



RADIOFÁRMACOS EN CÁNCER DE MAMA

Dr. Química – Javier Giglio

JORNADA DE ACTUALIZACIÓN – 28 de MAYO de
2016

CLASIFICACIÓN DE RADIOFÁRMACOS

- **Radiofármacos SPECT**
- Agentes de perfusión
 - ^{99m}Tc -Sestamibi
 - ^{99m}Tc -Tetrofosmin
- Mecanismos no específicos
 - ^{99m}Tc -MDP
 - ^{99m}Tc -Sulfur Colloid, nanopartículas, etc (ganglio centinela)
- Imagen de receptores
 - ^{131}I - Estradiol (receptor de estrógenos)
 - ^{123}I - Estradiol (receptor de estrógeno)



○ **Radiofármacos PET**

○ Metabolismo de la glucosa

- FDG (2-[18F]Fluoro-2-deoxy-D-glucose)

○ Imágenes de receptores

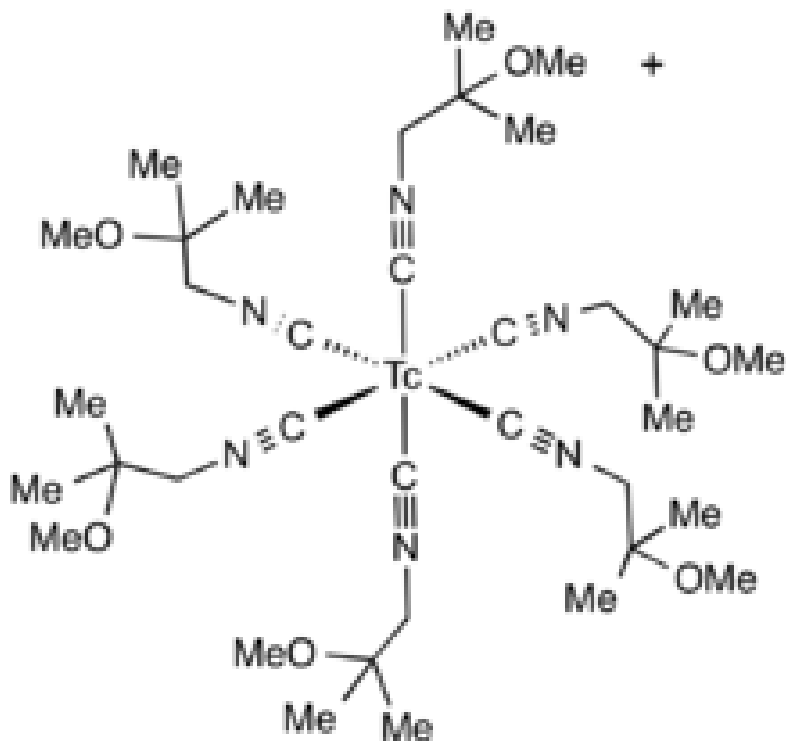
- 2[18F]Fluoro-16 α -ethyl-19-norprogesterone (receptores de progesterona)
- 16 β -[18F]Fluoroestradiol (receptor de estrógeno)

○ Otros

- 18-FLT, etc.

