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PET-CT as predictor: influencing your strategy

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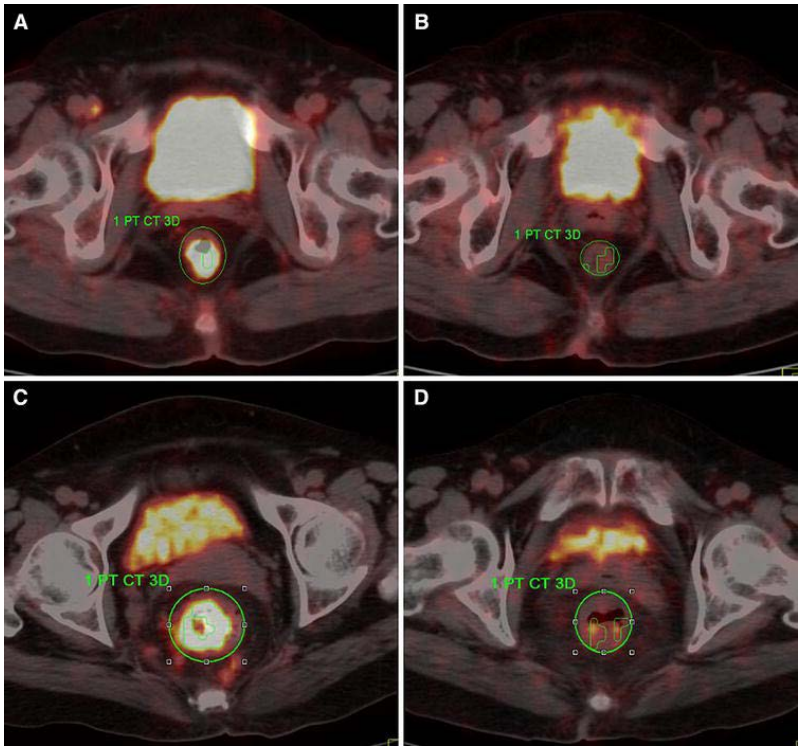
Afdeling Radiologie

LUMC



Background

- After neoadjuvant CRT 15–27% of the patients experience a pCR
- Could invasive surgery be avoided in this selected cohort of patients?
- Patients who achieve a pCR have a favourable long-term outcome with excellent local control and disease-free survival regardless of their initial T- and N-stages
- Does this support the feasibility of the ‘wait-and-see’ policy?
- Advantages for these patients: avoid the risks of surgical mortality and morbidity, and will spare them the need for a stoma
- What is needed: a precise selection of the eligible patients is mandatory

How to predict a pCR?

Gold standard:

histopathological analysis, only applicable in the postoperative setting → cannot be used for the “watch and wait” strategy

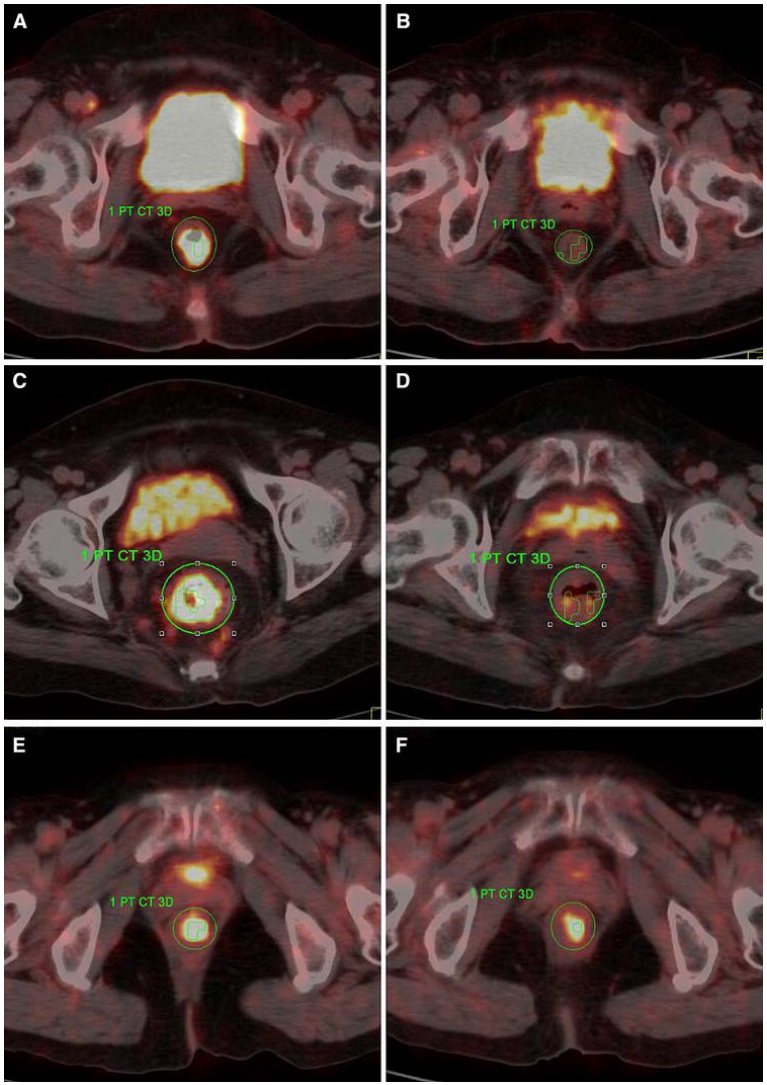
Lack of accuracy for restaging after CRT:

