OnkoLIS 2014, 6-7 februar
Scandic Oslo Airport Gardermoen
CNS tumores og lymfomer

PET-scan i lymfomdiagnostikk og monitorering av behandlingsrespons

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ARN, OUS
Aarhus Universitet / PET-Centeret,
Aarhus, Danmark

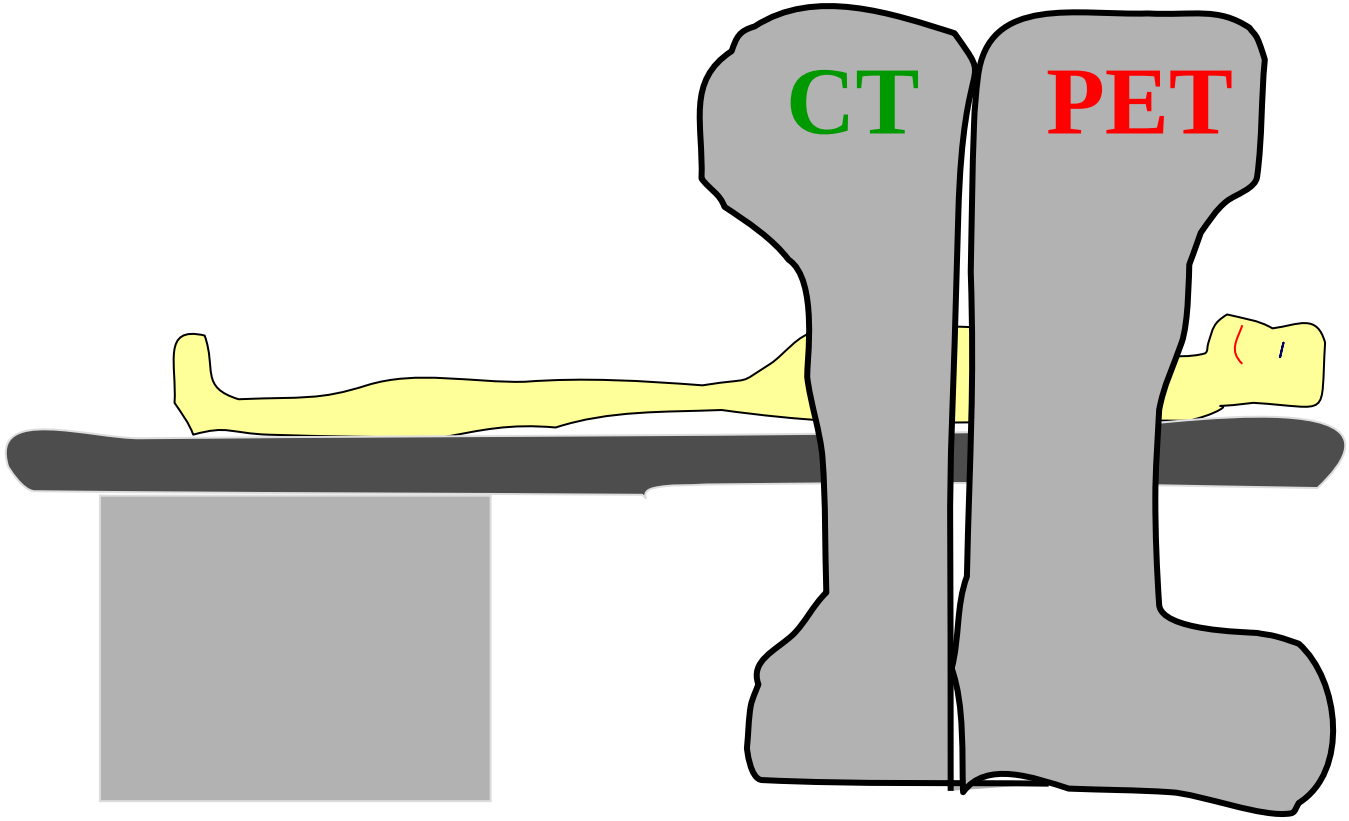
- CT ved PET/CT

- Attenueringskorreksjon og attenueringsartefakter ved PET/CT FDG

- Bruk av FDG PET/CT ved lymfom

PET-scan i lymfomdiagnostikk og monitorering av behandlingsrespons

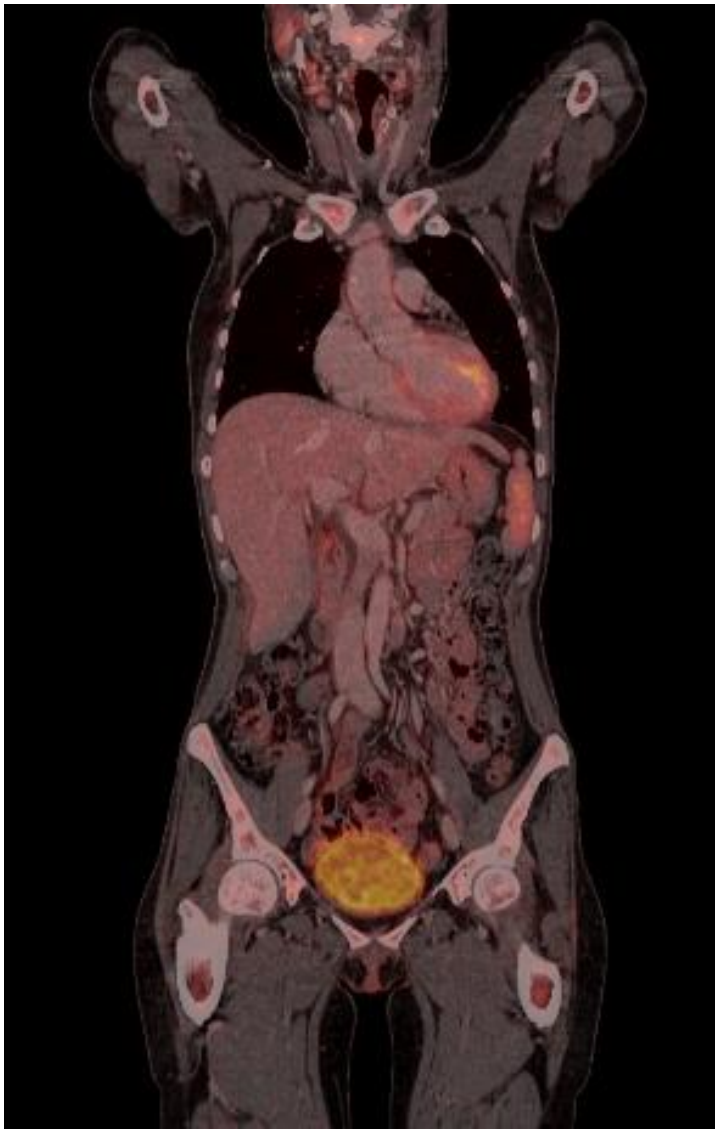
Hvorfor PET/CT og ikke bare PET?



CT i PET/CT

1. **Rask attenueringskorreksjon**
2. **Anatomisk lokalisering av PET funn**
3. **Diagnostisk CT-informasjon**
4. **One-stop shop (PET/CT m/ CECT)**
   (NB! Når indisert!!)

PET



PET/CECT

CT i PET/CT

1. **Rask attenueringskorreksjon**
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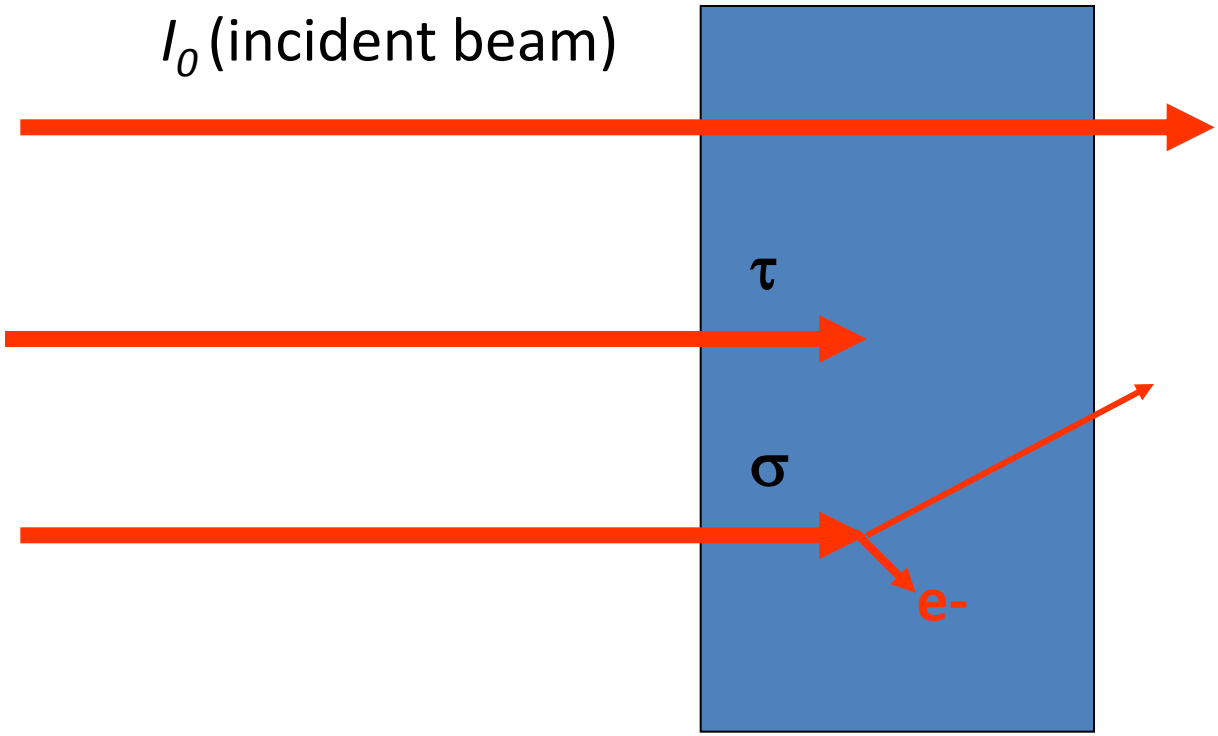
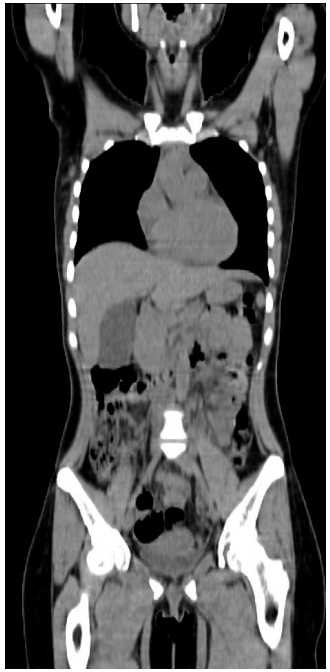
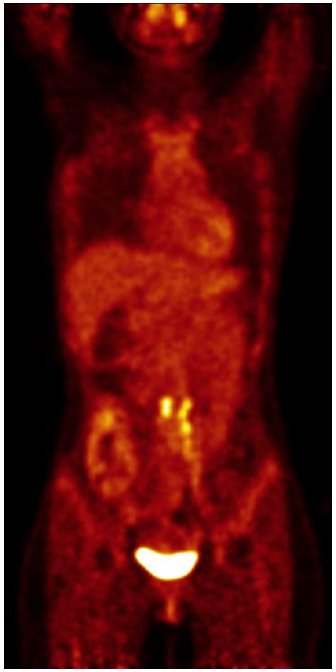


$$I_t = I_0 e^{-\mu x}$$

Når γ-stråler eller rtg-stråler passerer gjennom et absorberende medium vil noe av strålingen bli absorbert (*fotoelektrisk effekt*) eller bli spredt (*Compton scatter*). Denne svekkelsen av strålingen kalles **attenuering**.



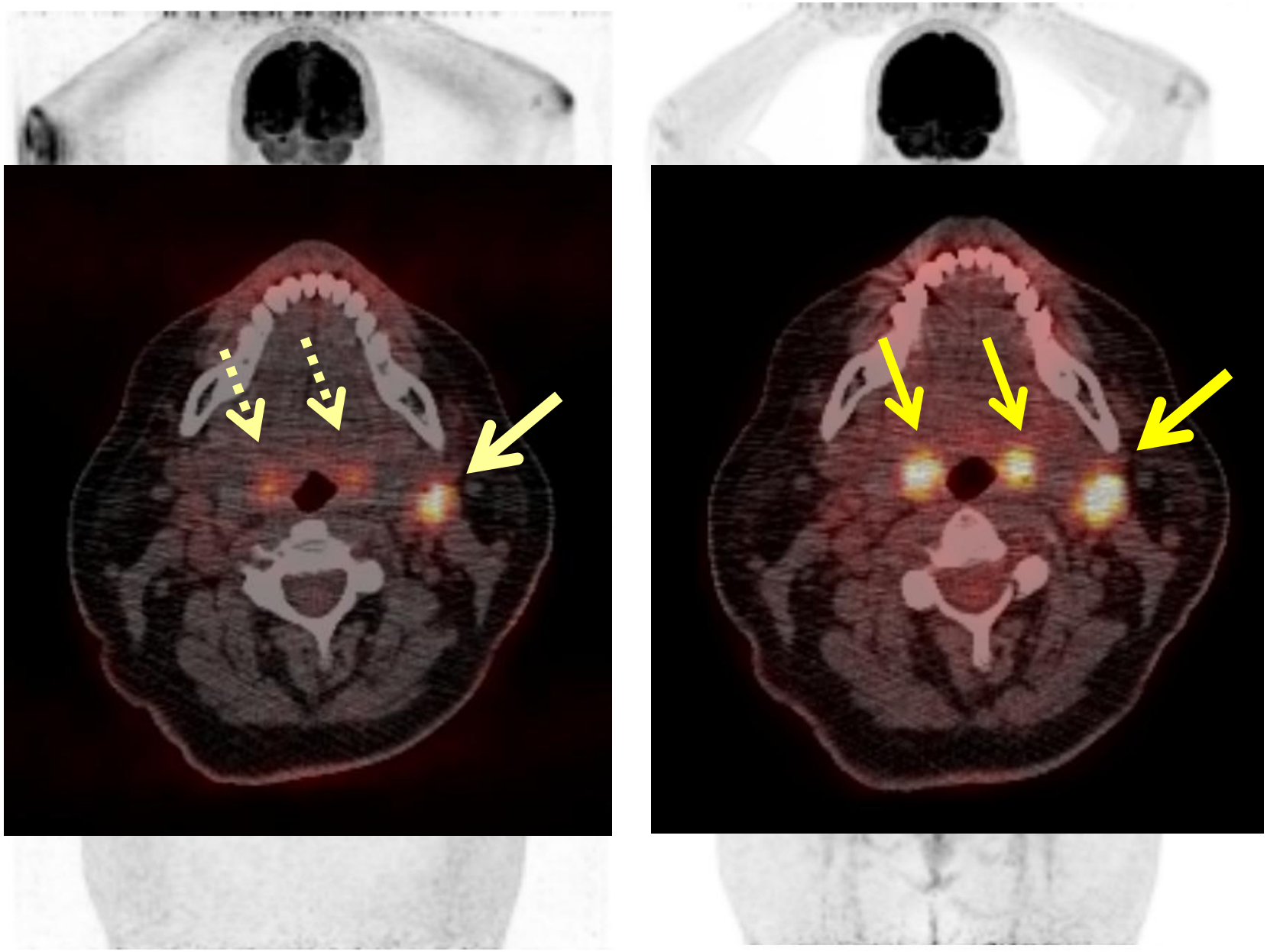


Ved **CT** er vevsattenuering grunnlaget for bildedannelsen.

Ved **nukleærmedisinske undersøkelser** ligger bildeinformasjonen i opptak og fordeling av det radiofarmasøytiske preparatet, mens vevsattenuering vil *fordreie* informasjonen.

