

On-line Table 1: Characteristics of eligible studies

Study	Year	Country	Age Range/Median (yr)	Male/Female	Primary Tumor	Radiotherapy Method	Tracer	Patients	Lesions	Analytic Method Used	Study Design	Follow-Up Time	Standard References	Cutoff Index*
Béloháček et al ²²	2003	Czech Republic	36–76	14:11	RCC, NSCLC, BC, NC, CC, melanoma	SRS	¹⁸ F-FDG	25	57	Lesions	Prospective	26 wk/mean	Histopathology + clinical and radiologic follow-up	U
Ceccon et al ⁸	2017	Germany	17–78/55 (mean)	14:48	NSCLC, BC, mixed cancer	SRS, WBRT, EFRT, brachytherapy	¹⁸ F-FET	62	76	Lesions	Retrospective	16 mo/median	Histopathology + clinical and radiologic follow-up	TBR _{mean} > 1.95 + presence of TAC slope < 0.37 SUV/h
Chao et al ³¹	2001	United States	U	U	LC, BC, RCC, HNC, EC, melanoma	SRS	¹⁸ F-FDG	36	36	Lesions	Retrospective	5.6 mo/median	Histopathology + radiologic follow-up	U
Cicone et al ²³	2015	Italy	38–84/64	19:23	LC, BC, RCC, GC, TC, CC, cervical cancer, melanoma, bladder cancer	SRS	¹⁸ F-FDOPA	42	50 (46 available)	Lesions	Prospective	16 mo/median	Histopathology + clinical and radiologic follow-up	SUV _{max} /Bkg _{max} (r-SUV)
Galdiks et al ³²	2012	Germany	17–70/53 (mean)	5:26	LC, BC, RCC, CC, SC, bone cancer	SRS, WBRT	¹⁸ F-FET	31	40	Lesions	Prospective	12 mo/median	Histopathology + clinical and radiologic follow-up	TAC curve pattern II and III + TBR _{mean} > 1.95
Guffens et al ³³	2015	Belgium	U	U	BC, LC, HNC cancer	U	¹⁸ F-FET	29	39	Lesions	Retrospective	U	Histology + clinical follow-up	TAC curve pattern II and III vs curve pattern I
Hatzoglou et al ³⁴	2016	United States	24–81/63	U	NSCLC, BC, melanoma	SRS, WBRT, PBRT	¹⁸ F-FDG	24	26	Lesions	Prospective	9 mo/median	Histopathology + clinical and radiologic follow-up	SUV _{max} lesion/SUV _{max} normal brain ≥ 1.4
Heesters et al ²⁴	2012	The Netherlands	U	U	U	SRS	¹¹ C-MET	26	U	Patients	Retrospective	U	Histopathology + clinical and radiologic follow-up	rSUV V20
Horley et al ³⁵	2011	United States	33–80/54	9:16	NSCLC, BC, LC, RCC, GCC, melanoma, NHL, bladder cancer	U	¹⁸ F-FDG	25	27 (30 scans)	Scans	Retrospective	18 mo/mean	Histopathology + radiologic follow-up	SUV _{max} lesion/SUV _{max} gray matter change with time (%)
Lai et al ³⁶	2015	United States	46–79	9:5	LC, BC, RCC, melanoma, esophageal cancer	SRS	¹⁸ F-FDG	14	U	Patients	Prospective	U	Histopathology	SUV _{max} > 3.0
Lizarraga et al ³⁷	2014	United States	21–77/58	6:26	LC, BC, TC, CC, OC, melanoma, testis cancer	SRS, WBRT	¹⁸ F-FDOPA	32	83	Lesions	Retrospective	U	Histopathology + clinical and radiologic follow-up	Visual scale
Lohmann et al ³⁸	2017	Germany	17–79	11:36	BC, EC, CC, OC, bronchial cancer	SRS, WBRT	¹⁸ F-FET	47	54	Lesions	Retrospective	12 mo/median	Histopathology + clinical and radiologic follow-up	TBR _{mean} + TBR _{max}
Matuszak et al ³⁸	2016	France	27–81/57	14:25	BC, RCC, CC, bronchial cancer	U	¹⁸ F-FDG	39	49	Lesions	Retrospective	U	Histopathology + clinical and radiologic follow-up	Visual scale (FDG 4 hr)
Romagna et al ³⁹	2016	Germany	61.9	11:11	NSCLC, BC, RCC, GC, melanoma	SRS, SBT	¹⁸ F-FET	22	34 (50 scans)	Scans	Prospective	28.3 mo/median	Histopathology + clinical and radiologic follow-up	Decreasing TACs + TBR _{max} > 2.15 + TBR _{mean} > 1.95
Terakawa et al ⁴⁰	2008	Japan	U	U	LC, BC, CC, RCC, OC, testis cancer	Conventional radiotherapy, SRS	¹¹ C-MET	51	56	Lesions	Retrospective	U	Histopathology + clinical and radiologic follow-up	SUV _{max} lesion/SUV _{mean} normal brain > 1.41