- Computed tomography (CT)
- Endorectal ultrasound (EUS)
- Conventional magnetic resonance imaging (MRI)

Growing interest in functional imaging techniques:

- Diffusion-weighted imaging (DWI-MRI)
- ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET/CT)

^{18}F-FDG-PET/CT



Complete pathologic response

Partial response

Non-response

QW Li et al. Abdom Radiol. 2016 41:14448-1455

18F-FDG PET for Predicting Response to Neoadjuvant Therapy in Rectal Cancer

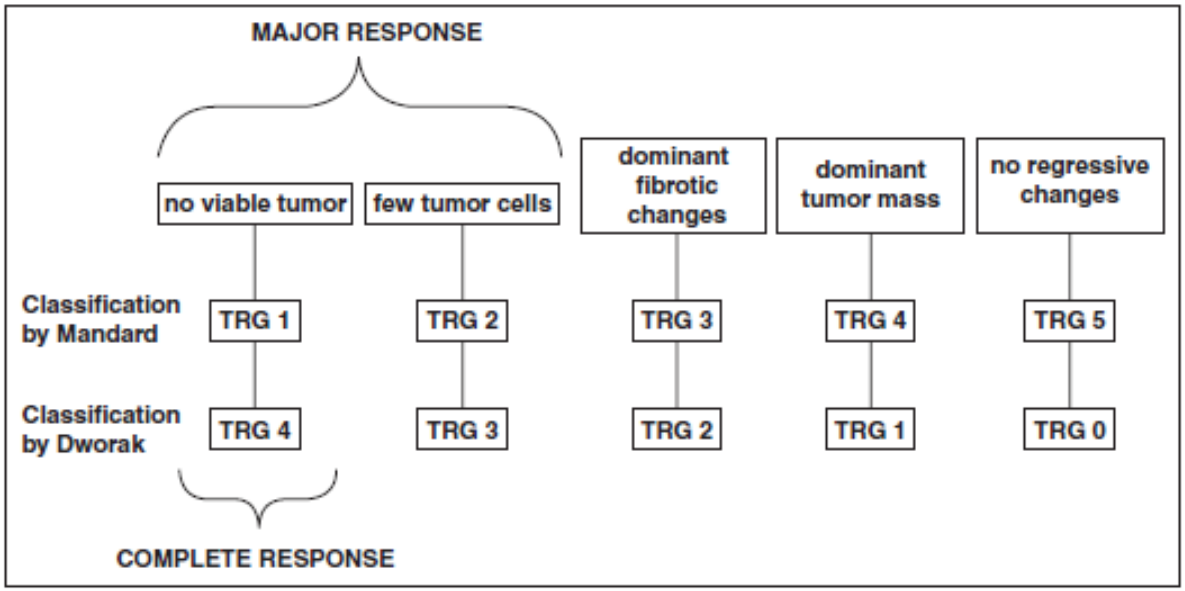
TABLE 3: Pooled Results for Entire Cohort of Studies and for Different Subdivisions