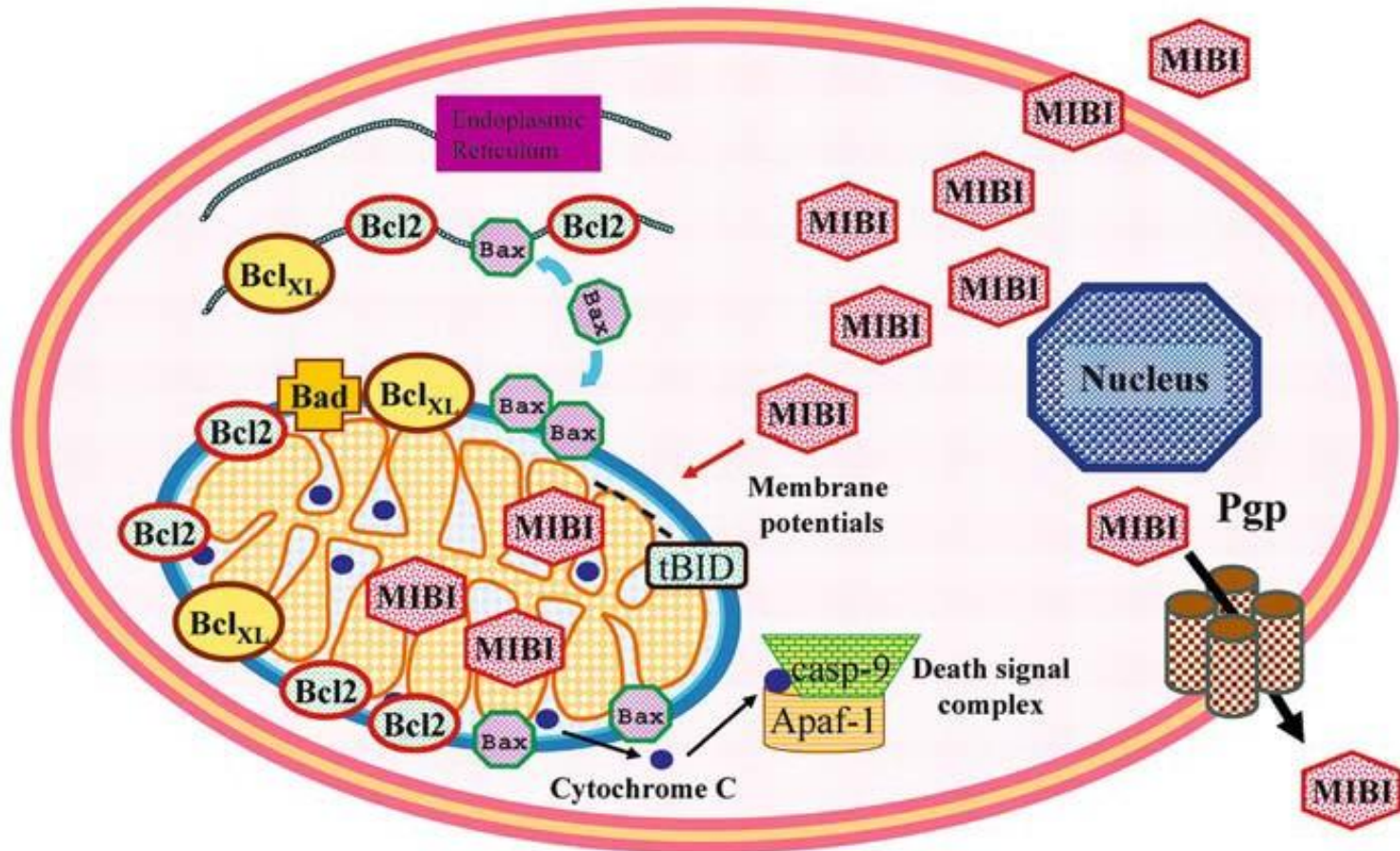


^{99m}Tc -SESTAMIBI



- $^{99m}\text{Tc}(\text{I})$ + 6 ligandos metoxy-isobutilisonitrile
- Introducido a principios de los 90 por Dupont.
- Fue el primer radiofármaco aprobado por la FDA para cancer de mama en junio de 1997.
- No es muy utilizado hoy en día por su baja especificidad frente a otras modalidades diagnósticas como la mamografía.

