Supplementary material S2

Results

Table of content:

APPENDIX S1 – OVERALL RISK OF BIAS AND APPLICABILITY SCORE PER BIOLOGICAL FACTOR

Figure A1.1 'Risk of Bias' and 'Applicability' assessment sorted by biological factor. Values indicate the number of studies within the respective QUADAS-2 'risk of bias' or 'applicability' class. Green or "low" indicates a low risk of bias in the study and/or low concern regarding applicability. Yellow or "unclear/medium" suggests either insufficient information provided or non-ideal study characteristics influencing applicability or risk of bias. Red or "high" signifies significant concerns regarding bias or applicability.

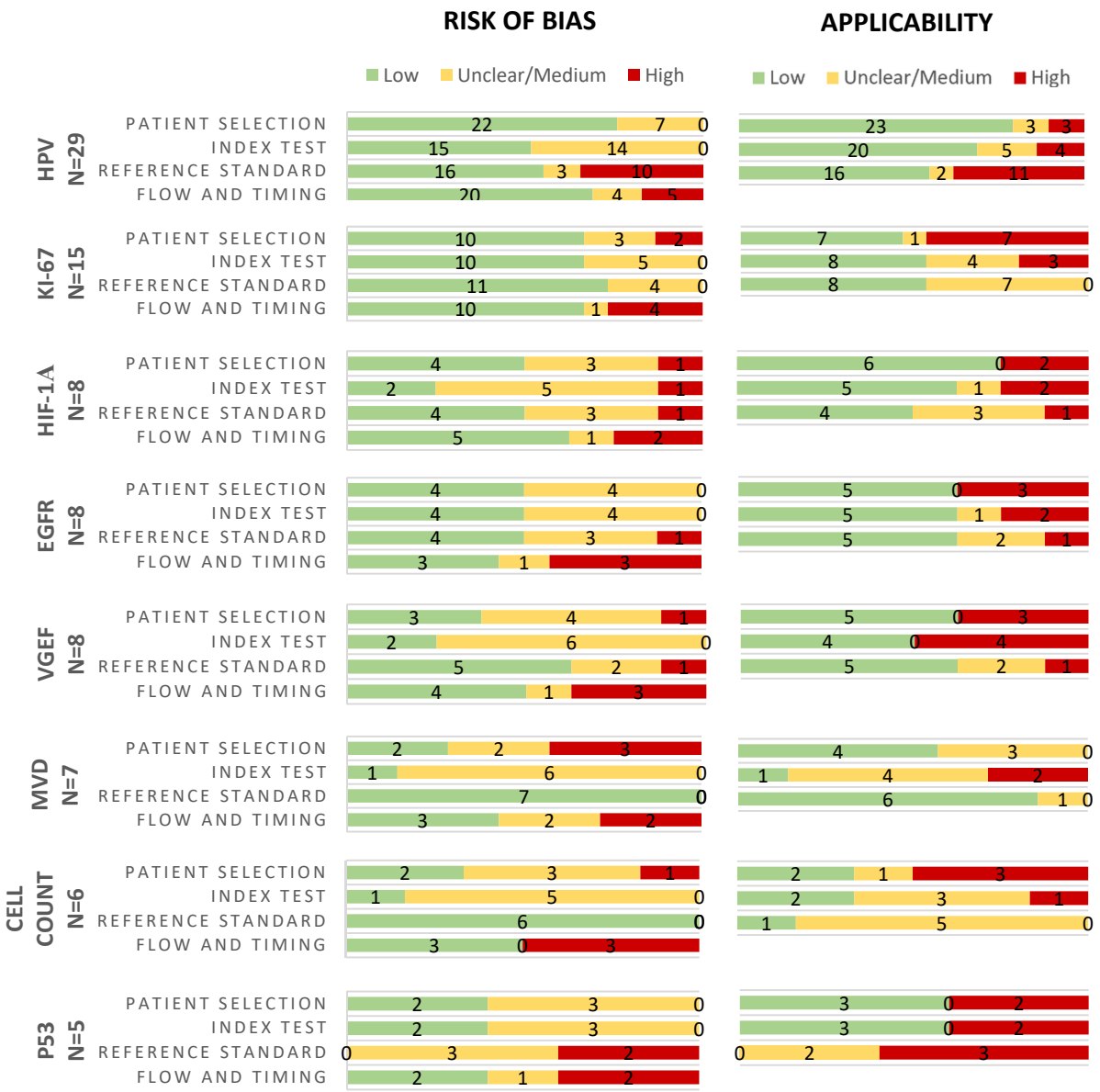

Table A2.1 'Risk of Bias' and 'Applicability' assessment for each independent study. Values indicate the numbers of studies within the respective QUADAS-2 'risk of bias' or 'applicability' class. Green or "low" indicates a low risk of bias in the study and/or low concern regarding applicability. Yellow or "unclear/medium" suggests either insufficient information provided or non-ideal study characteristics influencing applicability or risk of bias. Red or "high" signifies significant concerns regarding bias or applicability.

