET/CT], p=0.42) [29]. However, PET/MRI was found to have increased patient-level specificity for lung metastases (88.9%/91.1% versus 80.0%/82.2%, p=0.008), and lesion-level sensitivity for liver metastases (100%/80.0% versus 75.0%/70.0%, p<0.001) and bone metastases (98.1%/95.3% versus 99.1%/86.9%, p=0.012) in breast cancer [8].

Detection of Liver Metastases

Of the three studies that provided the required crude data for meta-analysis, two studies explored various solid malignancies [34,35], while the other investigated colorectal cancer [11] (Table 2).

At the lesion level (prevalence, 39.8% to 94.2%), the pooled sensitivity of PET/CT was 56% (95% CI, 46% to 66%) and the pooled specificity was 97% (95% CI, 92% to 99%) (Figure 9). Significant heterogeneity was observed among the studies for both sensitivity (I^2=85.9%, p<0.001) and specificity (I^2=66.3%, p=0.03). Positive LR, negative LR, and DOR were 17.9 (95% CI, 6.0 to 53.4), 0.46 (95% CI, 0.35 to 0.59), and 39 (95% CI, 11 to 144), respectively. The area under the SROC curve was 0.85 (95% CI, 0.81 to 0.87) (Figure 10). In comparison, the pooled sensitivity was 97% (95% CI, 93% to 98%) and the pooled specificity was 100% (95% CI, 0% to 100%) for PET/MRI (Figure 11). The I^2 statistic did not reveal the presence of significant heterogeneity for sensitivity (57.1%, p=0.07) or specificity (0%, p=1.00). Positive LR, negative LR, and DOR were 2.4 x 10^{11} (95% CI, 0 to unknown), 0.03 (95% CI, 0.02 to 0.07), and 6.9x 10^{12}

(95% CI, 0 to unknown), respectively. The area under the SROC curve was 1.00 (95% CI, 0.99 to 1.00) (Figure 12). Patient-based results also showed consistently greater sensitivity (98.2% to 100% versus 75.6% to 91.7%) and accuracy (98.6% to 100% versus 78.6% to 96.9%) for PET/MRI over PET/CT [11,34,35].

Figure 9. Forest plots of the combined sensitivity and specificity of PET/CT for the detection of liver metastases at the lesion level.

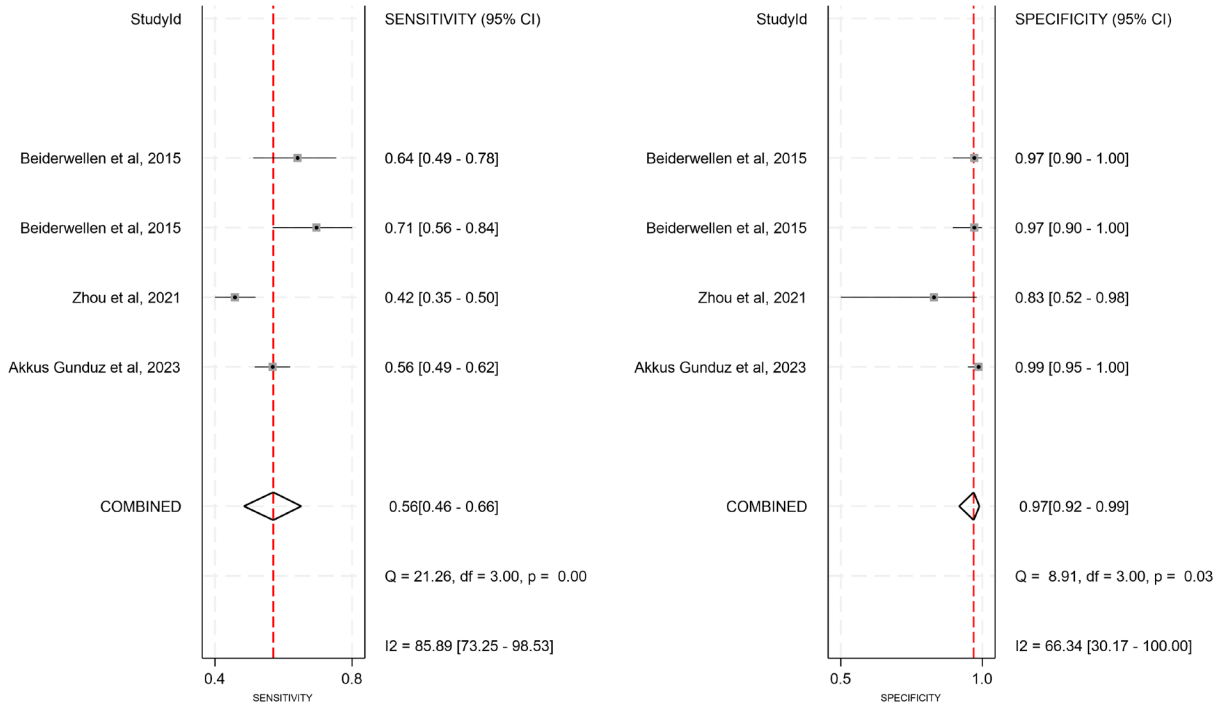


Figure 10. Summary receiver operating characteristic curve for PET/CT in the detection of liver metastases at the lesion level.

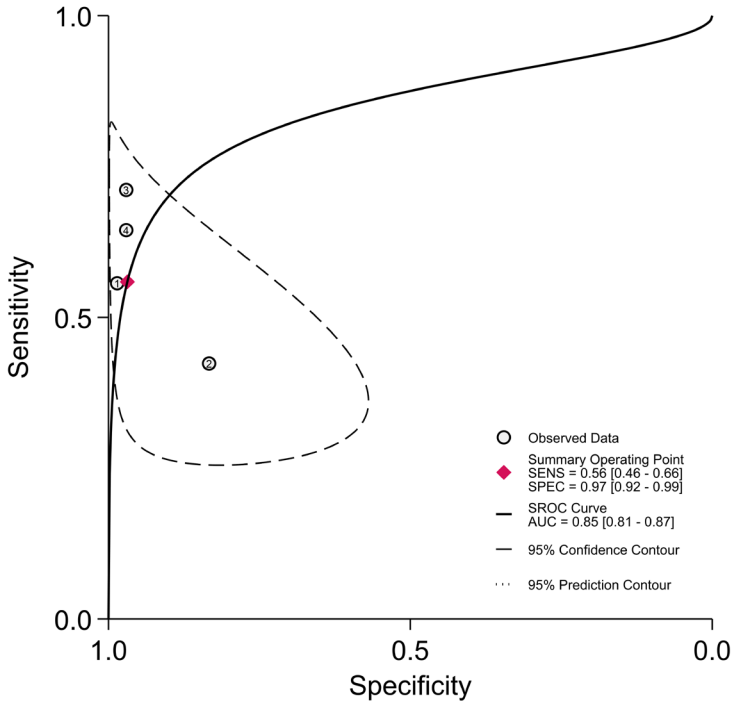


Figure 11. Forest plots of the combined sensitivity and specificity of PET/MRI for the detection of liver metastases at the lesion level.

