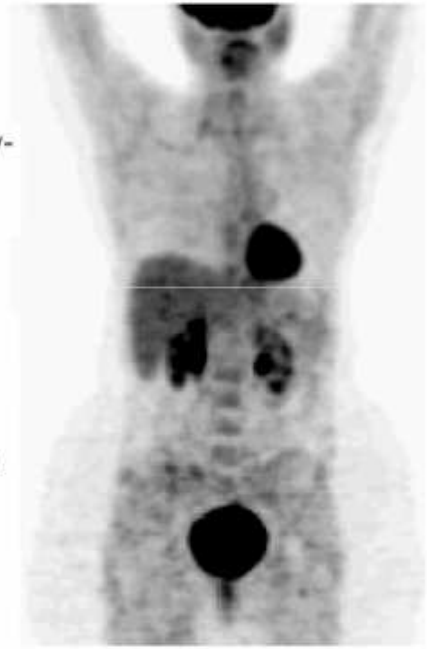
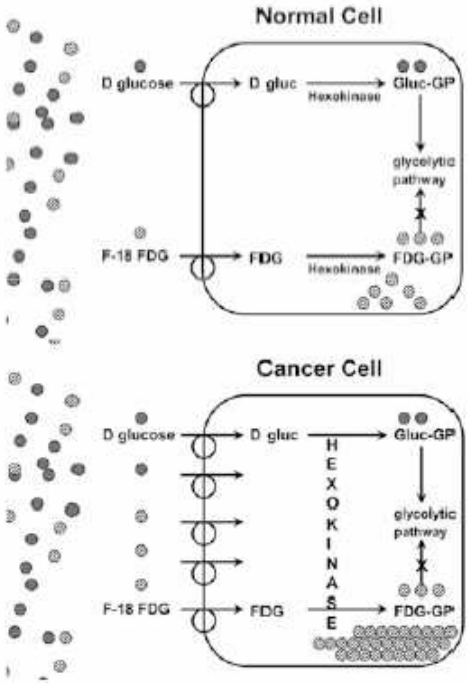
18F-FDG PET/TC
NEL CARCINOMA MAMMARIO

Paola Scapoli - MEDICINA NUCLEARE

Metabolismo del ^{18}F-FDG

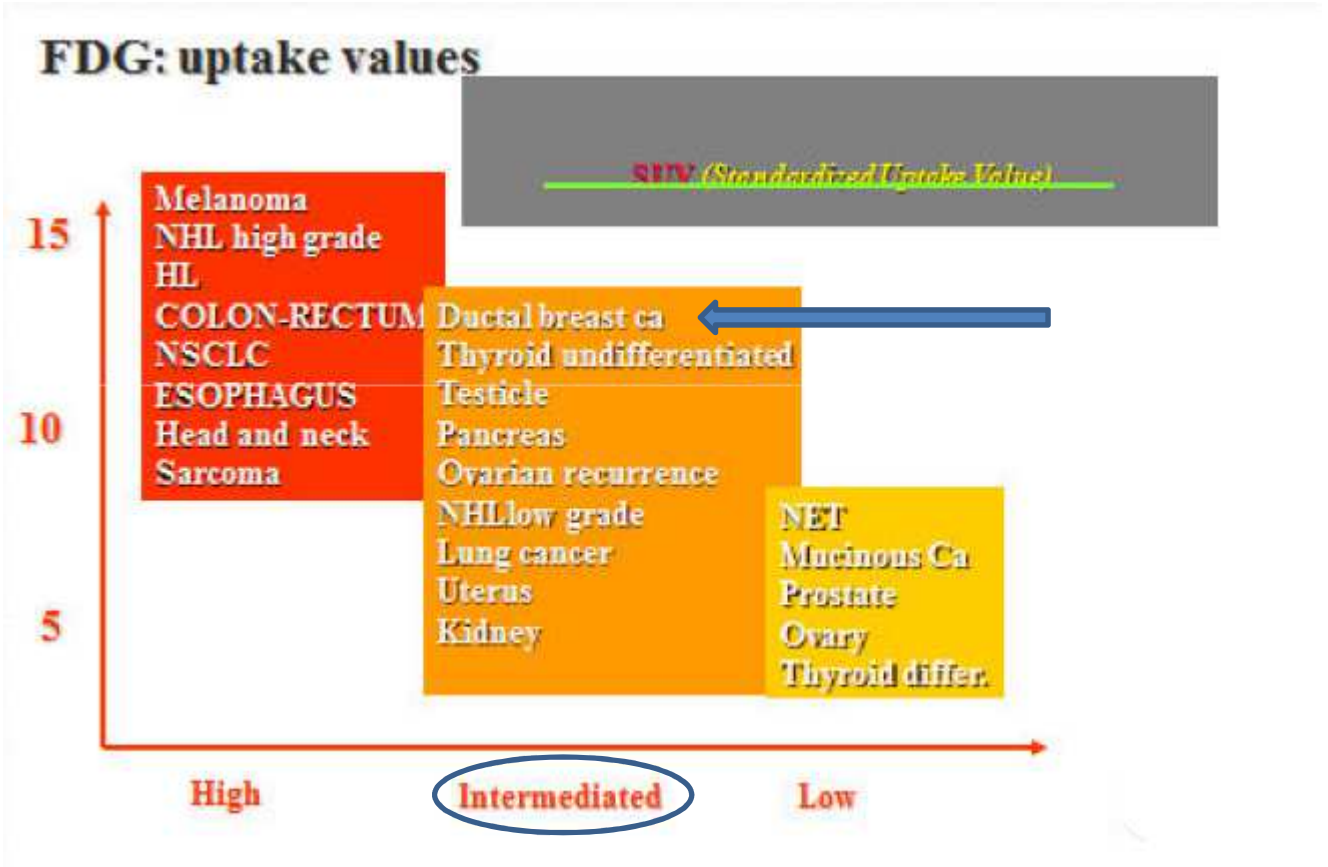
^{18}F-2-fluoro-2-deoxy-glucose (FDG)

