Nuclear Medicine
Odense University Hospital Denmark

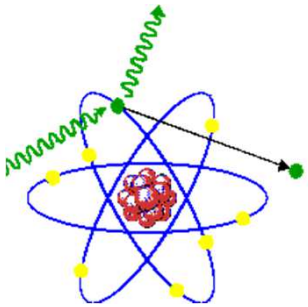
HVILKE MULIGHEDER GIVER FDG-PET/CT?

DBCG'S NACT SEMINAR 4. NOVEMBER 2019

Overlæge Malene Grubbe Hildebrandt
Nuklearmedicinsk Afdeling, Odense Universitetshospital

Region of Southern Denmark

PRINCIPLES OF NUCLEAR MEDICINE

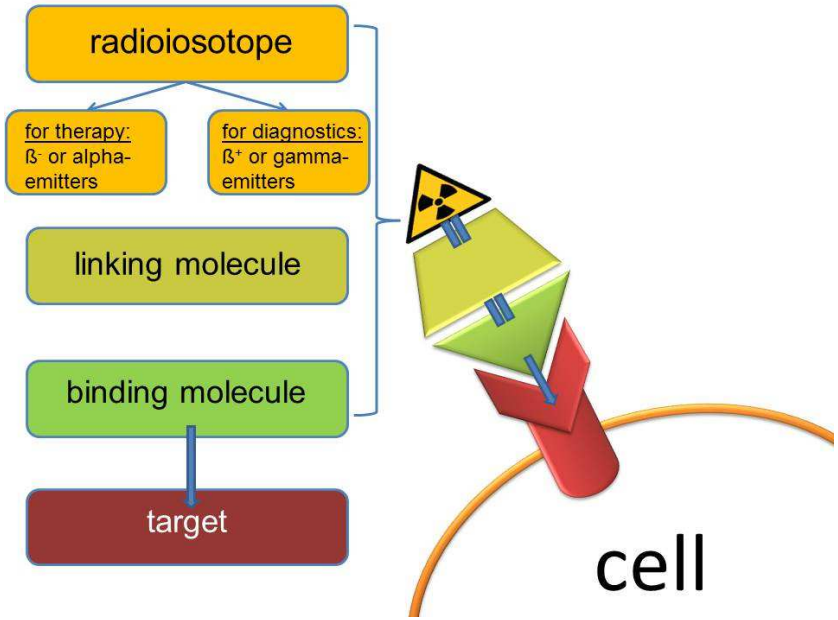


Radionuclide

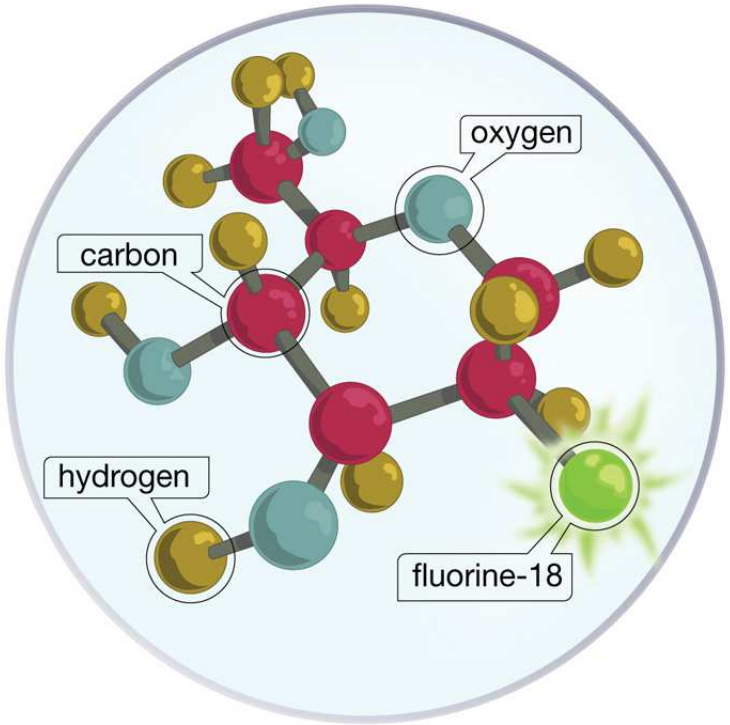
Linker

Molecule

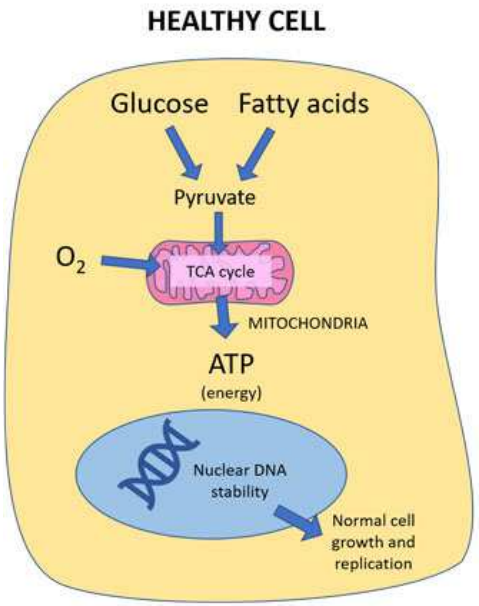
PRINCIPLES OF NUCLEAR MEDICINE

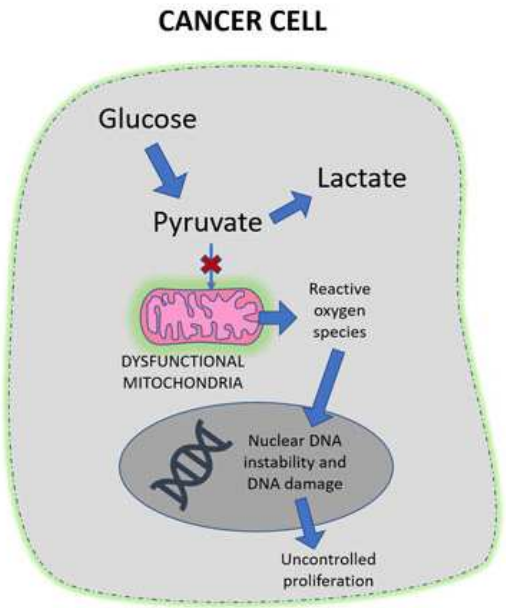


^{18}F-FLOURDEOXYGLUCOSE (FDG)