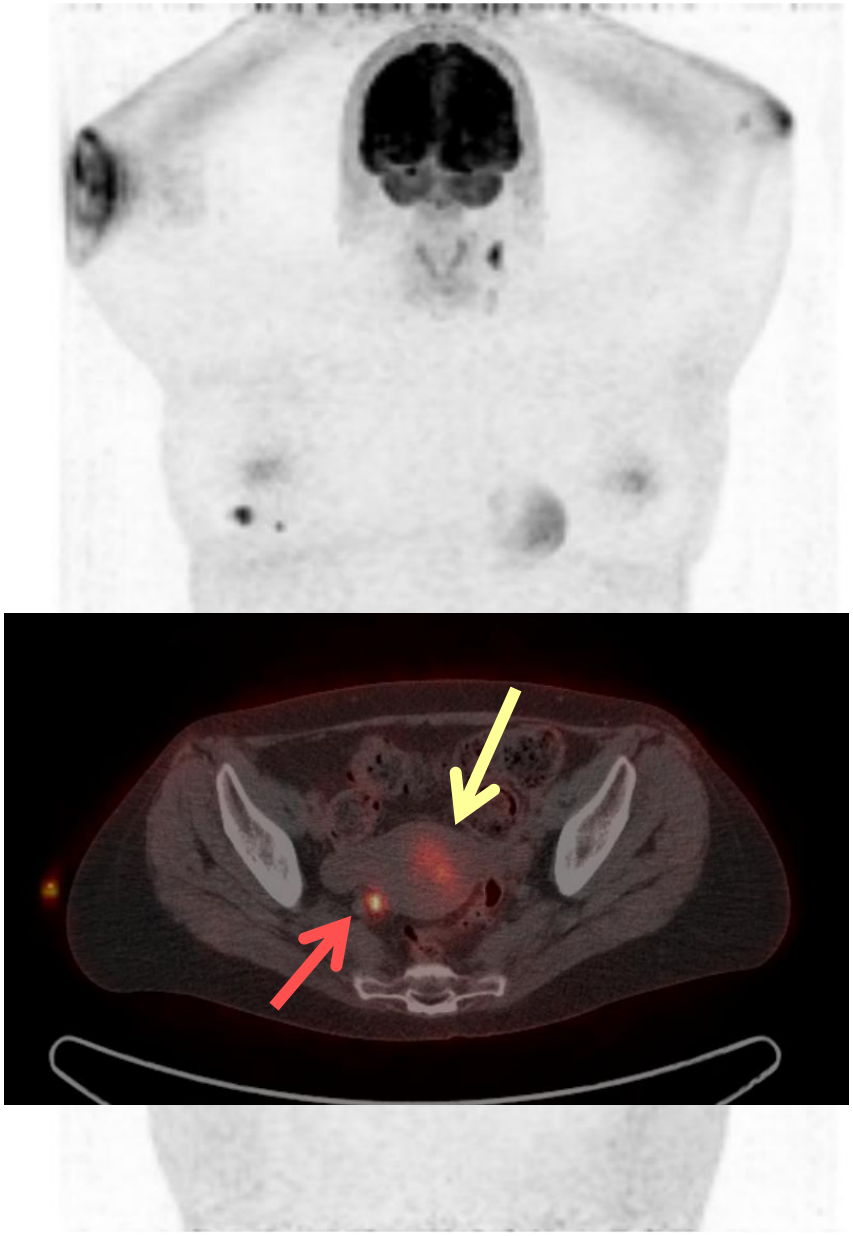
Ikke-attenuasjonskorrigert

CT-attenuasjonskorrigert



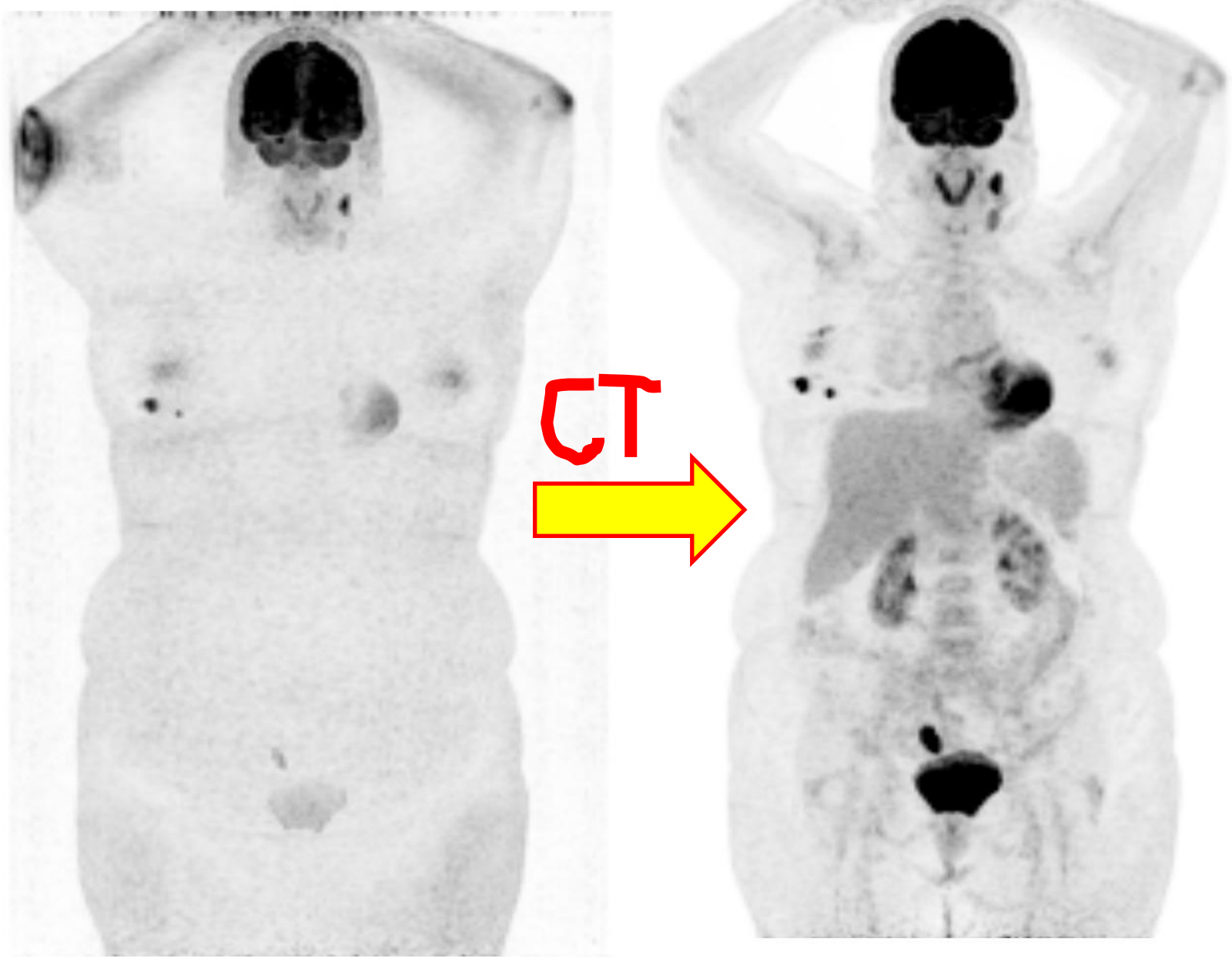
Ikke-attenuasjonskorrigert

CT-attenuasjonskorrigert



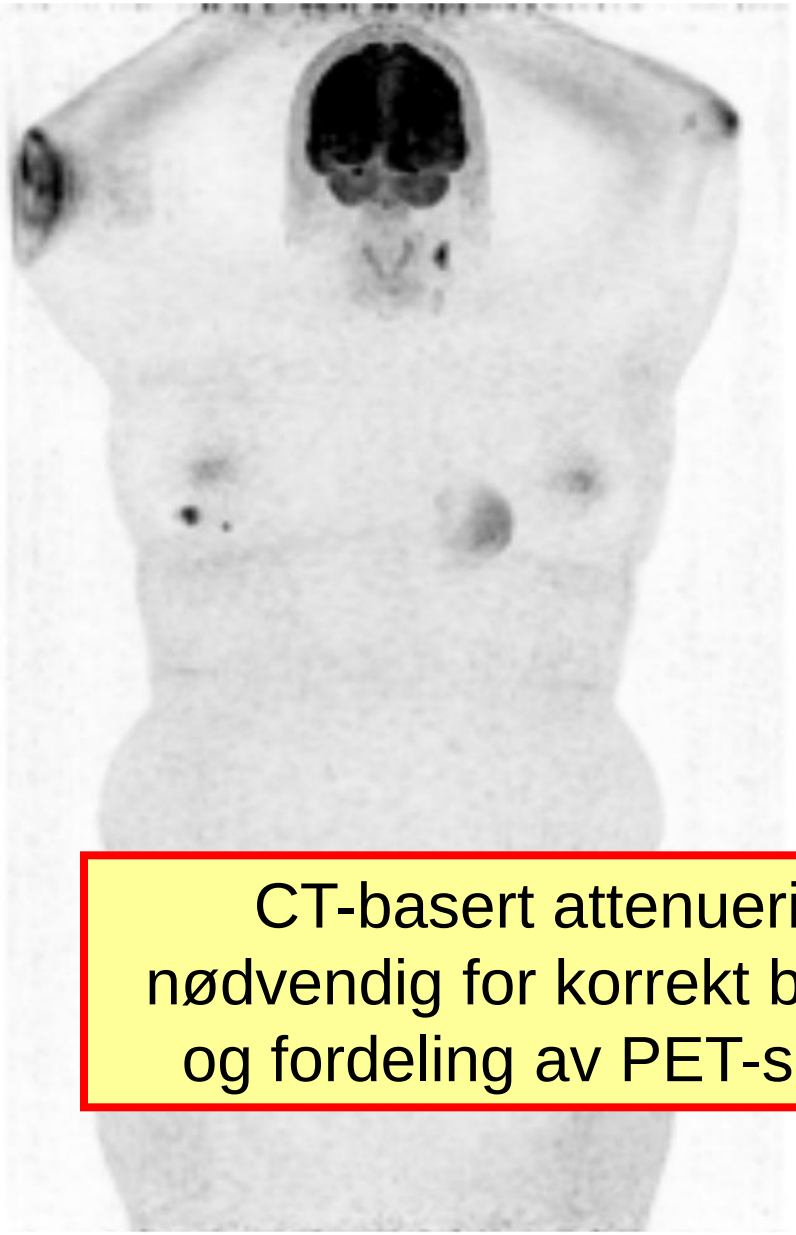
Ikke-attenuasjonskorrigert

CT-attenuasjonskorrigert



Ikke-attenuasjonskorrigert

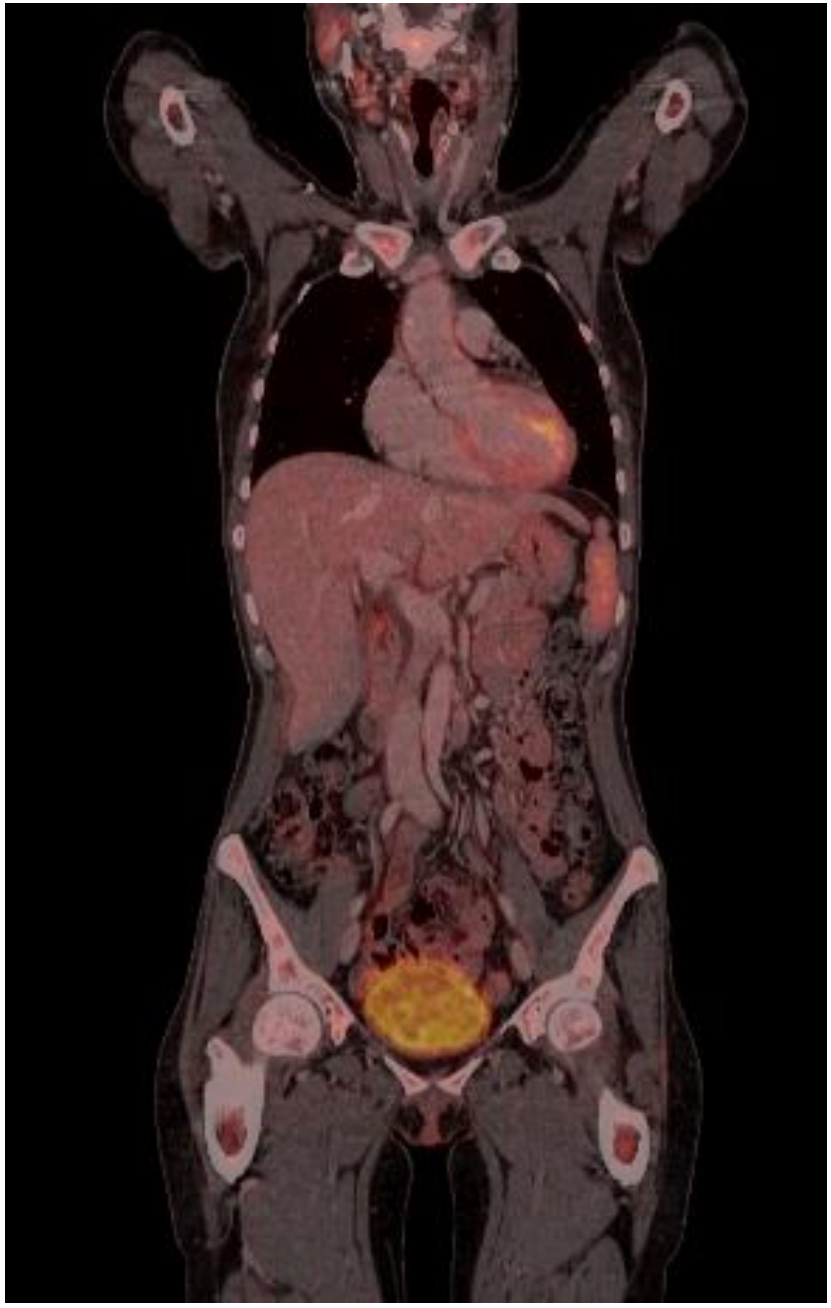
CT-attenuasjonskorrigert



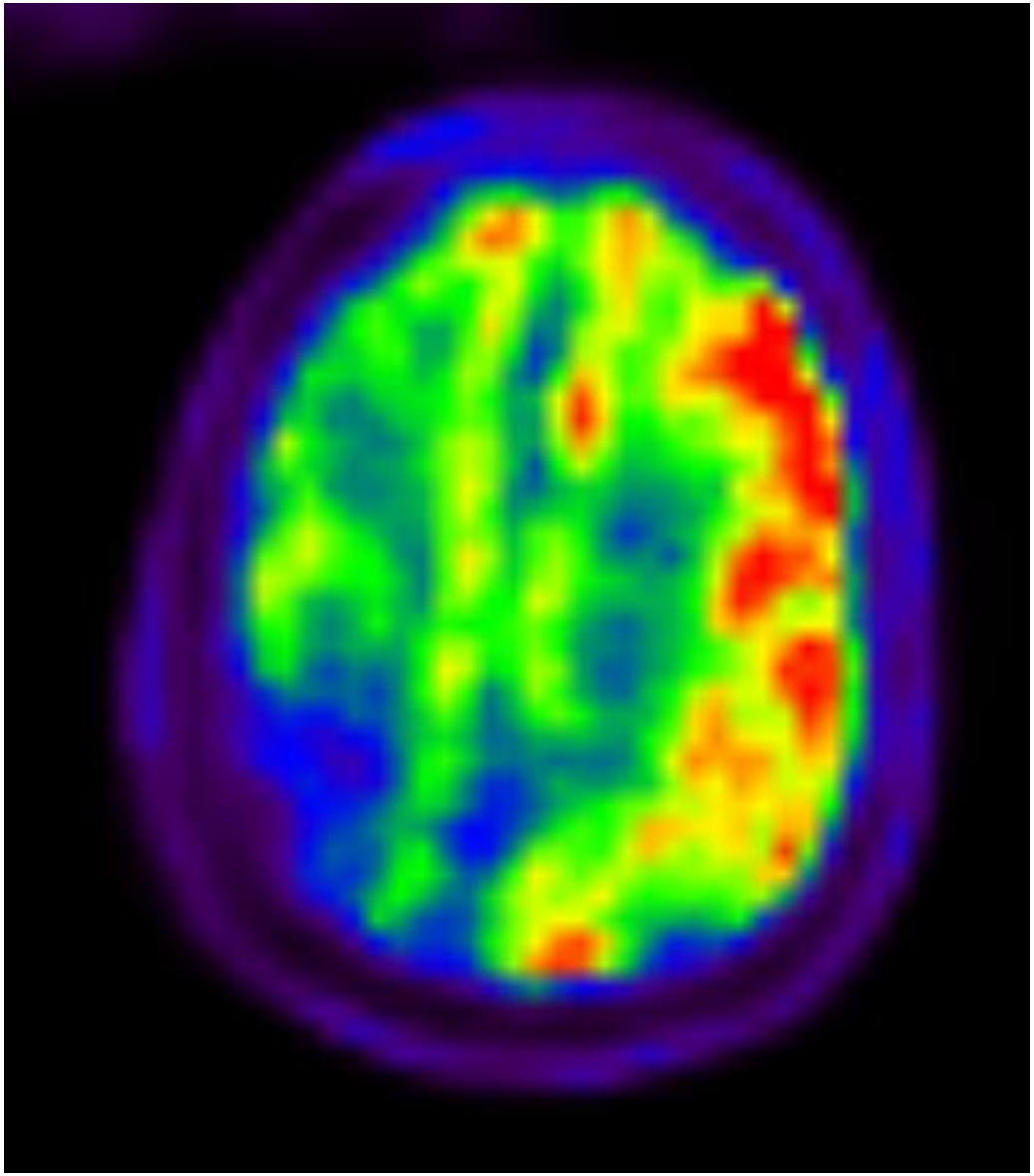
CT-basert attenueringskorreksjon er helt nødvendig for korrekt bildefremstilling av opptak og fordeling av PET-sporstoffet i kroppen……

Ikke-attenuasjonskorrigert

CT-attenuasjonskorrigert



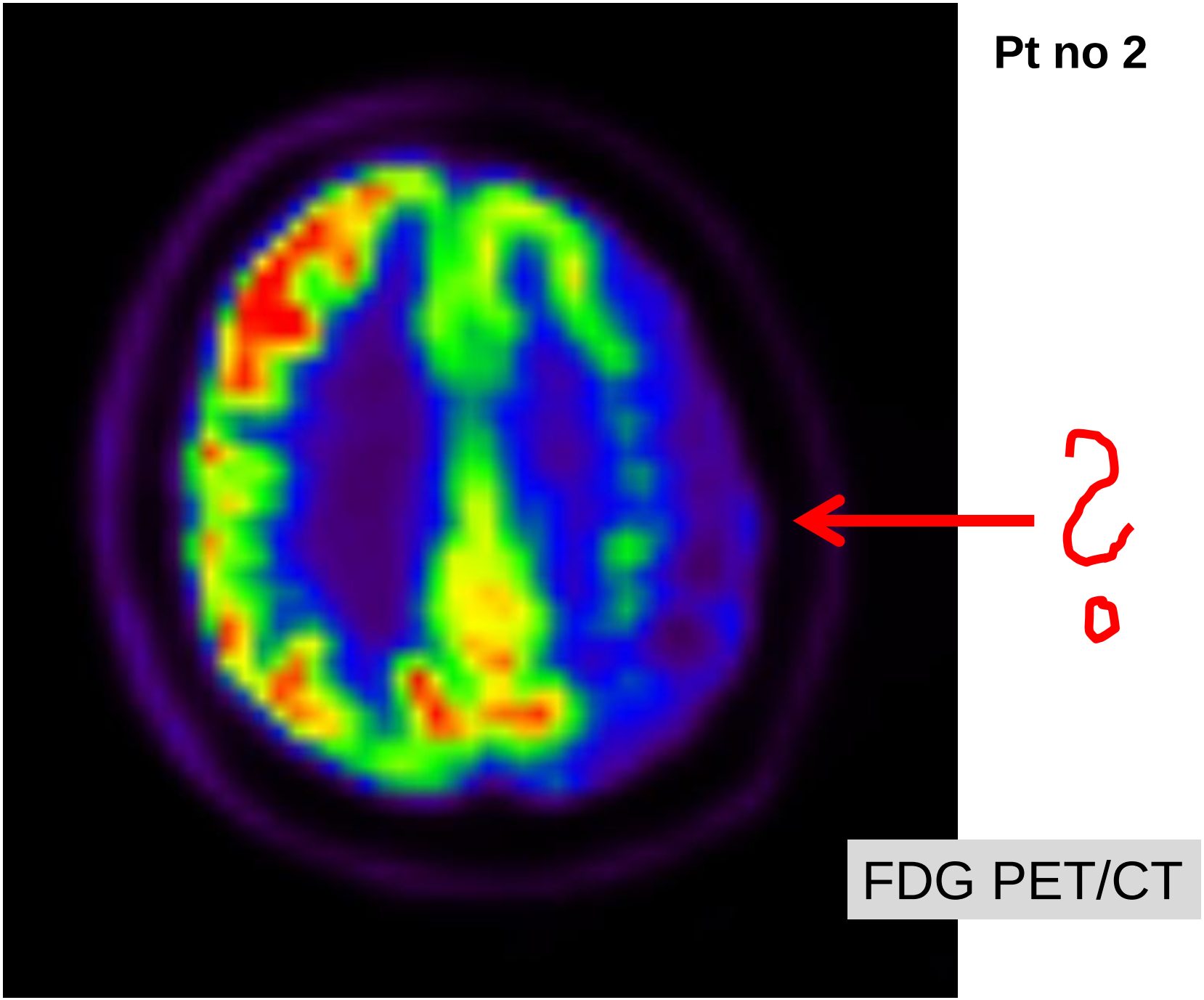
…… men
koregistreringen
MÅ være perfekt, ellers får man **misregistrerings-artefakter**

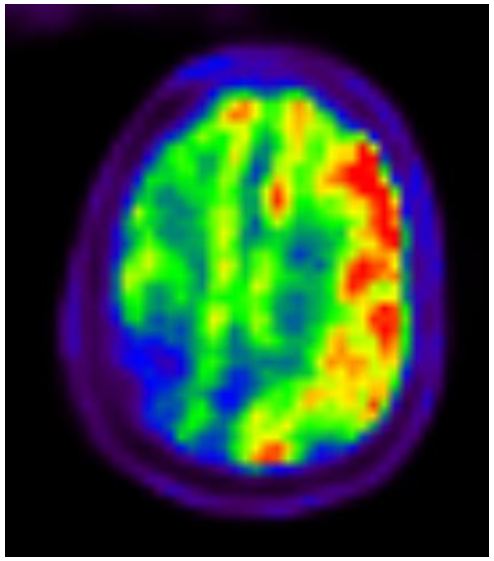


Pt no 1
FDG PET/CT

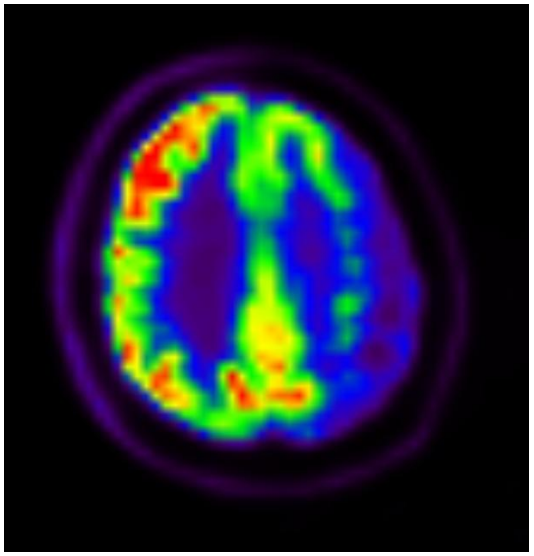
Tilfeldig funn:
Redusert opptak høyre cerebrale hemisfære

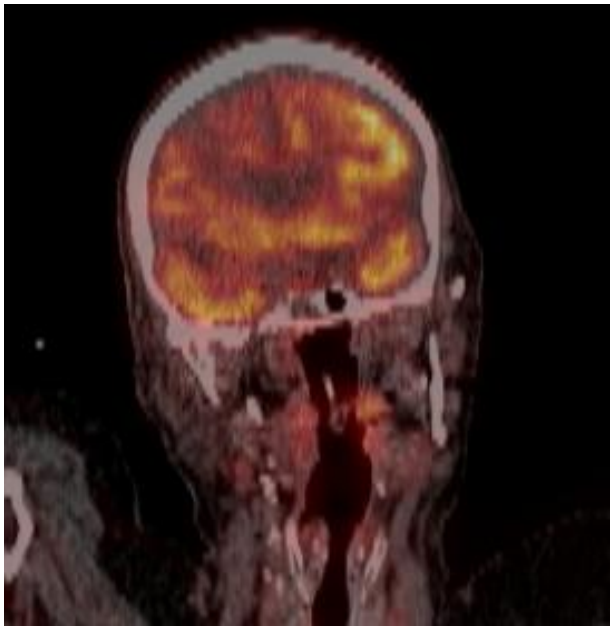
Årsak:
Carotisstenose høyre side


Pt no 2
FDG PET/CT

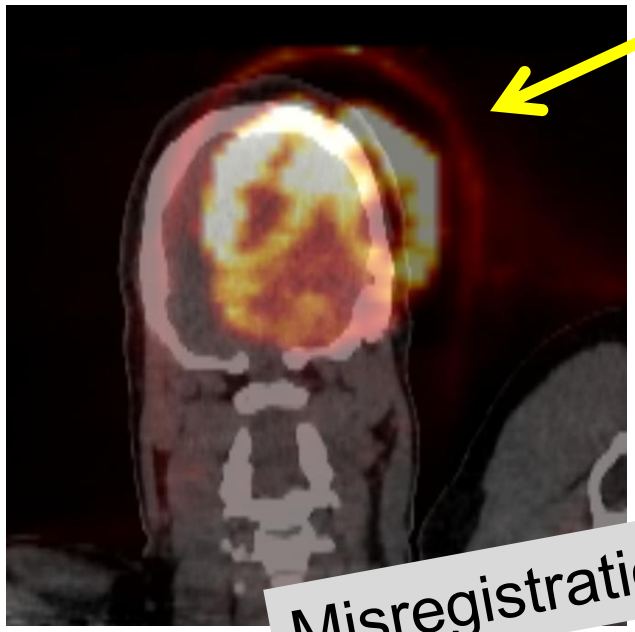


Axial brain
PET





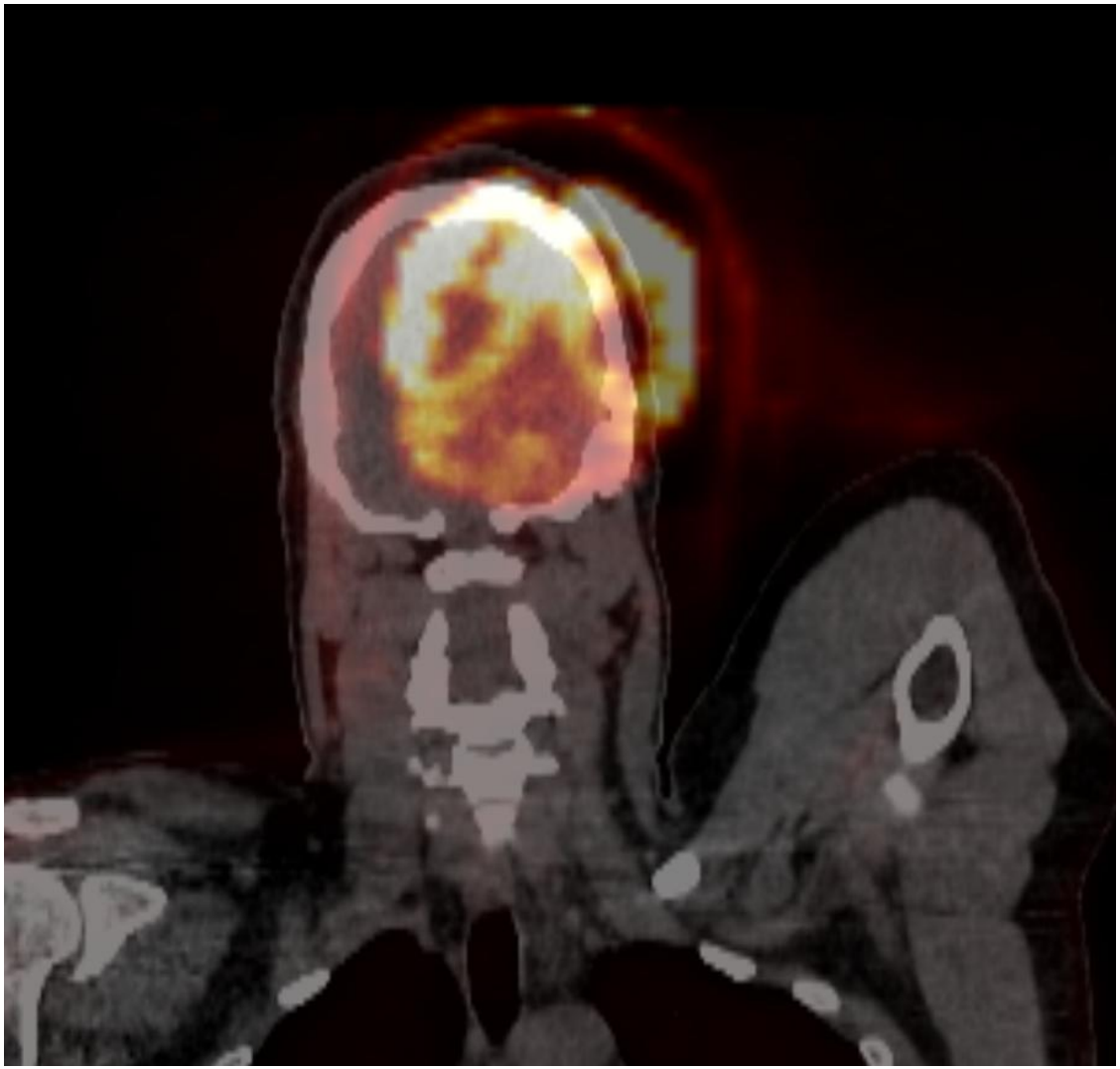
Coronal
PET/CT



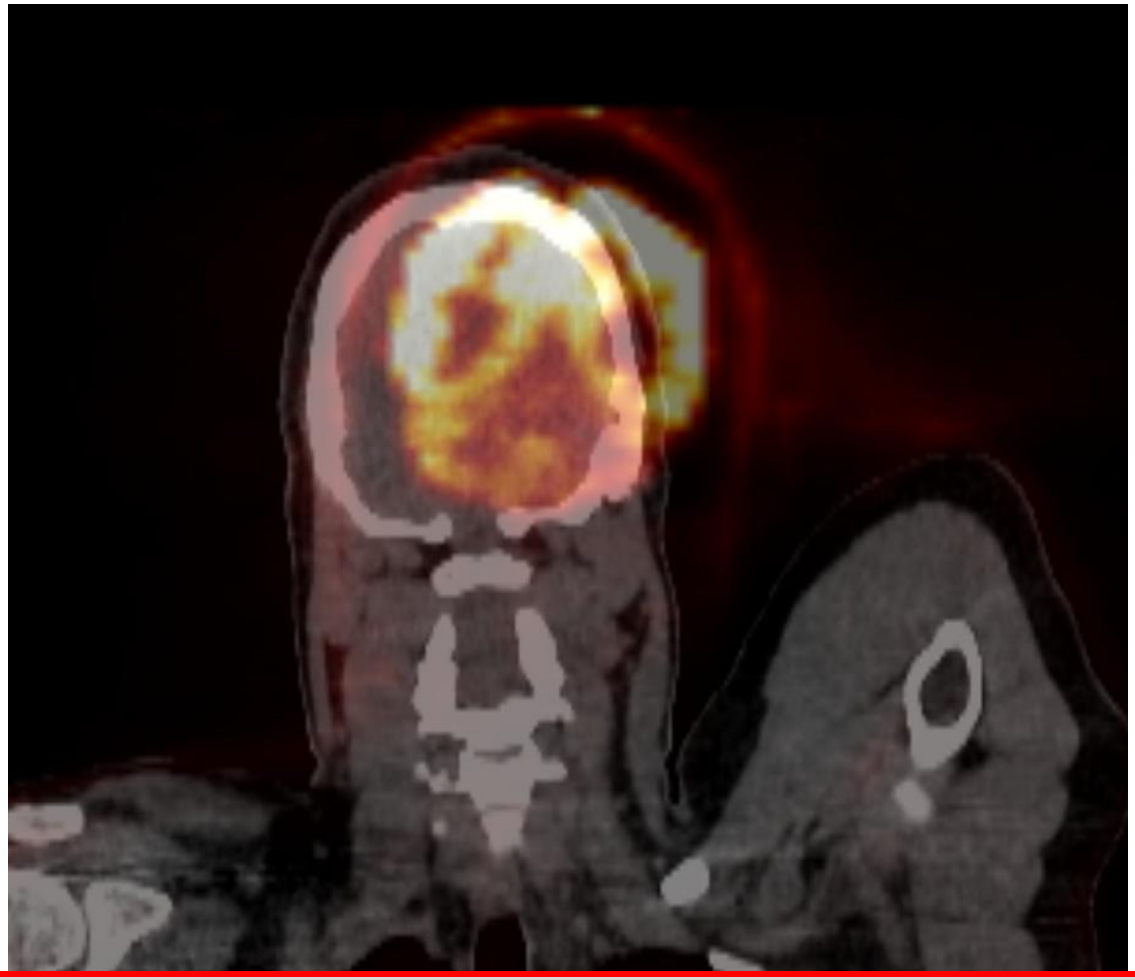
Misregistration !