Note:—U indicates unclear; RCC, renal cell carcinoma; NSCLC, non-small-cell lung cancer; BC, breast cancer; NC, nasopharyngeal cancer; CC, colorectal cancer; LC, lung cancer; HNC, head and neck cancer; EC, endometrial cancer; TC, thyroid cancer; GC, gastrointestinal cancer; SC, skin cancer; GCC, germ cell cancer; OC, ovarian cancer; NHL, non-Hodgkins lymphoma; WBRT, whole-brain radiation therapy; EFRT, external fractionated radiotherapy; PBRT, partial-brain radiation therapy; SBT, stereotactic iodine-125 brachytherapy; TBR, tumor-brain ratios; TAC, time-activity curve; SUV, standardized uptake value; SUV_{max}, maximum lesion SUV; rSUV V20, the ratio of SUV V20 (the brain volume receiving ≥20 Gy)/SUV uninvolved brain; Bkg_{max}, maximum background SUV.
^a TAC curve pattern (I, constantly increasing uptake; II, uptake peaking early [time-to-peak <20 min] followed by a plateau; III, uptake peaking early [time-to-peak <20 min] followed by a descent).

On-line Table 2: Quality assessment (QUADAS-2)

Study	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Bělohávek et al ²²	L	L	L	L	L	L	L
Ceccon et al ⁸	H	L	L	H	L	L	L
Chao et al ³¹	H	L	L	H	L	L	L
Cicone et al ²³	L	H	L	L	L	L	L
Galldiks et al ³²	L	L	L	L	L	L	L
Guffens et al ³³	H	U	L	L	L	L	L
Hatzoglou et al ³⁴	L	H	L	L	L	L	L
Heesters et al ²⁴	H	U	L	L	L	L	L
Horky et al ³⁵	H	H	L	L	H	L	L
Lai et al ³⁶	L	L	H	L	L	L	L
Lizarraga et al ³⁷	H	L	L	L	L	L	L
Lohmann et al ¹³	H	L	L	L	L	L	L
Matuszak et al ³⁸	H	L	L	L	L	L	L
Romagna et al ³⁹	L	H	L	L	L	L	L
Terakawa et al ⁴⁰	H	H	L	L	L	L	L

Note:—L indicates low risk; H, high risk; U, unclear.