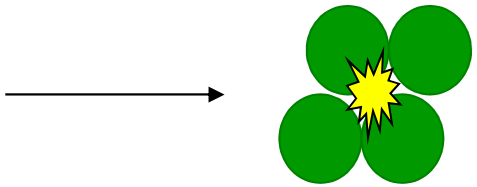


FDG-PET/CT – THE WARBURG EFFECT

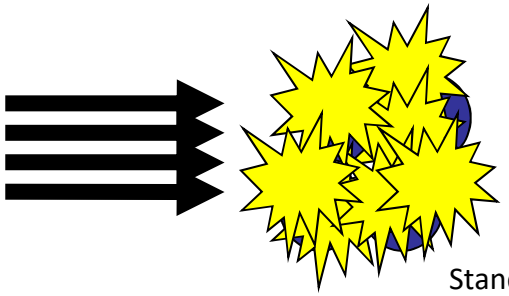




THE SUGAR MODEL



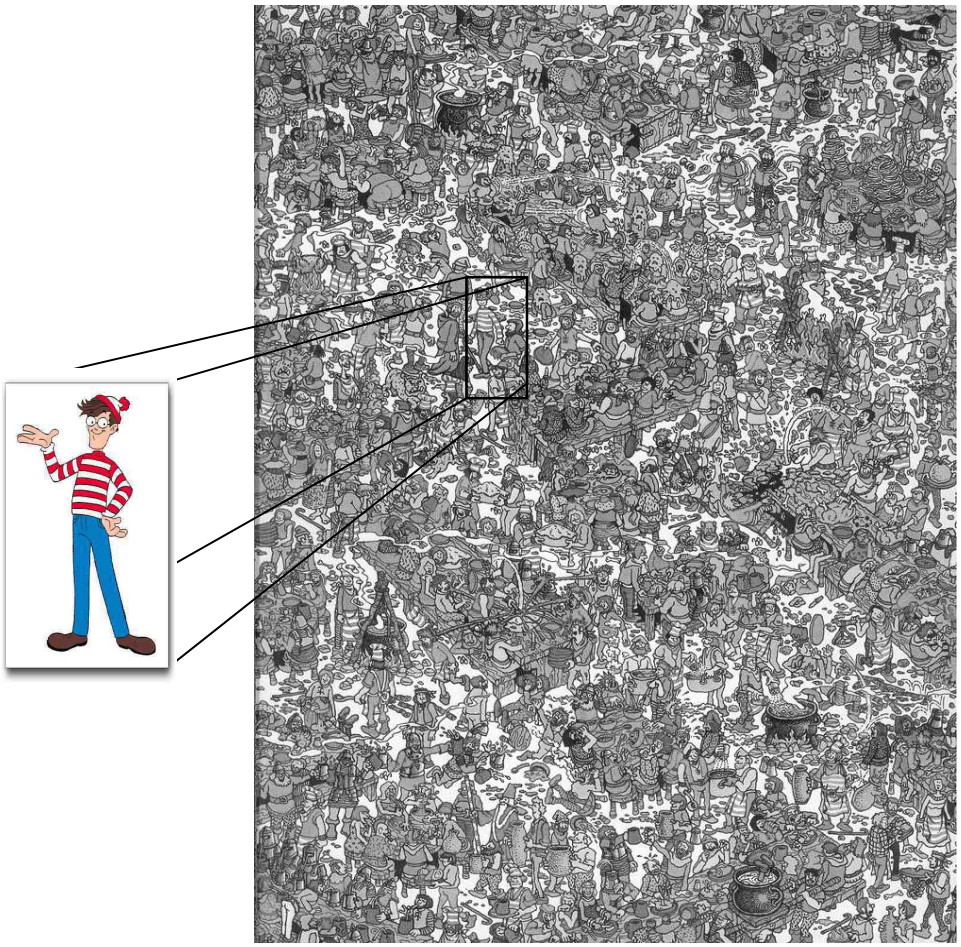
Normal cells



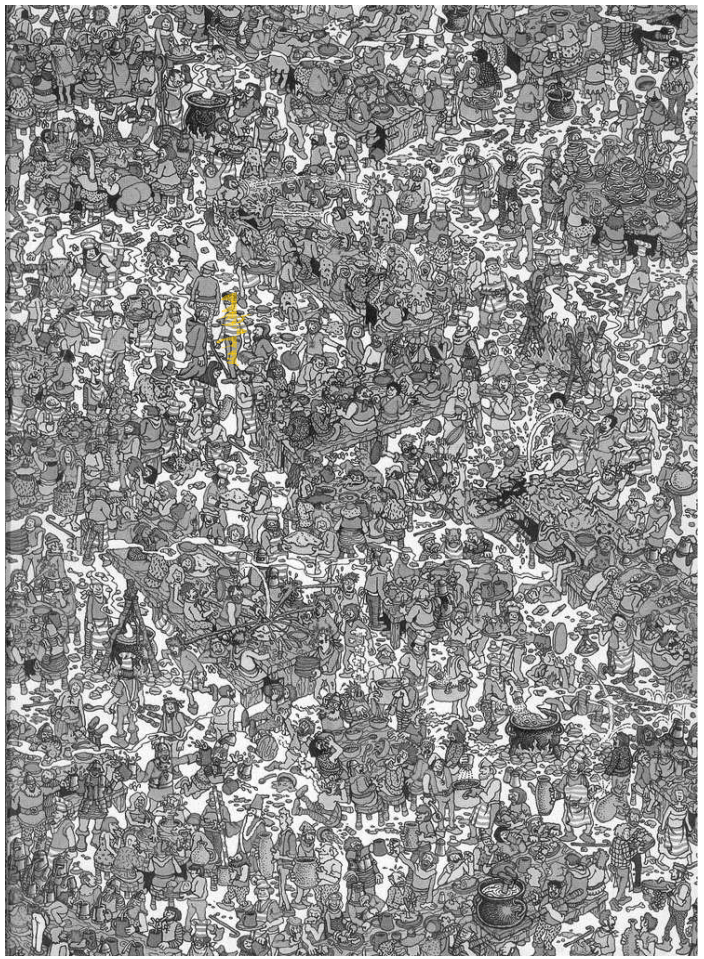
Cancer cells

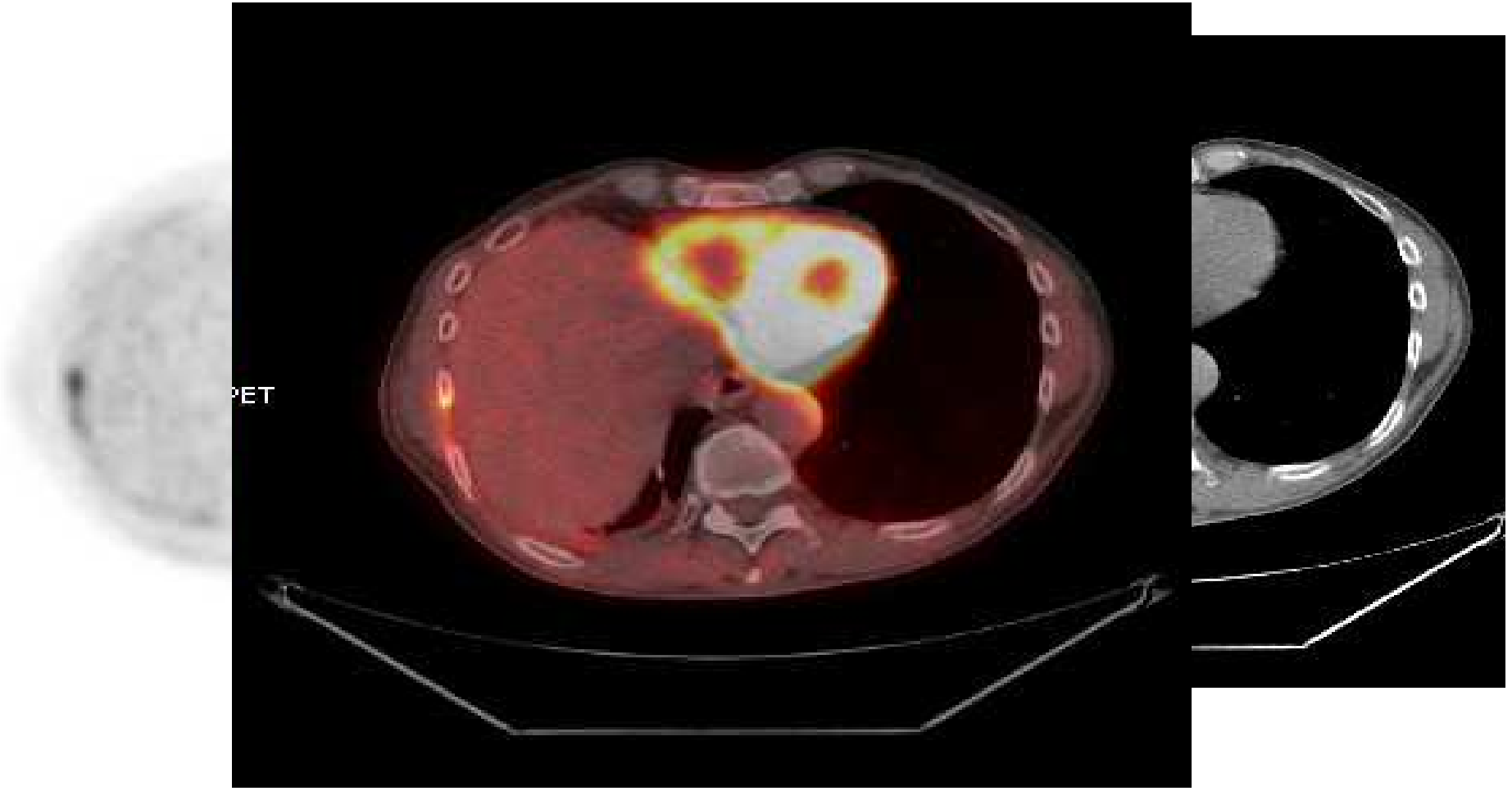
Standardized uptake value (SUV)