Mecanismo de captación



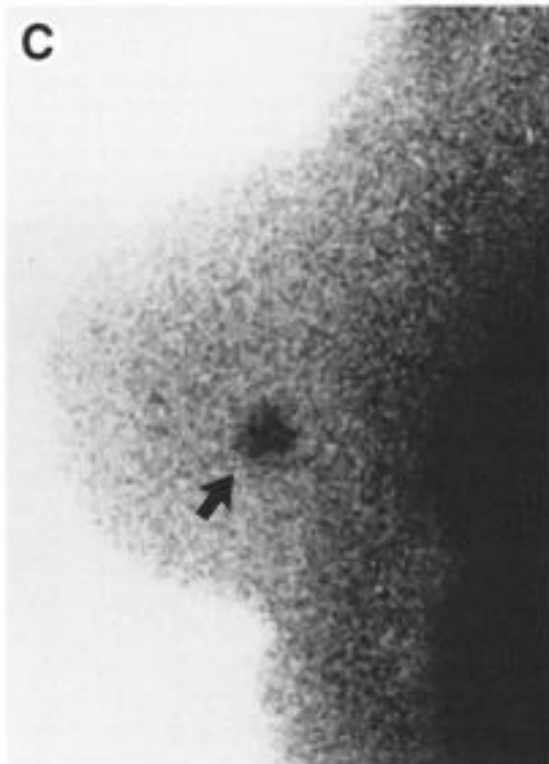
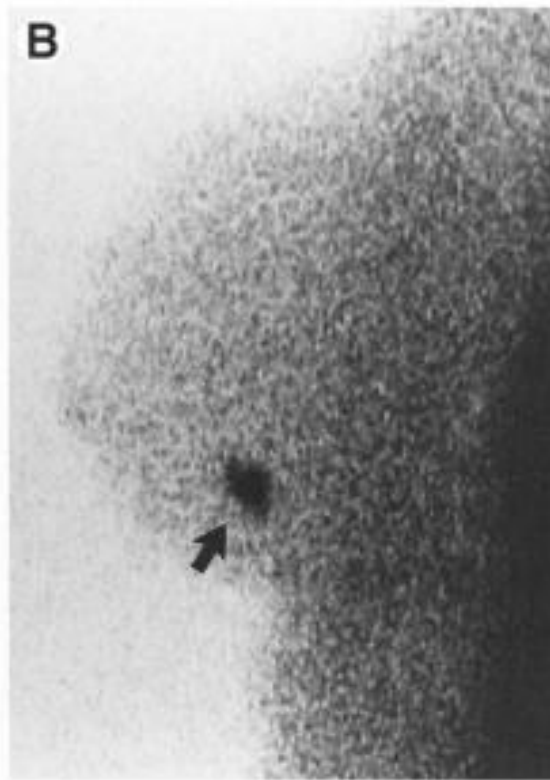
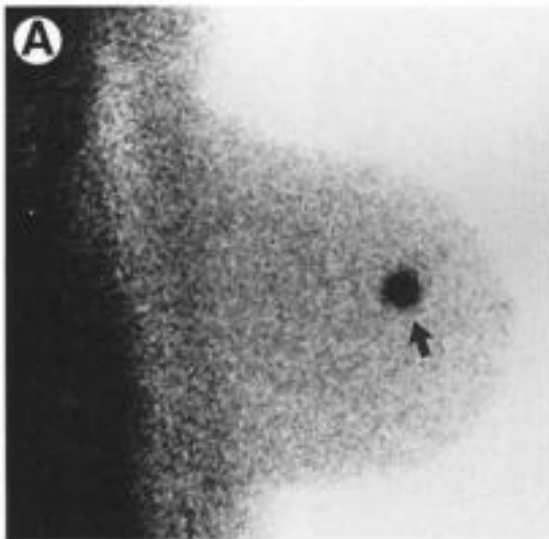
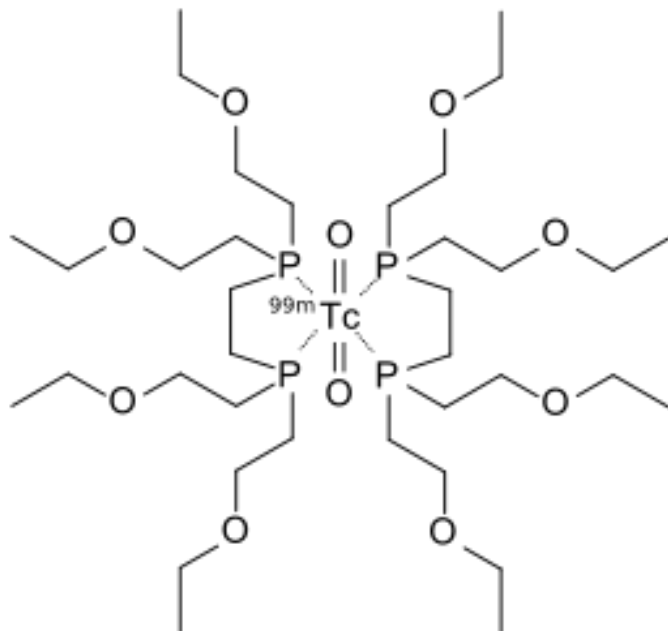


