Avbildning av onkologisk behandlingseffekt - Immunterapier

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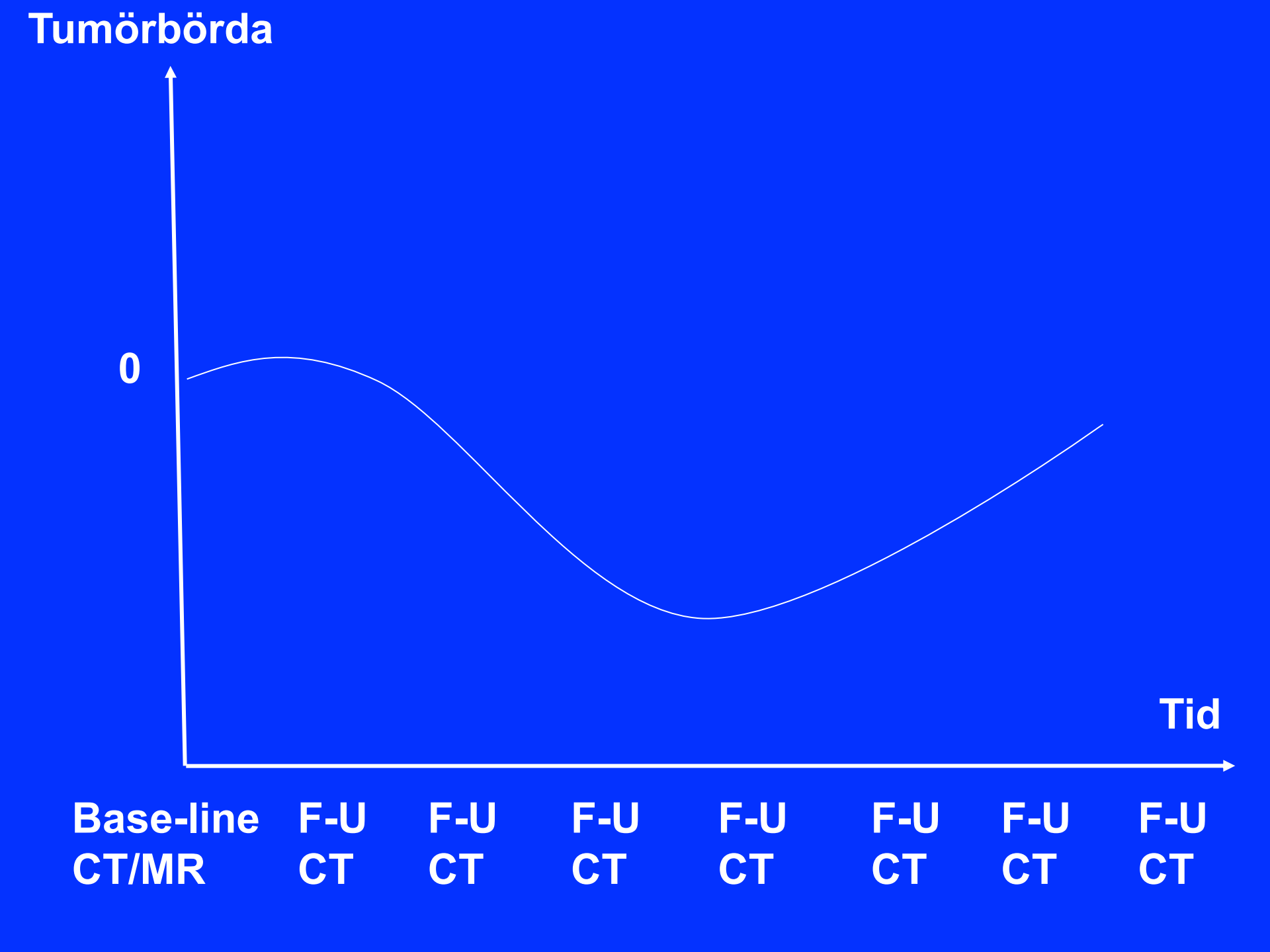
RECIST kriterierna

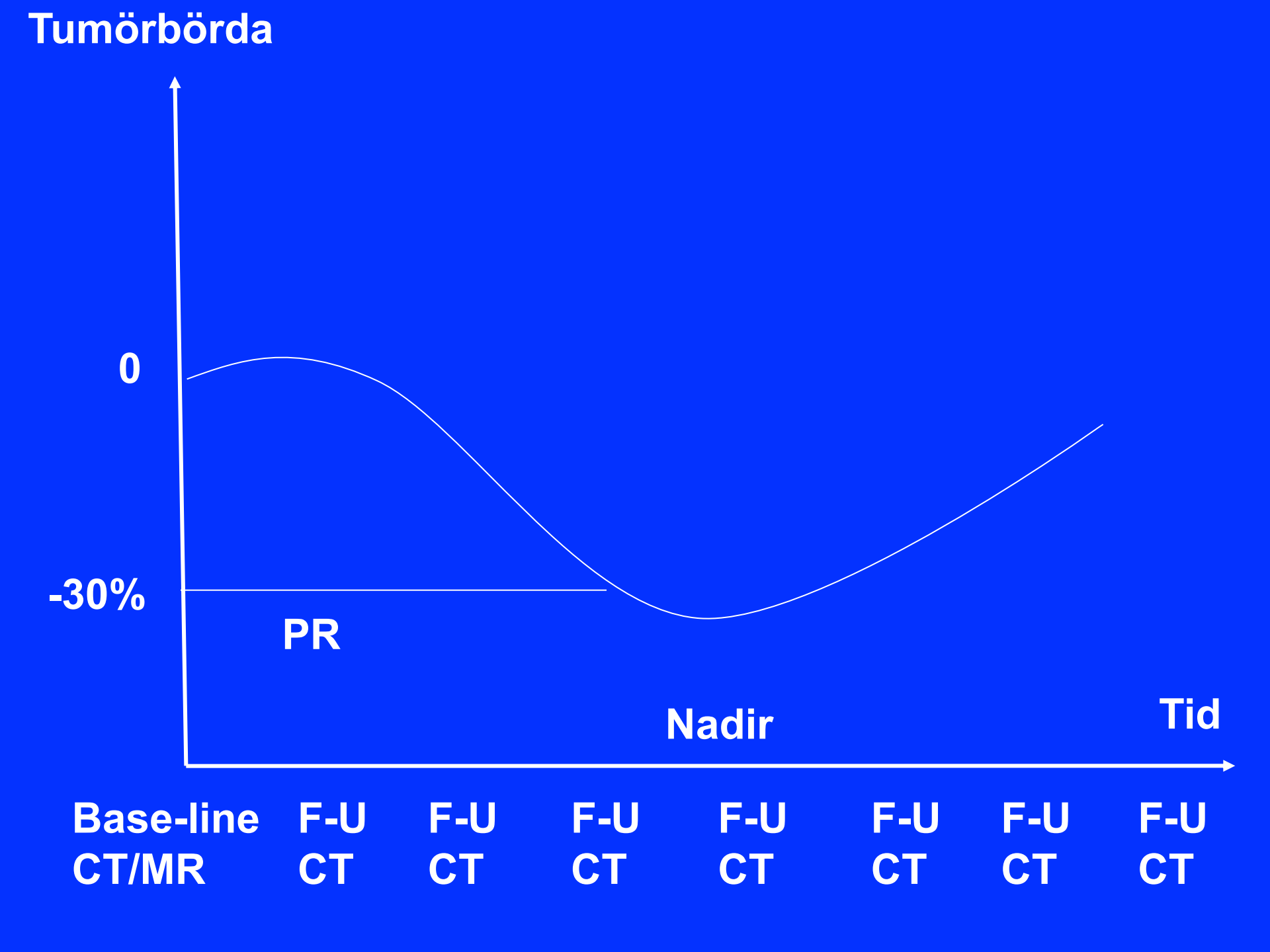
Response Evaluation Criteria In Solid Tumors

CT och MRT

Therasse P et al. J National Cancer Institute 2000 – **RECIST 1.0**

Eisenhauer E A et al. Eur J Cancer 2009 – **RECIST 1.1**


Tumörbörda
0
Tid
Base-line CT/MR
F-U CT
F-U CT
F-U CT
F-U CT
F-U CT
F-U CT
F-U CT


Tumörbörda
0
-30%
PR
Nadir
Tid
Base-line CT/MR
F-U CT
F-U CT
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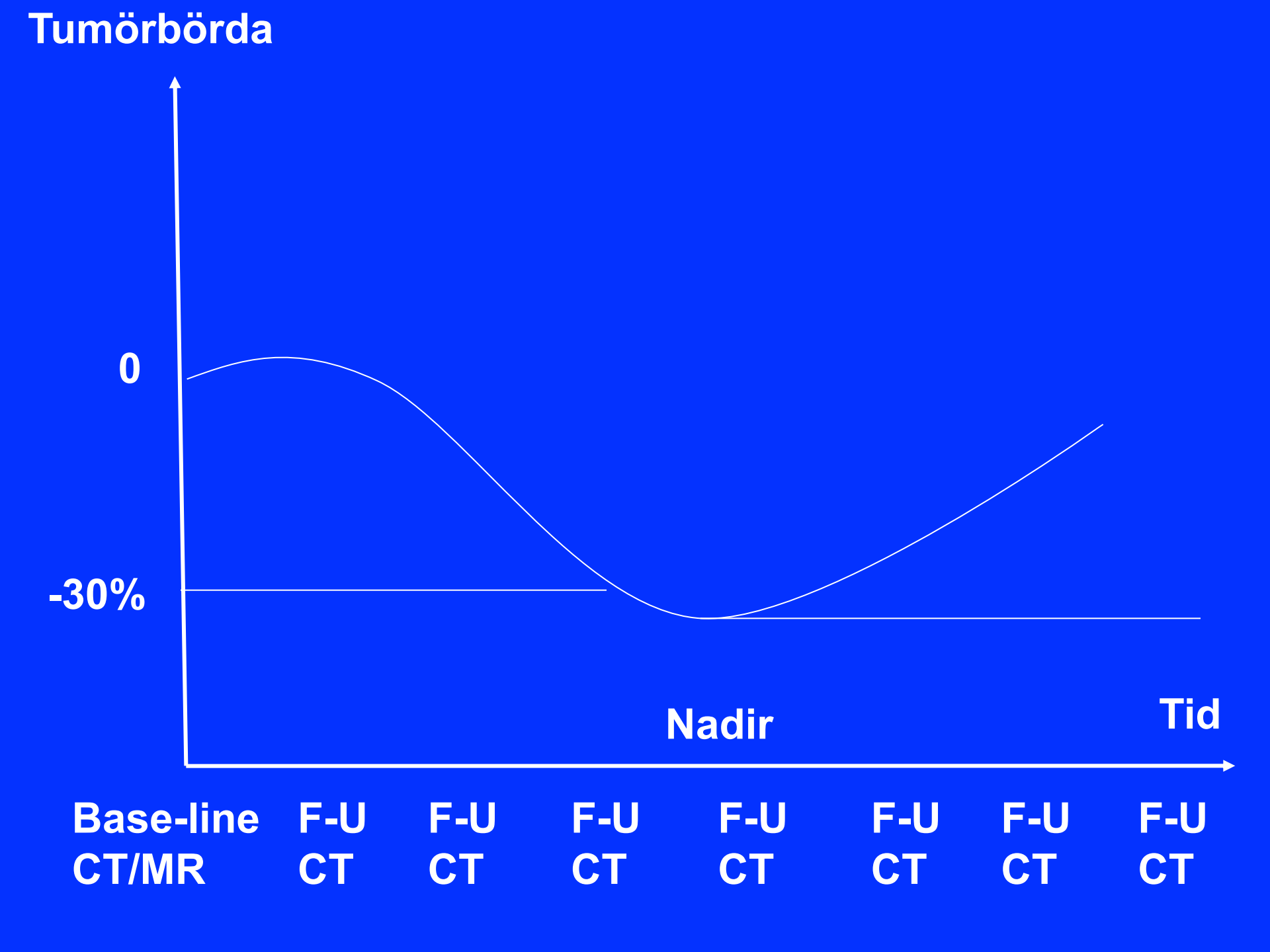
F-U CT