Radiology

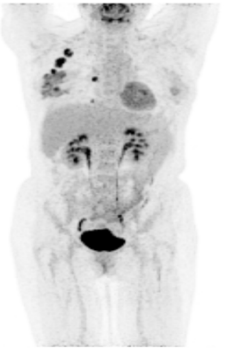


Nuclear medicine




PET

National vejledning



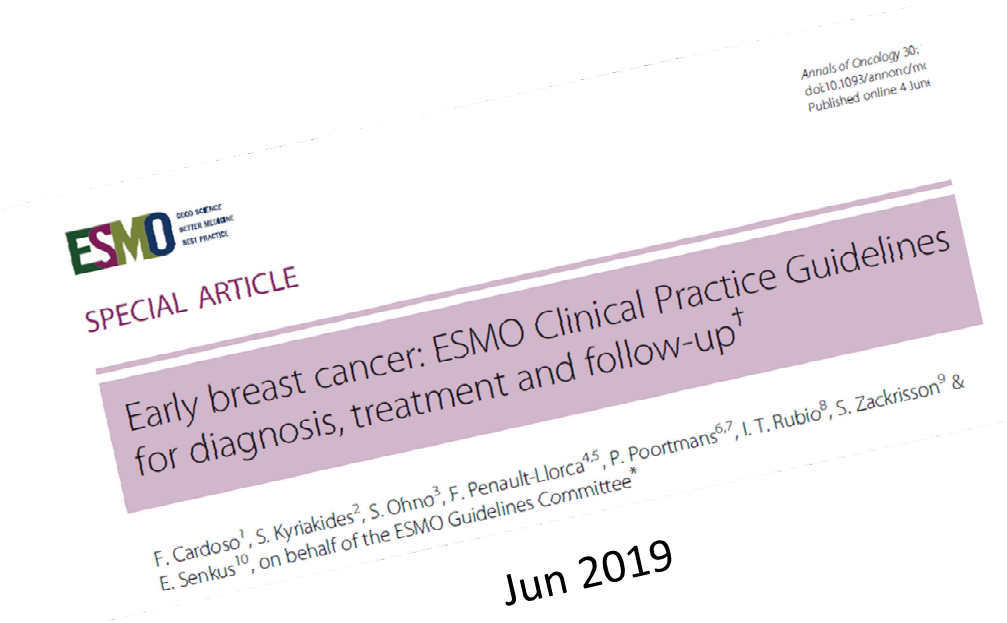
^{18}F-FDG-PET/CT ved brystkræft

Malene Grubbe Hildebrandt, Odense Universitetshospital
Mikkel Holm Vendelbo, Århus Universitetshospital
Mie Holm Vilstrup, Odense Universitetshospital
Charlotte Birk Christensen, Herlev Hospital
Helle Hendel, Herlev Hospital

Region of Southern Denmark

Nuclear Medicine
Odense University Hospital Denmark

ESMO – CLINICAL GUIDELINES



Annals of Oncology 30:
doi:10.1093/annonc/mx
Published online 4 June

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

SPECIAL ARTICLE

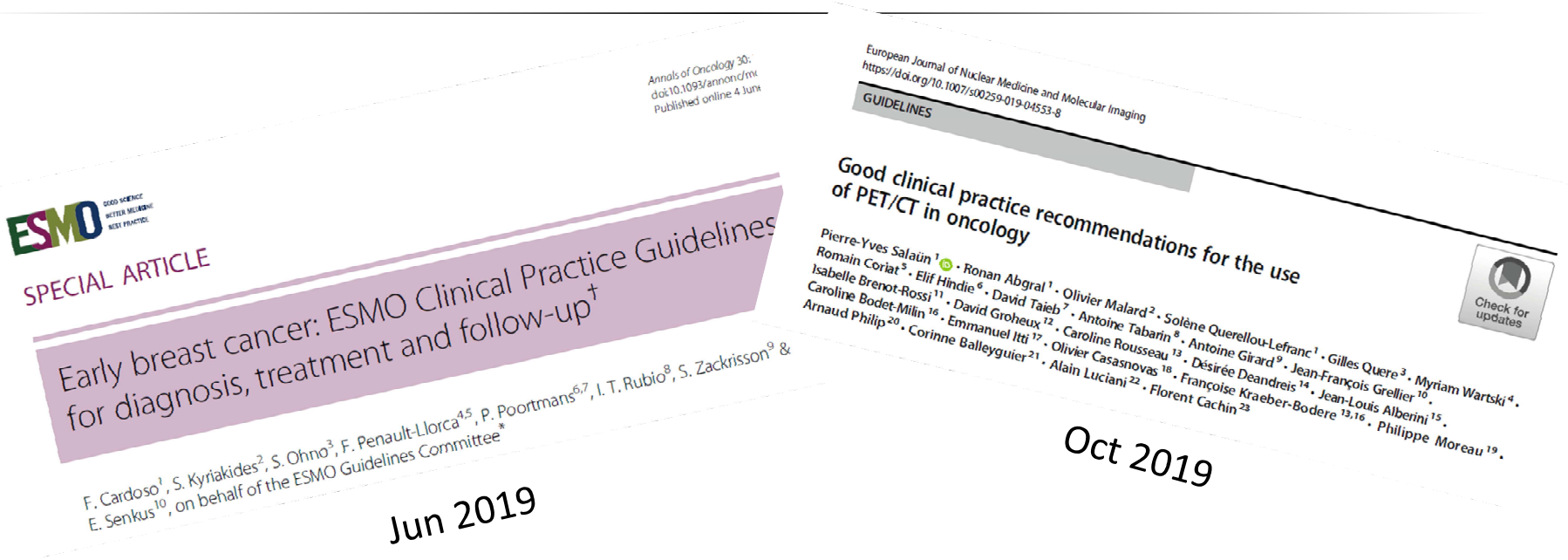
Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

F. Cardoso[1], S. Kyriakides[2], S. Ohno[3], F. Penault-Llorca[4,5], P. Poortmans[6,7], I. T. Rubio[8], S. Zackrisson[9] & E. Senkus[10], on behalf of the ESMO Guidelines Committee*

Jun 2019

ESMO – CLINICAL GUIDELINES

GCP RECOMMENDATIONS FOR USE OF PET/CT IN ONCOLOGY



Region of Southern Denmark

Nuclear Medicine
Odense University Hospital Denmark

NATIONAL VEJLEDNING

Brystkræftforløb	Anbefaling fra National PET/CT-gruppe
Diagnostik af primær brystkræft	FDG-PET/CT anbefales ikke til diagnostik af primær brystkræft*
Stadieinddeling ved primær brystkræft	FDG-PET/CT anbefales til udredning for fjernmetastasering ved: • klinisk mistanke herom • lokalavanceret brystkræft (Stadie III sygdom – se appendix) • inflammatorisk brystkræft (Stadie III sygdom – se appendix)
Responsevaluering ved lokalavanceret (primær) brystkræft	FDG-PET/CT anbefales ikke til responsevaluering efter neoadjuverende kemoterapi*
Opfølgningsforløb efter primær brystkræft	Der er ikke evidens for helkropsbilleddiagnostik som led i kontrol i opfølgningsforløb efter kurativt intenderet behandling for primær brystkræft*
Recidivopsporing	FDG-PET/CT anbefales til udredning for fjernmetastasering ved: • klinisk eller biokemisk mistanke om fjernrecidiv • biopsiverificeret lokoregionalt recidiv
Responsmonitorering ved metastaserende brystkræft	Der foreligger ikke tilstrækkelig evidens til anbefaling af FDG-PET/CT til responsmonitorering ved fjernmetastaserende (kronisk) brystkræft

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DIAGNOSTIK AF PRIMÆR BRYSTKRÆFT

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*Vurderet udelukkende ud fra aktuelle nationale og internationale retningslinjer

DIAGNOSTIK AF PRIMÆR BRYSTKRÆFT

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 30:
doi:10.1093/annonc/m
Published online 4 Jun

SPECIAL ARTICLE

Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

Recommendations:

- Regular (annual or every 2 years) mammography is recommended in women aged 50–69 years [I, A]. Regular mammography may also be done for women aged 40–49 and 70–74 years, although the evidence for benefit is less well established [II, B].
- In women with a strong familial history of breast cancer, with or without proven *BRCA* mutations, annual MRI and annual mammography (concomitant or alternating) are recommended [III, A].

European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-019-04553-8

GUIDELINES

Good clinical practice recommendations for the use of PET/CT in oncology

Recommendations The following recommendations are mainly supported by literature data:

FDG-PET/CT is not recommended for characterizing a breast lesion as 'diagnosing malignancy'.
When FDG exams performed for other reasons come up with incidental finding of an FDG-avid intra-mammary focus, it is recommended to pursue investigations, even though some benign lesions such as fibroadenomas may give false-positive uptake.