		Risk of Bias				Applicability		
Author, year	**Biological factors**	Patient Selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Ahn, 2021	HPV							
Boot, 2023	HPV							
Bos, 2021	HPV							
Bos, 2022	HPV							
Chan, 2016	HPV							
Chen T., 2015	HIF-1α							
Chen Y., 2023	EGFR							
Choi, 2016	HPV							
Dang, 2015	P53							
De Perrot, 2017	HPV							
Donaldson, 2015	VGEF							
Driessen, 2016	HPV							
Freihat, 2021	HPV							
Gao, 2021	Whole trancriptomic sequencing							
Giannitto, 2020	HPV							
Han, 2018	HPV							
Hu, 2018	HIF-1α, VGEF, MVD (CD34)							
Huang, 2021	HIF-1α, EGFR, KI-67							
Karabay, 2022	MVD (CD34,CD105)							
Kawaguchi, 2020	HPV							
Lenoir, 2022	HPV							
Li, 2023	HPV							
Liu, 2021	HIF-1α							
Martens, 2019	HPV							
Marzi, 2022	HPV							
Meyer, 2018 (A)	HPV, P53, HIF-1α, VGEF, EGFR							
Meyer, 2019 (B)	HPV, P53, HIF-1α, VGEF, EGFR							
Meyer,2019(C)	HPV, P53, HIF-1α, VGEF, EGFR, KI-67, CC							
Meyer, 2019 (D)	MVD (CD105)							
Meyer, 2019 (E)	MVD (CD105)							

Nakahira, 2014	HPV	
Park, 2022	HPV	
Piludu, 2021	HPV	
Rasmussen, 2020	VGEF, EGFR, KI-67, CC	
Rasmussen, 2020	P53	
Ravanelli, 2018	HPV	
Samolyk-Kogaczewska, 2020	HPV, KI-67	
Schouten, 2015	HPV	
Shima, 2023		
Sohn, 2020	HPV	
Suh, 2020	HPV	
Surov, 2016 (A)	KI-67, CC	
Surov, 2017 (B)	KI-67, MVD (CD31), CC	
Surov, 2018 (C)	KI-67, CC	
Surov, 2018 (D)	KI-67, CC	
Swartz, 2018	HIF-1α , KI-67	
Tekiki, 2021	VGEF, MVD (CD31)	
Tse, 2010	VGEF, EGFR	
Unestubo, 2009	MVD (CD34)	
Vidiri, 2019	HPV	
Wong, 2016	HPV	
Wu W., 2021	KI-67	
Wu, Y. 2023		
Zhang, 2020	Genes panel sequencing	

APPENDIX S3 – OVERVIEW OF PROPORTION MRI PARAMETER STUDIES REPORTING SIGNIFICANT ASSOCIATIONS WITH BIOLOGICAL FEATURES.

Tables depicting the frequency of reported significant correlations between the stated biological factors and the individual MRI parameter out of the total number of correlations of the researching studies, displayed as nr.Significant[significant references]/nr.Total[Other reporting references]. If the percentage of significant correlations exceeds 50%, the corresponding numbers are presented in bold font. The tables are sorted by MRI sequence technique: (A3.1) Diffusion parameters (including all IVIM and DKI parameters), (A3.2) Perfusion parameters (including pharmacokinetic models, time-signal intensity curve (TIC), and arterial spin labeling (ASL) parameters), and (A3.3) stand-alone conventional t1w and t2w imaging parameters.