Tumörbörda
0
-30%
Nadir
Tid
Base-line CT/MR
F-U CT
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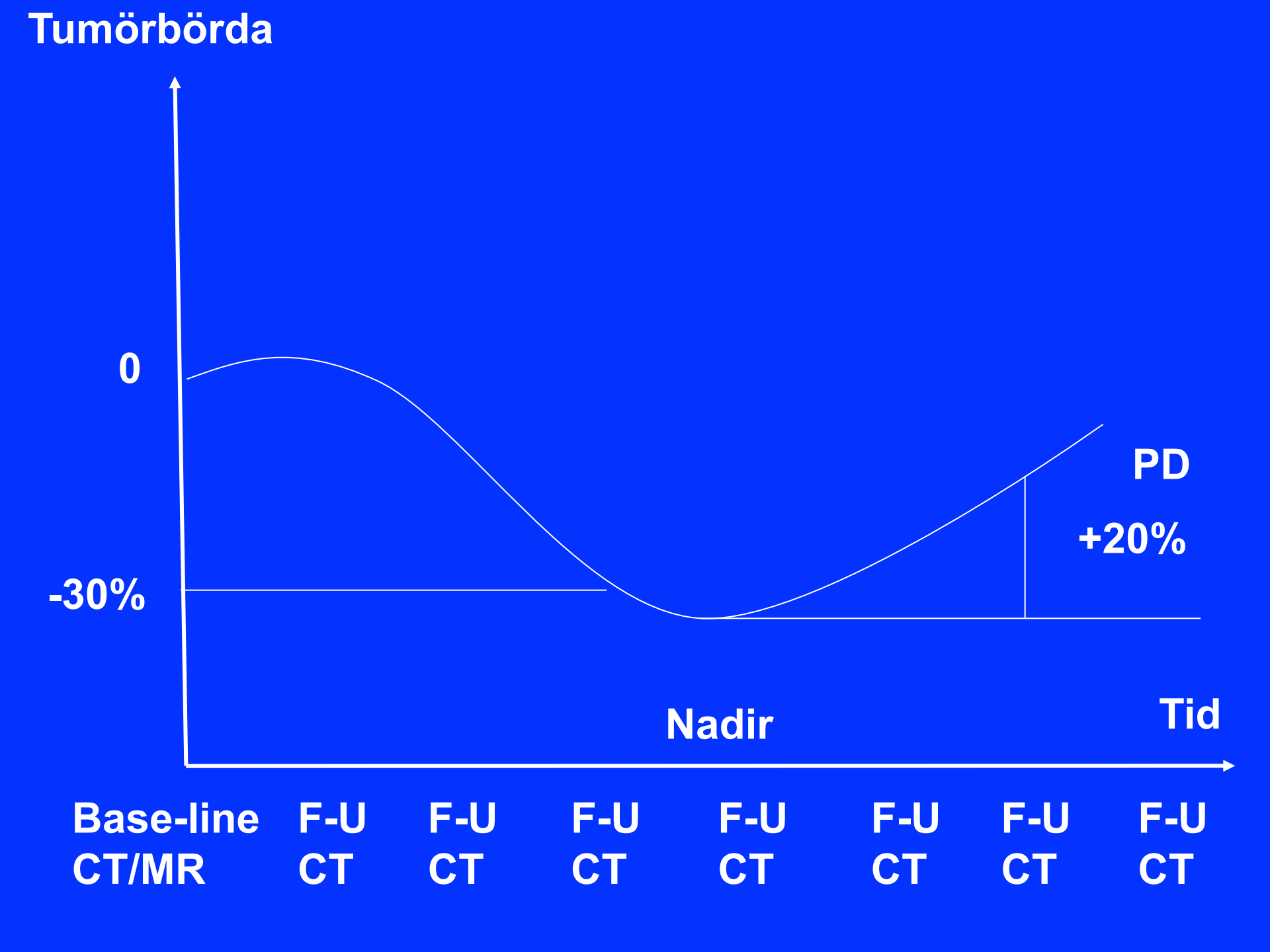
Tumörbörda
0
-30%
PD
+20%
Nadir
Tid
Base-line CT/MR
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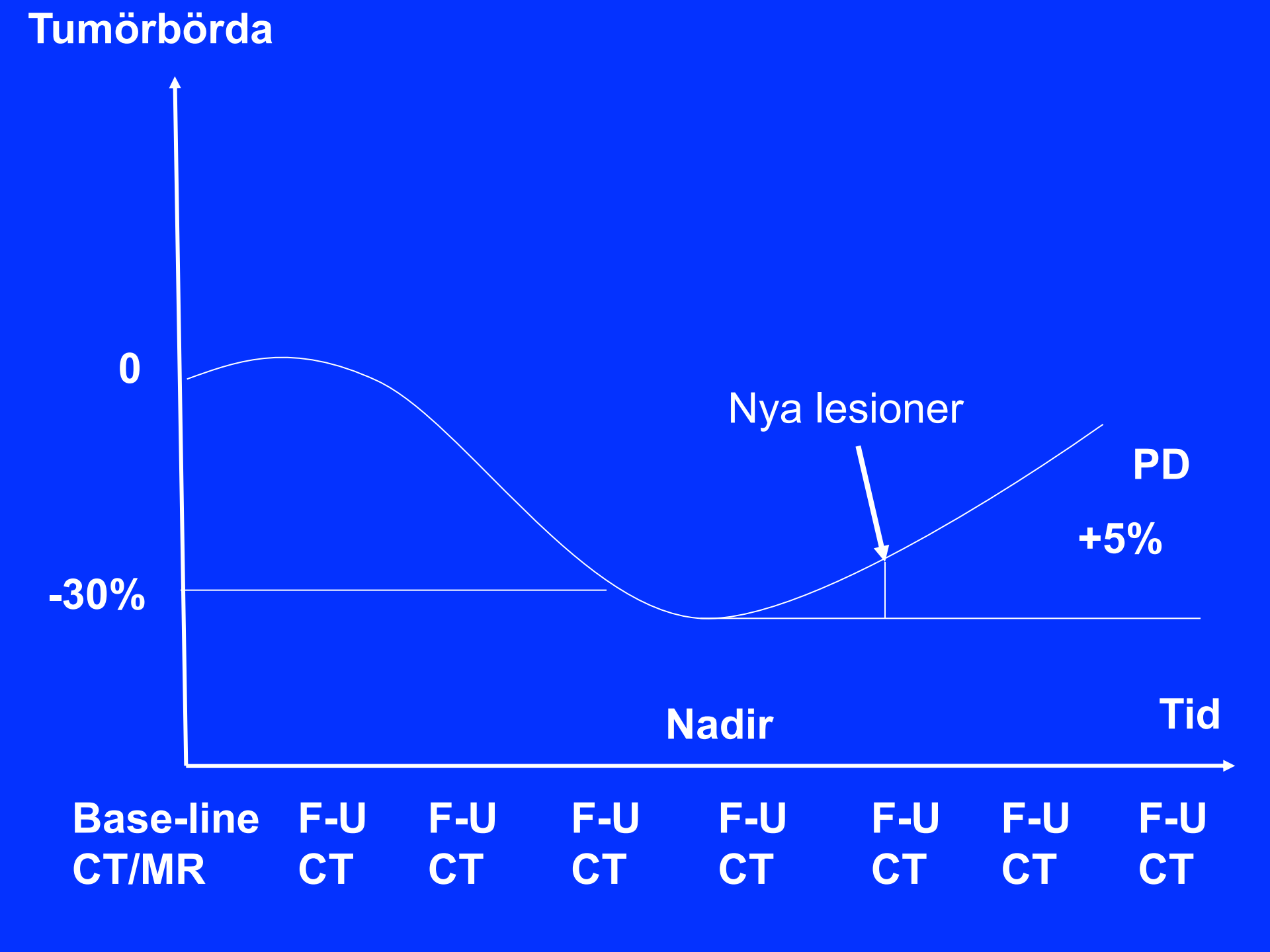
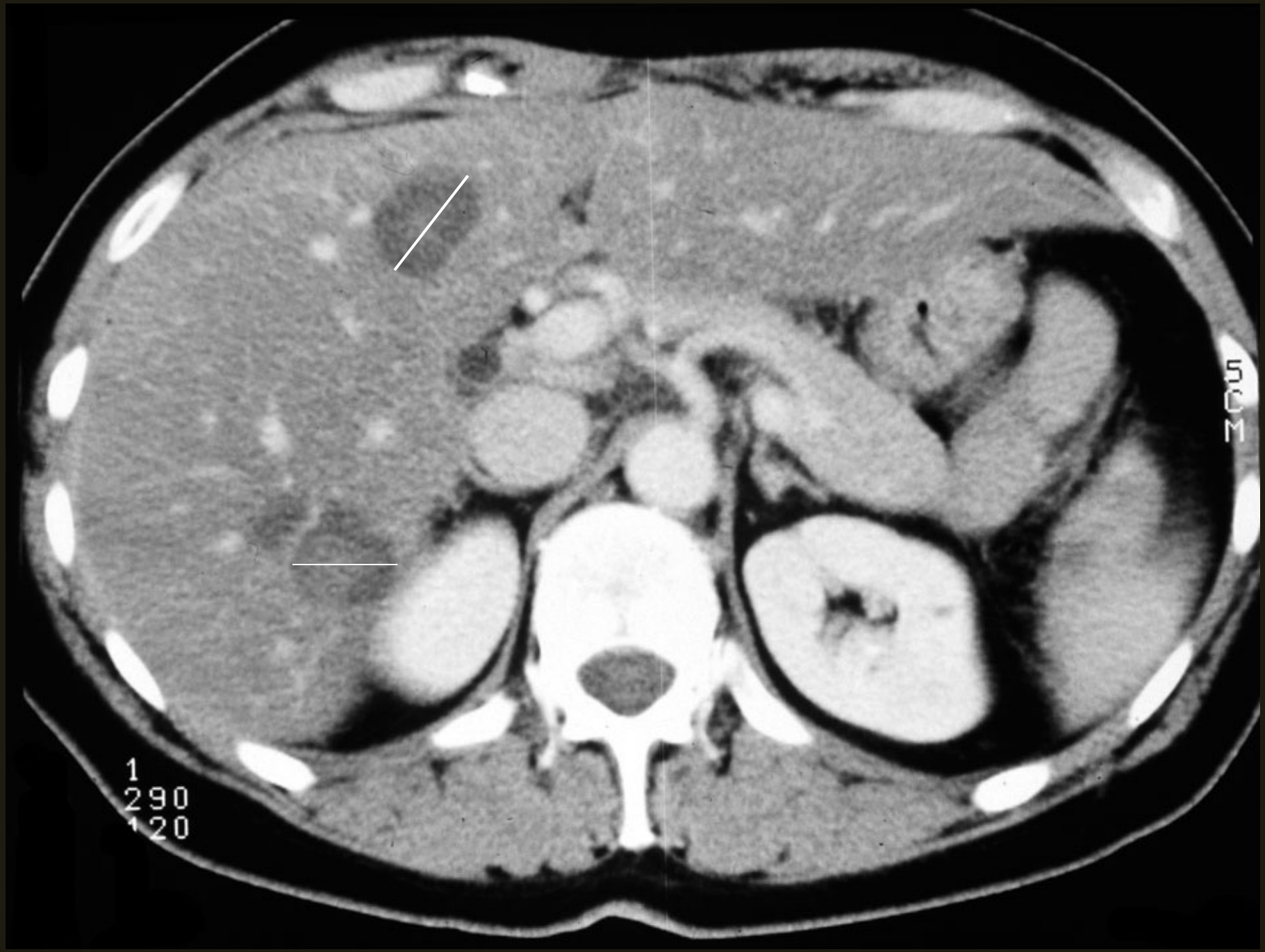
F-U CT
F-U CT