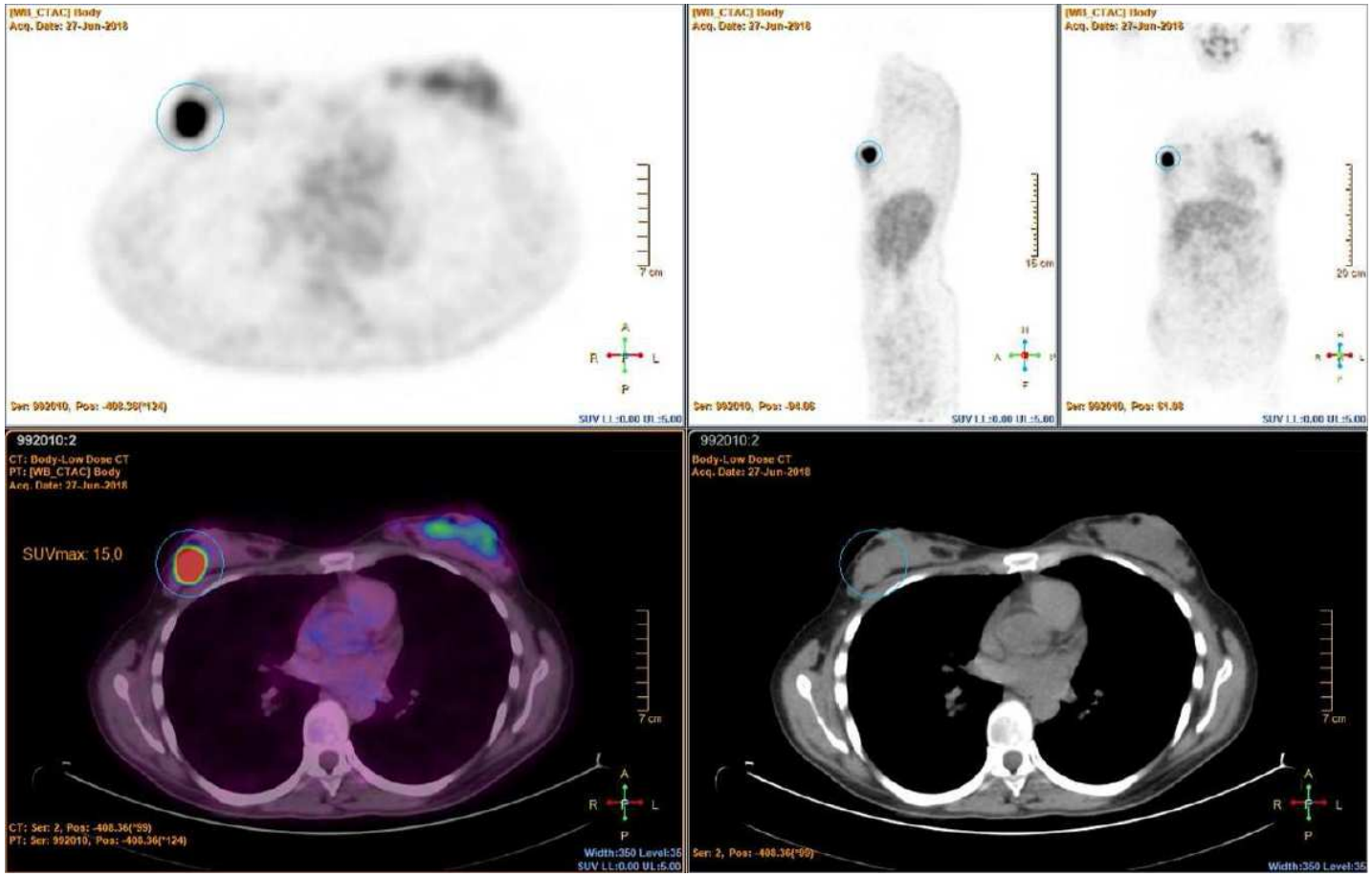


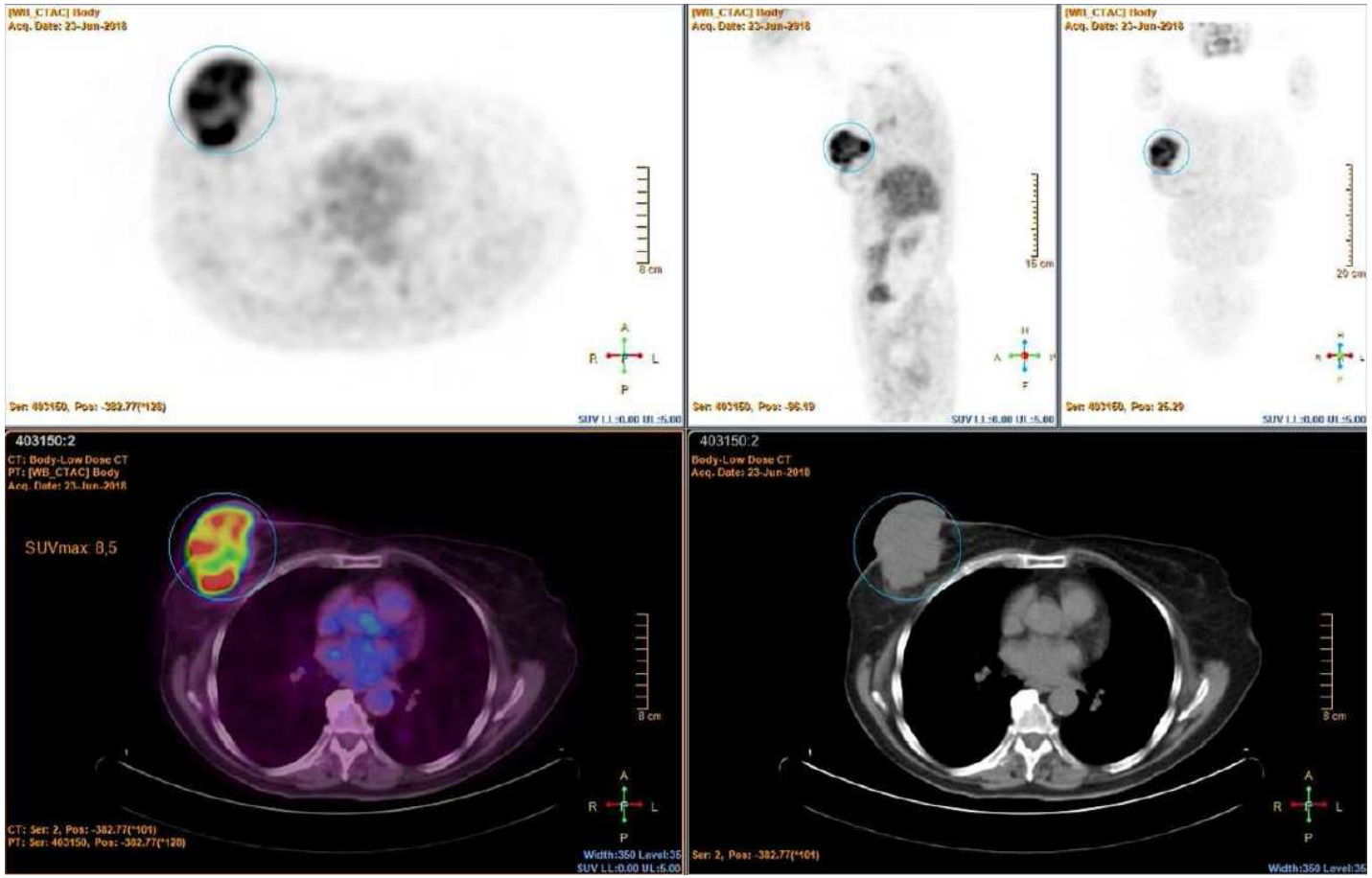


- Overexpression of GLUT
- Higher levels of Hexokinase
- Down-regulation of Glucose-6-phosphatase
- Anaerobic glycolysis
- General increase in metabolism from high growth rates