Category	Pooled Sensitivity (%)	Pooled Specificity (%)	Pooled Positive LR	Pooled Negative LR	Q*	AUC
Global cohort	73	77	3.09	0.37	0.76	0.83
Major	74	78	3.18	0.36	0.76	0.83
Complete	71	76	2.67	0.42	0.74	0.80
Major and postchemoradiotherapy	73	77	3.16	0.36	0.76	0.82
Complete and postchemoradiotherapy	70	74	2.37	0.45	0.73	0.79
Ad interim	84	81	3.79	0.28	0.82	0.89
Postchemoradiotherapy	72	77	3.01	0.38	0.75	0.82
Response index	74	72	2.6	0.38	0.75	0.81
SUV_{max} post	72	76	2.82	0.41	0.74	0.8
Visual response score	55	80	2.41	0.6	0.7	0.76
ΔTLG	72	86	4.41	0.37	NA	NA
ΔMTV	73	82	3.89	0.33	NA	NA

Note—Complete indicates pathologic absence of cancer cells, and major indicates pathologic absence of tumor cells or presence of rare residual cancer cells. Q* indicates point where sensitivity and specificity are equal. LR = log ratio, ΔTLG = percentage of total lesion glycolysis decrease, ΔMTV = percentage of metabolic tumor volume decrease. NA = not applicable.

AM Maffione et al. AJR AM Roentgenol. 2015 Jun;204(6):1261-8

Major response vs Complete response



AM Maffione et al. AJR AM Roentgenol. 2015 Jun;204(6):1261-8

Author	Grade	Comment
Dworak *et al.* [24]	0	No regression
	1	Dominant tumour mass with obvious fibrous and/or vasculopathy
	2	Dominantly fibrous changes with few tumour cells or groups
	3	Very few tumour cells in fibrotic tissue with or without mucous substance
	4	No tumour cells, only fibrotic mass. Total regression
Mandard *et al.* [29]	1	Complete regression, absence of residual cancer
	2	Presence of rare residual cancer cells scattered through fibrosis
	3	Increased number of cancer cells but fibrosis still predominates
	4	Residual cancer outgrowing fibrosis
	5	Absence of regressive change

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Koo et al. Clin Colorectal Cancer 2016 Dec;15(4):e213-e219.
ΔSUVmax significant predictor of pCR: sensitivity of 90.9% and specificity of 80.3%