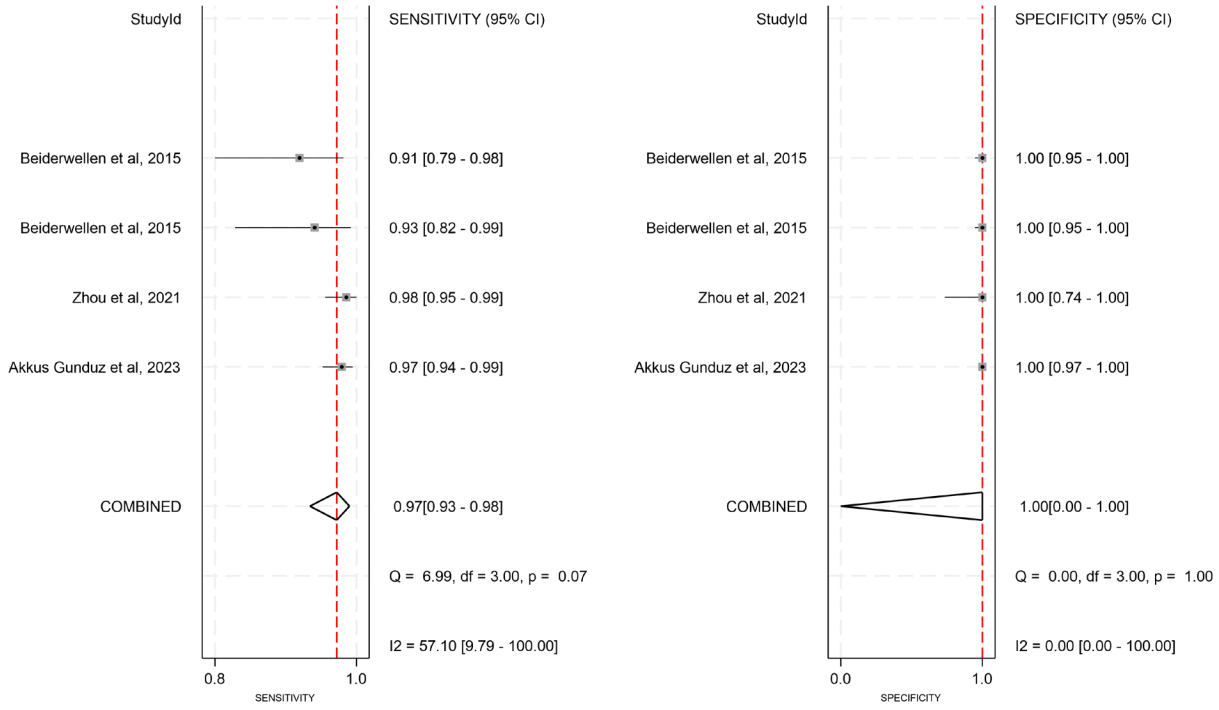
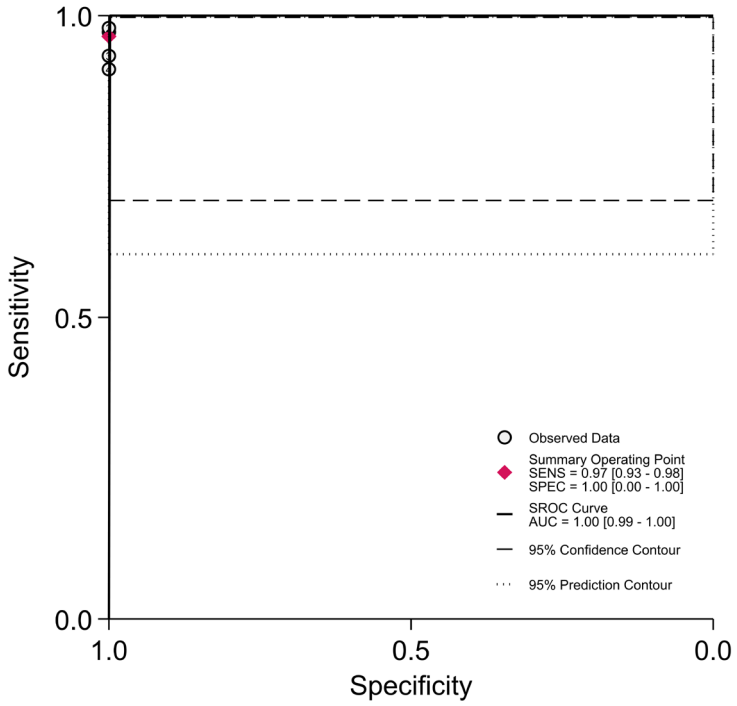


Figure 12. Summary receiver operating characteristic curve for PET/MRI in the detection of liver metastases at the lesion level.



Detection of Tumour Invasion

For endometrial cancer, PET/MRI provided a higher patient-level accuracy than PET/CT when assessing myometrial invasion (81.8% versus 54.1%, p<0.001) [16]. Another study also reported PET/MRI to be more accurate than PET/CT for myometrial invasion detection, but it did not reach statistical significance (93.0% versus 73.7%, p=1). Additionally, PET/MRI (91.2%) and PET/CT (89.5%, p=1) were similarly accurate in the diagnosis of cervical invasion [17]. Likewise, the patient-level evaluation of pleural invasion in non-small cell lung cancer was not significantly different between PET/MRI (area under the curve [AUC], 0.90) and PET/CT (AUC, 0.79, p=0.21) [30].

Detection of Recurrence and/or Metastases

Of the five studies that provided adequate data to allow for the generation of summary estimates, one study was of breast cancer [9], two studies were of pelvic malignancies [14,15], and two studies were of differentiated thyroid cancer [23,24] (Table 2).

Based on a per-patient analysis (prevalence, 73.0% to 88.4%), the pooled sensitivity and specificity of PET/CT were 95% (95% CI, 84% to 98%) and 97% (95% CI, 61% to 100%), respectively (Figure 13). Significant heterogeneity was noticed only for sensitivity (I^2=74.4%, p<0.001). Positive LR, negative LR, and DOR were 33.7 (95% CI, 1.7 to 674.2), 0.05 (95% CI, 0.02 to 0.17), and 640 (95% CI, 31 to 13,226), respectively. The area under the SROC curve was 0.99 (95% CI, 0.98 to 1.00) (Figure 14). For PET/MRI, the pooled sensitivity, specificity, positive LR, negative LR, and DOR were 96% (95% CI, 91% to 98%), 93% (95% CI, 68% to 99%), 13.3 (95% CI, 2.5 to 69.4), 0.04 (95% CI, 0.02 to 0.10), and 318 (95% CI, 41 to 2459), respectively. Neither sensitivity (I^2=0%, p=0.92) nor specificity (I^2=28.8%, p=0.23) showed significant heterogeneity (Figure 15). The area under the SROC curve was 0.97 (95% CI, 0.95 to 0.98) (Figure 16).

Figure 13. Forest plots of the combined sensitivity and specificity of PET/CT for the detection of recurrence and/or metastases at the patient level.

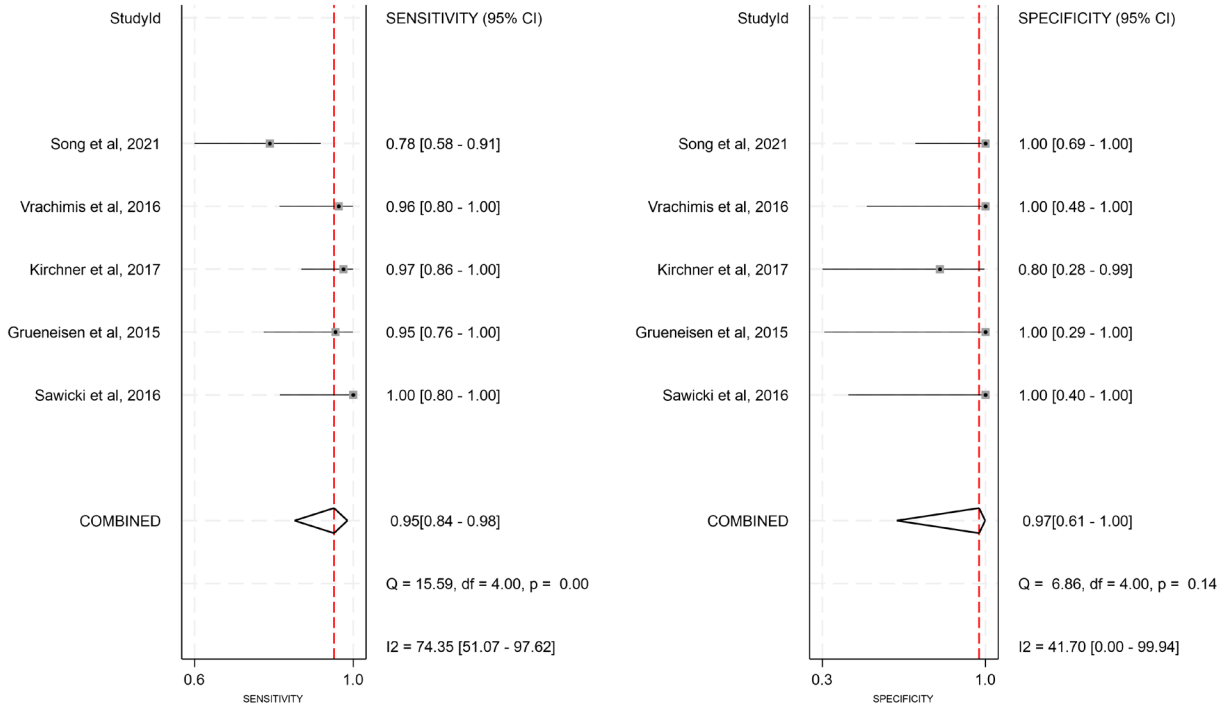


Figure 14. Summary receiver operating characteristic curve for PET/CT in the detection of recurrence and/or metastases at the patient level.

