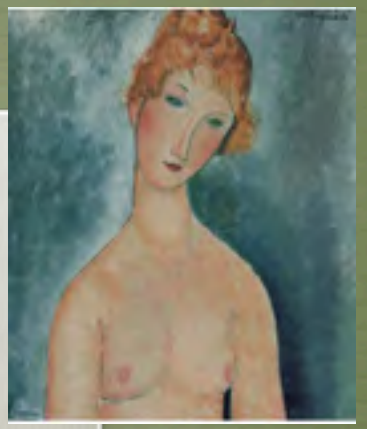
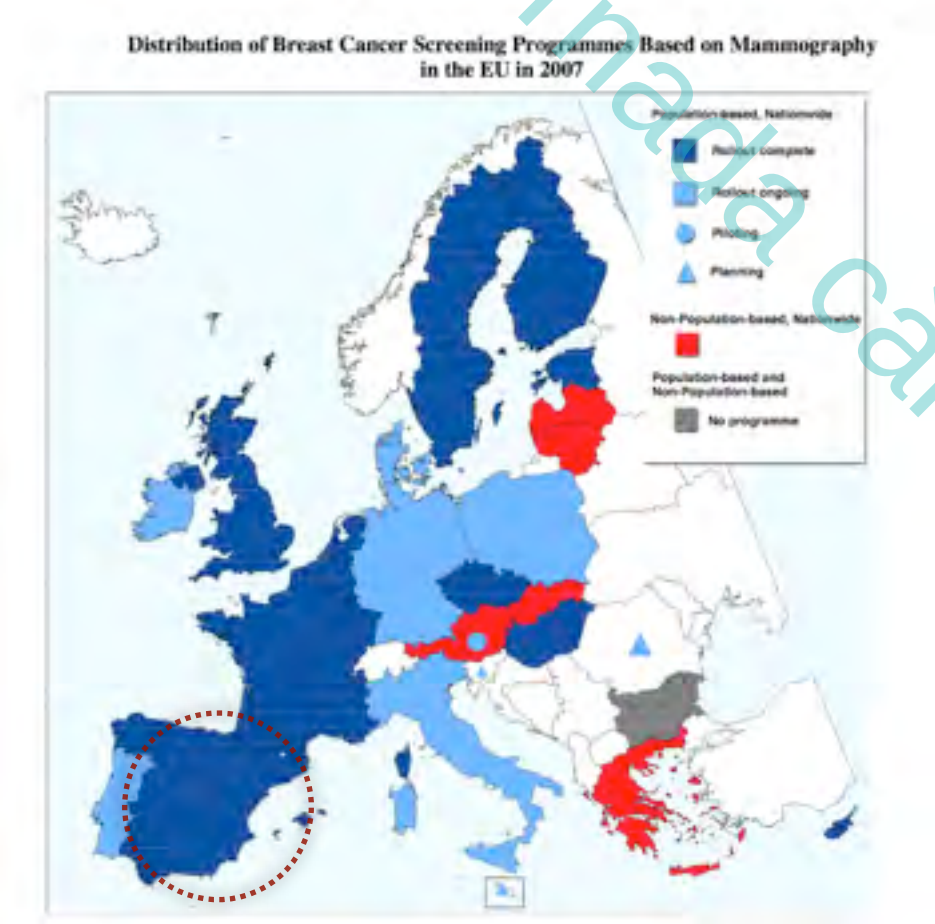


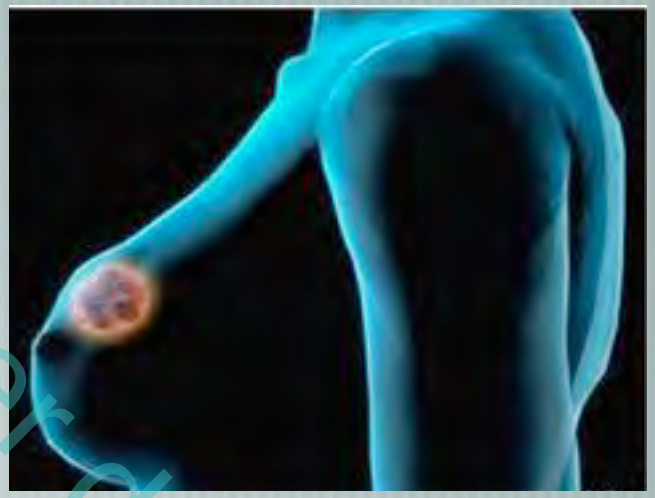
XVI JORNADA SOBRE EL CÀNCER DE MAMA: PERSONALITZACIÓ EN EL CÀNCER DE MAMA

VISIÓ DES DE LA MEDICINA NUCLEAR

Dr. Sergi Vidal-Sicart
Dr. Renato Valdés-Olmos



CANCER DE MAMA



EUROPA
150.000 NUEVOS CASOS POR AÑO (8%)

Personalización


XVI Jornada càncer de mama

Personalización en MN

- el mejor ejemplo de personalización es lo que haces a diario Sergi
- Lo del mapeo del drenaje que en cada paciente es diferente (localización GC, GC aberrantes, etc...)
- Lo otro es por ejemplo el establecimiento de la heterogeneidad que te lleva a personalizar las áreas activas para su eventual biopsia
- Con el MIBI podrías predecir si el tumor presenta rasgos de resistencia
- Con la FDG si es que se puede medir el efecto de las terapias de blanco sobre el tumor y los ganglios
- Como ves toda la MN es un ejemplo de personalización

Personalización

Tipo de Ca	Afectación	Curación	Incidencia
Carcinoma Ductal in Situ:	Conductos Mamarios, localizado, no produce metástasis	100%	43% en mujeres entre 40-49 años 92% en mujeres de 30-39 años
Carcinoma Ductal Infiltrante	Inicia en el Conducto Mamario y se extiende hasta el Tej. Adiposo y otras partes del Cuerpo	Ganglios -: 70% Ganglios +: 25%	85%
Carcinoma Lobular in Situ	Glándulas Mamarias, masa palpable, mujeres pre menopáusicas	85%	25-35%
Carcinoma Lobular infiltrante	Inicia en las Glándulas Mamarias se puede extender a otros tejidos del cuerpo	Ganglios -: 70% Ganglios +: 25%	10-15%
Carcinoma Inflamatorio	Agresivo, rápido. Cambia la apariencia de la piel. Puede afectar hasta los Huesos	De acuerdo al estadio	1%
Enfermedad de Paget	erosión plana en el Pezón, secreción en el pezón.	El dx puede durar hasta 1 año	

Personalización

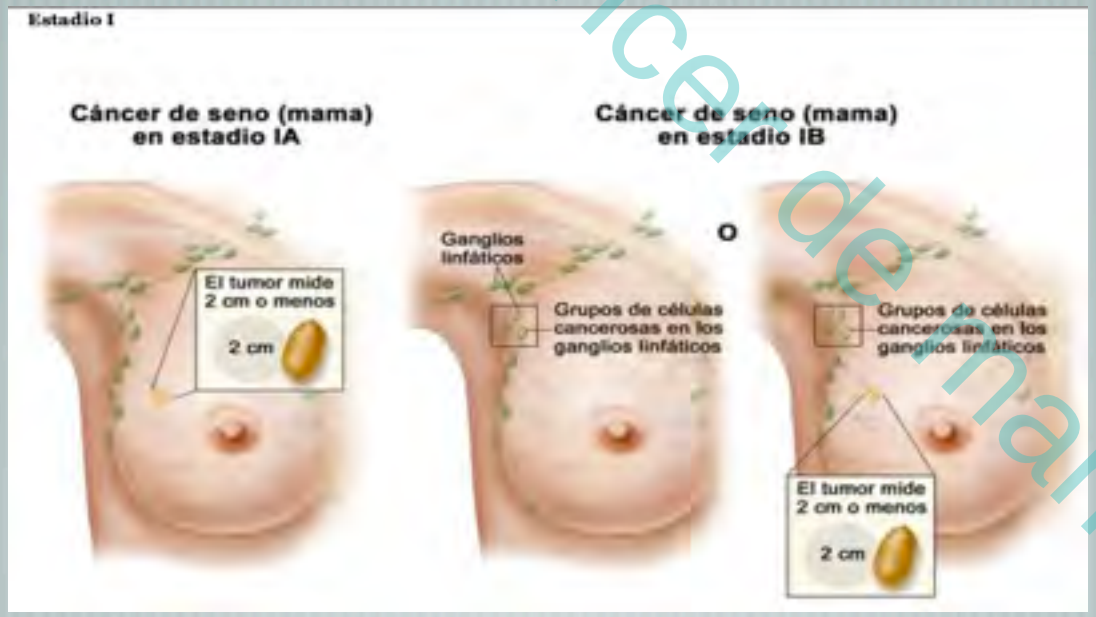
Estadio I	**Indica que el Tu es < de 2cm y no hay metástasis**	**Índice de supervivencia a 5 años es de 98%**
Estadio II	**1. No mide + de 2cm pero los ganglios están afectados** **2. Mide entre 2 y 5cm y puede o no haberse extendido** **3. Mide + de 5cm pero los GL axilares no están afectados**	**Índice de Supervivencia a 5 años es de 88 – 76%**
Estadio III	**III a:** **1. Mide < de 5cm y se ha diseminado a los GL axilares** **2. Mide + de 5cm y los GL axilares están afectados**	**Índice de Supervivencia a 5 años es de 56%**
	III b: **1. Se ha diseminado a otros tejidos de la mama (piel, costillas, musculo)** **2. Se ha diseminado a los GL dentro de la Pared torácica**	**Índice de Supervivencia a 5 años es de 46%**
Estadio IV	**El Ca se ha diseminado a otras estructuras del cuerpo**	**Índice de Supervivencia a 5 años es de 16%**

Personalización

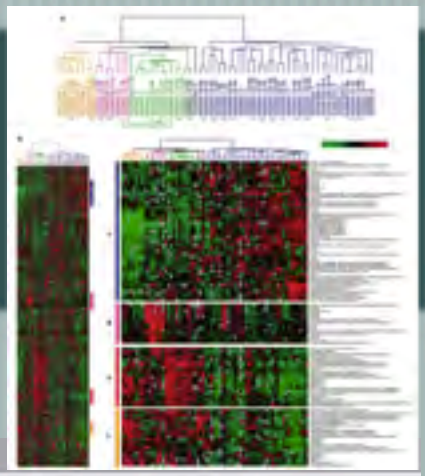
El reconocimiento de la *biología tumoral* ha cambiado el tratamiento del cáncer de mama

La recomendación de administrar un tratamiento sistémico se ve influida por los factores relacionados con el propio paciente y el tumor, no siendo el estado de los ganglios linfáticos el único condicionante para su elección

El diagnóstico en una fase más precoz, debido al cribado, ha dado lugar a lesiones cada vez más iniciales, a las que se les ha podido ofrecer un tratamiento conservador sobre la mama



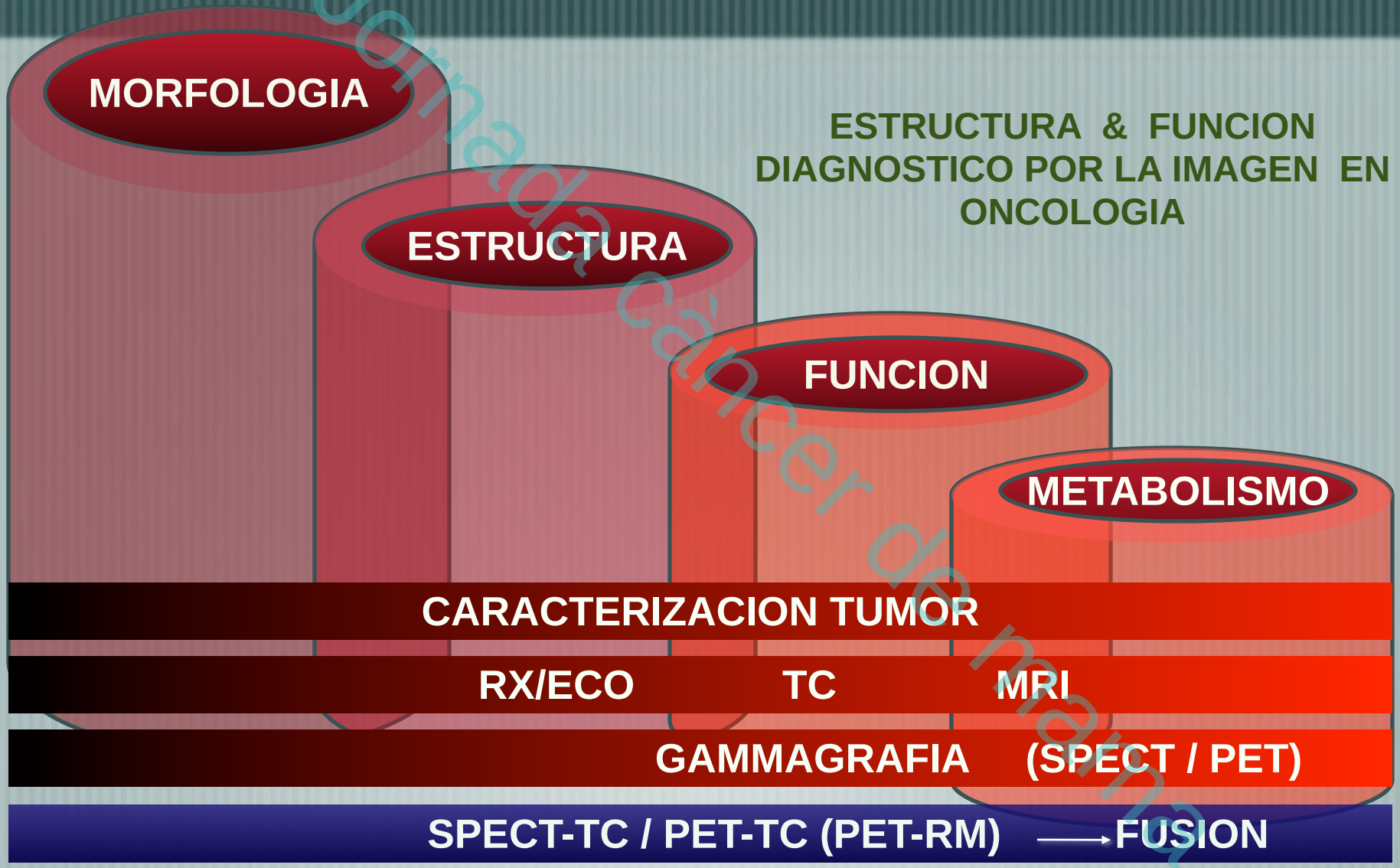
Personalización



Intrinsic Subtype (1)	Clinico-pathologic definition	Notes
Luminal A	**'Luminal A'** ER and/or PgR positive(76) HER2 negative (77) Ki-67 low (<14%)*	This cut-point for Ki-67 labelling index was established by comparison with PAM50 intrinsic subtyping (7). Local quality control of Ki-67 staining is important.
Luminal B**	**'Luminal B (HER2 negative)'** ER and/or PgR positive HER2 negative Ki-67 high	Genes indicative of higher proliferation are markers of poor prognosis in multiple genetic assays (78). If reliable Ki-67 measurement is not available, some alternative assessment of tumor proliferation such as grade may be used to distinguish between 'Luminal A' and 'Luminal B (HER2 negative)'.
	'Luminal B (HER2 positive)' ER and/or PgR positive Any Ki-67 HER2 over-expressed or amplified	Both endocrine and anti-HER2 therapy may be indicated.
Erb-B2 overexpression	**'HER2 positive (non luminal)'** HER2 over-expressed or amplified ER and PgR absent	
'Basal-like'	**'Triple negative (ductal)'** ER and PgR absent HER2 negative	Approximately 80% overlap between 'triple negative' and intrinsic 'basal-like' subtype but 'triple negative' also includes some special histological types such as (typical) medullary and adenoid cystic carcinoma with low risks of distant recurrence. Staining for basal keratins (79) although shown to aid selection of true basal-like tumors, is considered insufficiently reproducible for general use.

Goldhirsch A et al. Ann Oncol 2011; 22: 36-47

Personalización



ESTRUCTURA & FUNCION
DIAGNOSTICO POR LA IMAGEN EN ONCOLOGIA

¿Personalización?

clinical practice guidelines

Annals of Oncology 22 (Supplement 6): vi12–vi24, 2011
doi:10.1093/annonc/mdr371

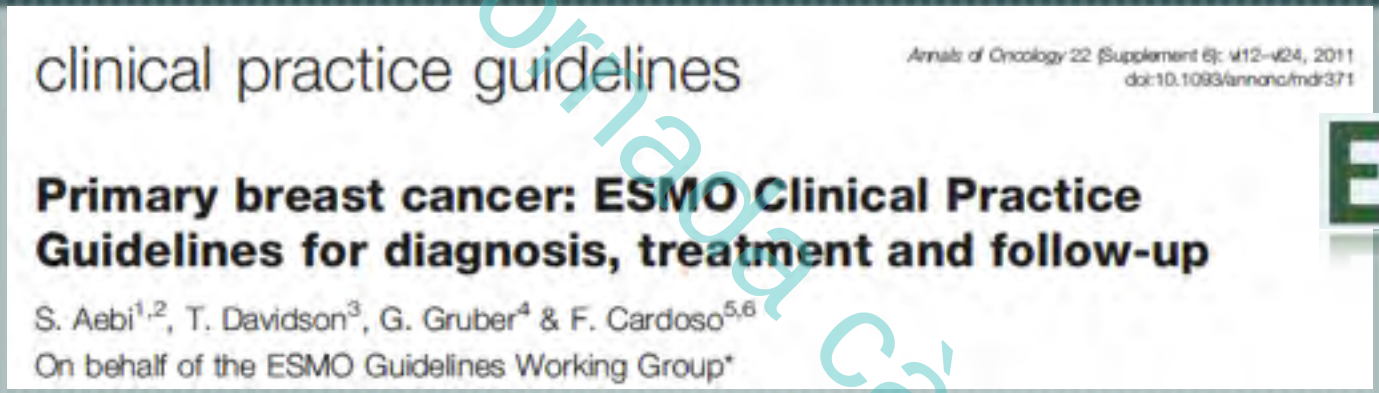
Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up

S. Aebi[1,2], T. Davidson[3], G. Gruber[4] & F. Cardoso[5,6]
On behalf of the ESMO Guidelines Working Group*

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Diagnóstico: Exploración clínica (palpación mama y axila)
Exploración radiológica: mamografía, ecografía, RM (mamas densas, prótesis, BCRA, multifocalidad...)
Exploración AP: BAG (o PAAF)

¿Personalización?


clinical practice guidelines

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On behalf of the ESMO Guidelines Working Group*

Estadificación y valoración de riesgo:

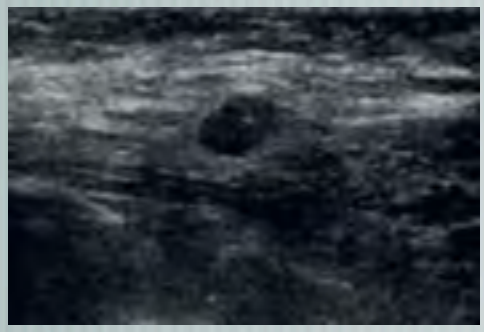
Historial médico
Historia familiar
Exploración física
Performance status
Valoración menopausia

Hemograma completo
Test hepáticos y renales
Fosfatasa alcalina
Calcio sérico

¿Personalización?

Estadificación prequirúrgica:

Estadios TNM
Evaluación por AP (tipo, grado)
Valoración clínica/ECO ganglios
Estatus receptores hormonales
HER2 neu



TS neoadyuvante:

RX tórax
ECO o TAC abdominal
Gammagrafía ósea

¿Personalización?

¿Personalización?

¿Personalización?

NCCN National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines)®

Breast Cancer

Version 3.2012

NCCN.org

NCCN Guidelines for Patients™ available at www.nccn.com

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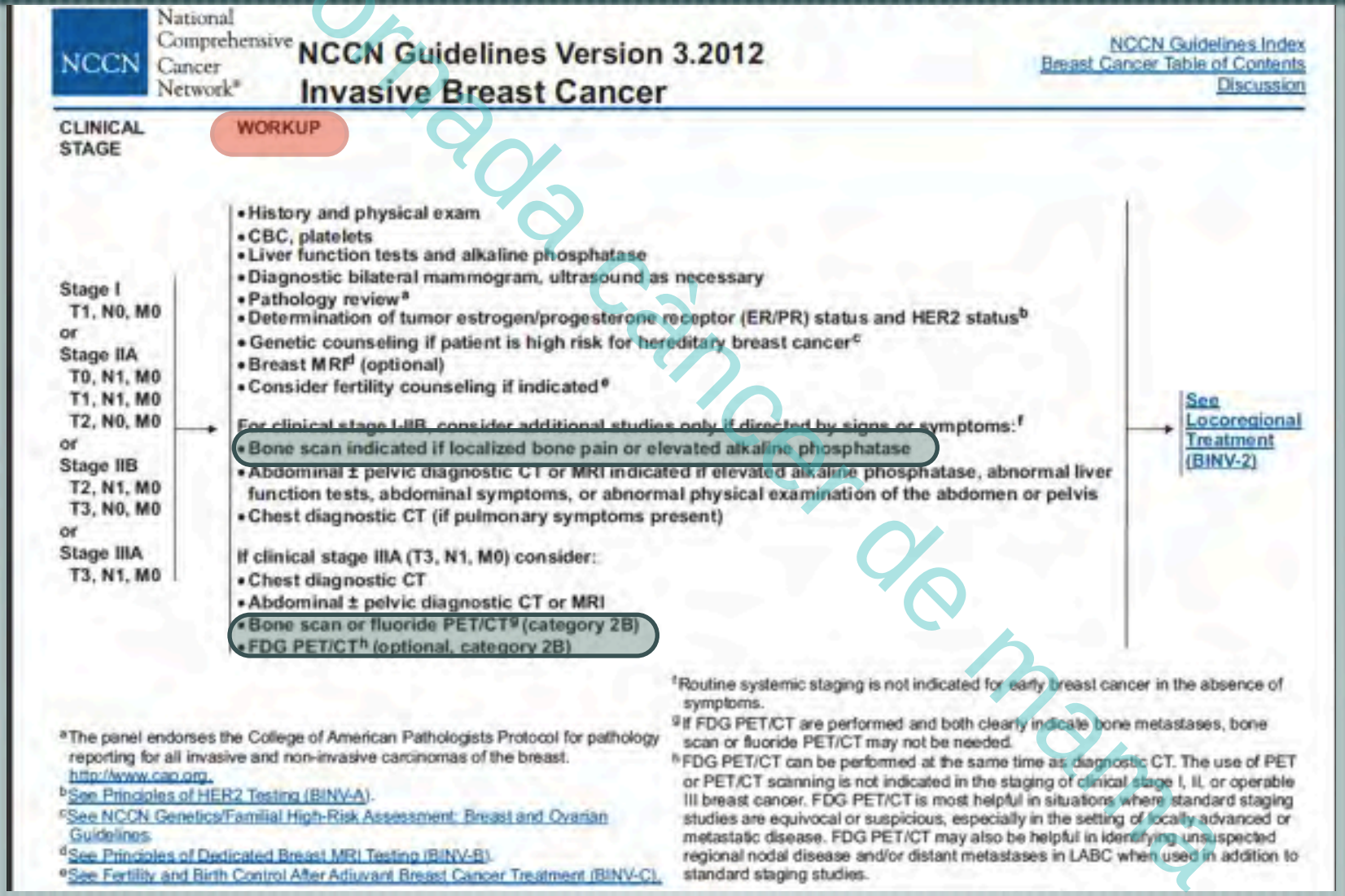

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2012
Invasive Breast Cancer

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Breast Cancer Table of Contents
Discussion

CLINICAL STAGE

WORKUP

Stage I
T1, N0, M0
or
Stage IIA
T0, N1, M0
T1, N1, M0
T2, N0, M0
or
Stage IIB
T2, N1, M0
T3, N0, M0
or
Stage IIIA
T3, N1, M0

- History and physical exam
- CBC, platelets
- Liver function tests and alkaline phosphatase
- Diagnostic bilateral mammogram, ultrasound as necessary
- Pathology review[a]
- Determination of tumor estrogen/progesterone receptor (ER/PR) status and HER2 status[b]
- Genetic counseling if patient is high risk for hereditary breast cancer[c]
- Breast MRI[d] (optional)
- Consider fertility counseling if indicated[e]

For clinical stage I-IIB, consider additional studies only if directed by signs or symptoms:[f]

- Bone scan indicated if localized bone pain or elevated alkaline phosphatase
- Abdominal ± pelvic diagnostic CT or MRI indicated if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, or abnormal physical examination of the abdomen or pelvis
- Chest diagnostic CT (if pulmonary symptoms present)

If clinical stage IIIA (T3, N1, M0) consider:

- Chest diagnostic CT
- Abdominal ± pelvic diagnostic CT or MRI
- Bone scan or fluoride PET/CT[g] (category 2B)
- FDG PET/CT[h] (optional, category 2B)

→ See Locoregional Treatment (BINV-2)

[a] The panel endorses the College of American Pathologists Protocol for pathology reporting for all invasive and non-invasive carcinomas of the breast. http://www.cap.org.
[b] See Principles of HER2 Testing (BINV-A).
[c] See NCCN Genetics/Familial High-Risk Assessment: Breast and Ovarian Guidelines.
[d] See Principles of Dedicated Breast MRI Testing (BINV-B).
[e] See Fertility and Birth Control After Adjuvant Breast Cancer Treatment (BINV-C).
[f] Routine systemic staging is not indicated for early breast cancer in the absence of symptoms.
[g] If FDG PET/CT are performed and both clearly indicate bone metastases, bone scan or fluoride PET/CT may not be needed.
[h] FDG PET/CT can be performed at the same time as diagnostic CT. The use of PET or PET/CT scanning is not indicated in the staging of clinical stage I, II, or operable 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. FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in LABC when used in addition to standard staging studies.

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Invasive Breast Cancer

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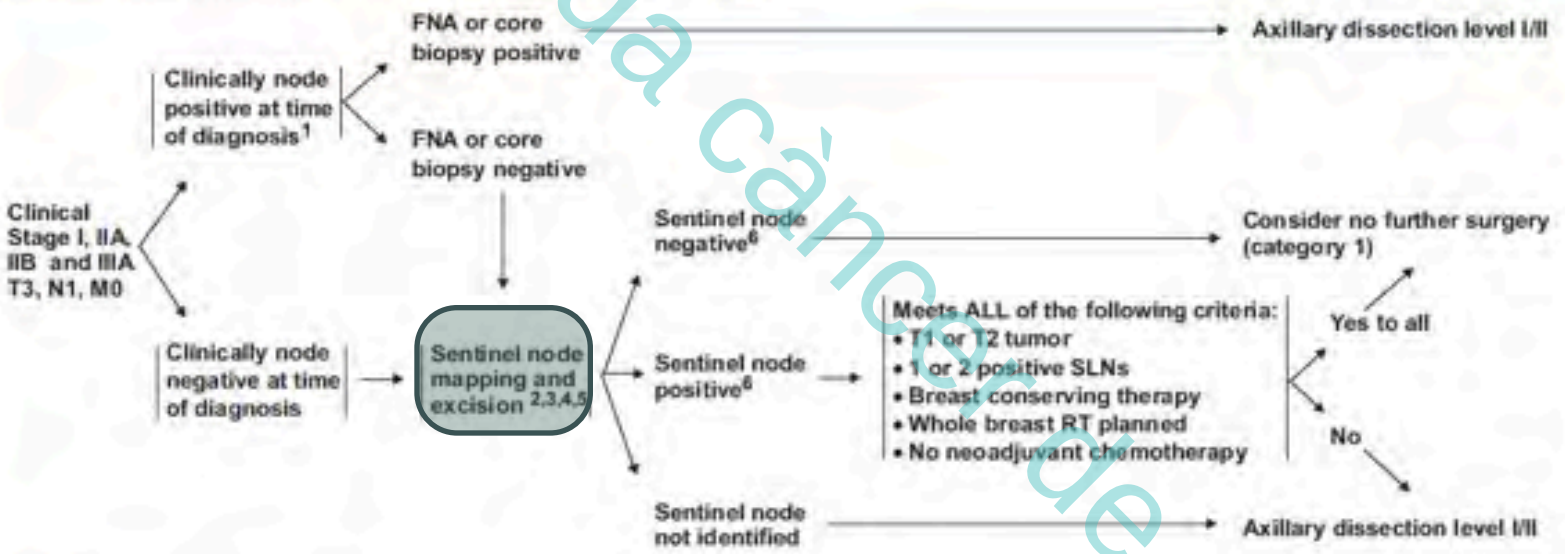
SURGICAL AXILLARY STAGING - STAGE I, IIA, IIB and IIIA T3, N1, M0



[1]Consider pathologic confirmation of malignancy in clinically positive nodes using ultrasound-guided FNA or core biopsy in determining if a patient needs axillary lymph node dissection.

[2]A sentinel node team must have documented experience with sentinel node biopsy in breast cancer. The team includes surgeon, radiologists, nuclear medicine physician, pathologist, and prior discussion with medical and radiation oncologists on use of sentinel node for treatment decisions.