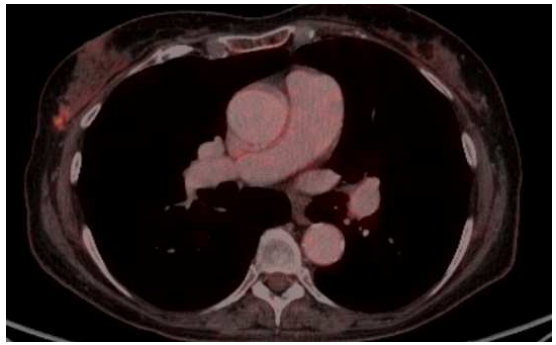
Aarstad *et al. European Journal of Hybrid Imaging* (2019) 3:16
https://doi.org/10.1186/s41824-019-0063-5

European Journal of Hybrid Imaging

REVIEW Open Access

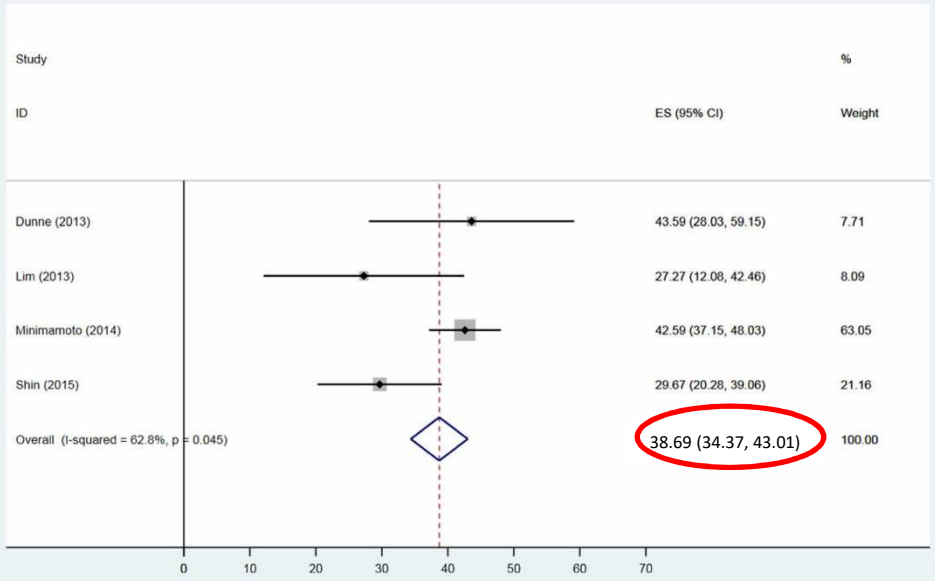
Prevalence of focal incidental breast uptake on FDG-PET/CT and risk of malignancy: a systematic review and meta-analysis

Else Marie Aarstad[1†], Petter Nordhaug[1†], Mohammad Naghavi-Behzad[1,2,3*], Lisbet Brønsro Larsen[4], Oke Gerke[2] and Malene Grubbe Hildebrandt[1,2,5]

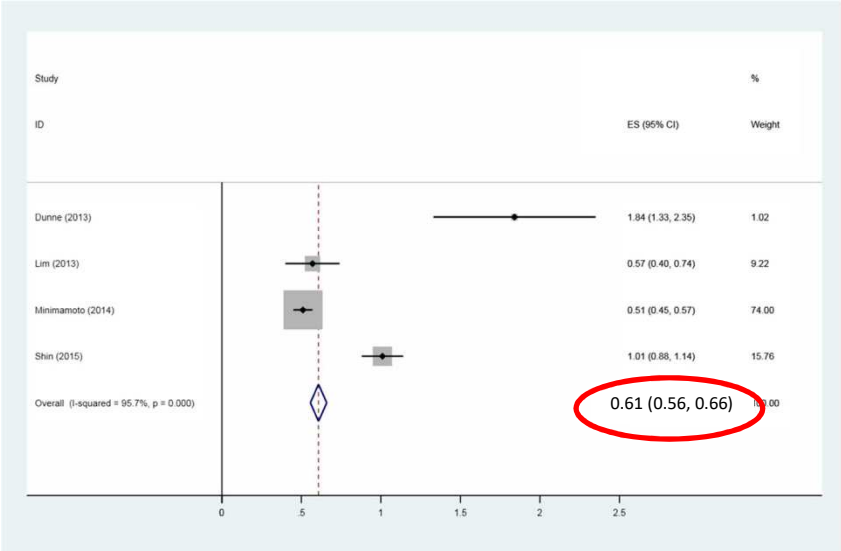


N=93,591 women in four studies

Risk of malignancy in focal incidental breast uptake on FDG-PET/CT



Prevalence of focal incidental breast uptake on FDG-PET/CT



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STADIEINDDELING AF PRIMÆR BRYSTKRÆFT

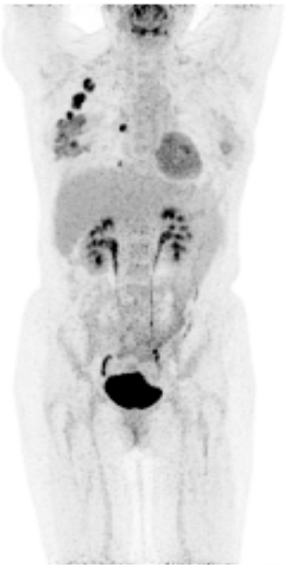
CA CANCER J CLIN 2017;67:290–303

Breast Cancer—Major Changes in the American Joint Committee on Cancer Eighth Edition Cancer Staging Manual

Armando E. Giuliano, MD[1]; James L. Connolly, MD[2]; Stephen B. Edge, MD[3]; Elizabeth A. Mittendorf, MD, PhD[4]; Hope S. Rugo, MD[5]; Lawrence J. Solin, MD[6]; Donald L. Weaver, MD[7]; David J. Winchester, MD[8]; Gabriel N. Hortobagyi, MD[9]

- T-staging
- N-staging
- M-staging
- *Integrering af biomarkører*

T stadie	N stadie	M stadie	Stadie
T1	N0	M0	IA
T0	N1mi*	M0	IB
T1	N1mi*	M0	IB
T0	N1	M0	IIA
T1	N2	M0	IIA
T2	N0	M0	IIA
T2	N1	M0	IIB
T3	N0	M0	IIB
T0	N2	M0	IIIA
T1	N2	M0	IIIA
T2	N2	M0	IIIA
T3	N1	M0	IIIA
T3	N2	M0	IIIA
T4	N0	M0	IIIB
T4	N1	M0	IIIB
T4	N2	M0	IIIB
Alle	N3	M0	IIIC
Alle	Alle	M1	IV



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T-STAGING PRIMÆR BRYSTKRÆFT

clinical practice guidelines

Annals of Oncology 26 (Supplement 5): v8–v30, 2015
doi:10.1093/annonc/mdv298

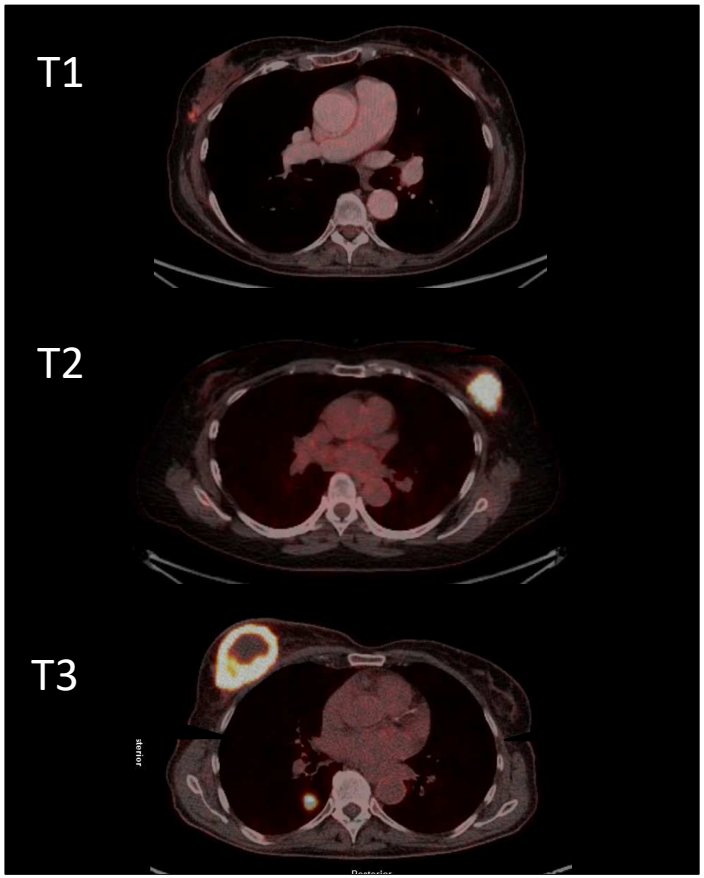
Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