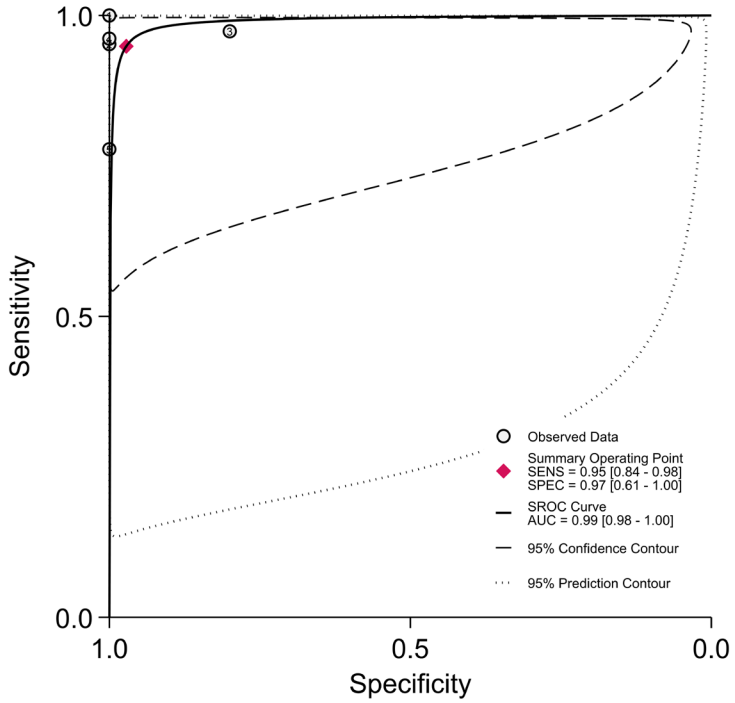


Figure 15. Forest plots of the combined sensitivity and specificity of PET/MRI for the detection of recurrence and/or metastases at the patient level.

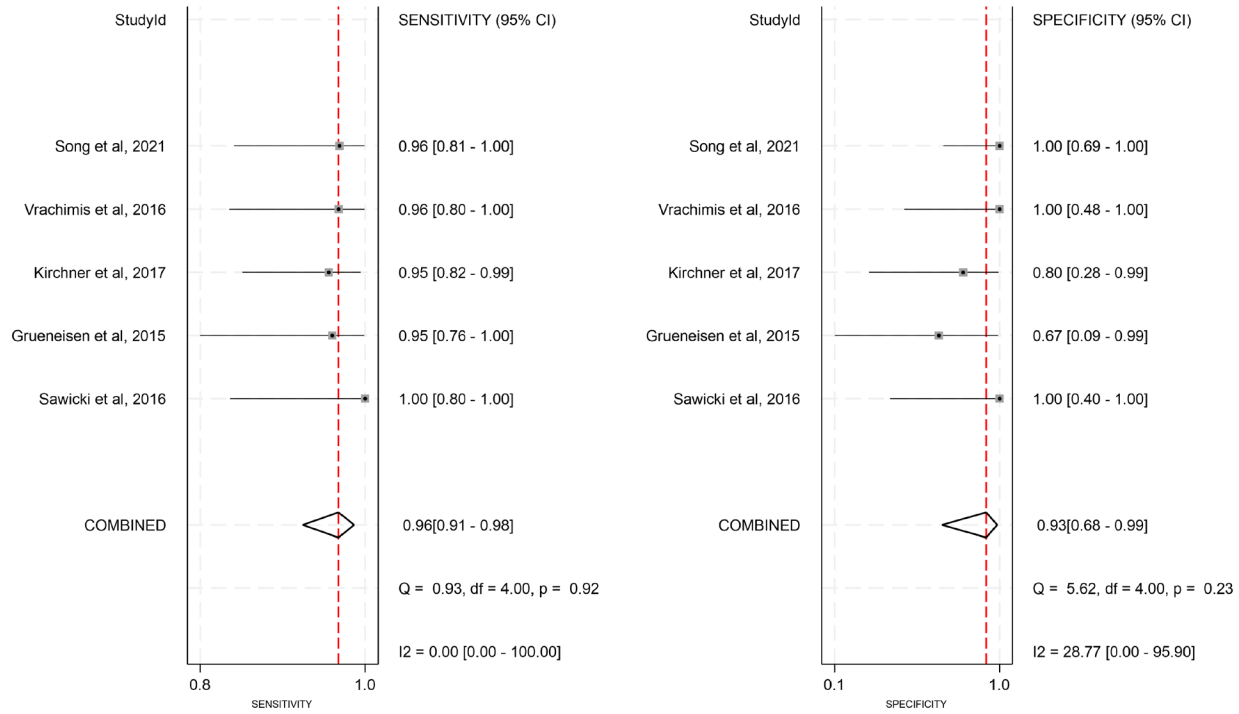
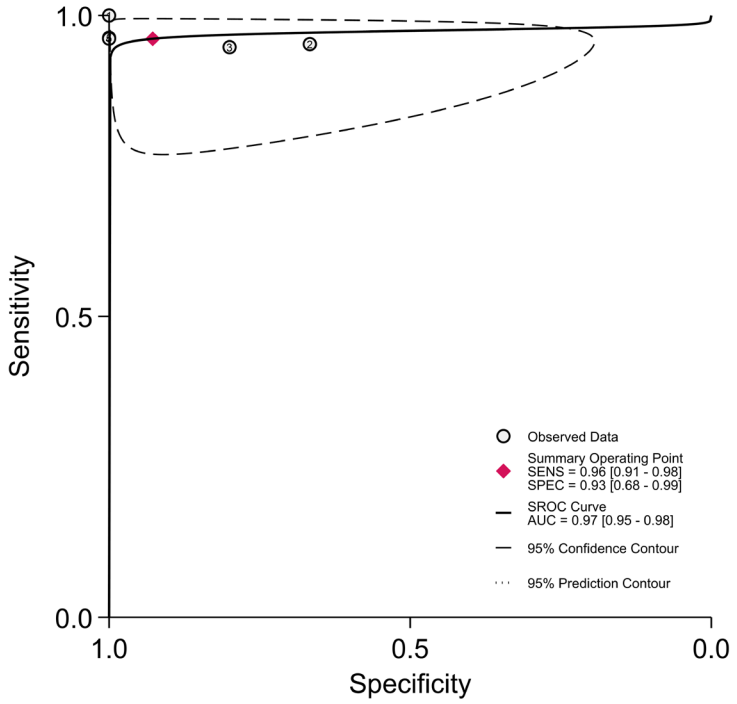


Figure 16. Summary receiver operating characteristic curve for PET/MRI in the detection of recurrence and/or metastases at the patient level.



For per lesion (prevalence, 59.2% to 86.6%), the pooled sensitivity of PET/CT was 91% (95% CI, 77% to 96%; I^2=95.1%, p<0.001) and the pooled specificity was 81% (95% CI, 72% to 88%; I^2=66.5%, p=0.02), with considerable heterogeneity (Figure 17). Positive LR, negative LR, and DOR were 4.8 (95% CI, 3.1 to 7.3), 0.12 (95% CI, 0.05 to 0.30), and 41 (95% CI, 13 to 124), respectively. The area under the SROC curve was 0.88 (95% CI, 0.85 to 0.91) (Figure 18). In contrast, pooled sensitivity and specificity for PET/MRI were 94% (95% CI, 78% to 99%) and 83% (95% CI, 76% to 88%), respectively. Significant heterogeneity was found for sensitivity (I^2=91.8%, p<0.001) but not for specificity (I^2=52.8%, p=0.08) (Figure 19). The area under the SROC curve was 0.87 (95% CI, 0.83 to 0.89) (Figure 20).

Figure 17. Forest plots of the combined sensitivity and specificity of PET/CT for the detection of recurrence and/or metastases at the lesion level.