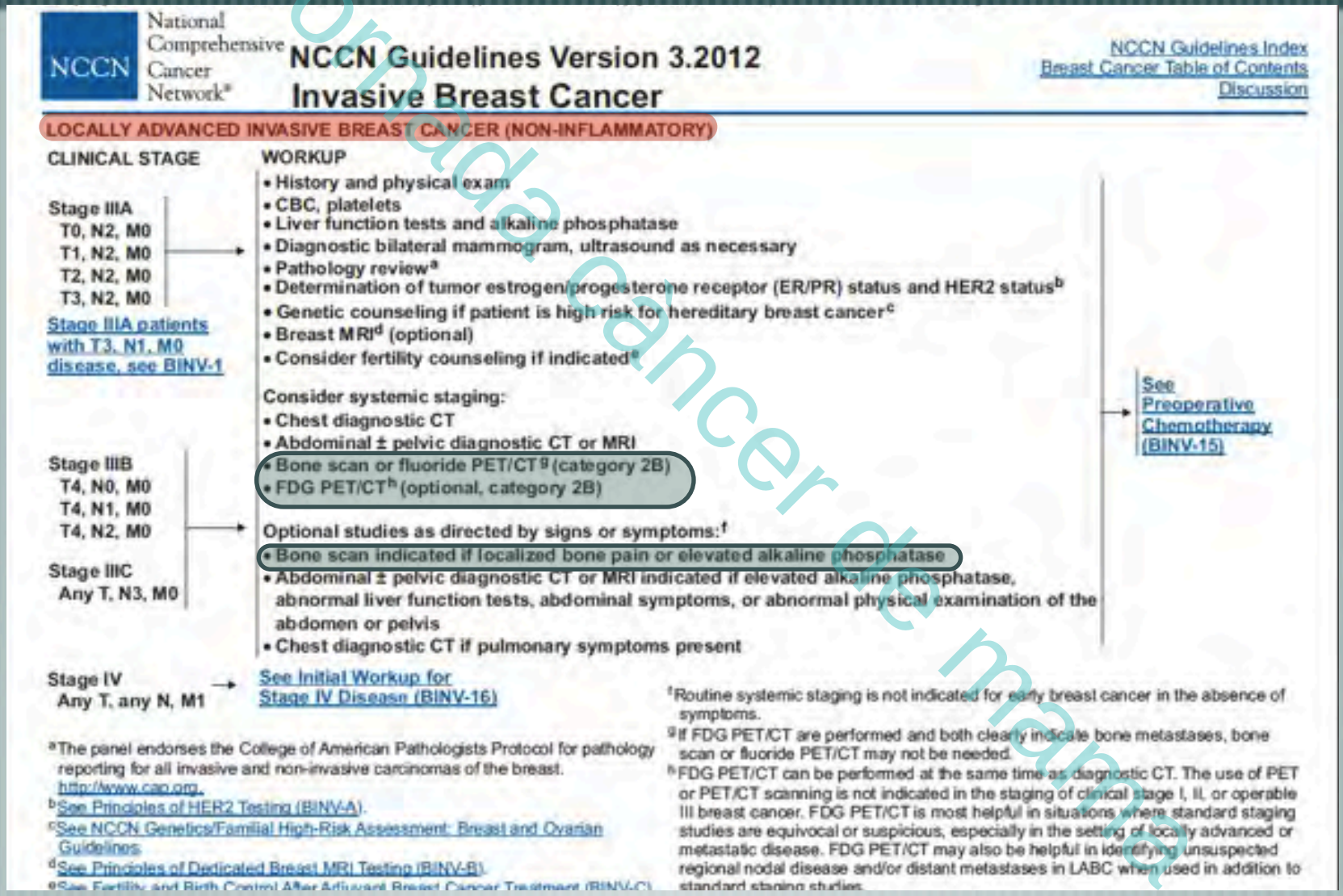
[3]Axillary sentinel node biopsy in all cases; internal mammary sentinel node biopsy is optional if drainage maps to internal mammary nodes (category 3).

[4]Sentinel lymph node mapping injections may be peritumoral, subareolar, or subdermal. However, only peritumoral injections map to the internal mammary lymph node(s).

[5]Results of randomized clinical trials indicate that there is a lower risk of mobidity associated with sentinel node mapping and excision than with level I/II axillary dissection.

[6]Sentinel node involvement is defined by multilevel node sectioning with hematoxylin and eosin (H&E) staining. Cytokeratin Immunohistochemistry (IHC) may be used for equivocal cases on H&E. Routine cytokeratin IHC to define node involvement is not recommended in clinical decision making.

¿Personalización?



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LOCALLY ADVANCED INVASIVE BREAST CANCER (NON-INFLAMMATORY)

CLINICAL STAGE

Stage IIIA
T0, N2, M0
T1, N2, M0
T2, N2, M0
T3, N2, M0

Stage IIIA patients with T3, N1, M0 disease, see BINV-1

Stage IIIB
T4, N0, M0
T4, N1, M0
T4, N2, M0

Stage IIIC
Any T, N3, M0

Stage IV
Any T, any N, M1 → See Initial Workup for Stage IV Disease (BINV-16)

WORKUP

- History and physical exam
- CBC, platelets
- Liver function tests and alkaline phosphatase
- Diagnostic bilateral mammogram, ultrasound as necessary
- Pathology review[a]
- Determination of tumor estrogen/progesterone receptor (ER/PR) status and HER2 status[b]
- Genetic counseling if patient is high risk for hereditary breast cancer[c]
- Breast MRI[d] (optional)
- Consider fertility counseling if indicated[e]

Consider systemic staging:
- Chest diagnostic CT
- Abdominal ± pelvic diagnostic CT or MRI
- Bone scan or fluoride PET/CT[g] (category 2B)
- FDG PET/CT[h] (optional, category 2B)

Optional studies as directed by signs or symptoms:[f]
- Bone scan indicated if localized bone pain or elevated alkaline phosphatase
- Abdominal ± pelvic diagnostic CT or MRI indicated if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, or abnormal physical examination of the abdomen or pelvis
- Chest diagnostic CT if pulmonary symptoms present

→ See Preoperative Chemotherapy (BINV-15)

[a] The panel endorses the College of American Pathologists Protocol for pathology reporting for all invasive and non-invasive carcinomas of the breast. http://www.cap.org.

[b] See Principles of HER2 Testing (BINV-A).

[c] See NCCN Genetics/Familial High-Risk Assessment: Breast and Ovarian Guidelines.

[d] See Principles of Dedicated Breast MRI Testing (BINV-B).

[e] See Fertility and Birth Control After Adjuvant Breast Cancer Treatment (BINV-C).

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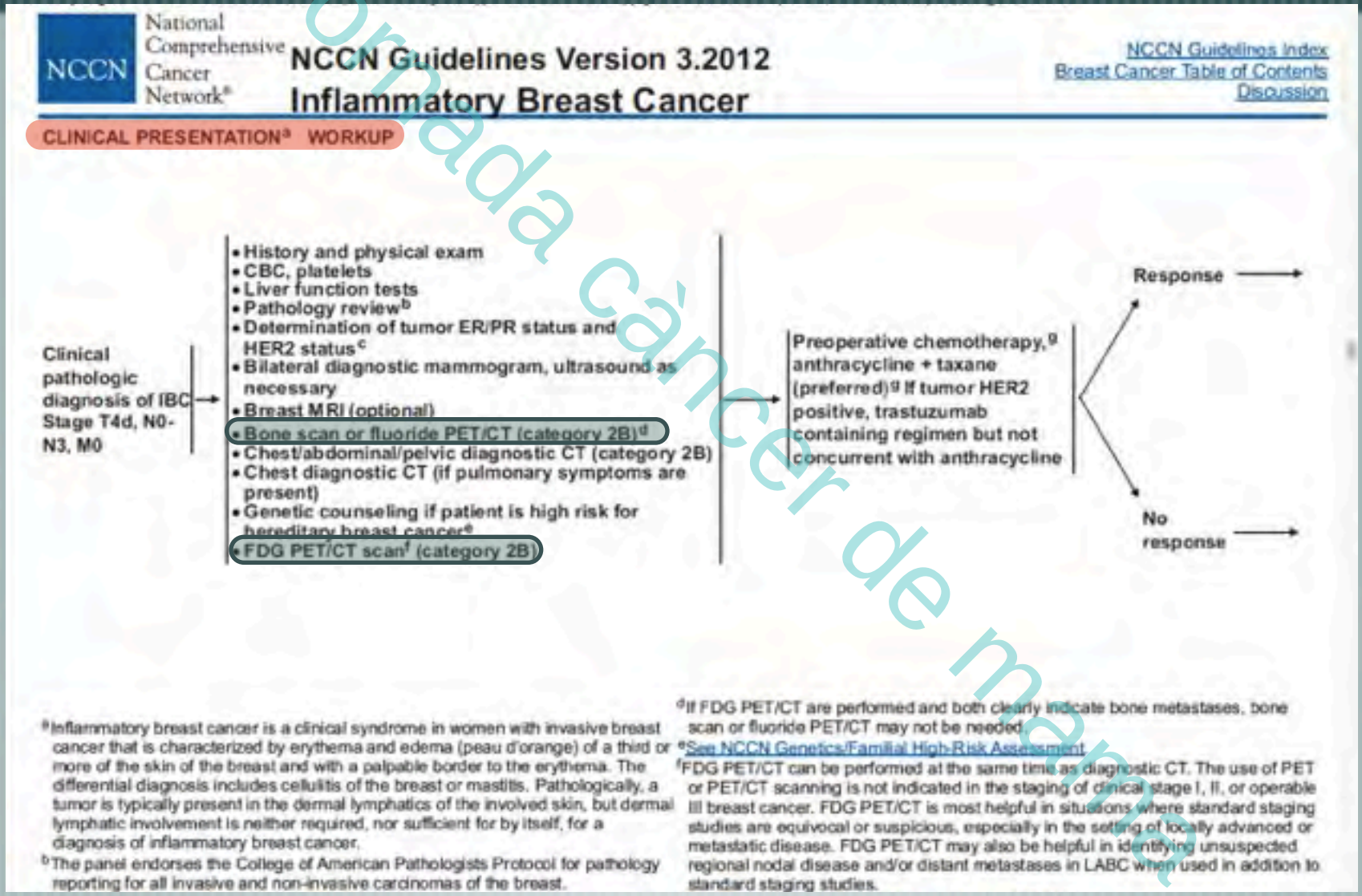

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PRINCIPLES OF MONITORING METASTATIC DISEASE

Suggested intervals of follow-up for patients with metastatic disease[1]

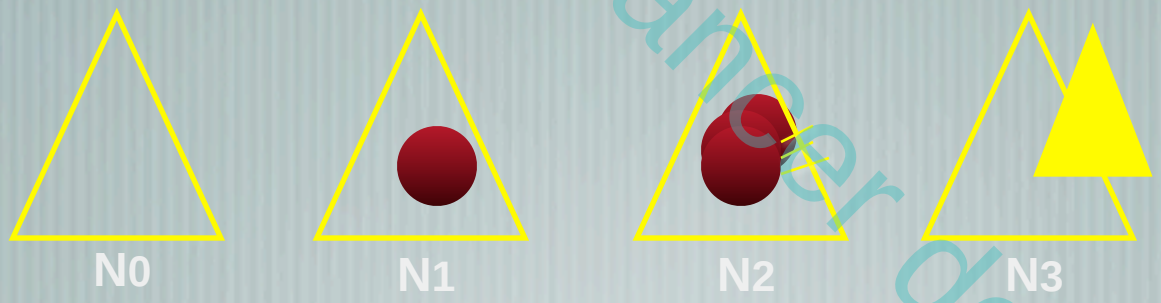
	Baseline prior to new therapy	Chemotherapy	Endocrine therapy	Restaging if concern for progression of disease
Symptom assessment	Yes	Prior to each cycle	Every 2-3 months	Yes
Physical examination	Yes	Prior to each cycle	Every 2-3 months	Yes
Performance status	Yes	Prior to each cycle	Every 2-3 months	Yes
Weight	Yes	Prior to each cycle	Every 2-3 months	Yes
LFTs, CBC	Yes	Prior to each cycle	Every 2-3 months	Yes
CT scan chest/abd/pelvis	Yes	Every 2-4 cycles	Every 2-6 months	Yes
Bone scan	Yes	Every 4 cycles	Every 4-6 months	Yes
PET/CT	Optional	Unknown	Unknown	Optional
Tumor markers	Optional	Optional	Optional	Optional

[1] In patients who have long-term stable disease, the frequency of monitoring can be reduced

TNM

ESTADIFICACION & IMAGEN DIAGNOSTICA

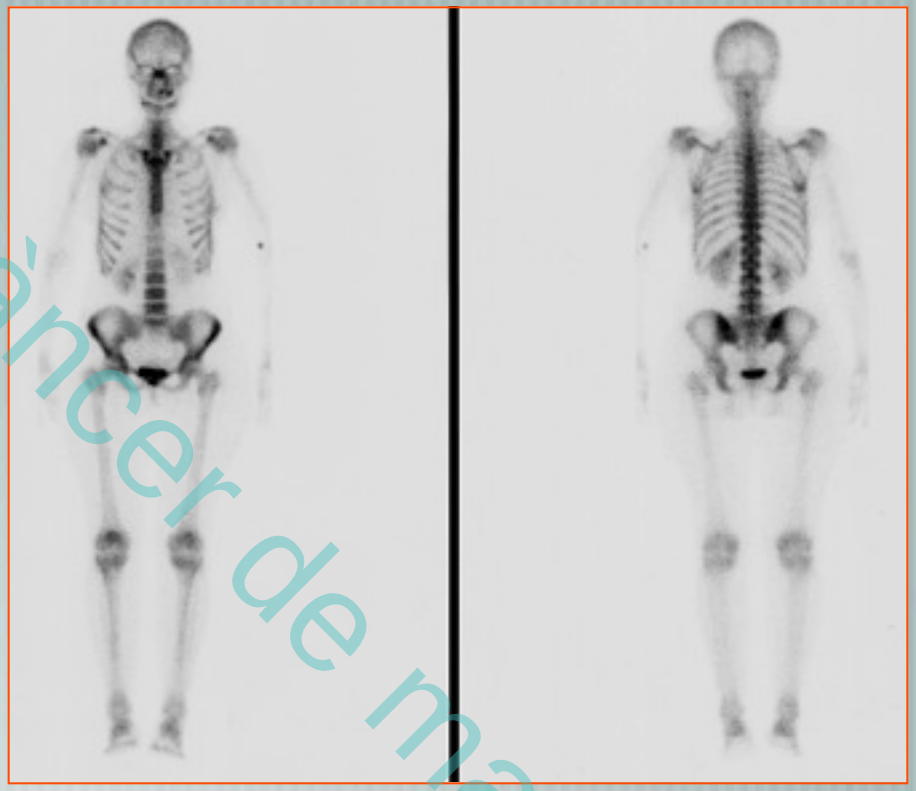
ESTADIO	I	II	III	IV	
TUMOR	T1	T2	T3	T4	RADIOLOGIA
GANGLIO LINFATICO	N0	N1	N2	N3	RADIOLOGIA / MEDICINA NUCLEAR
METASTASIS A DISTANCIA			M+		MEDICINA NUCLEAR / RADIOLOGIA



Personalización en MN

Gammagrafía ósea

- Técnica planar de imagen
- Gammagrafía de cuerpo entero
- Difosfonatos marcados con Tc99m
- Trazas
- Visualizar *in vivo* mineralización
- Muy sensible para detectar incrementos en osteogénesis
- Hallazgos poco específicos



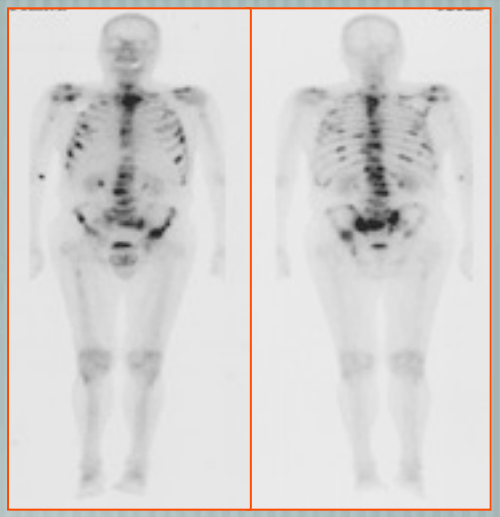
<u>Caracterización imágenes</u>

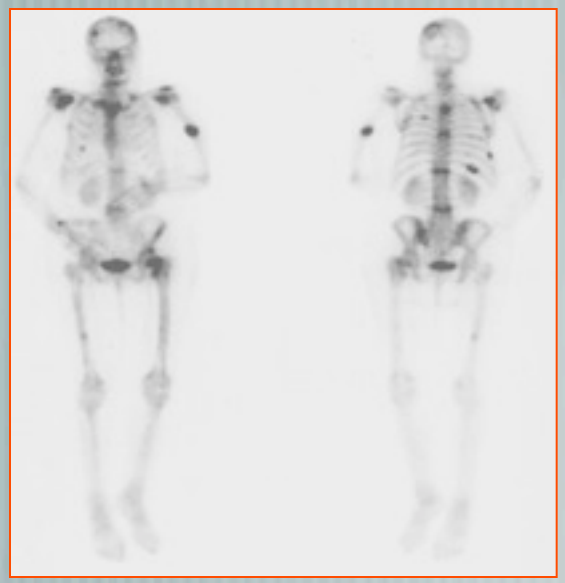
- Detección precoz M1
- Sensibilidad elevada para detectar M1

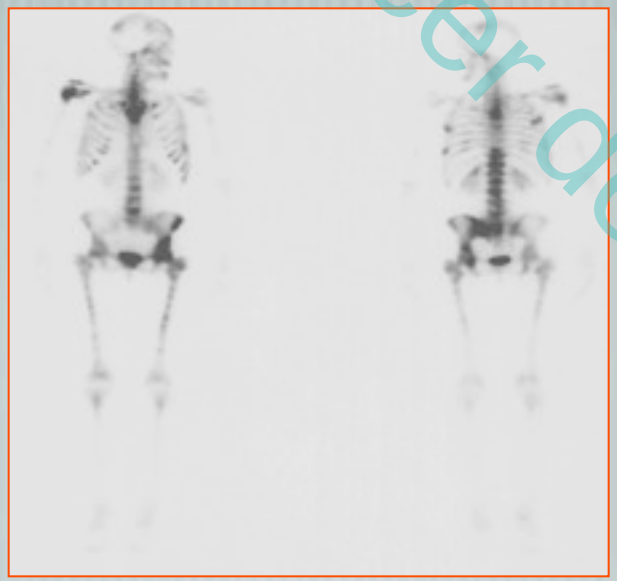
Personalización en MN

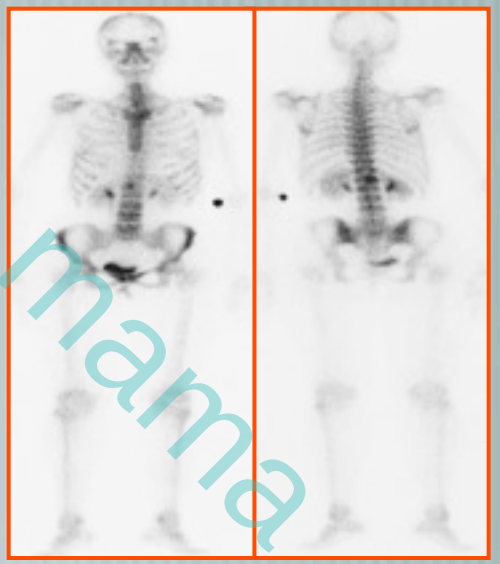
Patrones gammagráficos de M1

- Múltiples imágenes hipercaptantes
- Patrón medular
- Superscan
- Hipercaptación única
- Lesión fría (única o múltiples)









Personalización en MN

Indicaciones en cáncer de mama

- Estadificación

  - En estadio I y II si existe dolor óseo o elevación de fosfatasas alcalinas (*).
  - En estadio III

  (*) Si se practica la GO sistemáticamente : Modificaremos la estrategia diagnóstica en un 3% de los estadios I y en un 6% de los II. En las GO negativas, tendremos un estudio basal para comparar con las GO del seguimiento.

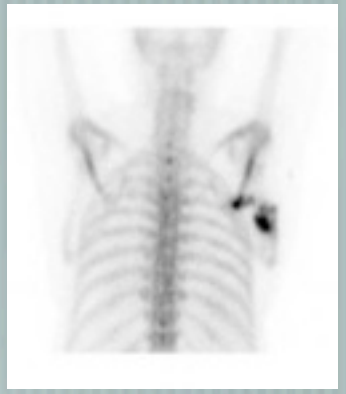
- Seguimiento

  - En estadio I y II : GO cada 6 meses durante 2 primeros años. Resto : 1 cada año
  - En cualquier momento evolutivo si aparece dolor óseo

- Control del tratamiento

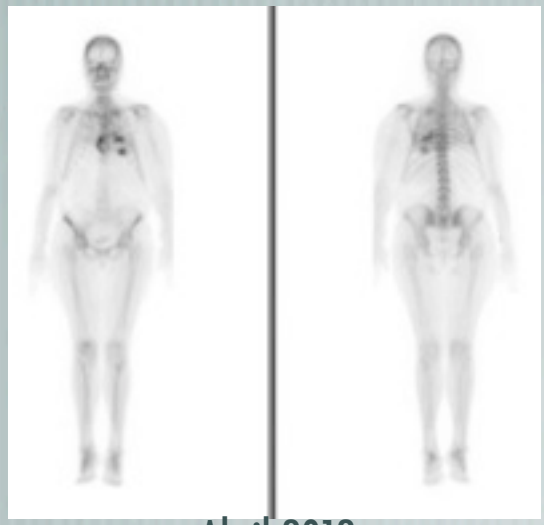
Personalización en MN

Control tratamiento (*)

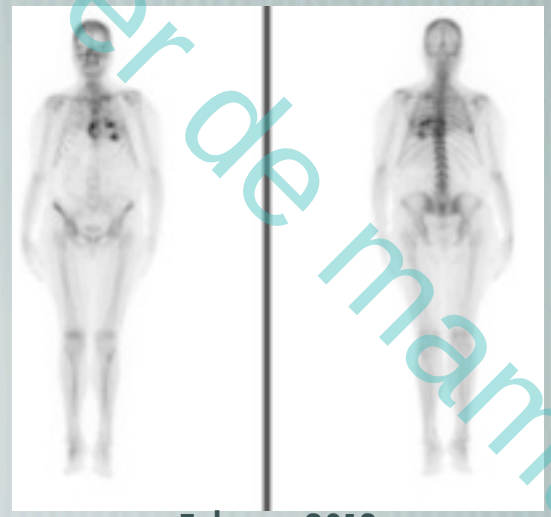


No respuesta : Persistencia de imágenes hipercaptantes
R. Completa : Desaparición de imágenes hipercaptantes
R. Parcial : Disminución en nº e intensidad de captación
Empeoramiento : Aumento en nº e intensidad de captación

(*) A tener en cuenta : Evolución radiológica (Rx o TAC)
Quimio/Hormonoterapia : Fenómeno “flare”



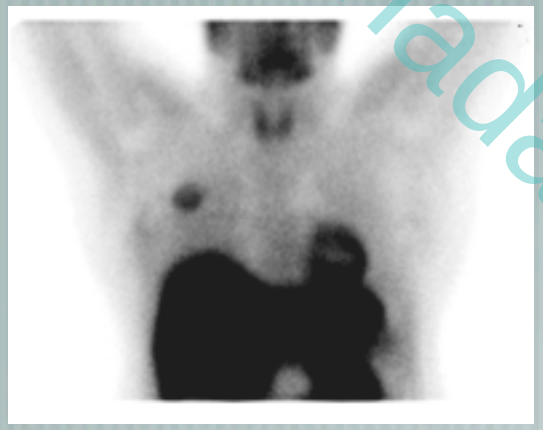
Abril 2012

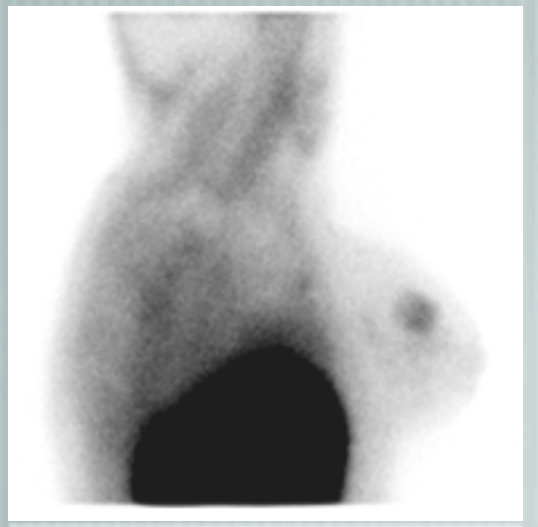


Febrero 2013

Personalización con MN

Radiotrazadores utilizados





201-Tl

99m-Tc-HDP

99m-Tc-Sestamibi

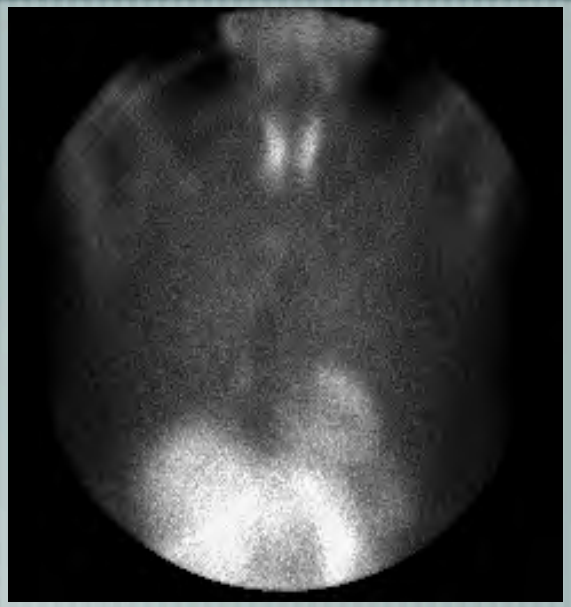
99m-Tc.Tetrofosmin

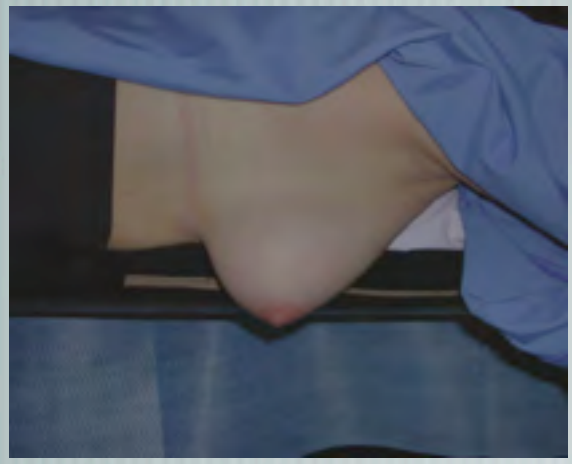
111-In-pentetreótido

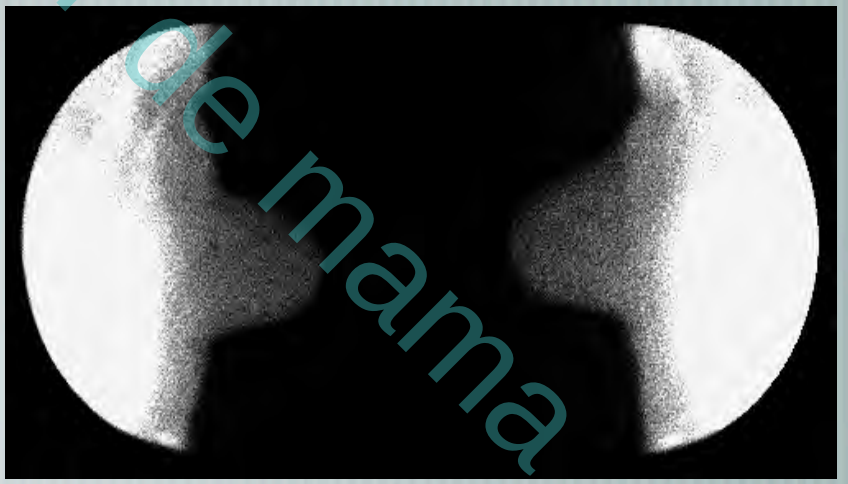
Personalización en MN

Gammagrafía mamaria con 99mTc-MIBI

Técnica de imagen funcional
Radiotrazador se acumula en tumor mamario y ganglios metastáticos
Uso limitado por escasa sensibilidad en tumores pequeños y micrometástasis
Mejoría resultados con SPECT