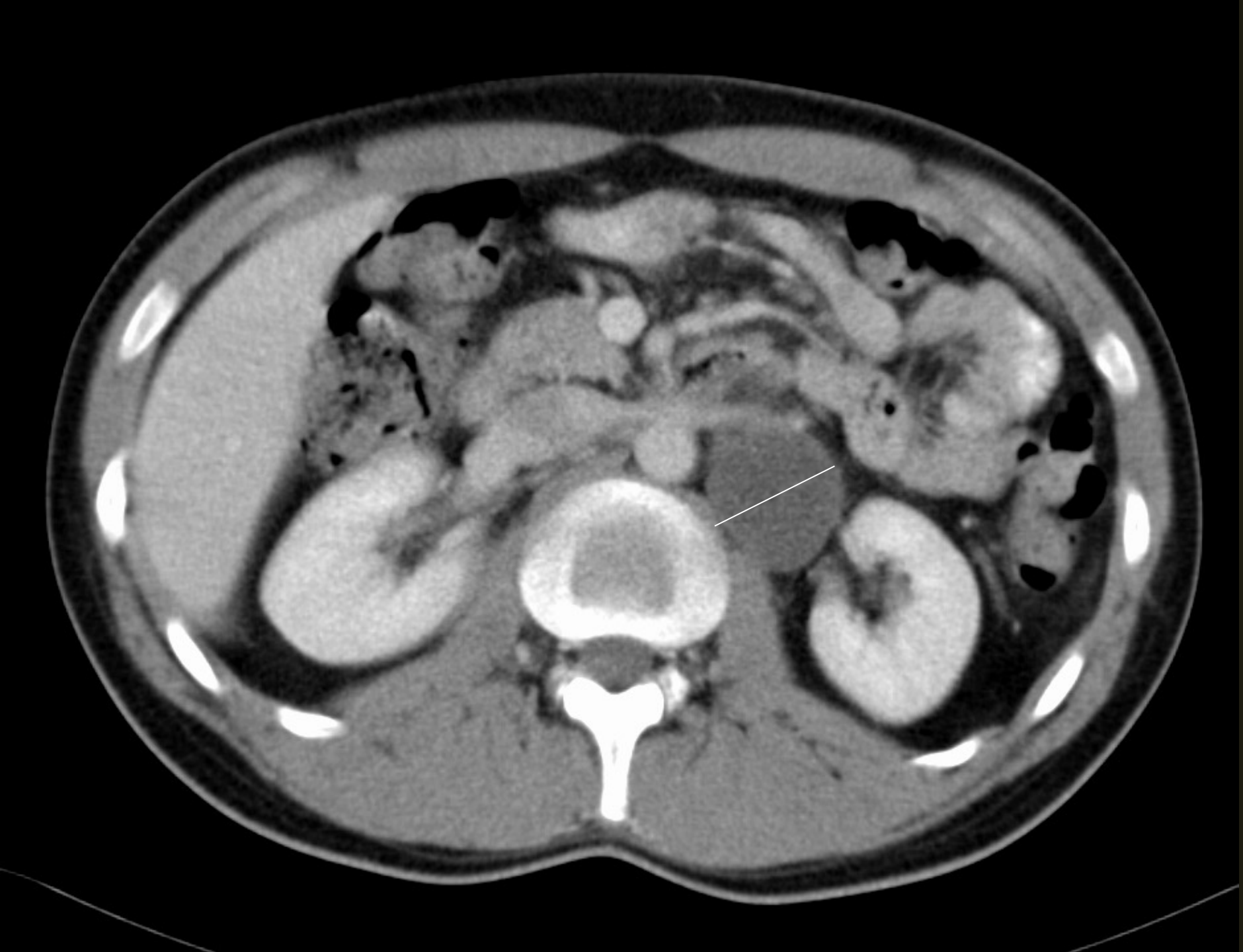

Tumörbörda
0
-30%
Nya lesioner
PD
+5%
Nadir
Tid
Base-line CT/MR
F-U CT
F-U CT
F-U CT
F-U CT
F-U CT
F-U CT
F-U CT

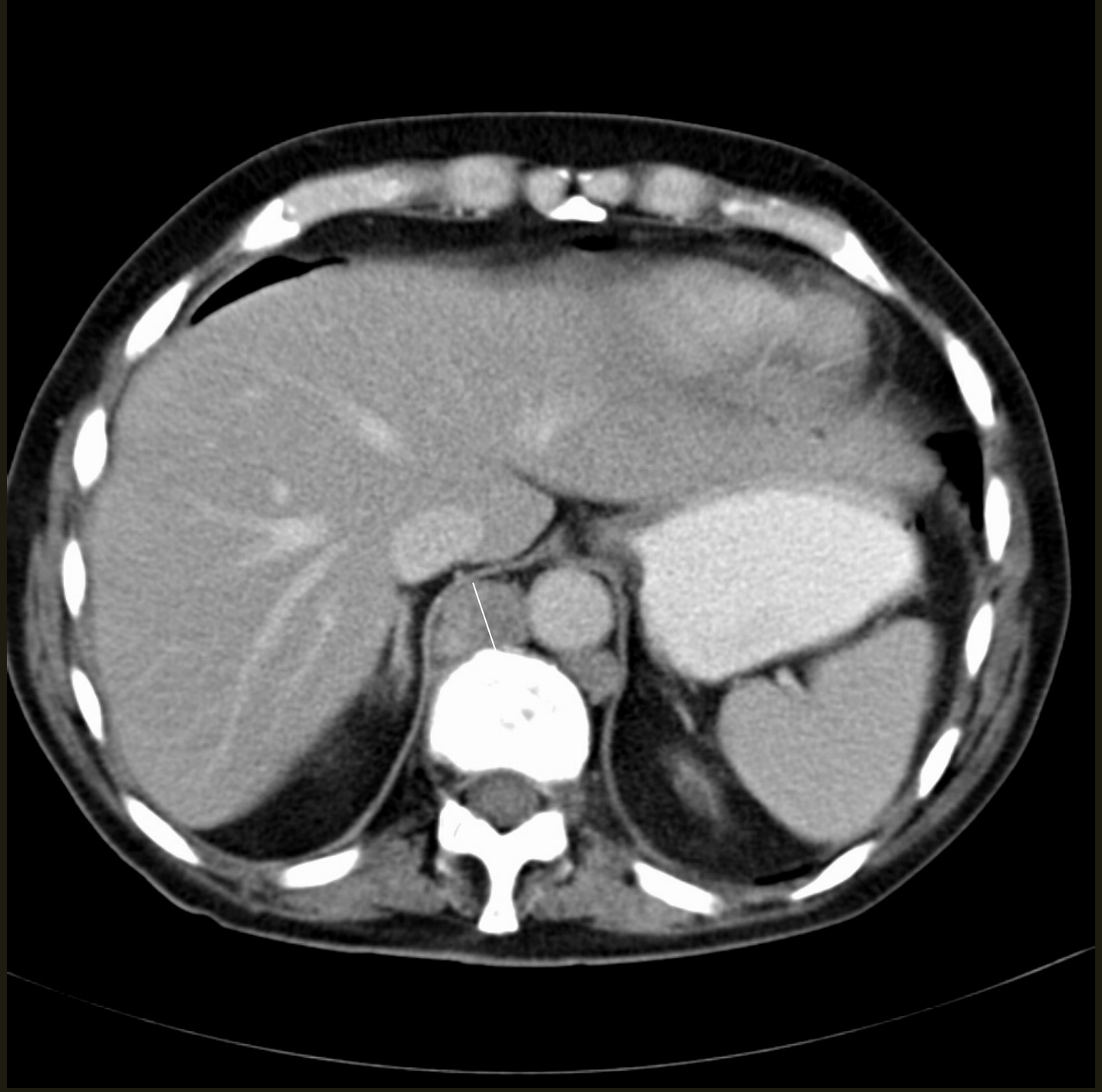
RECIST 1.1

- Max 5 lesioner
- Max 2 per organ

- Mäter lesionernas längsta diameter
- Lymfkörtlar kortaste diameter >15mm
- Summan av de längsta diametrarna


1
290
120
5CM





RECIST 1.1

CT Baseline		**CT follow-up**
Levermetastaser		
52 mm		41 mm
48 mm		38 mm
Lgll. metastaser		
31 mm		23 mm
27 mm		19 mm
Lung-T		
57 mm		41 mm
Summa: 215 mm	**0,75**	Summa: 162 mm

RECIST 1.1

Complete Response (CR) = 0

Partial Response (PR) ≤ 30%, Inga nya T

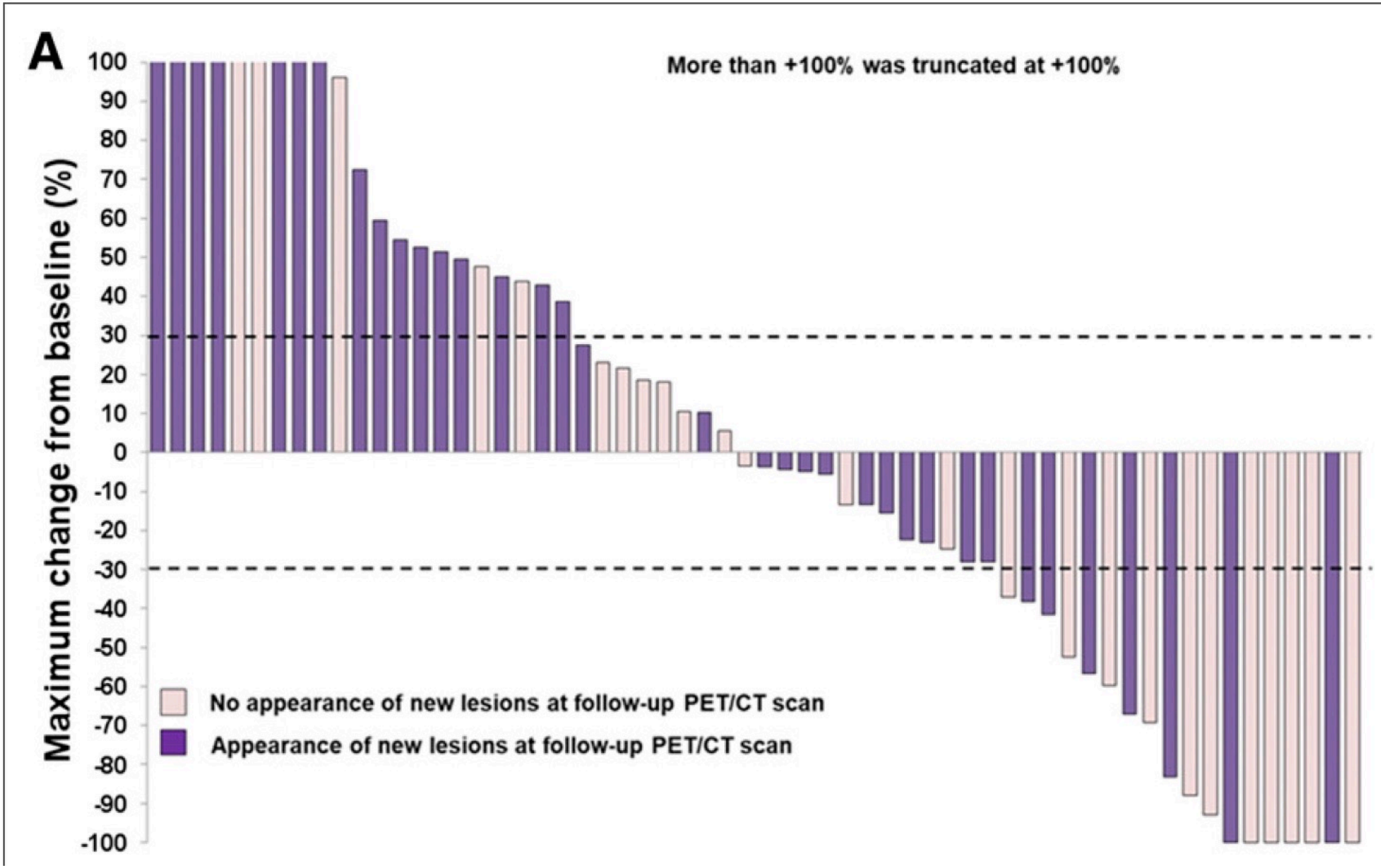
Progressive Disease (PD) ≥ 20% och/eller nya T

Stable Disease (SD) Not PR, Not PD

Varför behöver vi andra kriterier än RECIST för att mäta terapirespons?

- Det finns situationer som inte RECIST kan hantera

- Vid s.k. molekylära ”targeted therapies” krymper inte alltid tumörerna vid terapisvar t.ex. tyrosinkinas-hämmare vid GIST och NETs
- ”Pseudoprogress” vid ^{177}Lu-terapi (PRRT) av NETs
- ”Pseudoprogress” vid immunterapier
- Nya lesioner är alltid progress vid immunterapier



Kimiteru I et al. J Nucl Med 2019; 60:335–341

irRECIST Modifications and Clarifications

1. 0 Baseline: Measurable Lesion Definitions and Target Lesion Selection

Follow the definitions from RECIST 1.1.

Measurable lesions must be accurately measured in at least one dimension with a minimum size of:

- 10 mm in the longest diameter by CT or MRI scan (or no less than double the slice thickness) for non-nodal lesions and ⩾15 mm in short axis for nodal lesions
- 10 mm caliper measurement by clinical exam
- 20 mm by chest X-ray

1.1. Baseline: Non-measurable Lesion Definitions

Follow the definitions from RECIST 1.1

Non-target lesions will include:

- Measurable lesions not selected as target lesions
- All sites of non-measurable disease, such as neoplastic masses that are too small to measure because their longest uninterrupted diameter is < 10 mm (or < two times the axial slice thickness), ie. the longest per-pendicular diameter is ⩾10 and < 15 mm.
- Other types of lesions that are confidently felt to represent neoplastic tissue, but are difficult to measure in a reproducible manner. These include bone metastases, leptomeningeal metastases, malignant ascites, pleural or pericardial effusions, ascites, inflammatory breast disease, lymphangitis cutis/pulmonis, cystic lesions, ill-defined abdominal masses, skin lesions, etc.