A3.1 STAND-ALONE CONVENTIONAL T1W AND T2W IMAGING PARAMETERS

		Conventional T1W(+c), T2W, DWI or not specified								**DWI**	**T1W**		**T2W**	
BIOLOGICAL FACTOR		Volume		Diameter		Necrosis on MRI				SIR	SIR	HSL	SIR	LSL
HPV	All	0/5[A,B,D,E‡,F]		0/1[E*]		-				0/1[C]	0/1[C]	-	0/1[C]	-
	P16	0/1[E]		0/1[E]		-				0/1[C]	0/1[C]	-	0/1[C]	-
	P16+PCR	0/4[A,D,E,F]		0/1[E]		-				-	-	-	-	-
	Other	0/1[B]		-		-				-	-	-	-	-
Ki-67		0/1[E]		0/1[E]		-				-	-	0/1[I]	-	0/1[I]
HIF-1α		-		-		1/1[I]				-	-	-	-	-
		Conventional T1W(+c)												
		Mean	Min	Max	Median	Mode	SD	Kurtosis	Skewness	Entropy	P10	P25	P75	P90
HPV	All	0/2[G,H]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
	P16	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
	Other	0/1[H]	-	-	-	-	0/1[H]	1/1[H]	0/1[H]	0/1[H]	-	-	-	-
Ki-67		0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
HIF-1α		0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
EGFR		0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
VGEF		0/1[G*]	0/1[G]	0/1[G]	0/1[G*]	0/1[G*]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	1/1[G*]	0/1[G*]	0/1[G]	0/1[G]
Tumor cell count		0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
p53		0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	1/1[G*]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
		Conventional T2W												
		Mean	Min	Max	Median	Mode	SD	Kurtosis	Skewness	Entropy	P10	P25	P75	P90
HPV	All	1[H]/2[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
	P16	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]

Other	1/1[H]	-	-	-	-	0/1[H]	0/1[H]	0/1[H]	0/1[H]	-	-	-	-
Ki-67	0/1[G*]	0/1[G]	0/1[G]	0/1[G*]	0/1[G*]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G*]	0/1[G*]
HIF-1α	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G†]	0/1[G]	0/1[G]	0/1[G†]
EGFR	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
VGEF	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G*]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
Tumor cell count	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G*]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
p53	0/1[G*]	0/1[G]	0/1[G†]	0/1[G*]	0/1[G*]	0/1[G†]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G*]	0/1[G*]	0/1[G†]

Table shows the proportion of studies (number significant / number not significant) reporting significant associations between different functional MRI parameters and biological features as indicated. Proportions of more than half testing the indicated association are highlighted in bold.

Abbreviations = Min: minimum; max: maximum; SD: Standard deviation; P10,P25,P75,P90: percentile 10, 25, 75, 90; SIR: signal intensity ratio; HSL: High signal lesion; LSL: low signal lesion; SD: standard deviation; P10/25/75/90: percentile
*Note: *Significant for P16 positive subgroup analyses; †significant in P16 negative subgroup analyses; ⁂Volume defined by CT or PET/MRI*

a. Driessen, 2016 (article reference: [35])
b. Han, 2018 (article reference: [38])
c. Kawaguchi, 2020 (article reference: [43])
d. Martens, 2019 (article reference: [45])
e. Samolyk-Kogaczewska, 2020 (article reference: [56])
f. Vidiri, 2019 (article reference: [69])
g. Meyer, 2019 (article reference: [49])
h. Ravanelli, 2018 (article reference: [55])
i. Chen T., 2015 (article reference: [31])

A3.2 DIFFUSION PARAMETERS

		Apparent diffusion coefficient (ADC) (10^{-3} мм^2/s)												
Biological factor		Mean	Min	Max	Median	Mode	SD	Kurtosis	Skewness	Entropy	P10	P25	P75	P90
HPV	All	**10[A-D,G,H,J-L,N] /15[E,F,I,M,O]**	3[F,H,J] /7[B,E,I,M]	**2[B,H]/3[I]**	1[B]/2[I]	0/1[I]	1[H]/2[L]	2[B,G]/5[H,I,L]	2[B,G]/5[H,I,L]	0/2[I,L]	0/1[I]	1[B]/2[I]	1[B]/2[I]	0/1[I]
	P16	**3[A,D,J]/5[F,I]**	**2[F,J]/3[I]**	0/1[I]	0/1[I]	0/1[I]	-	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]
	PCR+P16	**6[B,C,G,H,K,N]/7[M]**	1[H]/3[B,M]	**2/2[B,H]**	**1/1[B]**	-	**1/1[H]**	**2[B,G]/3[H]**	**2[B,G]/3[H]**	-	-	**1/1[B]**	**1/1[B]**	-
	Other	1[L]/3[E,O]	0/1[E]	-	-	-	0/1[L]	0/1[L]	0/1[L]	0/1[L]	-	-	-	-
Ki-67		**5[Q-T,X]/6[U]**	1[S]/3[R,U]	2[R,S]/2	**1/1[S]**	**1/1[S]**	0/1[S]	0/1[S]	0/1[S]	0/1[S]	**1/1[S]**	**1/1[S]**	**1/1[S]**	**1/1[S]**
HIF-1α		0/2[T,I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I*]	0/1[I]	0/1[I*]	0/1[I]	0/1[I*]
EGFR		0/4[Q,I,V,Z]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]
VGEF		0/2[Q,I]	0/1[I]	0/1[I]	0/1[I]	0/1[I†]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I]