Pt no 1

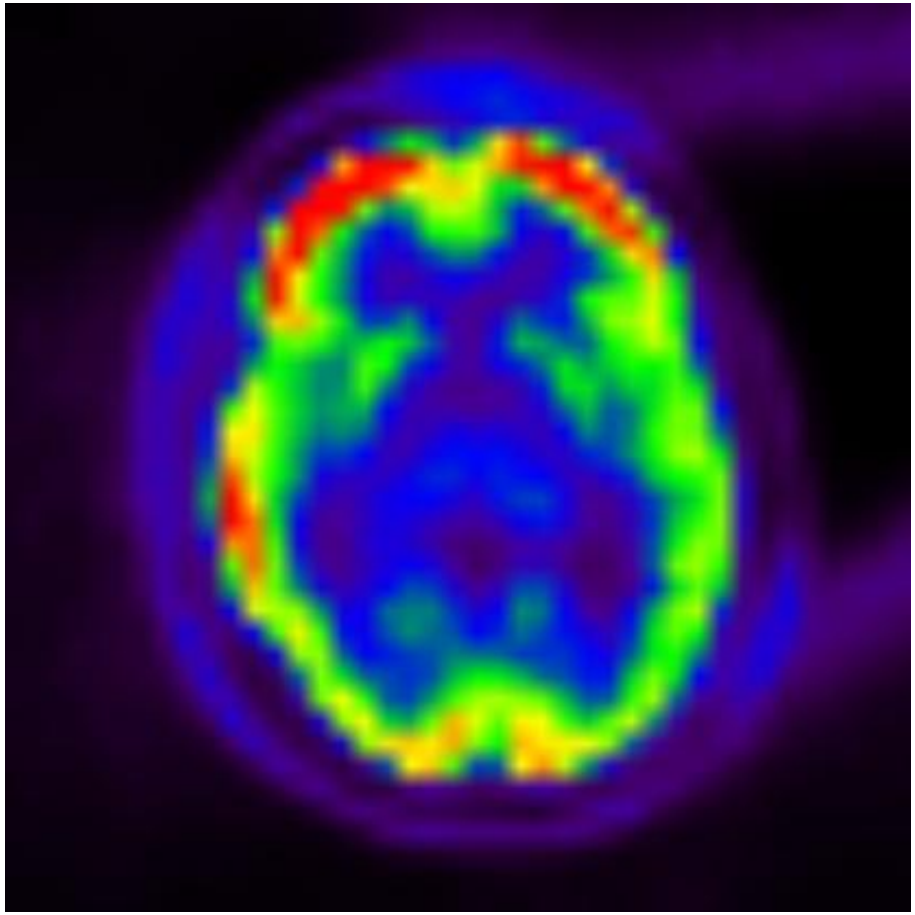
Pt no 2



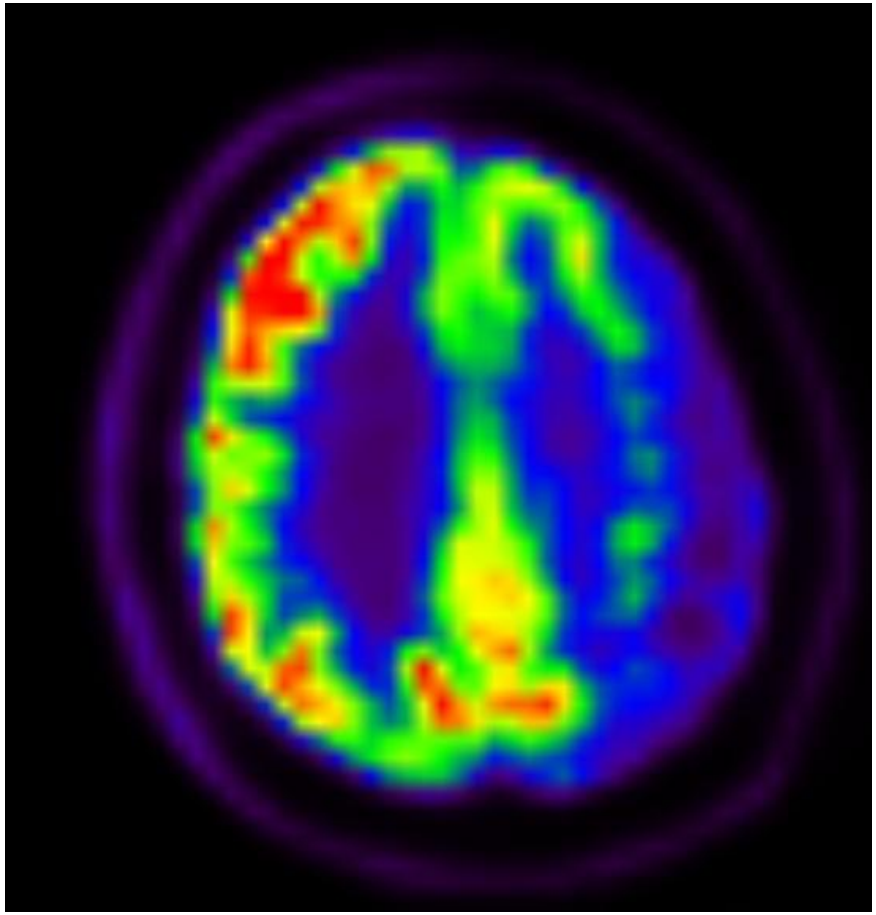
Alvorlig **misregistrering** mellom PET og CT resulterer i feil attenueringskorreksjon



De områder av hjernen som ligger utenfor CT-avbildningen blir *ikke* attenueringskorrigert og fremstår med lavere FDG-opptak

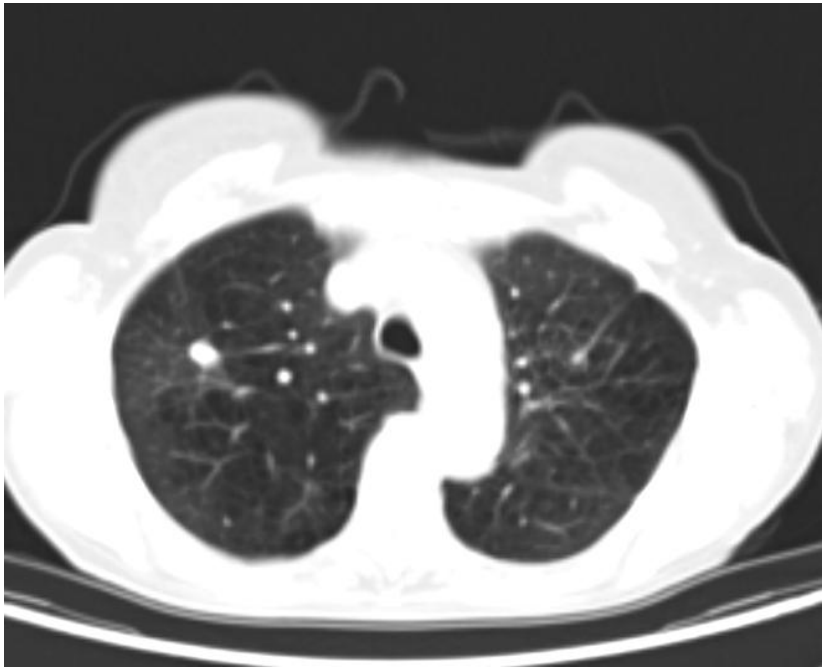


Ikke-attenueringskorrigert:
Symmetrisk kortikalt opptak

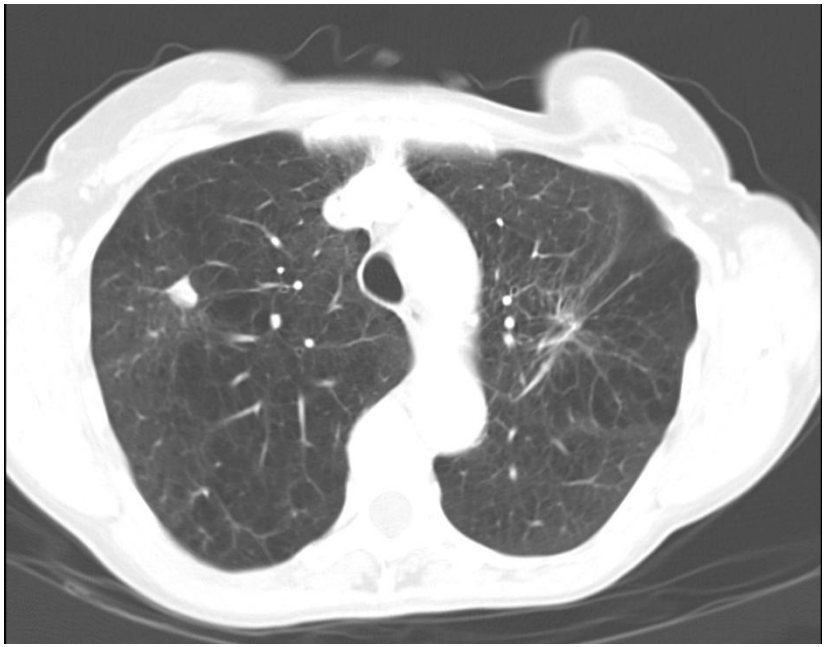


Attenueringskorrigert, men *feilaktig* pga hodebevegelse med misregistrering PET og CT som følge

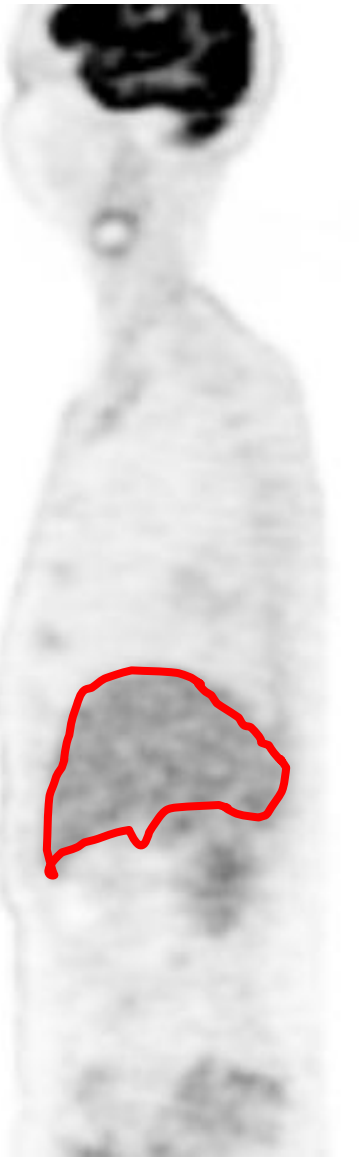
Inspiratorisk breath-hold er optimalt for dCT av thorax og abdomen, men gir betydelig misregistrering mellom PET og CT på PET/CT som resulterer i betydelige bildeartefakter og unøyaktig kvantitering



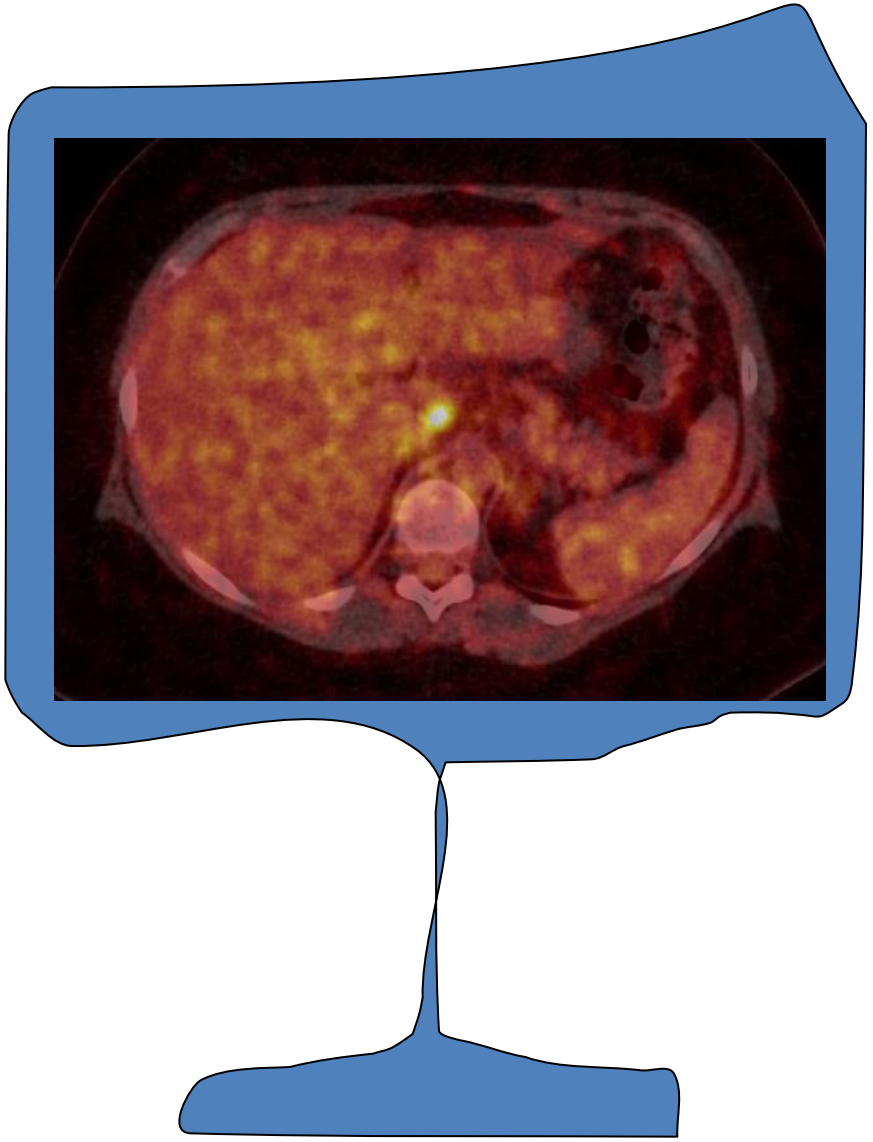
Lavdose CT (PET/CT) under rolig pusting

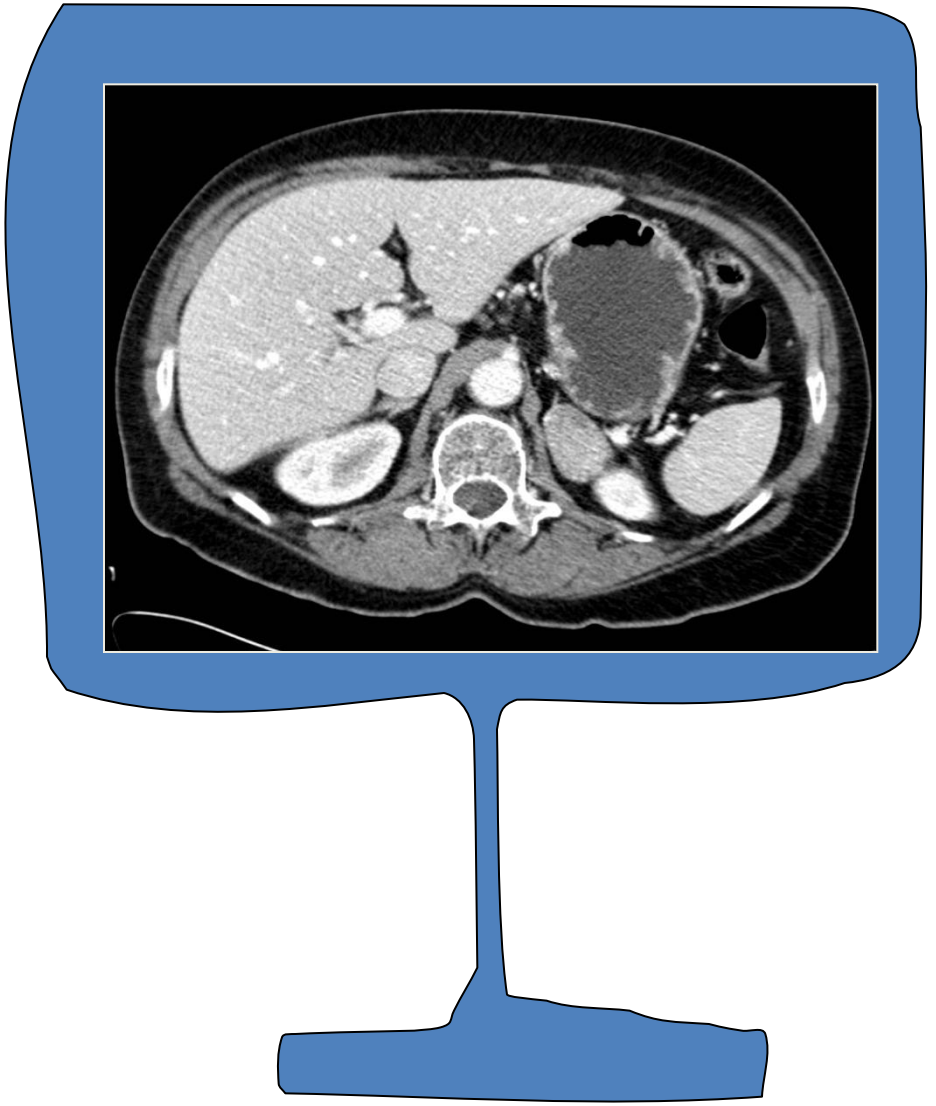


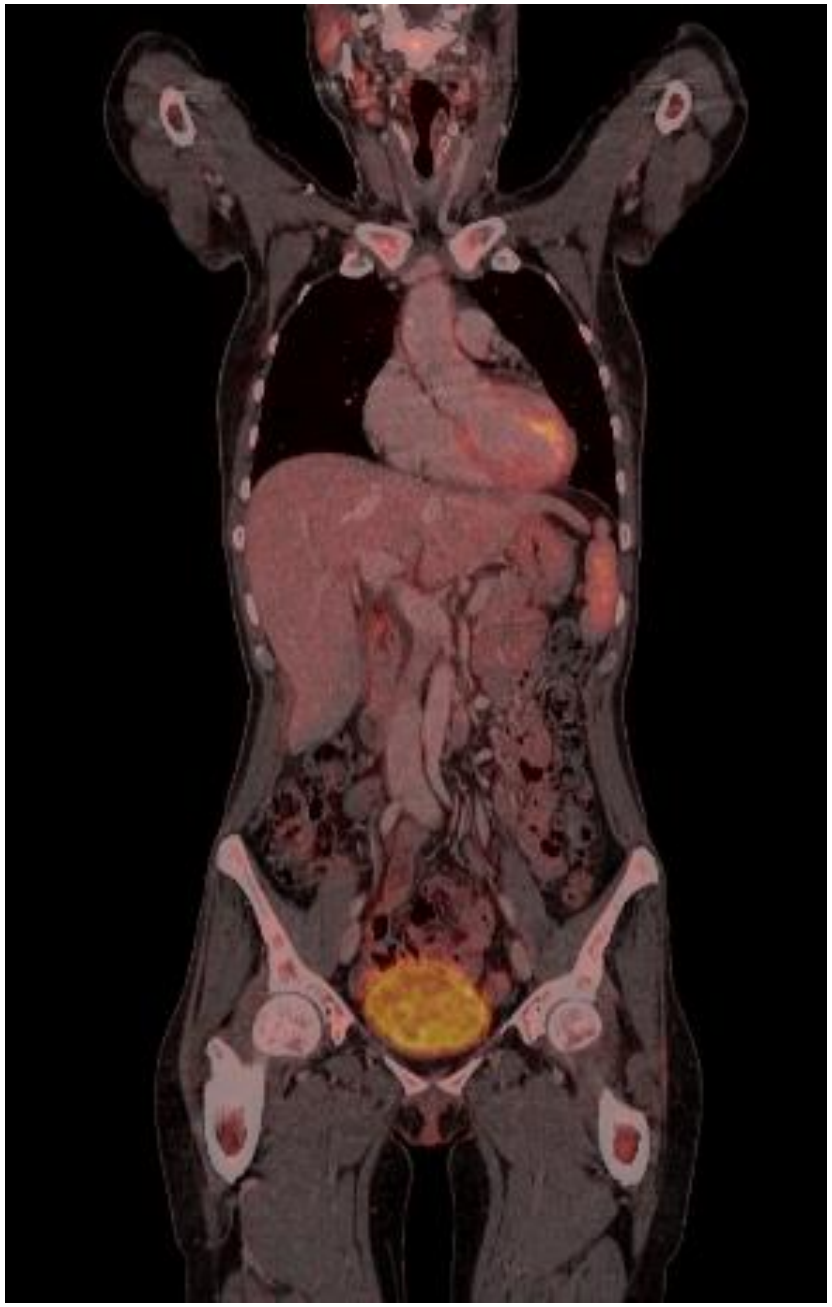
Diagnostisk CT under inspiratorisk breath-hold



sagittal







Københavnmodellen

Is contrast enhanced CT necessary in addition to PET/CT?

…… less clear (Sally Barrington et al Br J Haem 2013).

The use of contrast-enhanced CT did not alter stage nore change in managemnent in 4 series.

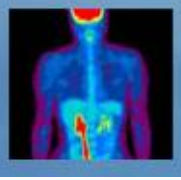
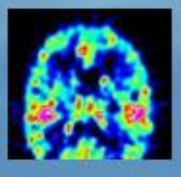
Gollub MJ. J Nucl Med 2007; 48: 1583-91.
Rodríguez-Vigil B et al. J Nucl Med 2006; 47: 1643-1648.
Elstrom R. Annals of Oncol 2008; 19: 1770-73.
Pinilla et al. The Quarterly J Nucl Med Mol Imaging 2011; 55: 567-75.

If a contrast enhanced CT is performed at staging and there is no additional benefits, subsequent examinations should be performed at lower dose

Sally Barrington 2013

NOPR

NATIONAL ONCOLOGIC PET REGISTRY


- Den hyppigste planen, dersom PET ikke hadde vært tilgjengelig, var alternativ bildediagnostikk (oftest CT eller MR). Dette gjaldt **9518** pasienter.

- For disse 9518 pasientene ble etter utført PET ytterligere bildediagnostikk funnet indisert hos kun **552** pasienter (552/9518 = 6%) .

Hillner BE et al. National Oncologic PET Registry.
J Clin Oncol 2008; 26: 2155-61.

Brenner DJ, Hall EJ.

Are Patients Being Irradiated Unnecessarily? Computed Tomography -- An Increasing Source of Radiation Exposure.

:

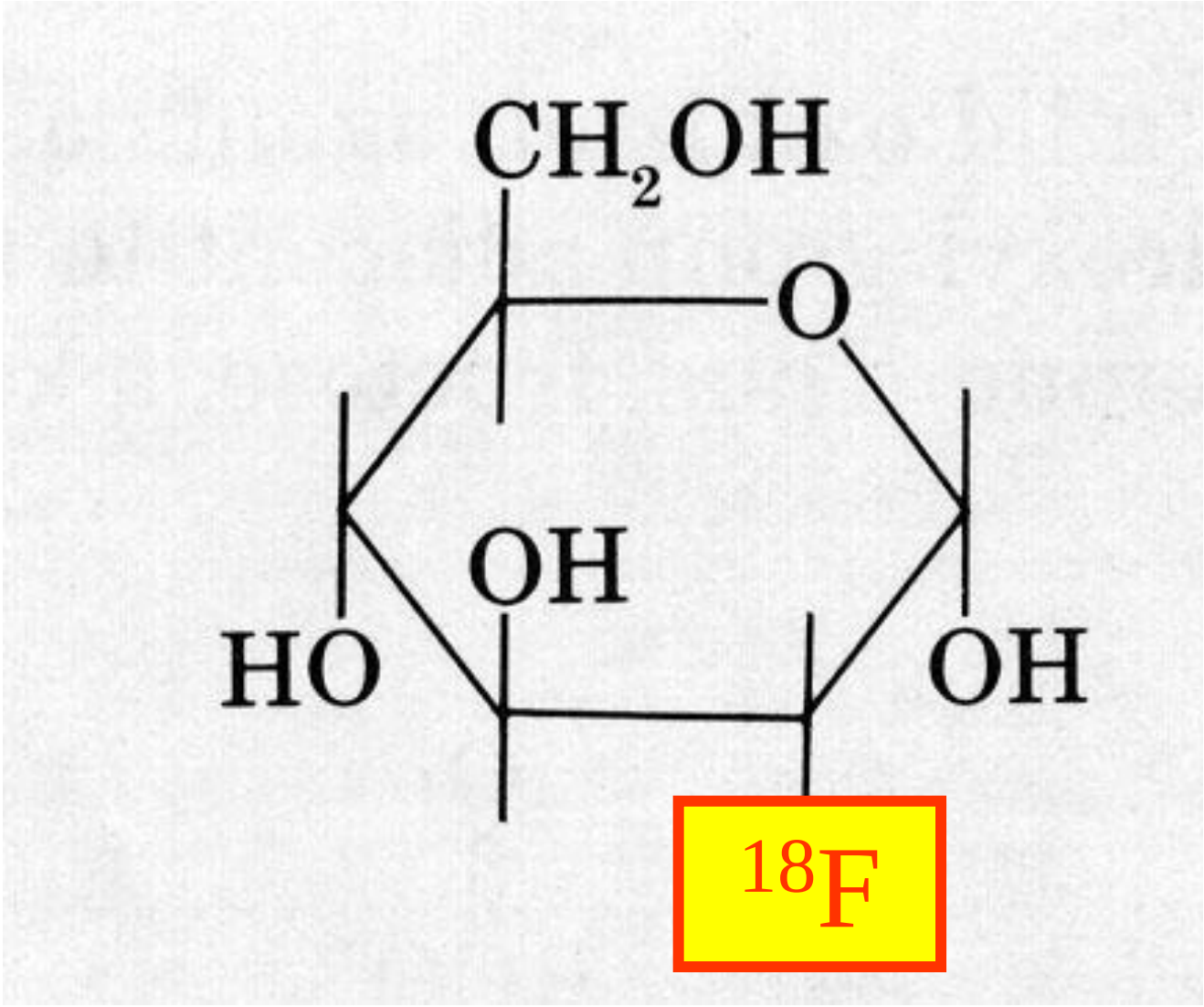
N Engl J Med ***2007***; 357: 2277-2284.