Intensità di captazione di ^{18}F-FDG in diversi tumori




[WB_CTAC] Body
Acq. Date: 27-Jun-2018
992010:2
CT: Body-Low Dose CT
PT: [WB_CTAC] Body
SUVmax: 15,0
Body-Low Dose CT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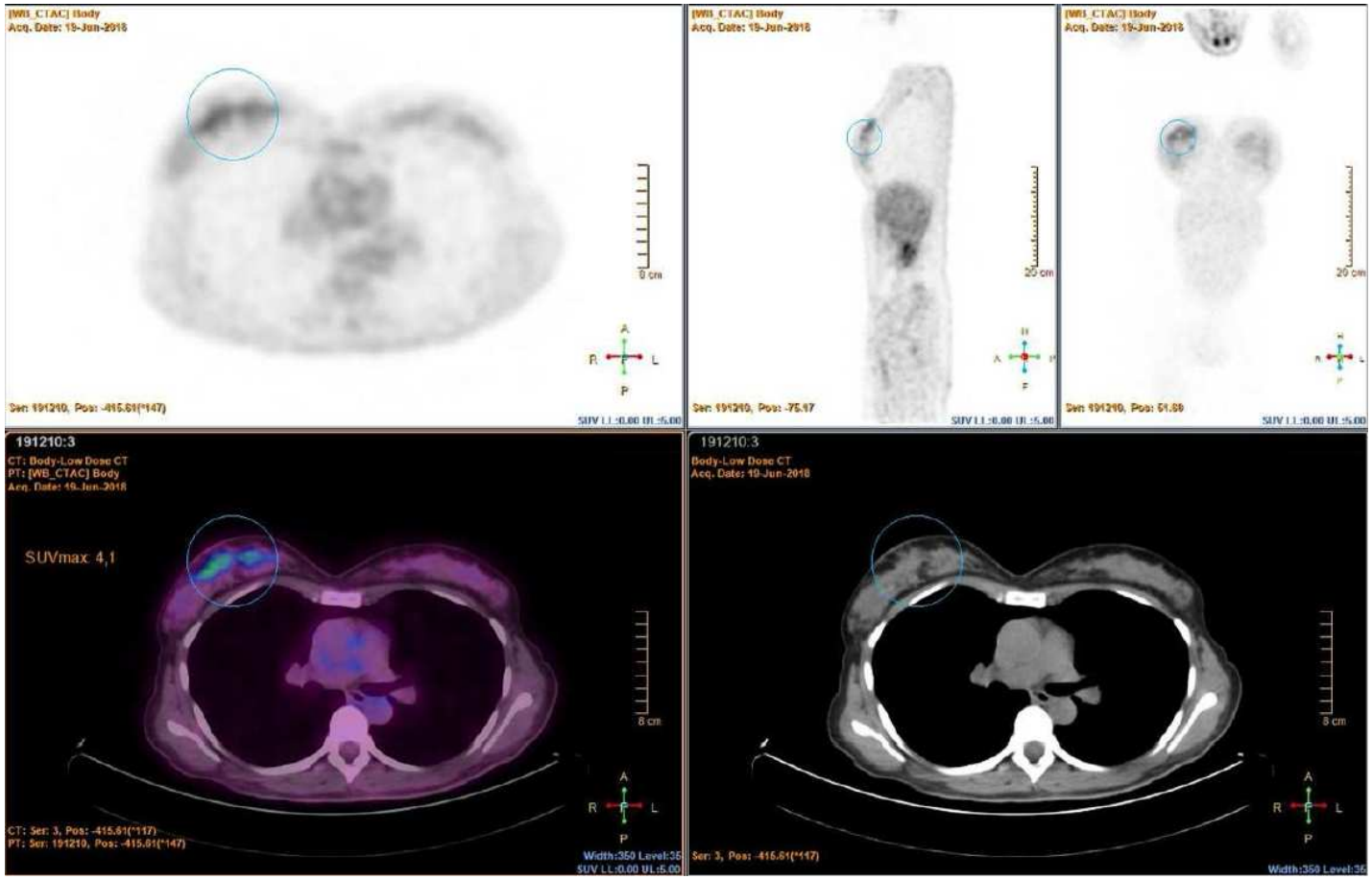
Body-Low Dose CT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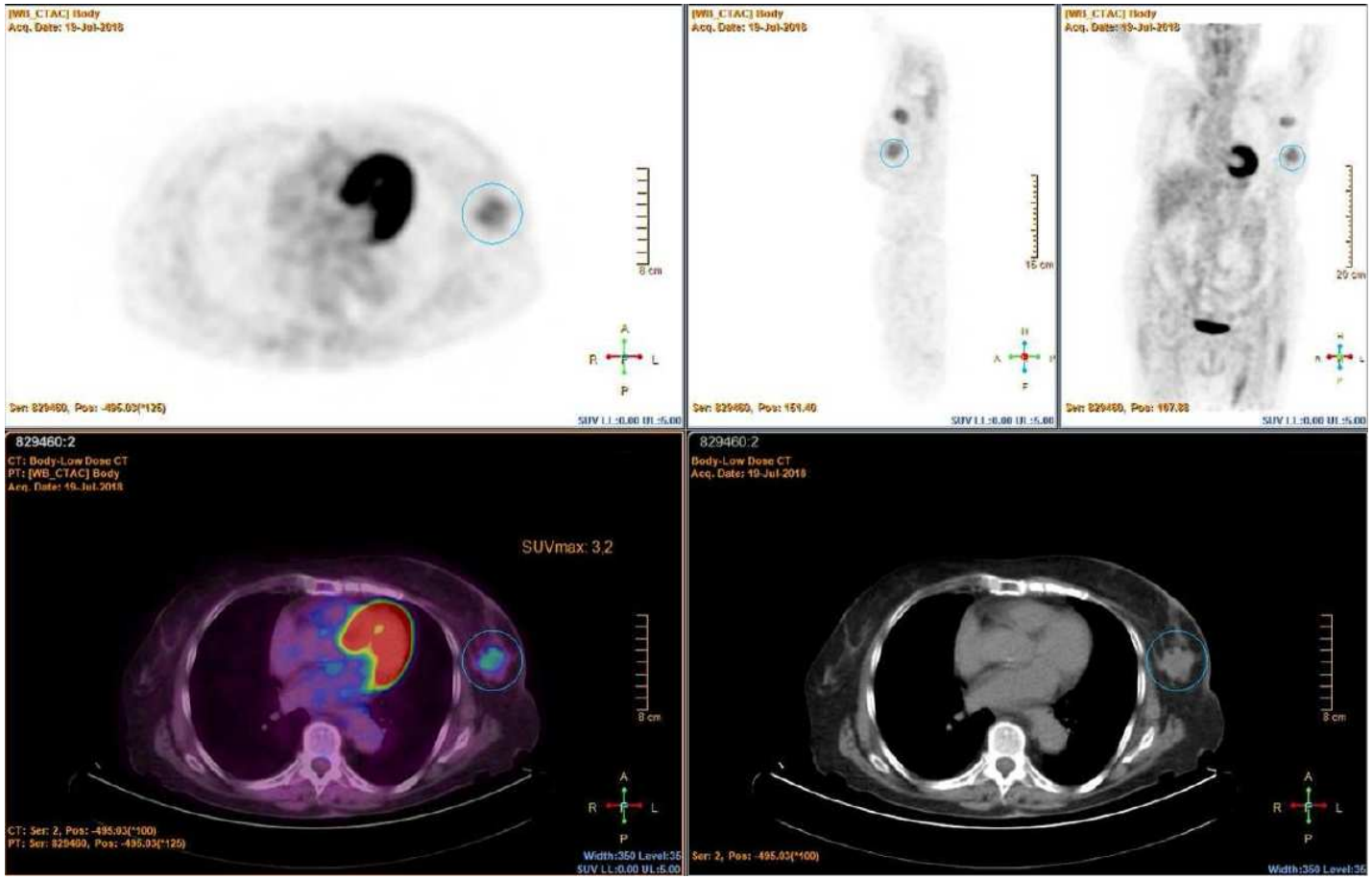
Acq. Date: 19-Jun-2018
SUVmax 4,1
Body-Low Dose CT
Acq. Date: 19-Jun-2018