MVD	All	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]
	CD105	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]	0/1[W]
Tumor cell count		1[S]/3[Q,R]	1[S]/2[R]	0/2[R,S]	**1/1[S]**	**1/1[S]**	0/1[S]	**1/1[S]**	0/1[S]	0/1[S]	**1/1[S]**	**1/1[S]**	**1/1[S]**	**1/1[S]**
p53		1[Q]/2[I]	0/1[I]	**1/1[I†]**	0/1[I]	0/1[I]	0/1[I]	0/1[I*]	0/1[I]	0/1[I]	0/1[I]	0/1[I]	0/1[I†]	0/1[I†]

		ADC (10^{-3} мм^2/s)			**Intravoxel incoherent motion (IVIM) (10^{-3} мм^2/s)**									
		IQR	P10-P90	GTV	D_t	ƒ(%)	D*	D* x ƒ	D_t min	D* min	ƒ min	D_t max	D* max	ƒ max
HPV	All	**1/1[B]**	**1/1[H]**	0/1[H]	**3/3[K,N,P]**	0/1[N]	0/1[N]	0/1[N]	-	-	-	-	-	-
	PCR+P16	**1/1[B]**	**1/1[H]**	0/1[H]	**3/3[K,N,P]**	0/1[N]	0/1[N]	0/1[N]	-	-	-	-	-	-
Ki-67		-	-	-	0/1[U]	0/1[U]	0/1[U]	-	0/1[U]	0/1[U]	0/1[U]	-	-	-

	Diffusion Kurtosis imaging (DKI) (10^{-3} mm^2/s)												
	K	D_k	DDC	α	D_{slow}	MK	Ka	Kr	FAk	MD	Da	Dr	FA
Ki-67	**1/1[X]**	**1/1[X]**	**1/1[X]**	0/1[X]	**1/1[X]**	**1/1[Y]**	**1/1[Y]**	**1/1[Y]**	0/1[Y]	**1/1[Y]**	**1/1[Y]**	**1/1[Y]**	0/1[Y]

Table shows the proportion of studies (number significant / number not significant) reporting significant associations between different functional MRI parameters and biological features as indicated. Proportions of more than half testing the indicated association are highlighted in bold.

Abbreviations: Min: minimum; max: maximum; SD: Standard deviation; P10,P25,P75,P90: percentile 10, 25, 75, 90; IQR: interquartile range; P10-P90: ADC between percentile 10 and 90; GTV: gross tumor volume; D_t: tissue diffusion coefficient; f: perfusion fraction; D: perfusion related diffusion coefficient; K: kurtosis value; D_K: the kurtosis-corrected diffusion coefficient; DDC: distributed diffusion coefficient; α: diffusion heterogeneity, D_{slow}: slow diffusion coefficient; MK: mean kurtosis; Ka: axial kurtosis; Kr: radial kurtosis; FAk: fractional anisotropy of kurtosis; MD: mean diffusivity; DA: axial diffusivity; Dr: radial diffusivity; FA: fractional anisotropy*
*Notes: *Significant for P16 positive subgroup analyses; †significant in P16 negative subgroup analyses*

a. Chan, 2016 (article reference: [29])
b. De Perrot, 2017 (article reference: [34])
c. Driessen, 2016 (article reference: [35])
d. Freihat, 2021 (article reference: [36])
e. Han, 2018 (article reference: [38])
f. Kawaguchi, 2020 (article reference: [43])
g. Lenoir, 2022 (article reference: [44])
h. Martens, 2019 (article reference: [45])
i. Meyer, 2018 (article reference: [47])
j. Nakahira, 2014 (article reference: [52])
k. Piludu, 2021 (article reference: [54])
l. Ravanelli, 2018 (article reference: [55])
m. Schouten, 2015 (article reference: [57])
n. Vidiri, 2019 (article reference: [69])
o. Wong, 2016 (article reference: [70])
p. Marzi, 2022 (article reference: [46])
q. Rasmussen, 2020 (article reference: [60])
r. Surov, 2016 (article reference: [61])

s. Surov, 2018 (article reference: [63])
t. Swartz, 2018 (article reference: [65])
u. Wu W., 2021 (article reference: [71])
v. Tse, 2010 (article reference: [67])
w. Meyer, 2019 (article reference: [51])
x. Shima, 2023 (article reference: [72])
y. Wu Y., 2023 (article reference: [73])
z. Chen Y., 2023 (article reference: [75])