E. Senkus[1], S. Kyriakides[2], S. Ohno[3], F. Penault-Llorca[4,5], P. Poortmans[6], E. Rutgers[7], S. Zackrisson[8] & F. Cardoso[9], on behalf of the ESMO Guidelines Committee*

Primary tumour (T)[a,b,c,d]

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma *in situ*
Tis (DCIS)	Ductal carcinoma *in situ*
Tis (LCIS)	Lobular carcinoma *in situ*
Tis (Paget's)	Paget's disease (Paget disease) of the nipple NOT associated with invasive carcinoma and/or carcinoma *in situ* (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget's disease are categorised based on the size and characteristics of the parenchymal disease, although the presence of Paget's disease should still be noted.
T1	Tumour ≤20 mm in greatest dimension
T1mi	Tumour ≤1 mm in greatest dimension
T1a	Tumour >1 mm but ≤5 mm in greatest dimension
T1b	Tumour >5 mm but ≤10 mm in greatest dimension
T1c	Tumour >10 mm but ≤20 mm in greatest dimension
T2	Tu… …greatest dimension

T1	Tumour ≤20 mm in greatest dimension
T1mi	Tumour ≤1 mm in greatest dimension
T1a	Tumour >1 mm but ≤5 mm in greatest dimension
T1b	Tumour >5 mm but ≤10 mm in greatest dimension
T1c	Tumour >10 mm but ≤20 mm in greatest dimension
T2	Tumour >20 mm but ≤50 mm in greatest dimension
T3	Tumour >50 mm in greatest dimension



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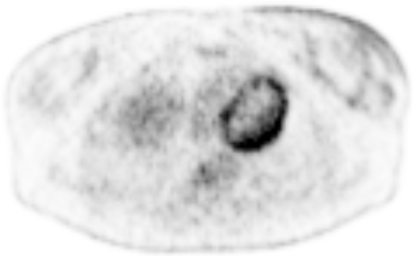
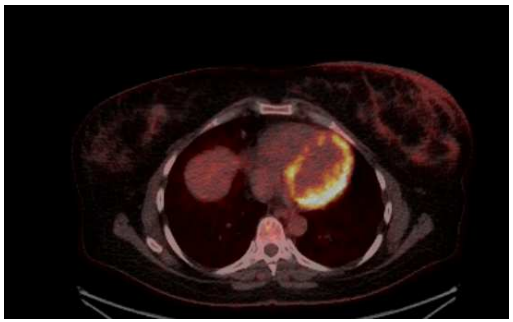
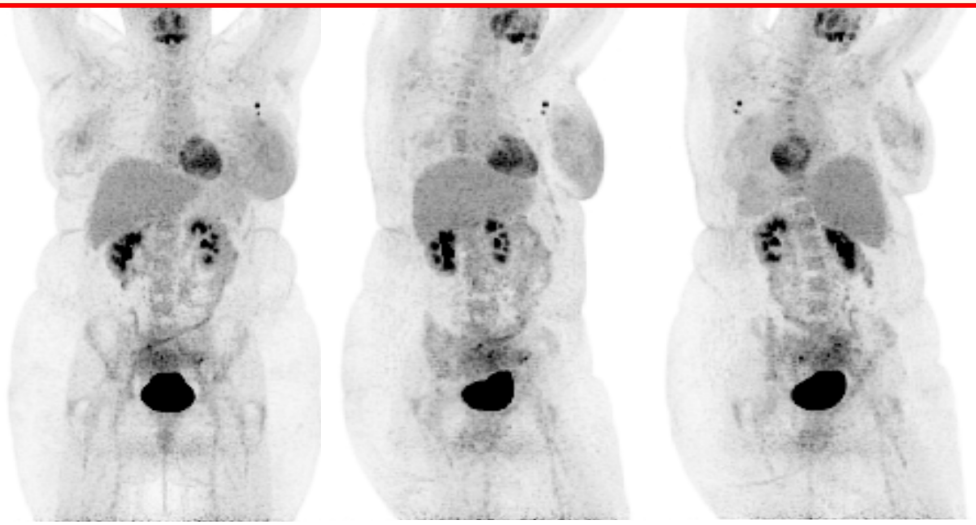




T4	Tumour of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules)[e]
T4a	Extension to the chest wall, not including only pectoralis muscle adherence/invasion
T4b	Ulceration and/or ipsilateral satellite nodules and/or oedema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma
T4c	Both T4a and T4b
T4d	Inflammatory carcinoma[f]



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T-STAGING PRIMÆR BRYSTKRÆFT

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 30:
doi:10.1093/annonc/m
Published online 4 Jun

SPECIAL ARTICLE

Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

Recommendations:

- Breast imaging should involve bilateral mammogram and US of breasts and axillae in all cases [I, A]; MRI is recommended in case of uncertainties following standard imaging and in special clinical situations [I, A].
- Pathological evaluation includes histology from the primary tumour and cytology/histology of the axillary nodes (if involvement is suspected) [I, A].
- Pathological report should include histological type, grade, IHC evaluation of ER, PgR (for invasive cancer), HER2 (for invasive cancer) and some form of proliferation markers (e.g. Ki67 for invasive cancer) [I, A]. Tumours should be grouped into surrogate intrinsic subtypes, defined by routine histology and IHC data [I, A].

European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-019-04553-8

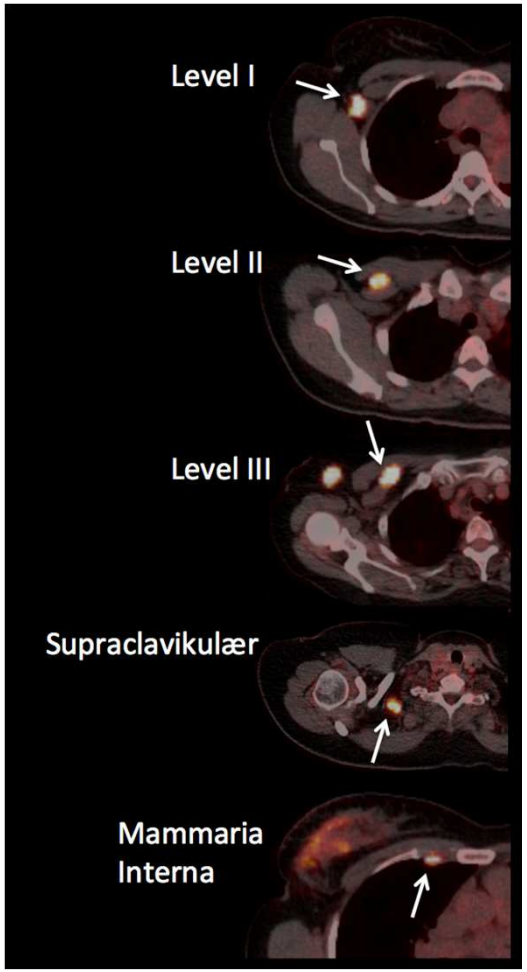
GUIDELINES

Good clinical practice recommendations for the use of PET/CT in oncology

Recommendations The following recommendation is mainly supported by literature data:

FDG-PET/CT is currently not recommended for assessing multifocality or determining the precise T status of a breast cancer in the TNM staging system.

N-STAGING PRIMÆR BRYSTKRÆFT



Lavt axillært (level I)

Midt axillært (level II)

Infraclavikulært (level III)

Supraclavikulært

Parasternalt ved mammaria interna karrene

Billede udlånt af Mikkel Holm Vendelbo

N-STAGING PRIMÆR BRYSTKRÆFT

ESMO

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doi:10.1093/annonc/m
Published online 4 Jun

SPECIAL ARTICLE

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Recommendations:

- SLNB, rather than full nodal clearance, is the standard of care for axillary staging in early, clinically node-negative breast cancer [II, A].
- Further axillary surgery following positive SLNB is not required in case of low axillary disease burden (micrometastases or 1–2 SLNs containing metastases, treated with postoperative tangential breast RT) [II, A].
- Axillary radiation is a valid alternative in patients with positive SLNB, irrespective of the type of breast surgery [II, A].