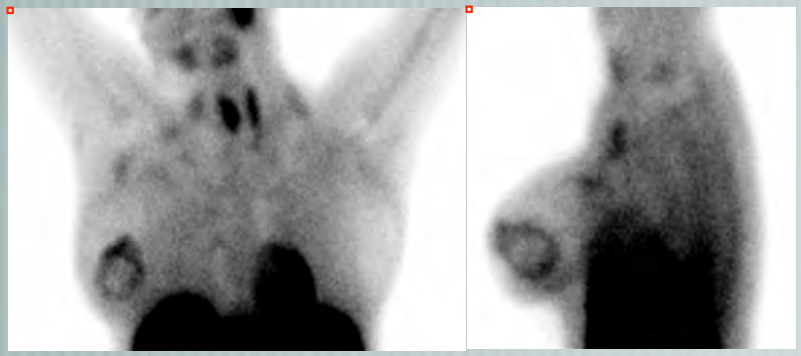


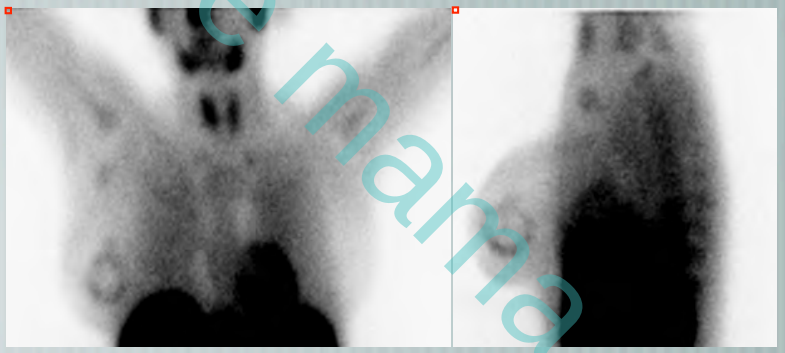
Personalización en MN

Gammagrafía mamaria con 99mTc-MIBI

Indicaciones

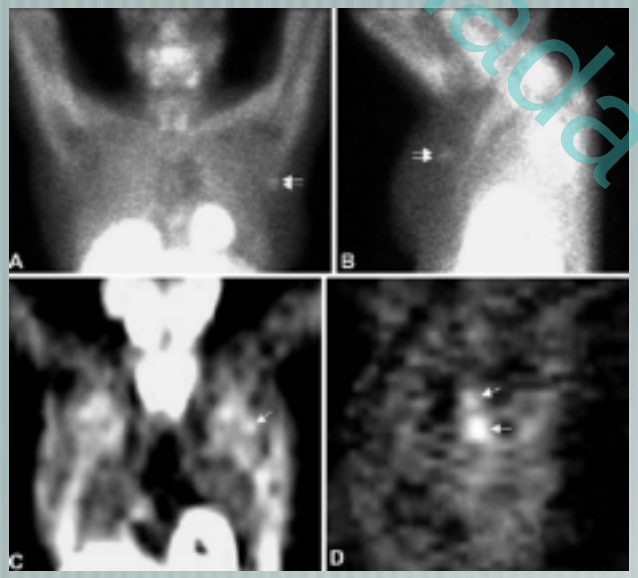
No como sistema de screening
Diagnóstico complementario a la mamografía (no diagnóstica o dudosa)
Tejido mamario denso (25% mujeres)
Alteraciones yatrógenas (IQ, RT, QT, Biopsia)
Implantes protésicos mamarios
Valoración multifocalidad
Evaluación respuesta a QT (ganglios +)



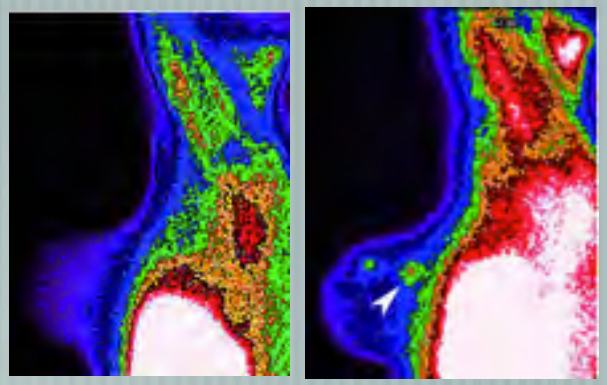


Personalización en MN

Pin-hole SPECT



SPECT



Authors	Year	Ref.	Patient number	Scan	Sensitivity (%)	Specificity (%)	Accuracy (%)	NPV (%)	PPV (%)
Spanu et al.	2000	[79]	112	P-SPECT	100 (53/53)	93.6 (44/47)	97	100	94.6
				SPECT	96.2 (51/53)	93.6 (44/47)	95	95.6	94.4
				Planar	56.6 (30/53)	100 (47/47)	77	67.1	100
Spanu et al.	2003	[80]	188[a]	P-SPECT	93.2 (69/74)	92.4 (97/105)	92.7	95	89.6
				SPECT	85.1 (63/74)	94.3 (99/105)	90.5	90	91.3
				Planar	36.5 (27/74)	99 (104/105)	73.2	68.9	96.4

Table 1 Efficacy of SPECT scintimammography in differentiating between benign and malignant small lesions (172 cases)

Sensitivity	100.0%
Specificity	93.5%
Positive predictive value	92.5%
Negative predictive value	100.0%
Test efficacy	96.5%

Table 2 Efficacy of SPECT scintimammography in differentiating between axillary lymph nodes involved or not by tumor cells (80 patients with breast cancer ≤3 cm)

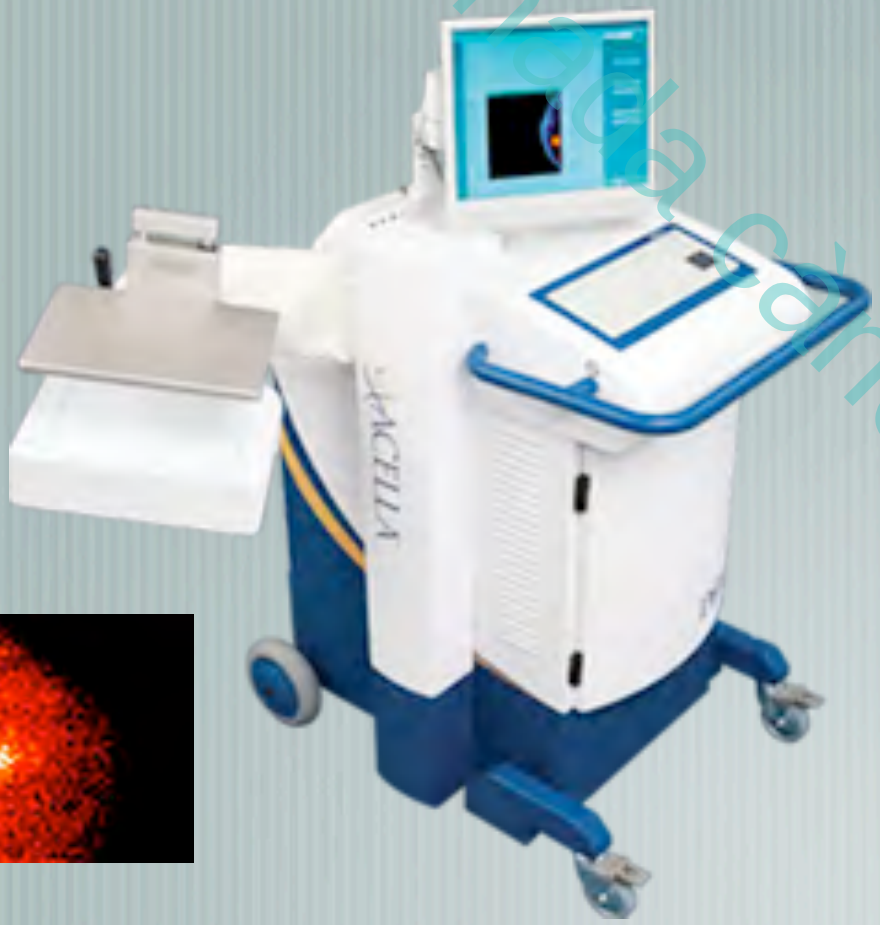
Sensitivity	83.4%
Specificity	97.5%
Positive predictive value	97.0%
Negative predictive value	85.0%
Test efficacy	90.0%

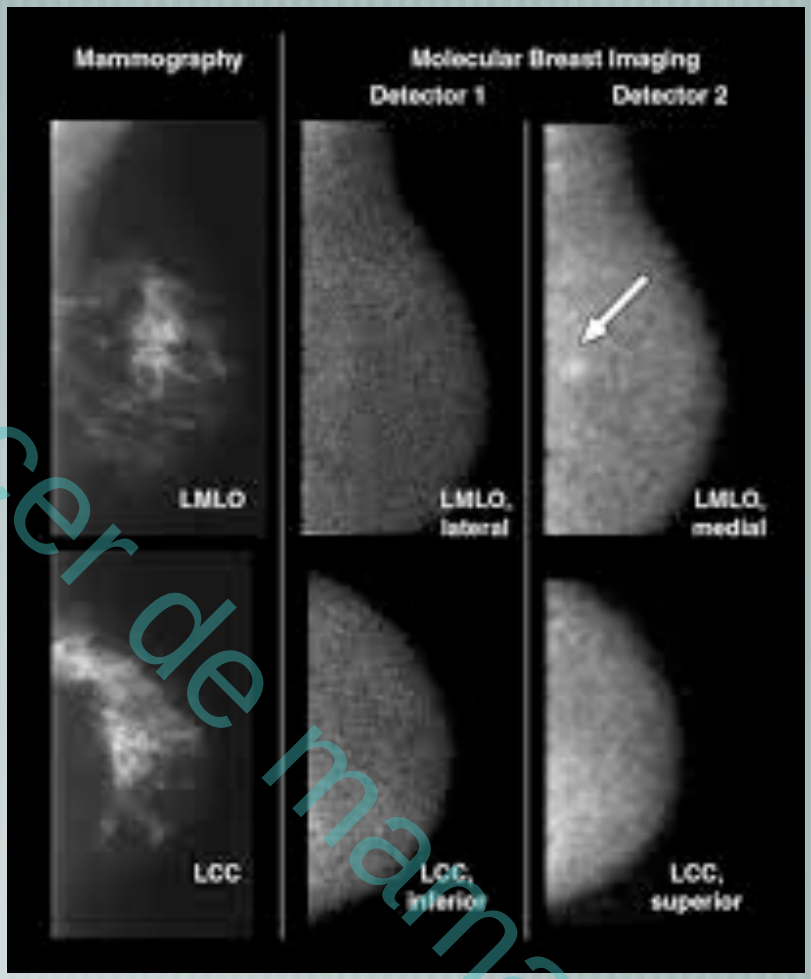
Madeddu G et al. Eur J Nucl Med Mol Imaging 2004; 31: S23-S34

De Cesare A et al. World J Surg 2011; 35: 2668-2672

Personalización en MN

Gammacámaras dedicadas





Personalización en MN

Gammagrafía mamaria con 99mTc-MIBI

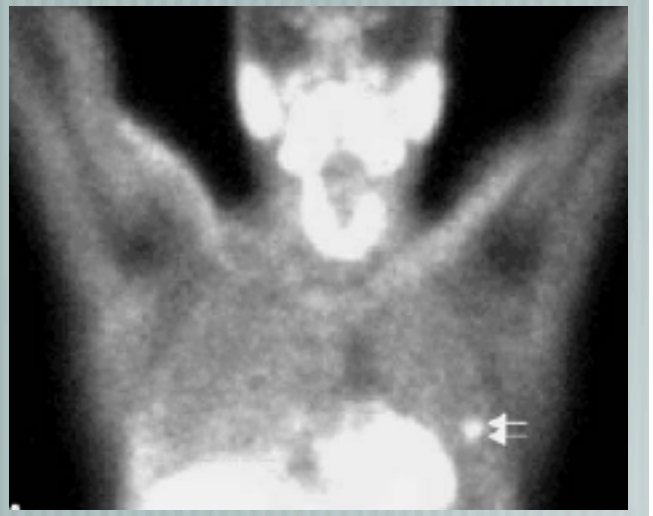


Table 4 Breast-Specific Gamma Camera Clinical Indications

A. Patients with recently detected breast malignancy
   1. Evaluating the extent of disease (initial staging)
   2. Detecting multicentric, multi-focal, or bilateral disease
   3. Assessing response to neoadjuvant chemotherapy
   4. Breast scintigraphy is addressed in the ACR's Appropriateness Criteria Panel on Breast Imaging[35]
B. Patients at high risk for breast malignancy
   1. Suspected recurrence
   2. Limited mammogram or previous malignancy was occult on mammogram
C. Patients with indeterminate breast abnormalities and remaining diagnostic concerns
   1. Nipple discharge with abnormal mammogram and/or sonographic abnormality with or without contrast ductography
   2. Bloody nipple discharge with normal mammogram and/or ductogram
   3. Significant nipple discharge with unsuccessful ductogram
   4. Evaluation of lesions when patient reassurance is warranted (BI-RADS 3)
   5. Evaluation of lesions identified by other breast imaging techniques, palpable or non-palpable
   6. Evaluation of palpable abnormalities not demonstrated by mammography or ultra-sound
   7. Evaluation of multiple masses demonstrated on breast imaging
   8. To aid in biopsy targeting
   9. Evaluation of diffuse or multiple clusters of microcalcifications
   10. Evaluation of breasts for occult disease in cases of axillary lymph node metastases with unknown primary
   11. Unexplained architectural distortion
   12. Evaluation of suspicious mammographic finding seen on one view only
   13. Evaluation of enhancing areas seen on MRI to increase specificity
D. Patients with technically difficult breast imaging
   1. Radiodense breast tissue
   2. Implants, free silicone, or paraffin injections compromising the mammogram
E. Patients for whom Breast MRI would be indicated
   1. MRI is diagnostically indicated, but not possible
      a. implanted pacemakers or pumps
      b. ferromagnetic surgical implants
      c. risk of nephrogenic systemic fibrosis response to gadolinium.
      d. body habitus exceeding the inside of the MRI bore
      e. patients with breasts too large to be evaluated within the breast coil
      f. patients with acute claustrophobia
      g. other factors limiting compliance with a prescribed MRI study.
   2. As an alternative for patients who meet MRI screening criteria: BRCA1, BRCA2 mutations; parent, sibling, or child BRCA+; Lifetime risk of 20%-25% established; chest radiation between ages 10 and 30
F. Monitor neoadjuvant tumor response in patients undergoing preoperative chemotherapy
   1. Determine the impact of therapy
   2. Surgical planning for residual disease

Adapted from SNM Guideline for Breast Scintigraphy with breast-specific gamma cameras version 1.0 June 4, 2010.[34]
BIRADS, Breast Imaging-Reporting and Data System[32]; MRI, magnetic resonance imaging.

Personalización en MN

TOMOGRAFIA POR EMISION DE POSITRONES (PET)

La FDG marcada con 18F es captada por el tejido metabólicamente activo

Detección tumor primario

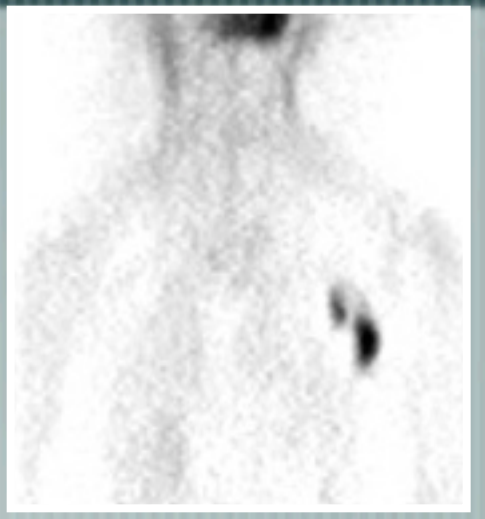
Util en sospecha de recidiva en cáncer de mama

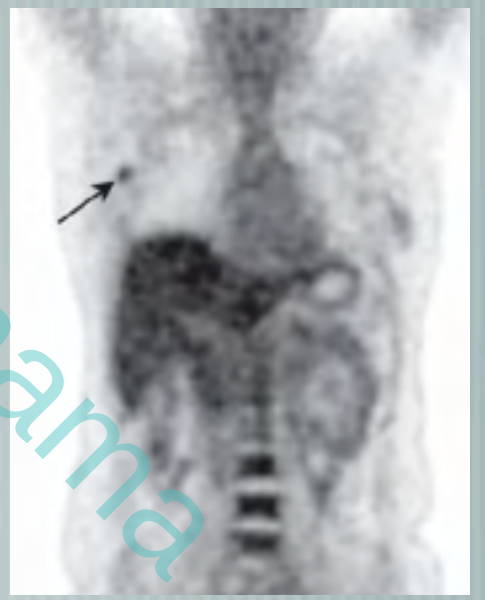
Diferenciación cambios postquirúrgicos de recurrencia

Valoración de metástasis a distancia

Evaluación respuesta al tratamiento

Valoración de metástasis axilares/extraaxilares (depende tamaño)

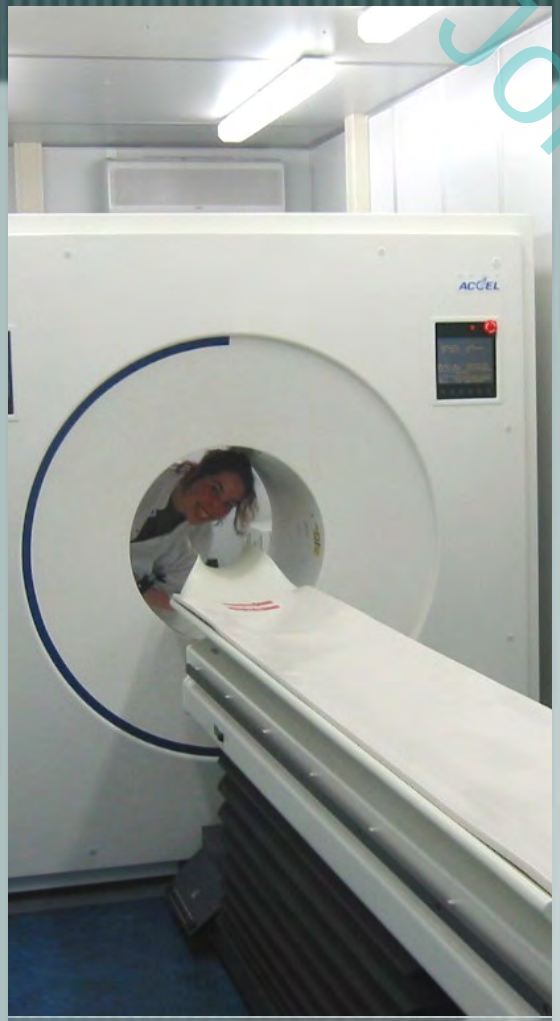




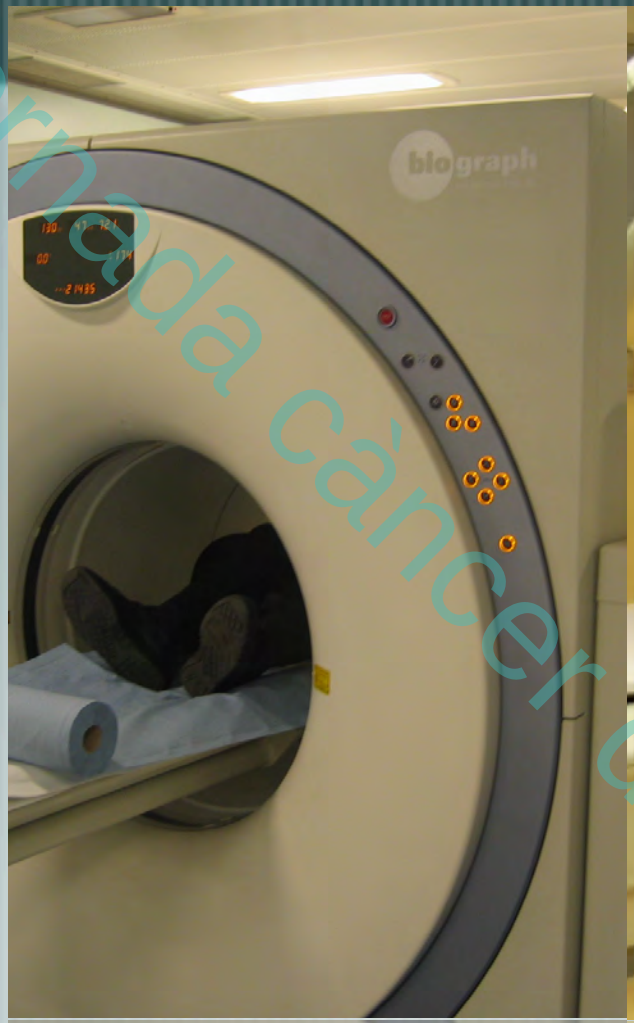
2004 n= 360 pacientes (Sensibilidad 61%/ Especificidad 80%)