1.8 Baseline: No Disease at Baseline

If a patient has no measurable and no non-measurable disease at baseline the radiologist will assign 'No Disease' (irND) as the overall tumor assessment for any available follow-up timepoints unless new measurable lesions are identified and contribute to the TMTB.

2.0 Follow-up: Recording of Target and New Measureable Lesion Measurements

The longest diameters of non-nodal target and new non-nodal measurable lesions, and short axes of nodal target and new nodal measurable lesions will be recorded. Together they determine the Total Measured Tumor Burden (TMTB) at follow-up.

2.1 Follow-up: Definition of Measurable New Lesions

In order to be selected as new measurable lesions (⩽ 2 lesions per organ, ⩽ 5 lesions total, per timepoint), new lesions must meet criteria as defined for baseline target lesion selection and meet the same minimum size requirements of 10 mm in long diameter and minimum 15 mm in short axis for new measurable lymph nodes. New measurable lesions shall be prioritized according to size, and the largest lesions shall be selected as new measured lesions.

2.4 irRC Overall Tumor Assessments

irCR, complete disappearance of all measurable and non-measurable lesions. Lymph nodes must decrease to < 10 mm in short axis. Confirmation of response is not mandatory.

irPR, decrease of ⩾ 30% in TMTB relative to baseline, non-target lesions are irNN, and no unequivocal progression of new non-measurable lesions.

irSD, failure to meet criteria for irCR or irPR in the absence of irPD.

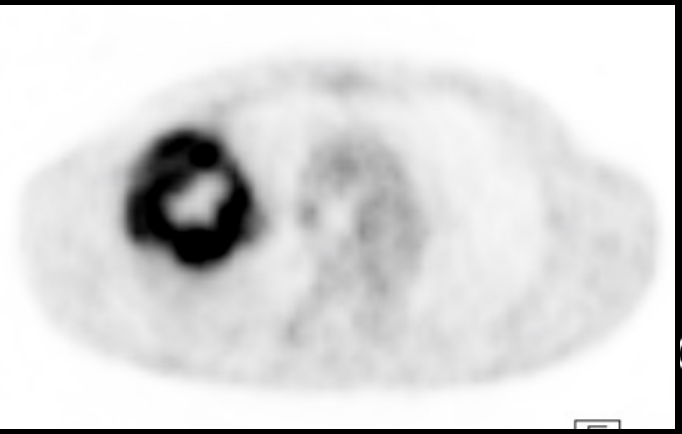
irNN, no target disease was identified at baseline and at follow-up the patient fails to meet criteria for irCR or irPD.

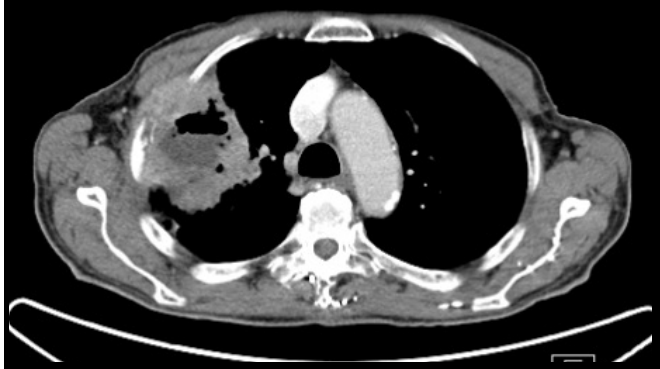
irPD, minimum 20% increase and minimum 5 mm absolute increase in TMTB compared to nadir, or irPD for non-target or new non-measurable lesions. Confirmation of progression is recommended minimum 4 weeks after the first irPD assessment.

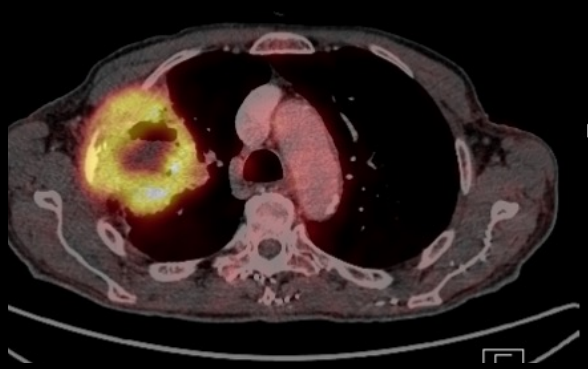
irNE, used in exceptional cases where insufficient data exists.

irND, in adjuvant setting when no disease is detected.

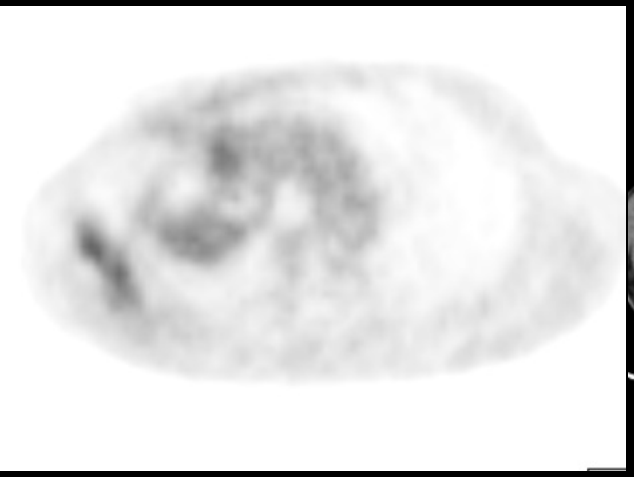
2011-03-29 Adenocarcinoma of the lung

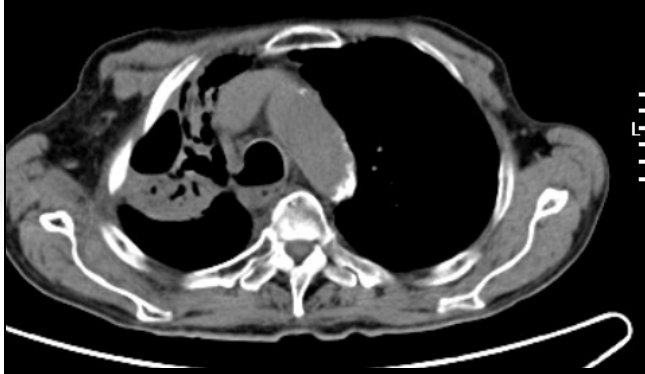


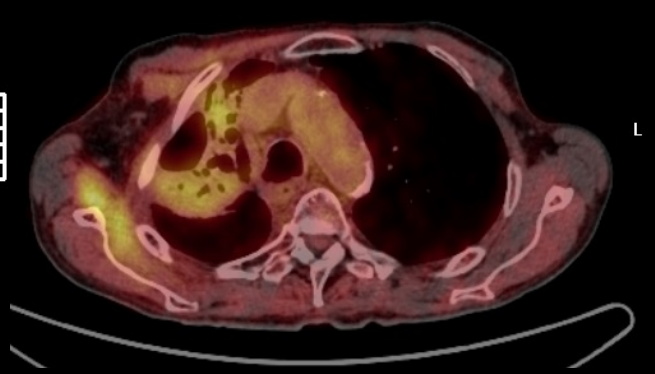




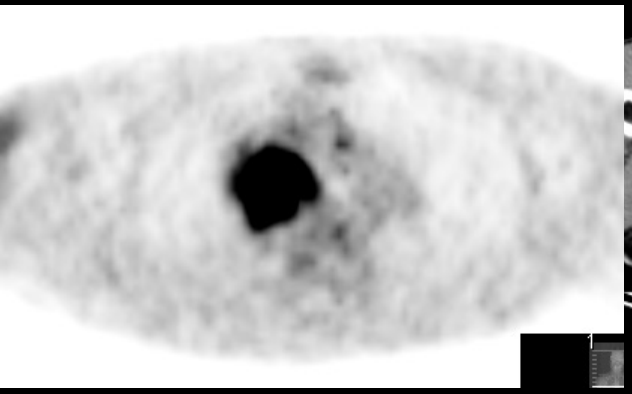
2012-02-10 Following radio-chemotherapy

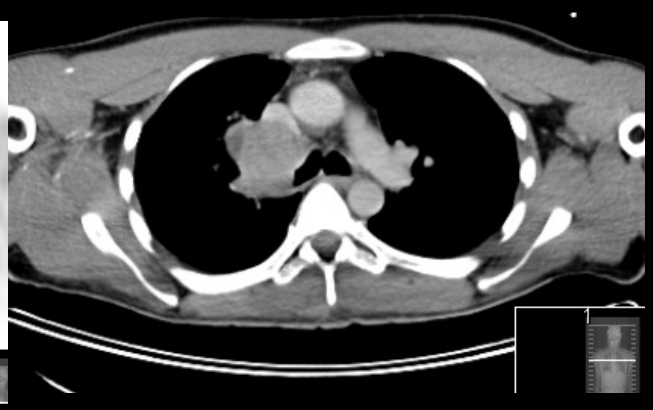


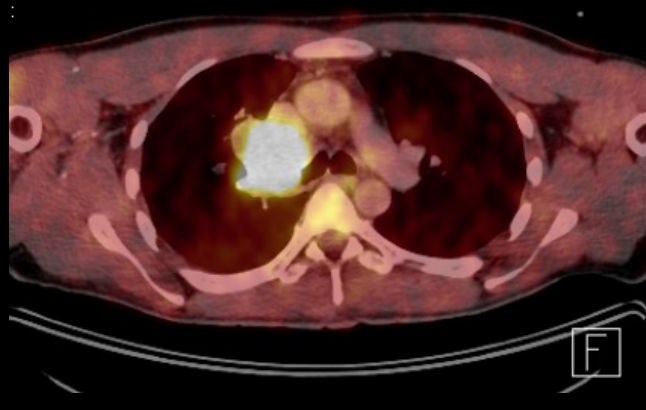




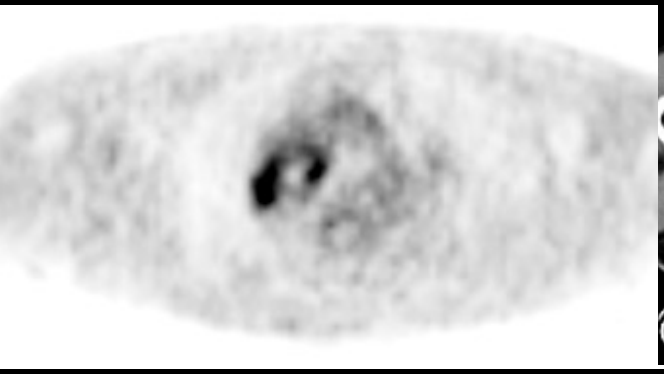
2010-10-07 Metastatic melanoma

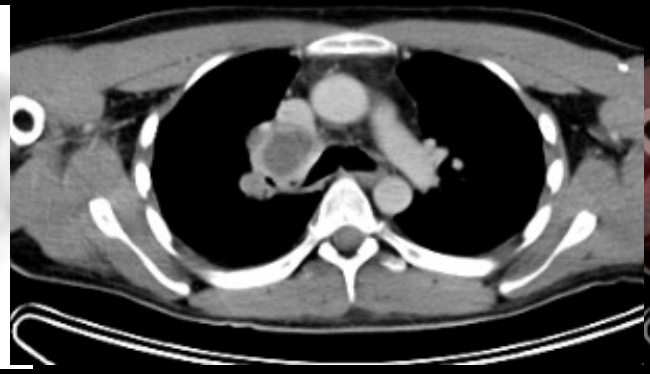


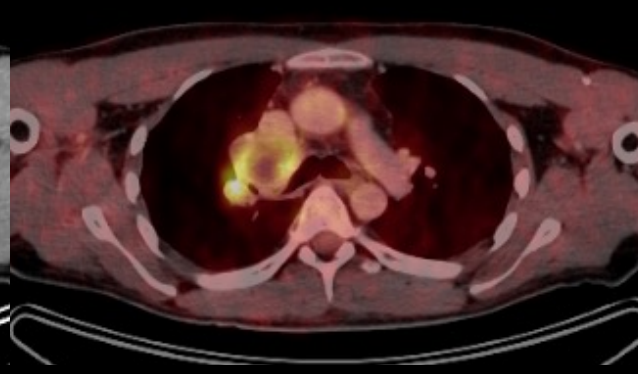




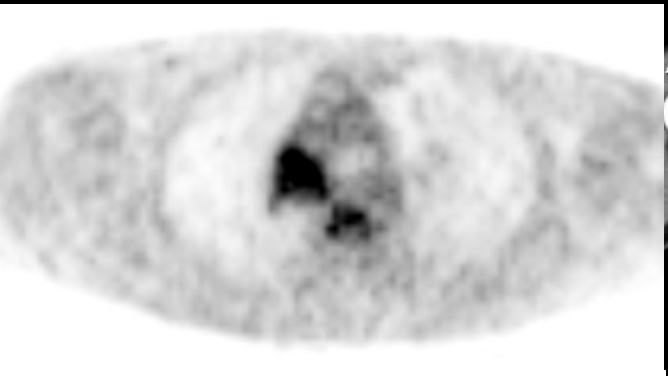
2010-12-21 Following treatment with paclitaxel & carboplatin