A3.2 PERFUSION PARAMETERS

		Volume transfer constant (K^{trans})												
Biological factor		Mean	Min	Max	Median	Mode	SD	Kurtosis	Skewness	Entropy	P10	P25	P75	P90
HPV	All	$1^{B}/4^{C-E}$	$0/1^{D}$	$0/1^{D}$	$1^{B}/2^{D}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$1^{B}/2^{D}$	$1^{B}/2^{D}$	$0/1^{D}$
	P16	$1^{B}/2^{D}$	$0/1^{D}$	$0/1^{D}$	$1^{B}/2^{D}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$1^{B}/2^{D}$	$1^{B}/2^{D}$	$0/1^{D}$
	PCR+P16	$0/1^{E}$	-	-	-	-	-	-	-	-	-	-	-	-
	Other	$0/1^{C}$	-	-	-	-	-	-	-	-	-	-	-	-
Ki-67		$1^{I}/4^{F,H,J}$	**$1/1^{J}$**	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	**$1/1^{J}$**	$0/1^{J}$	**$1/1^{J}$**	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$
HIF-1α		$0/3^{D,F,K}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D*}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$
EGFR		$2^{B,F}/5^{D,H,Q}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/2^{B,D}$	$0/1^{D*}$	$0/1^{D}$	$0/2^{B,D}$	$0/2^{B,D}$	$0/1^{D}$
VGEF		$0/3^{D,H,K}$	$0/1^{D}$	$0/1^{D*}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$
MVD	All	$1^{G*}/4^{I,K,O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$
	CD31	$0/1^{I}$	-	-	-	-	-	-	-	-	-	-	-	-
	CD34	$1^{G*}/2^{K}$	-	-	-	-	-	-	-	-	-	-	-	-
	CD105	$0/2^{G*,O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$	$0/1^{O}$
Tumor cell count		$0/3^{H,I,J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$1/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$
p53		$1^{H}/2^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$
		Rate constant (K_{ep})												
		Mean	Min	Max	Median	Mode	SD	Kurtosis	Skewness	Entropy	P10	P25	P75	P90
HPV	All	$0/4^{B-E}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$1^{D}/2^{B}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$1^{B}/2^{D}$	$0/2^{B,D}$	$0/1^{D}$
	P16	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$1^{D}/2^{B}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$1^{B}/2^{D}$	$0/2^{B,D}$	$0/1^{D}$
	PCR+P16	$0/1^{E}$	-	-	-	-	-	-	-	-	-	-	-	-
	Other	$0/1^{C}$	-	-	-	-	-	-	-	-	-	-	-	-
Ki-67		$0/3^{F,I,J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	**$1/1^{J}$**	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$
HIF-1α		$0/3^{D,F,K}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D*}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$
EGFR		$1^{B}/4^{D,F,Q}$	$0/1^{D}$	$0/1^{D}$	$1^{B}/2^{D}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/2^{B,D}$	**$1/1^{D}$**	$0/1^{D}$	$1^{B}/2^{D}$	$1^{B}/2^{D}$	$0/1^{D}$
VGEF		$1/2^{D,K}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D*}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$