Wahl R et al. J Clin Oncol 2004; 22: 277-285

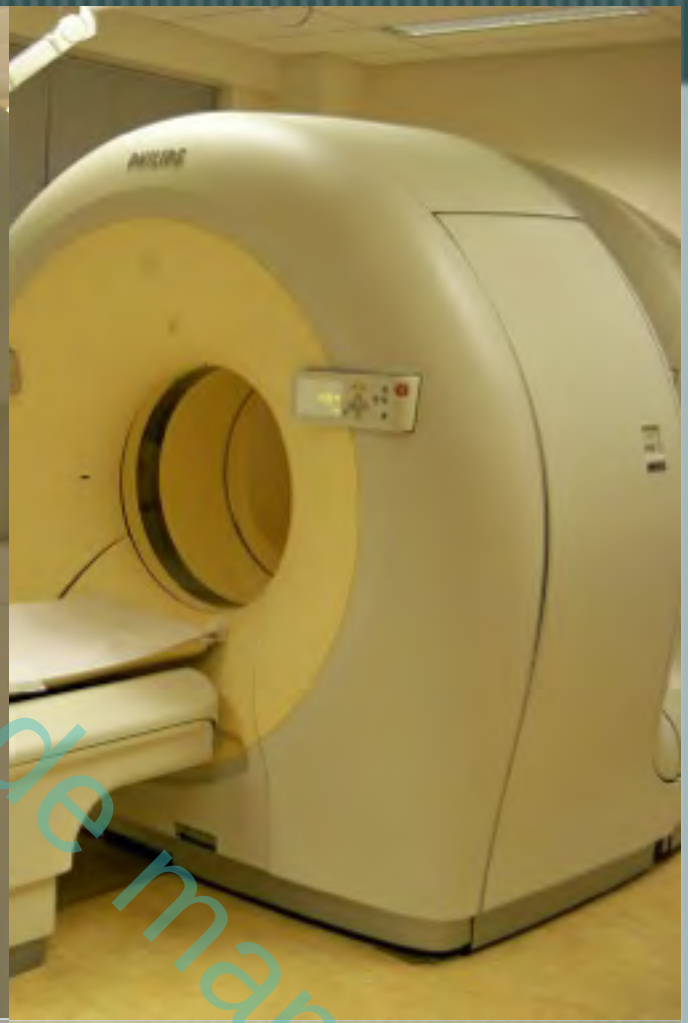
Personalización en MN



PET

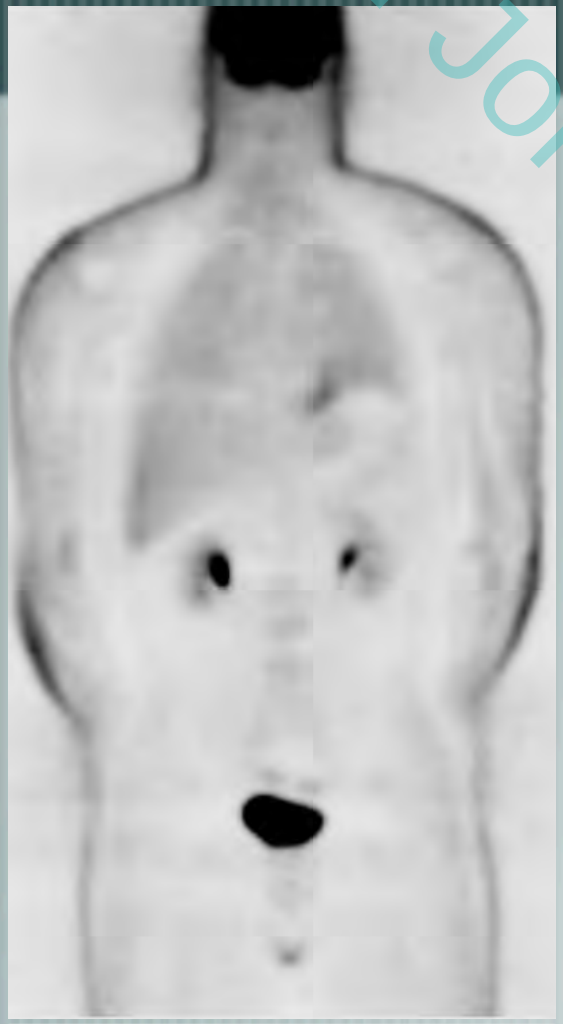


PET-TC

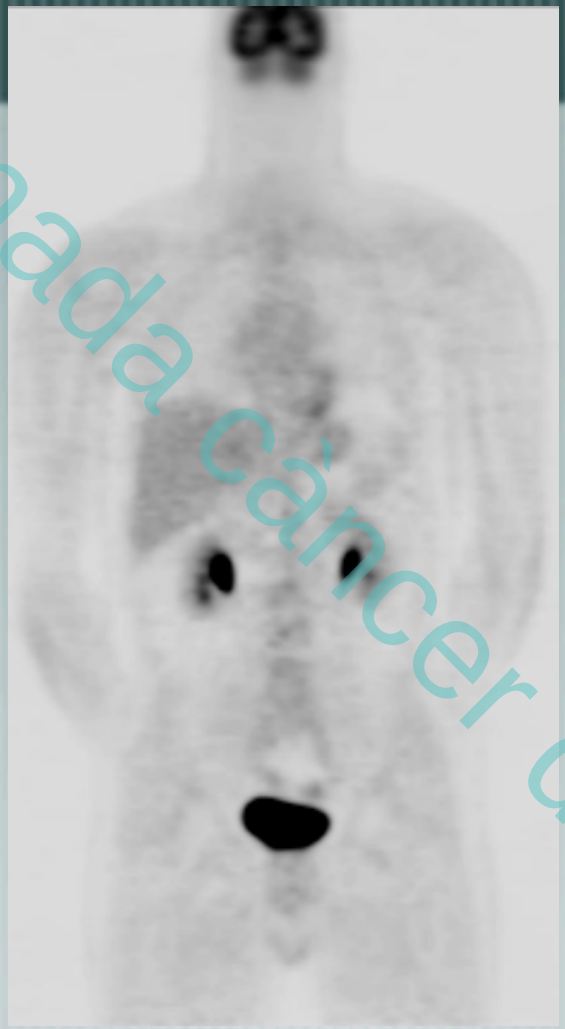


PET-TC TOF/HD

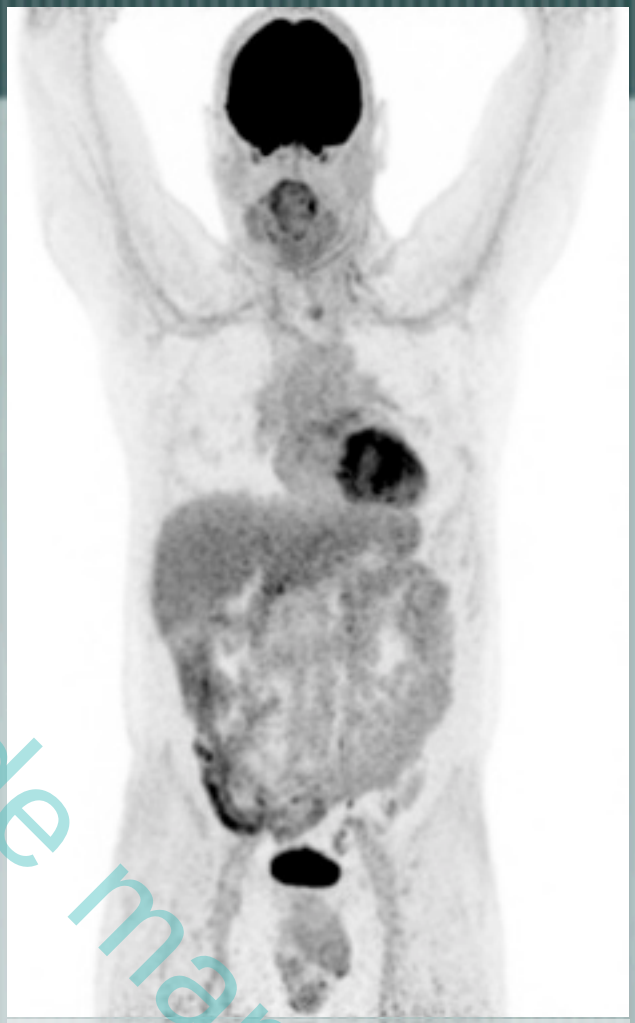
Personalización en MN



90s

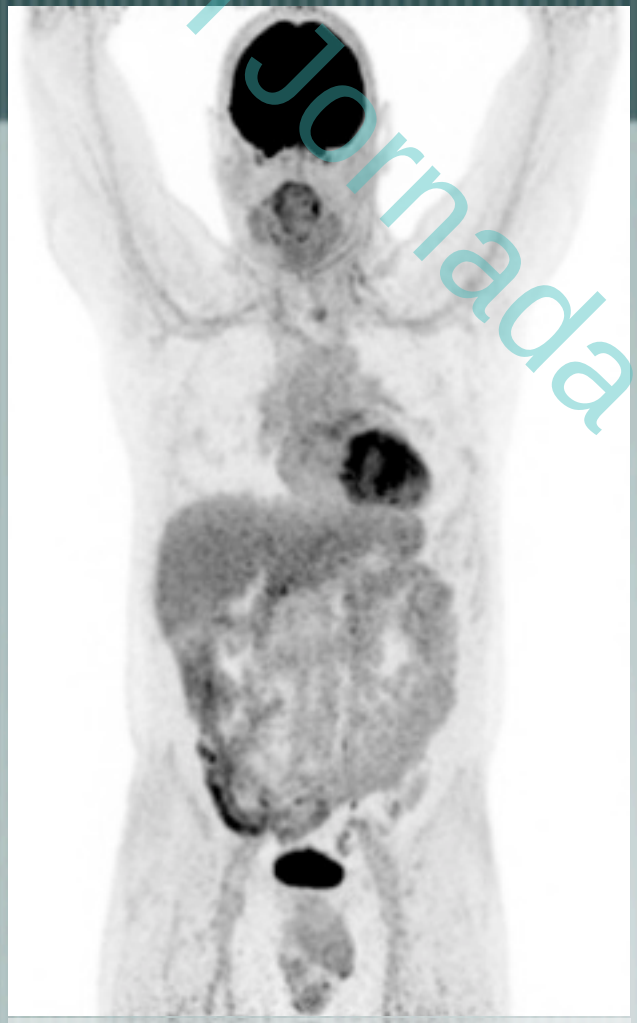


2000

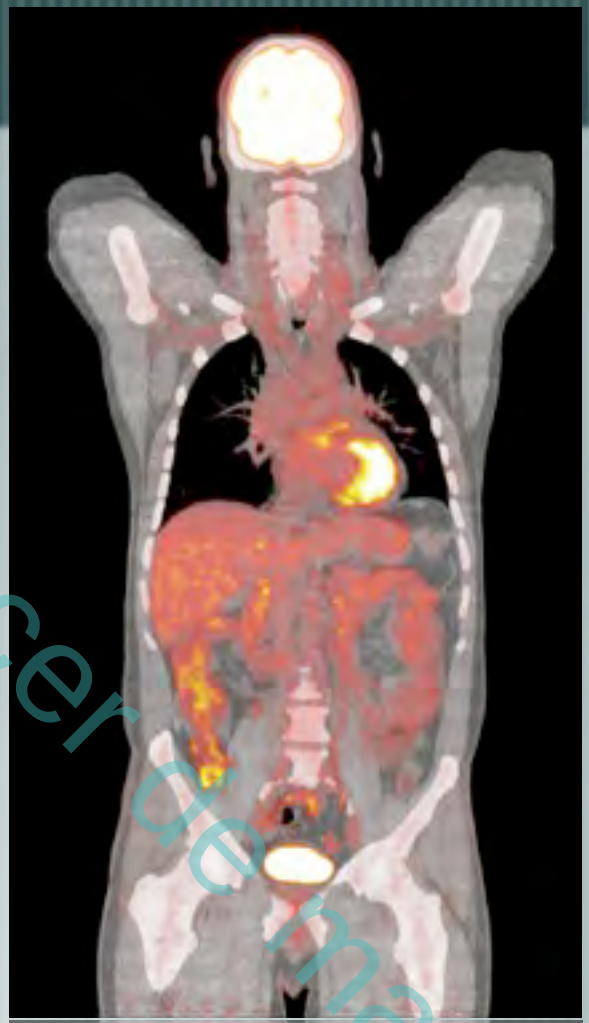


2006

Personalización en MN

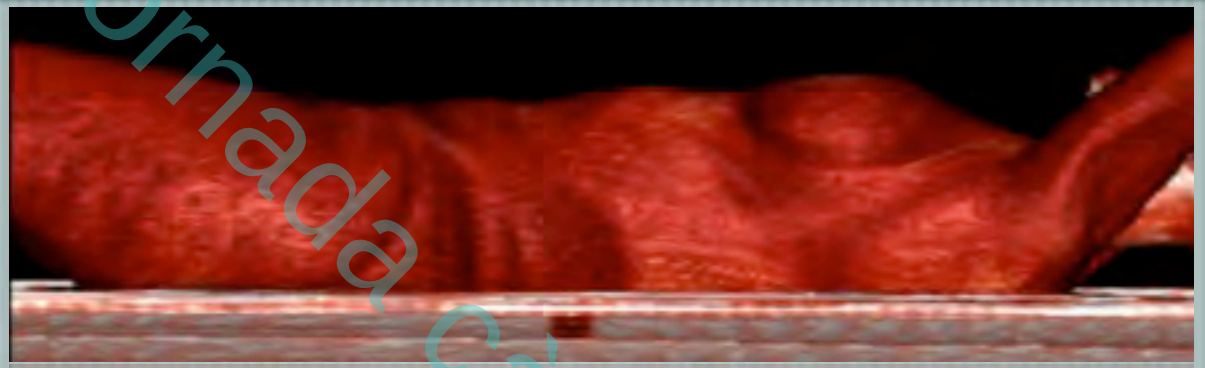


PET

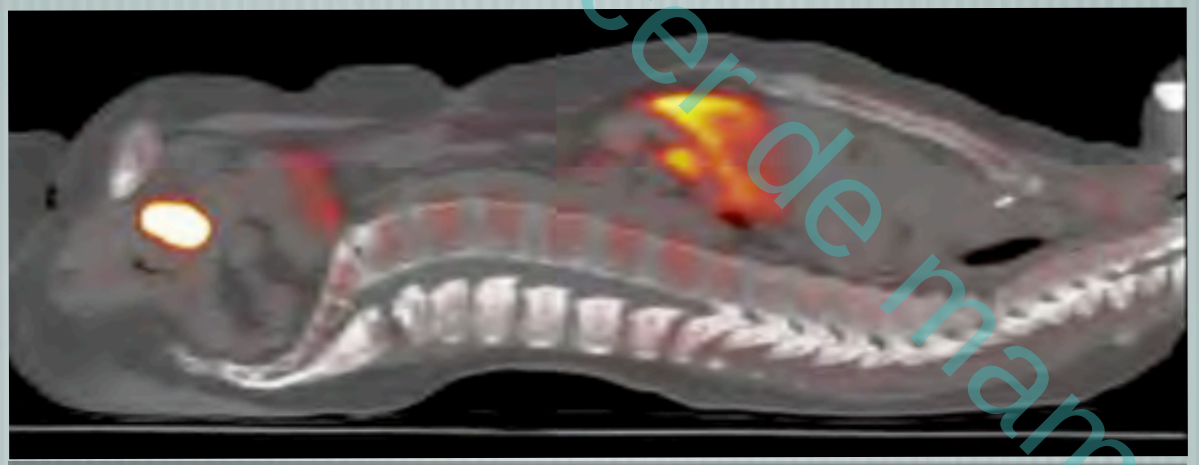


PET-TC

Personalización en MN

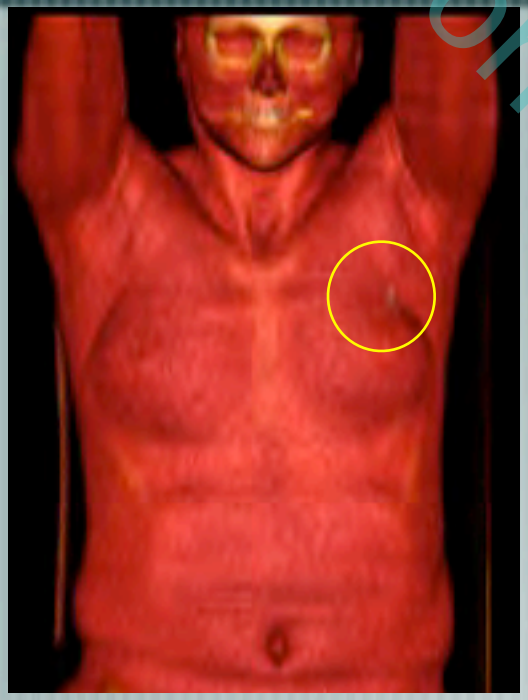


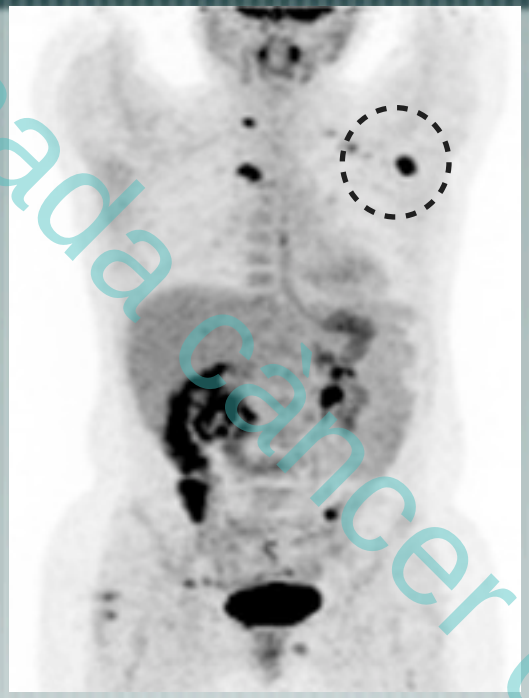
DISEMINACION A DISTANCIA

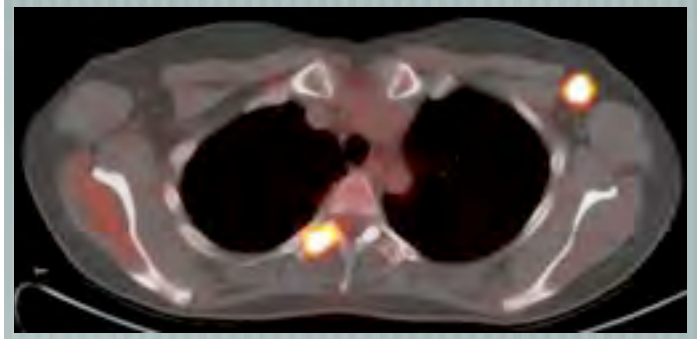


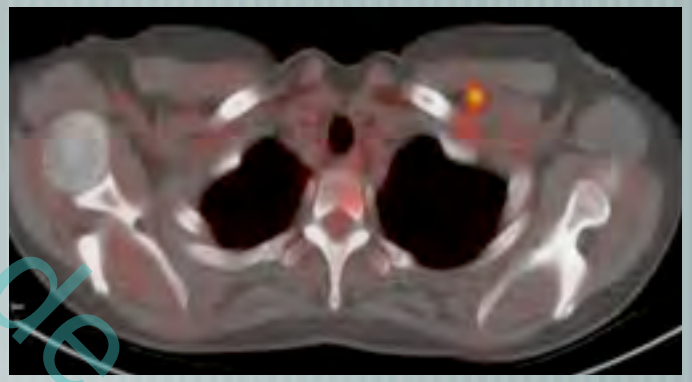
PET-TC SUPINO cortes 5 mm TC BAJA DOSIS

Personalización en MN









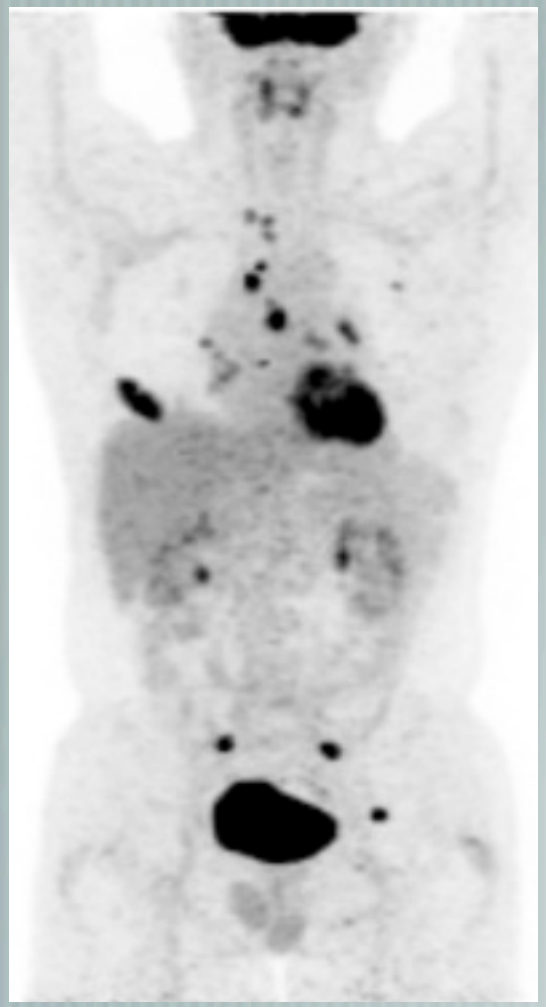
Evaluación loco-regional

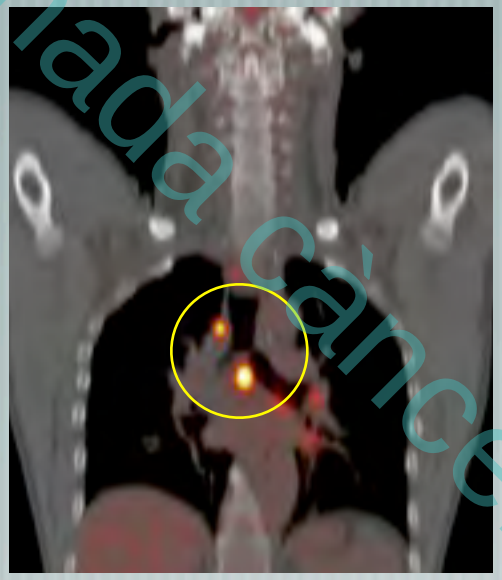
2007-2009
5 series N= 24-183
Tumores T1-T2

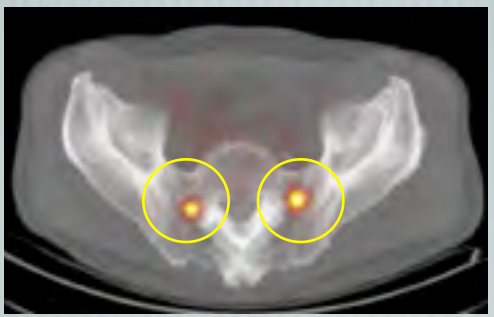
SENSIBILIDAD 48% - 95%
ESPECIFICIDAD 84%-100%

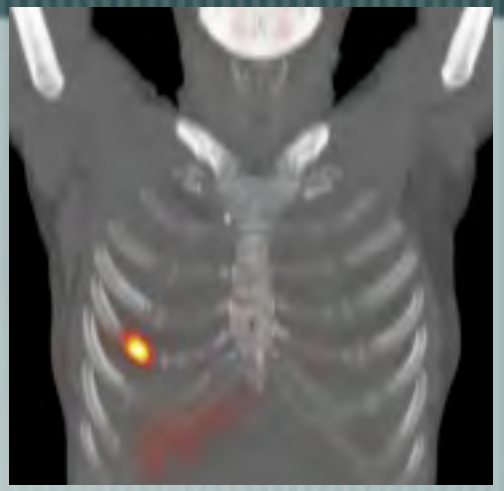
Peare R et al. Breast Cancer Res 2010;123:281-290

Personalización en MN









ELEVACION
MARCADORES TUMORALES
(CA15-3 / CEA)

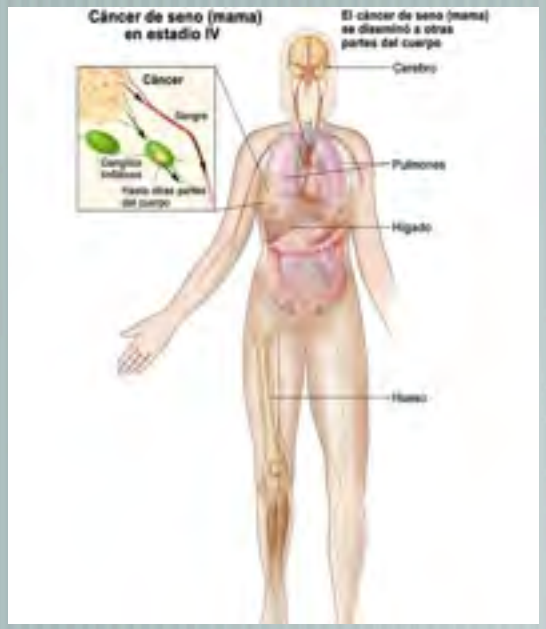
N = 228
SENSIBILIDAD 94%
ESPECIFICIDAD 85%
CAMBIO MANEJO 54%

Champion L et al. Cancer 2010;117:1621-29

Personalización en MN

FDG PET-TC

Metástasis a distancia



N =154 (ESTADIO II/III)
QUIMIOTERAPIA NEOADJUVANTE

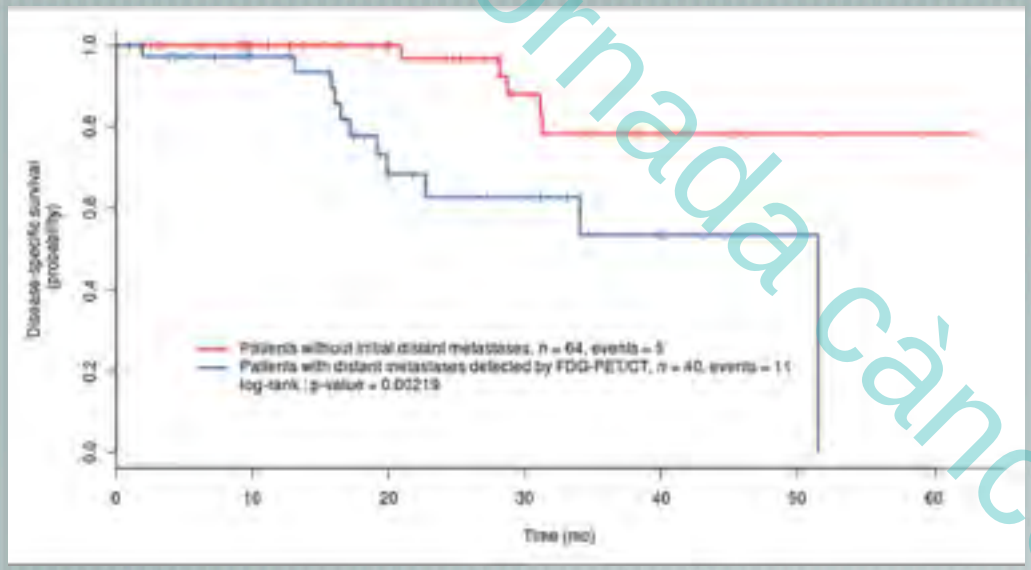
RX-TORAX, ECOGRAFIA HIGADO, GAMMAGRAFIA OSEA

42 NUEVAS LESIONES
25 PACIENTES
(OSEAS, GANGLIOS LINFATICOS, ORGANOS, NUEVO TP)
CONFIRMADAS EN 20 PACIENTES
(16 SOLO PET-CT +)
FALSOS-POSITIVOS IN 4

CAMBIO MANEJO
13/154 PACIENTES (8%)

Koolen B et al. Breast Cancer Research & Treatment, 2011,

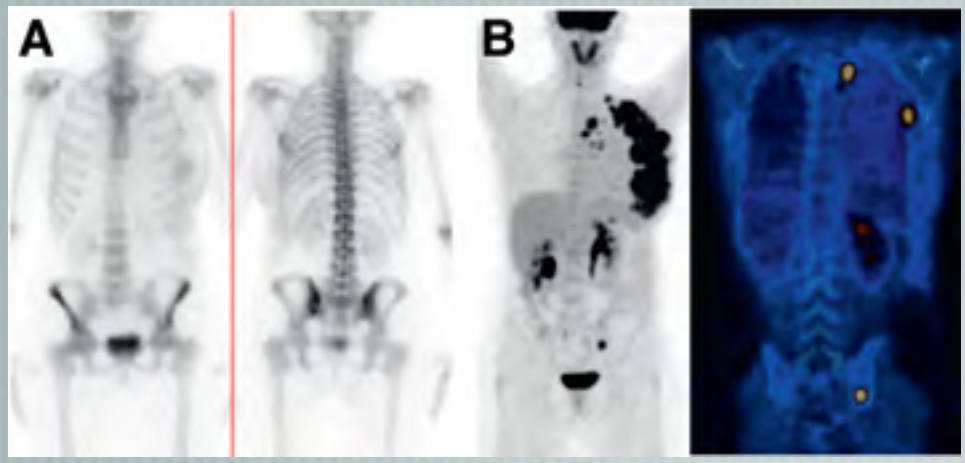
Personalización en MN

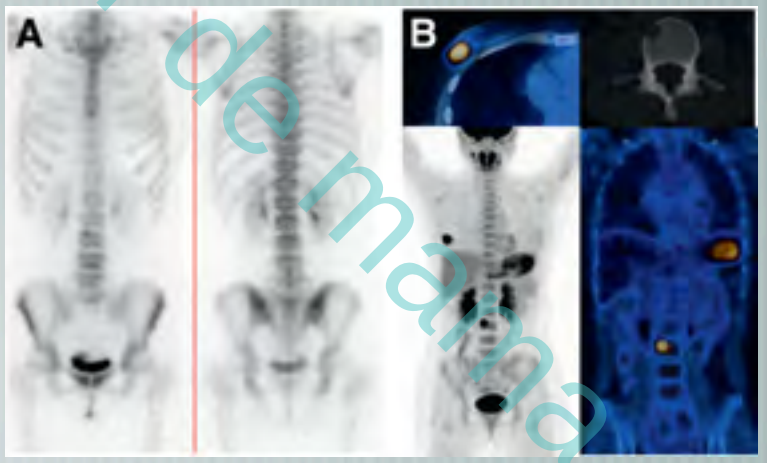


^{18}F-FDG PET/CT in Staging Patients with Locally Advanced or Inflammatory Breast Cancer: Comparison to Conventional Staging

In this series of 117 LABC patients, almost all lesions detected by conventional imaging were also depicted with ^{18}F-FDG PET/CT, which also showed additional lesions. PET/CT had the clear advantage of examining the chest, abdomen, and bones in a single session. ^{18}F-FDG PET/CT offered powerful prognostic stratification at initial staging.

J Nucl Med 2013; 54:5–11





Personalización en MN

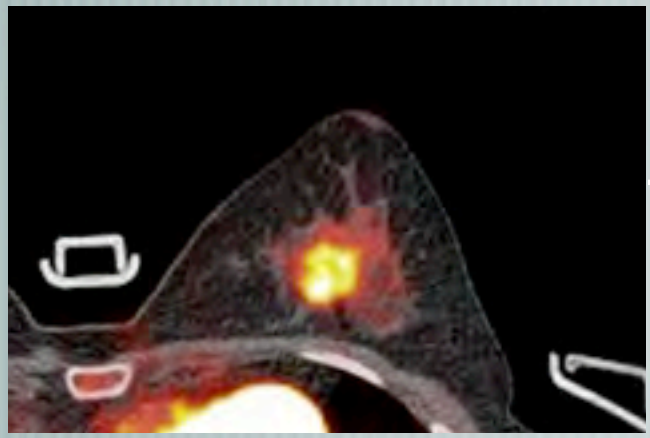
DETECCION TUMOR PRIMARIO

(Avril N et al, JCO 2000;18:3495)

FDG-PET

< 1cm 57%
> 1cm 91%

ESPECIFICIDAD ~ 90%



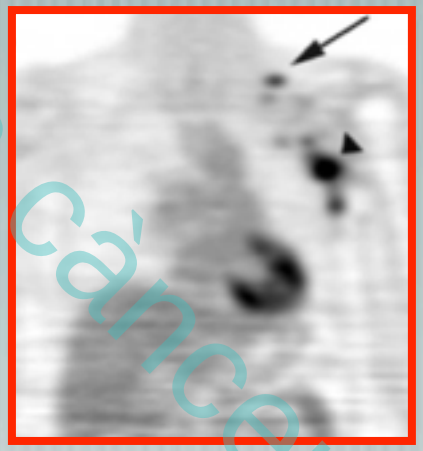
FDG-PET/TC

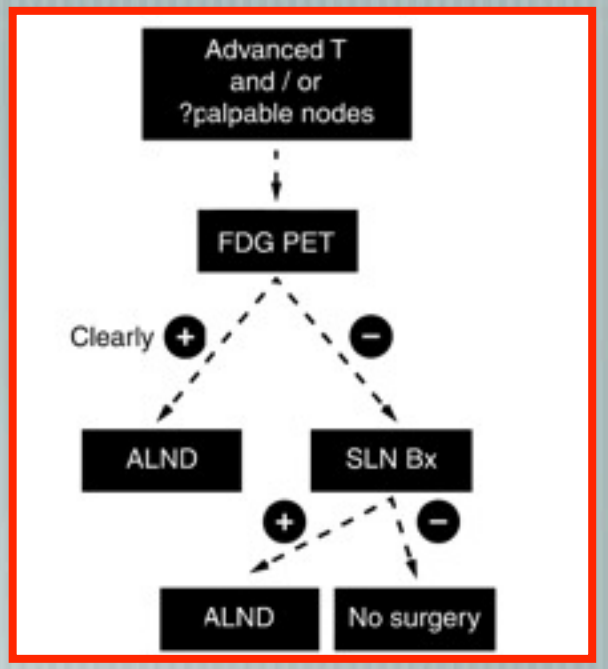
Personalización en MN

Table 1 Largest Prospective Series Comparing Axillary Nodal Staging Using FDG-PET With Pathologic Results of Axillary Lymph Node Dissection in Patients With Breast Cancer

Series	Number of Patients	Sensitivity	Specificity
Adler, 1997[44]	52	95 (19/20)	66 (21/32)
Utech, 1996[45]	122	100 (44/44)	75 (60/80)
Avril overall, 1996[46]	51	79 (19/24)	96 (26/27)
T1 tumors	18	33 (2/6)	100 (12/12)
>T1 tumors	23	94 (17/18)	100 (5/5)
Crippa, 1998[28]	72	85 (23/27)	91 (41/45)
Smith, 1998[47]	50	90 (19/21)	97 (28/29)
Greco, 2001[48]	167	94 (68/72)	86 (82/95)
Schirrmeister, 2001[49]	113	79 (27/34)	92 (73/79)
Wahl, 2004[40]	308	61	80
Lovrics, 2004[50]	90	40	97

Numbers in parentheses are patient numbers used to derive sensitivity and specificity values.





Estadificación tumor primario Tamaño < 1 cm (S = 57% vs 91%)

Carcinoma in situ (S = 25%)

Estadificación axilar Incremento de falsos negativos

Micrometástasis

Macrometástasis (necrosis, grado tumoral...)