Six percent of all cancers in the United States may be attributable to the radiation from CT studies.

Approximately one-third of all CT scans may not be justified. Twenty million adults and >1 million children are being irradiated unnecessarily.

Brenner DJ, Hall EJ. *N Engl J Med* 2007; 357: 2277-2284

PET-scan i lymfomdiagnostikk og monitorering av behandlingsrespons



2-DEOXY-2-[^{18}F]FLUORO-D-GLUCOSE


FDG


FDG PET/CT

Warburg O, Posener K, Negelein E.

Ueber den Stoffwechsel der Tumoren.

Biochemische Zeitschrift **1924**; 152: 319-344.

Warburg O.

On metabolism of tumors.

Constable,

London, England ***1930***.

Malignant transformation of cells is associated with an increased glycolytic rate.

Otto Heinrich Warburg 1883-1970

glucose

^{18}F-FDG

glucose transport proteins

GLUT-1

HK-2

hexokinase

glucose-6-P

^{18}F-FDG-6-P

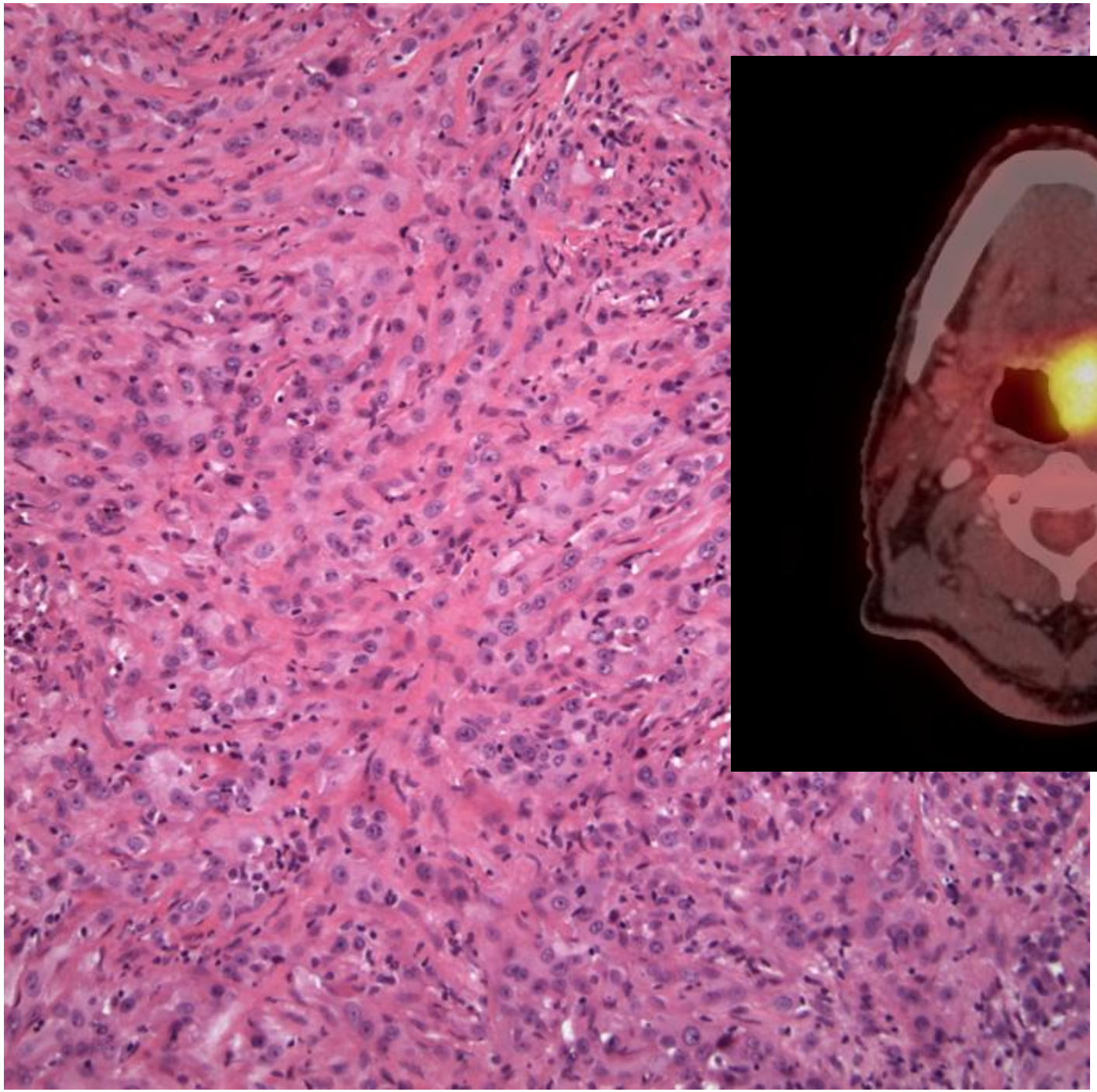
phosphatase

Aerob ned-brytning

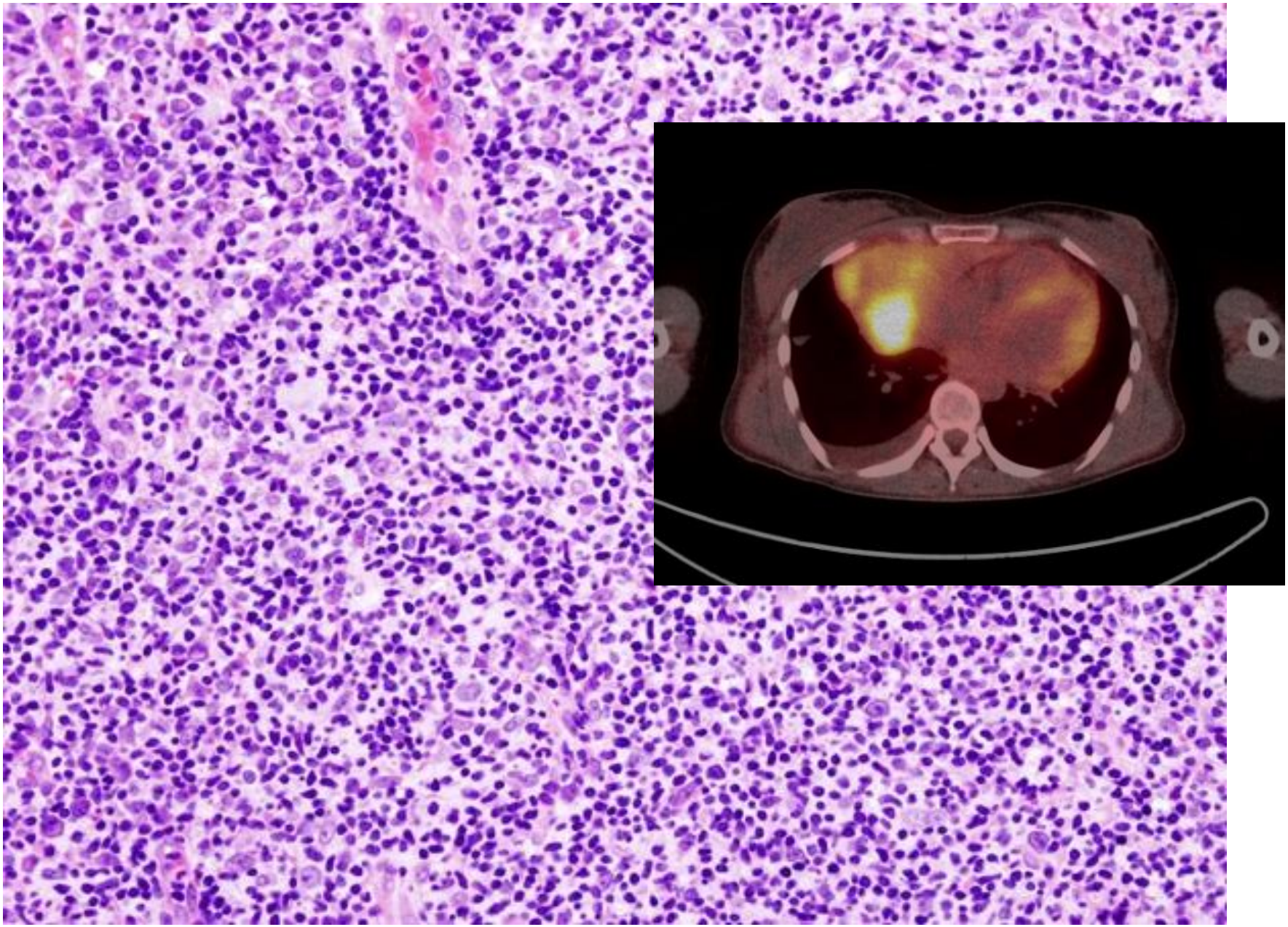
$CO_2 + H_2O$

glycogen

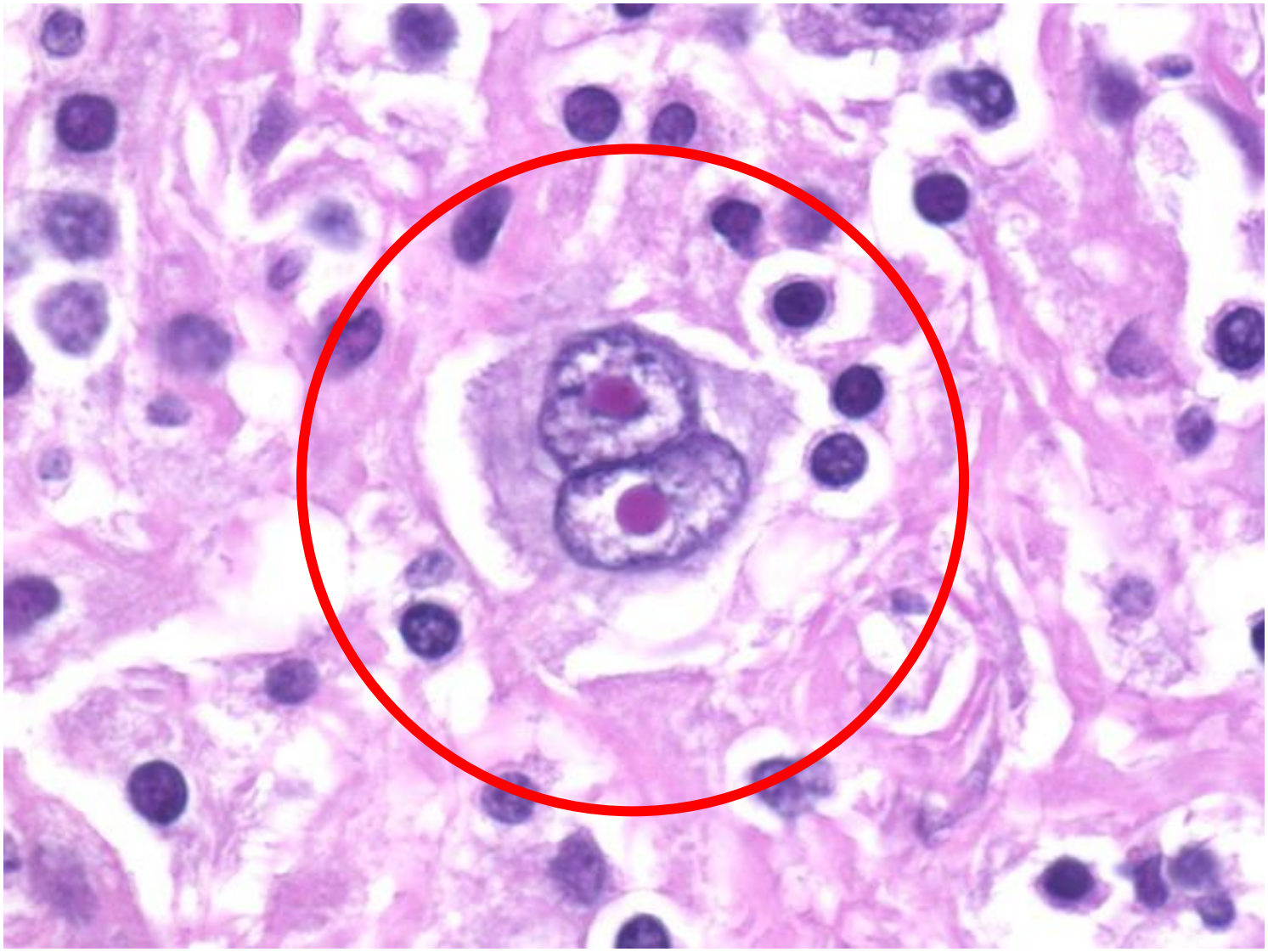
Anaerob degradering



SCC



Diffuse large B-cell lymphoma (DLBCL)



Hodgkin´s lymfom:

Reed Sternberg celler omgitt av reaktive lymfocytter..

Otto Heinrich Warburg 1883-1970

glucose

^{18}F-FDG

glucose transport proteins

GLUT-1

HK-2

hexokinase

glucose-6-P

^{18}F-FDG-6-P

phosphatase

Aerob ned-brytning

$CO_2 + H_2O$

glycogen

Anaerob degradering

Hvorfor fungerer FDG PET/CT for HL?

FDG er en god biomarkør for inflammatoriske celler i tumors microenvironment

Gallamin A. Haematologica 2010: 95: 1046-48.

Aggressive lymfom har vanligvis meget høyt FDG-opptak og høyere enn indolente lymfomer : **SUVmax** ofte høyere enn cerebral cortex (=12)

Indolente lymfomer har generelt lavere FDG-opptak enn cerebral cortex

Schoder et al J Clin Oncol 2005: 23: 4643-51.

God korrelasjon **SUVmax** og **Ki67** index.

Watanabe et al Leukemia and lymphoma 2010: 51: 279-83.

Aggressive lymfom har vanligvis meget høyt FDG-opptak og høyere enn indolente lymfomer : SUVmax ofte høyere enn cerebral cortex (>13)

Indolente lymfomer har generelt lavere FDG-opptak enn cerebral cortex <10

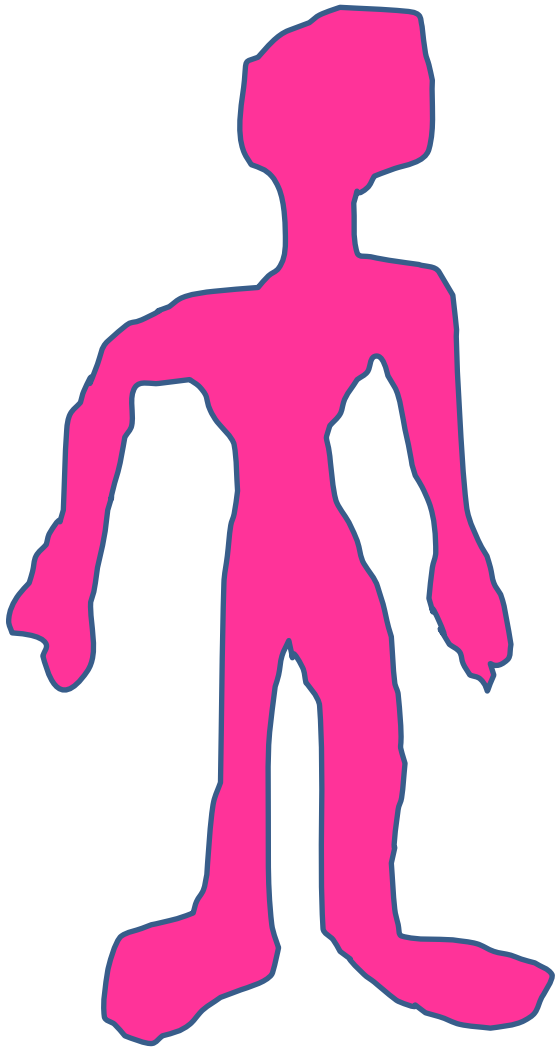
Schoder et al J Clin Oncol 2005: 23: 4643-51.

God korrelasjon **SUVmax** og Ki67 index.

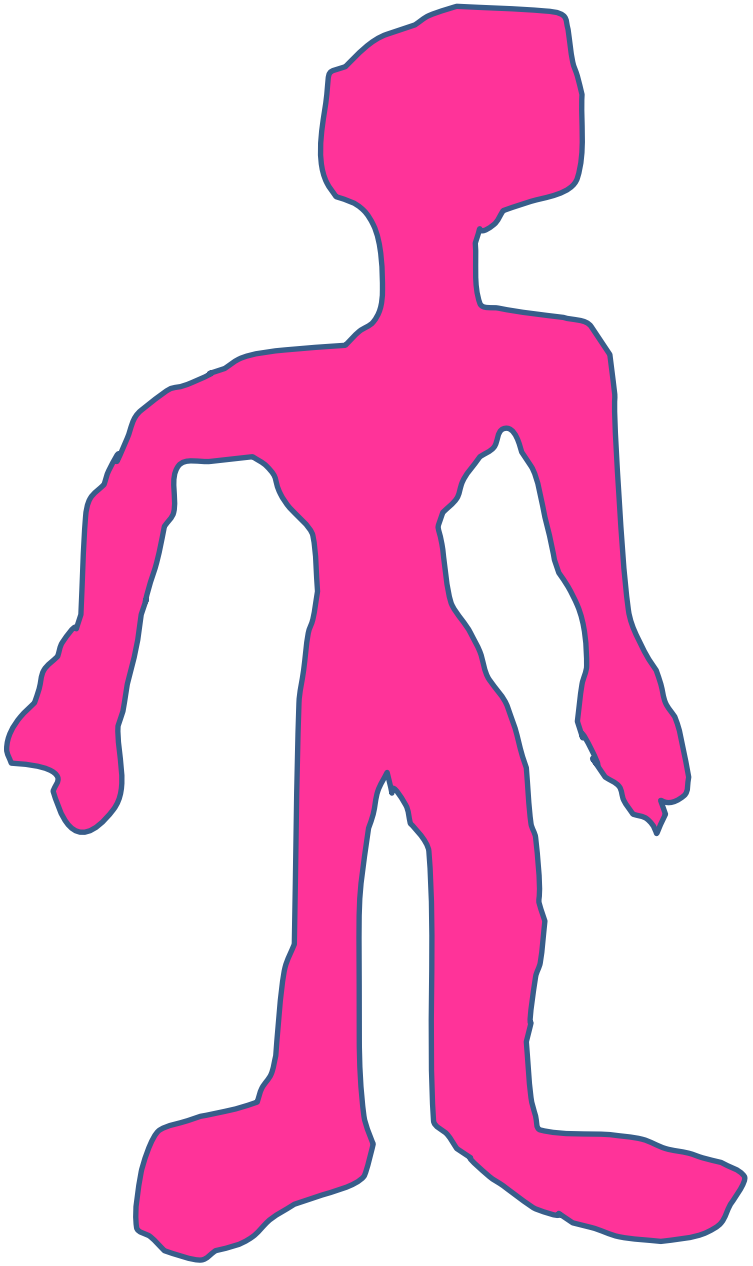
Watanabe et al Leukemia and lymphoma 2010: 51: 279-83.

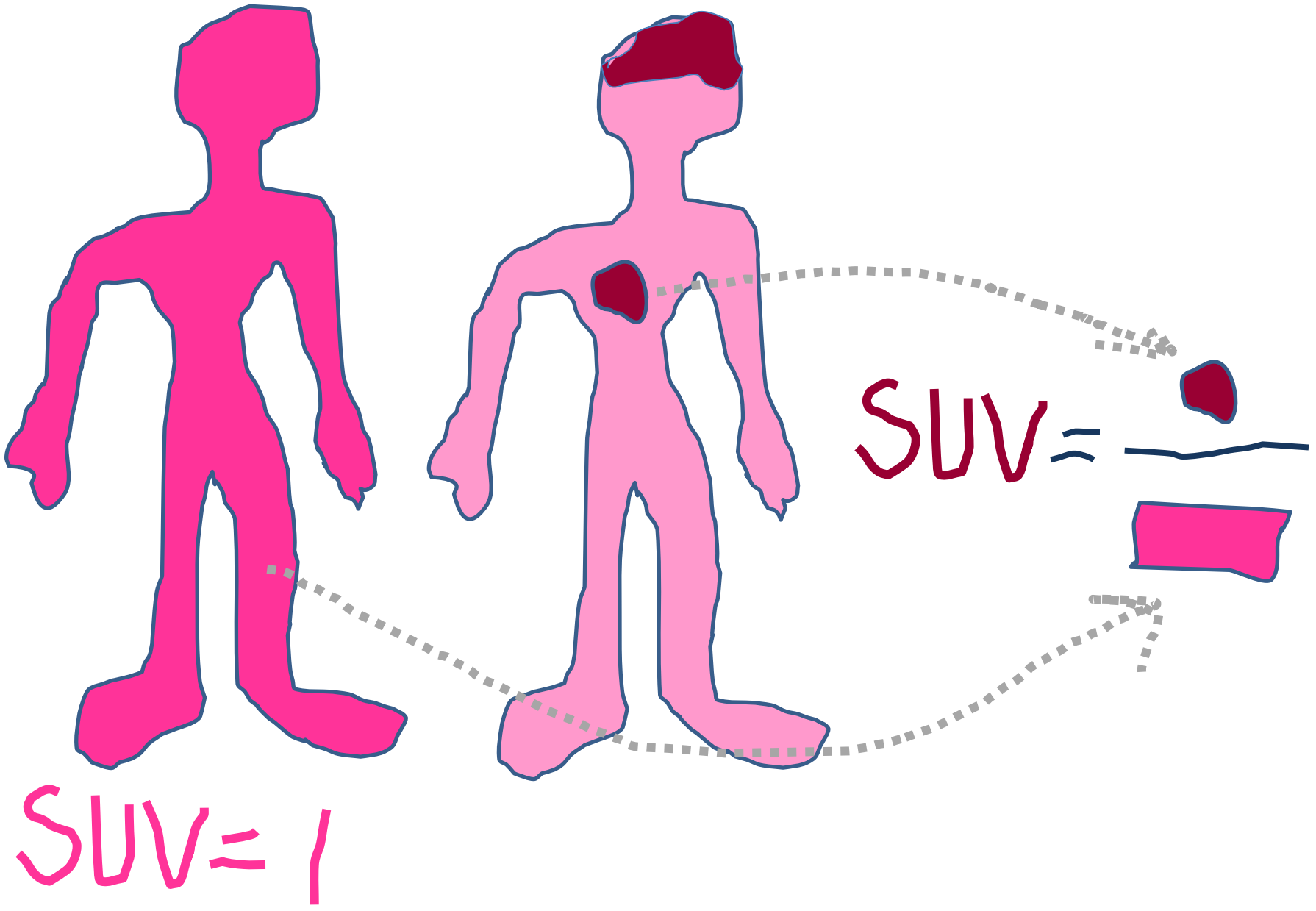
Standardized **U**ptake **V**alue

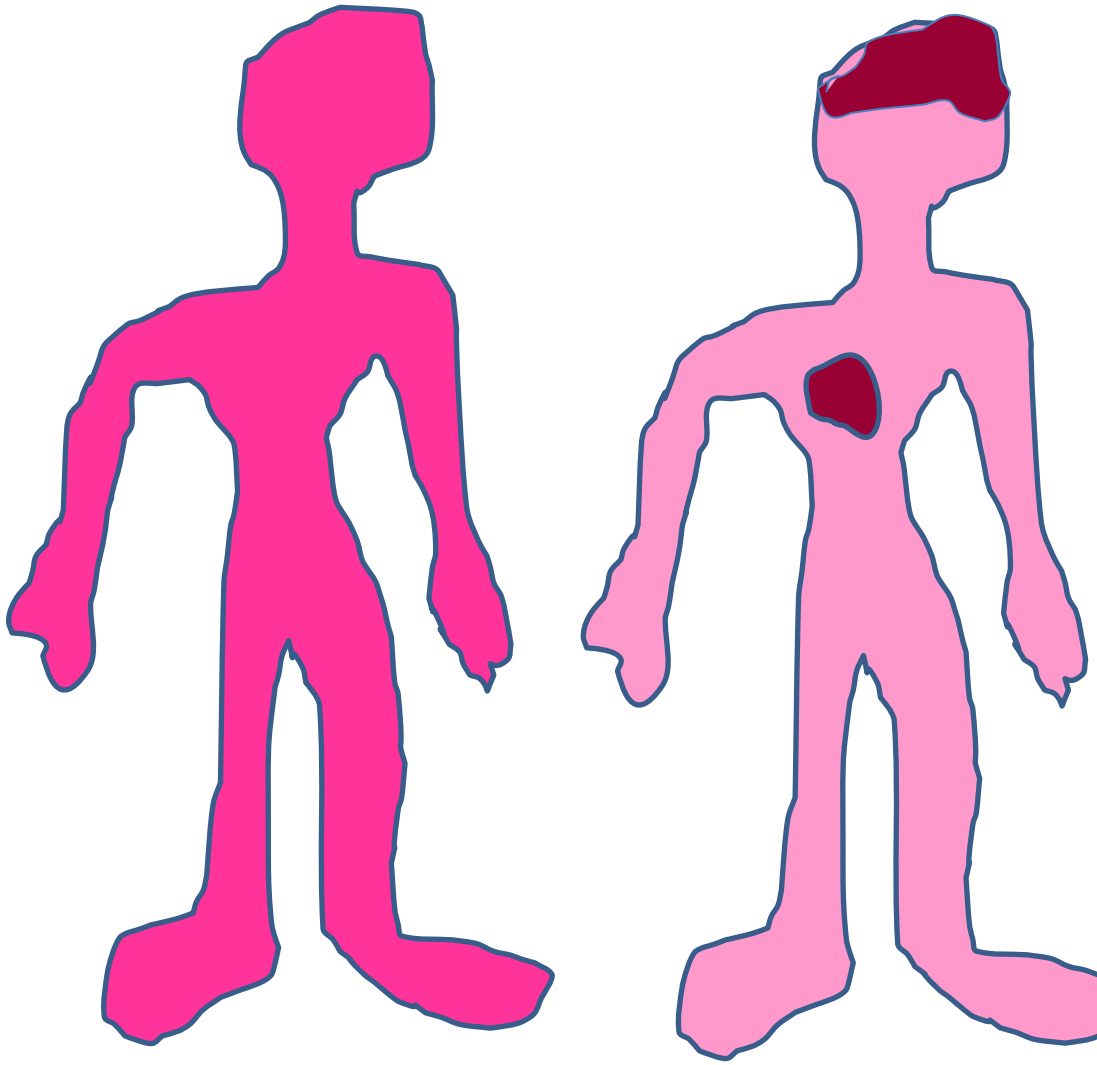
$$SUV = \frac{\text{Aktivitetskonsentrasjon i vevet (kBq/g)}}{\frac{\text{Decay-korrigert injisert aktivitet (kBq)}}{\text{Kroppsvekt (g)}}}$$