ISTITUTO DI CANDIOLO - IRCCS

HETEROGENEITY AFFECTS TUMOR VISUALIZATION ON FDG PET/CT

- HISTOLOGY — IDC/no-special-type >>> ILC
- RECEPTOR STATUS — TNBC >>> non-TNBC
- TUMOR GRADE — GRADE 3 >>> GRADE 2/1
- PROLIFERATION INDEX — statistically significant positive correlation between proliferation index and FDG uptake in IDC

STAGING

Review

Tumor Biology

Tumor Biology
October 2017: 1–23

DOI: 10.1177/1010428317728285
journals.sagepub.com/home/tub
SAGE

18F-FDG PET/CT in breast cancer: Evidence-based recommendations in initial staging

Ana Paula Caresia Aroztegui[1], Ana María García Vicente[2], Soledad Alvarez Ruiz[3], Roberto Carlos Delgado Bolton[4], Javier Orcajo Rincon[5], Jose Ramon Garcia Garzon[6], Maria de Arcocha Torres[7] and Maria Jose Garcia-Velloso[8], on behalf of the Oncology Task Force of the Spanish Society of Nuclear Medicine and Molecular Imaging

Abstract

Current guidelines do not systematically recommend 18F-FDG PET/CT for breast cancer staging; and the recommendations and level of evidence supporting its use in different groups of patients vary among guidelines. This review summarizes the evidence about the role of 18F-FDG PET/CT in breast cancer staging and the therapeutic and prognostic impact accumulated in the last decade. Other related aspects, such as the association of metabolic information with biology and prognosis are considered and evidence-based recommendations for the use of 18F-FDG PET/CT in breast cancer staging are offered. We systematically searched MEDLINE for articles reporting studies with at least 30 patients related to clinical questions following the Problem/Population, Intervention, Comparison, and Outcome framework. We critically reviewed the selected articles and elaborated evidence tables structuring the summarized information into methodology, results, and limitations. The level of evidence and the grades of recommendation for the use of 18F-FDG PET/CT in different contexts are summarized. Level III evidence supports the use of 18F-FDG PET/CT for initial staging in patients with recently diagnosed breast cancer; the diagnostic and therapeutic impact of the 18F-FDG PET/CT findings is sufficient for a weak recommendation in this population. In patients with locally advanced breast cancer, level II evidence supports the use of 18F-FDG PET/CT for initial staging; the diagnostic and therapeutic impact of the 18F-FDG PET/CT findings is sufficient for a strong recommendation in this population. In patients with recently diagnosed breast cancer, the metabolic information from baseline 18F-FDG PET/CT is associated with tumor biology and has prognostic implications, supported by level II evidence. In conclusion, 18F-FDG PET/CT is not recommended for staging all patients with early breast cancer, although evidence of improved regional and systemic staging supports its use in locally advanced breast cancer. Baseline tumor glycolytic activity is associated with tumor biology and prognosis.

Review

Tumor Biology

Tumor Biology
October 2017: 1–23

DOI: 10.1177/1010428317728285
journals.sagepub.com/home/tub
SAGE

18F-FDG PET/CT in breast cancer: Evidence-based recommendations in initial staging