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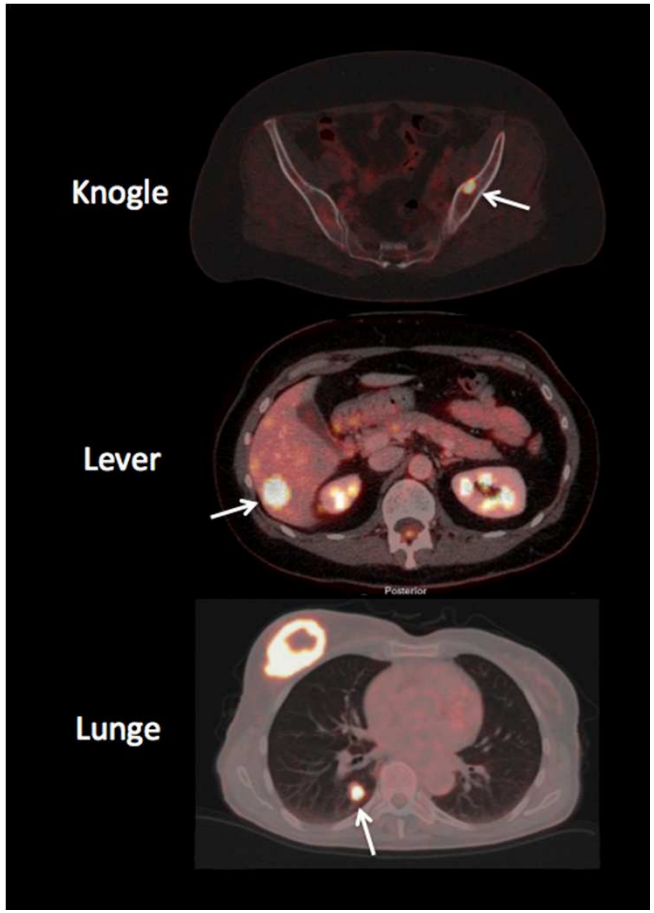
GUIDELINES

Good clinical practice recommendations for the use of PET/CT in oncology

Recommendations The following recommendation is mainly supported by literature data:

FDG-PET/CT is not recommended to replace sentinel node biopsy.

M-STAGING PRIMÆR BRYSTKRÆFT



Knoglemetastase

Levermetastase

Lungemetastase

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M-STAGING PRIMÆR BRYSTKRÆFT

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Published online 4 Jun

SPECIAL ARTICLE

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Recommendations:

- Imaging of chest, abdomen and bone is recommended for higher-risk patients (high tumour burden, aggressive biology, signs, symptoms or laboratory values suggesting the presence of metastases) [III, A].
- FDG-PET-CT scanning may be useful when conventional methods are inconclusive [V, A] and may replace traditional imaging for staging in high-risk patients [V, B].

European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-019-04553-8

GUIDELINES

Good clinical practice recommendations for the use of PET/CT in oncology

Recommendations The following recommendations are mainly supported by literature data:

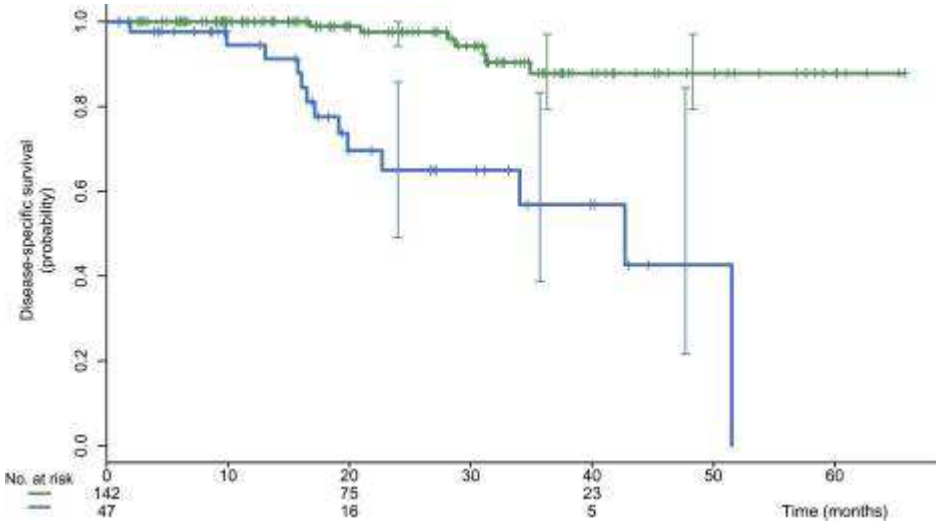
FDG-PET/CT is recommended for initial staging in patients with clinical stage ≥ IIB breast cancer and is better when performed before surgery.
FDG-PET/CT can be proposed for staging patients with clinical stage IIA (T1N1 or T2N0) breast cancer and is better when performed before surgery.
FDG-PET/CT is not recommended for staging patients with clinical stage I (T1N0) breast cancer.

Prognostic Impact of ^{18}FDG-PET-CT Findings in Clinical Stage III and IIB Breast Cancer

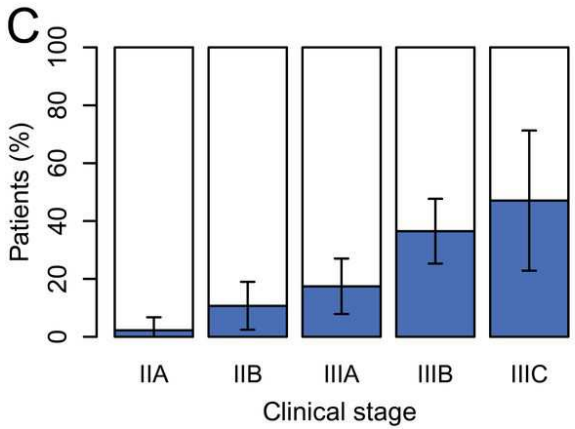
Table 2. Fluorodeoxyglucose positron emission tomography/computed tomography (^{18}FDG-PET-CT) findings according to tumor phenotype and Scarff-Bloom-Richardson (SBR) grade*

PET-CT findings	ER positive†/ HER2 negative‡	HER2 positive‡	TNBC	Grade 3	Grades 1 and 2	Total
Total patients	130§	51§	69§	119‖	126‖	254
Patients with N3 lymph nodes	21 (16%)	16 (31%)	19 (28%)	34 (29%)	17 (13%)	57 (22%)
Total patients with distant metastases	28 (22%)	13 (26%)	11 (16%)	20 (17%)	27 (21%)	53 (21%)
Only bone metastases	13 (10%)	5 (10%)	2 (3%)	7 (6%)	11 (9%)	21 (8%)
Extra-skeletal metastases only	5 (4%)	6 (12%)	7 (10%)	9 (8%)	8 (6%)	18 (7%)
Skeletal and extra-skeletal metastases	10 (8%)	2 (4%)	2 (3%)	4 (3%)	8 (6%)	14 (6%)