18F-FDG PET for Predicting Response to Neoadjuvant Therapy in Rectal Cancer

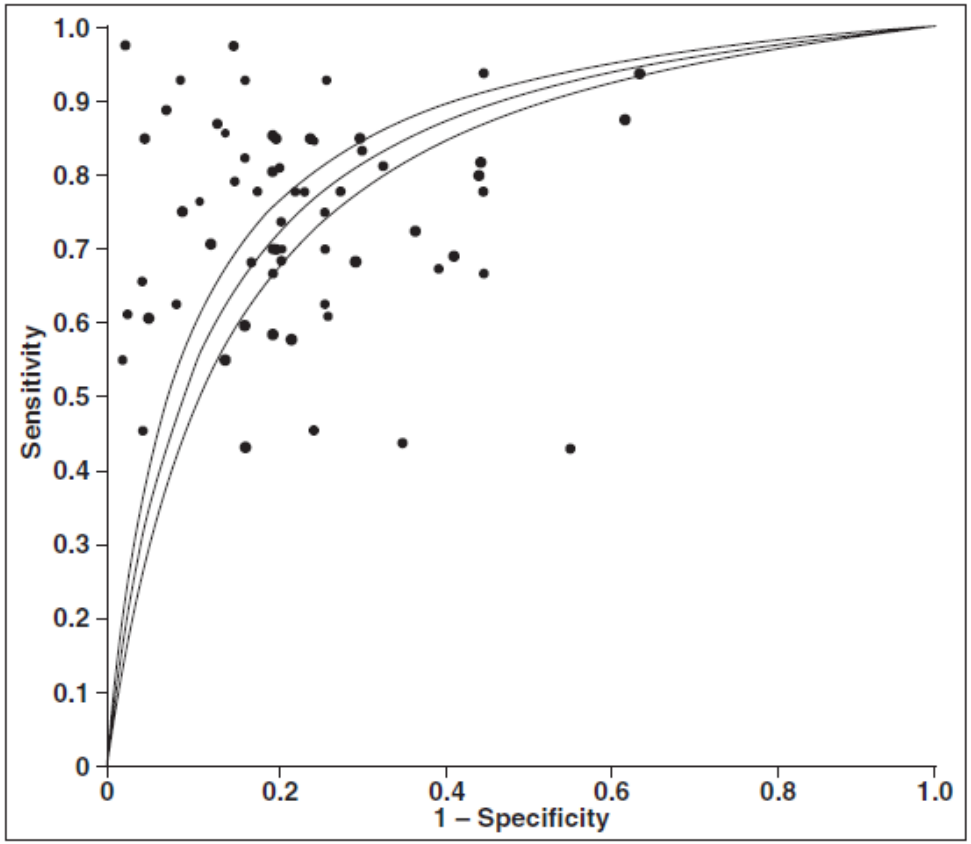


Fig. 4—Graph shows summary ROC values for global cohort. AUC = 0.8263, standard error of AUC = 0.0112, Q statistic = 0.7592, standard error of Q statistic = 0.0102.