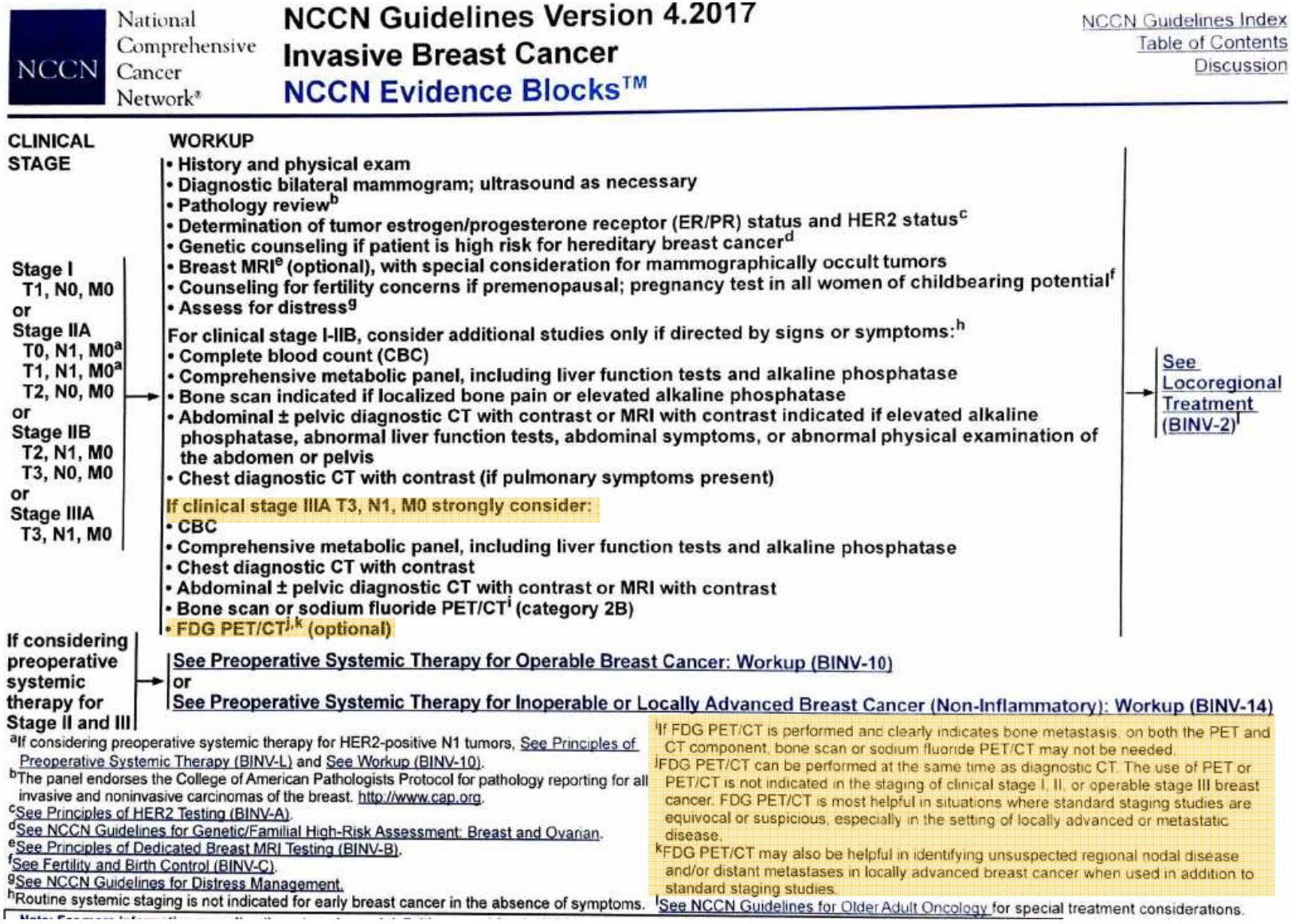
Table 1. Evidence level and grade of recommendations for 18F-FDG PET/CT in staging breast cancer as reported in current clinical guidelines.

Guideline	Evidence level /grade of recommendation	Recommendation description
SEOM 2015	I/A[a]	Suspicion of distant metastases: When anomalies are detected in laboratory tests, or when disease is detected at advanced stage (stage III), a more extensive study is performed using PET/CT or thoracic–abdominal CT and bone scan (if bone symptoms, elevation of alkaline phosphatase, lactose dehydrogenase, or calcium are present).
	III/C[a]	Determination of metastatic spread in standard staging.
ESMO 2015	V/A[b]	Locally advanced breast cancer with inconclusive conventional diagnostic methods.
	V/B[b]	PET/CT scanning can replace traditional imaging for staging in high-risk patients who are candidates for neoadjuvant chemotherapy, as well as those with locally advanced and/or inflammatory disease due to their high risk of having metastatic disease.
NCCN 2016	II/B[c]	Bone scan or sodium fluoride PET/CT: only in patients presenting with localized bone pain or elevated alkaline phosphatase. FDG PET/CT is most helpful in situations where standard imaging results are equivocal or suspicious. However, limited studies support a potential role of FDG PET/CT to detect regional node involvement as well as distant metastases in locally advanced breast cancer, including T3, N1, and M0 disease. The NCCC panel suggests that bone scan may be omitted if FDG PET/CT results are positive for bone metastases.
NICE 2015	Not referred	PET/CT should only be used to make a new diagnosis of metastases for patients with locally advanced breast cancer whose imaging is suspicious but not diagnostic of metastatic disease.

18F-FDG PET/CT: fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography; NCCC: Norris Cotton Cancer Center.
[a]Strength of recommendation (five categories, A–E)/quality of evidence (three categories, I–III).
[b]Grade of recommendation (six categories, 1A–2C).
[c]Categories of evidence and consensus (four categories, 1, 2a, 2b and 3).

Ca mammario localmente avanzato

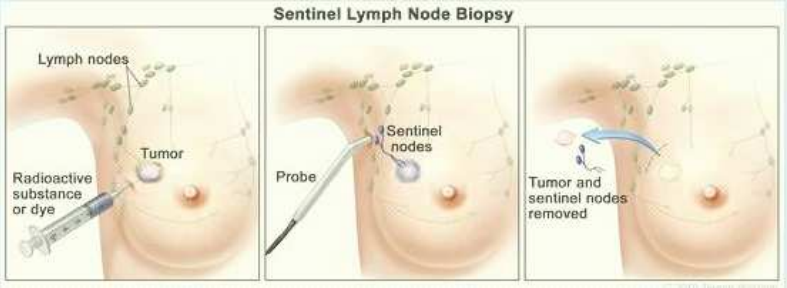
Presenza di segni/sintomi suggestivi per mts
e/o
reperti dubbi all'imaging standard