Eubank WB et al. Semin Nucl Med 2005; 35: 84-99
Hodgson NC et al. J Clin Oncol 2008; 26: 712-720

Personalización en MN

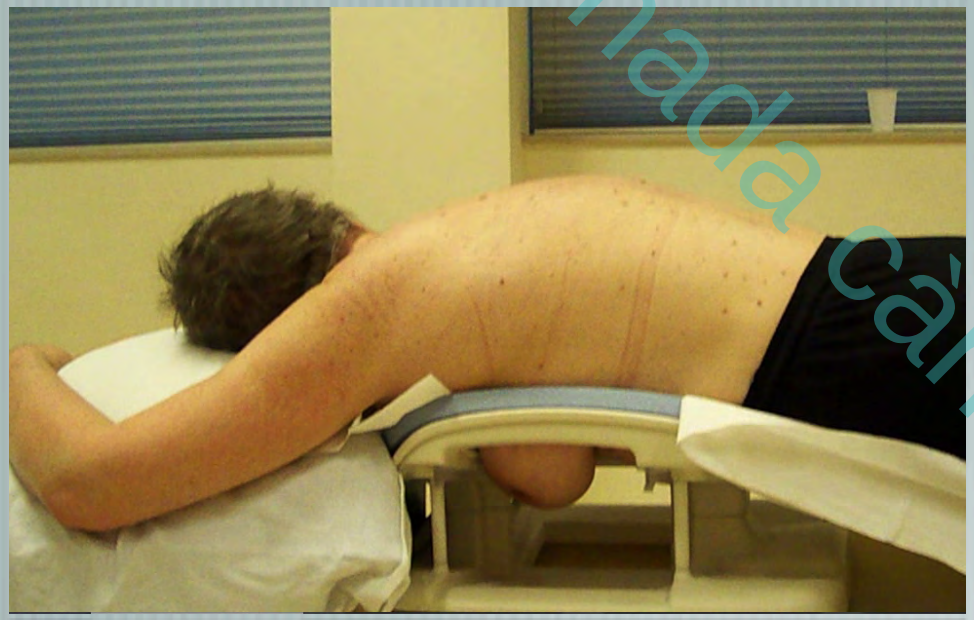
	PET	GC
SENSIBILIDAD	43.7%	96.6%
ESPECIFICIDAD	97.1%	100.0%
VPN	67.1%	97.1%
VPP	92.7%	100.0%

- BAJA SENSIBILIDAD
  - PET negativa: bajo valor predictivo
- ALTO VALOR PREDICTIVO POSITIVO
  - linfadenectomía sin GC si PET +

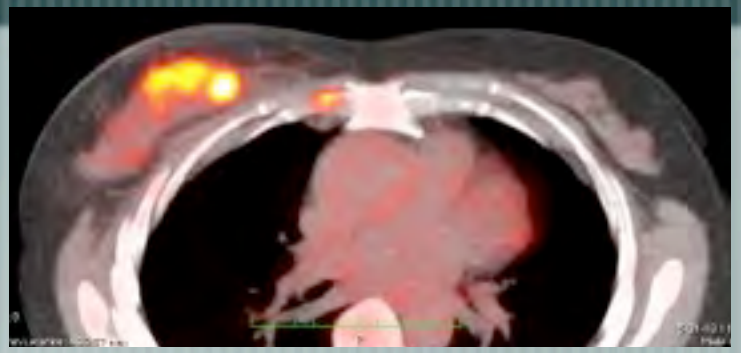
Veronesi U et al. Ann Oncol 2007; 18: 473-478

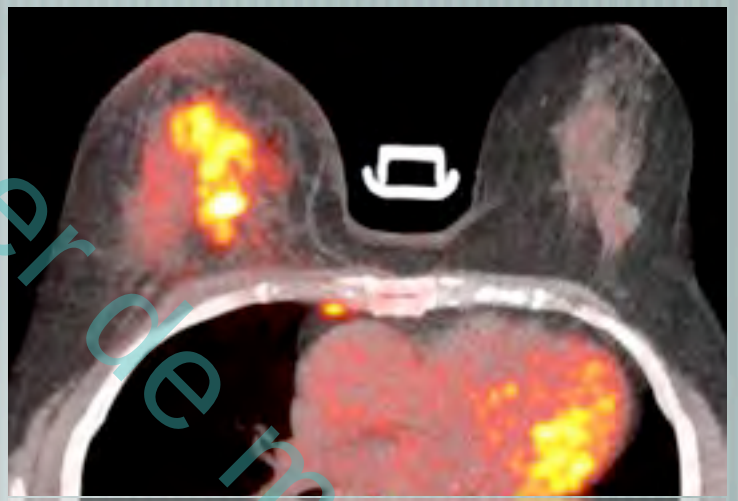
Personalización en MN

Evaluación loco-regional



PET-CT EN POSICION PRONO cortes 2 mm

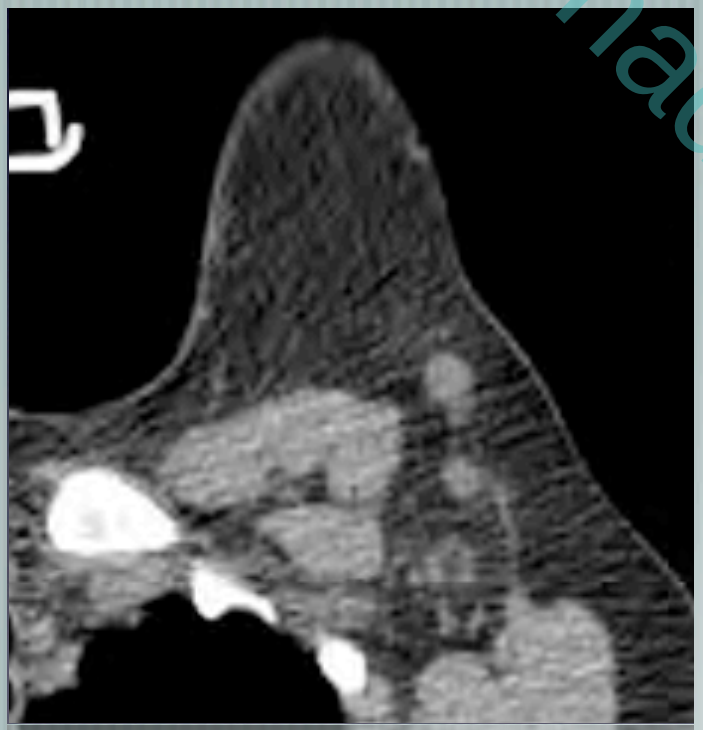


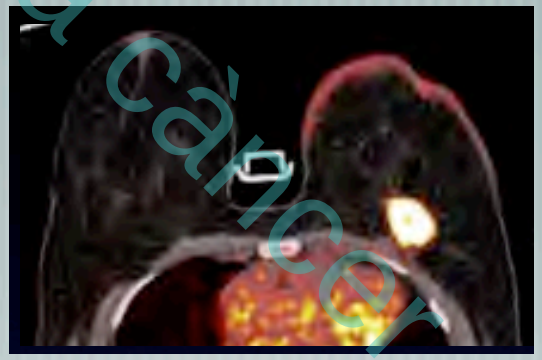


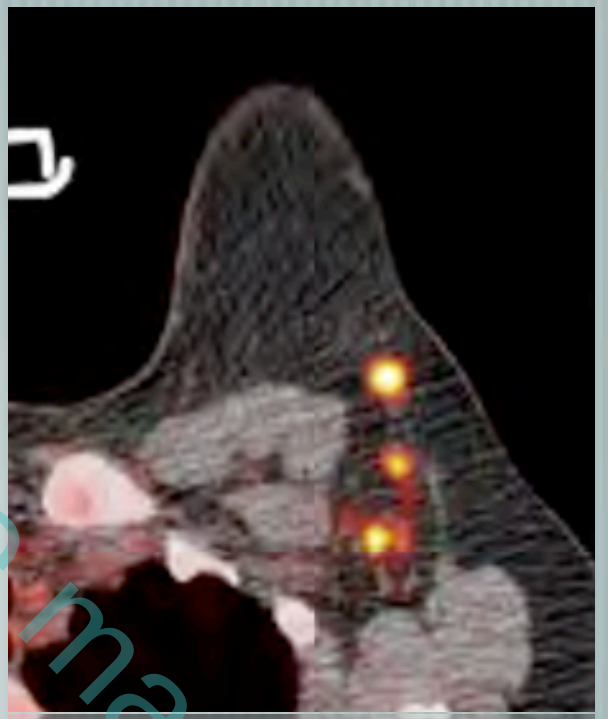
MEJOR RESOLUCION
MENOS ARTEFACTOS RESPIRATORIOS
MEJOR DEFINICION TUMORES
MEJOR IDENTIFICACION GANGLIOS

Vidal-Sicart S et al. Rev Esp Med Nucl 2010;29:230-235

Personalización en MN

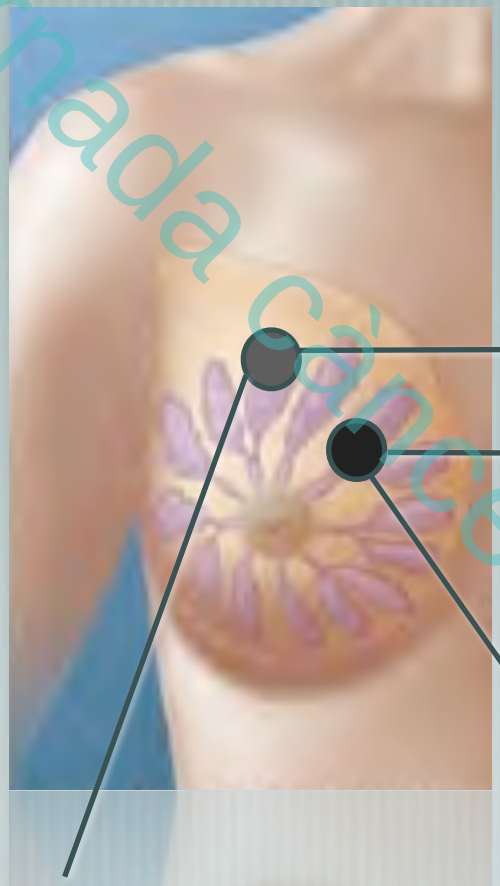






Personalización en MN

CARACTERIZACION TUMOR (SUVmax)



CARCINOMA INVASIVO MAMA

^{18}F-FDG
CAPTACION
AUMENTADA

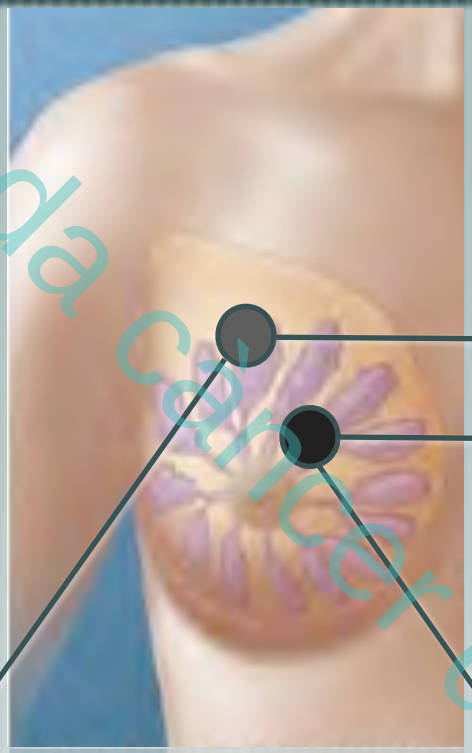
CARCINOMA LOBULILLAR
MENOS CAPTACION FDG

CARCINOMA DUCTAL
MAYOR CAPTACION FDG

Personalización en MN

CARACTERIZACION TUMOR (SUVmax)

146/159 PACIENTES
ESTADIO II/III(92%)
CAPTACION TUMORAL ADECUADA PARA EVALUACION



CARCINOMA INVASIVO MAMA

^{18}F-FDG
CAPTACION AUMENTADA

LOBULILLAR
67% (14/21)
mediana SUVmax 4,4

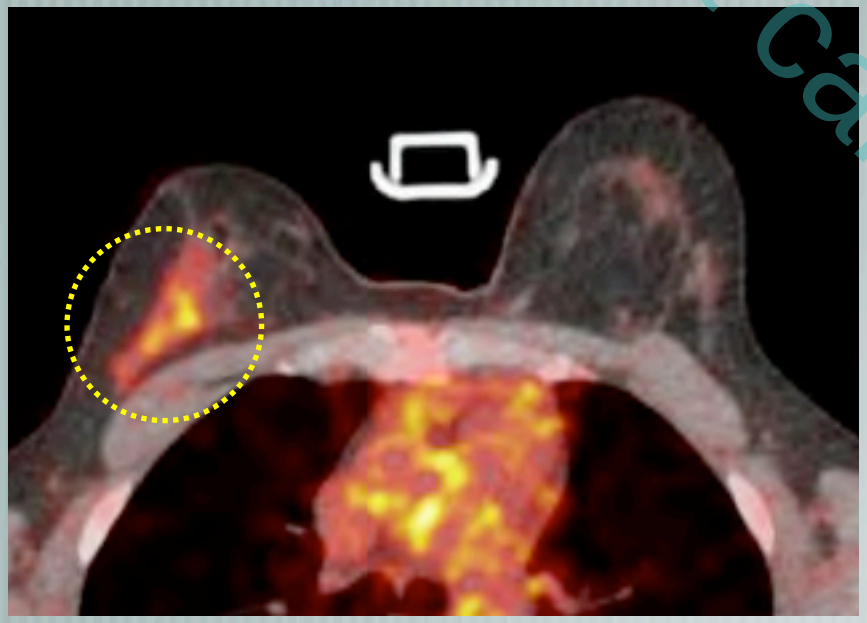
DUCTAL
95% (124/131)
mediana SUVmax 6,8

Koolen B et al. EJNMMI 2012; 39: 1830-38

Personalización en MN

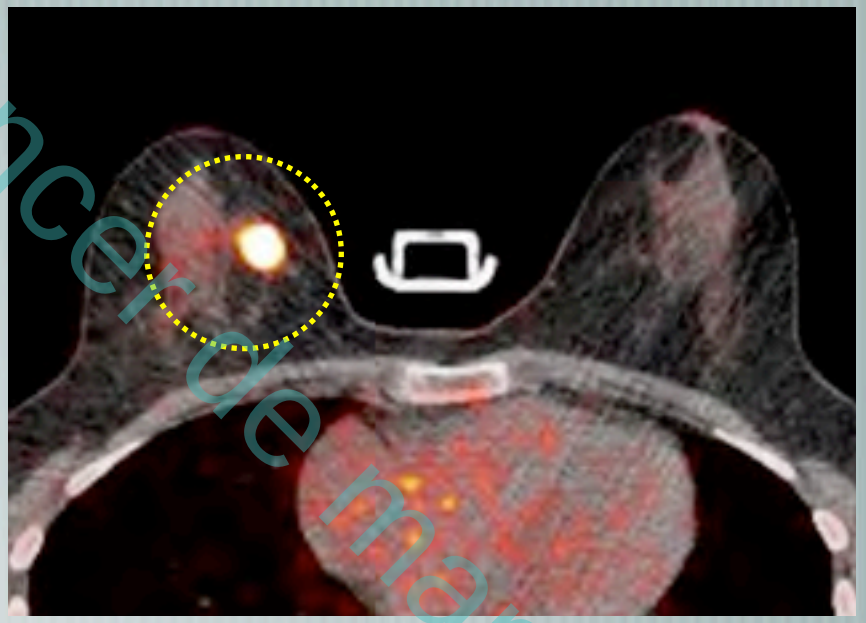
DIFERENTES TIPOS CARCINOMA MAMA

SUVmax 2.5



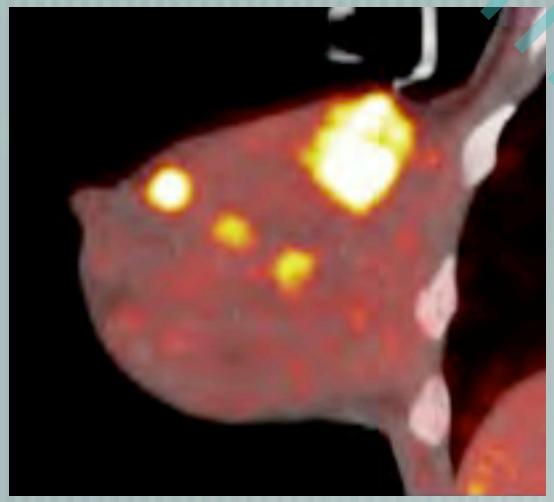
LOBULILLAR

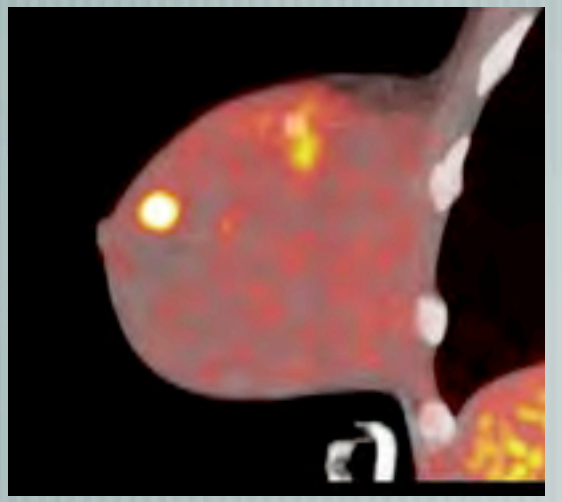
SUVmax 10



DUCTAL

Personalización en MN





PERFIL GENETICO

MATERIAL OBTENIDO
BIOPSIA GUIADA
POR ECOGRAFIA O
ESTEREOTAXIA

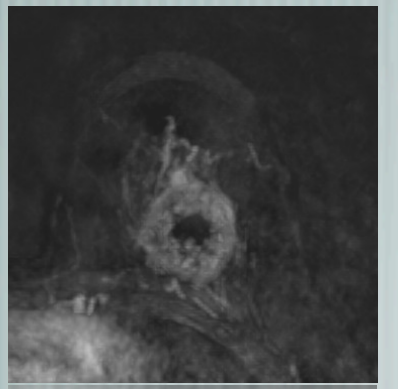
PREDICCION
RESPUESTA TERAPEUTICA
&
PRONOSTICO

Personalización en MN

ER (+)

SUVmax = 5.4

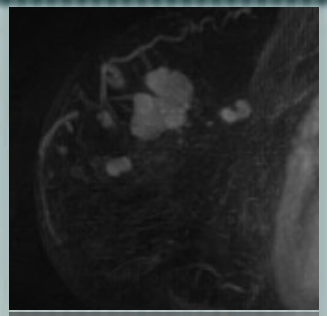
(95%CI 3.7-7.1)

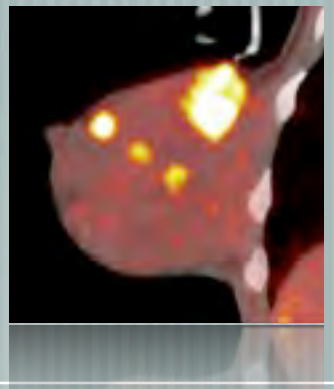


HER2 (+)

SUVmax = 5.9

(95%CI 3.3-8.6)

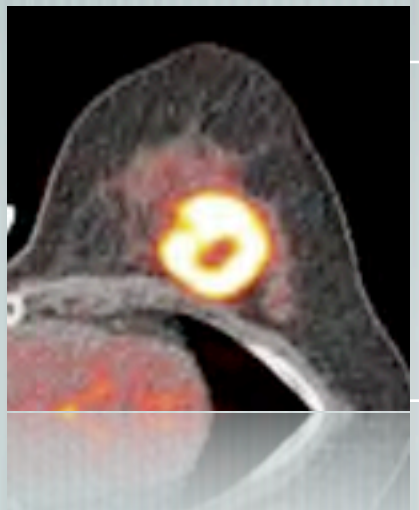




TRIPLE (-)

SUVmax = 11.1

(95%CI 3.7-16.1)

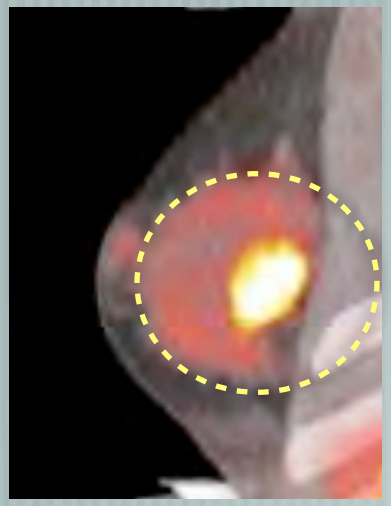


Straver M et al.Eur J Nucl Med 2010

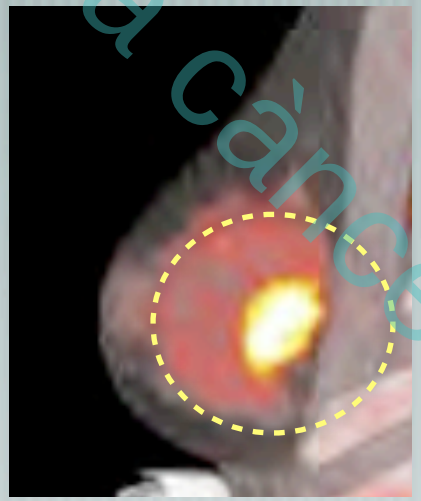
Personalización en MN

RESPUESTA TUMORAL

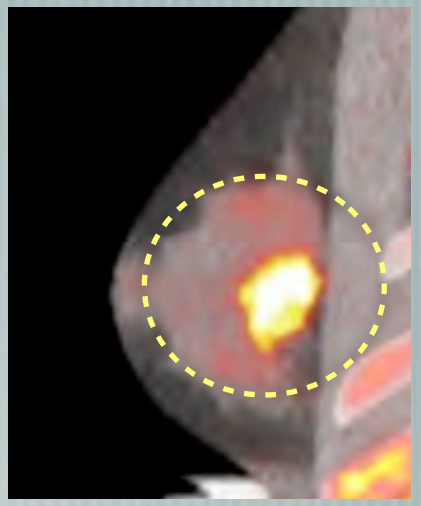
DIFERENCIACION PACIENTES RESPONDEDORES DE LOS NO RESPONDEDORES



PRE-QUIMIOTERAPIA



1 x QUIMIOTERAPIA



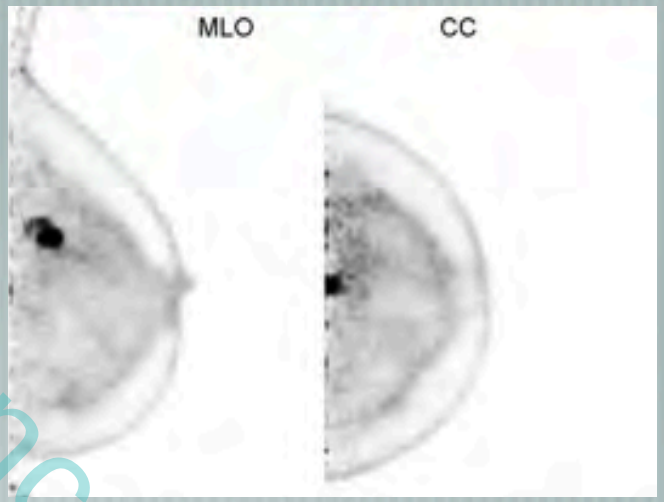
3 x QUIMIOTERAPIA

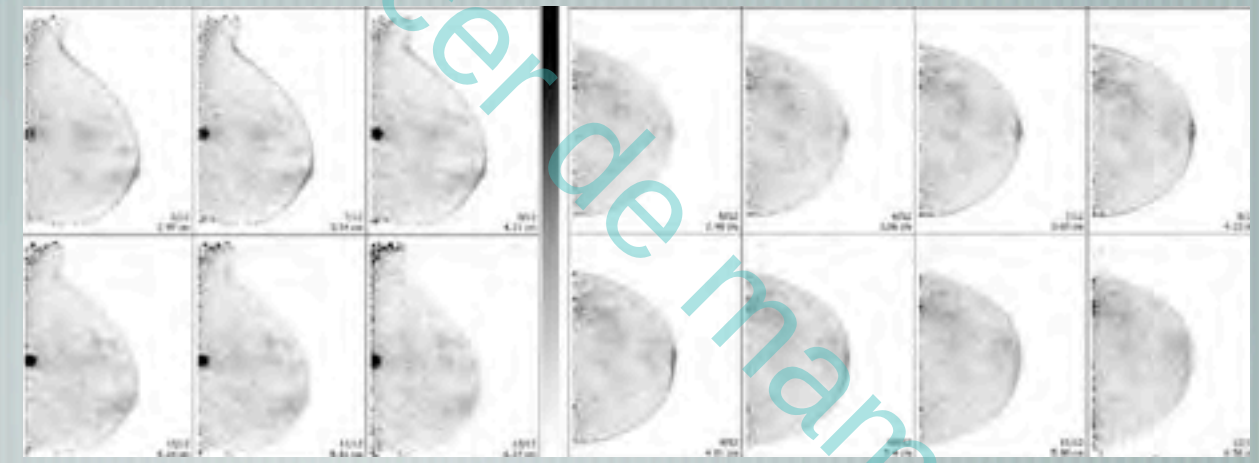
SENSIBILIDAD 93% ESPECIFICIDAD 75%

Kumar A et al. Eur Radiol 2009;19:1347-1357

Personalización en MN

PEM - FLEX-SOLO II



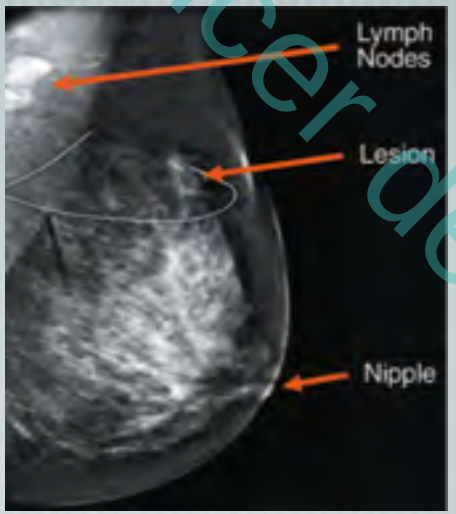


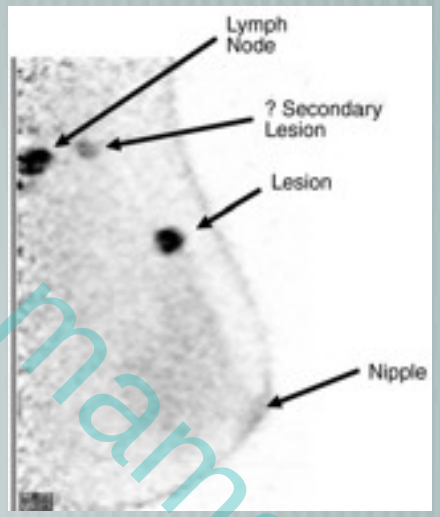
600 MBq ^{18}F-FDG - 7min/toma - 60 min p.i.

Personalización en MN

Table 1. Characteristics of nuclear cameras used in breast cancer imaging

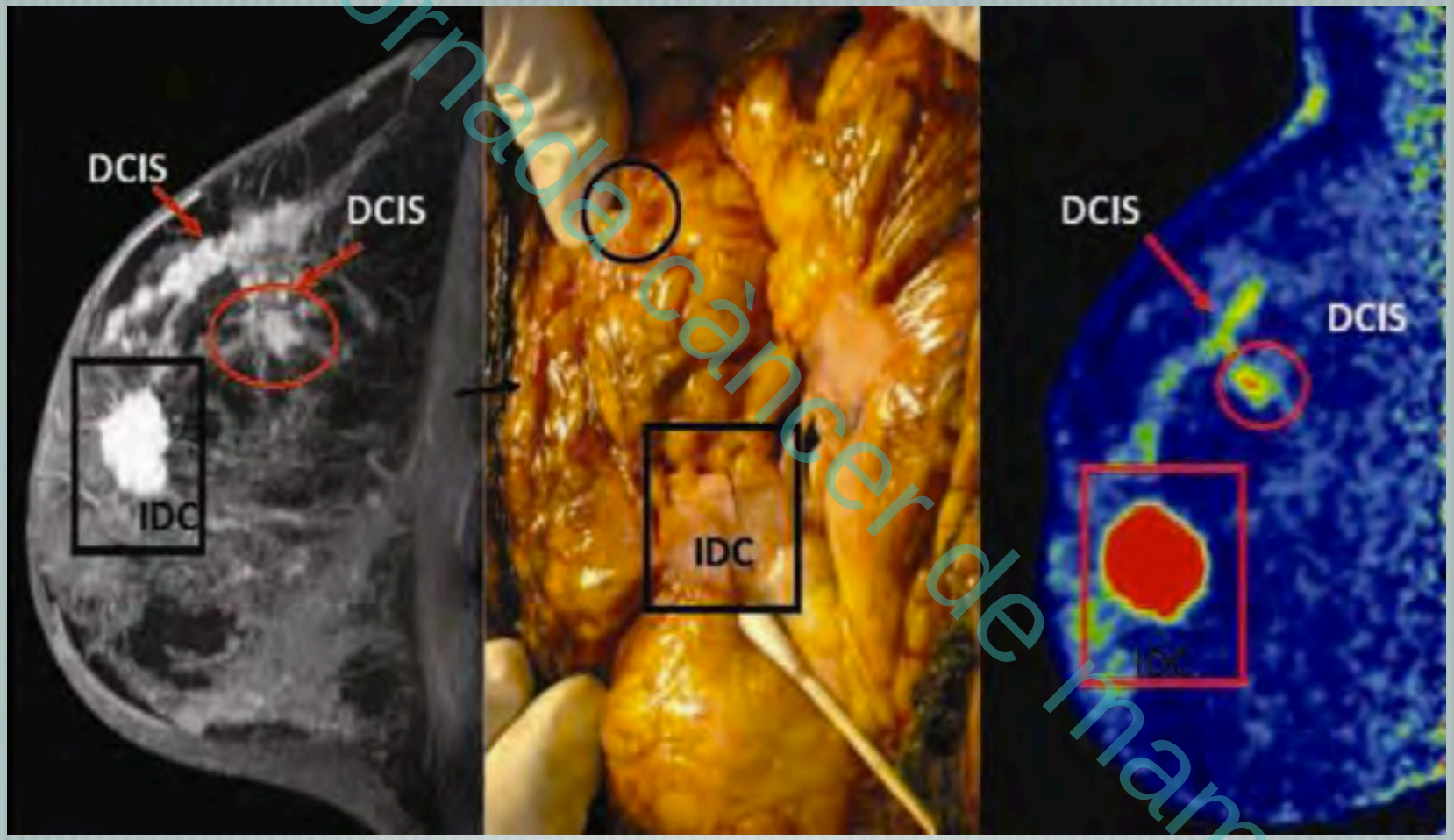
	Whole-body scintimammography	Breast-specific scintimammography	Whole-body PET	PEM
Type of radiotracer detected	Single photon	Single photon	Positron	Positron
Limit of resolution	5.0 mm	3.0 mm	5.0 mm	1.5 mm
Type of collimation	Lead collimator	Lead collimator	Timing collimation	Timing collimation
Position of patient	Lying	Sitting	Lying	Sitting
Breast immobilization	No	No	No	Yes
Respiratory motion	Yes	Some	Yes	No
Detector close to breast	No	Yes	No	Yes
Mimics mammographic views	No	Yes	No	Yes
Provides tomographic views	No	No	Yes	Yes