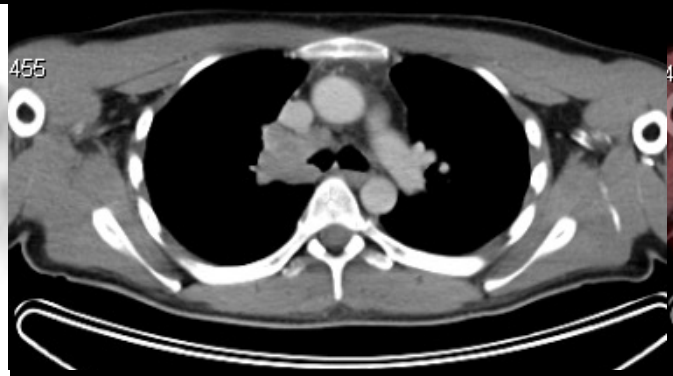


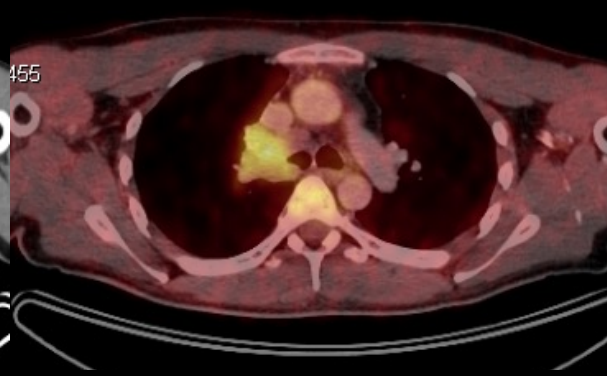




2011-08-19



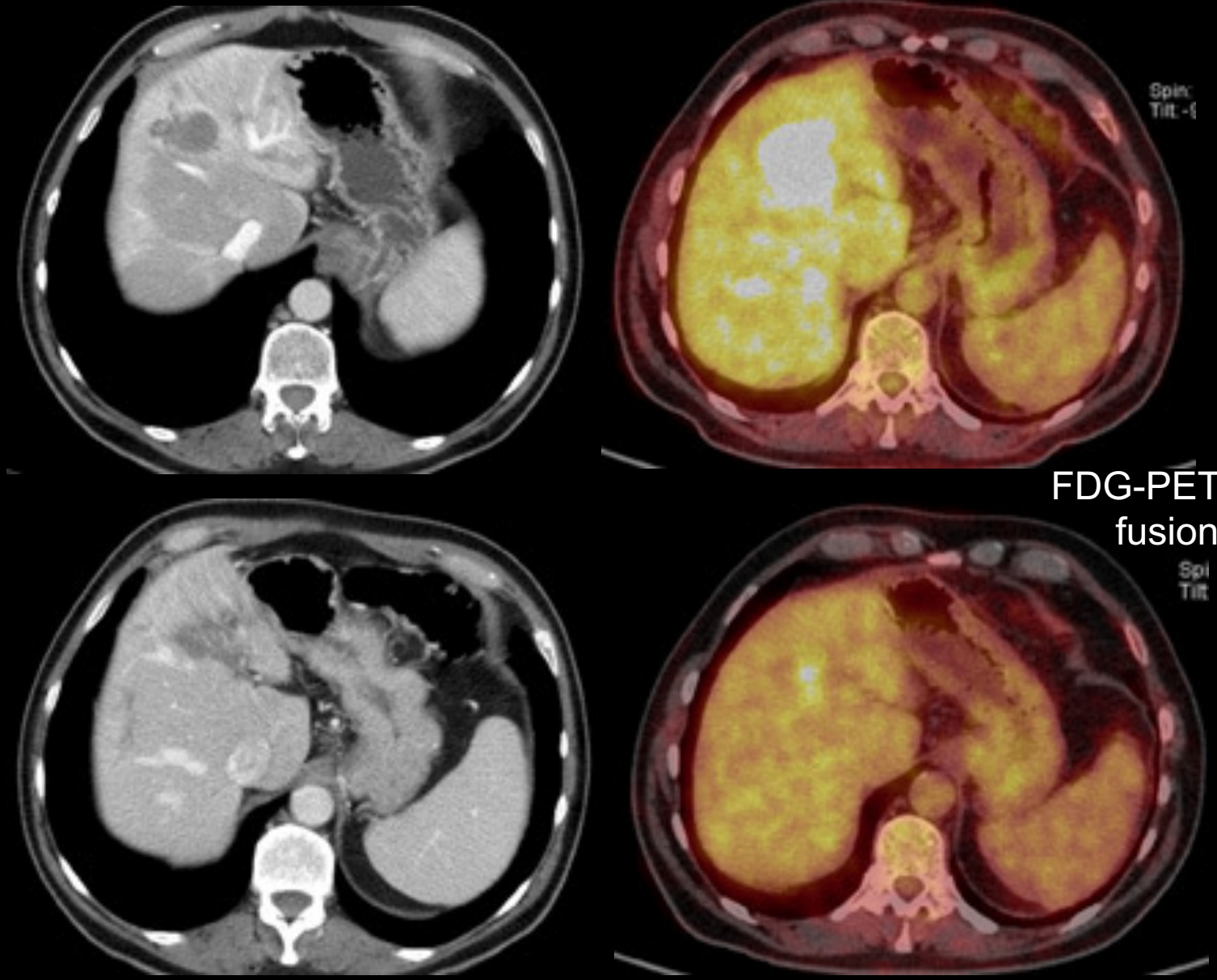




Njurcancer och levermetastaser - Bevacizumab

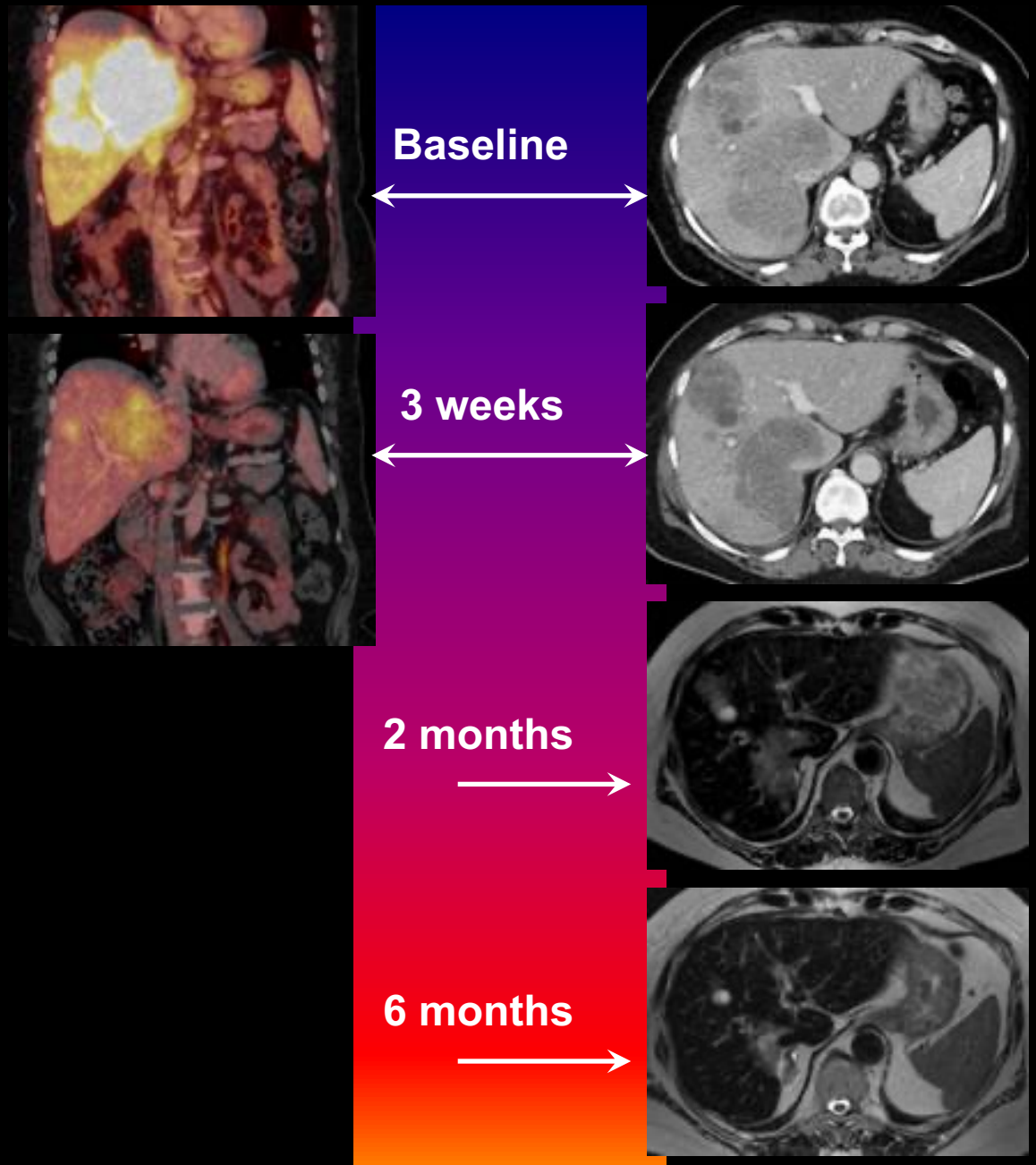
Baseline

Follow-up



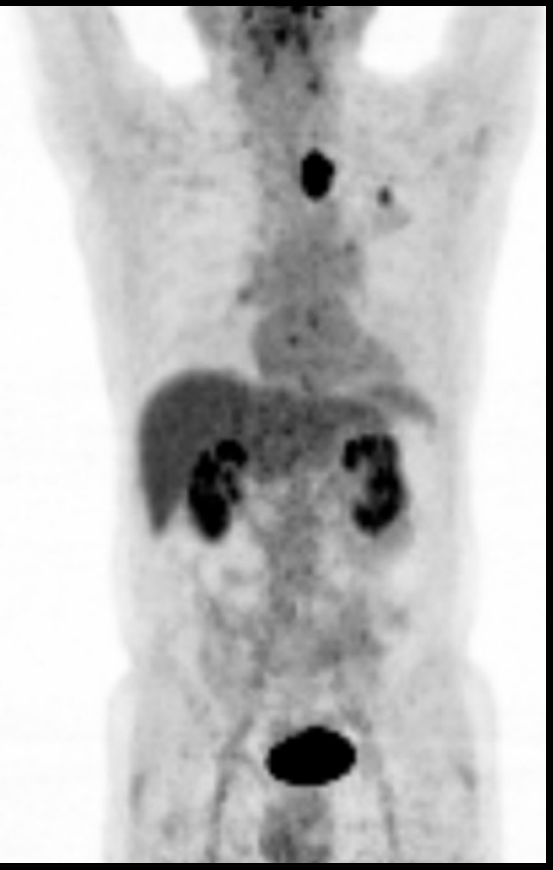
FDG-PET/CT fusion

Bröstcancer och levermetastaser - Sunitinib

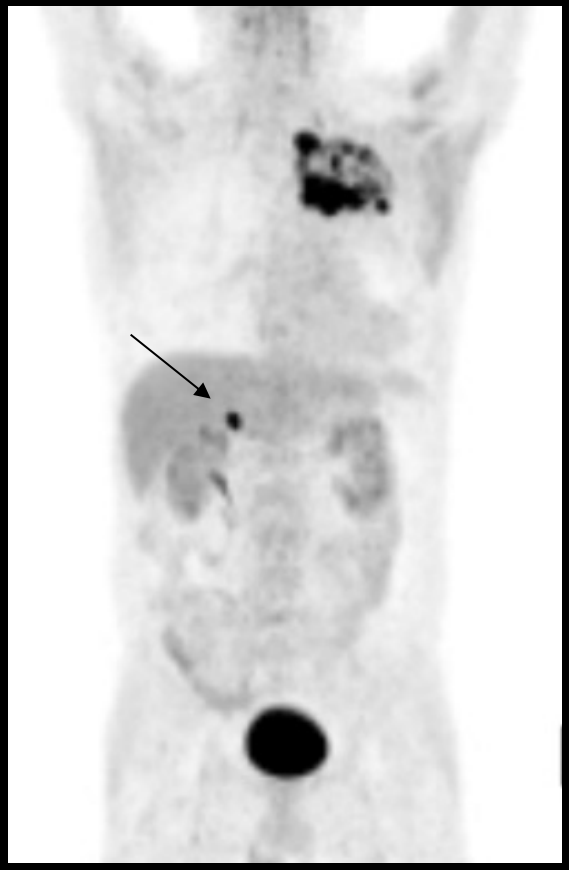


FDG-PET/CT = PR

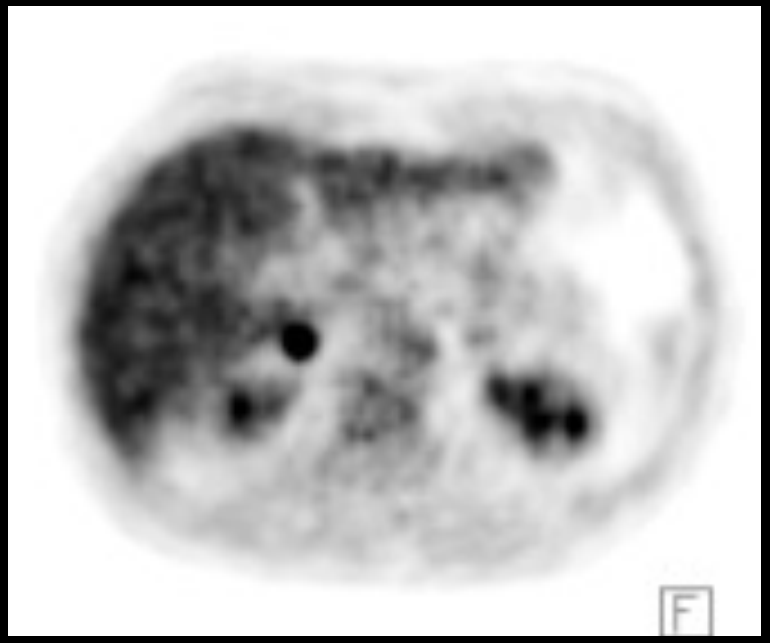
MRI = PR

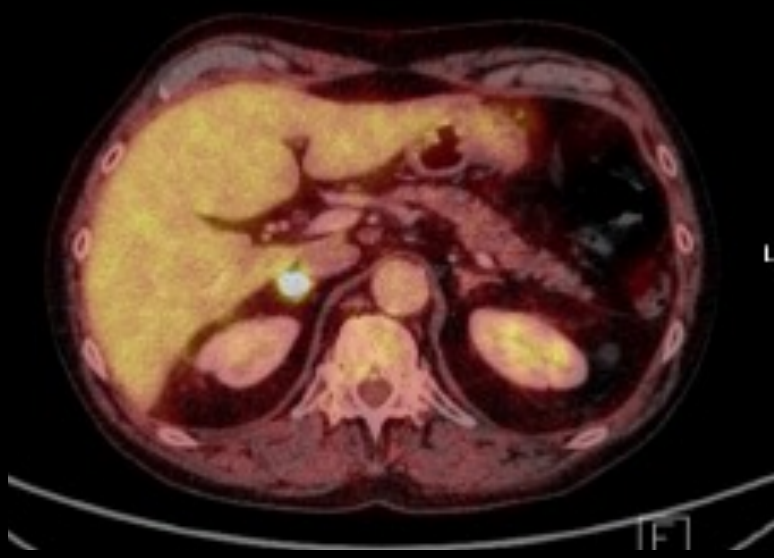


2010-02-17

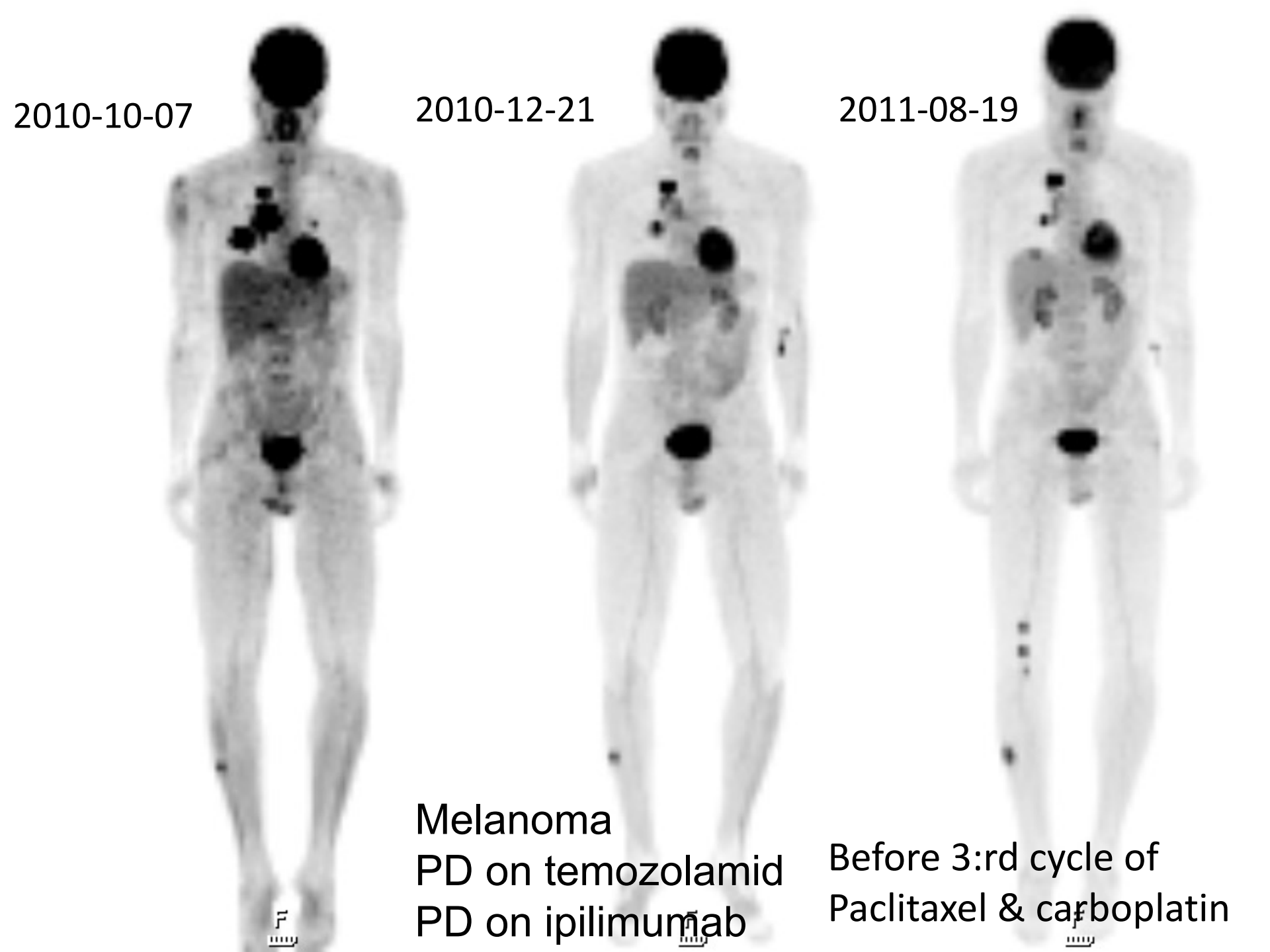


2011-12-12

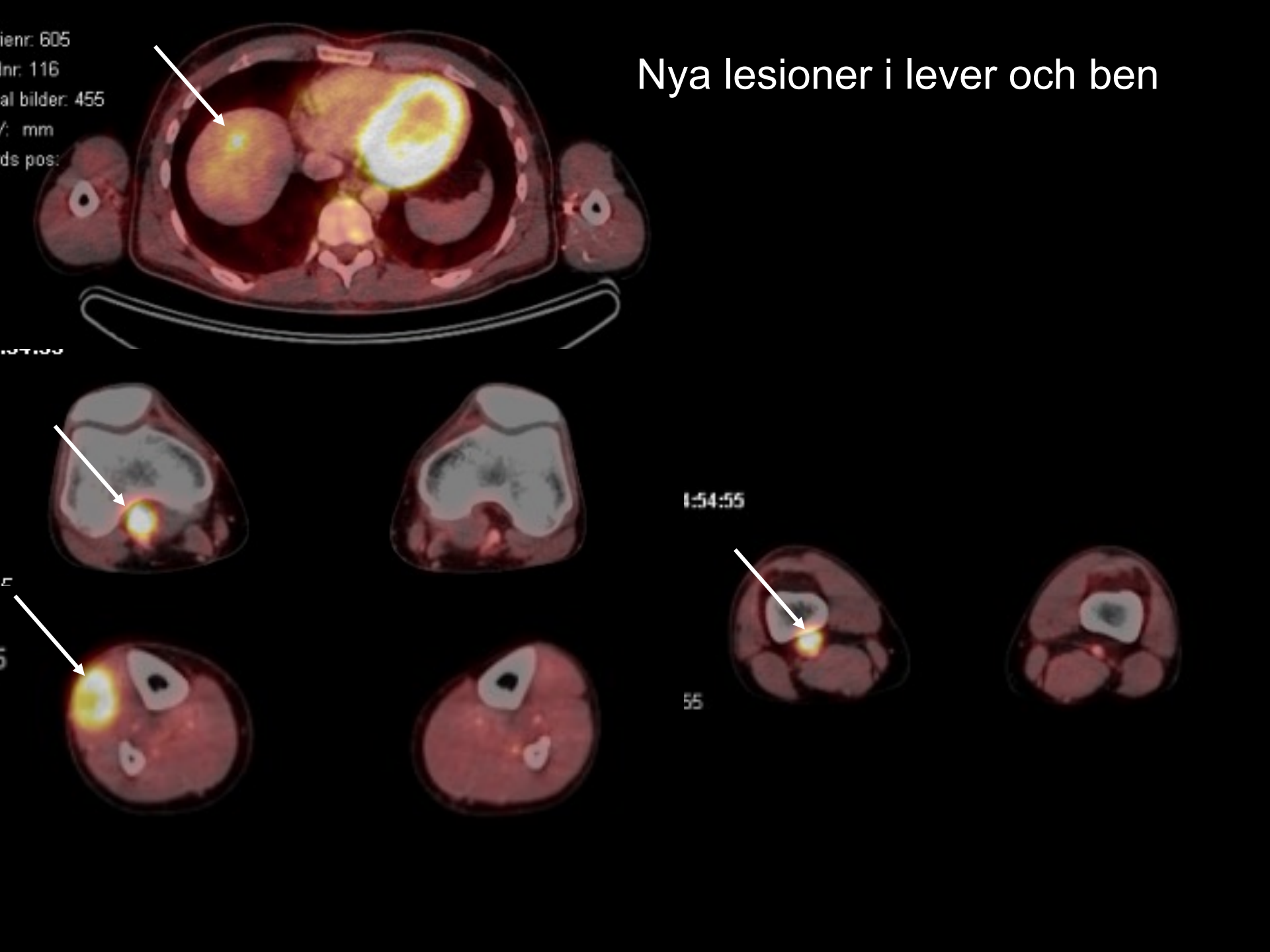




Adenocarcinoma of the lung


2010-10-07
2010-12-21
2011-08-19
Melanoma
PD on temozolamid
PD on ipilimumab
Before 3:rd cycle of
Paclitaxel & carboplatin

Nya lesioner i lever och ben



Standardiserat Upptags Värde (SUV)

Radioaktivitetskoncentrationen (Bq/mL) i PET-bilden

Mängden FDG (Bq) varierar
3-5 MBq/kg kroppsvikt
210 -350 MBq

Kroppsvikten (g) varierar mellan patienterna

$$\frac{\text{Radioaktivitetskoncentration i PET-bilden(Bq / ml)}}{\text{Injicerad aktivitet (Bq) / Kroppsvikt (g)}} = \textbf{SUV}$$

EORTC criteria - European Organization for Research and Treatment of Cancer

FDG-PET - SUV

CMR (komplett metabol respons) = 0

PMR (partiell metabol respons) =

SUV minskar 15-25% efter 1 cykel kemoterapi

SUV minskar >25% efter >1 cykel kemoterapi

PMD (progressiv metabol sjukdom) =

SUV ökning >25%,

Ökning av FDG-upptagets längd >20%

Nya lesioner

PERCIST criteria
(PET Response in Solid Tumors)
Wahl R. JNM 2009

SUV korrigerat för Lean Body Mass = SUL

1,2 cm ROIs, = SUL_{peak}

5 lesioner, 2 per organ

PERCIST criteria (PET Response in Solid Tumors)