SUV= 1




SUV = 1
SUV =



SUV= 1

Ved FDG PET har:

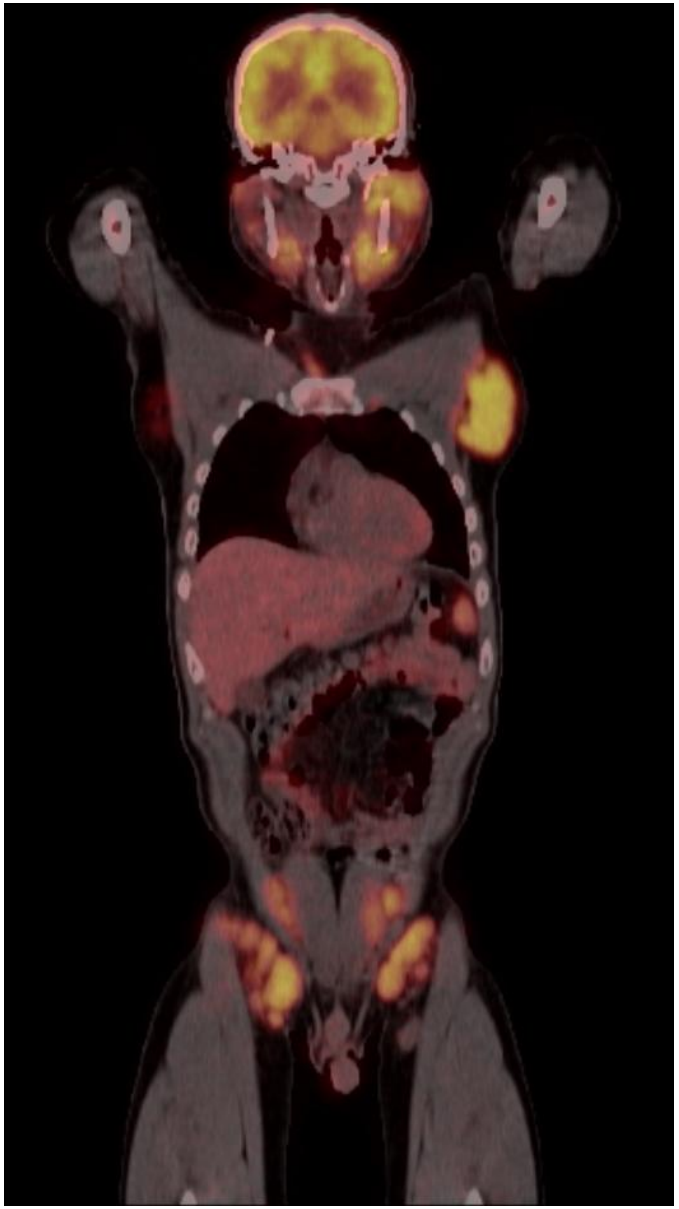
blod SUVmax=2
lever SUVmax=3

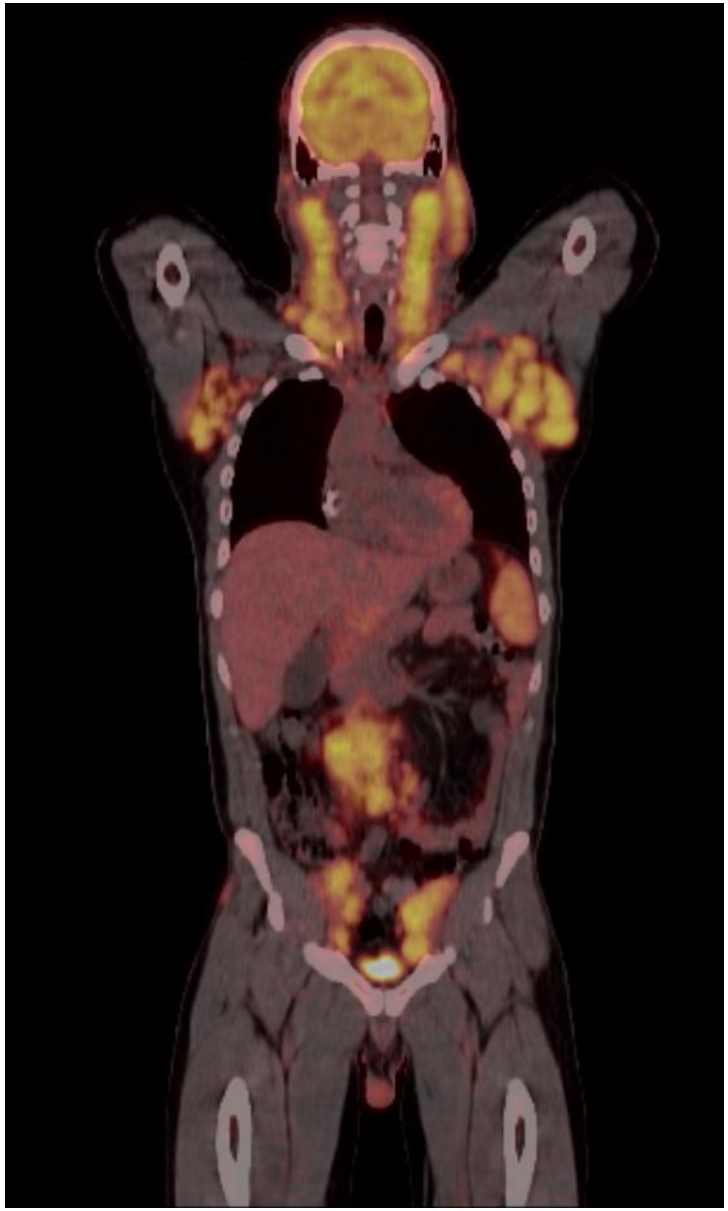
hjernebark SUVmax=12

maligne tumores
SUVmax=4 -15

Høyt **FDG-opptak** også ved **Burkitt** (Karantanis et al), **Mantle celle lymfom** (MCL) og aggressive T-cellelymfomer.

Mer variabelt **FDG-opptak** i **småcellet lymfocytisk lymfom** (50-83%), **ekstranodal marginalsone lymfom** (54-67%), i lymfomer med affeksjon av **hud,** samt i **KLL**.





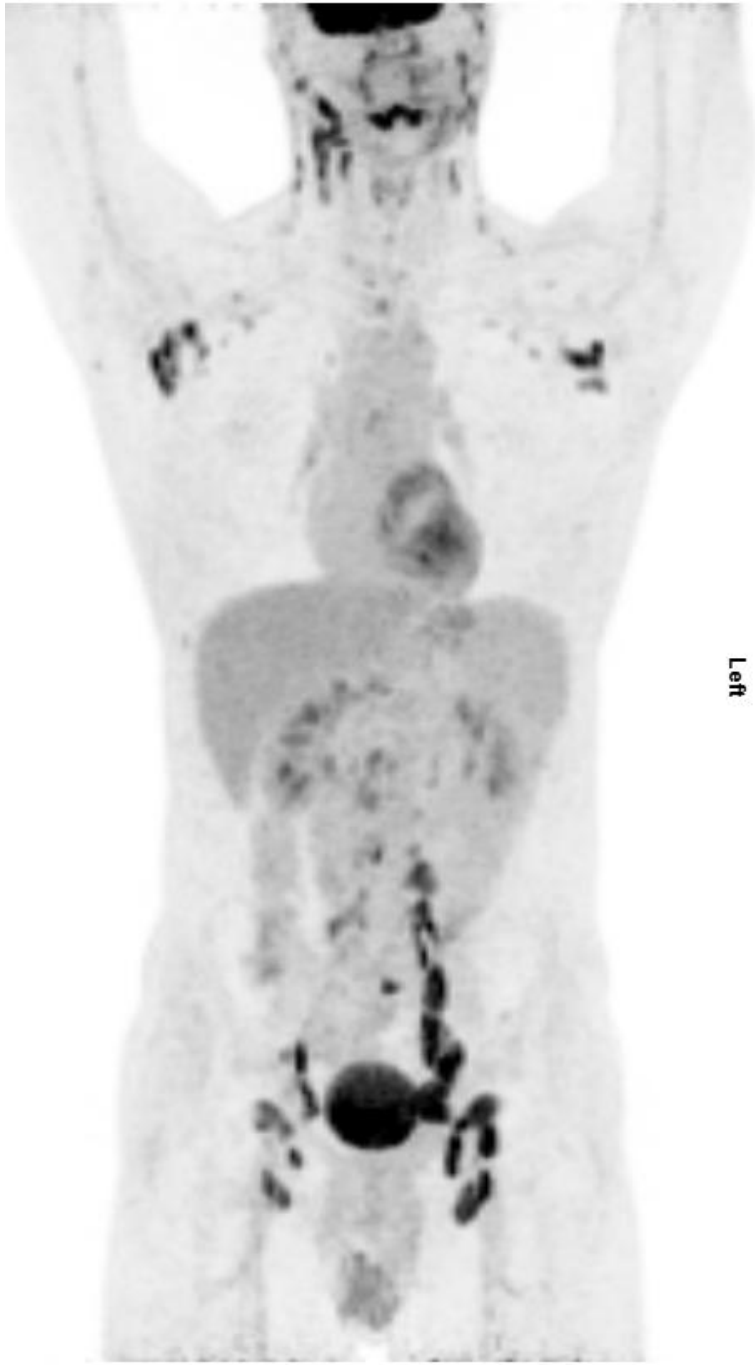
M 22
HL (St IV)

FDG
PET-CT:
Baseline
(initial staging)

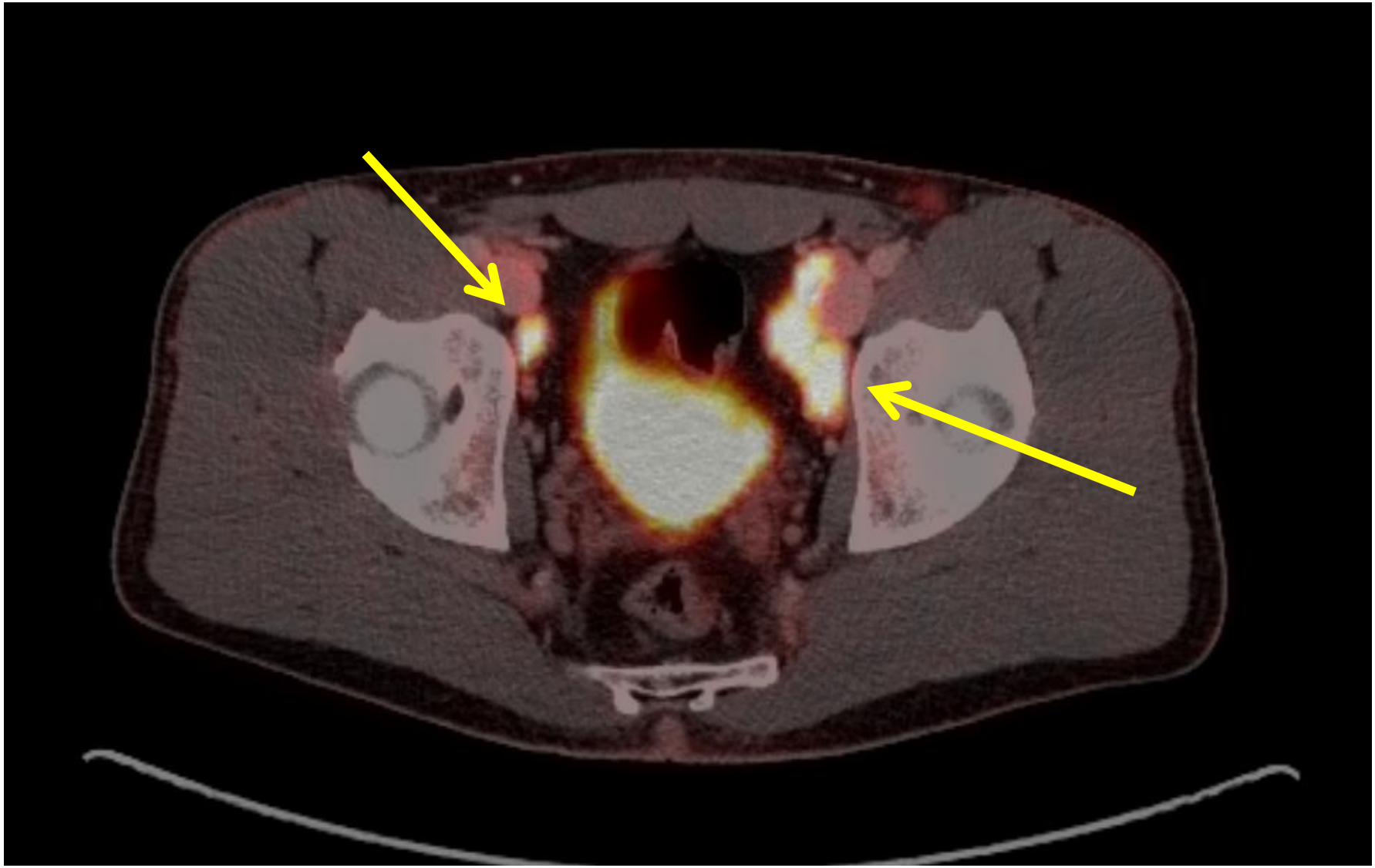
Utbredelse:

LN hals
LN aksiller
milt
LN abdomen
LN bekken
LN lysker

Koronale snitt ant => post

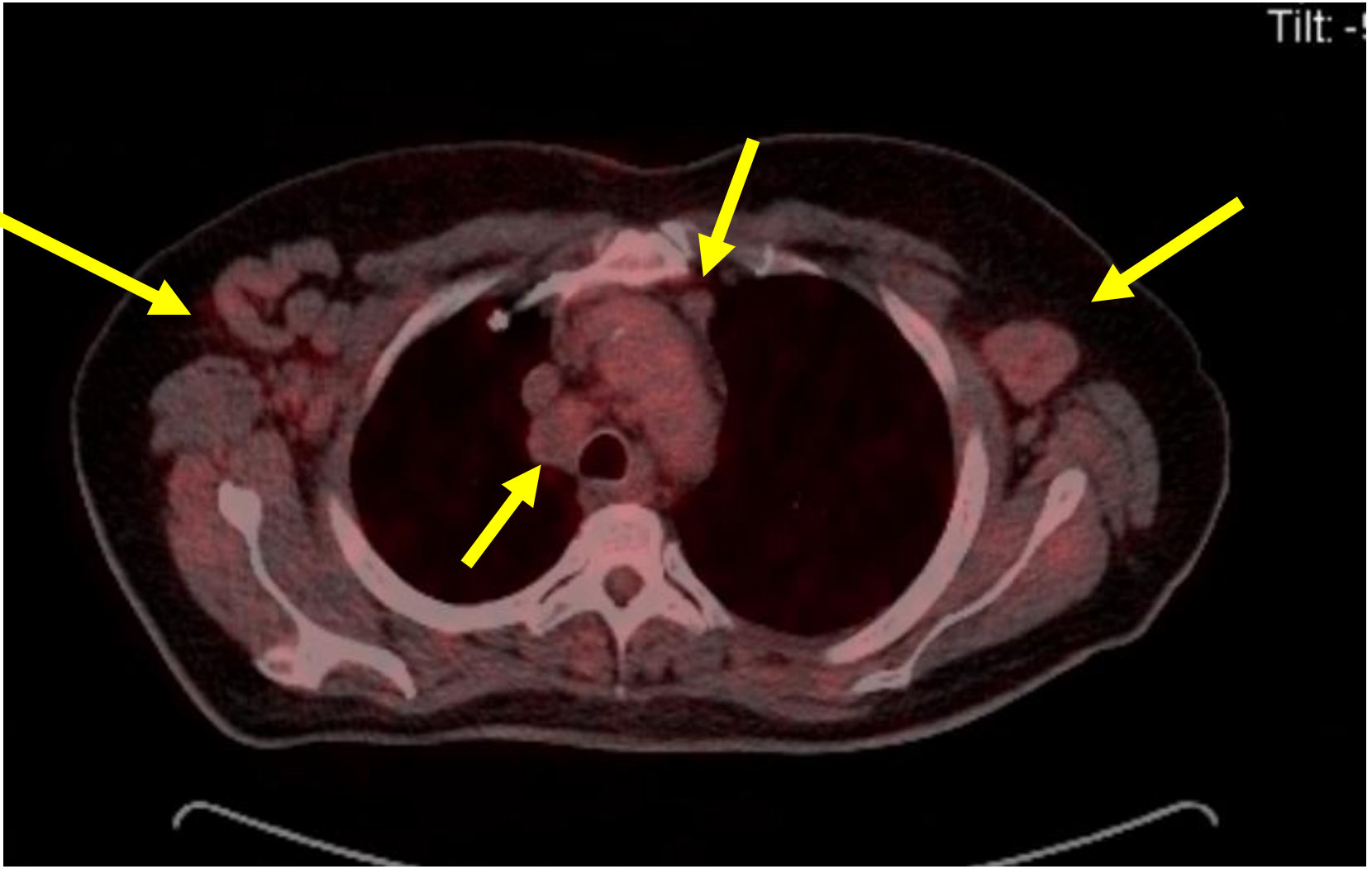


M 33 år
FL



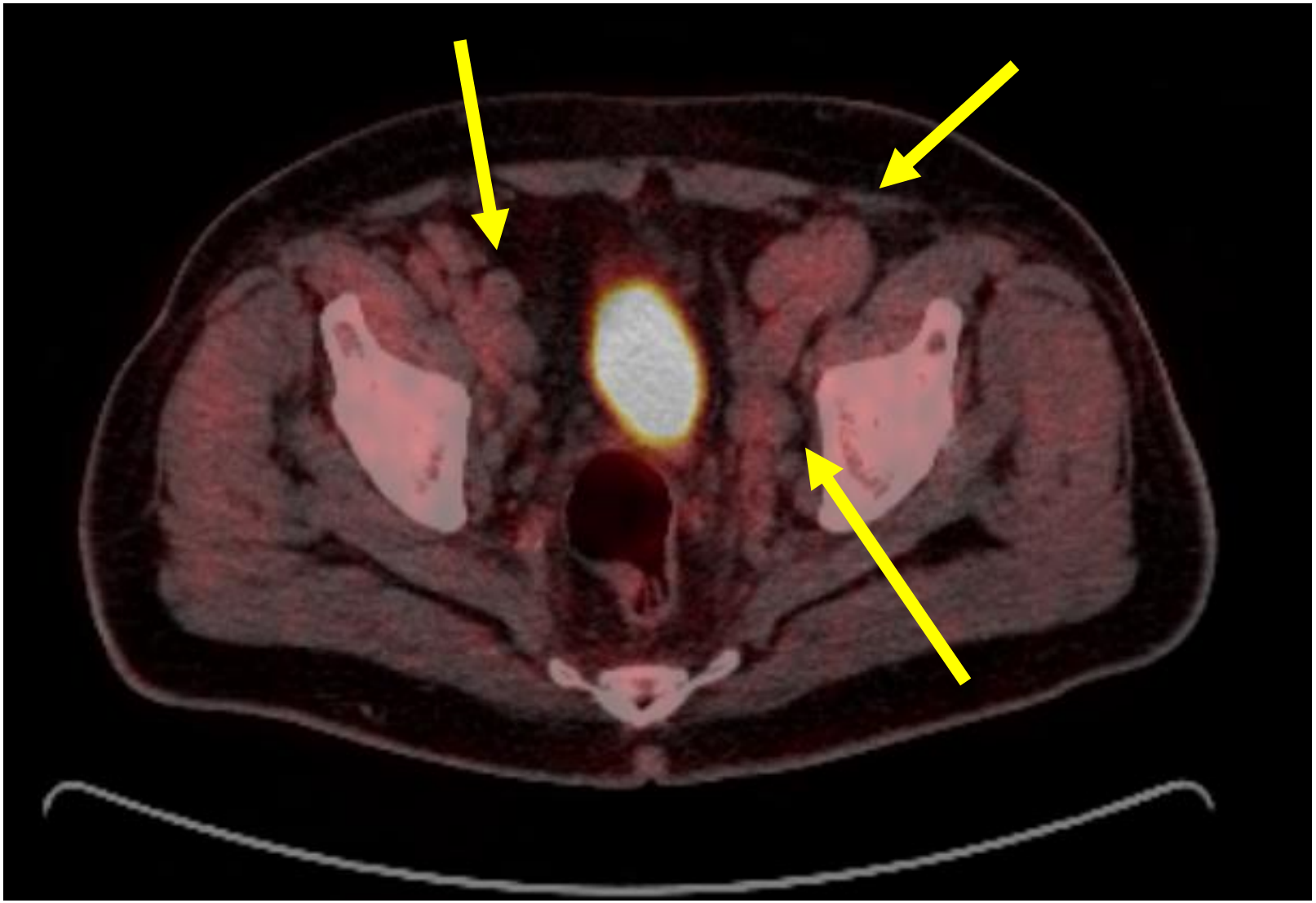
M 68

Lavgradig follikulært lymfom

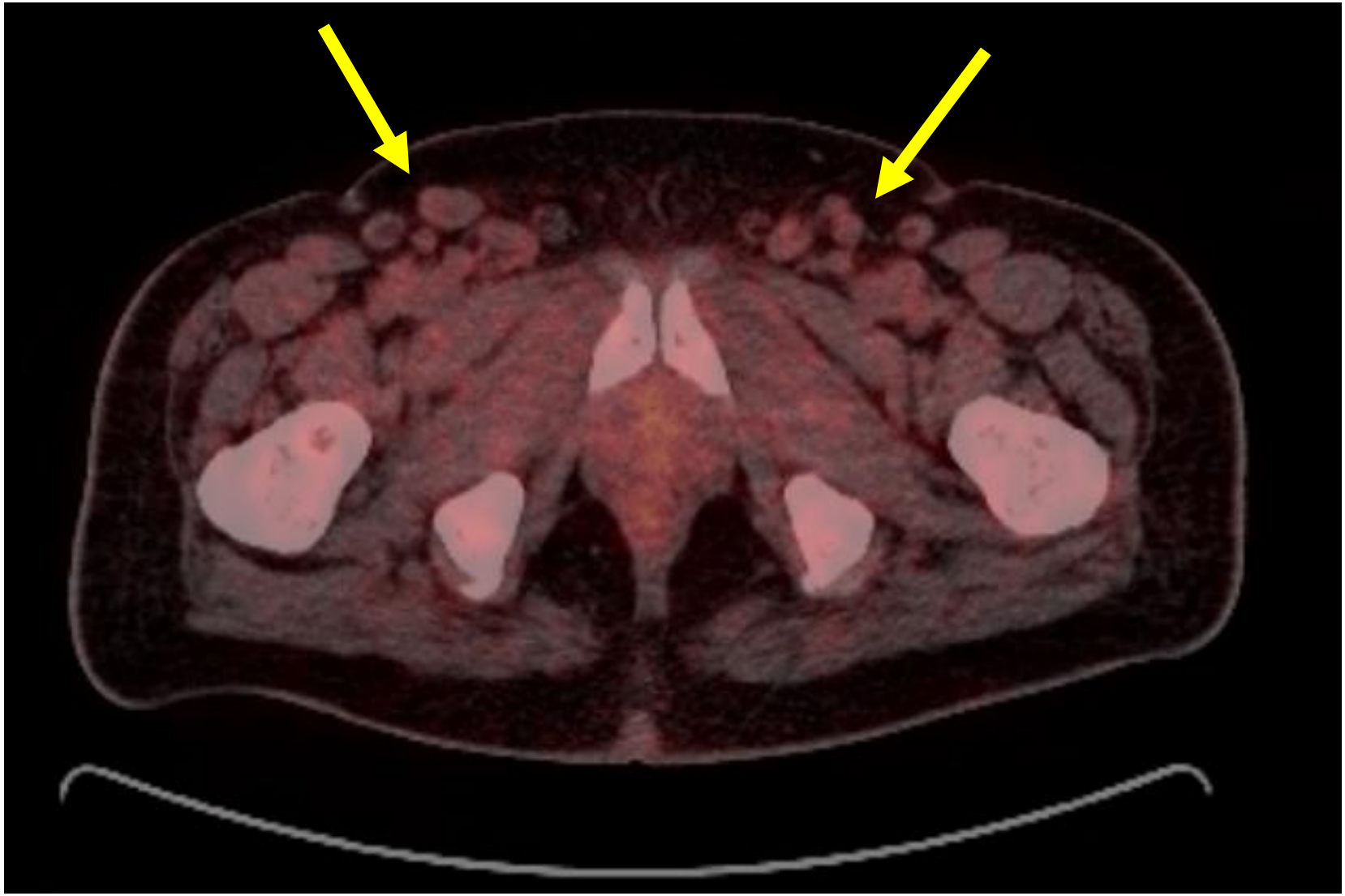


Lavgradig lymfom

Lavgradig lymfom



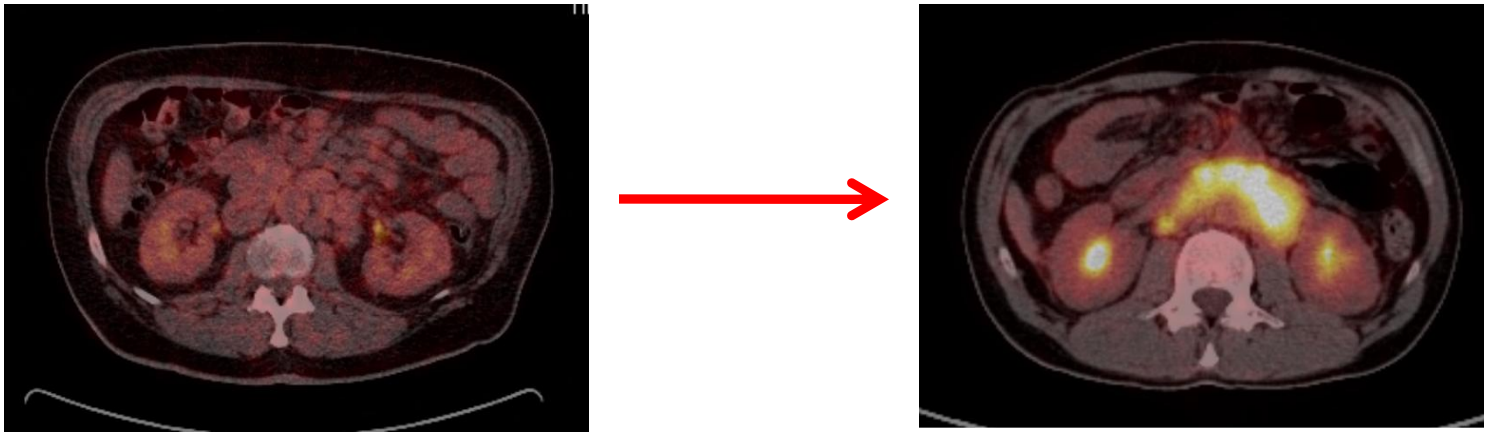
Lavgradig lymfom

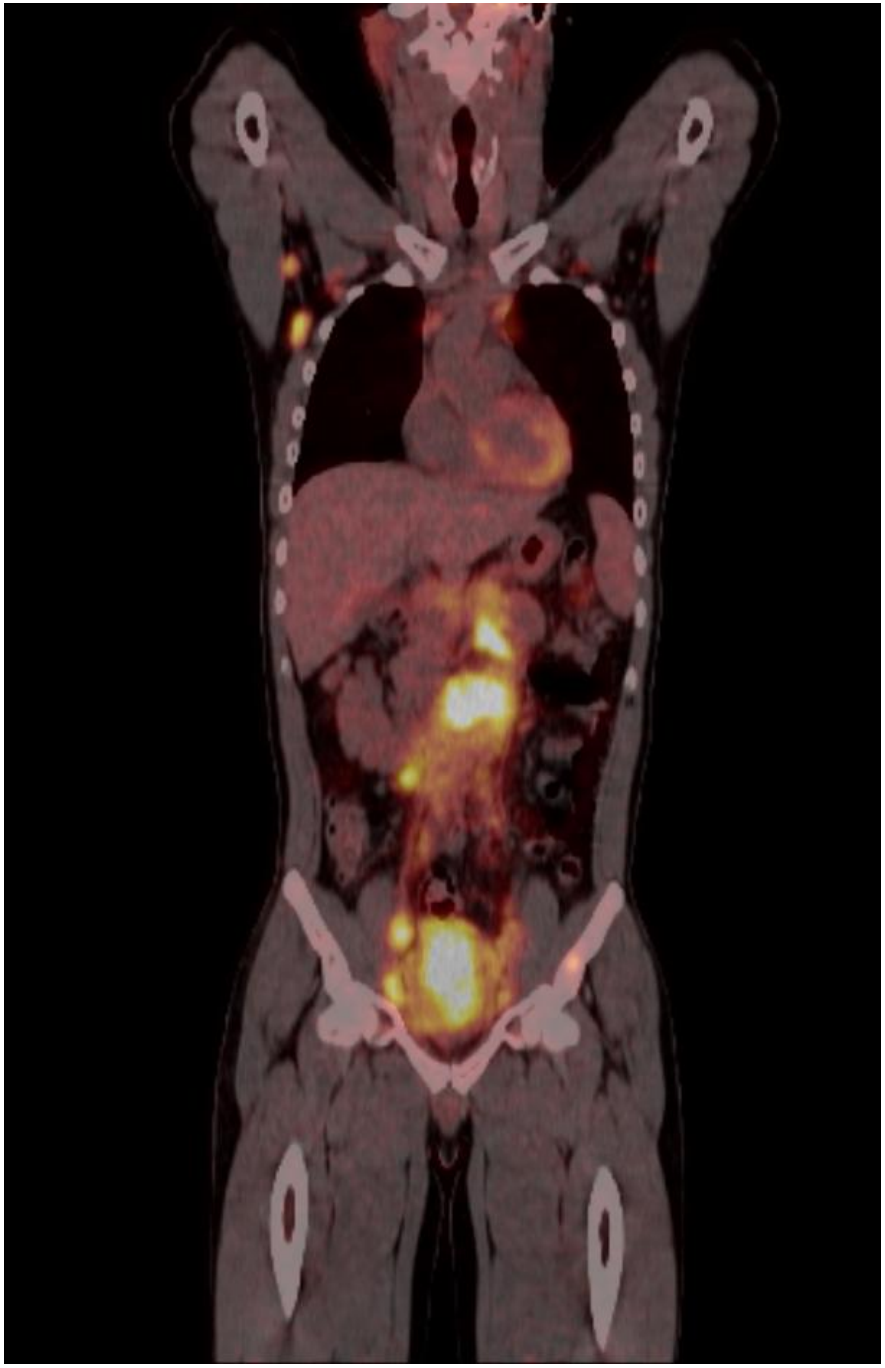


Lavgradig lymfom

Lavgradige lymfomer **kan transformere** til høygradige.

FDG **PET-CT** kan være nyttig for avsløre transformering og egnet angi biosisted



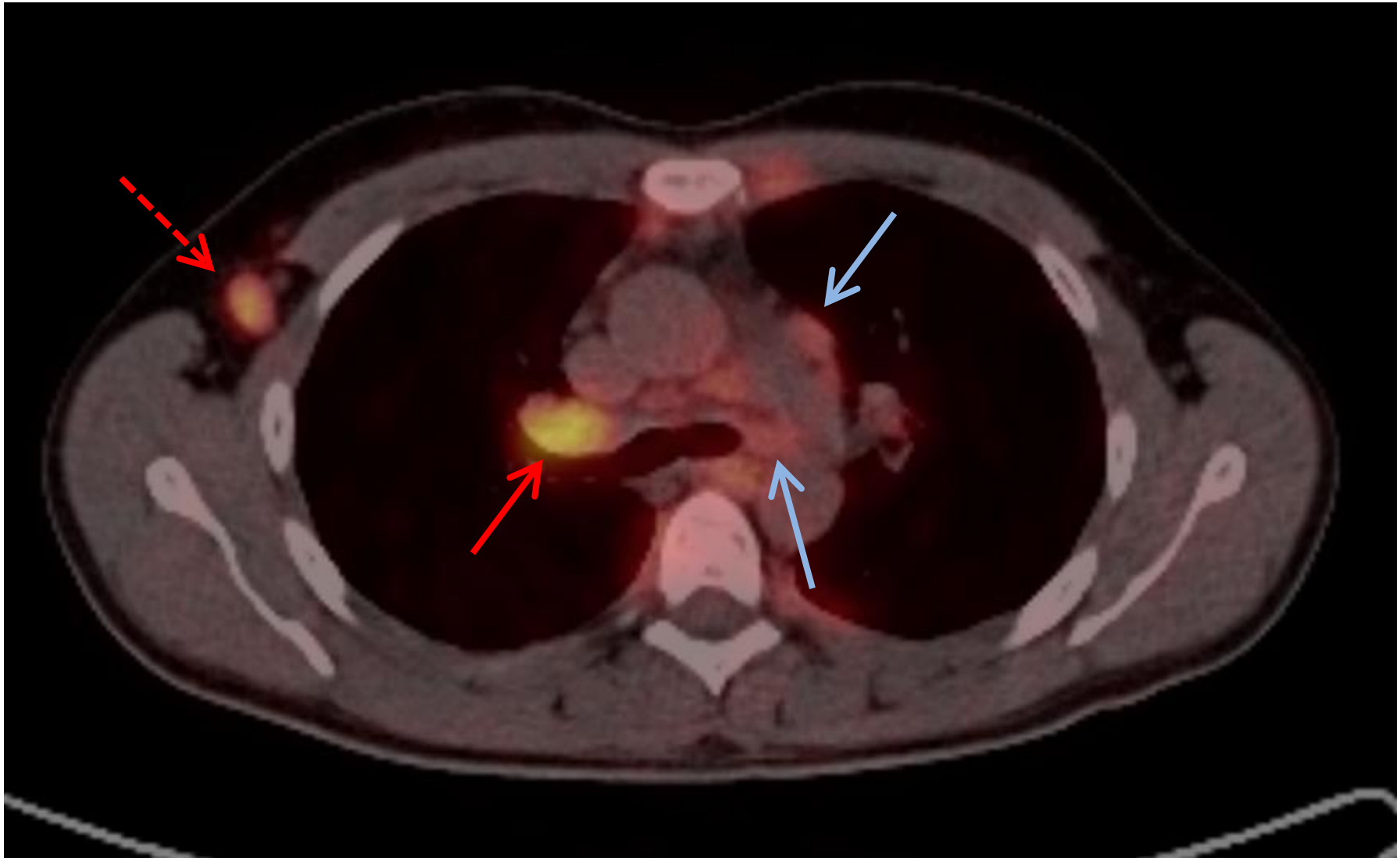


M 42

Follikulært lymfom (transformert lavgradig)

PET/CT: Baseline

mediastinum
aksiller
retroperitonealt
langs bekkenkart



Blandingsintensitet ved **transformert** lavgradig NHL

INDIKASJONER FDG PET/CT VED LYMFOM

1. Primær stadieinndeling (undersøke sykdomsutbredelse, sikre at tumor er FDG-avid, RT)
2. Evaluering av terapirespons under pågående behandling (forutsi endelig behandingseffekt)
3. For evaluering av terapirespons etter avsluttet behandling og RT planlegging
4. Påvise transformert lymfom
5. Veilede biopsitakning
6. Ved mistanke om recidiv
7. Restaging

Benmargsaffeksjon:

PET/CT mer **sensitiv** enn benmargsbiopi for å vise **fokal benmargsaffeksjon** ved både HL og NHL

El-Galaly et al J Clin Oncol 2012: 30: 4508-14.
Berthet et al J Nucl Med 2013;1244-50: 54
Khan et al. Blood 2013: 122: 61-67.

…… unntak er at

PET/CT ***mindre sensitiv*** enn benmargsbiopsi

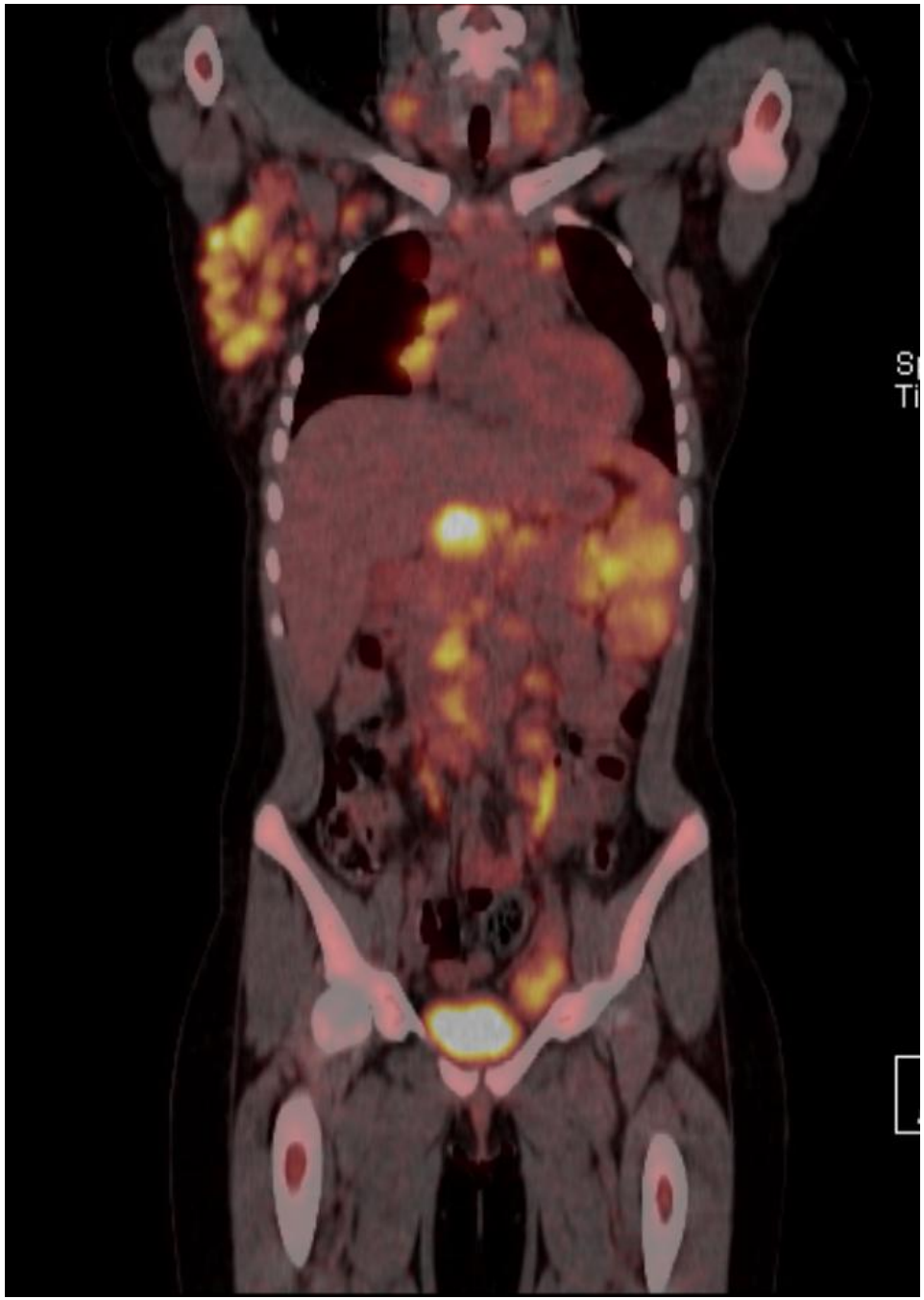
ved indolent lymfom fordi da ofte diffus

sykdom

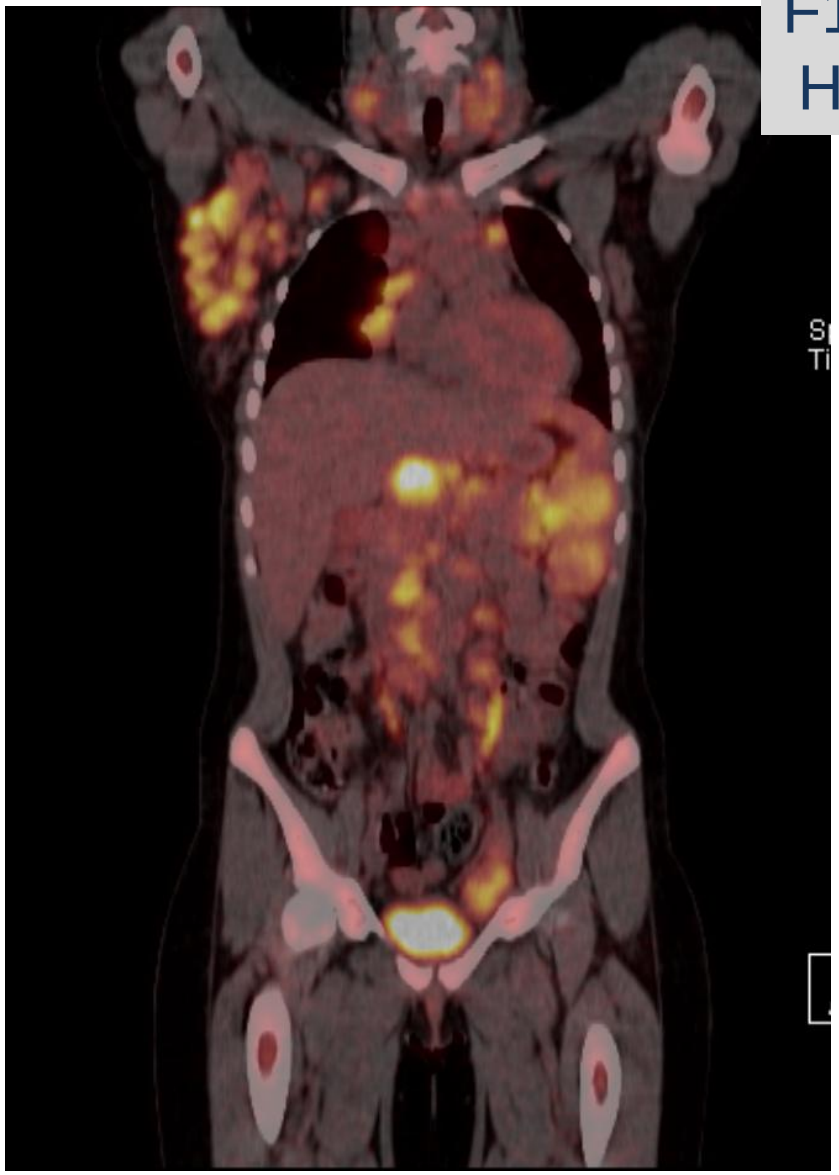
F18
HL

Baseline PET-CT

(RATHL-studien)