Pooled Response Index (RI): 63%

Pooled SUVmax postcutoff: 4.4

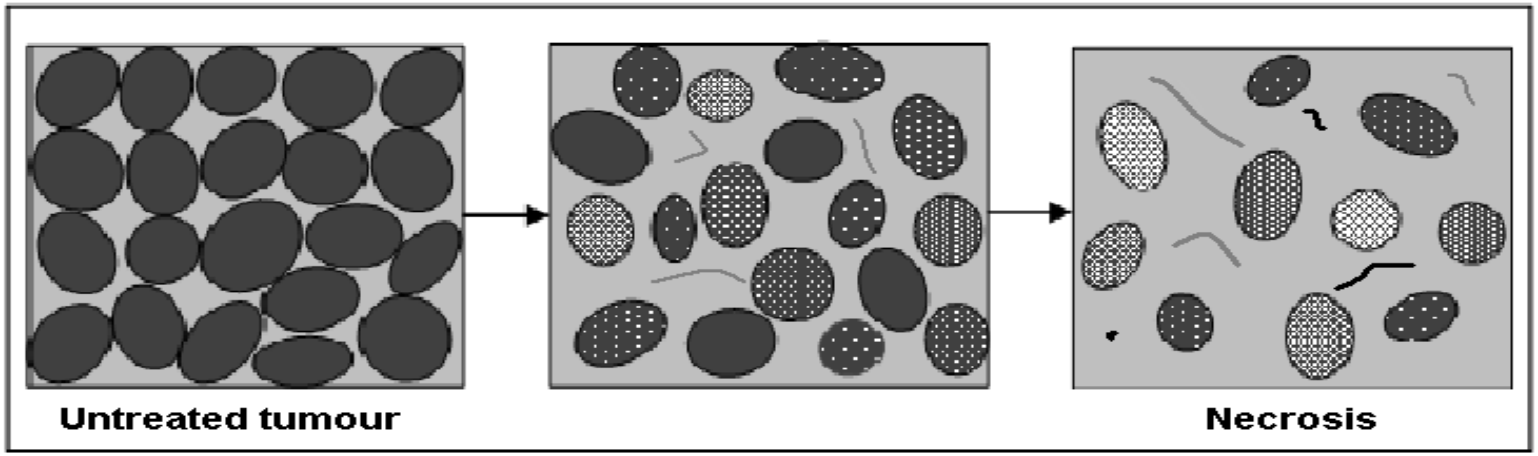
Pooled time to PET during CRT: 1.5 wks

Pooled time to PET after CRT: 6.5 wks

AM Maffione et al. AJR AM Roentgenol. 2015 Jun;204(6):1261-8

Diffusion-weighted MRI

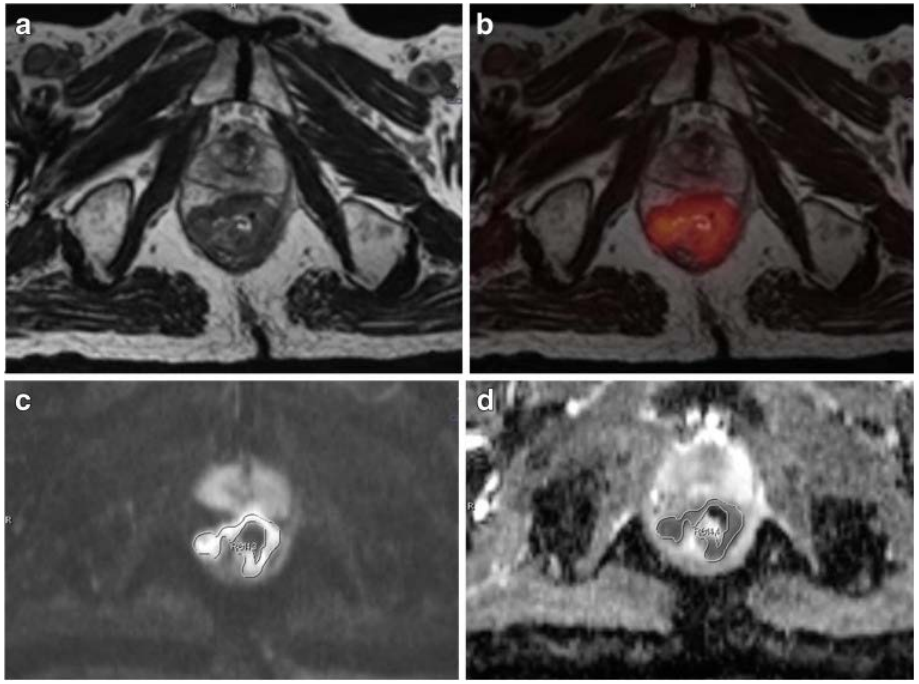
Low ⟶ Water proton mobility ⟶ High