National Comprehensive Cancer Network
NCCN Guidelines Version 4.2017
Invasive Breast Cancer
NCCN Evidence Blocks™
NCCN Guidelines Index
Table of Contents
Discussion
CLINICAL STAGE
WORKUP
• History and physical exam
• Diagnostic bilateral mammogram; ultrasound as necessary
• Pathology review[b]
• Determination of tumor estrogen/progesterone receptor (ER/PR) status and HER2 status[c]
• Genetic counseling if patient is high risk for hereditary breast cancer[d]
• Breast MRI[e] (optional), with special consideration for mammographically occult tumors
• Counseling for fertility concerns if premenopausal; pregnancy test in all women of childbearing potential[f]
• Assess for distress[g]
Stage I
T1, N0, M0
or
Stage IIA
T0, N1, M0[a]
T1, N1, M0[a]
T2, N0, M0
or
Stage IIB
T2, N1, M0
T3, N0, M0
or
Stage IIIA
T3, N1, M0
For clinical stage I-IIB, consider additional studies only if directed by signs or symptoms:[h]
• Complete blood count (CBC)
• Comprehensive metabolic panel, including liver function tests and alkaline phosphatase
• Bone scan indicated if localized bone pain or elevated alkaline phosphatase
• Abdominal ± pelvic diagnostic CT with contrast or MRI with contrast indicated if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, or abnormal physical examination of the abdomen or pelvis
• Chest diagnostic CT with contrast (if pulmonary symptoms present)
If clinical stage IIIA T3, N1, M0 strongly consider:
• CBC
• Comprehensive metabolic panel, including liver function tests and alkaline phosphatase
• Chest diagnostic CT with contrast
• Abdominal ± pelvic diagnostic CT with contrast or MRI with contrast
• Bone scan or sodium fluoride PET/CT[i] (category 2B)
• FDG PET/CT[j,k] (optional)
See Locoregional Treatment (BINV-2)[l]
If considering preoperative systemic therapy for Stage II and III
See Preoperative Systemic Therapy for Operable Breast Cancer: Workup (BINV-10)
or
See Preoperative Systemic Therapy for Inoperable or Locally Advanced Breast Cancer (Non-Inflammatory): Workup (BINV-14)
[a]If considering preoperative systemic therapy for HER2-positive N1 tumors, See Principles of Preoperative Systemic Therapy (BINV-L) and See Workup (BINV-10).
[b]The panel endorses the College of American Pathologists Protocol for pathology reporting for all invasive and noninvasive carcinomas of the breast. http://www.cap.org.
[c]See Principles of HER2 Testing (BINV-A).
[d]See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian.
[e]See Principles of Dedicated Breast MRI Testing (BINV-B).
[f]See Fertility and Birth Control (BINV-C).
[g]See NCCN Guidelines for Distress Management.
[h]Routine systemic staging is not indicated for early breast cancer in the absence of symptoms.
[i]If FDG PET/CT is performed and clearly indicates bone metastasis on both the PET and CT component, bone scan or sodium fluoride PET/CT may not be needed.
[j]FDG PET/CT can be performed at the same time as diagnostic CT. The use of PET or PET/CT is not indicated in the staging of clinical stage I, II, or operable stage III breast cancer. FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease.
[k]FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in locally advanced breast cancer when used in addition to standard staging studies.
[l]See NCCN Guidelines for Older Adult Oncology for special treatment considerations.

STAGING: N

STADIO I e II (N0): non indicazione a PET/TC con FDG

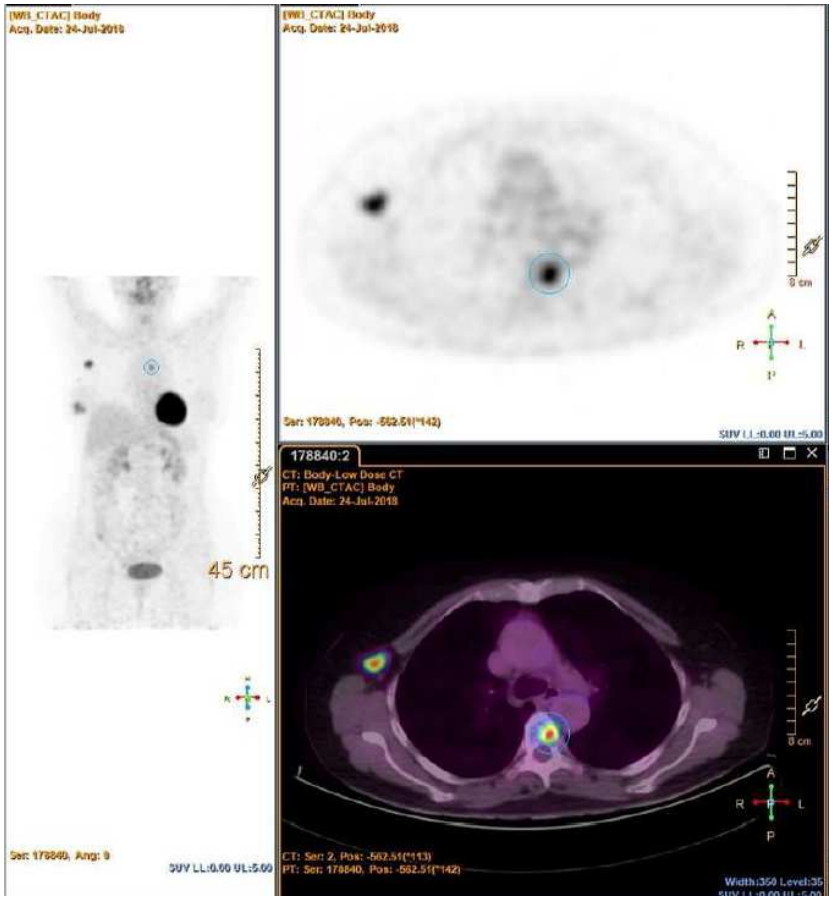
Minore sensibilità e specificità rispetto alla biopsia del linfonodo sentinella nella valutazione dei linfonodi ascellari
(63% e 94% vs 93% e 100%)



STADIO II (N1) e III (localmente avanzato): utile l'esecuzione di PET/TC con FDG prima della chirurgia o della terapia neoadiuvante

Possibilità di identificare adenopatie extra-ascellari

STAGING: M



Elevata «detection rate» di metastasi a distanza, specie nei tumori localmente avanzati (> 20% dei casi)

UPSTAGING

con significativo impatto sull'approccio terapeutico

In sintesi…

Early breast cancer → non indicazione alla PET/TC con FDG
(eventuale indicazione come indagine di II livello per approfondire reperti dubbi all'imaging radiologico)

indicata esecuzione di scintigrafia ossea in presenza di segni/sintomi suggestivi per metastasi scheletriche

Locally advanced breast cancer → indicazione alla PET/TC con FDG

«Zona grigia» → pazienti affette da ca mammario in stadio IIA-IIB

Facciamo o non facciamo la PET?