F18
HL



Baseline

Etter 2 kjemoterapikurer

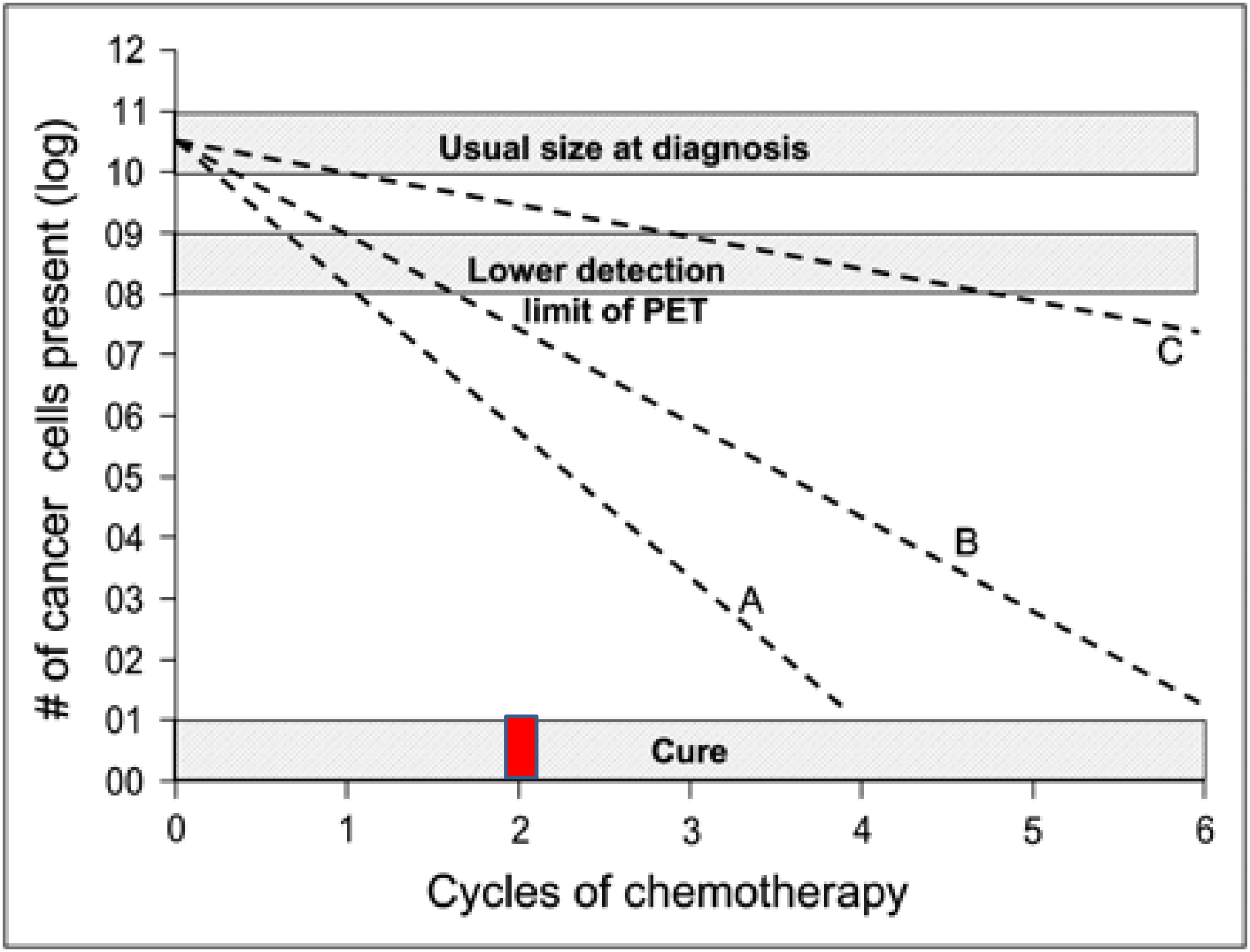
Deauville score 2

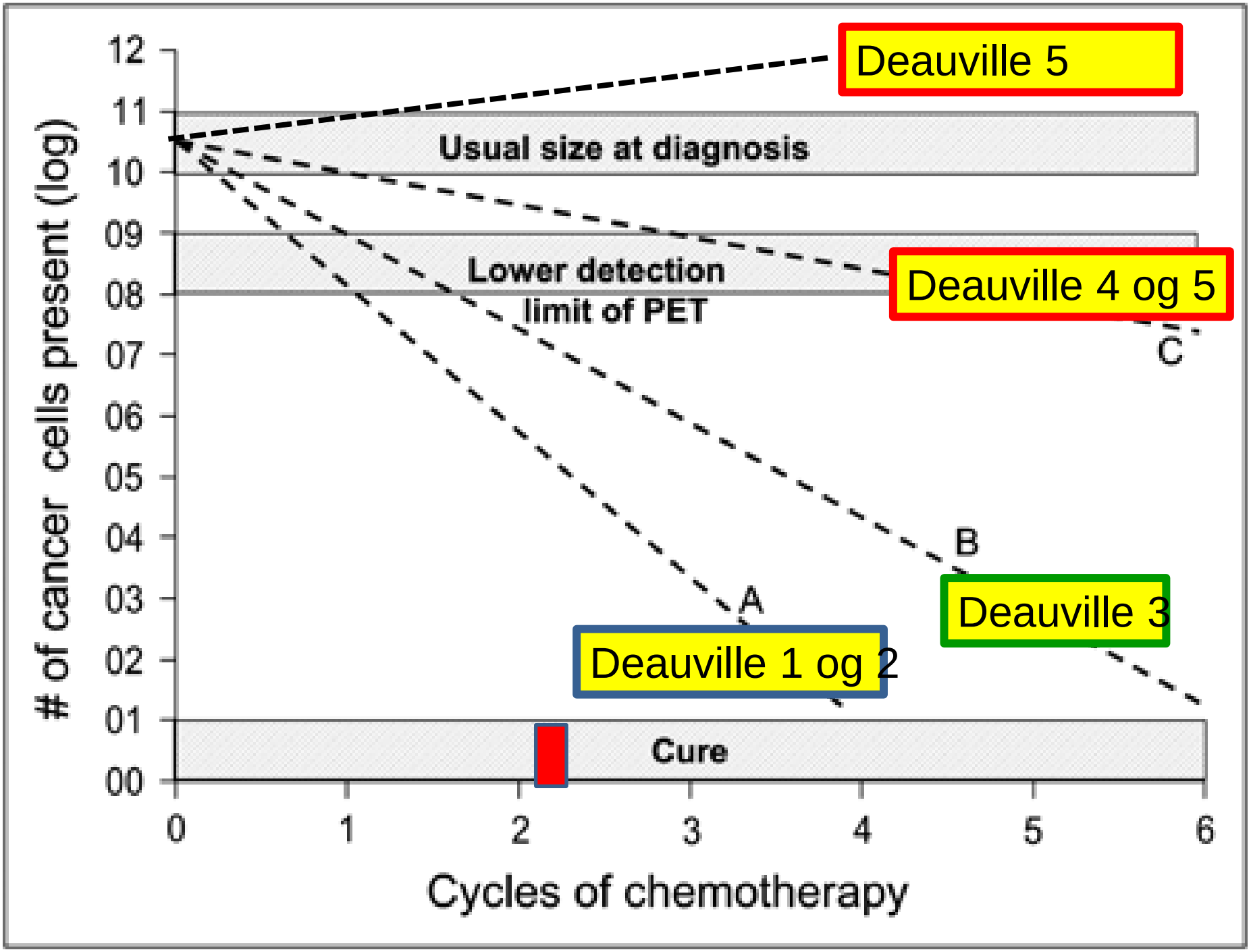
”Ikke tegn til rester av viabelt tumorvev”

Deauville score 2

”Ikke tegn til rester av viabelt tumorvev”

”God behandlingsrespons”
(resultatet indikerer at pasienten vill gå i komplett remisjon med den aktuelle behandling): God prognose!”


12
11
10
09
08
07
06
05
04
03
02
01
00
# of cancer cells present (log)
Usual size at diagnosis
Lower detection
limit of PET
C
B
A
Cure
0
1
2
3
4
5
6
Cycles of chemotherapy


Deauville 5
Usual size at diagnosis
Lower detection
limit of PET
Deauville 4 og 5
C
B
A
Deauville 3
Deauville 1 og 2
Cure
12
11
10
09
08
07
06
05
04
03
02
01
00
0
1
2
3
4
5
6
# of cancer cells present (log)
Cycles of chemotherapy

Sluttevaluering med FDG

PET/CT *ikke* indisert dersom

negativ interim !!

Sally Barrington, 2013

1st International Meeting on Interim PET in Lymphoma

Deauville (France), Centre International, April 3rd-4th,2009

Organization Committee

M. Meignan (France), A. Gallamini (Italy), C. Haioun (France)

Score 1: no residual uptake above the background level,

Score 2: residual uptake ≤ mediastinum blood pool

Score 3: residual uptake greater than the mediastinum but not greater than the liver

Score 4: residual uptake moderately increased compared with the liver

Score 5: residual uptake markedly increased compared with the liver or new sites of disease.

Early PET / interim PET/CT

Deauville score (sammenligner lesjon med høyest opptak på interim med blod mediastinum / lever)

dSUV

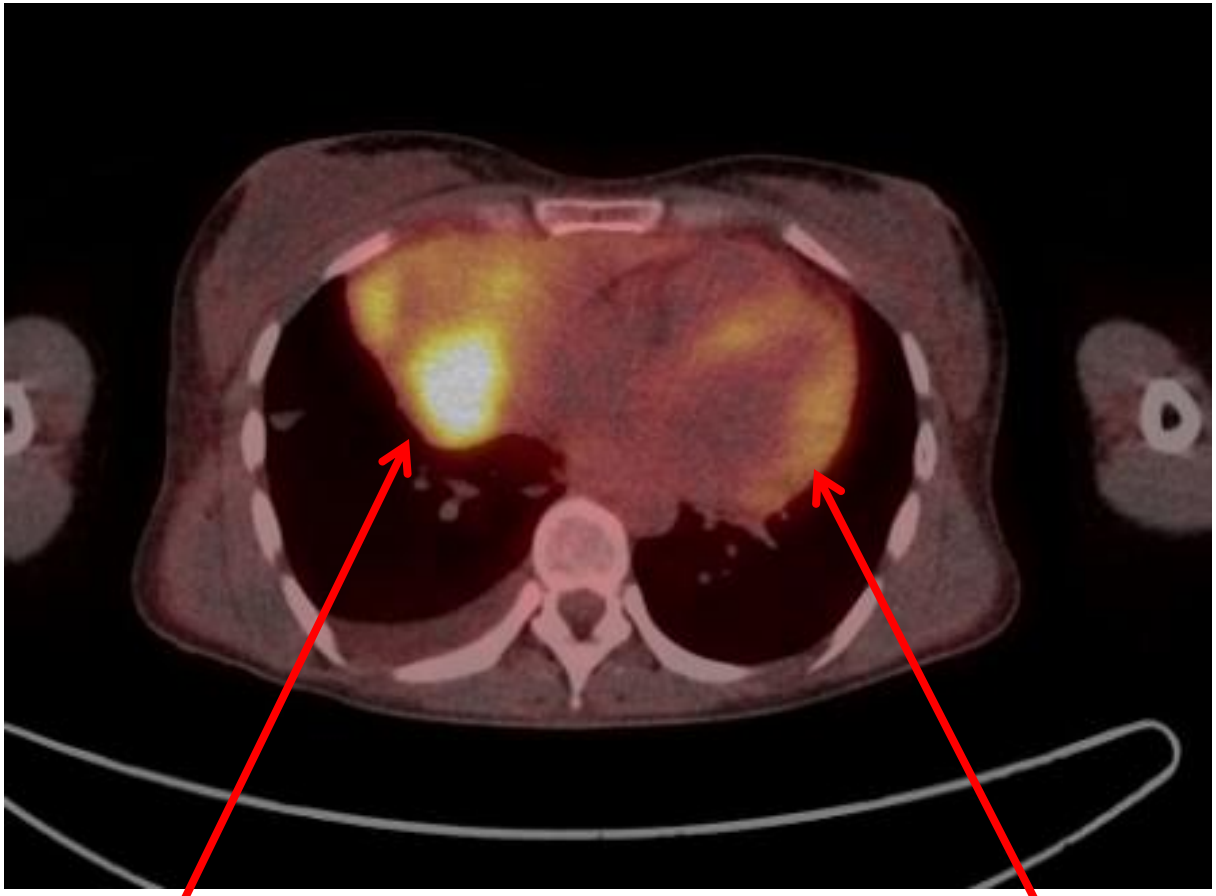
Etter 2 sykluser 66% reduksjon

Etter 4 sykluser 70% reduksjon

Interim best egnet for HL og DLBCL fordi disse responederer raskest på kjemoterapi

F 32

DLBCL

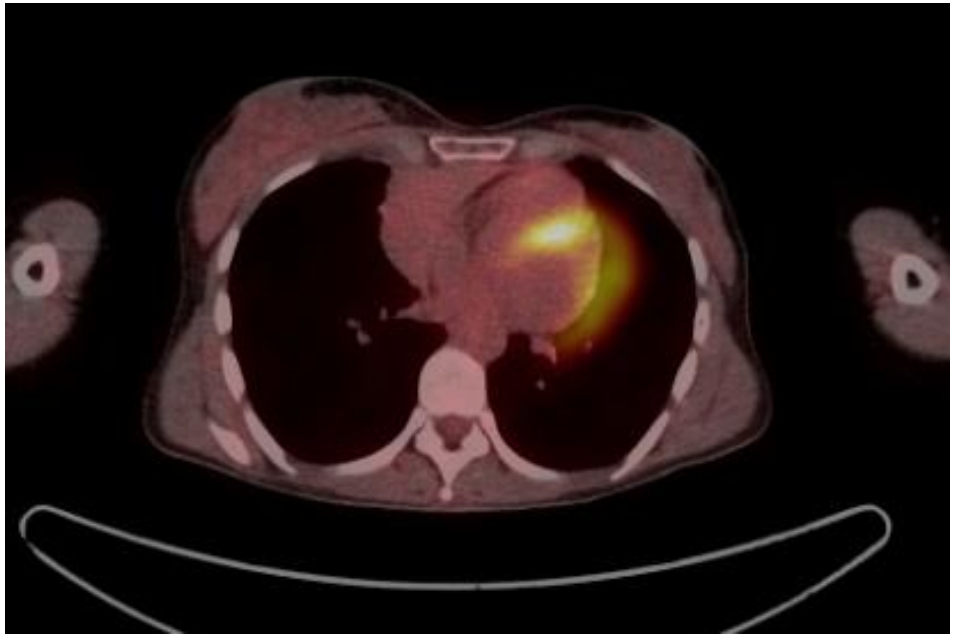


Baseline studie

Høyt opptak av FDG i mediastinal tumor

Fysiologisk opptak av FDG i myokard

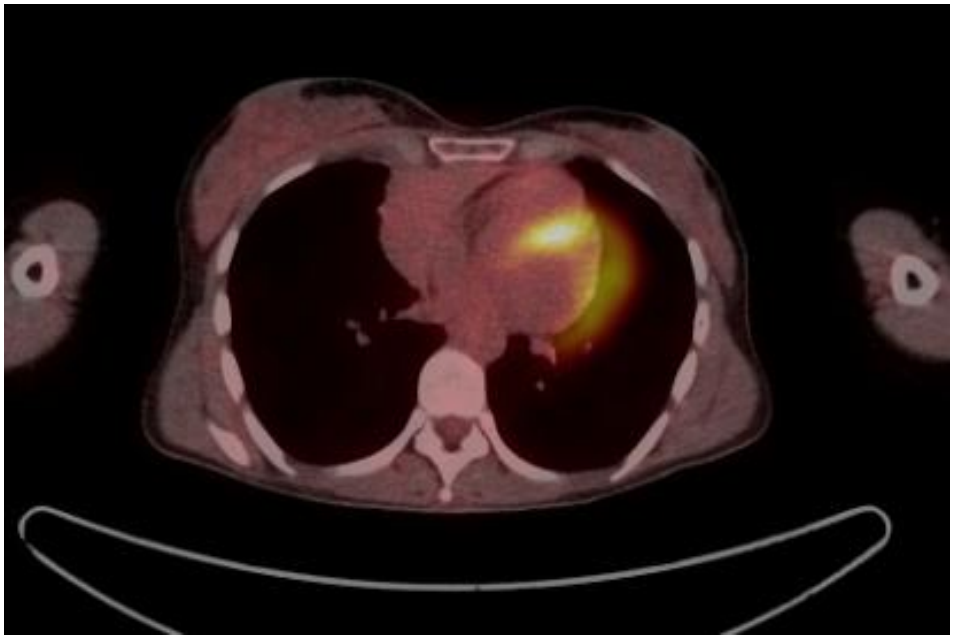
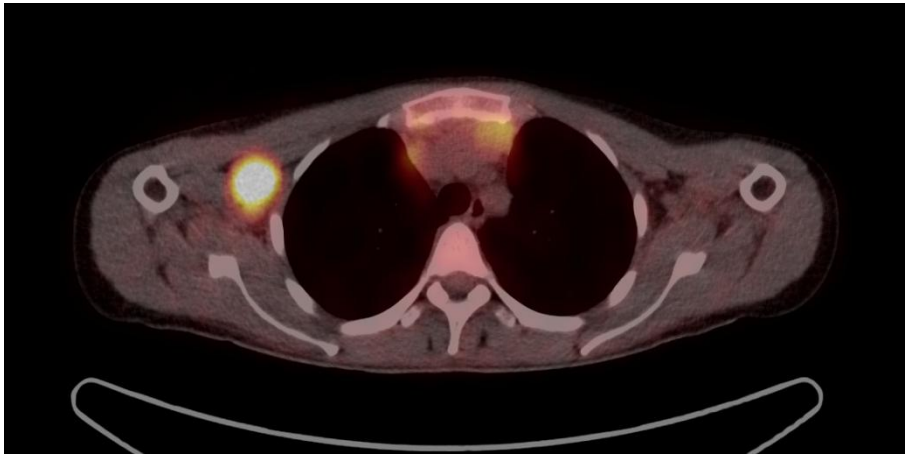
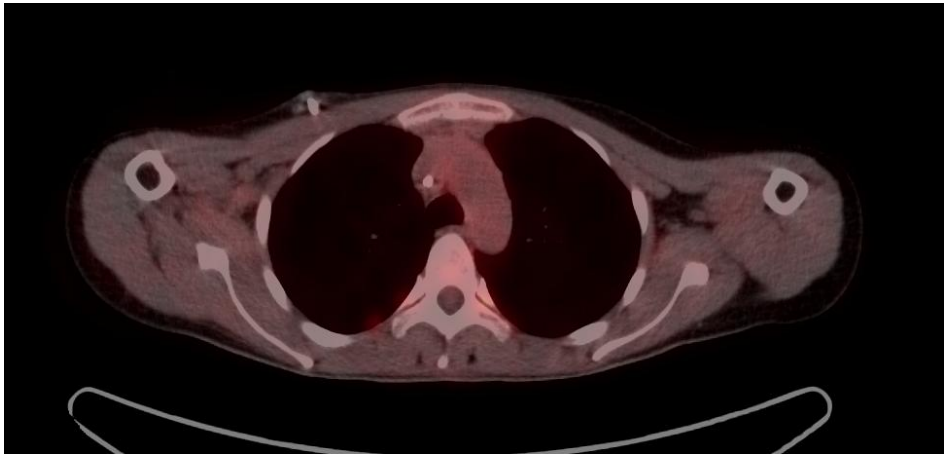
F32.DLBCL. Sluttevaluering



Baselinestudie

Tre uker etter avsluttet kjemopterapi:

Opptak resttumor har FDG-opptak lik blodbakgrunn

Konklusjon: Ikke holdepunkt for rester av viablet tumorvev.

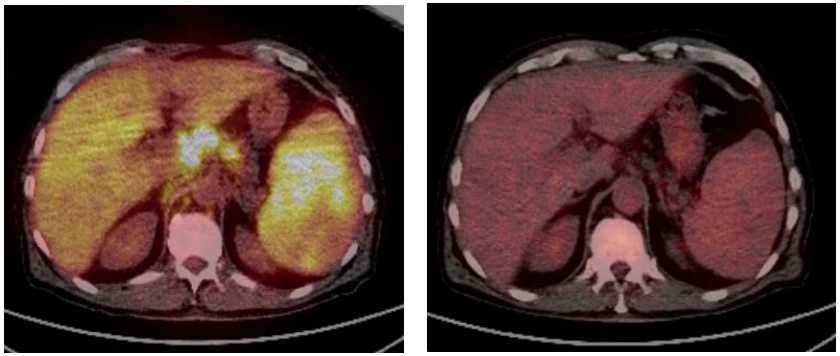
Komplett metabolsk respons.

Juweid ME, Stroobants S, Hoekstra OS, et al.

Use of PET for
Response Assessment of Lymphoma:

Consensus of the Imaging Subcommitee of International Harmonization Project in Lymphoma.

J Clin Oncol ***2007***; 25: 571-8.



Complete response (CR)

……. a post-treatment residual mass of any size on CT is permitted as long as it is PET negative.

Consensus of the Imaging Subcommitee of International Harmonization Project in Lymphoma.

J Clin Oncol ***2007***; 25: 571-8.

Høyt opptak **benmarg**:

Reaktiv benmarg
(sekundært til **kjemoterapi)**

Høyt opptak i stor **milt**
(diffust fordelt > lever (**GcSF**).

Diffust

benmargsopptak

reaktivt (kjemo) særlig

ved HL,

Men sees også hos

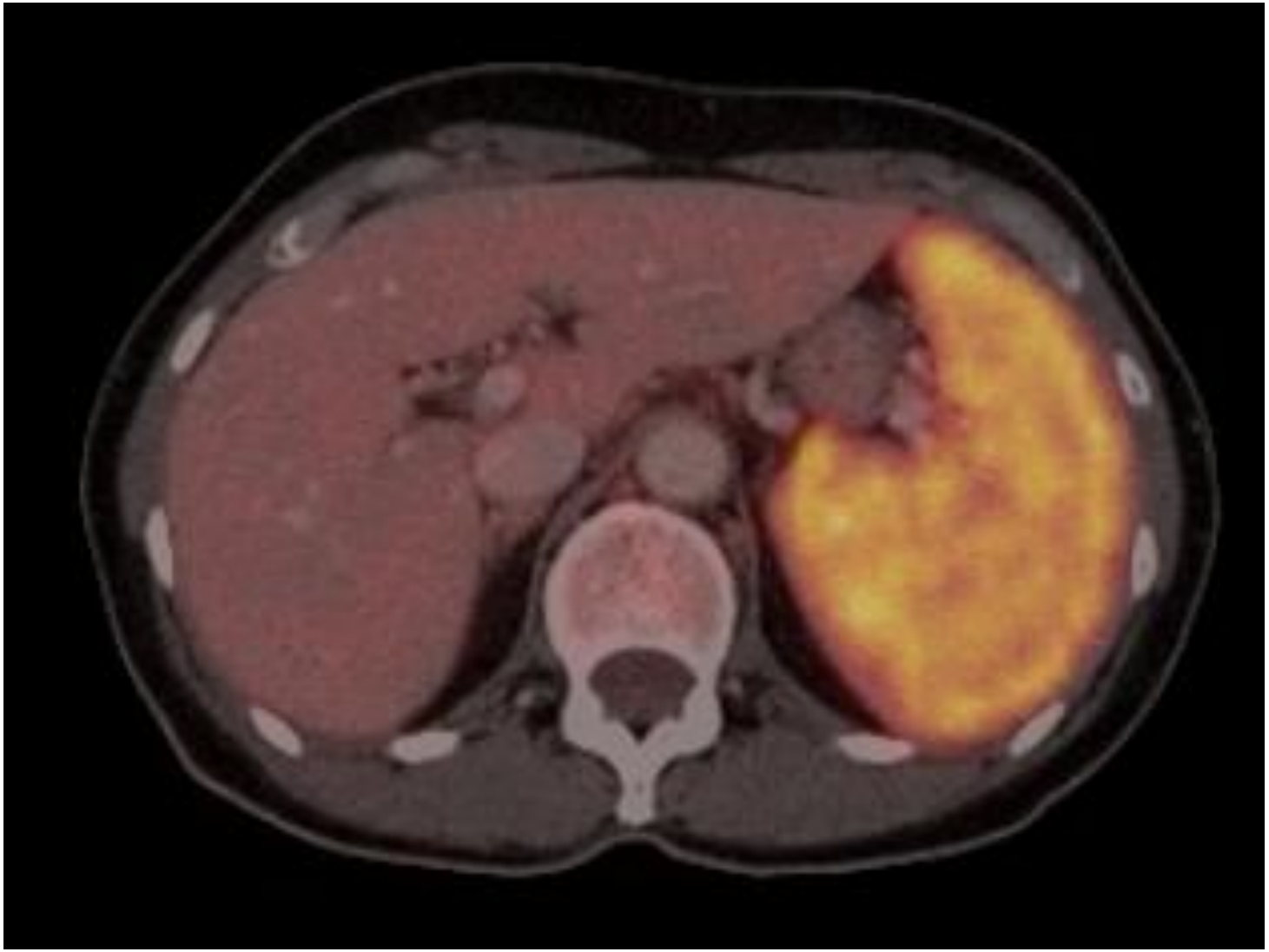
ungen pasienter ved

sykdomsdebut *før*

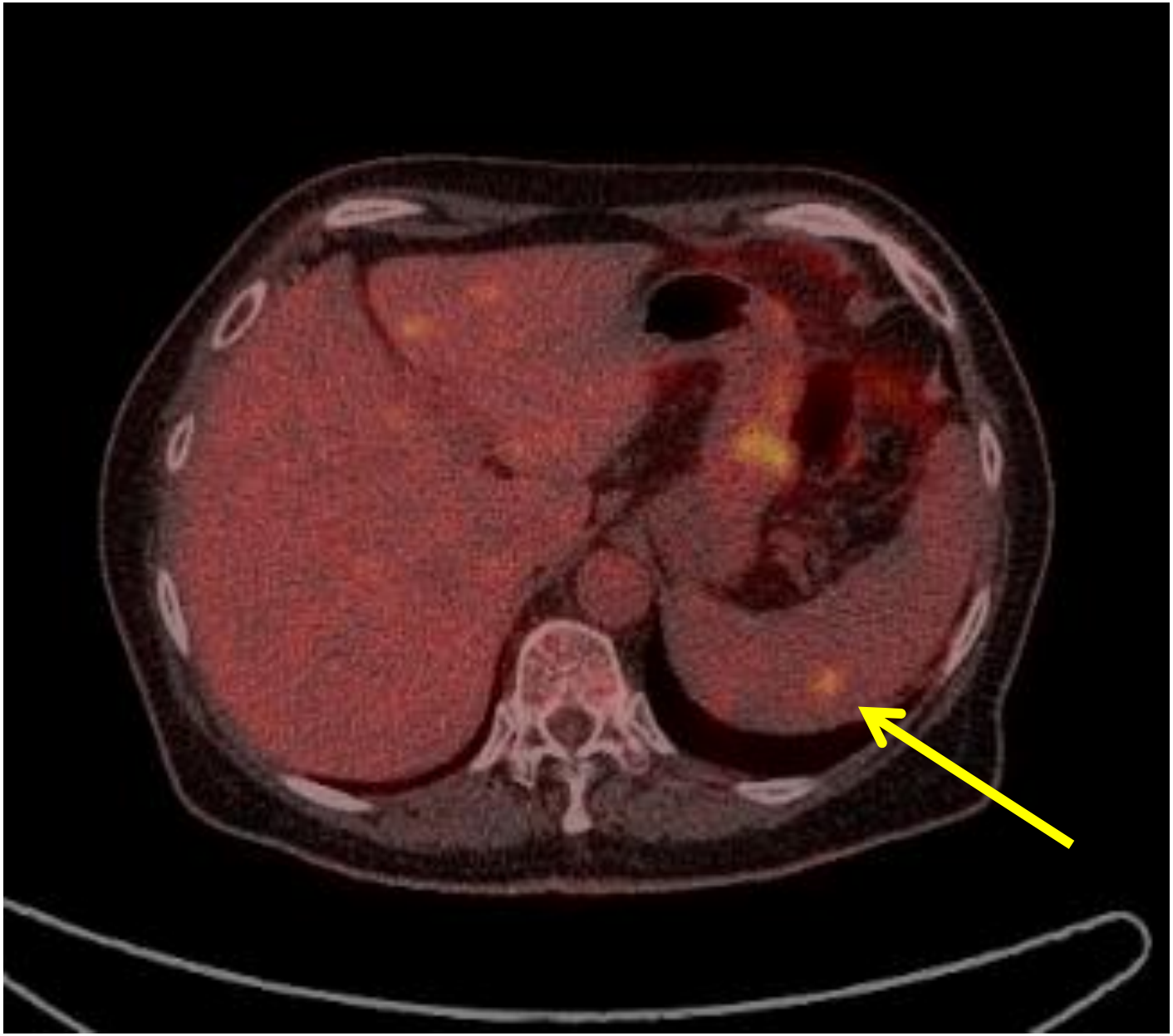
behandling!