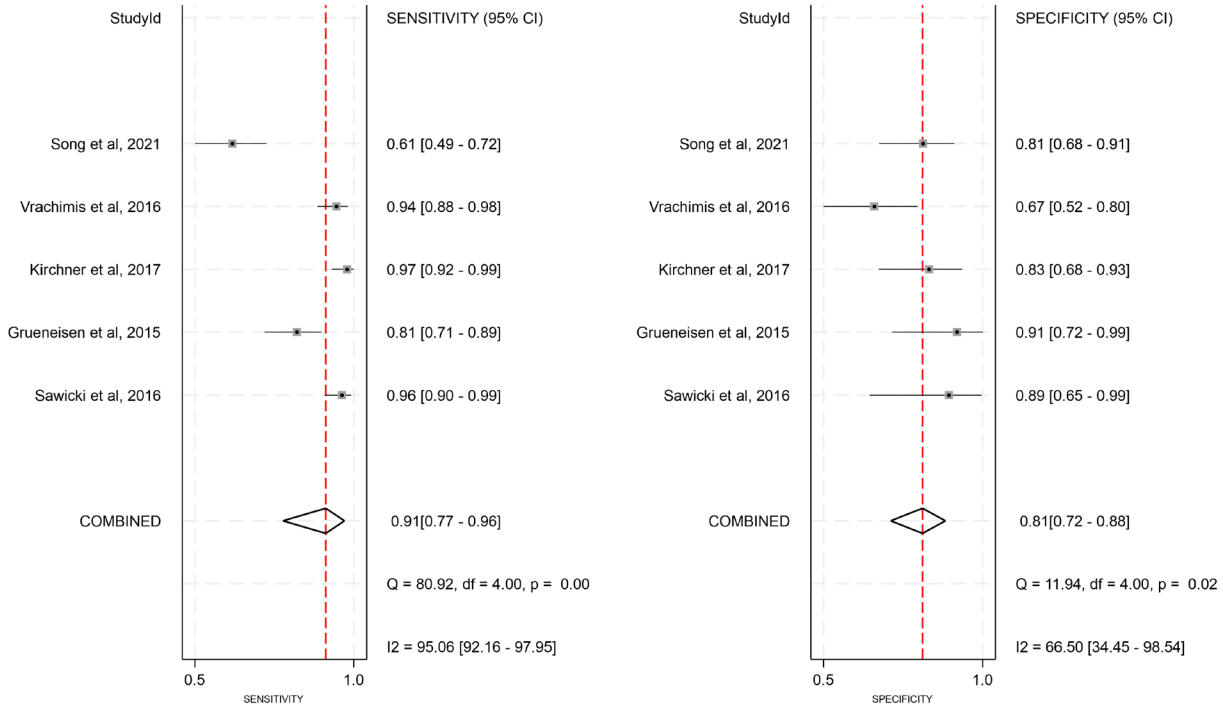


Figure 18. Summary receiver operating characteristic curve for PET/CT in the detection of recurrence and/or metastases at the lesion level.

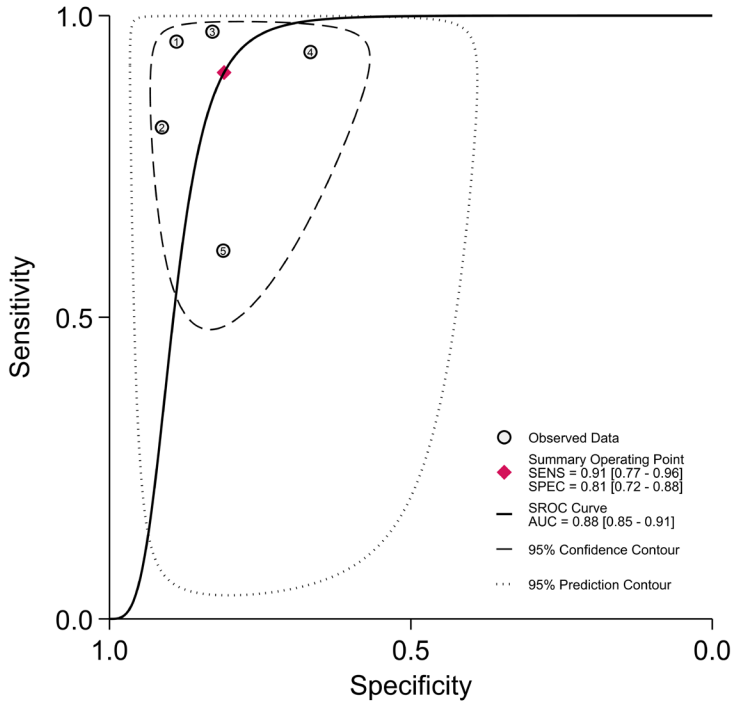


Figure 19. Forest plots of the combined sensitivity and specificity of PET/MRI for the detection of recurrence and/or metastases at the lesion level.

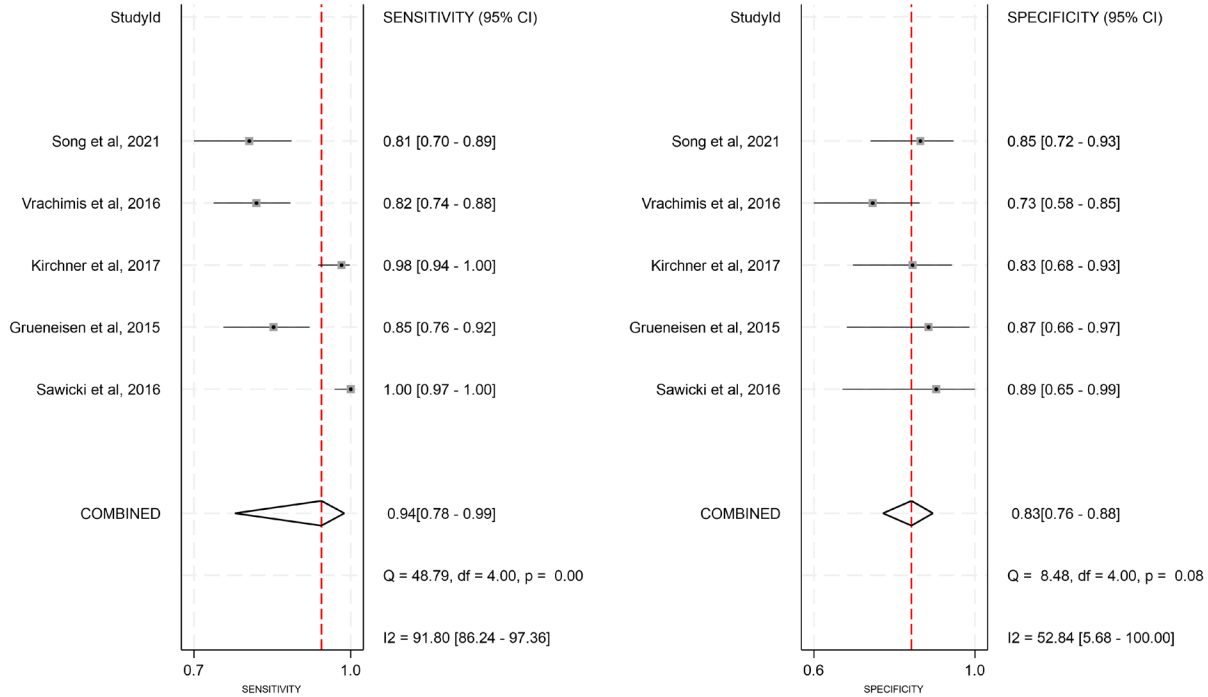
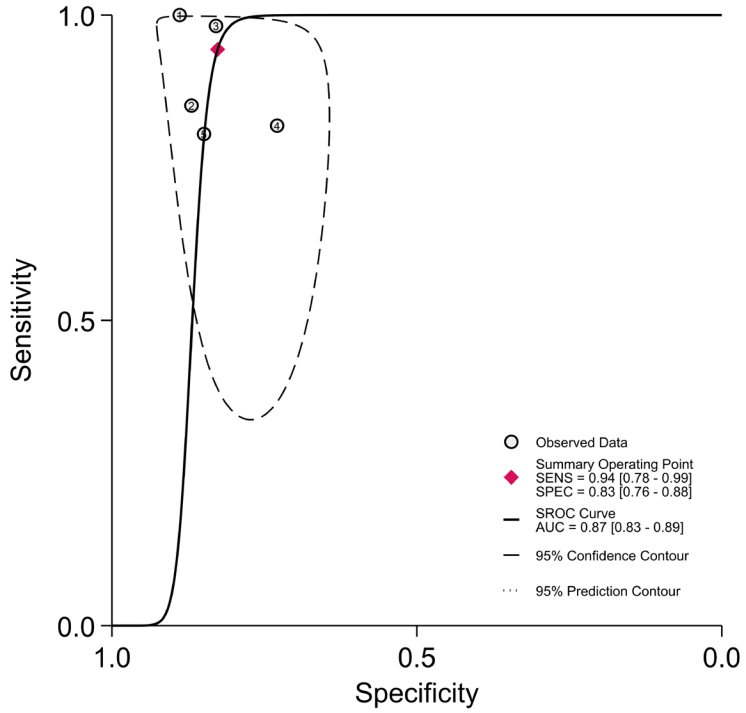


Figure 20. Summary receiver operating characteristic curve for PET/MRI in the detection of recurrence and/or metastases at the lesion level.