Schilling K et al. Eur J Nucl Med Mol Imaging 2010; 38: 23-26

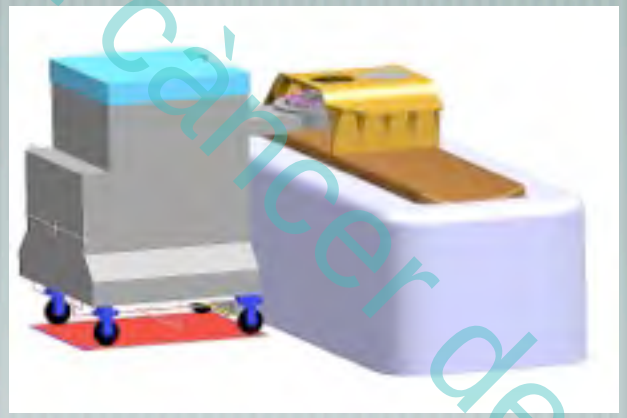
Personalización en MN

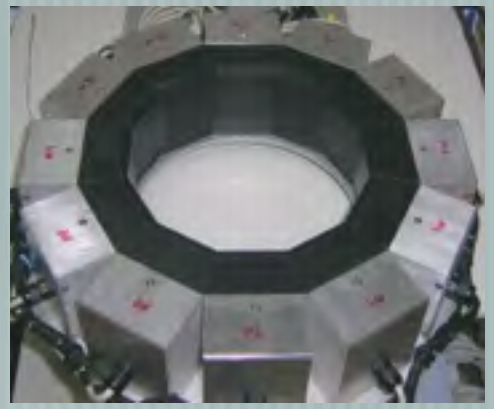


Personalización en MN

PEM - MAMMI

proyecto EU



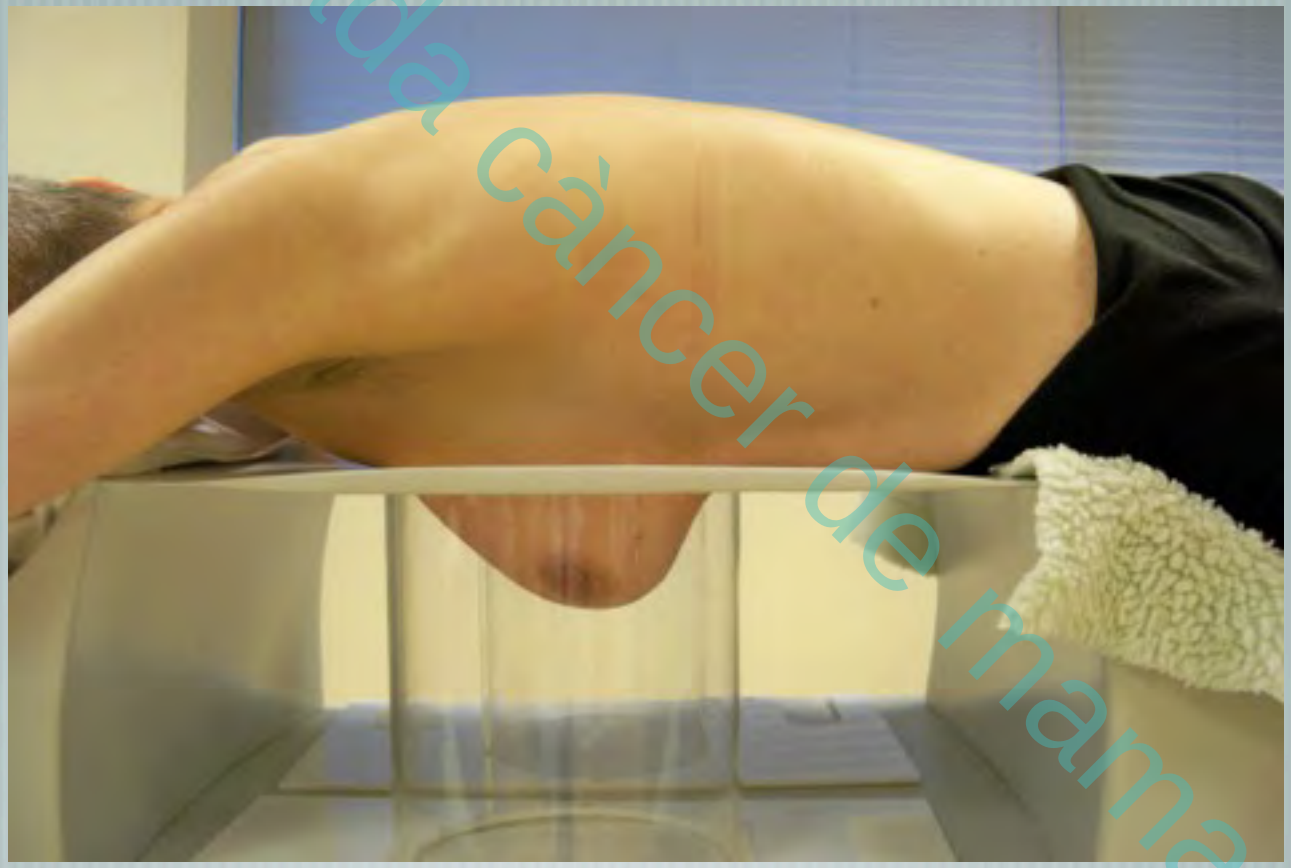


ANILLO 12 DETECTORES CON CRISTALES LYSO MONOLITICOS

Personalización en MN

POSICION MAMA COLGANTE

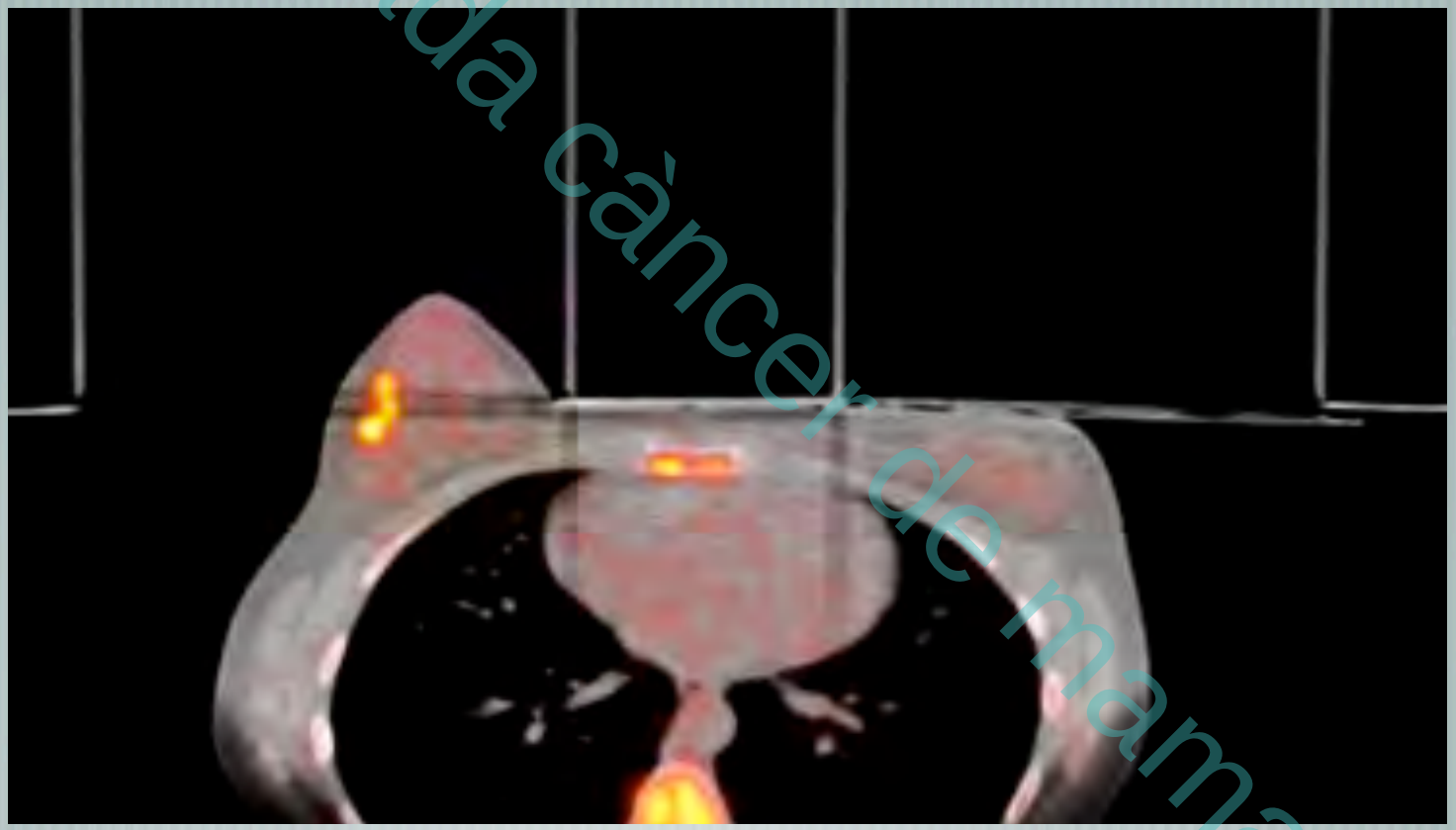
DEL PET-TT AL MAMMI-PEM



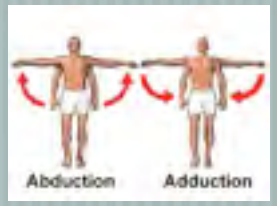
Personalización en MN

POSICION MAMA COLGANTE

DEL PET-TC AL MAMMI-PEM



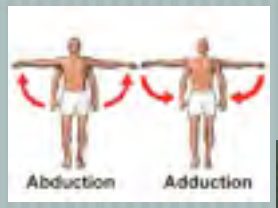
Personalización en MN



DEL PET-TC AL MAMMI-PEM

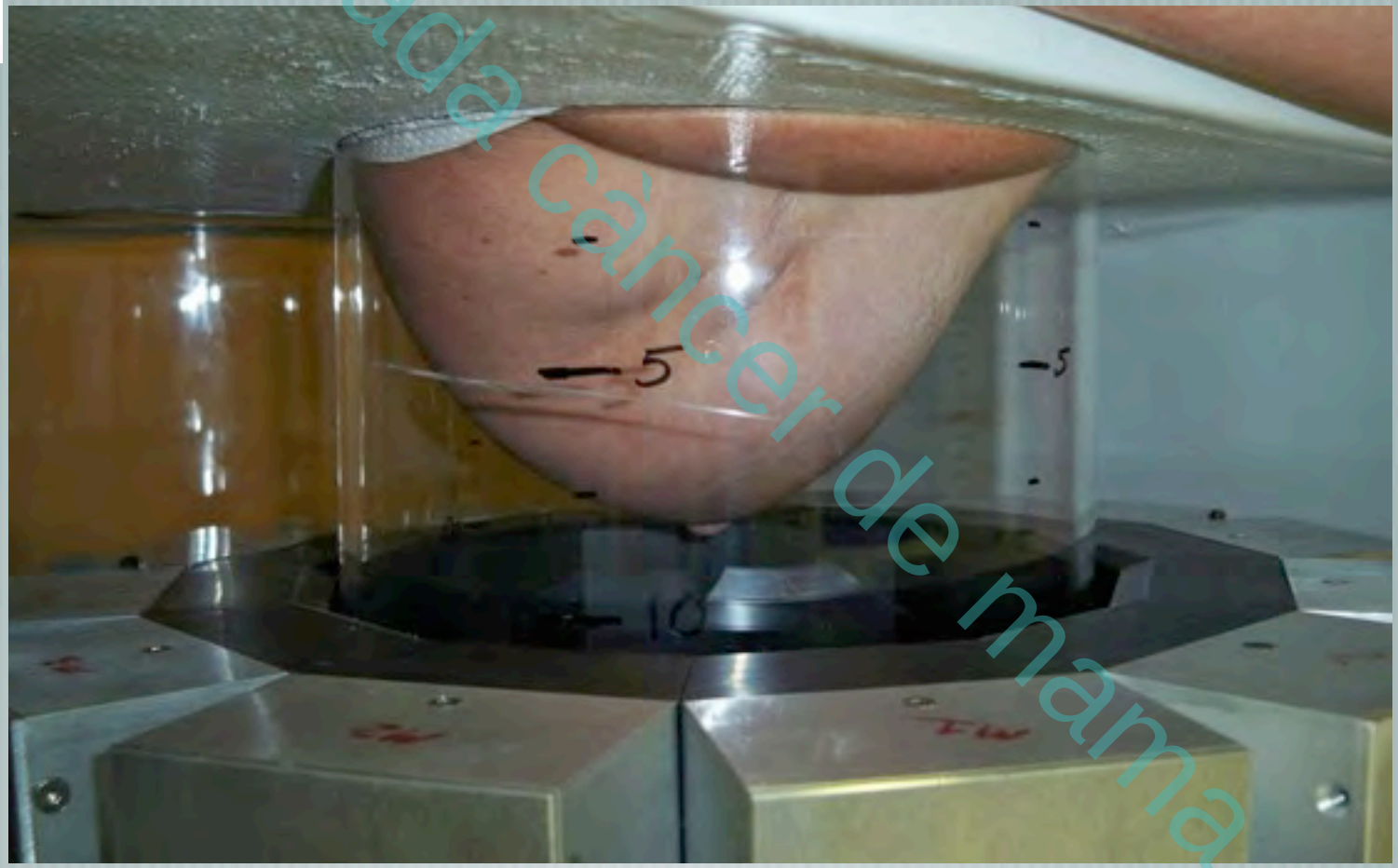
POSICION MAMA COLGANTE + ADDUCCION BRAZO

Personalización en MN

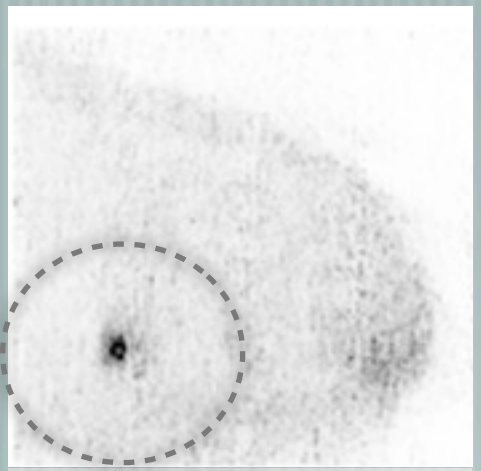


DEL PET-TC AL MAMMI-PEM

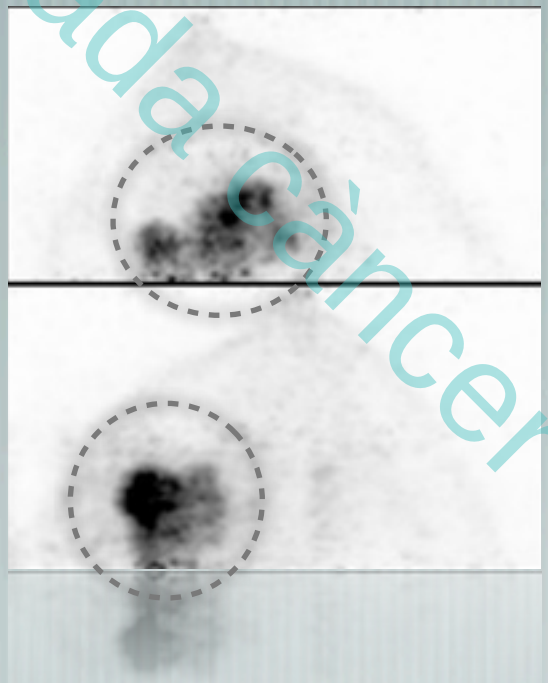
POSICION MAMA COLGANTE + ADDUCCION BRAZO



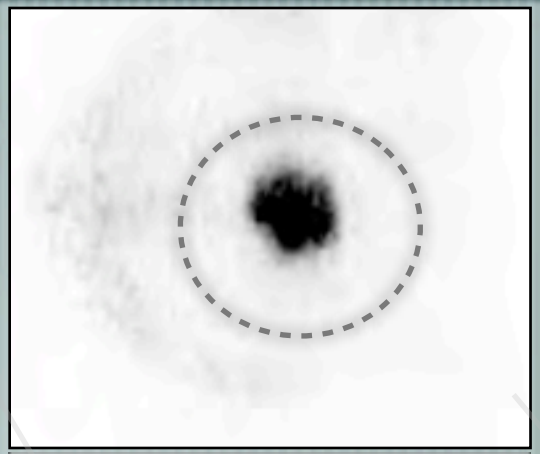
Personalización en MN

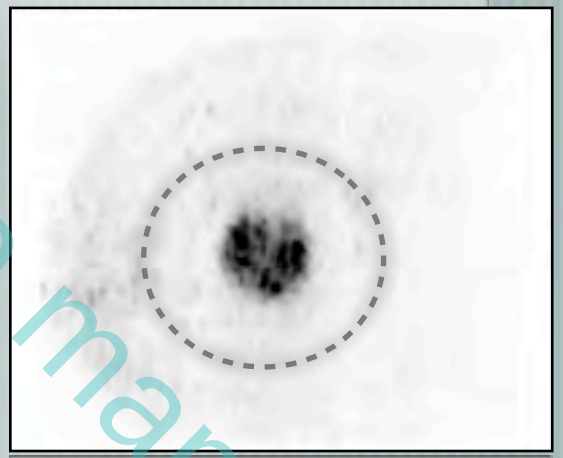


LESIONES PEQUEÑAS



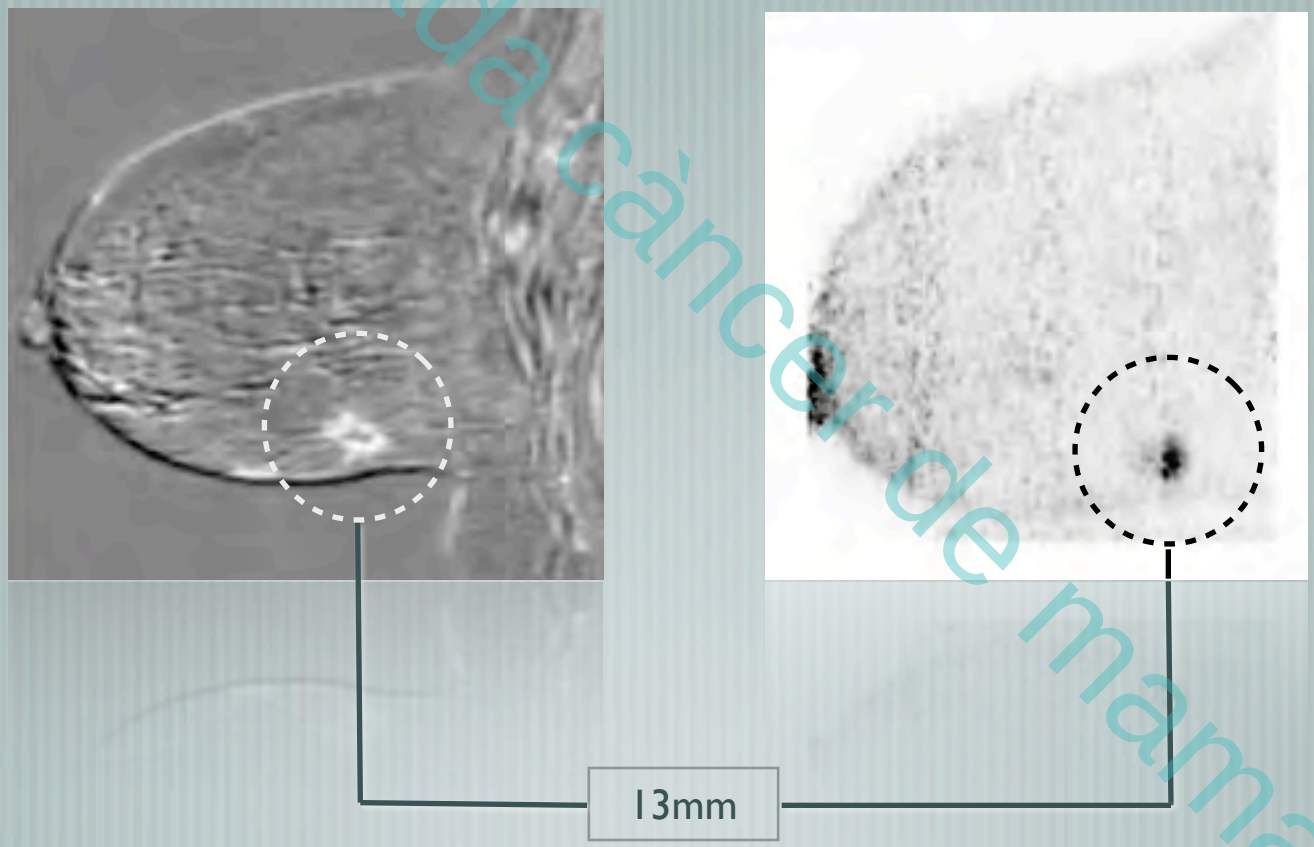
LESIONES HETEROGENEAS





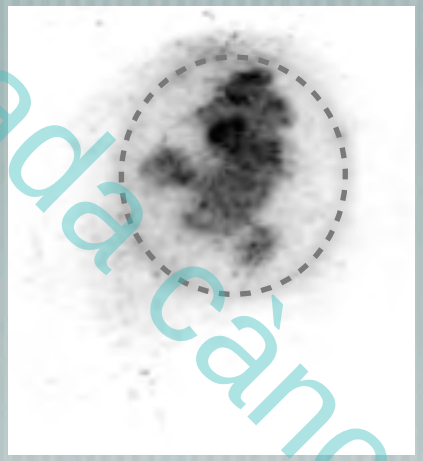
LESIONES RESISTENTES

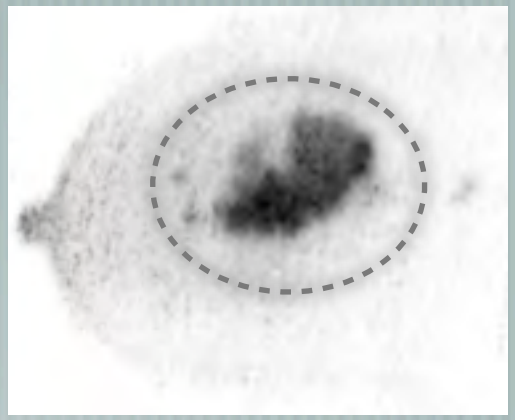
Personalización en MN



Personalización en MN

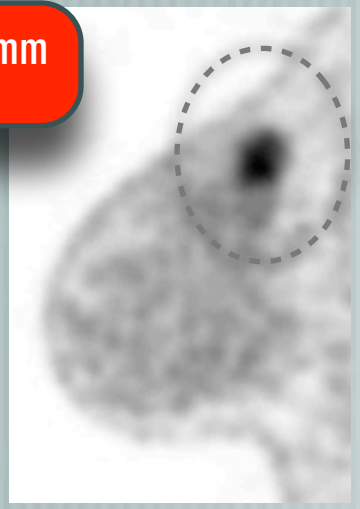
MAMMI

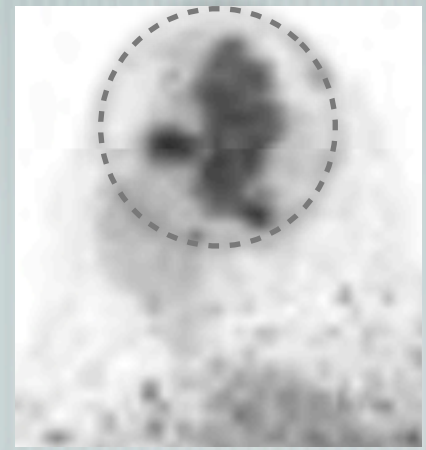


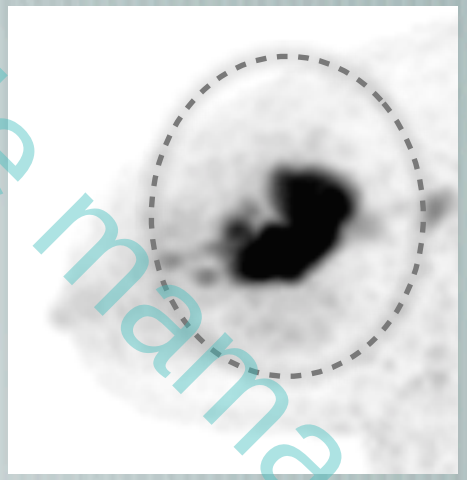


LESIONES HETEROGENEAS

PET/CT 2mm







Personalización en MN

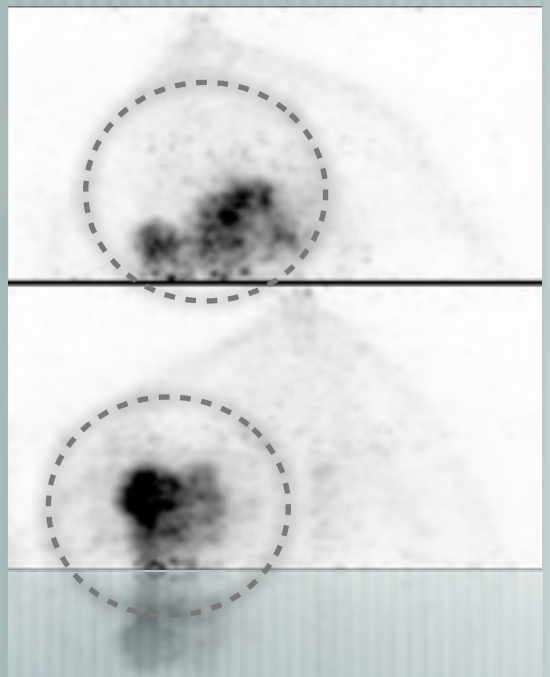
ORIGINAL ARTICLE

Intratumor Heterogeneity and Branched Evolution Revealed by Multiregion Sequencing

Marco Gerlinger, M.D., Andrew J. Rowan, B.Sc., Stuart Horswell, M.Math., James Larkin, M.D., Ph.D., David

The NEW ENGLAND JOURNAL of MEDICINE

BIOPSIAS MULTIPLES



Sci Transl Med 28 March 2012:
Vol. 4, Issue 127, p. 127ps10
Sci. Transl. Med. DOI: 10.1126/scitranslmed.3003854

PERSPECTIVE

TUMOR HETEROGENEITY

Intratumor Heterogeneity: Seeing the Wood for the Trees

Timothy A. Yap[1*], Marco Gerlinger[2,3*], P. Andrew Futreal[4], Lajos P

Fig. 1. A trunk-branch model of intratumor hetero

Personalización en MN

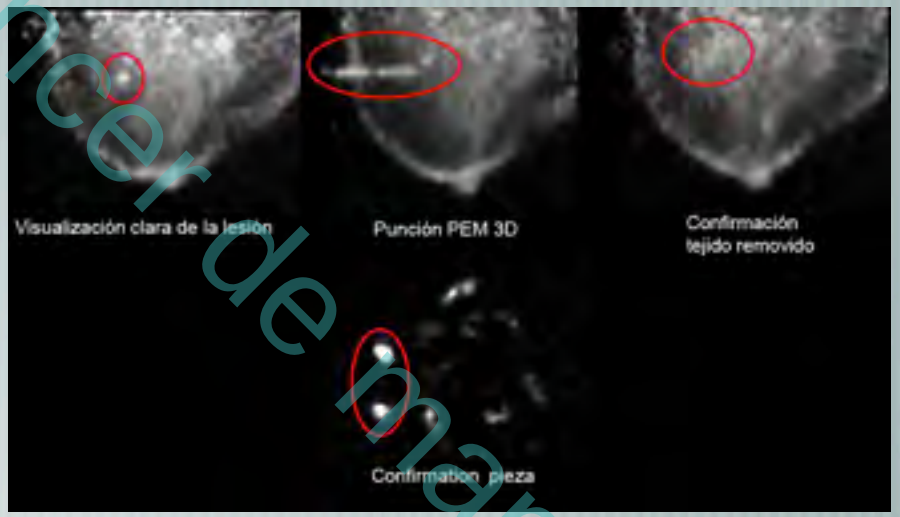
INDICACIONES CLINICAS PEM

MAMOGRAFIA NO CONCLUSIVA
MAMAS DENSAS
CIRUGIA PREVIA REDUCTIVA DE MAMA
TUMORES OCULTOS
RESPUESTA TERAPEUTICA TUMOR PRIMARIO

CARACTERIZACION TUMOR (SUVmax)
BIOPSIA GUIADA POR FDG

Personalización en MN

Biopsia guiada por FDG



Personalización en MN

N = 19

24 biopsias

370 MBq ^{18}F-FDG

Tamaño Lesiones

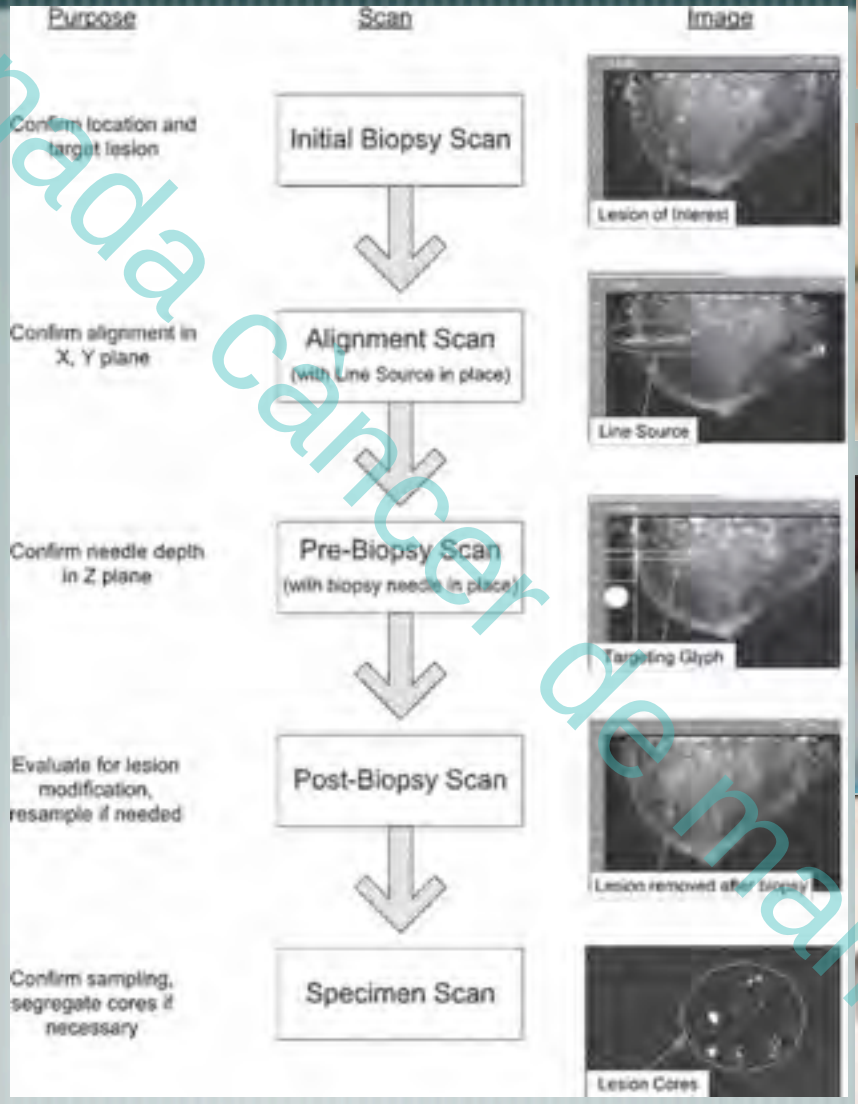
3mm - 55mm

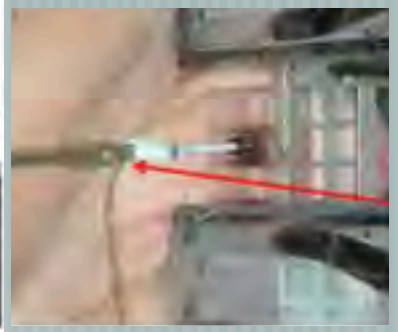
(mediana 7,5mm)