Baseline FDG PET/CT

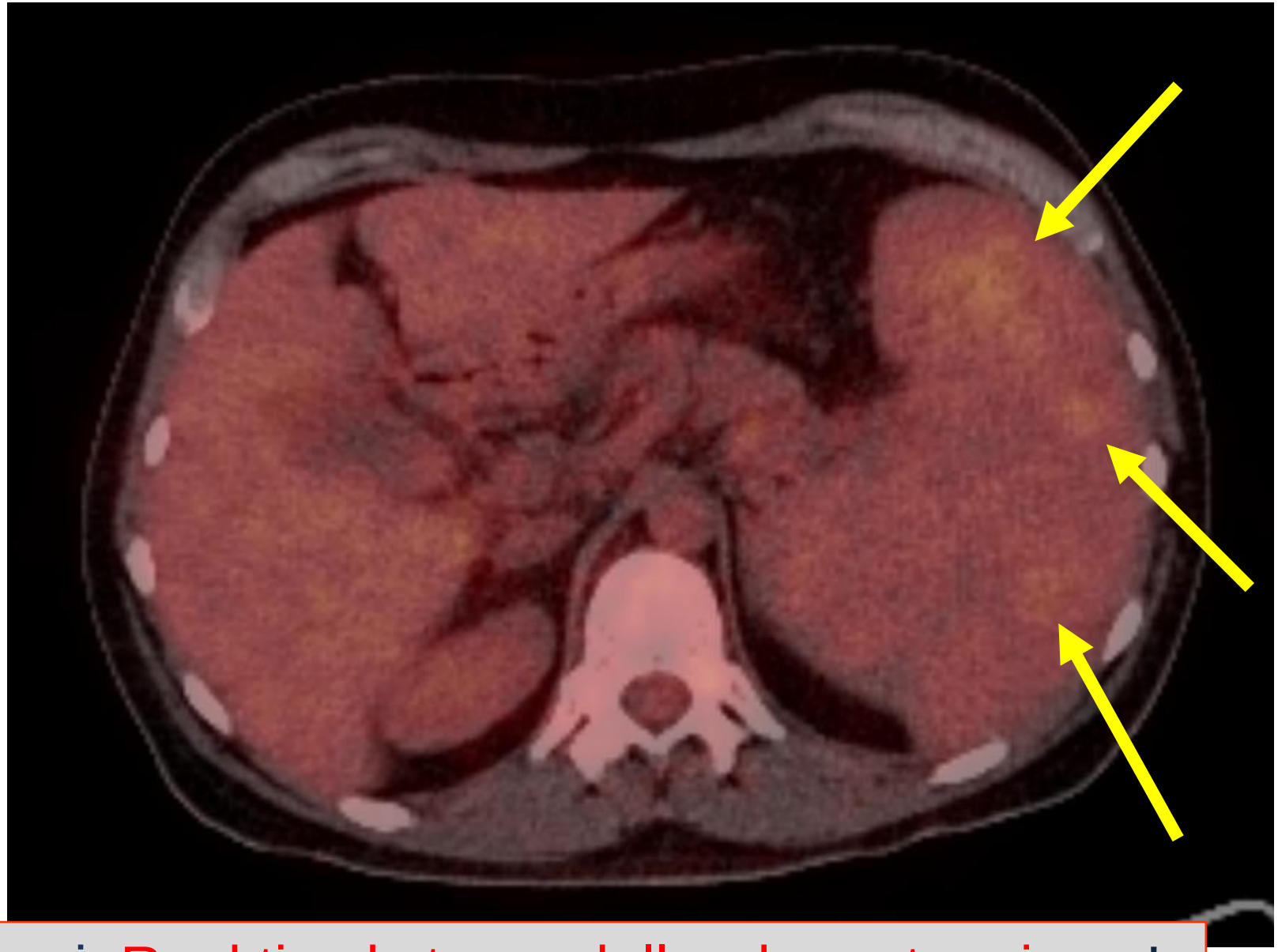
Hyperplastisk thymus



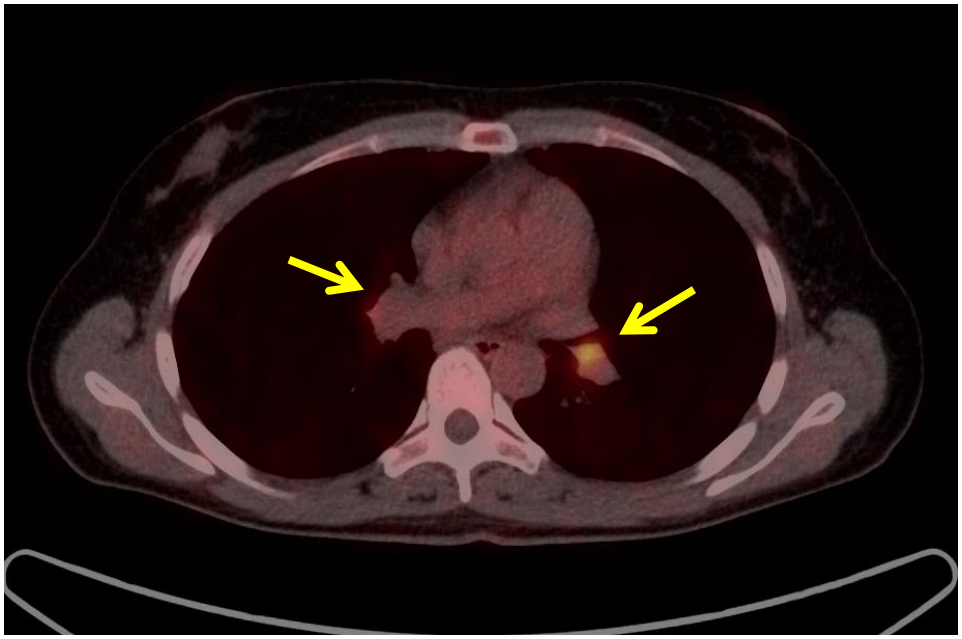
Diffus miltaffeksjon



Fokal miltaffeksjon



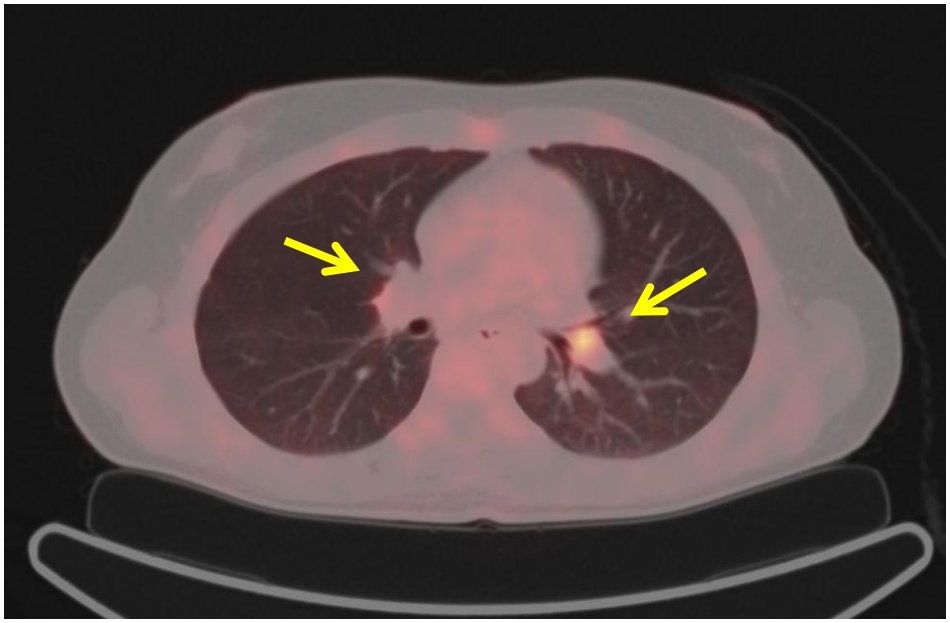
Biopsi: Reaktiv ekstramedullær hematopoiese !

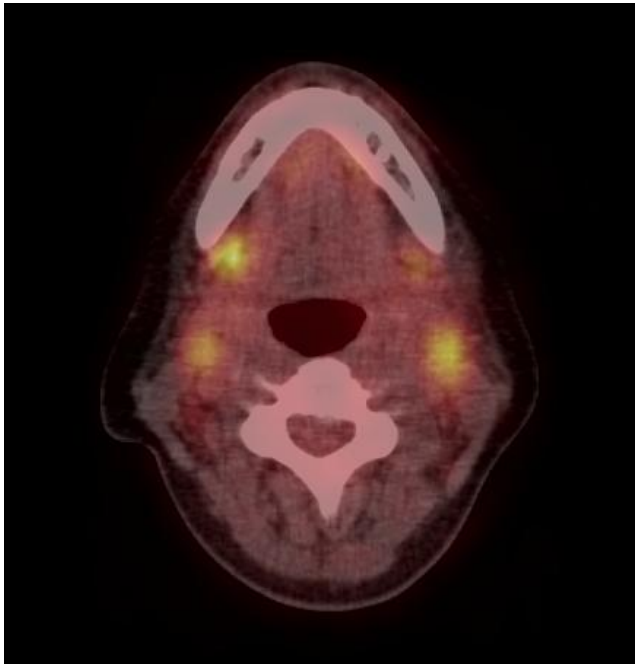


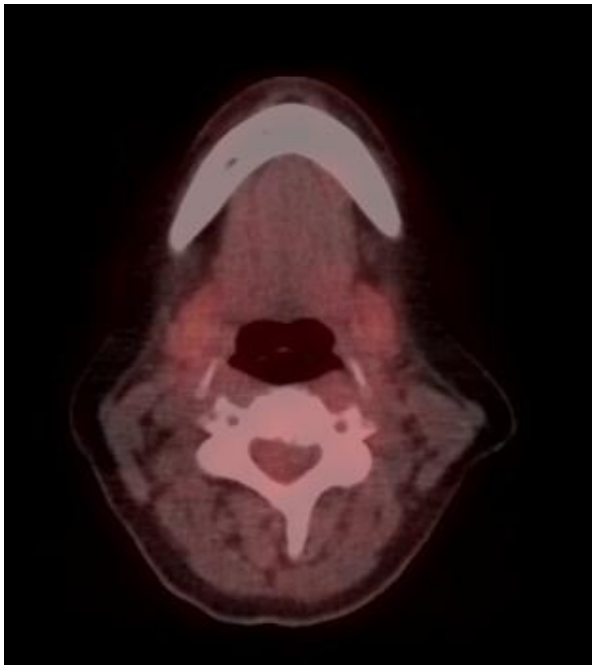
F 38
DLBCL (behandlingsresistent)

Nå sluttevaluering etter
3. runde med kjemoterapi
og HMAS

Klinisk og CT ikke holdepunkt
for rester av viabelt tumorvev,
men PET/CT ……

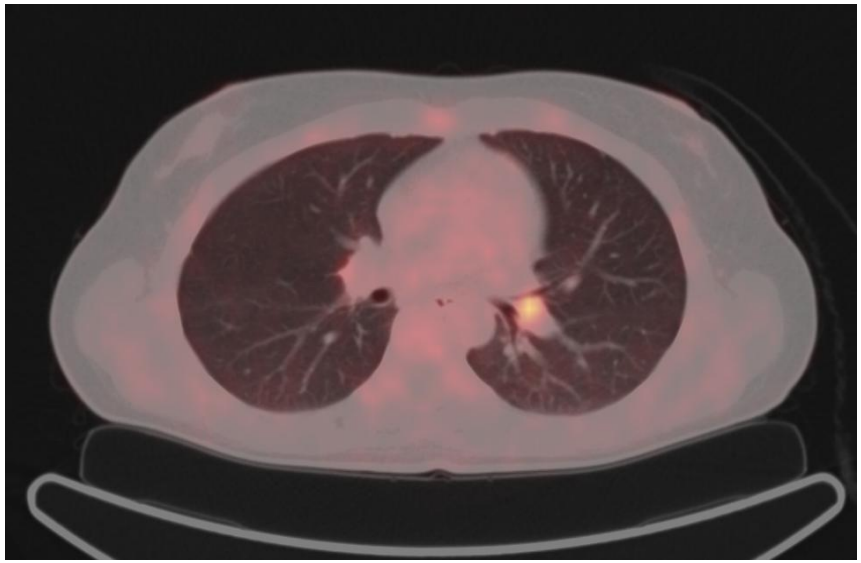


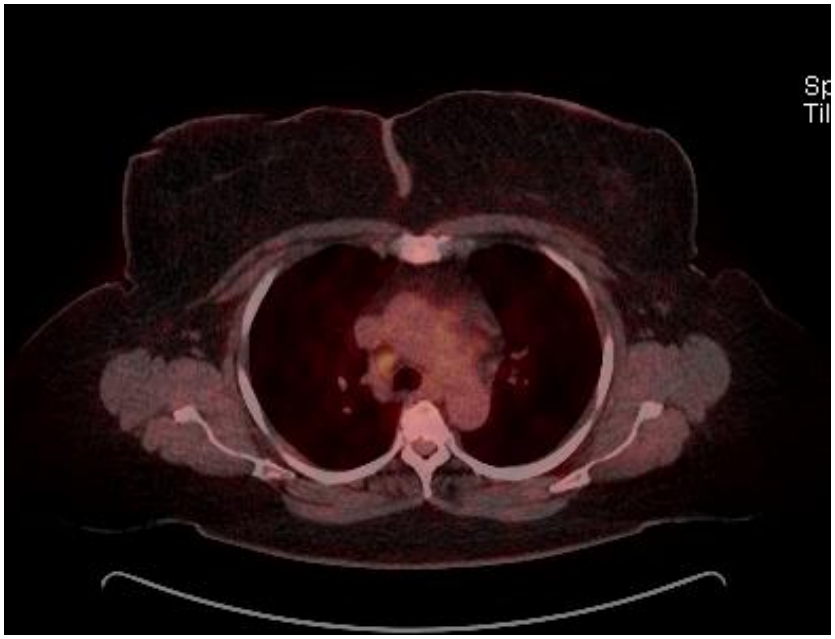


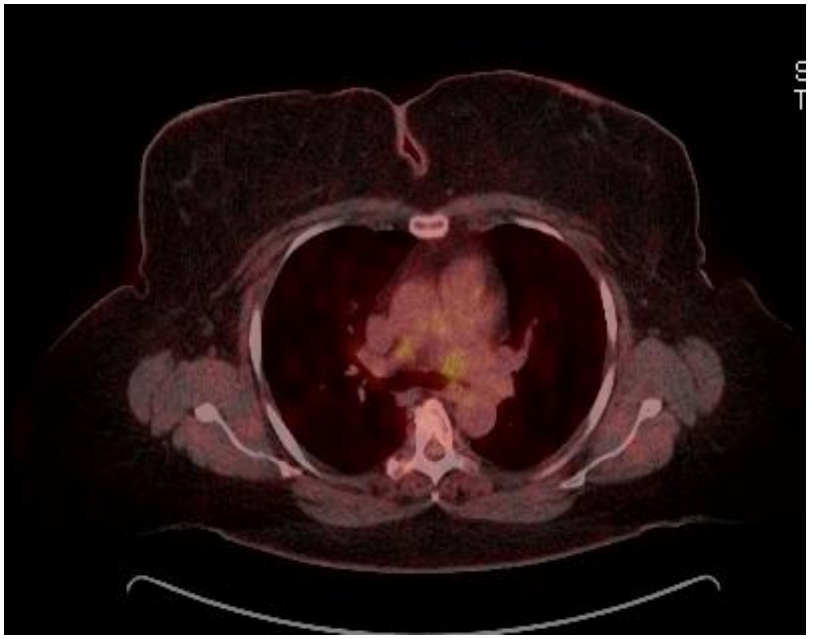


Kontroll PET-CT
etter 3 uker: **Negativ**

Normalisering er forenlig med forandringer sekundært til **infeksjon** 3 uker tidligere.







FDG-avide lymfeknuter lokalisert i mediastinum inkludert begge lungehili med annen utbredelse enn ved initial sykdom:

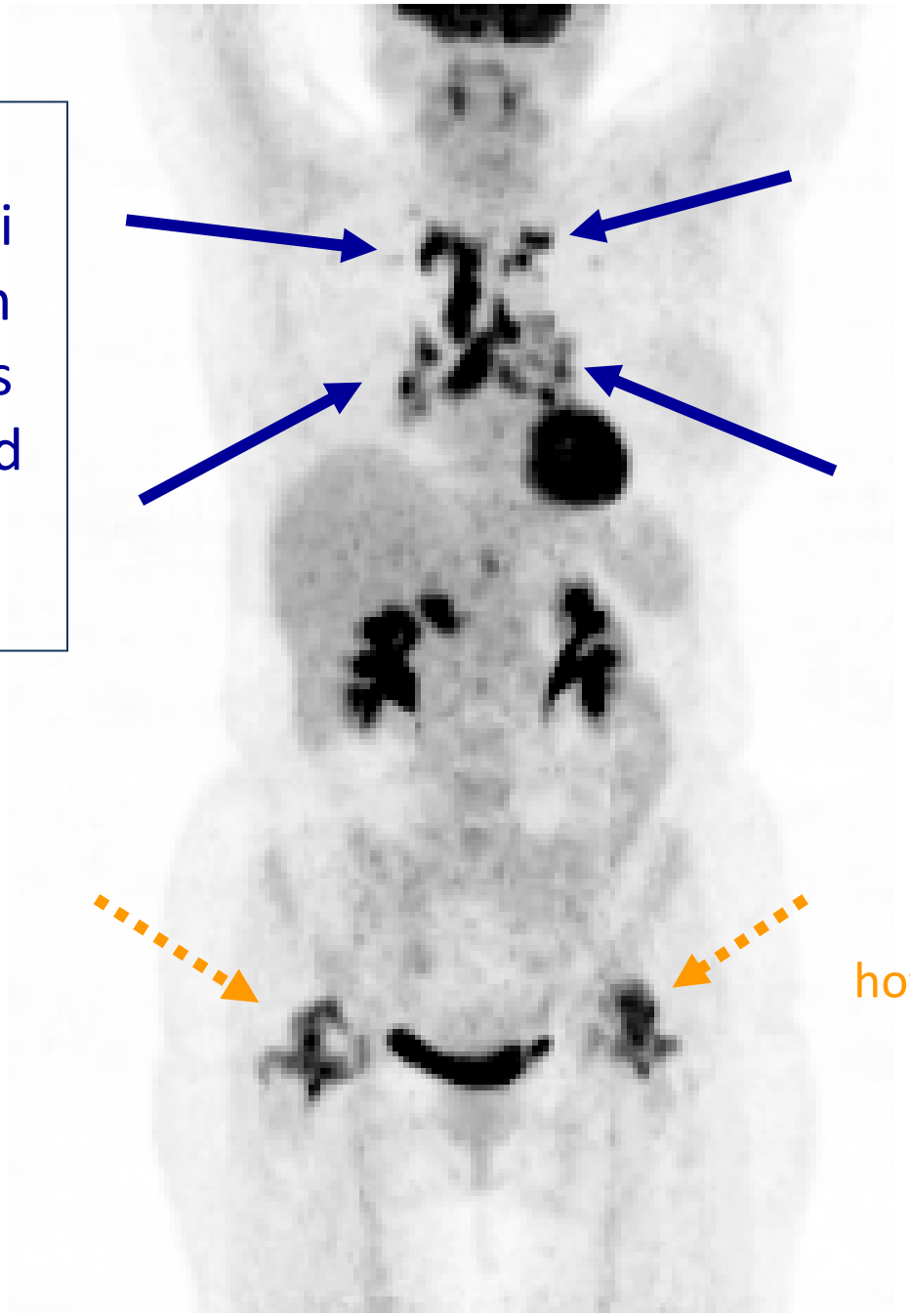
Sarkoidose **?**

Deauville score

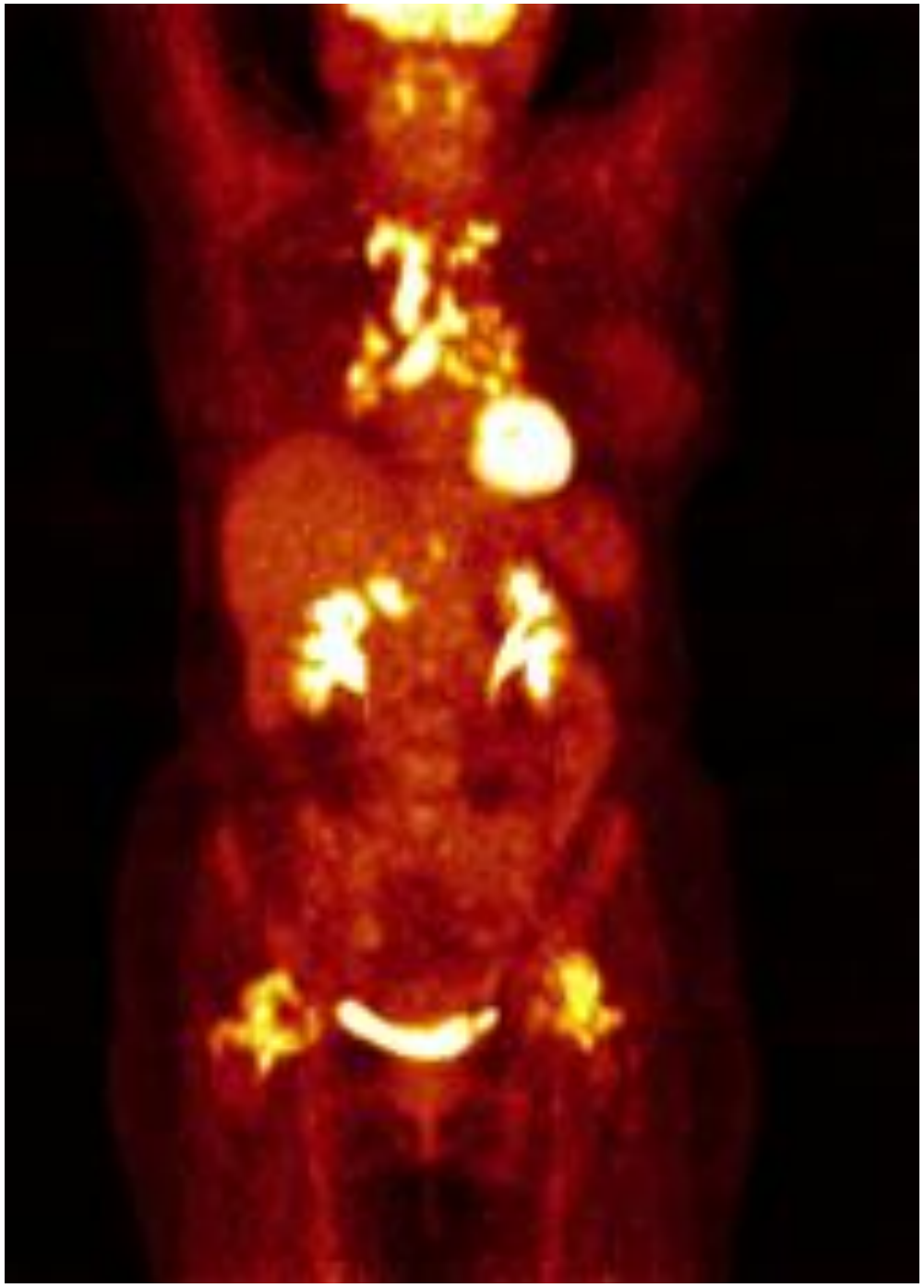
A new lesion (not present on baseline PET) in a patient who is responding to treatment at other sites is unlikely to be lymphoma.

(Deauville score X)

Forstørrete lymfeknuter i mediastinum og lungehilus bilateralt med intenst FDG opptak



Reaktiv inflammasjon omkring hofteleddsproteser



Sarkoidose

INDIKASJONER FDG PET/CT VED LYMFOM

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3. For evaluering av terapirespons etter avsluttet behandling og RT planlegging
4. Påvise transformert lymfom
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6. Ved mistanke om recidiv
7. Restaging