MVD	All	$1^{o}/4^{G*,i,k}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	**$1/1^{o}$**	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	**$1/1^{o}$**	**$1/1^{o}$**	**$1/1^{o}$**	$0/1^{o}$
	CD31	$0/1^{I}$	-	-	-	-	-	-	-	-	-	-	-	-
	CD34	$0/2^{G*,K}$	-	-	-	-	-	-	-	-	-	-	-	-
	CD105	$1^{o}/2^{G*}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	**$1/1^{o}$**	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$1/1^{o}$	$1/1^{o}$	$1/1^{o}$	$0/1^{o}$
Tumor cell count		$0/2^{I,J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$
p53		$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$
		Extravascular space (V_e)												
		Mean	Min	Max	Median	Mode	SD	Kurtosis	Skewness	Entropy	P10	P25	P75	P90
HPV	All	$0/4^{B-E}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$o/2^{B,D}$	$0/2^{B,D}$	$0/1^{D}$
	P16	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/2^{B,D}$	$0/1^{D}$
	PCR+P16	$0/1^{E}$	-	-	-	-	-	-	-	-	-	-	-	-
	Other	$0/1^{C}$	-	-	-	-	-	-	-	-	-	-	-	-
Ki-67		$0/3^{F,I,J}$	**$1/1^{J}$**	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	**$1/1^{J}$**	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$
HIF-1α		$1/3^{D,F,K}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$
EGFR		$1/4^{B,D,F,Q}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D}$	$0/2^{B,D}$	$0/2^{B,D}$	$0/1^{D}$	$0/1^{D\dagger}$	$0/2^{B,D}$	$0/2^{B,D}$	$0/1^{D}$
VGEF		$0/2^{D,K}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$
MVD	All	$0/4^{G*,i,k,o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$
	CD31	$0/1^{I}$	-	-	-	-	-	-	-	-	-	-	-	-
	CD34	$0/2^{G*,K}$	-	-	-	-	-	-	-	-	-	-	-	-
	CD105	$0/2^{G*,O}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$	$0/1^{o}$
Tumor cell count		$0/2^{I,J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	**$1/1^{J}$**	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$	$0/1^{J}$
p53		$0/1^{D}$	$0/1^{D}$	$0/1^{D\dagger}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$	$0/1^{D}$
		V_p	**DCE-AUC**			**QTM**		**Time-signal intensity curve(TIC)**						
		Mean	60 sec	90 sec	TBF	|u|	D	RE	ME	MRE	TTP	WIR	WOR	AUC
HPV	All	$0/1^{C}$	$0/1^{C}$	$0/1^{E}$	-	-	-	-	-	-	-	-	-	-
	PCR+P16	-	-	$0/1^{E}$	-	-	-	-	-	-	-	-	-	-
	Other	$0/1^{C}$	$0/1^{C}$	-	-	-	-	-	-	-	-	-	-	-
Ki-67		-	-	-	$0/1^{F}$	**$1/1^{F}$**	$0/1^{F}$	-	-	-	-	-	-	-
HIF-1α		$0/1^{K}$	-	-	**$1/1^{F}$**	**$1/1^{F}$**	$0/1^{F}$	**$1/1^{L}$**	**$1/1^{L}$**	**$1/1^{L}$**	$0/1^{L}$	$0/1^{L}$	$0/1^{L}$	$0/1^{L}$
EGFR		-	-	-	$0/1^{F}$	$0/1^{F}$	$0/1^{F}$	-	-	-	-	-	-	-
VGEF		**$1/1^{K}$**	-	-	-	-	-	-	-	-	-	-	-	
MVD	All	$0/1^{K}$	-	-	-	-	-	-	-	-	-	-	-	$0/2^{G*,i}$
	CD31	-	-	-	-	-	-	-	-	-	-	-	-	$0/1^{I}$
	CD34	$0/1^{K}$	-	-	-	-	-	-	-	-	-	-	-	$0/1^{G}$

	CD105	-	-	-	-	-	-	-	-	-	-	-	0/1[G]
		2 Compartment model (2CXM)						**Arterial spin labeling (ASL)**					
		Fb	PS	Vb	Ve	MTT	Mean	SD	CV	Skewness	Kurtosis	TBF P5	TBF P95
HPV	All	-	-	-	-	-	0/1[A]	**1/1[A]**	0/1[A]	0/1[A]	0/1[A]	0/1[A]	**1/1[A]**
	PCR+P16	-	-	-	-	-	0/1[A]	**1/1[A]**	0/1[A]	0/1[A]	0/1[A]	0/1[A]	**1/1[A]**
	Other	-	-	-	-	-	-	-	-	-	-	-	-
VGEF		**1/1[M]**	0/1[M]	0/1[M]	0/1[M]	0/1[M]	-	-	-	-	-	-	-

		Contrast Index (CI)				
		CI max	CI gain max	CI-peak	T-max	CI-gain/CI-max ratio
VGEF		0/1[N]	0/1[N]	0/1[N]	0/1[N]	-
MVD	All	0/2[N,P]	**2/2[N,P]**	0/1[N]	**1/1[N]**	**1/1[P]**
	CD31	0/1[N]	**1/1[N]**	0/1[N]	**1/1[N]**	-
	CD34	0/1[P]	**1/1[P]**	-	-	**1/1[P]**

Table shows the proportion of studies (number significant / number not significant) reporting significant associations between different functional MRI parameters and biological features as indicated. Proportions of more than half testing the indicated association are highlighted in bold.