Wahl R. JNM 2009

CMR = 0

PMR = SUL minskar ≥ 30% och ≥0,8 SUL
Och ingen ökning >30% av SUL i andra lesioner
Och ingen ökning >70% i storlek av andra lesioner

PMD = SUL ökar ≥ 30% och ≥0,8 SUL och/eller
ökning >75% i total lesion glycolysis (TLG) och/eller
Nya lesioner
PMD behöver konfirmeras inom 1 månad

MTV

Metabolic tumour volume = MTV (mL)

Segmentering av hela den FDG-upptagande tumörvolymen

Functional (Tumour) Volume = FV

Table 3 Lung cancer studies including multiple methods to measure MTV

First author (ref)	Design	Purpose	Pt no.	Segmentation methods	Findings
Mehta et al. [52]	Retrospective	Predict outcome	288	40%, 50%	Comparable (predictive)
Arslan et al. [53]	Retrospective	Predict outcome	25	SUV 2.5 / 50%	Comparable (predictive)
Yoo Ie et al. [54]	Retrospective	Predict outcome	58	SUV 2.5 / 25%, 50%, 75% / liver based	Liver based threshold was inferior. The others were comparable.
Lin et al. [55]	Retrospective	Predict outcome	60	SUV 2.5 / 40%, 50%	SUV 2.5 was better than 40%, 50%.
Abelson et al. [56]	Retrospective	Predict outcome	54	SUV 2, 4, 7, 10 / 50%	SUV 7, 10 were better than the others.
Kim et al. [57]	Retrospective	Predict outcome	91	SUV 2.5, 3.0, 3.5, 4.0	Comparable (predictive)
Harris et al. [58]	Retrospective	Predict outcome	29	50% / Gradient	Comparable (predictive)
Carvalho et al. [59]	Retrospective	Predict outcome	220	2.5, 3, 4 / 40%, 50%	Comparable (not predictive)
Lee et al. [60]	Retrospective	Predict outcome	57	40%, 50%	Comparable (not predictive)
Park et al. [61]	Retrospective	Predict occult LN metastasis	39	SUV 1.5, 2.0, 2.5, 3.0	Comparable, SUV 2.0 selected
Burger et al. [23]	Retrospective	Predict treatment response	44	42% / BSV	BSV had higher correlation with response.
Burger et al. [62]	Retrospective	Compare accuracy of the tumor delineation	50	2.5 / 42% / BSV	BSV had higher correlation with reference volume.
Chen et al. [63]	Retrospective	Compare accuracy of the tumor delineation	37	SUV 2.5 / 40%, 50% / Adaptive	Adaptive method had higher correlation with CT volume.
Yu et al. [64]	Prospective	Compare accuracy of the tumor delineation	15	SUV 1.5~5.5 / 15~60%	Optimal relative and absolute thresholds were 31% ± 11% and 3.0 ± 1.6.
Biehl et al. [33]	Retrospective	Compare accuracy of the tumor delineation	20	10%, 20%, 30%, 40%, 50%	The optimal threshold is different according to CT volume.
Laffon et al. [65]	Retrospective	Assess variability of TLG measurement	13	40%, 50%, 60%, 70%, 80%	Variability was the lowest in 40%.

BSV background subtracted volume, *SUV* standardized uptake value, __% relative fixed threshold using __% of SUVmax of the tumor, *TLG* total lesion glycolysis, *CT* computed tomography

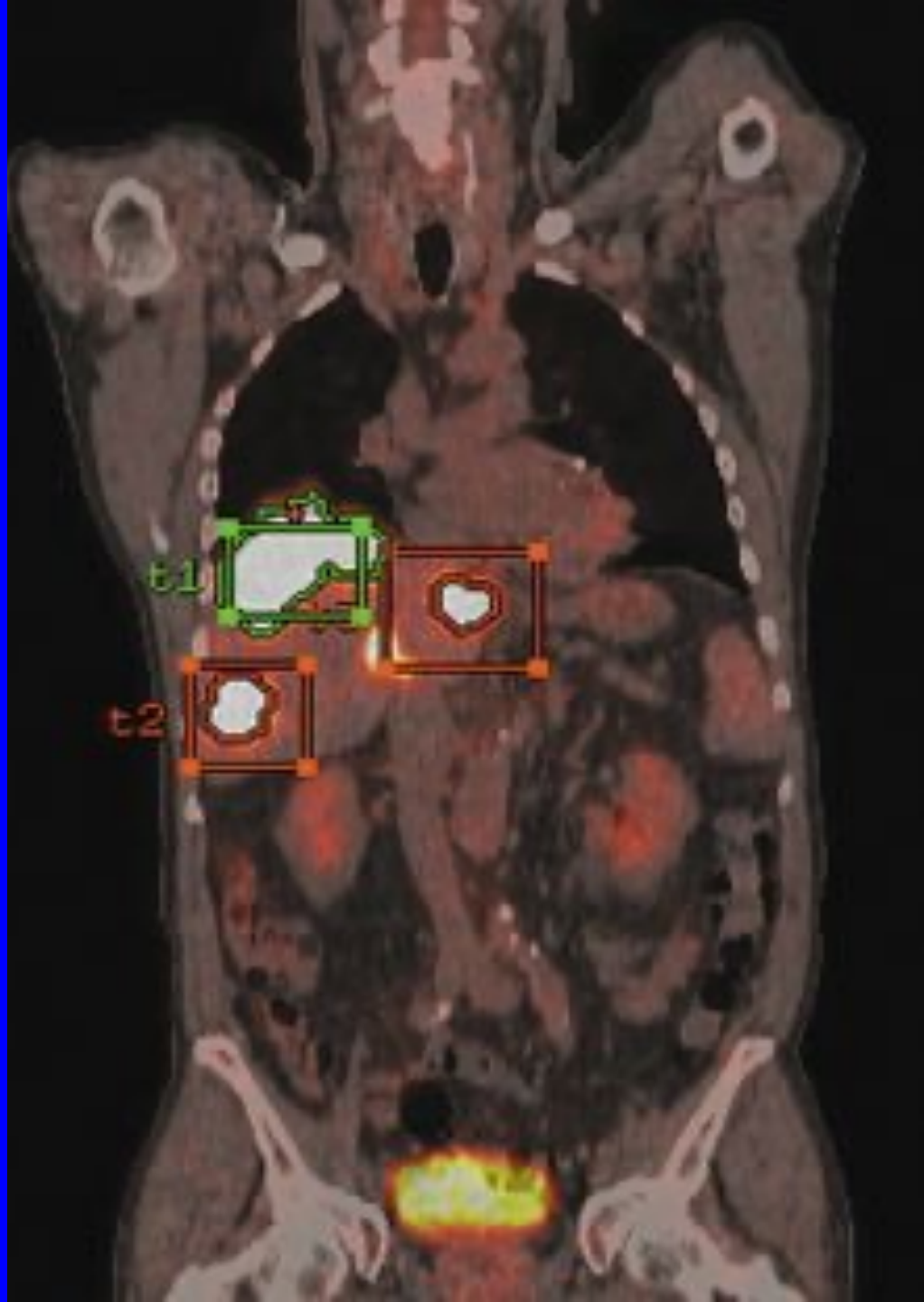
Im HJ I et al. Nucl Med Mol Imaging 2018; 52:5–15

TLG

Tumour Lesion Glycolysis = TLG

$TLG = MTV \times SUV_{mean}$

1.Co-registration
of baseline and follow-up
PET/CT
2. Automatic delineation
of tumour VOIs and editing
3. Propagation and editing
4. Quantification
of tumour VOIs
SUVmean
SUVmax
Functional volume
5. Reporting



Finding List | Patient and Exam Data | Options

Lesion [#]	Status / Type		Functional Volume [cm³]		Functional Volume C... [%]		SUV Max [SUVbw g/ml]		TLG [SUVbw g]		TLG Change [%]		Slice Number [#]	
-	2006 06-20	2006 08-29	2006 06-20	2006 08-29	2006 06-20	2006 08-29	2006 06-20	2006 08-29	2006 06-20	2006 08-29	2006 06-20	2006 08-29	2006 06-20	2006 08-29
1	N	N	0.6	0.0	-	-100.0	6.1	-	3.4	-	-	-100.0	81	81
2	N	N	1.2	0.0	-	-100.0	10.2	-	8.5	-	-	-100.0	89	89
3	N	N	4.4	0.0	-	-100.0	13.7	-	29.5	-	-	-100.0	110	115
4	T	T	21.6	0.7	-	-96.7	12.4	9.3	139.3	4.1	-	-97.1	114	117
5	N	N	14.2	0.0	-	-100.0	12.6	-	100.7	-	-	-100.0	112	112
6	N	N	1.1	0.0	-	-100.0	7.6	-	6.1	-	-	-100.0	114	116
7	T	T	6.3	0.0	-	-100.0	8.4	-	34.3	-	-	-100.0	125	124
8	T	T	8.6	0.0	-	-100.0	11.8	-	59.4	-	-	-100.0	129	133
9	T	T	18.8	3.2	-	-83.1	10.2	13.0	116.8	22.0	-	-81.1	133	128
10	T	Inflamma...	47.9	1.1	-	-97.6	13.0	13.0	329.6	11.1	-	-96.6	138	128
11	-	Inflamma...	-	45.2	-	∞	-	41.7	-	1233.2	-	∞	-	270
Summary	-	-	124.6	50.2	-	-59.7	13.7	41.7	827.7	1270.4	-	53.5	-	-

PD: Progressive disease SD: Stable disease PR: Partial response CR: Complete response

Conclusion:

Lesion 9 shows a increased SUVmax. This is most likely the consequence of the 83% volume shrinking.
Lesion 11 corresponds to a inflammatory reaction.

The conclusions as entered will appear on the report and can be burned on the cd. They will also be saved in the IDA file for later use.

Response	CT-based criteria		PET-based criteria		
	RECIST 1.1	irRC		PERCIST 1.0	EORTC
Complete response	Disappearance of all TLs and NLs; all LNs < 10 mm short axis	Resolution of all lesions (whether measurable or not) and no new lesions	Complete metabolic response	Complete resolution of ^{18}F-FDG uptake within measurable TL and disappearance of all other lesions to BBP levels	Complete resolution of ^{18}F-FDG uptake within TV so that it is indistinguishable from surrounding NT
Partial response	≥30% decrease in SoDs of TLs; NLs may persist but not unequivocally progress	Decrease in TB ≥ 50%, measured as SoPs of 2 largest perpendicular diameters of all ILs, relative to BL	Partial metabolic response	>30% RD and >0.8 AD in SUL_{peak} of HL	Reduction of 15%–25% in tumor SUV after 1 CoT and >25% after more than 1 CoT
Stable disease	Neither sufficient TR nor TG to qualify for PR or PD	Not meeting criteria for irCR or irPR, in absence of irPD	Stable metabolic disease	Not meeting criteria for CMR, PMR, or PMD	Increase in tumor SUV of <25% or decrease of <15% and no visible increase in extent of ^{18}F-FDG TU (20% in LD)
Progressive disease	≥20% increase in sum of diameters of TLs or unequivocal progression of NL or appearance of new lesion	Increase in TB ≥ 25% relative to nadir, measured as SoPs of 2 largest perpendicular diameters of all ILs	Progressive metabolic disease	>30% RI and >0.8 AI in SUL_{peak} of HL or unequivocal progression of ^{18}F-FDG–avid NL or appearance of new ^{18}F-FDG–avid lesion	Increase from BL in tumor SUV of >25% within tumor region, visible increase in extent of ^{18}F-FDG TU (20% in LD), or appearance of new ^{18}F-FDG uptake in MLs

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TL = target lesion; NL = nontarget lesion; LN = lymph node; BBP = background blood-pool; TV = tumor volume; NT = normal tissue; SoDs = sum of diameters; TB = tumor burden; SoPs = sum of the products; IL = index lesion; BL = baseline; RD = relative decrease; AD = absolute decrease; SUL_{peak} = average SUV corrected by lean body mass within a 1-cm^3 spheric volume of interest; HL = hottest lesion; CoT = cycle of therapy; TR = tumor regression; TG = tumor growth; PR = partial response; PD = progressive disease; irCR = immune-related complete response; irPR = immune-related partial response; irPD = immune-related progressive disease; CMR = complete metabolic response; PMR = partial metabolic response; PMD = progressive metabolic disease; TU = tumor uptake; LD = longest dimension; RI = relative increase; AI = absolute increase; ML = metastatic lesion; SUV = for EORTC we used SUV_{max} (maximum voxel value of SUV).