Tiempo Biopsia

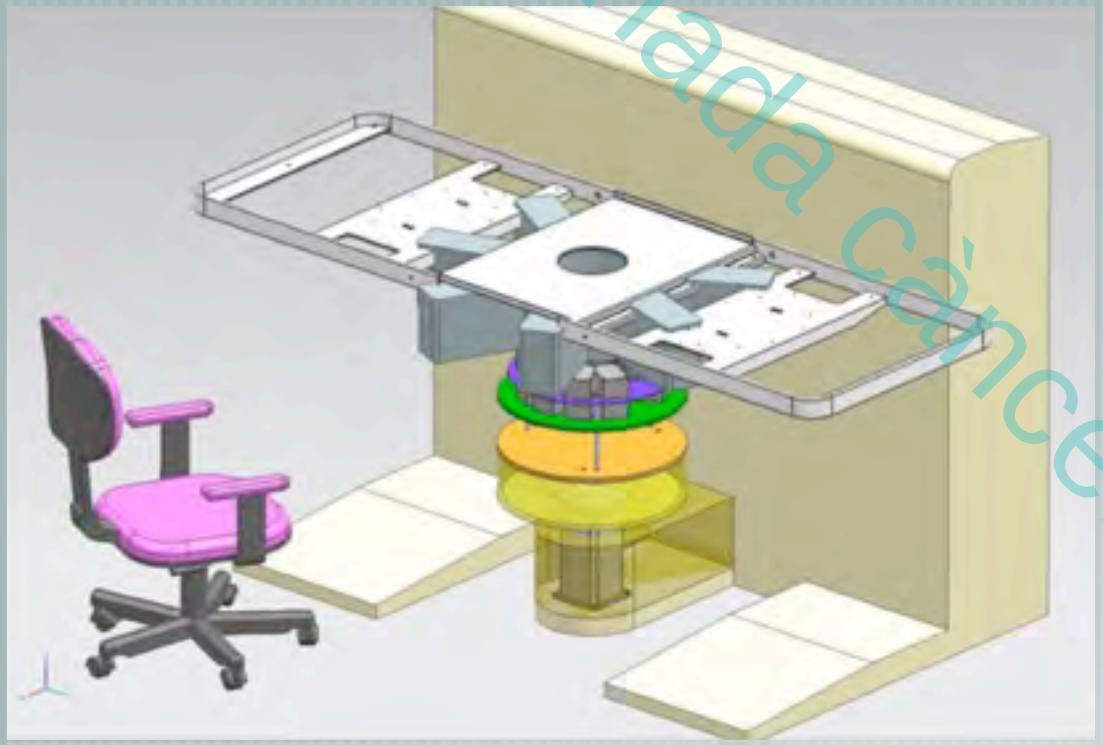
19-119 min

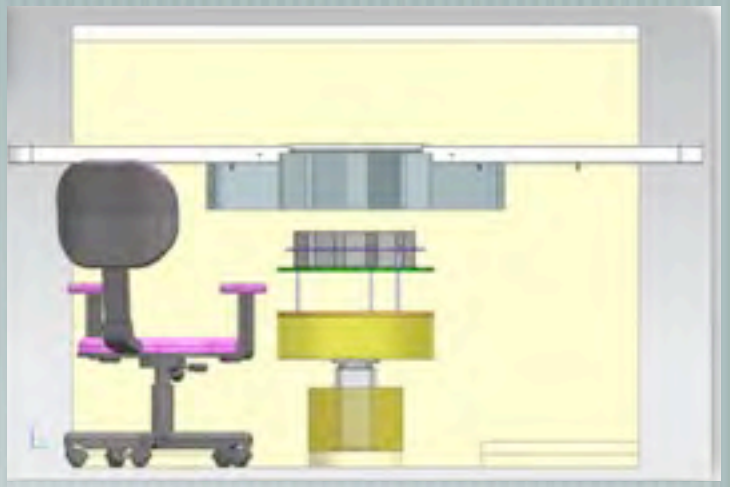
Kalinyak JE et al. Breast J 2011; 2:143-51

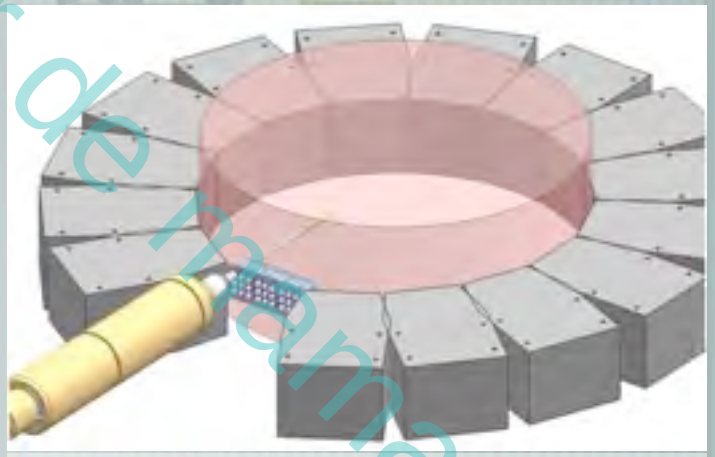




Personalización en MN

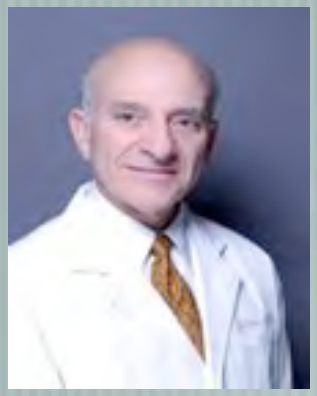






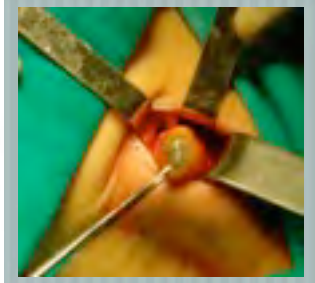
Personalización en MN

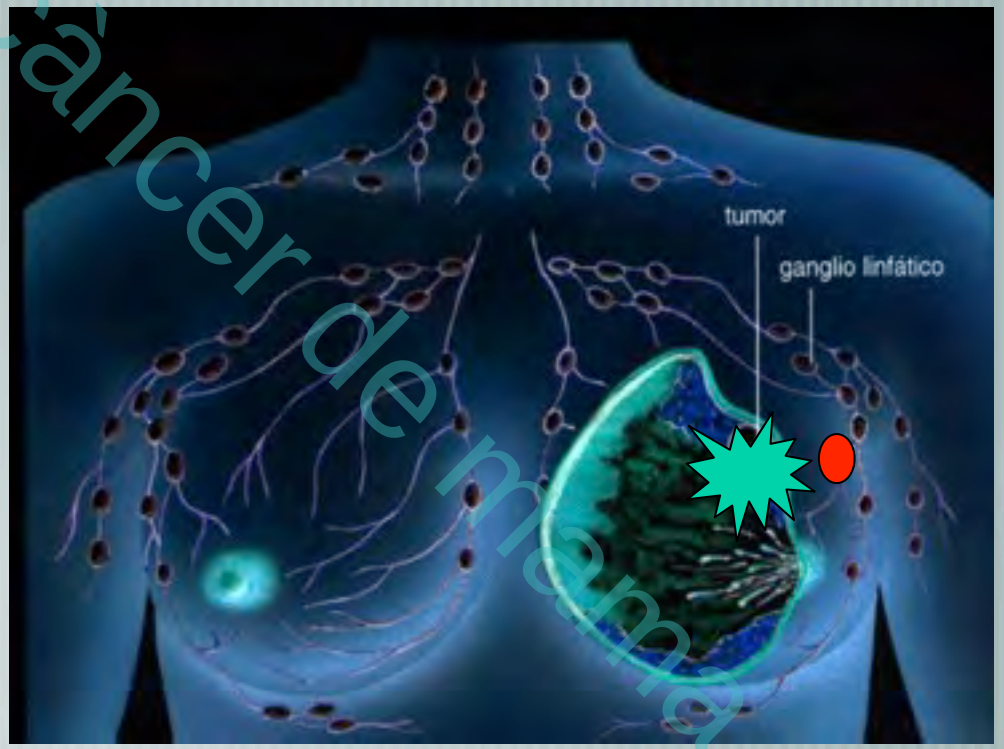
1994



JOHN WAYNE CANCER INSTITUTE
at Saint John's Health Center

Lymphatic Mapping and Sentinel Lymphadenectomy for Breast Cancer

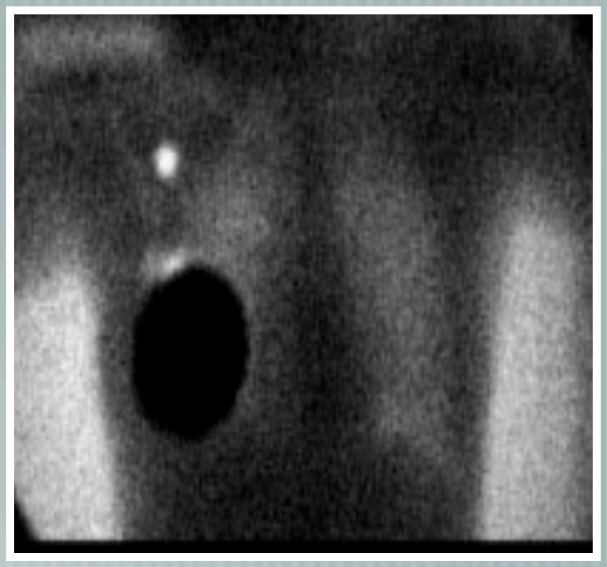




El **GANGLIO CENTINELA**
será la primera adenopatía
invadida en caso de
diseminación metastática
por vía linfática

Personalización en MN

GANGLIO CENTINELA

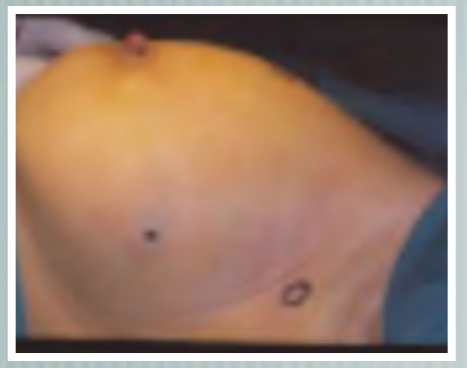


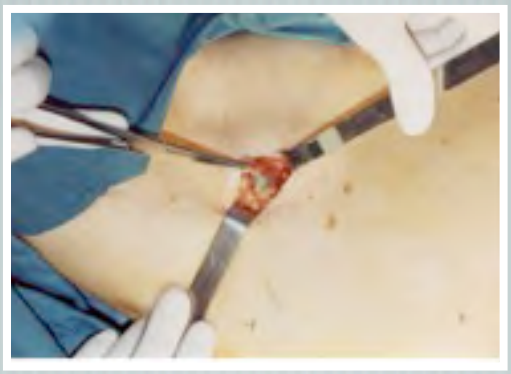
Ventajas

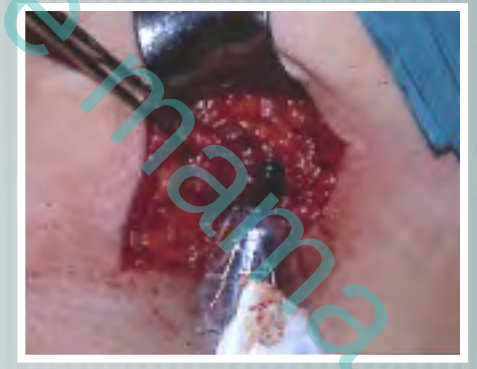
Procedimiento sencillo y económico
Morbilidad mínima
VP del resto de los GL > 95%
Permite ahorrar linfadenectomías innecesarias

Inconvenientes

No detección del GS en 2-10% de los casos
Falsos negativos (5%)







Personalización en MN

Personalización en MN

Características de la paciente

Edad
IMC
Cirugía previa

Características del tumor

Unifocal
Multicéntrico
Microcalcificaciones
Palpable/No palpable

Personalización en MN

Propósito de la linfogammagrafía

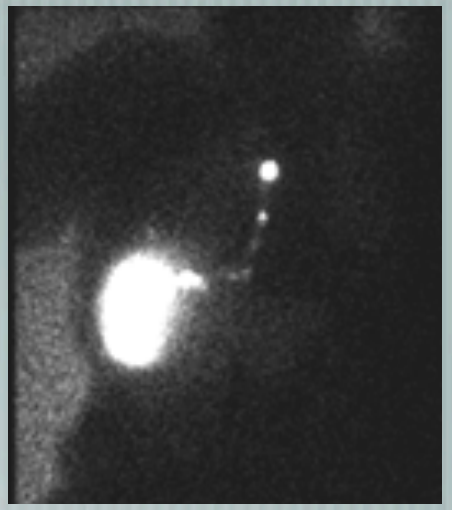
Indicar el área linfática de drenaje

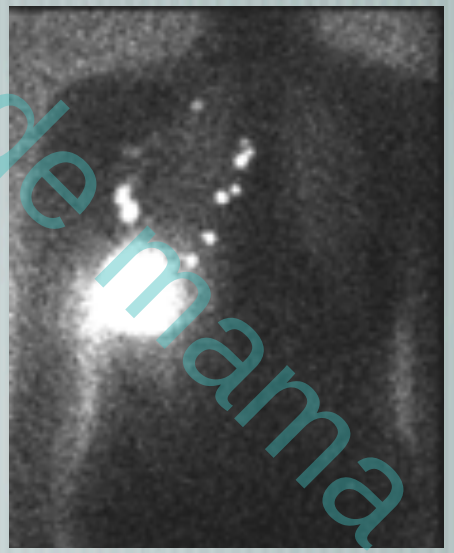
Determinar el número de GC

Diferenciar los GC de los secundarios

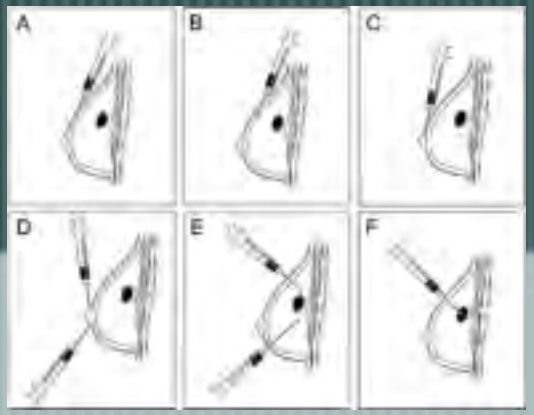
Localizar los GC aberrantes

Marcar la localización de los GC





Personalización en MN



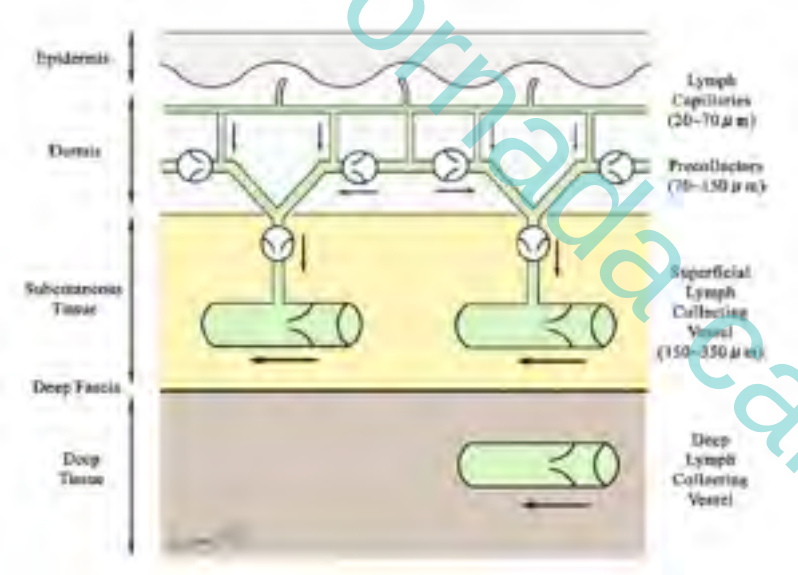
Método inyección

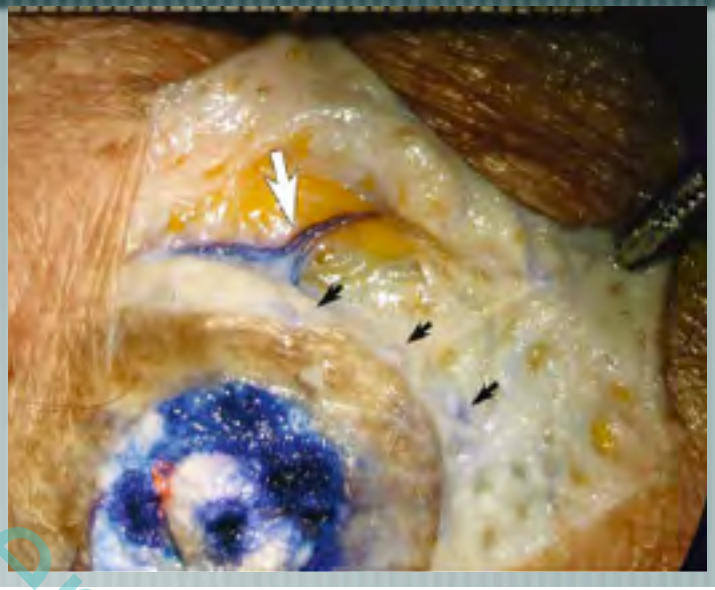
Región	Peritumoral	Intradérmica/ Subdérmica	Periareolar/ Subareolar	Intratumoral
Axila	92.0% (rango, 86%-100%)	96.4% (rango, 93%-100%)	98.4% (rango, 94.2%-100%)	92.0% (rango, 88%-96%)
Mamaria interna	4.9% (rango, 0%-25.3%)	0.6% (rango, 0%-4%)	0%	18.4% (rango, 13%-43%)
Otras	0.6% (rango, 0%-8.4%)	0%	0%	4.3% (rango, 0%-33.1%)

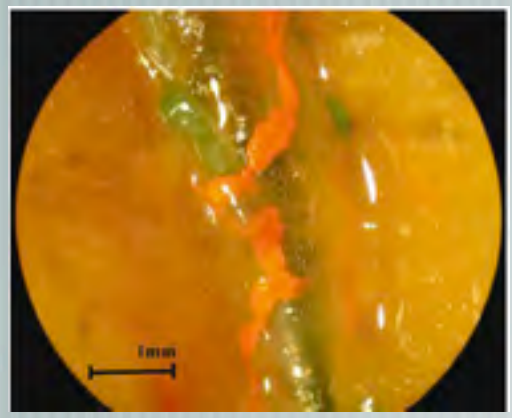
Harlow et al. ACS Surgery 2005

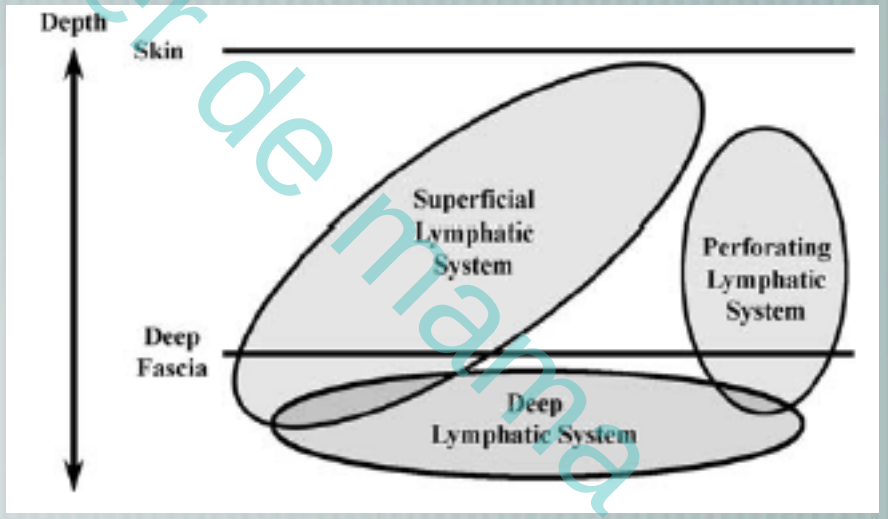
Ortega M et al. Rev Esp Med Nucl 2004; 23: 153-161

Personalización en MN







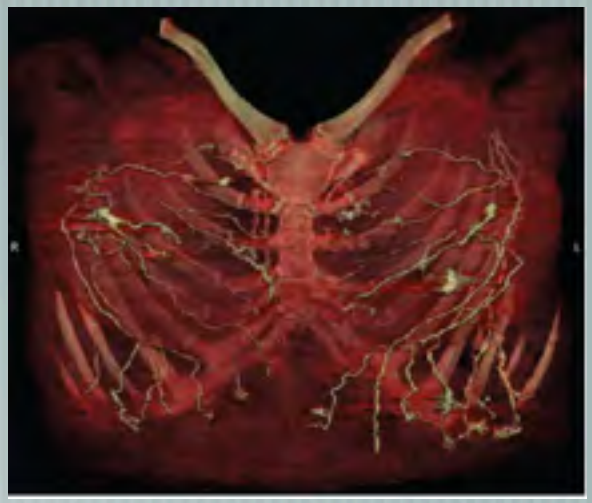


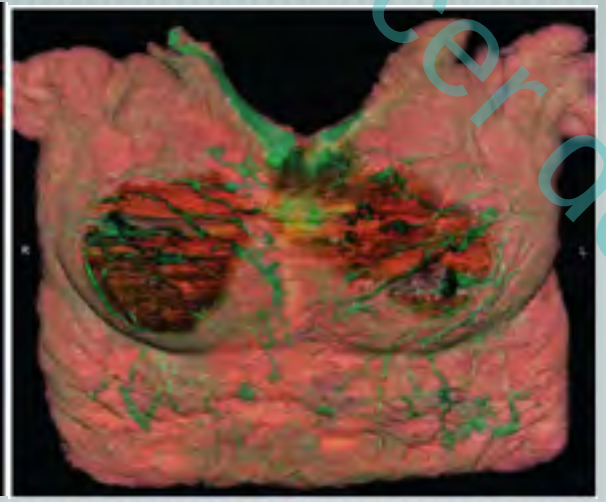
Suami H et al. Ann Surg Oncol 2008; 15: 863-871

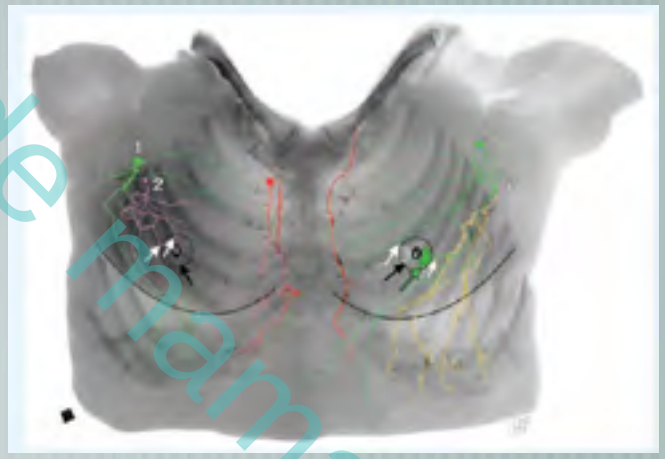
Personalización en MN

SISTEMA LINFATICO MAMARIO

Patrón de drenaje radial hacia los ganglios axilares
Predominio de los linfáticos superficiales
Patrones asimétricos entre las mamas



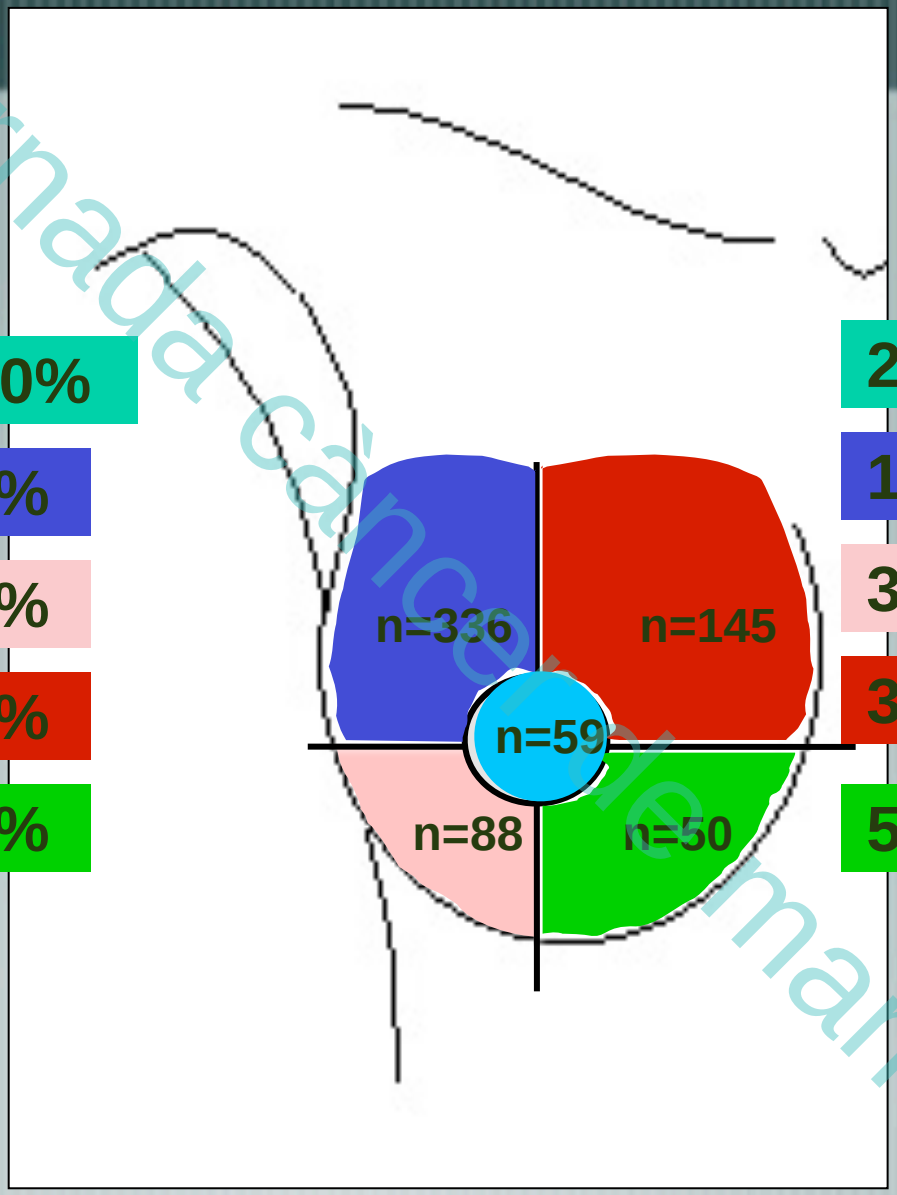




Pan et al. Clin Breast Cancer 2009; 9: 86-91

Personalización en MN

Drenaje Tumoral



DRENAJE AXILAR

DRENAJE MAMARIA INTERNA

Estourgie S et al.