*Abbreviations = Min: minimum; max: maximum; SD: Standard deviation; P10,P25,P75,P90: percentile 10, 25, 75, 90; Vp: fractional plasma volume; QTM: Quantitative transport mapping; RE: relative enhancement; ME: maximum enhancement; MRE: maximum relative enhancement; TTP: time to peak; WIR: wash-in rate; WOR: wash-out rate; AUC: Area under the curve; Fb: perfusion; PS: Capillary permeability, Vb: blood volume; Ve: Extravascular extracellular space volume; MTT: whole blood mean transit time; CV: Coefficient of variance, TBF: tumor blood flow. Notes: *Significant for P16 positive subgroup analyses; †significant in P16 negative subgroup analyses; ⁂study tested two MVD IHC markers.*

a. Ahn, 2021 (article reference: [25])
b. Choi, 2016 (article reference: [30])
c. Han, 2018 (article reference: [38])
d. Meyer, 2019 (article reference: [48])
e. Piludu, 2021 (article reference: [54])
f. Huang, 2021 (article reference: [40])
g. Karabay, 2022 (article reference: [41])
h. Rasmussen, 2020 (article reference: [60])
i. Surov, 2017 (article reference: [62])
j. Surov, 2018 (article reference: [64])
k. Hu, 2018 (article reference: [39])
l. Lui, 2021 (article reference: [42])
m. Donaldson, 2011 (article reference: [33])
n. Tekiki, 2021 (article reference: [66])
o. Meyer, 2019 (article reference: [50])
p. Unetsubo, 2009 (article reference: [68])
q. Chen Y., 2023 (article reference: [75])

APPENDIX S4 – SIGNIFICANCE OVERVIEW FOR BIOLOGICAL FEATURES WITH LESS THAN FOUR REPORTING SOURCES

Tables depicting the frequency of reported significant results for each individual MRI parameter out of the total number of researched studies, displayed as nr.Significant[significant references]/nr.Total[Other reporting references]. If the percentage of significant studies exceeds 50%, the corresponding numbers are presented in bold font. The tables are sorted by MRI sequence technique: (A4.1) Diffusion parameters (including all IVIM and DKI parameters), (A4.2) Perfusion parameters (including pharmacokinetic models, time-signal intensity curve (TIC), and arterial spin labeling (ASL) parameters), and (A4.3) stand-alone conventional t1w and t2w imaging parameters.

A4.1 STAND-ALONE CONVENTIONAL T1W AND T2W IMAGING PARAMETERS

	Conventional T1W or T2W (not specified)		
Biological factor	Volume	Diameter	Primary tumor necrosis on MRI
PD-L1	-	-	**1/1[M]**
EBV	0/1[N]	0/1[N]	-

Abbreviations = Min: minimum; max: maximum; SD: Standard deviation; P10,P25,P75,P90: percentile 10, 25, 75, 90

A4.2 DIFFUSION

		ADC												
Biological factor		Mean	Min	Max	Median	Mode	SD	Kurtosis	Skewness	Entropy	P10	P25	P75	P90
Nuclei Area	Total	**2/2[A,B]**	1[B]/2[A]	0/2[A,B]	**1/1[B]**	0/1[B]	0/1[B]	0/1[B]	0/1[B]	0/1[B]	0/1[B]	**1/1[B]**	0/1[B]	**1/1[B]**
	Average	0/2[A,B]	0/2[A,B]	0/2[A,B]	0/1[B]	0/1[B]	0/1[B]	0/1[B]	0/1[B]	0/1[B]	0/1[B]	0/1[B]	0/1[B]	0/1[B]
HER2		0/2[C,D]	0/1[C]	0/1[C]	0/1[C]	**1/1[C]**	-	0/1[C]	0/1[C]	0/1[C]	0/1[C]	0/1[C]	0/1[C]	0/1[C]
CD3 cell count		0/1[E]	-	-	-	-	-	-	-	-	-	-	-	-
CAIX		0/1[F]	-	-	-	-	-	-	-	-	-	-	-	-
PD-L1		**1/1[F]**	-	-	-	-	-	-	-	-	-	-	-	-
Blc-2		1[F]/2[D]	-	-	-	-	-	-	-	-	-	-	-	-
GLUT-1		0/1[F]	-	-	-	-	-	-	-	-	-	-	-	-
IL6/ IL8/ IL10		0/1[D]	-	-	-	-	-	-	-	-	-	-	-	-
Bak / Bax		0/1[D]	-	-	-	-	-	-	-	-	-	-	-	-

COX-2	0/1[D]	-	-	-	-	-	-	-	-	-	-	-	-
HER2	0/1[C,D]	0/1[C]	0/1[C]	0/1[C]	1/1[C]	0/1[C]	0/1[C]	0/1[C]	0/1[C]	0/1[C]	0/1[C]	0/1[C]	0/1[C]
Tumor stroma ratio	0/1[O]	-	-	-	-	-	-	-	-	-	-	-	-

Abbreviations = Min: minimum; max: maximum; SD: Standard deviation; P10,P25,P75,P90: percentile 10, 25, 75, 90.