N=254

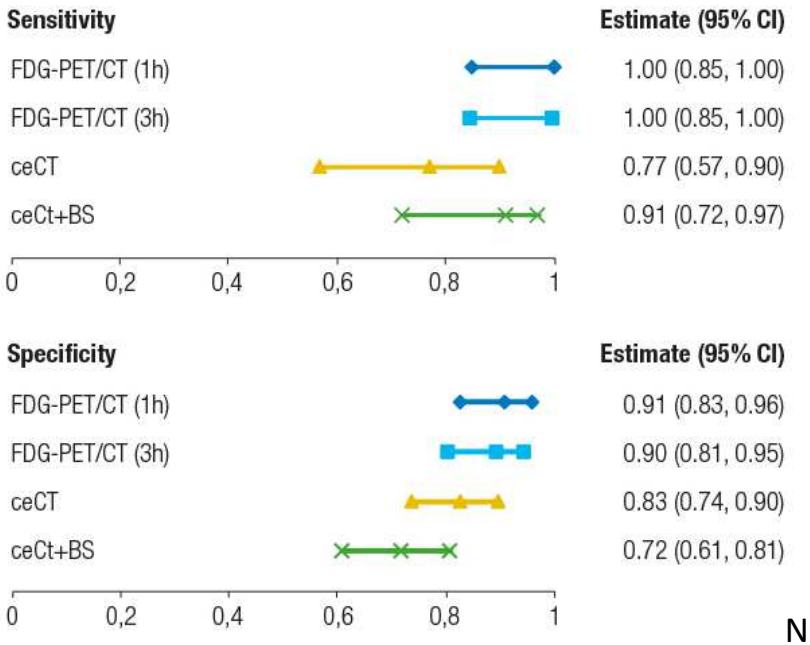


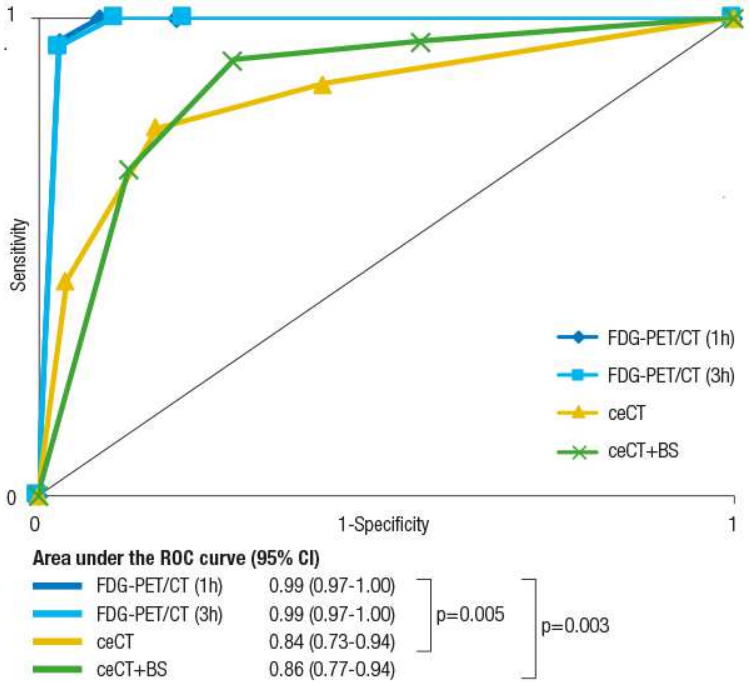
Yield of FDG-PET-CT in diagnosis of metastasis



RECIDIVOPSPORING- PROSPECTIVE ACCURACY STUDY

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT





N=100

Nuclear Medicine
Odense University Hospital Denmark

Region of Southern Denmark

STADIEINDDELING PRIMÆR BRYSTKRÆFT

Breast
Committe

Armando E. Gi
Hope S. Rugo, MD[5];

Table 1 Correlations between clinicopathological and SUVmax values

	Number (%)	SUVmax (mean±SD)	p value
Tumour invasive size (cm)			
1–2	127 (41.2)	3.51±2.14	<0.0001
>2	181 (58.8 %)	6.60±3.92	
ER status			
Positive	227 (73.7)	4.73±3.30	<0.0001
Negative	81 (26.3)	7.00±4.73	
PR status			
Positive	160 (51.9)	4.48±3.03	<0.0001
Negative	148 (48.1)	6.24±4.00	
HER2 status			
Negative	251 (81.5)	4.94±3.49	0.00029
Positive	57 (18.5)	7.02±3.81	
Ki-67 index (%)			
<14	103 (33.4)	3.70±2.50	<0.0001
≧14	205 (66.6)	6.14±3.84	
Nuclear grade			
1	167 (54.2)	4.00±2.66	<0.0001
2	75 (24.4)	6.31±3.89	
3	66 (21.4)	7.56±4.04	
Histology			
Invasive ductal carcinoma	282 (91.6)	5.51±3.66	0.0014
Invasive lobular carcinoma	13 (4.2)	3.10±1.56	
Others	13 (4.2)	3.62±3.57	
Axillary lymph node metastasis			
Absent	173 (56.2)	4.19±2.83	<0.0001
Present	135 (43.8)	6.78±4.02	
Stage			
I	94 (30.5)	3.17±1.83	<0.0001
II	165 (53.6)	5.44±3.18	
III	23 (7.5)	10.01±4.50	
IV	26 (8.4)	8.22±4.34	

CA CANCER J CLIN 2017;67:290–3

erican Joint
Staging Manual

Mittendorf, MD, PhD[4];
; Gabriel N. Hortobagyi, MD[9]

Eur J Nucl Med Mol Imaging (2015) 42:1371–1377
DOI 10.1007/s00259-015-3070-1

ORIGINAL ARTICLE

Association between ^{18}F-FDG uptake and molecular subtype of breast cancer

Kazuhiro Kitajima[1] · Kazuhito Fukushima[1] · Yasuo Miyoshi[2] · Arisa Nishimukai[2] · Seiichi Hirota[3] · Yoko Igarashi[1] · Takayuki Katsuura[1] · Kaoru Maruyama[1] · Shozo Hirota[4]

Højere FDG-aktivitet		Lavere FDG-aktivitet
Invasivt duktalt karcinom	>	Invasivt lobulært karcinom
Anaplasigrad 3	>	Anaplasigrad 1-2
Østrogenreceptornegativ	>	Østrogenreceptorpositiv
HER2-receptorpositiv	>	HER2-receptornegativ
Triple-negativ	>	Ikke triple-negativ
Højt KI-index	>	Lavt KI-index

NATIONAL VEJLEDNING

Brystkræftforløb	Anbefaling fra National PET/CT-gruppe
Diagnostik af primær brystkræft	FDG-PET/CT anbefales ikke til diagnostik af primær brystkræft*
Stadieinddeling ved primær brystkræft	FDG-PET/CT anbefales til udredning for fjernmetastasering ved: • klinisk mistanke herom • lokalavanceret brystkræft (Stadie III sygdom – se appendix) • inflammatorisk brystkræft (Stadie III sygdom – se appendix)
Responsevaluering ved lokalavanceret (primær) brystkræft	FDG-PET/CT anbefales ikke til responsevaluering efter neoadjuverende kemoterapi*
Opfølgningsforløb efter primær brystkræft	Der er ikke evidens for helkropsbilleddiagnostik som led i kontrol i opfølgningsforløb efter kurativt intenderet behandling for primær brystkræft*
Recidivopsporing	FDG-PET/CT anbefales til udredning for fjernmetastasering ved: • klinisk eller biokemisk mistanke om fjernrecidiv • biopsiverificeret lokoregionalt recidiv
Responsmonitorering ved metastaserende brystkræft	Der foreligger ikke tilstrækkelig evidens til anbefaling af FDG-PET/CT til responsmonitorering ved fjernmetastaserende (kronisk) brystkræft

PET/CT TIL RESPONSEVALUERING VED NACT

ESMO

Annals of Oncology 30:
doi:10.1093/annonc/m
Published online 4 Jun

SPECIAL ARTICLE

Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

This topic is not addressed

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GUIDELINES

Good clinical practice recommendations for the use of PET/CT in oncology

Recommendations The following recommendations are mainly supported by literature data:

FDG-PET/CT can be proposed for early evaluation of response to neoadjuvant therapy, particularly in triple negative or HER2+ disease, but it is currently not recommended to modify treatment on the basis of FDG-PET/CT results.

FDG-PET/CT is not recommended as an intervention to search for residual breast tumour at the end of neoadjuvant treatment.

RESPONSEVALUERING VED NACT

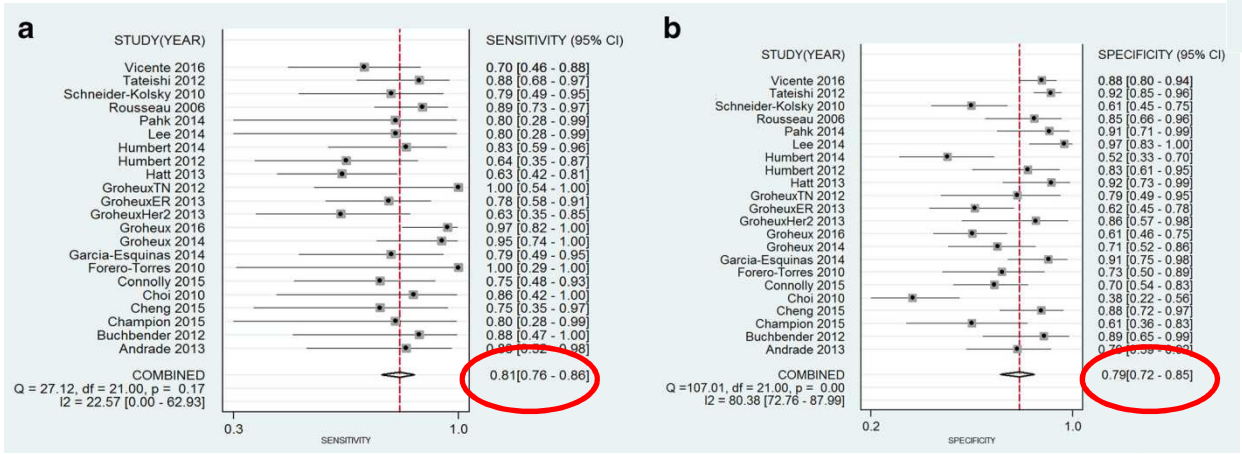
Eur Radiol (2017) 27:4786–4796
DOI 10.1007/s00330-017-4831-y