Fig 3. ^{99m}Tc -sestamibi scintimammography in three different patients with primary breast cancers (invasive ductal carcinoma in patients A and B, and invasive lobular carcinoma in patient C) measuring between 1 and 2 cm in diameter (arrows). Contrary to benign disease, the abnormal uptake is more focalized, well-circumscribed, moderate-to-important in intensity, and there is a good target-to-background ratio.

The Role of
 ^{99m}Tc -Sestamibi
 and Other
 Conventional
 Radiopharmaceutic
 als in Breast
 Cancer Diagnosis.
 Raymond Taillefer

^{99m}Tc -Tetrofosmin



- $^{99m}\text{Tc(V)} + 2$ ligandos 1,2-*bis*[di-(2-ethoxietil)fosfino]etano
- Myoview ([GE Healthcare](#))

Technetium-99m-Tetrofosmin as a New Radiopharmaceutical for Myocardial Perfusion Imaging

J. Duncan Kelly, Alan M. Forster, Brian Higley, Colin M. Archer, Fong S. Booker, Lewis R. Canning, K. Wai Chiu, Barbara Edwards, Harjit K. Gill, Mary McPartlin, Katharine R. Nagle, Ian A. Latham, Roger D. Pickett, Anthony E. Storey and Peter M. Webbon

Pharmaceuticals Research and Development, Amersham International plc, Buckinghamshire, United Kingdom; School of Chemistry, University of North London, London, United Kingdom; Department of Medicine, Royal Veterinary College, North Mymms, Hatfield, Hertfordshire, United Kingdom

J NucIMed
1993,34:222



Tc-99m Tetrofosmin Scintimammography for the Detection of Recurrent Breast Cancer in a Patient with Equivocal Mammography Study

[Samir Hussein](#),^{1,*} [Sukhpal Sawhney](#),¹ and [Adil Al-Jarrah](#)²

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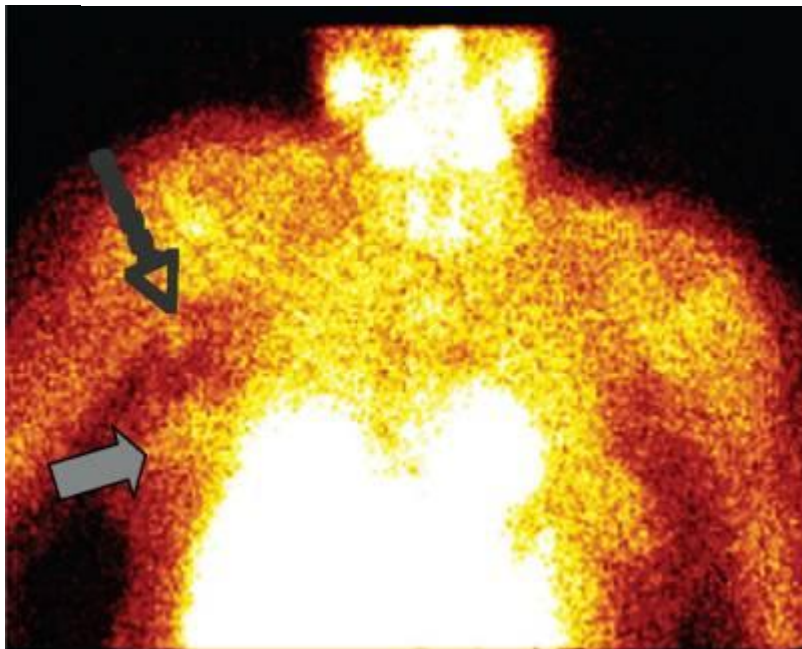
This article has been [cited by](#) other articles in PMC.