Impact on Patient Management

For the initial staging of cervical or high-risk endometrial carcinoma, PET/MRI detected parametrial invasion in 11.1% (2/18) of patients that were missed by PET/CT. Consequently, treatment plan was modified from radical hysterectomy to chemoradiotherapy in these patients [19]. In the staging and restaging of patients with colorectal cancer or solid malignancies with suspicious liver lesions, additional information obtained from PET/MRI after PET/CT influenced the clinical decision making of 9.0% to 41.4% of cases [11,34]. Furthermore, PET/MRI was shown to have impacted the care of patients with non-small cell lung cancer slightly more often than PET/CT. PET/MRI changed the therapeutic strategy in 5.2% (4/77) of cases (e.g., from a curative to a palliative approach, and from resection combined with adjuvant chemotherapy to induction chemotherapy followed by curative chemoradiotherapy or to induction chemoradiotherapy followed by resection). On the other hand, PET/CT revised the treatment recommendation in 2.6% (2/77) of cases (e.g., from resection to induction chemotherapy followed by curative chemoradiotherapy) [32].

Ongoing, Unpublished, or Incomplete Studies

The National Library of Medicine Database (http://www.clinicaltrials.gov/) was searched on October 4, 2023, for potential trials meeting the selection criteria for this systematic review. There was one ongoing trial identified that would be eligible for inclusion in the future update of this evidence summary.

The Value of PET/MRI for the Assessment of Lymph Node Metastasis and Other Prognostic Factors in Patients With Rectal Cancer	
Protocol ID:	NCT03846882
Study type:	Observational
Estimated enrollment:	100
Last updated:	February 20, 2019
Estimated study completion date:	December 31, 2023
Sponsor:	Region Västerbotten
Status:	Recruiting

DISCUSSION

The present systematic review was conducted to compare the diagnostic performance of PET/CT and PET/MRI in oncology for TNM staging across different tumour types and to identify indications where PET/MRI may provide a material clinical benefit. While several new radiotracers have entered into clinical practice, the study scope was limited to FDG where there is greatest clinical experience to date. Both PET and MRI separately have shown their utility in diagnosing and staging different types of cancer, assessing treatment response, detecting recurrence, and evaluating metastases [36,37]. While PET/CT has established itself as a robust diagnostic tool, its limitations, such as low soft tissue contrast and higher radiation exposure, prompt the exploration of PET/MRI as a potential alternative.

The 29 included studies examined various cancer types and anatomical regions, offering a comprehensive overview of the evidence. It is worth noting that the methodological approach and study design in this review were predominantly prospective, with three-fifths of the studies conducted in this manner. This is an improvement since our last review [2]. Based on this more mature evidence, PET/MRI generally demonstrated comparable or superior sensitivity and specificity relative to PET/CT in several applications. This trend was most evident in breast and colorectal cancer staging [7,8,13] as well as detecting primary tumour of the cervix [18]. For breast cancer, the improvement in staging performance was not just limited to local staging as would be expected, but also enhanced M staging via better detection of liver and bone metastases. These results further support our earlier findings highlighting the improved soft tissue contrast and differentiation capabilities of MRI. The incorporation of dedicated MRI sequences, such as DWI, may have contributed to this performance increase in tumour detection and characterization.

Several methodological aspects merit consideration. it is important to underline the evident statistical heterogeneity observed in certain meta-analyzed outcomes. The significant I^2 values for sensitivity and specificity among the studies emphasized the variability in imaging acquisition protocols, especially those concerning the dedicated MRI sequences of PET/MRI or the use of contrast in the CT portion of PET/CT. This variability in protocols and potential biases in some studies might limit the generalizability of the results, prompting caution in drawing definitive conclusions. Additionally, the risk of bias in patient selection, particularly in studies with constrained criteria, limits the generalizability of the findings. For example, those able to tolerate longer imaging time with PET/MRI may be biologically different than those able to only undergo faster scanning with PET/CT. These limitations, coupled with the variability in imaging protocols, contribute to the low to moderate grading of the quality of evidence.

Since our previous review, many challenges remain, including the comparability of standardized uptake value (SUV) derived from MR-based simulated tissue attenuation maps compared to more accurate maps available from CT. Better estimates as well as machine learning-derived simulated attenuation maps have reduced modality-specific differences. As well, the field of PET imaging has generally moved away from using SUV in isolation, but rather

toward using internal reference standards to define the presence of disease, such as the Deauville or Hopkins criteria for lymphoma and head and neck malignancies, respectively. Furthermore, the prolonged study acquisition time of PET/MRI due to detailed characterization with MRI sequences poses a practical challenge to patient throughput and convenience. There needs to be a balance between the need for detailed MRI assessment and scan time, and the detailed MRI protocol should be tailored to the specific tumour being staged. The variability in imaging acquisition protocols, particularly the dedicated MRI sequences of PET/MRI, introduces inconsistency in the results. These factors underscore the need for standardization in imaging protocols to ensure quality, generalizability, and consistency of PET/MRI offered by different providers.

The current evidence base showcases the potential of PET/MRI as an integral diagnostic tool, possibly superseding PET/CT in specific applications. It holds promise in improving lesion detection and characterization, particularly in regions requiring high soft tissue contrast. However, the extended study acquisition time with MRI and the need for standardized protocols are challenges that must be addressed to streamline its integration into routine clinical practice. Although not yet widely available, especially on PET/MRI platforms, the recent introduction of artificial intelligence-powered MR image reconstruction technology that takes advantage of convolutional neural networks to accelerate MR scans may improve workflow efficiency and improve patient experience, enabling acquisition of larger-volume data in shorter acquisition times.

CONCLUSIONS

PET/MRI has emerged as a promising modality, offering diagnostic performance equal to, if not better than PET/CT in various oncologic applications. Its advantages, rooted in the superior soft tissue contrast of MRI, enable better tumour detection and characterization. However, the discrepancies in imaging protocols and the associated heterogeneity observed across studies signal the need for standardized guidelines. Future research should aim to establish uniform imaging acquisition protocols and validate the clinical utility and cost-effectiveness of PET/MRI in diverse clinical settings.

INTERNAL REVIEW

The evidence summary was reviewed by Xiaomei Yao (Assistant Managing Director) and Jonathan Sussman (Scientific Director). The Working Group was responsible for ensuring any necessary changes were made.

Acceptance by the Ontario PET Steering Committee

After internal review, the report was presented to the Ontario PET Steering Committee. The committee reviewed and formally approved the document on April 18, 2024

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- Om Patel for conducting a data audit.
- Sara Miller for copy editing.

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Appendix 1: Affiliations and Conflict of Interest Declarations

Name	Affiliation	Declarations of interest
Amit Singnurkar, MDCM, MPH, FRCPC Nuclear Medicine Physician	Department of Medical Imaging, University of Toronto, Sunnybrook Health Sciences Centre	Received $500 or more in a single year from Isologic Innovative Radiopharmaceuticals for a speaking engagement.
Raymond Poon, MPH Health Research Methodologist	Department of Oncology, McMaster University, Juravinski Hospital Site	No conflict declared
Ur Metser, MD, FRCPC Radiologist	Department of Medical Imaging, University of Toronto, Princess Margaret Cancer Centre	Received $500 or more in a single year from POINT Biopharma to act in a consulting capacity; principal investigator for several clinical trials on PET imaging in general including PET/MRI.