A4.3 PERFUSION PARAMETERS

		Volume transfer constant (K^{trans})												
Biological factor		Mean	Min	Max	Median	Mode	SD	Kurtosis	Skewness	Entropy	P10	P25	P75	P90
Nuclei Area	Total	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
	Average	0/1[G]	**1/1[G]**	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
CAIX		0/2[F,H]	-	-	-	-	-	-	-	-	-	-	-	-
PD-L1		0/1[F]	-	-	-	-	-	-	-	-	-	-	-	-
Blc-2		0/1[F]	-	-	-	-	-	-	-	-	-	-	-	-
GLUT-1		0/1[F]	-	-	-	-	-	-	-	-	-	-	-	-
EBV		0/1[I]	-	-	-	-	-	-	-	-	-	-	-	-
Tumor stroma ratio		0/1[P]	0/1[P]	0/1[P]	0/1[P]	0/1[P]	-	0/1[P]	0/1[P]	**1/1[P]**	0/1[P]	0/1[P]	0/1[P]	0/1[P]
Tumor infiltrating lymphocytes		0/1[P]	0/1[P]	0/1[P]	0/1[P]	0/1[P]	-	0/1[P]	0/1[P]	0/1[P]	0/1[P]	0/1[P]	0/1[P]	0/1[P]
		Rate constant (K_{ep})												
		Mean	Min	Max	Median	Mode	SD	Kurtosis	Skewness	Entropy	P10	P25	P75	P90
Nuclei Area	Total	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
	Average	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
CAIX		0/1[H]	-	-	-	-	-	-	-	-	-	-	-	-
EBV		**1/1[I]**	-	-	-	-	-	-	-	-	-	-	-	-
Tumor stroma ratio		0/1[P]	0/1[P]	0/1[P]	0/1[P]	0/1[P]	-	0/1[P]	0/1[P]	0/1[P]	0/1[P]	0/1[P]	0/1[P]	0/1[P]
		Extravascular space (V_e)												
		Mean	Min	Max	Median	Mode	SD	Kurtosis	Skewness	Entropy	P10	P25	P75	P90
Nuclei Area	Total	0/1[G]	0/1[G]	**1/1[G]**	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	**1/1[G]**	0/1[G]	0/1[G]	0/1[G]	0/1[G]
	Average	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]	0/1[G]
CAIX		0/1[H]	-	-	-	-	-	-	-	-	-	-	-	-
EBV		**1/1[I]**	-	-	-	-	-	-	-	-	-	-	-	-
Tumor stroma ratio		0/1[P]	0/1[P]	0/1[P]	0/1[P]	0/1[P]	-	0/1[P]	**1/1[P]**	0/1[P]	0/1[P]	0/1[P]	**1/1[P]**	**1/1[P]**

	Fractional plasma volume (V_p)												
	Mean	Min	Max	Median	Mode	SD	Kurtosis	Skewness	Entropy	P10	P25	P75	P90
EBV	0/1[I]	-	-	-	-	-	-	-	-	-	-	-	-
	Contrast Index (CI)												
	CI max		CI gain max		CI-peak		T-max		CI-gain/CI-max ratio				
PD-L1	**1/1**[J]		**1/1**[J]		**1/1**[J]		0/1[J]		-				
PCNA	1[L]/2[K]		**2/2**[K,L]		-		-		**1/1**[K]				

Abbreviations = Min: minimum; max: maximum; SD: Standard deviation; P10,P25,P75,P90: percentile 10, 25, 75, 90.

Notes: †significant in P16 negative subgroup analyses. Abbreviations = SD: standard deviation; P10/25/75/90: percentile

a. Surov, 2016 (article reference: [61])
b. Surov, 2018 (article reference: [63])
c. Meyer, 2018 (article reference: [47])
d. Tse, 2010 (article reference: [67])
e. Swartz, 2018 (article reference: [65])
f. Rasmussen, 2020 (article reference: [60])
g. Surov, 2018 (article reference: [64])
h. Newbold, 2009 (article reference: [80])
i. Sriyook, 2021 (article reference: [78])
j. Tekiki, 2021 (article reference: [66])
k. Unetsubo, 2009 (article reference: [68])
l. Konouchi, 2003 (article reference: [79])
m. Chen T., 2015 (article reference: [31])
n. Samolyk-Kogaczewska, 2020 (article reference: [56])
o. Choi, 2017 (article reference: [81])
p. Meyer, 2021 (article reference: [82])]