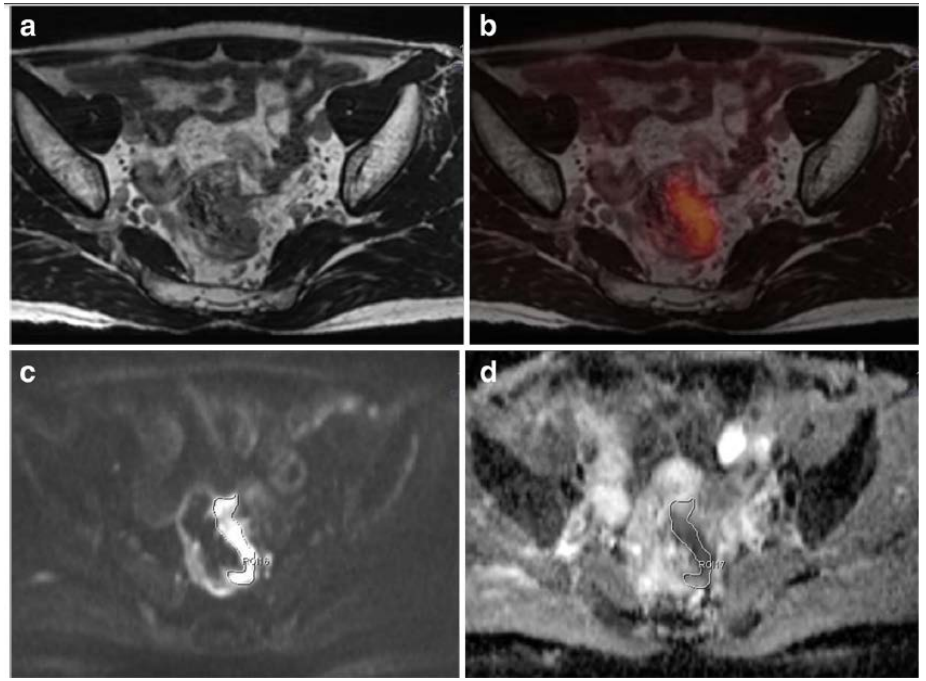


Low ⟶ apparent diffusion coefficient ⟶ High

ADC

^{18}F-FDG PET-DWI acquired on a hybrid PET-MRI

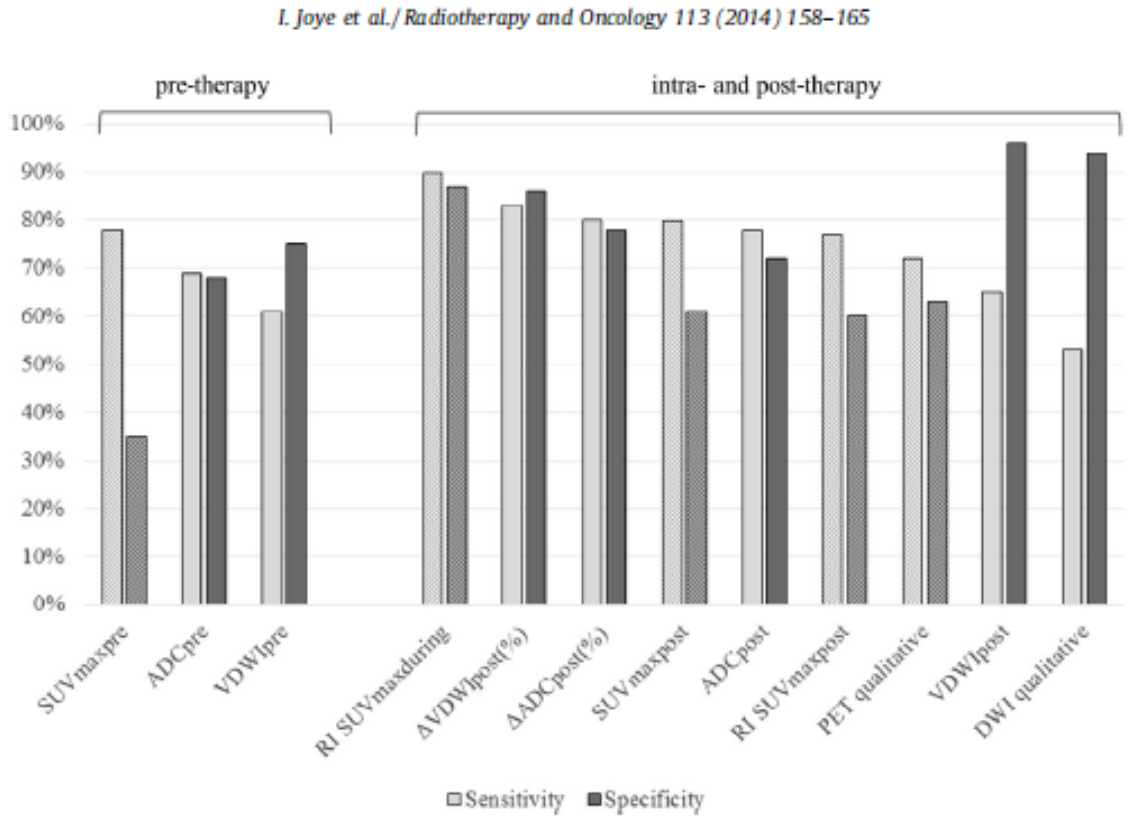




(A) Axial T2-weighted SPACE image
(B) Fused ^{18} F-FDG PET and axial T2-weighted SPACE images
(C) b1000 diffusion image
(D) ADC map