Abstract

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This is a case report describing a patient at Sultan Qaboos University Hospital, Oman, with recurrent local breast cancer and axillary lymph node metastasis. The cancer was detected with $^{99}\text{Tc-m}$ tetrofosmin scintimammography after an equivocal mammography study.

Keywords: Breast Scintigraphy, Tc-99m Tetrofosmin, Mammography, Breast Cancer, Case report, Oman



Tc-99m Tetrofosmin showing abnormal uptake in the right breast (grey wide arrow), and abnormal uptake in the right axilla (black dotted arrow)



La utilidad de la mamografía radioisotópica con ^{99m}Tc -tetrofosmin en cáncer de mama cuando la mamografía y el ultrasonido resultan inespecíficos

The usefulness of radioisotopic mammography with TC-99m-tetrofosmin in breast cancer when mammography and ultrasound are not specific

E Estrada-Lobato, RG Meza-Hernández

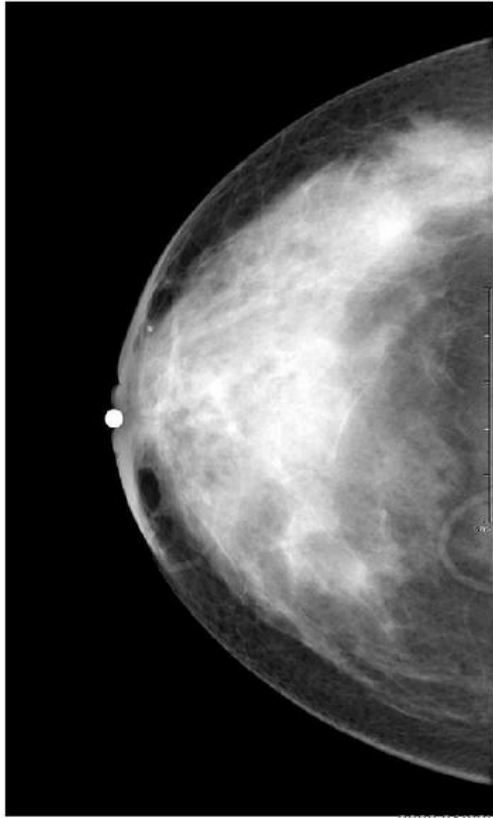
Revista Mexicana de Medicina Nuclear e Imagen Molecular



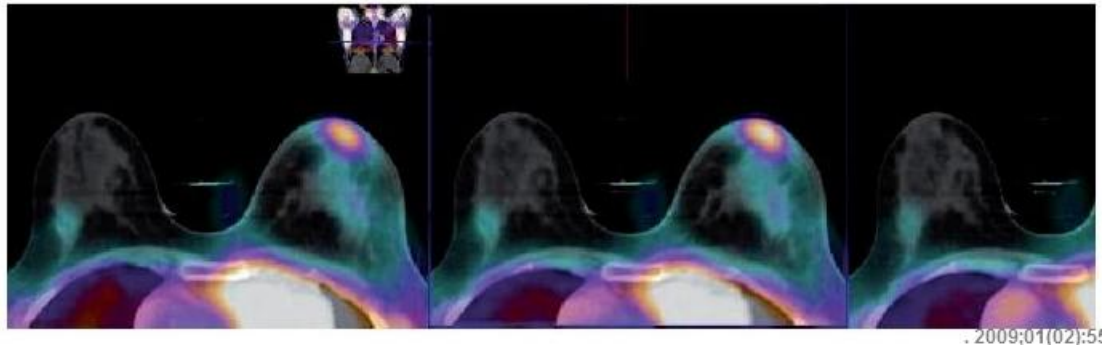
Vol. 01. Núm. 02. Octubre - Diciembre 2009
◀ Documento Anterior - Documento Siguiente ▶