Appendix 2: Literature Search Strategy

The search was conducted in MEDLINE (1946 to Present), Embase (1974 to 2023 January 25), and Cochrane Database of Systematic Reviews (2005 to January 25, 2023) from July 2015 to January 25, 2023.

Medline and Embase

Section A: Disease and/or population	1. cancer$.mp. or tumo?r$.mp. or carcinoma$.mp. or neoplas$.mp. or metastas$.mp. or malignan$.mp. or adenocarcinoma$.mp. or sarcoma$.mp. or myosarcoma$.mp. or rhabdomyosarcoma$.mp. or angiosarcoma$.mp. or h?emangiosarcoma$.mp. or lymphangiosarcoma$.mp. or stewart-treves syndrome$.mp. or h?emangiopericytoma$.mp. or cystosarcoma$.mp. or phyllodes.mp. or dermatofibrosarcoma$.mp. or fibrosarcoma$.mp. or gastrointestinal stromal tumo?r$.mp. or GIST.mp. or leiomyosarcoma$.mp. or liposarcoma$.mp. or MFH.mp. or MPNST.mp. or myxosarcoma$.mp. or neurofibrosarcoma$.mp. or synovioma$.mp. or adamantinoma$.mp. or PNET.mp. or chondrosarcoma$.mp. or mesenchymoma$.mp. or osteoclastoma$.mp. or osteosarcoma$.mp. or chordoma$.mp. or dermatofibrosarcoma protuberan$.mp. or DFSP.mp. or carcinosarcoma$.mp. or melanoma$.mp. or myeloma$.mp. or lymphoma$.mp. or leukemia$.mp.
Section B: Intervention or diagnostic test	2. exp Deoxyglucose/ or deoxyglucose.mp. or deoxy-glucose.mp. or fluorodeoxyglucose.mp. or 18fluorodeoxyglucose.mp. or fludeoxyglucose.mp. or fdg$.mp. or 18fdg.mp. or f-18-dg.mp. or fluoro-2-deoxy-d-glucose.mp. or 2fluoro-2deoxyglucose.mp. or fluoro-d-glucose.mp.
	3. exp Tomography, Emission-computed/
	4. (positron adj emission adj tomograph$).mp.
	5. (pet$ or pet scan$).mp.
	6. or/3-5
	7. 2 and 6
	8. (magnetic resonance imag$ or magnetic resonance spectroscop$).mp.
	9. (dynamic adj4 (MRI or magnet$)).mp.
	10. (diffusion weight$ adj3 (MRI or magnet$)).mp.
	11. (MPMRI or MP-MRI or MR$2 or DWI$ or DW-MRI or DCE$ or NMR$ or fmri).mp.
	12. (T1-weighted or T2-weighted).mp. adj3 imag$.mp.
	13. (MR$1 adj (imag$ or spectroscop$ or scan$ or tomograph$)).mp.
	14. (magnet$ adj (imag$ or spectroscop$ or scan$ or resonance)).mp.
	15. exp Magnetic Resonance Imaging/ or exp Magnetic Resonance Spectroscopy/
	16. or/8-15
	17. 7 and 16
	18. (tomograph$ or ct scan$).mp.

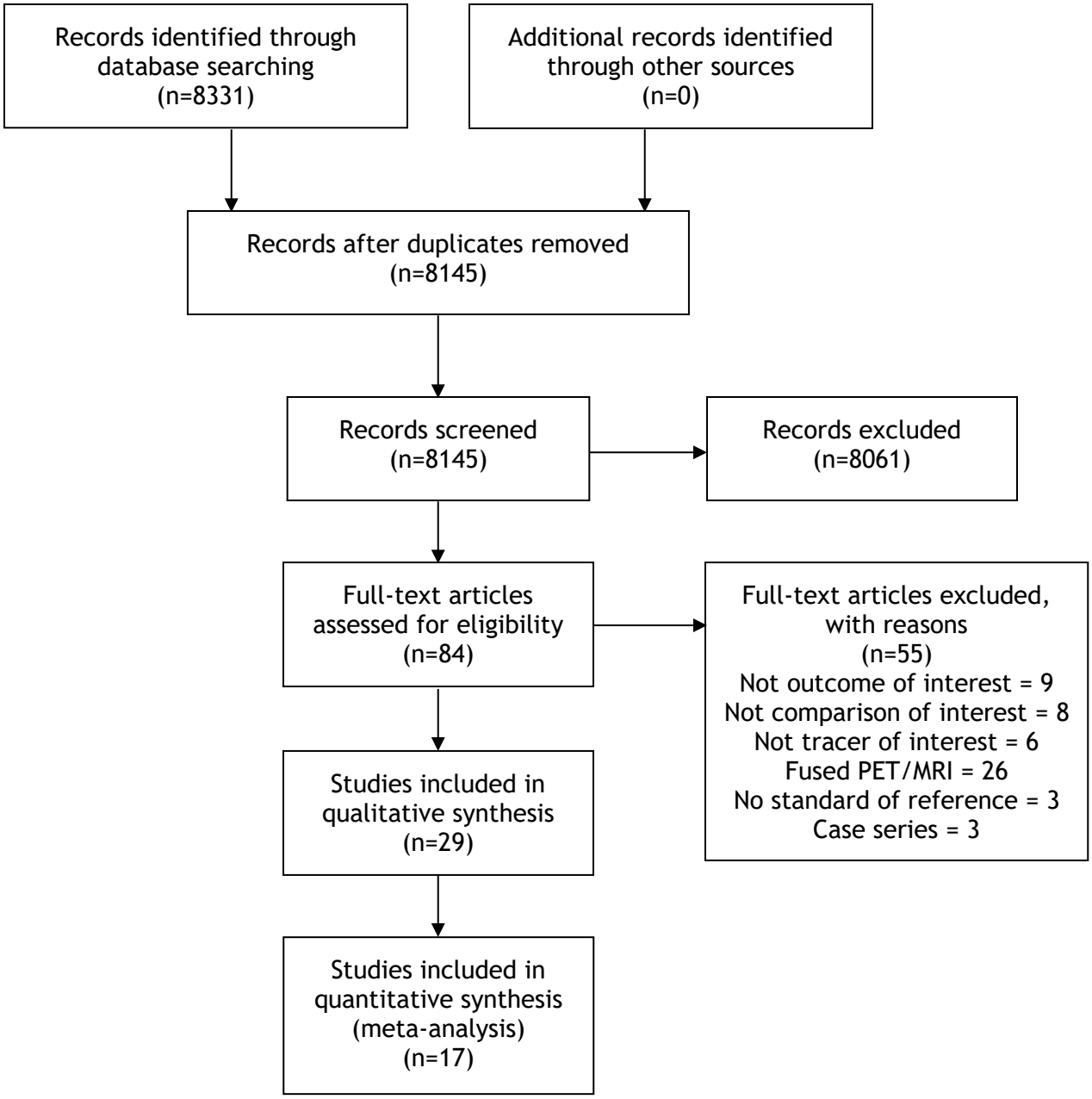
	19. ct.mp.
	20. scan$.mp.
	21. 19 and 20
	22. 18 or 21
	23. 7 and 22
	24. 17 and 23
	25. (positron emission tomography computed tomography or pet ct or pet-ct or pet$ct).mp.
	26. (positron emission tomography magnetic resonance imaging or pet mr$ or pet-mr$ or petmr).mp.
	27. 25 and 26
	28. 24 or 27
Section C: Exclusion strategy	29. (conference or conference proceeding$ or conference paper$ or in brief or invited comment$).ti,ab.
	30. (editorial or note or letter or erratum or short survey).pt. or abstract report$/ or letter$/ or case stud$/
	31. animal/ not human/
	32. or/29-31
Combining Sections A, B, and C	33. 1 and 28
	34. 33 not 32
Limiting the final search by date and language	35. **[Medline]** (201507: or 201508: or 201509: or 201510: or 201511: or 201512: or 2016: or 2017: or 2018: or 2019: or 2020: or 2021: or 2022: or 2023:).ed. **[Embase]** (201507$ or 201508$ or 201509$ or 201510$ or 201511$ or 201512$ or 2016$ or 2017$ or 2018$ or 2019$ or 2020$ or 2021$ or 2022$ or 2023$).ew.
	36. 34 and 35
	37. limit 36 to English language