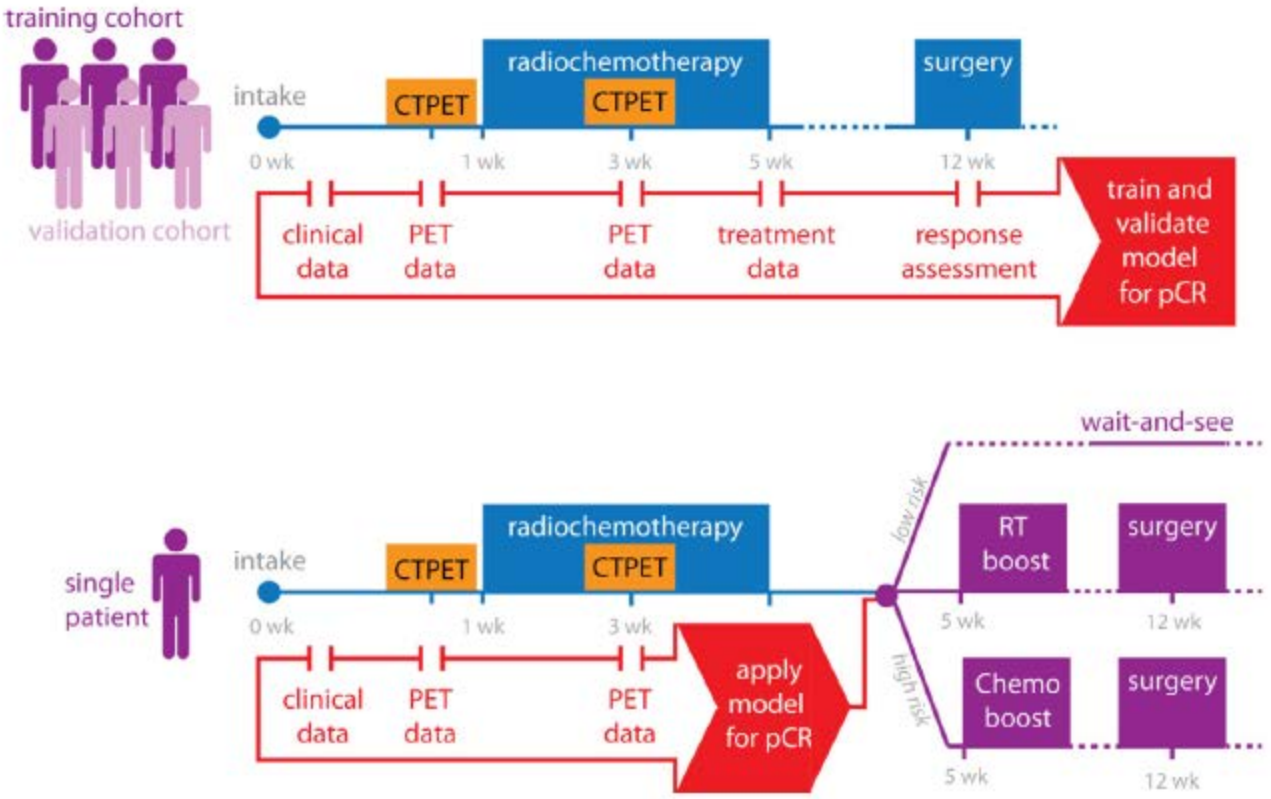
JH Jeong et al. Nucl Med Mol Imaging. 2016 Jun;50(2):150-6

Diffusion-weighted MRI and ^{18}F-FDG PET/CT in the prediction of pCR after RCT



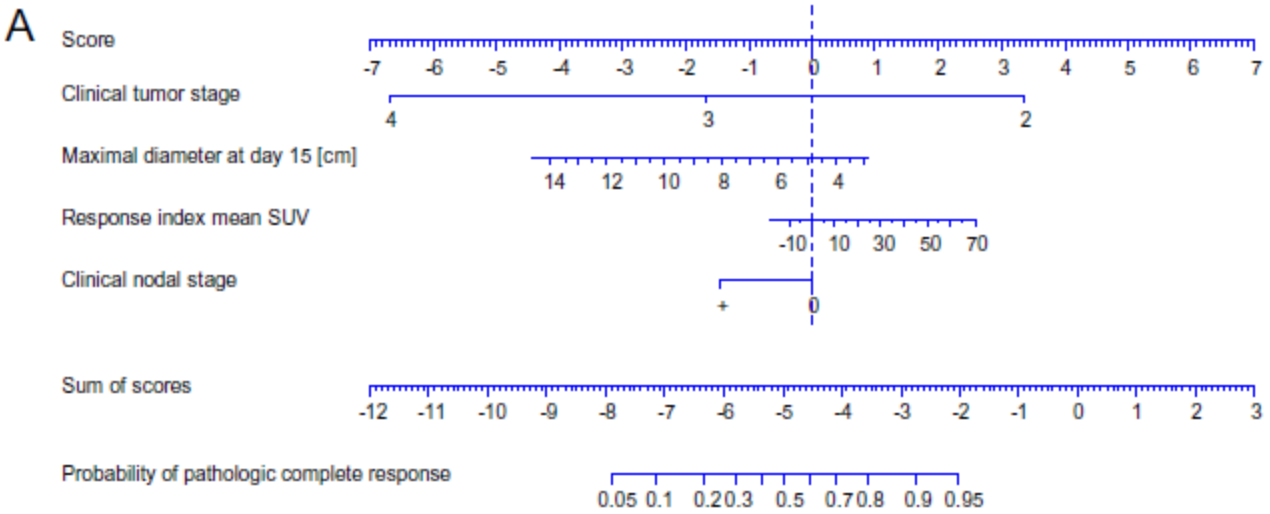
Joye I et al. Radiother Oncol. 2014 Nov;113(2):158-65