SYSTEMATIC REVIEWS

Preoperative [18]fluorodeoxyglucose-positron emission tomography/computed tomography in early stage breast cancer: Rates of distant metastases

Vincent Vinh-Hung, Hendrik Everaert, Karim Farid, Navid Djassemi, Jacqueline Baudin-Veronique, Stefanos Bougas, Yuriy Michailovich, Clarisse Joachim-Contaret, Elsa Cécilia-Joseph, Claire Verschraegen, Nam P Nguyen

World Journal of Radiology

World J Radiol 2017 July 28; 9(7): 312-320

T2 N1 M0, T3 N0 M0

Table 2 Prevalence of occult distant metastases in clinical stage II patients who had [18]fluorodeoxyglucose-positron emission tomography scan as part of a staging workup before or immediately after surgery

Ref.	Subjects, *n*	Age, median	Distant metastases rate		
			II A	II B	All
Groheux *et al*[17]	84	NS	2.80% (1/36)	8.30% (4/48)	5.95%
Gunalp *et al*[23]	100	51	19.60% (10/51)	40.80% (20/49)	30%
Cochet *et al*[24]	142	51	9.10% (2/22)	7.00% (4/57)	7.60%
Jeong *et al*[25]	70	54.9	0% (0/64)	0% (0/6)	0%
Riedl *et al*[27]	91	36.2	5% (2/44)	17% (8/47)	10.90%
Nursal *et al*[31]	315	51.5	9.50% (19/199)	17.20% (20/116)	12.40%
Ulaner *et al*[32]	169	51	5% (4/82)	15% (13/87)	9.50%
Lebon *et al*[33]	124	45.2	11% (7/64)	15% (9/60)	12.90%
Ulaner *et al*[34]	483	52.7	4.20% (6/143)	13.80% (26/188)	9.70%
All	1578	47.8	7.20% (0%-19.6%)	15.80% (0%-40.8%)	11.40% (0%-12.9%)

Large tumors
Axillary lymph node metastasis

Young age (< 40 years old)

TUMOR BIOLOGY

ISTITUTO DI CANDIOLO - IRCCS

ANNALS OF ONCOLOGY

letters to the editor

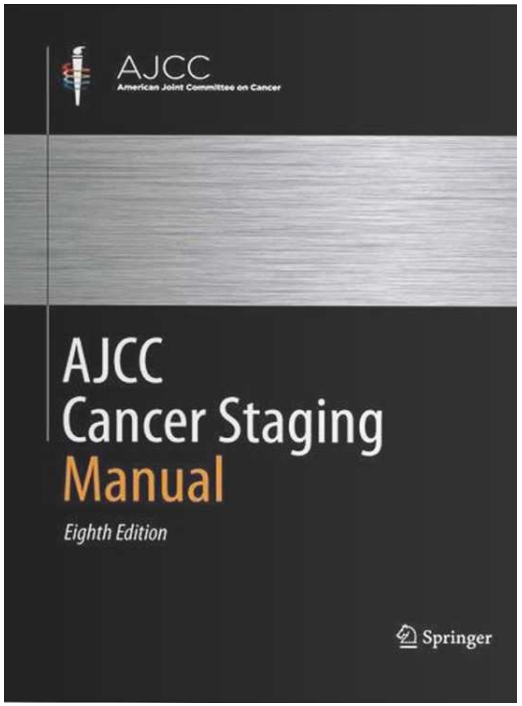
Preoperative PET/CT in early-stage breast cancer: is the TNM classification enough?

L. Gilardi[1], L. Fumagalli[2] & G. Paganelli[1*]

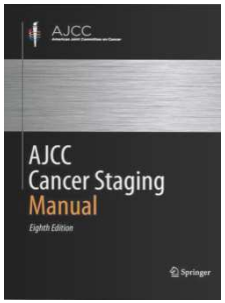
Divisions of [1]Nuclear Medicine;
[2]Medical Oncology, European Institute of Oncology, Milan, Italy

However, each TNM subgroup does not consider the biology of tumors cells and includes tumors with very different behaviors. Breast cancer is indeed a heterogeneous disease in terms of histology, dissemination modality, therapeutic response and prognosis. The tumors can be classified into subtypes distinguished by pervasive difference in their gene expression patterns [3]. These differences can be defined by genetic array testing or by a common histopathological determination of the expression of estrogen receptors, progesterone receptors, c-erbB2 and Ki67, that are actually considered sufficient to guide the systemic therapeutic plan [4].

The decision to carry out an FDG-PET/CT scan in the initial evaluation of patients with early breast cancer should probably take into account these biological differences as it is quite well established that some more aggressive subtypes of breast cancer have a greater probability to develop systemic disseminations even in the case of a relative small tumor. This could make the imaging procedure more useful, further improving its impact on the management of patients. Obviously, this is an impression that should be validated through a targeted prospective study with a large number of patients.



STADIO IIB



When TNM is…	And Grade is…	And HER2 Status is…	And ER Status is…	And PR Status is…	Then the Clinical Prognostic Stage Group is…
T2 N1*** M0 T3 N0 M0	G1	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
	G2	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIIB
	G3	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IIB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB

Facciamo la PET alle pazienti con TNBC in stadio IIB?

- Esiguità di dati in letteratura
- Pochi studi, per lo più retrospettivi e monocentrici
- Popolazioni eterogenee di pazienti
- Reperti PET non sempre confermati da EI

Eur J Nucl Med Mol Imaging. 2016 October ; 43(11): 1937–1944. doi:10.1007/s00259-016-3402-9.

^{18}F-FDG-PET/CT for Systemic Staging of Newly Diagnosed Triple-Negative Breast Cancer

Gary A. Ulaner[1,2], Raychel Castillo[1,2], Debra A. Goldman[3], Jonathan Wills[4], Christopher C
n[3]