Cochrane Database of Systematic Reviews

Section A: Disease and/or population	1. cancer$.mp. or tumo?r$.mp. or carcinoma$.mp. or neoplas$.mp. or metastas$.mp. or malignan$.mp. or adenocarcinoma$.mp. or sarcoma$.mp. or myosarcoma$.mp. or rhabdomyosarcoma$.mp. or angiosarcoma$.mp. or h?emangiosarcoma$.mp. or lymphangiosarcoma$.mp. or stewart-treves syndrome$.mp. or h?emangiopericytoma$.mp. or cystosarcoma$.mp. or phyllodes.mp. or dermatofibrosarcoma$.mp. or fibrosarcoma$.mp. or gastrointestinal stromal tumo?r$.mp. or GIST.mp. or leiomyosarcoma$.mp. or liposarcoma$.mp. or MFH.mp. or MPNST.mp. or myxosarcoma$.mp. or neurofibrosarcoma$.mp. or synovioma$.mp. or adamantinoma$.mp. or PNET.mp. or chondrosarcoma$.mp. or mesenchymoma$.mp. or osteoclastoma$.mp. or osteosarcoma$.mp. or chordoma$.mp. or dermatofibrosarcoma protuberan$.mp. or DFSP.mp. or carcinosarcoma$.mp. or melanoma$.mp. or myeloma$.mp. or lymphoma$.mp. or leukemia$.mp.
Section B: Intervention or diagnostic test	2. deoxyglucose.mp. or deoxy-glucose.mp. or fluorodeoxyglucose.mp. or 18fluorodeoxyglucose.mp. or fludeoxyglucose.mp. or fdg$.mp. or 18fdg.mp. or f-18-dg.mp. or

	fluoro-2-deoxy-d-glucose.mp. or 2fluoro-2deoxyglucose.mp. or fluoro-d-glucose.mp.
	3. (positron adj emission adj tomograph$).mp.
	4. (pet$ or pet scan$).mp.
	5. or/3-4
	6. 2 and 5
	7. (magnetic resonance imag$ or magnetic resonance spectroscop$).mp.
	8. (dynamic adj4 (MRI or magnet$)).mp.
	9. (diffusion weight$ adj3 (MRI or magnet$)).mp.
	10. (MPMRI or MP-MRI or MR$2 or DWI$ or DW-MRI or DCE$ or NMR$ or fmri).mp.
	11. (T1-weighted or T2-weighted).mp. adj3 imag$.mp.
	12. (MR$1 adj (imag$ or spectroscop$ or scan$ or tomograph$)).mp.
	13. (magnet$ adj (imag$ or spectroscop$ or scan$ or resonance)).mp.
	14. or/7-13
	15. 6 and 14
	16. (tomograph$ or ct scan$).mp.
	17. ct.mp.
	18. scan$.mp.
	19. 17 and 18
	20. 16 or 19
	21. 6 and 20
	22. 15 or 21
	23. (positron emission tomography computed tomography or pet ct or pet-ct or pet$ct).mp.
	24. (positron emission tomography magnetic resonance imaging or pet mr$ or pet-mr$ or petmr).mp.
	25. 23 or 24
	26. 2 and 25
	27. 22 or 26
Combining Sections A and B	28. 1 and 27
	29. (2015 or 2016 or 2017 or 2018 or 2019 or 2020 or 2021 or 2022 or 2023).yr.
	30. 28 and 29

Appendix 3: PRISMA Flow Diagram



Appendix 4: Tumour Subtypes and Technical Details of PET/MRI

Study, year	Tumour subtypes (number of patients)	Single injection protocol	Time from injection to PET/CT acquisition (minutes)	Time from injection to PET/MRI acquisition (minutes)	Acquisition area	Device/MRI sequences	Intravenous contrast
Breast Cancer							
Catalano et al, 2017 [7]	Invasive ductal carcinoma (51)	Yes	60	90	Whole-body	**Biograph mMR:** DWI, STIR, T1W Dixon, T2W HASTE, T1W VIBE	Yes
Melsaether et al, 2016 [8]	Not specified (51)	Yes	45	167±36	Vertex to thigh	**Biograph mMR:** VIBE Dixon, T1W VIBE, EPI DWI	Yes
Sawicki et al, 2016 [9]	Invasive ductal carcinoma (12), invasive lobular carcinoma (4), not specified (5)	Yes	62.9±13.1	124.8±28.9	Skull base to midthigh	**Biograph mMR:** VIBE Dixon, T2W HASTE, EPI DWI, T2W TIRM, T1W VIBE	Yes
Esophageal Cancer							
Wang et al, 2022 [10]	Squamous cell carcinoma (35)	Yes	60±10	Not specified	Lower neck to upper abdomen	**uPMR 790:** T1W Dixon, T2W RT, DWI	No
Gastrointestinal Cancer							
Akkus Gunduz et al, 2023 [11]	Adenocarcinoma (69), mucinous carcinoma (7), signet ring cell carcinoma (1), adenocarcinoma + mucinous carcinoma (1)	Yes	60	Not specified	Liver	**Signa PET/MR:** T2W SSFSE, T2W FSE, dual echo, EPI DWI, DISCO	Yes
Liu et al, 2019 [12]	Tubular adenocarcinoma (21), signet ring cell carcinoma (2), adenocarcinomas + signet ring cell carcinoma + mucinous adenocarcinoma (5), adenocarcinoma + neuroendocrine cell carcinoma (2)	No	PET/MRI was performed 3 days after PET/CT		Vertex to thigh, stomach	**Biograph mMR:** T1W VIBE, T2W TSE, DWI, 2-point Dixon, HASTE, SS-EPI DWI, ADC	No

Catalano et al, 2017 [13]	Not specified (26)	Yes	60	<180	Skull to midthigh	**Biograph mMR:** T1W VIBE, STIR, DWI, T2W HASTE	No
Gynecologic Cancer							
Grueneisen et al, 2015 [14]	Not specified (24)	Yes	60	132±25	Skull base to midthigh	**Biograph mMR:** T1W VIBE Dixon, EPI DWI, T2W TIRM, T2W HASTE, T1W VIBE, T2W TSE	Yes
Kirchner et al, 2017 [15]	Not specified (43)	Yes	Not specified	150±47	Skull base to midthigh	**Biograph mMR:** T1W VIBE Dixon, T2W HASTE, T1W VIBE	Yes
Bian et al, 2019 [16]	Adenocarcinoma (81)	No	Not available		Abdomen and pelvis	**Biograph mMR:** T1W VIBE Dixon, T2W HASTE, T2W FSE, DWI, 3D VIBE	No
Yu et al, 2022 [17]	Endometrioid adenocarcinoma (49), non-endometrioid adenocarcinoma (8)	Yes	60	33±12*	Pelvis	**Signa PET/MR:** T1W Dixon, T2W Dixon, DWI, ADC	No
Gong et al, 2021 [18]	Not specified (124)	No	Not available		Vertex to midthigh, pelvis	**Biograph mMR:** STIR, HASTE, T2W TSE, T1W TSE, EPI DWI	Yes
Schwartz et al, 2018 [19]	Not specified (18)	Yes	55	55±12*	Abdomen and pelvis	**Biograph mMR:** T1W VIBE Dixon, T2W HASTE, T2W FSE, DWI, 3D VIBE	No
Head and Neck Cancer							
Chan et al, 2018 [20]	Keratinizing squamous cell carcinoma (2), non-keratinizing squamous cell carcinoma (19), undifferentiated carcinoma (92)	Yes	50-70	57.9±25.6*	Whole-body, head and neck	**Biograph mMR:** T1W VIBE Dixon, T2W HASTE, STIR, T1W TSE, T2W TSE, T1W VIBE	Yes