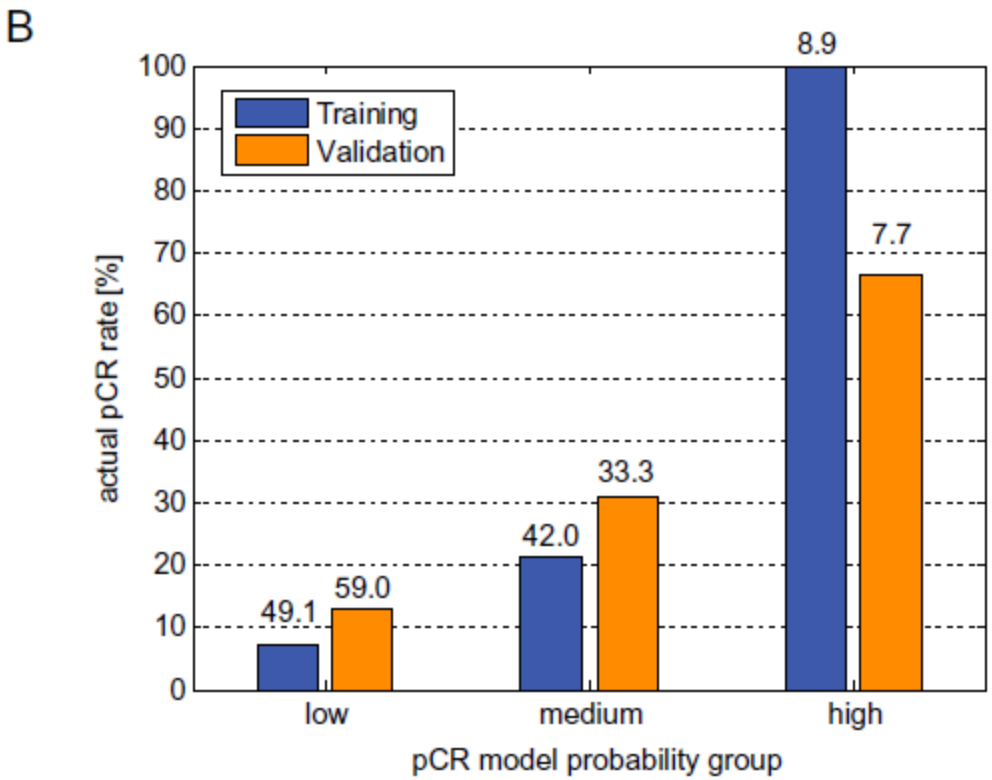
Nomogram predicting response after RCT using PET-CT: A multicentric study with external validation



RG van Stiphout et al. Radiother Oncol. 2014 Nov;113(2):215-22

Nomogram for response using PET during treatment in rectal cancer





RG van Stiphout et al. Radiother Oncol. 2014 Nov;113(2):215-22

Take home messages

FDG-PET/CT:

- pooled sensitivity: 73%
- pooled specificity: 77%
- pooled AUC: 0.83
- best predictor: interim PET (during CRT) – sens 84%, spec 81%
- RI, SUVmax, and VRA most frequent parameters used
- pooled RI and SUVmax postcutoff values were 63% and 4.4
- pooled time to PET during and after CRT was 1.5 and 6.5 weeks

DWI-MRI:

- best response: low pretreatment ADC + increase in ADC + decrease in SUV
- pooled analysis: qualitative DWI 5–10 wks after CRT >> ADC-parameters

Future research must focus on FDG-PET-DW-MRI + clinical data + molecular biomarkers → costs has to be compared to cost reductions due to better outcomes and fewer complications