On-line Table 3: Meta-regression and subgroup analysis^a

Covariate	Number of Studies	Pooled Sensitivity	Pooled Specificity	Joint P Value
Study design				
Prospective	6	0.90 (0.83–0.96)	0.88 (0.83–0.94)	.38
Retrospective	9	0.82 (0.77–0.88)	0.87 (0.82–0.93)	.38
Country				
United States	5	0.83 (0.73–0.92)	0.84 (0.76–0.92)	.52
Germany	4	0.87 (0.80–0.95)	0.90 (0.84–0.96)	.66
Others	6	0.84 (0.77–0.92)	0.89 (0.83–0.95)	.91
Radiotherapy methods				
SRS only	5	0.84 (0.74–0.94)	0.90 (0.84–0.96)	.76
SRS + other methods	7	0.86 (0.78–0.91)	0.86 (0.80–0.91)	.39
Unclear	3	0.85 (0.76–0.95)	0.94 (0.86–1.00)	.49
Tracer				
¹¹ C-MET	2	0.86 (0.74–0.98)	0.79 (0.66–0.93)	.31
¹⁸ F-FDOPA	2	0.86 (0.74–0.97)	0.88 (0.79–0.97)	.99
¹⁸ F-FET	5	0.83 (0.76–0.91)	0.89 (0.83–0.95)	.77
¹⁸ F-FDG	6	0.85 (0.77–0.94)	0.90 (0.83–0.96)	.81
Cutoff index				
Quantitative methods without TAC curve pattern	7	0.86 (0.79–0.93)	0.86 (0.80–0.93)	.70
Quantitative methods with TAC curve pattern	4	0.84 (0.76–0.93)	0.88 (0.81–0.96)	.98
Visual scale	2	0.88 (0.78–0.97)	0.88 (0.79–0.97)	.83
Unclear	2	0.74 (0.55–0.92)	0.90 (0.82–0.98)	.26
Method of quantification				
Lesions	11	0.82 (0.77–0.87)	0.88 (0.84–0.92)	.07
Patients	2	0.91 (0.78–1.00)	0.84 (0.65–1.00)	.60
Scans	2	0.95 (0.88–1.00)	0.88 (0.77–0.99)	.11
Sample size	15	0.85 (0.79–0.89)	0.88 (0.83–0.91)	.81
Median age	6	0.89 (0.81–0.94)	0.87 (0.80–0.92)	.67
Male percentage	10	0.97 (0.48–1.00)	0.91 (0.44–0.99)	.69

Note:—TAC indicates time-activity curve.

^a Data in parentheses are 95% CIs.

On-line Table 4: Sensitivity analysis

Excluding Studies	Pooled Sensitivity (95% CI)	Comparison with Overall (P Value) ^a	Pooled Specificity (95% CI)	Comparison with Overall (P Value) ^a
Overall	0.85 (0.79–0.89)	–	0.88 (0.83–0.91)	–
Bělohávek et al ²²	0.85 (0.79–0.90)	>.05	0.87 (0.82–0.91)	>.05
Ceccon et al ⁸	0.85 (0.79–0.90)	>.05	0.87 (0.82–0.91)	>.05
Chao et al ³¹	0.86 (0.80–0.90)	>.05	0.88 (0.84–0.92)	>.05
Cicone et al ²³	0.84 (0.79–0.89)	>.05	0.87 (0.83–0.91)	>.05
Galldiks et al ³²	0.84 (0.78–0.88)	>.05	0.88 (0.83–0.91)	>.05
Guffens et al ³³	0.86 (0.81–0.90)	>.05	0.88 (0.83–0.92)	>.05
Hatzoglou et al ³⁴	0.85 (0.79–0.89)	>.05	0.88 (0.84–0.92)	>.05
Heesters et al ²⁴	0.84 (0.78–0.89)	>.05	0.88 (0.83–0.91)	>.05
Horky et al ³⁵	0.84 (0.78–0.88)	>.05	0.87 (0.83–0.91)	>.05
Lai et al ³⁶	0.85 (0.79–0.89)	>.05	0.88 (0.84–0.92)	>.05
Lizarraga et al ³⁷	0.85 (0.79–0.90)	>.05	0.88 (0.83–0.92)	>.05
Lohmann et al ¹³	0.85 (0.79–0.90)	>.05	0.88 (0.83–0.91)	>.05
Matuszak et al ¹³⁸	0.84 (0.78–0.88)	>.05	0.87 (0.83–0.91)	>.05
Romagna et al ¹³⁹	0.84 (0.78–0.89)	>.05	0.88 (0.83–0.92)	>.05
Terakawa et al ⁴⁰	0.85 (0.79–0.90)	>.05	0.89 (0.85–0.92)	>.05
Guffens et al ³³ and Heesters et al ²⁴	0.85 (0.80–0.89)	>.05	0.88 (0.83–0.92)	>.05

Note:— indicates not applicable.

^a P < .05 was considered statistically significant.