Ann Surg 2004; 239:232-237

Personalización en MN

LINFOGAMMAGRAFIA

↓

IDENTIFICA LOS GANGLIOS CENTINELAS

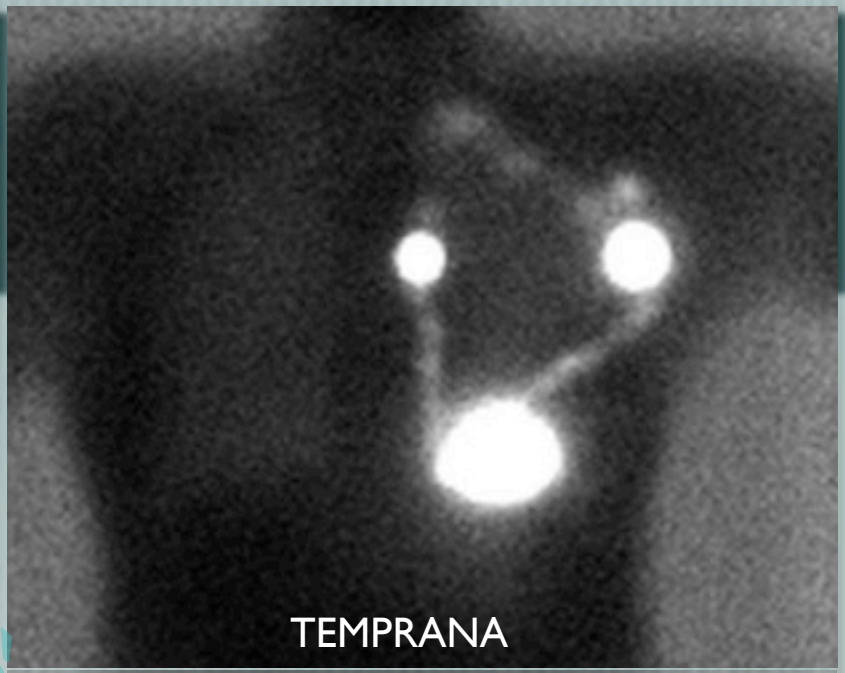
↓

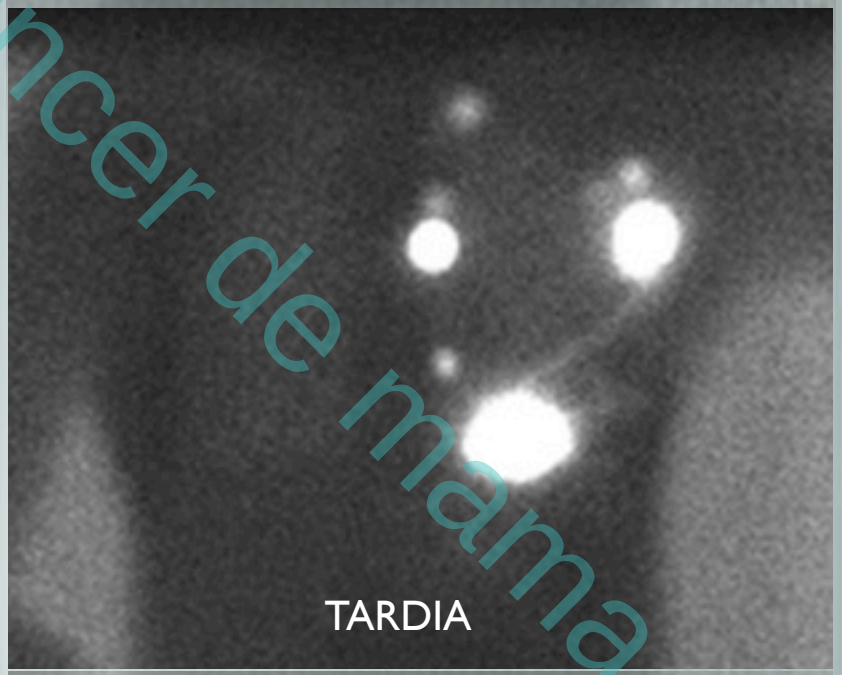
IMAGEN SECUENCIAL

↓

CRITERIOS
VISUALIZACION VIAS LINFATICAS
TIEMPO DE APARICION
GRUPO GANGLIONAR
INTENSIDAD CAPTACION

CATEGORIAS





Personalización en MN

CRITERIOS
VISUALIZACION VIAS LINFATICAS
TIEMPO DE APARICION
GRUPO GANGLIONAR
INTENSIDAD CAPTACION

↓

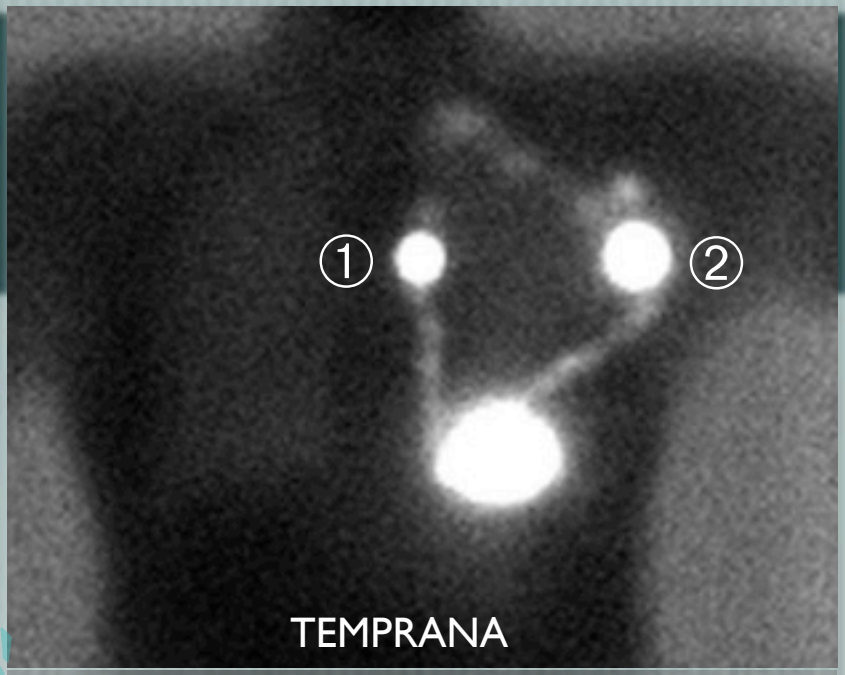
CATEGORIAS

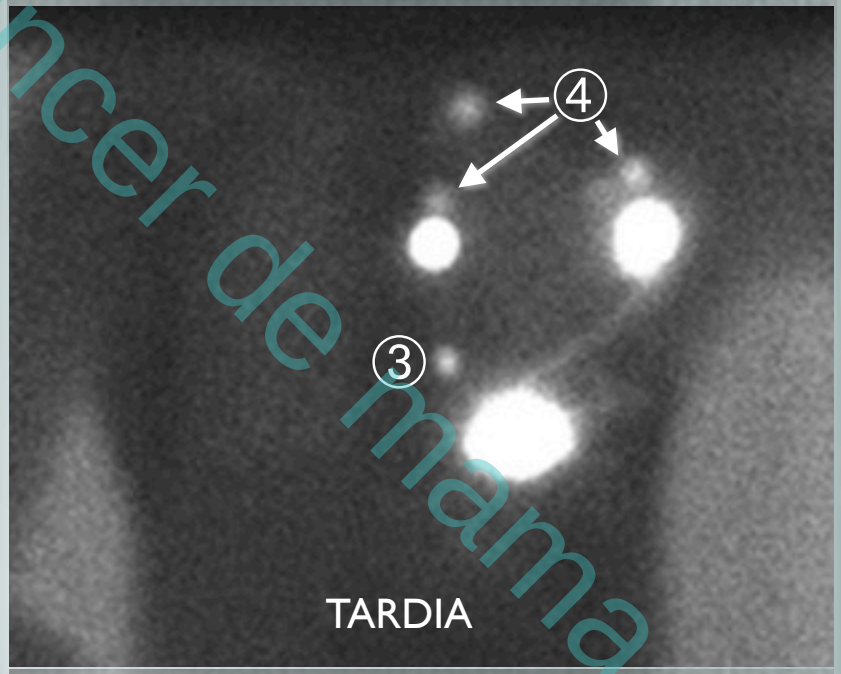
↓

DEFINITIVAMENTE GC
VIA LINFATICA PROPIA DIRECTA
GANGLIO UNICO APARICION PRECOZ-TARDIA

ALTA PROBABILIDAD GC
GANGLIO NO UNICO APARECIENDO ENTRE SITIO INYECCION Y GC
GANGLIO NO UNICO CAPTACION CRECIENTE

BAJA PROBABILIDAD GC
GANGLIOS SUBSECUENTES DE MENOR CAPTACION





Personalización en MN

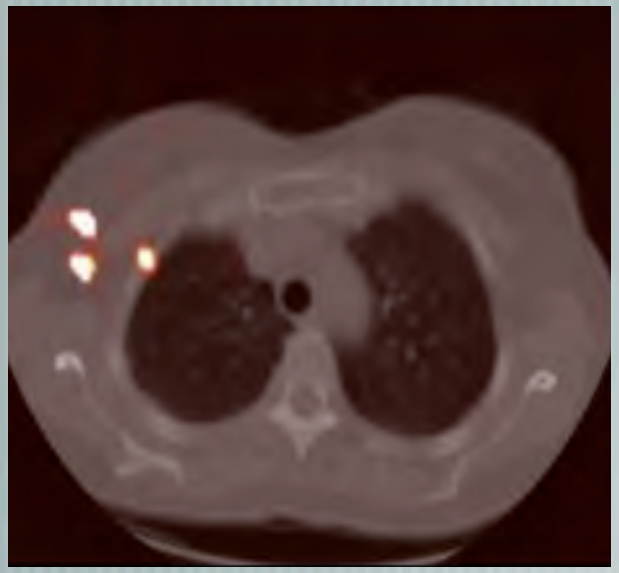
Linfogammagrafía

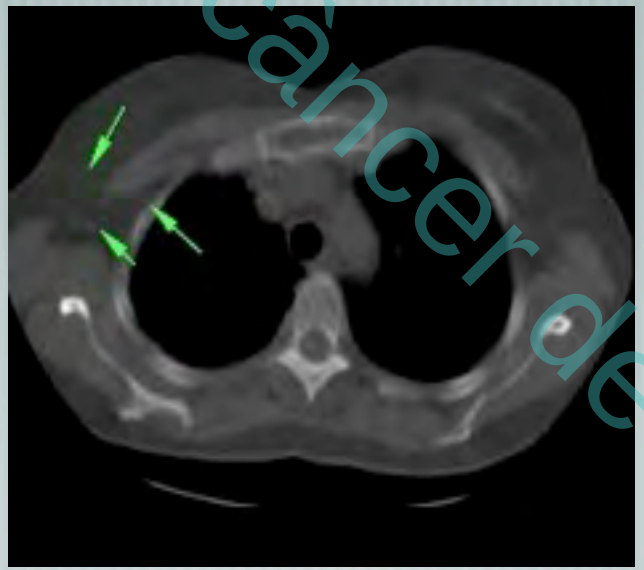
Identifica los GCs

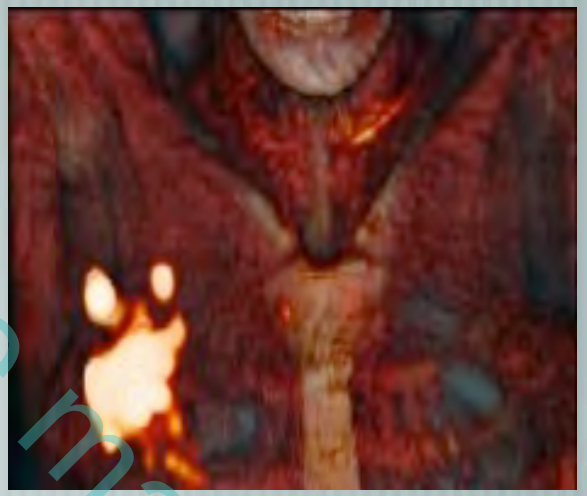
SPECT-CT

Situación anatómica GC

No sustituye a la linfogammagrafía

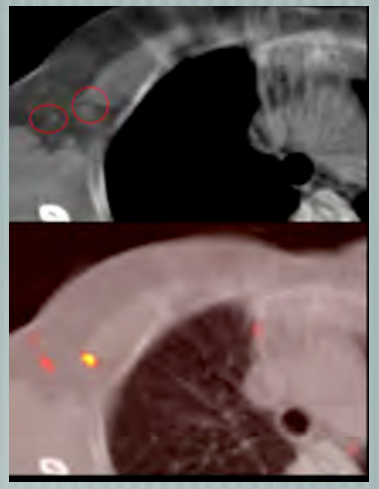






Personalización en MN

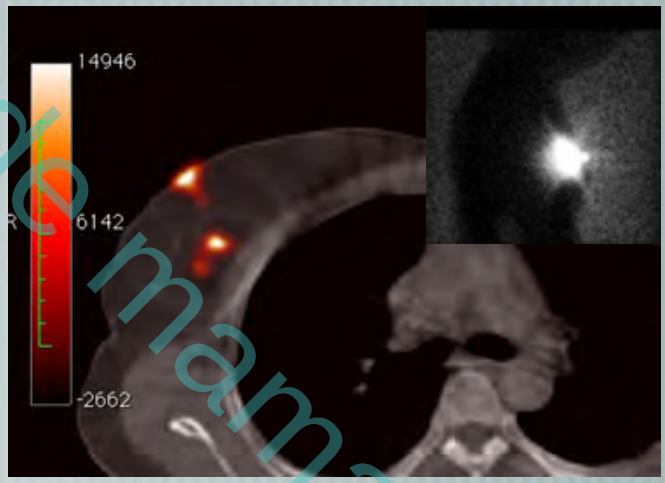
Indicaciones de la SPECT/CT



Patrones de drenaje no habitual

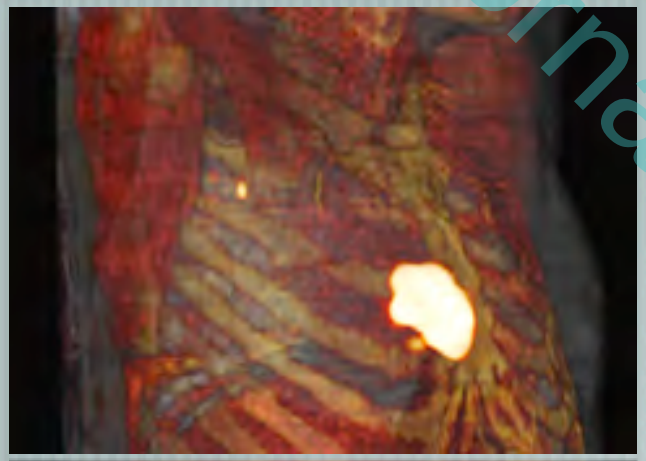
Dificultades en la interpretación de las imágenes planares
- Escasa actividad
- GC cerca de zona inyección
- Ganglios profundos

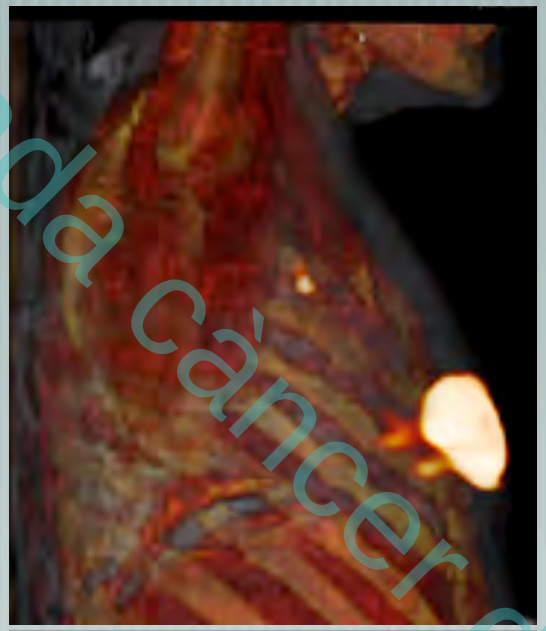
Ausencia de visualización en las imágenes planares

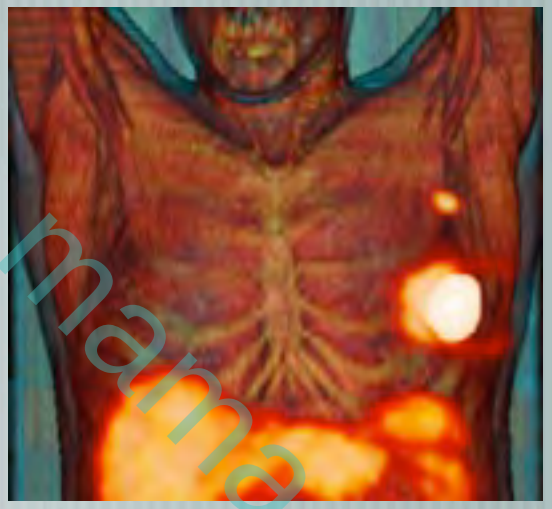


Husarik D et al. Semin Nucl Med 2007; 37: 29-33
Van der Ploeg IM et al. J Nucl Med 2007; 48: 1756-1760
Mucientes J et al. Rev Esp Med Nucl 2008; 27: 183-190
Van der Ploeg IM et al. Ann Surg Oncol 2009; 16: 1537-1542

Personalización en MN







SPECT-CT

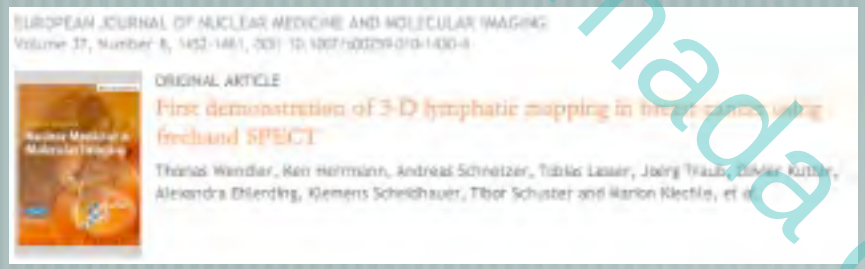
Información adicional para la cirugía

42% (48/134)

19 GC adicionales
4 GC (+)

Van der Ploeg IM et al. Eur J Nucl Med Mol Imaging 2009; 36:903-09

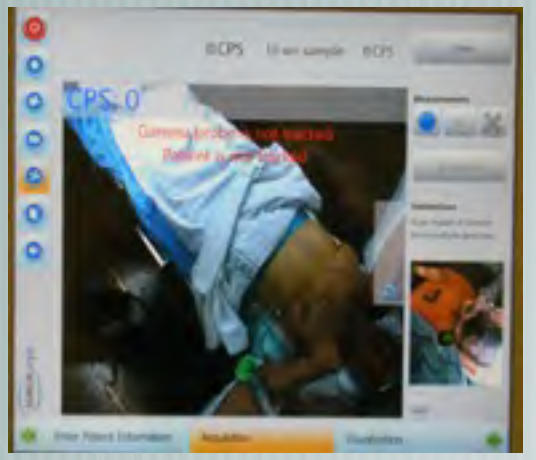
Personalización en MN

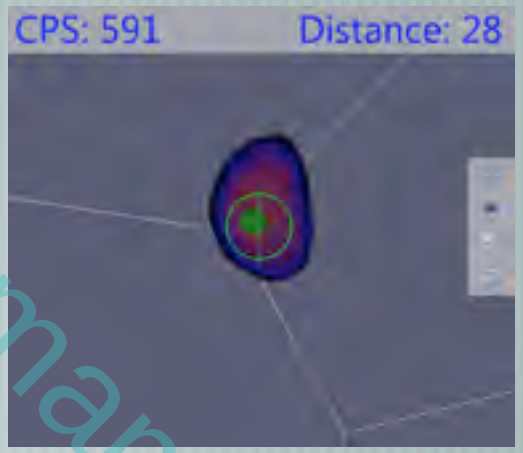

EUROPEAN JOURNAL OF NUCLEAR MEDICINE AND MOLECULAR IMAGING

ORIGINAL ARTICLE

First demonstration of 3-D lymphatic mapping in breast cancer using freehand SPECT

Thomas Wendler, Ken Herrmann, Andreas Schnelzer, Tobias Lasser, Joerg Traub, Didier Kutter, Alexandra Ehlerding, Klemens Scheidhauer, Tibor Schuster and Marion Kiechle, et al.





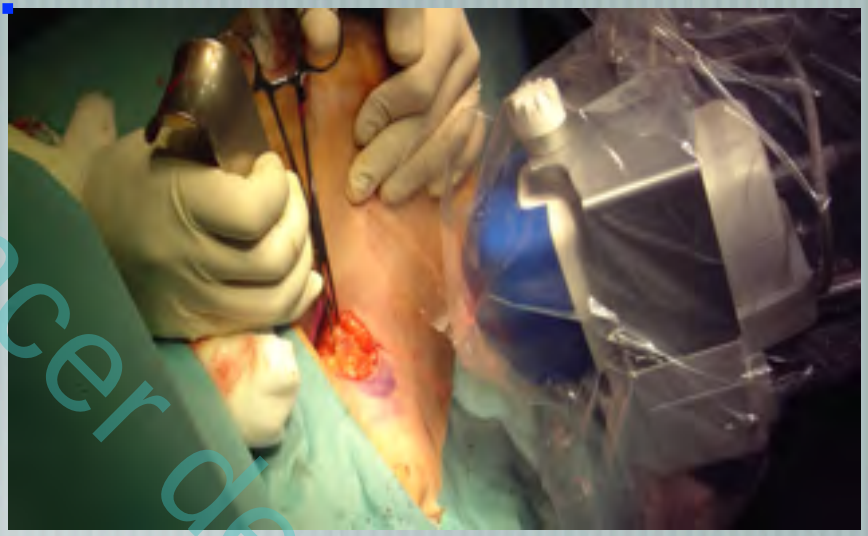
Personalización en MN

Imagen intraoperatoria

Re-evaluación de la incisión al adaptarla a la posición quirúrgica

Localización

Control post-exéresis GC



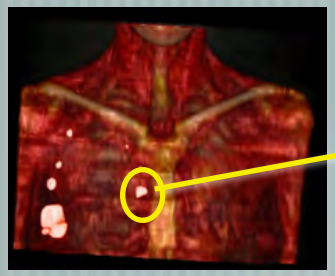
Personalización en MN

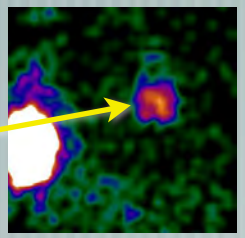
Imagen intraoperatoria

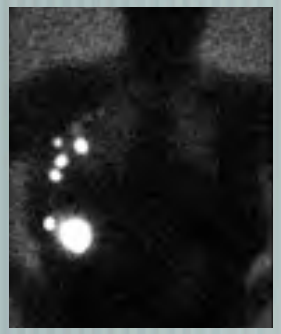
Added Value of Intraoperative Real-Time Imaging in Searches for Difficult-to-Locate Sentinel Nodes

Sergi Vidal-Sicart[1,2], Pilar Paredes[1], Gabriel Zanzi[3], Jaume Pahisa[1,2], Sergio Martínez-Rolán[1], Xavier Cigarini[3], Antoni Vilalta[4], Ramón Rull[5], and Francesca Puig[1,2]

[1]Nuclear Medicine Department (CDIC), Hospital Clínic Barcelona, Barcelona, Spain; [2]Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Hospital Clínic Barcelona, Barcelona, Spain; [3]Gynecology Department (CEIEN), Hospital Clínic Barcelona, Barcelona, Spain; [4]Dermatology Department (CMM), Hospital Clínic Barcelona, Barcelona, Spain; and [5]Surgery Department (CMM), Hospital Clínic Barcelona, Barcelona, Spain







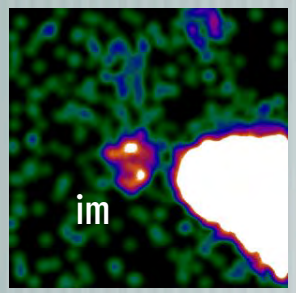


TABLE 1. Patient Characteristics and Results

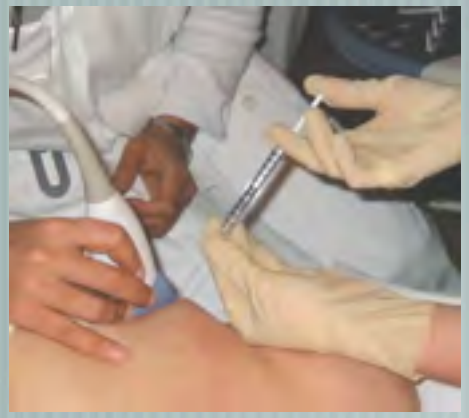
Patient no.	Age (y)	Location	Drainage	SN harvested	Time (min)*	Pathology
Melanoma						
1	50	Parietal	Occipital/retro-SCM	2 occipital, 1 retro-SCM	10	Negative
2	45	Right lower limb	Popliteal/inguinal	1 popliteal, 1 inguinal	6	Inguinal positive
3	71	Nose	Submandibular	2 left submandibular, 2 right submandibular	10	Negative
4	36	Frontal	Parotid	2 parotid, 1 preauricular, 1 SCM	10	Negative
5	65	Facial	Submandibular	1 submandibular	5	Negative
Breast cancer						
6	43	Right upper outer	AX/IM	1 AX, 1 IM	10	IM positive
7	66	Left central lower	AX/IMC	1 AX, 1 IMC	10	Negative
8	47	Right upper inner	AX/IMC	2 AX, 2 IMC	20	Negative
9	63	Left upper innner	AX/IM	1 AX, 1 IM	7	AX positive
10	47	Right upper inner	AX/IMC	1 AX, 1 IMC	12	Negative
11	53	Left upper inner	IMC	1 IMC	10	Negative
12	52	Right lower outer	AX/IMC	2 AX, 1 IMC	10	Negative
13	49	Left central inner	AX	2 AX	7	AX positive†
14	56	Left upper inner	AX/IMC	2 AX, 2 IMC	14	Negative
Gynecologic						
15	43	Cervix	Left pelvic	1 external iliac	4	Negative
16	33	Cervix	Bilateral pelvic	1 right hypogastric, 1 left external iliac	7	Negative
17	69	Endometrium	Right pelvic	1 obturator, 1 iliac	10	Obturator positive
18	37	Cervix	Right pelvic	1 obturator, 1 parametrial	10	Obturator positive
19	66	Vulva (labia majora)	Bilateral inguinal	2 right inguinal, 2 left obturator	5	Negative
20	34	Endometrium	Right paraaortic	2 precaval	20	Negative

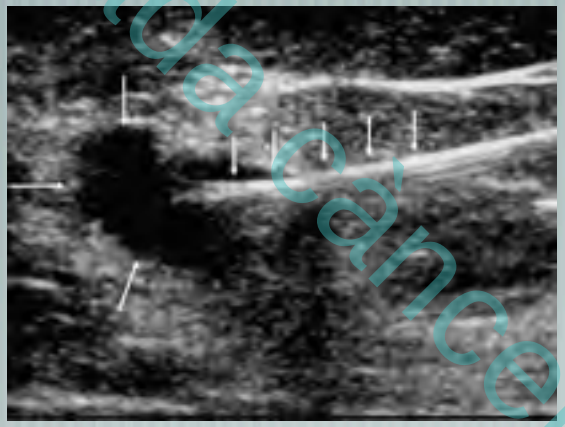
*Time to localize and excise sentinel node with γ-camera and counting probe.
†Only 1 of 2 sentinel nodes was positive.
AX = axilla; SCM = sternocleidomastoid muscle; IM = intramammary; IMC = inner mammary chain; SN = sentinel lymph node

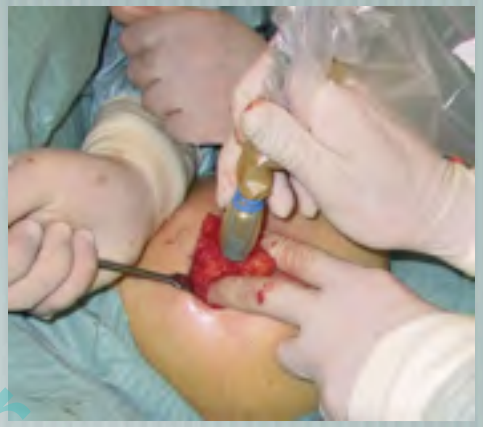
J Nucl Med 2010; 51: 1229-1235

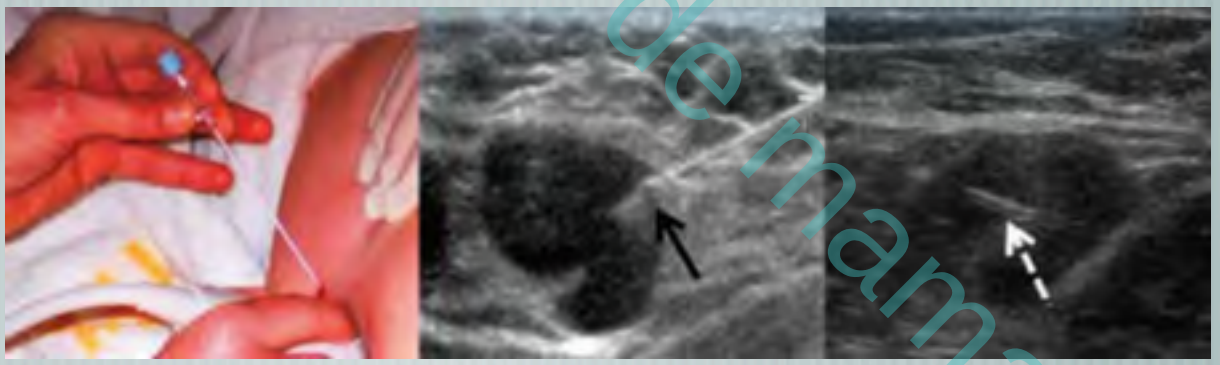
Personalización en MN

ROLL/RSL (lesiones no palpables)









Personalización

Personalización

CONCLUSIONES

La personalización en el cáncer de mama es, desde mi punto de vista, lo que hacemos todos los profesionales implicados día a día.

No sólo por las características clínicas de la paciente, su perfil genético, su tamaño, etc... sino por adaptarnos a "la paciente en sí", puesto que cada una de ellas es diferente y tiene percepciones distintas de su enfermedad

Personalización