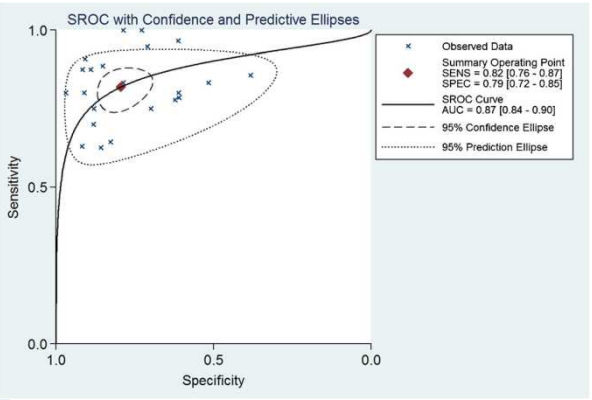
CrossMark

BREAST

The accuracy of ^{18}F-FDG PET/CT in predicting the pathological response to neoadjuvant chemotherapy in patients with breast cancer: a meta-analysis and systematic review

Fangfang Tian[1] · Guohua Shen[1] · Yunfu Deng[2] · Wei Diao[1] · Zhiyun Jia[1]





N=1119 BC patients, 22 studies
Two FDG-PET/CT scans
Diagnostic value of ΔSUV_{max}
Reference standard: Pathological response

It is advisable to perform post-therapy PET after second cycle of chemotherapy.

NATIONAL VEJLEDNING

Brystkræftforløb	Anbefaling fra National PET/CT-gruppe
Diagnostik af primær brystkræft	FDG-PET/CT anbefales ikke til diagnostik af primær brystkræft*
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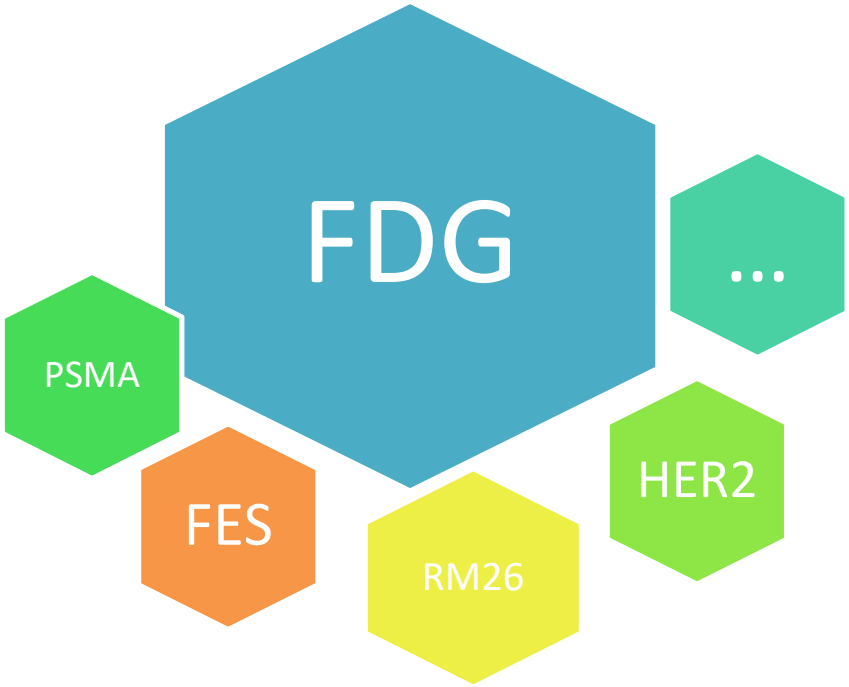
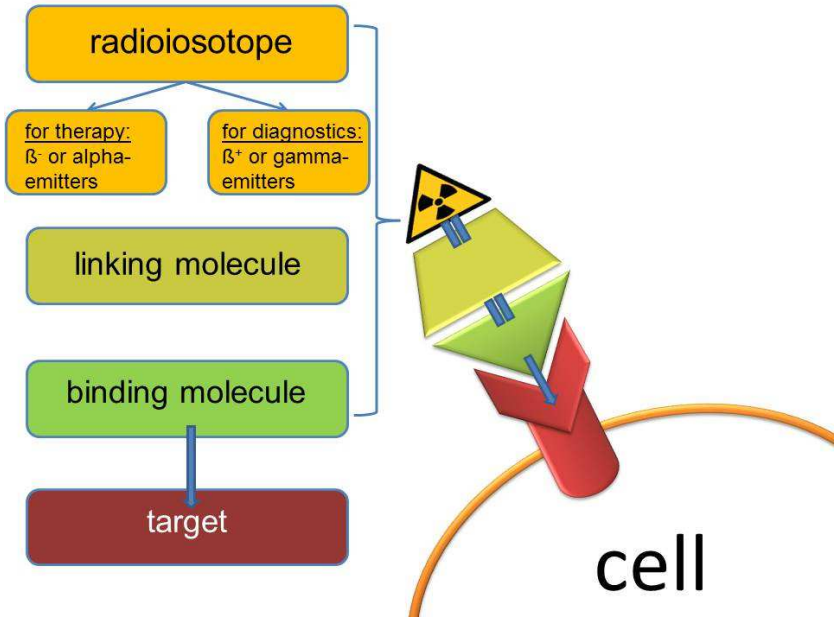
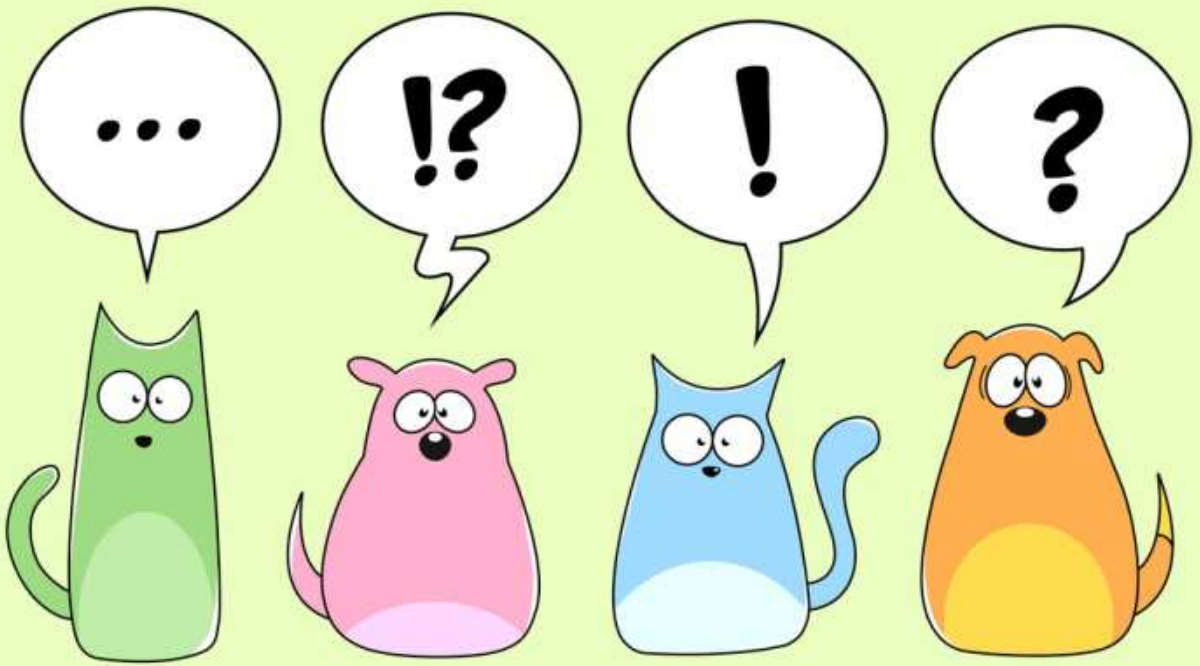
PERSPEKTIVER FOR PET/CT



PERSPEKTIVER FOR PET/CT





Tak for jeres opmærksomhed