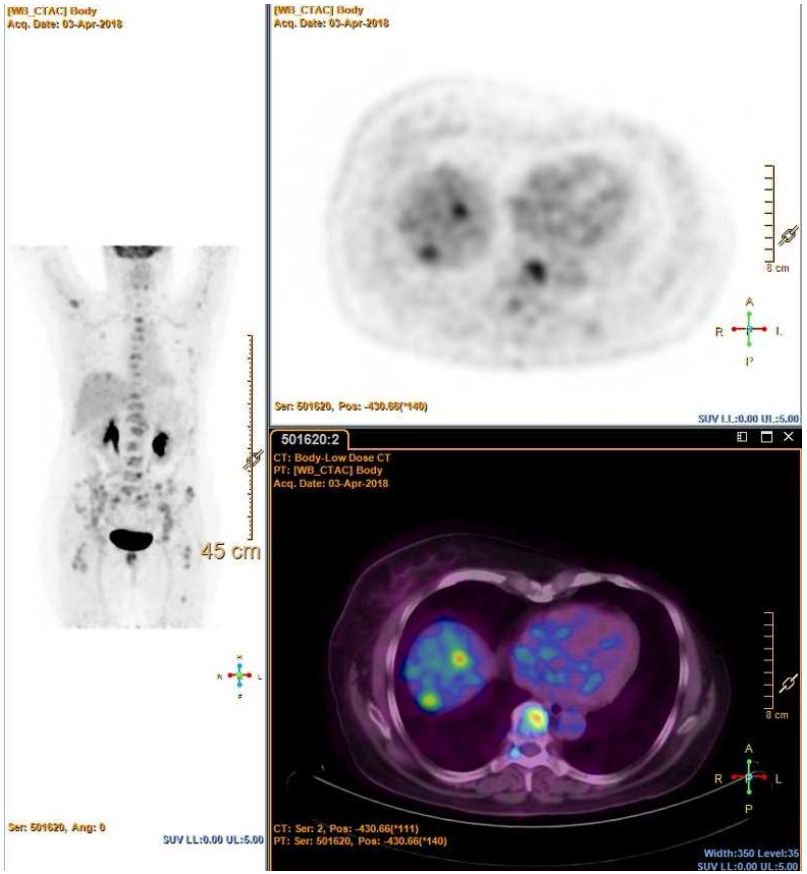
CONCLUSION

Fifteen percent of patients with initial stage IIB TNBC demonstrated unsuspected distant metastases, and were upstaged to stage IV, on ^{18}F-FDG-PET/CT. Although NCCN guidelines recommend against systemic staging with ^{18}F-FDG-PET/CT in patients with stage II breast cancer, our data suggest that patients with the aggressive triple negative receptor phenotype benefit from ^{18}F-FDG-PET/CT staging at least as early as stage IIB. Prospective evaluation of the impact that the receptor phenotype has on the utility of ^{18}F-FDG-PET/CT for systemic staging of patients with breast cancer is warranted.

Necessità di studi prospettici!

RESTAGING

Sospetto clinico e/o radiologico di recidiva loco-regionale/metastasi
Aumento dei markers



Elevata accuratezza diagnostica della FDG PET/TC

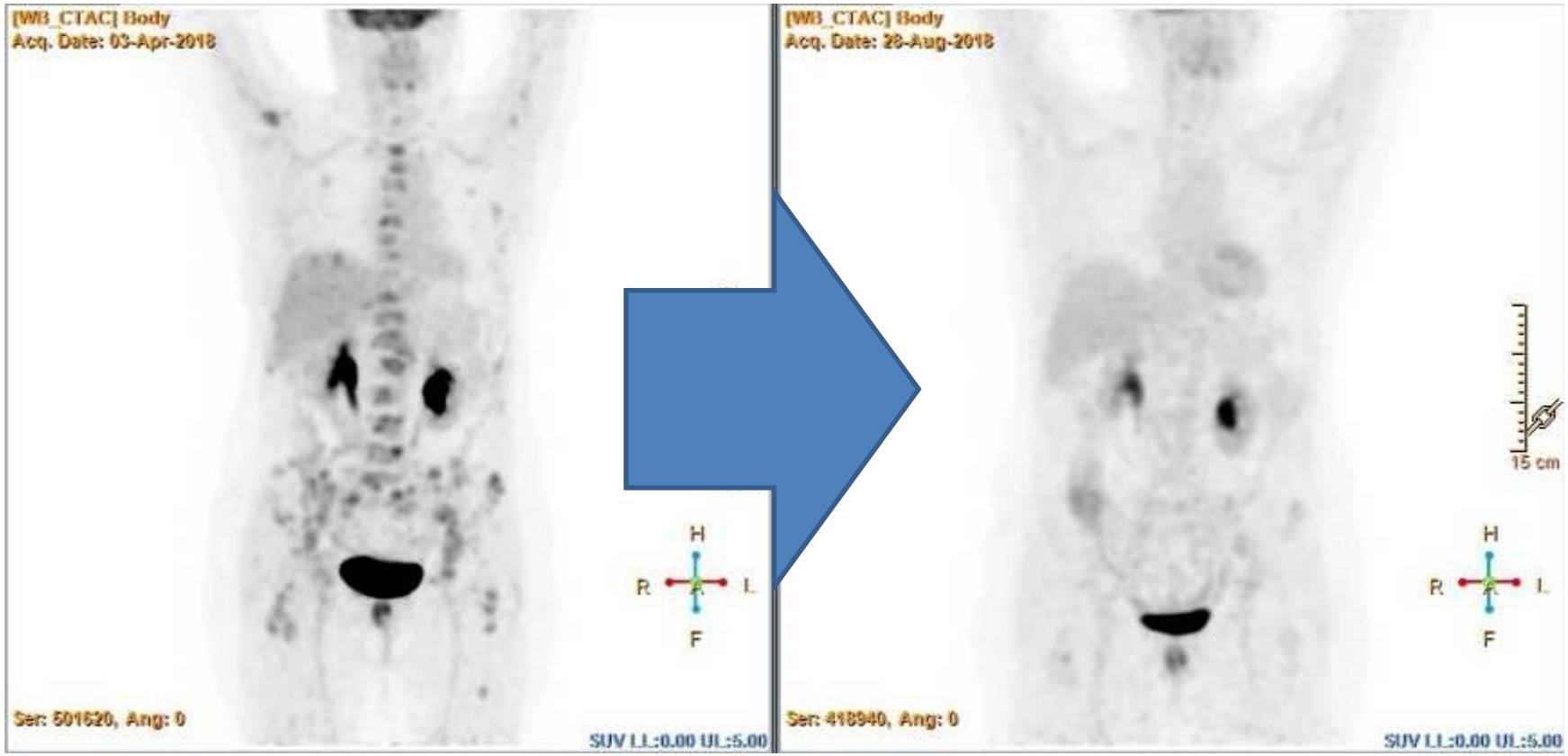
VANTAGGI
- Indagine «total-body»
- Possibilità di discriminare tra tessuto fibrotico e malattia
- Identificazione precoce di metastasi

Attualmente non indicata in LG
(indagine <u>opzionale</u> in caso di reperti dubbi)

Change management > 30% dei casi

Nel follow-up?

TREATMENT RESPONSE



ISTITUTO DI CANDIOLO - IRCCS

KEY POINTS

- Changes in metabolic activity generally occur earlier than changes in tumor size.
- The metabolic information provided by PET has been shown to be valuable for the early assessment of the response to neoadjuvant chemotherapy, but the methodology for image acquisition and analysis needs to be standardized; breast cancer subtype and treatment type need to be considered in interpreting the change in fludeoxyglucose uptake with therapy.
- In the metastatic setting, there is evidences that PET/computed tomography (CT) performed better than CT alone, especially to assess the response in bone metastases.
- In the metastatic setting, PET/CT has the ability to evaluate different sites of metastases in a single examination and to detect a heterogeneous response (coexistence of responding and nonresponding lesions within the same patient).
- The use of PET/CT in patients with metastatic breast cancer is hampered by the absence of consensus of the criteria to use to assess the response, of the number of metastatic sites to analyze, and of the optimal date to perform PET during treatment.

18F-FDG PET/TC
NEL CARCINOMA MAMMARIO

GRAZIE PER L'ATTENZIONE!

Paola Scapoli - MEDICINA NUCLEARE