Huang et al, 2020 [21]	Squamous cell carcinoma (20)	Yes	81.3±33	14±12*	Skull base to thoracic inlet	**Signa PET/MR:** T1W FSE, T2W FRFSE, STIR DWI, Dixon	No
Yeh et al, 2020 [22]	Squamous cell carcinoma (198)	Yes	50-70	49.2*	Whole-body, head and neck	**Biograph mMR:** VIBE Dixon, T2W HASTE, STIR, T1W TSE, T2W TSE, T1W VIBE	Yes
Vrachimis et al, 2016 [23]	Not specified (31)	Yes	64±11	121±26	Neck and thorax	**Biograph mMR:** T1W VIBE 2-point Dixon, T2W TSE Dixon, T2W TSE, T1W TSE, EPI STIR DWI, T1W TSE Dixon, T2W HASTE, EPI SPAIR DWI, T1W VIBE	Yes
Song et al, 2021 [24]	Papillary thyroid carcinoma (29), papillary thyroid microcarcinoma (4), papillary thyroid carcinoma + papillary thyroid microcarcinoma (3), follicular thyroid carcinoma (1)	Yes	60	120	Neck	**Signa PET/MR:** T1W FSE, T2W FSE, DWI	No
Slouka et al, 2020 [25]	Spinocellular carcinoma (75), mucoepidermoid carcinoma (2), myoepithelial carcinoma (2), salivary ductal carcinoma (3), low differentiated large cell diffuse carcinoma (1), acinocellular carcinoma (2), biphasic adenocarcinoma (1), epithelial-myoepithelial carcinoma (2), papillary carcinoma (2)	No	Not available		Head and neck, head to thigh	**Biograph mMR:** T2W STIR, T2W TSE, DWI, ADC, T1W VIBE, T1W VIBE 2-point Dixon	Yes
Hematologic Cancer							

Picardi et al, 2021 [26]	Nodular sclerosis (41), mixed cellularity (14), lymphocyte rich (3), lymphocyte depleted (2)	Yes	71±15	126±26	Whole-body	**Biograph mMR:** T1W VIBE 2-point Dixon, STIR, DWI, ADC, T2W HASTE, T1W VIBE	No
Giraudo et al, 2016 [27]	Mucosa-associated lymphoid tissue (15), mantle cell lymphoma (5), Hodgkin (4), marginal zone lymphoma (3), Burkitt (2), follicular lymphoma (2), diffuse large B-cell lymphoma (2), T-cell lymphoma (1)	Yes	45-60	100-150	Vertex to upper thigh	**Biograph mMR:** T1W VIBE 2-point Dixon, T2W HASTE, SS-EPI SPAIR DWI	No
Melanoma							
Schaarschmidt et al, 2018 [28]	Superficial spreading melanoma (22), nodular melanoma (11), acral lentiginous melanoma (2), desmoplastic melanoma (1), amelanotic melanoma (1), spitzoid melanoma (1), spindle cell melanoma (1), not specified (13)	Yes	60	186±48	Whole-body	**Biograph mMR:** T1W VIBE Dixon, T1W FLASH, T2W HASTE, T2W TIRM, DWI, T1W VIBE	No
Berzaczy et al, 2020 [29]	Not specified (22)	Yes	45-60	100-150	Vertex to upper thigh	**Biograph mMR:** T1W VIBE 2-point Dixon, T1W VIBE, T2W HASTE	Yes
Non-Small Cell Lung Cancer							
Wang et al, 2023 [30]	Adenocarcinoma (41), squamous cell carcinoma (10), adenosquamous cell carcinoma (1)	Yes	Not specified	167±62	Thorax	**uPMR 790:** T1W TSE, T2W BLADE, STIR BLADE, DWI	No
Kirchner et al, 2019 [31]	Adenocarcinoma (59), squamous cell carcinoma (21), large cell carcinoma (2), not specified (2)	Yes	60	120±16	Thorax	**Biograph mMR:** VIBE 2-point Dixon, T2W BLADE, T2W TrueFISP, T2W	Yes

Schaarschmidt et al, 2017 [32]	Adenocarcinoma (46), squamous cell carcinoma (22), other (9)	Yes	63±16	145±34	Thorax	HASTE, T1W FLASH, EPI DWI **Biograph mMR:** VIBE Dixon, T2W BLADE, T2W TrueFISP, T2W HASTE, T1W FLASH, EPI DWI	Yes
Lee et al, 2016 [33]	Adenocarcinoma (32), squamous cell carcinoma (8), mixed small cell carcinoma and adenocarcinoma (1), adenosquamous carcinoma (1), mucoepidermoid carcinoma (1), not specified (2)	Yes	15.0±6.7**	60	Head to midthigh	**Biograph mMR:** VIBE Dixon, T1W TSE, T2W HASTE, 3D VIBE, SPAIR DWI, ADC	Yes
Various Sites							
Beiderwellen et al, 2015 [34]	Not specified (32)	Yes	60	148±51	Whole-body	**Biograph mMR:** T1W VIBE 2-point Dixon, T1W FLASH, T2W HASTE, EPI DWI, T2W TSE, T1W VIBE	Yes
Zhou et al, 2021 [35]	Not specified (70)	Yes	60	142.9±23.9	Abdomen	**uPMR 790:** T2W FSE, DWI, T1W DE	No

Abbreviations: ADC, apparent diffusion coefficient; BLADE (PROPELLER), periodically rotated overlapping parallel lines with enhanced reconstruction; CT, computed tomography; DE, dual echo; DWI, diffusion-weighted imaging; DISCO, dynamic scan optimization; EPI, echo planar imaging; FLASH, fast low angle shot; FR, fast recovery; FSE, fast spin echo; HASTE, half-Fourier single shot turbo spin echo; MRI, magnetic resonance imaging; PET, positron emission tomography; RT, respiratory-triggered; SPAIR, spectral adiabatic inversion recovery; SS, single shot; STIR, short tau inversion recovery; TIRM, turbo inversion recovery magnitude; T1W, T1-weighted; T2W, T2-weighted; TrueFISP, true fast imaging with steady-state precession; TSE, turbo spin echo; VIBE, volumetric interpolated breath-hold examination

*mean time interval between PET/CT and PET/MRI

**mean time after completion of PET/MRI

Appendix 5: QUADAS-2 Assessment of Study Quality

Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Breast Cancer							
Catalano et al, 2017 [7]	L	L	U	L	L	L	L
Melsaether et al, 2016 [8]	L	L	U	L	L	L	L
Sawicki et al, 2016 [9]	L	L	U	L	L	L	L
Esophageal Cancer							
Wang et al, 2022 [10]	L	L	U	L	L	L	L
Gastrointestinal Cancer							
Akkus Gunduz et al, 2023 [11]	L	L	U	L	L	L	L
Liu et al, 2019 [12]	L	L	U	L	L	L	L
Catalano et al, 2017 [13]	L	L	U	L	L	L	L
Gynecologic Cancer							
Grueneisen et al, 2015 [14]	L	U	H	L	L	L	L
Kirchner et al, 2017 [15]	L	L	U	L	L	L	L
Bian et al, 2019 [16]	L	L	U	L	L	L	L
Yu et al, 2022 [17]	L	U	U	L	L	L	L
Gong et al, 2021 [18]	L	U	U	L	L	L	L
Schwartz et al, 2018 [19]	L	L	U	L	L	H	L
Head and Neck Cancer							
Chan et al, 2018 [20]	L	L	U	L	L	L	L

Huang et al, 2020 [21]	L	L	L	L	L	L	L
Yeh et al, 2020 [22]	L	L	U	L	L	L	L
Vrachimis et al, 2016 [23]	L	L	U	L	L	L	L
Song et al, 2021 [24]	L	U	U	L	L	L	L
Slouka et al, 2020 [25]	L	U	U	L	L	L	L
Hematologic Cancer							
Picardi et al, 2021 [26]	L	L	U	L	L	L	L
Giraudo et al, 2016 [27]	L	L	U	L	L	L	L
Melanoma							
Schaarschmidt et al, 2018 [28]	L	U	U	L	L	L	L
Berzaczy et al, 2020 [29]	L	L	U	L	L	L	L
Non-Small Cell Lung Cancer							
Wang et al, 2023 [30]	L	L	U	L	L	L	L
Kirchner et al, 2019 [31]	L	L	U	L	L	L	L
Schaarschmidt et al, 2017 [32]	L	L	L	L	L	L	L
Lee et al, 2016 [33]	L	L	U	L	L	L	L
Various Sites							
Zhou et al, 2021 [34]	H	L	U	L	L	L	L
Beiderwellen et al, 2015 [35]	L	L	U	L	L	L	L

L=Low Risk H=High Risk U=Unclear Risk

Appendix 6: Evidence Summary History

GUIDELINE VERSION	SYSTEMATIC REVIEW		PUBLICATIONS	NOTES and KEY CHANGES
	Search Dates	Data		
PET ES-16	Up to July 2015	Full Report	Peer review publication. Web publication.	None
PET ES-16 Version 2	July 2015 to January 2023	New data added to original Full Report	Updated web publication.	None