Table 1 Available and/or proposed response criteria for use with FDG PET

Response	EORTC[a]	PERCIST[b]	PECRIT[c]			PERCIMT[c]
Complete response (CR)	Complete resolution of FDG uptake	Disappearance of all metabolically active tumours	RECIST 1.1 (disappearance of all target lesions; reduction in short axis of target lymph nodes to <1 cm; no new lesions)		Clinical benefit	Complete resolution of all preexisting ^{18}F-FDG-avid lesions; no new ^{18}F-FDG-avid lesions
Partial response (PR)	Minimum reduction of ±15–25% in tumour SUV after one cycle of chemotherapy, and >25% after more than one treatment cycle	Decline in SULpeak by 0.8 unit (>30%) between the most intense lesion before treatment and the most intense lesion after treatment	RECIST 1.1 (decrease in target lesion diameter sum >30%)		Clinical benefit	Complete resolution of some preexisting ^{18}F-FDG-avid lesions. No new, ^{18}F-FDG avid lesions.
Stable disease (SD)	increase in SUV of less than 25% or a decrease of less than 15%	Does not meet other criteria	Does not meet other criteria	Change in SUL peak of the hottest lesion of >15%	Clinical benefit	Neither PD nor PR/CR
				Change in SUL peak of the hottest lesion of ≤15%	No clinical benefit	
Progressive disease (PD)	Increase in tumour FDG uptake of >25%; increase in maximum tumour of >20%; new metastases	Increase in SULpeak of >30% or the appearance of a new metabolically active lesion	RECIST 1.1 (increase in target lesion diameter sum of >20% and at least 5 mm or new lesions)		No clinical benefit	Four or more new lesions of <1 cm in functional diameter or three or more new lesions of >1.0 cm in functional diameter or two or more new lesions of more than 1.5 cm in functional diameter

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Table 1 FDG PET Assessment of Melanoma Tumor Response and Prognosis

Author	Date	N	Treatment(s)	Time Points	Follow-Up	Outcome	Conclusions
Sachpekidi[40]	2014	22	Ipi	Base, 2 cycles, 4 cycles	5-25 mo	PFS, OS, EORTC	Response at cycle 2 PET corresponds to cycle 4 outcome
Breki[101]	2016	31	Ipi	Base, 2 cycles, 4 cycles	NS	TO	Fractal dimension has potential as a predictive marker of ICI response
Cho[42]	2017	20	Ipi, Nivo, BMS	Base, 3-4 wk, 4 mo	10-184 wk	BOR	PERCIST and RECIST at 3-4 wk corresponds to BOR
Seith[102]	2018	10	Nivo, Pembro	Base, 2 wk, 3 mo	148-814 days	PFS, OS	Status at week 2 may predict long term response
Anwar[45]	2018	41	Ipi	End of Therapy	Median 21.4 mo (6.3-41.9)	BCR	PERCIMT criteria—new lesions with cut-off threshold for size and number as PD
Sachpekidis[103]	2018	25	Ipi	Base, 2 cycles, end of Tx (4 cycles)	Mean 59 wk (16-153)	BCR	PERCIMT criteria correlates with clinical outcome vs. quant. PET parameters
Sachpekidis[104]	2018	41	Ipi	Base, 2 cycles	21.4 mo (6.3-41.9)	BCR	PERCIMT criteria more sensitive than EORTC criteria
Tan[44]	2018	104	Nivo, Pembro	1 year	Median 30.1 mo	PFS	Patients with CMR at 1 year have ongoing response to therapy
Sachpekidis[105]	2019	16	Ipi	Base, 2 cycles, end of Tx (4 cycles)	0.1-63.3 mo	PFS	Pts with AEs have longer PFS
Sachpekidis[106]	2019	41	Ipi	Base, 2 cycles, end of Tx (4 cycles)	Median 21.4 mo (6.3-41.9)	BCR	Mediastinal lymph node activation assoc. with disease control
Ito[43]	2019	60	Ipi	Base, end of Tx (Median 12.2 wk; 1.0-11.1)	Median 14.9 mo (2.6-68.0)	OS	Response by PERCIST assoc. with OS. New FDG avid lesions not assoc. with OS
Ito[48]	2019	142	Ipi	Base	Median 14.7 mo (10.4-18.9)	OS	Baseline MTV assoc. with OS
Nobashi[107]	2019	21*	Ipi, Nivo, Pembro	Base, end of Tx (91 ± 38 days)	Median 378 days (97-1544)	BOR	Decreased tumor burden at 1st restaging assoc. with CB at 1 year
Sanil[108]	2019	34	NS	Base	Median 29.5 mo (3-288)	PFS, OS	Tumor heterogeneity index assoc. with OS
Amrane[109]	2019	37	Ipi, Nivo, Pembro	Base, 14 wk	22.5 - 42.8 mo	PFS, OS	PET response by iRECIST or PERCIST correlates with PFS, OS
Seban[49]	2019	55	NS (anti-PD-1)	Base	Median 20.7 mo (1.0-72.6)	PFS, OS, BOR	Low TLG correlates to prolonged PFS, OS.
Annovazzi[46]	2020	57	Ipi, Nivo, Pembro	Base, 12-18 wk	6 mo	Clinical benefit	PET at 3-4 mo predicts outcome at 6 mo. Similar performance of MTV, PERCIMT, EORTC, TLG criteria

Ipi, ipilimumab; Nivo, nivolumab; Pembro, pemborlizumab; BMS, BMS-936559; NS, not specified; ICI, immune checkpoint inhibitor therapy; PD, progressive disease; Base, Baseline prior to therapy; wk, weeks; mo, months; Tx, treatment; PFS, progression-free survival; OS, overall survival; TO, therapeutic outcome; BOR, best overall response; BCR, best clinical response; PD, progressive disease; PERCIMT, PET Response Evaluation Criteria for Immunotherapy; EORTC, European Organization for Research and Treatment of Cancer; MTV, metabolic tumor volume; TLG, total lesion glycolysis.

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Table 2 Principal studies investigating the role of FDG PET/CT in the evaluation of response of solid tumours to immunotherapy

Reference	Study type	Number of patients	Tumour	Treatment	Response criteria	Results
[20]	Prospective	22	Melanoma	Ipilimumab	EORTC after two cycles of treatment (early) and at the end of treatment after four cycles (late)	Early response evaluation after (two cycles) is predictive of final treatment outcome in patients with PMD and SMD
[26]	Prospective	27	Melanoma	20 pembrolizumab, 7 nivolumab	Visual analysis (qualitative visual inspection, positive when FDG uptake greater than background activity or hepatic uptake; Deauville score)	43% of patients who had residual disease by CT criteria, either PR or SD, were FDG-negative
[36]	Prospective	31	Melanoma	Ipilimumab	Fractal and multifractal analysis before and after two and after four cycles of treatment	Operator-independent method with a correct classification rate of 83.3%
[23]	Prospective	20	Melanoma	16 Ipilimumab, 1 nivolumab, 3 BMS-936559	RECIST 1.1 and PERCIST at early (4 weeks) and late assessment (4 months)	Combined anatomical and functional data at 21–28 days (PECRIT) criteria predicted response with 100% sensitivity, 93% specificity and 95% accuracy. Introduction of clinical benefit in response criteria
[22]	Prospective	24	NSCLC	Nivolumab	RECIST 1.1 versus PERCIST; additional semiquantitative analyses (SUVmax, MTV, TLG)	Metabolic response on PET (especially TLG) associated with therapeutic response and survival at 1 month after nivolumab
[28]	Prospective	27	NSCLC	23 nivolumab, 4 pembrolizumab	Baseline semiquantitative analysis	SUVmax ≤17.1 (sensitivity 88.9%) or a SUVmean ≤8.3 (sensitivity 100%) identified fast progression after 8 weeks of therapy
[24]	Prospective enrolment, retrospective PET analysis	41	Melanoma	Ipilimumab	RECIST and appearance of new FDG-avid lesions (PERCIMT); patients were dichotomized into those with and those without clinical benefit	A cut-off of four newly emerged FDG-avid lesions on posttreatment PET/CT gave reliable indication of treatment failure
[25]	Prospective	41	Melanoma	Ipilimumab	EORTC and PERCIMT after two cycles of immunotherapy	PERCIMT to interim PET/CT provides a more sensitive predictor of final response than EORTC criteria

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Response criteria	Results
EORTC after two cycles of treatment (early) and at the end of treatment after four cycles (late)	Early response evaluation after (two cycles) is predictive of final treatment outcome in patients with PMD and SMD
Visual analysis (qualitative visual inspection, positive when FDG uptake greater than background activity or hepatic uptake; Deauville score)	43% of patients who had residual disease by CT criteria, either PR or SD, were FDG-negative
Fractal and multifractal analysis before and after two and after four cycles of treatment	Operator-independent method with a correct classification rate of 83.3%
RECIST 1.1 and PERCIST at early (4 weeks) and late assessment (4 months)	Combined anatomical and functional data at 21–28 days (PECRIT) criteria predicted response with 100% sensitivity, 93% specificity and 95% accuracy. Introduction of clinical benefit in response criteria
RECIST 1.1 versus PERCIST; additional semiquantitative analyses (SUVmax, MTV, TLG)	Metabolic response on PET (especially TLG) associated with therapeutic response and survival at 1 month after nivolumab
Baseline semiquantitative analysis	SUVmax ≤17.1 (sensitivity 88.9%) or a SUVmean ≤8.3 (sensitivity 100%) identified fast progression after 8 weeks of therapy
RECIST and appearance of new FDG-avid lesions (PERCIMT); patients were dichotomized into those with and those without clinical benefit	A cut-off of four newly emerged FDG-avid lesions on posttreatment PET/CT gave reliable indication of treatment failure
EORTC and PERCIMT after two cycles of immunotherapy	PERCIMT to interim PET/CT provides a more sensitive predictor of final response than EORTC criteria

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Table 2 FDG PET Findings of Immune-Related Adverse Events (irAE)

irAE	Author	N	FDG PET Finding
Colitis	Barina et al[110]	86	Elevated uptake in a portion of, or throughout, the colon. Inflammation may be focal or diffuse. Inflammation can also involve other parts of the GI tract (esophagitis, gastritis, ileitis)
	Lang et al[60]	100	
	Iravani et al[59]	5	
	Wachsmann et al[111]	1	
	Gandy et al[112]	2	
	Bronstein et al[71]	1	
Hepatitis	Raad et al[113]	1	Elevated diffuse or focal uptake throughout the liver.
	Iravani et al[59]	1	
Pneumonitis	Raad et al[113]	1	Elevated lung uptake. Appearance can be focal (organizing pattern), or diffuse (ground glass opacity pattern, hypersensitivity pattern), and my only involve parts of the lung (interstitial pattern)
	Garcia-Gomez et al[114]	1	
	Razzouk-Cadet et al[62]	1	
	Iravani et al[59]	4	
	Gandy et al[112]	1	
Sarcoidosis	Tirumani et al[67]	1	Elevated bilateral uptake in mediastinal and hilar lymph nodes. May also include enlargement of existing nodes or appearance of new nodes on CT.
	Zhang et al[115]	1	
	Iravani et al[59]	2	
	Gandy et al[112]	1	
Pancreatitis	Alabed et al[116]	1	Diffuse elevated pancreatic uptake.
	Das et al[117]	1	
	Wachsmann et al[111]	1	
	Iravani et al[59]	1	
	Gandy et al[112]	1	
Hypophysitis	Wachsmann et al[111]	1	Elevated focal uptake in the pituitary. Assessment may be difficult due to normal brain uptake.
	Iravani et al[59]	1	
	Gandy et al[112]	1	
	Bronstein et al[71]	1	
Thymic hyperplasia	Mencel et al[118]	2	Elevated diffuse uptake in the thymus.
Fasciitis	Bronstein et al[71]	1	Elevated diffuse uptake in fascia.
Myositis	Iravani et al[59]	1	Elevated diffuse uptake in muscle.
	Bronstein et al[71]	1	
	Zimmer et al[72]	1	
Arthritis/arthropathy	Iravani et al[59]	1	Elevated uptake in joints.
	Gandy et al[112]	1	
Nephritis	Qualls et al[73]	1	Marked increased uptake in the renal cortex.

N are number of patients assessed with ^{18}F-FDG PET in each study. This may be less than the total number of patients analyzed.

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Sammanfattning

Morfologiska kriterier

Immunresponsanpassade morfologiska kriterier
som hanterar nya lesioner

Metabola/Funktionella kriterier - FDG-PET/CT
- Enstaka lesioner
- Definierat antal lesioner
- MTV/FV
- TLG

Dessa kriterier prövas och i olika studier jämförs med varandra och korreleras mot PFS, OS