Opciones





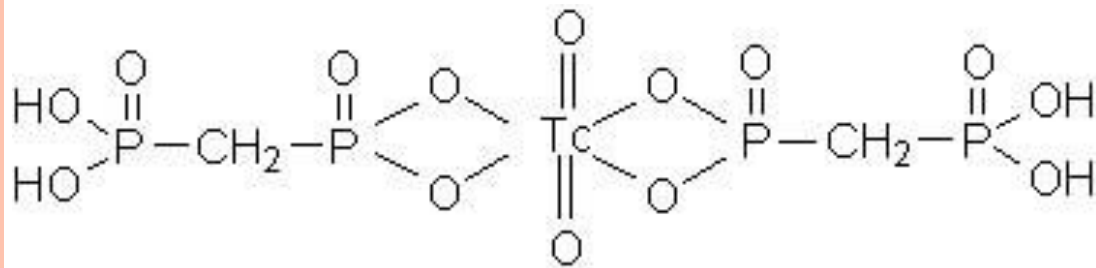
Proyección cráneo-caudal de mama derecha la cual demuestra un patrón glandular denso sin lesiones sospechosas.



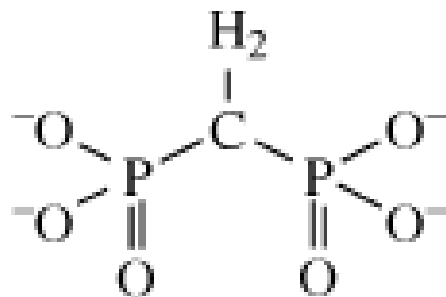
Fusión de imágenes de tomografía computarizada y SPECT con ^{99m}Tc tetrofosmin mostrando la hipercaptación del radiofármaco en tumoración izquierda y la zona sospechosa de captación en mama derecha.



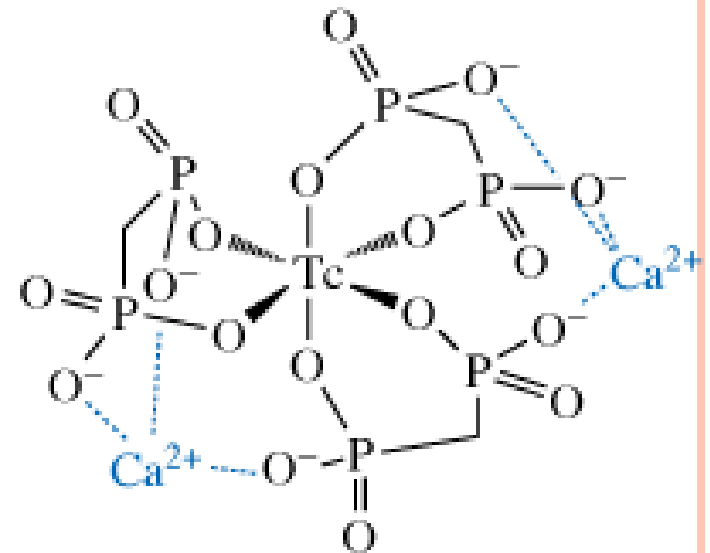
^{99m}Tc -MDP (methylene diphosphonate)



$[^{99m}\text{Tc}]$ Medronate



9.10



9.11

Posible interacción con los iones Ca de la hidroxiapatita de los huesos

- A mediados de 1970, Subramanian et al] introdujo el ^{99m}Tc -MDP como un nuevo radiofármaco para hueso.
- Hay muchos informes que demuestren que varios tipos de cáncer se han detectado concomitantemente a una centellografía ósea con ^{99m}Tc -MDP.

Mecanismo de captación del ^{99m}Tc -MDP

- Varios factores están propuestos como implicados en la captación de ^{99m}Tc -MDP en las células tumorales de los tejidos blandos:
 - Aumento del flujo sanguíneo
 - Aumento del contenido de calcio intracelular
 - Neoangiogénesis
 - Espacio extracelular ampliado
 - cambios en el pH
 - calcificaciones microscópicas, etc



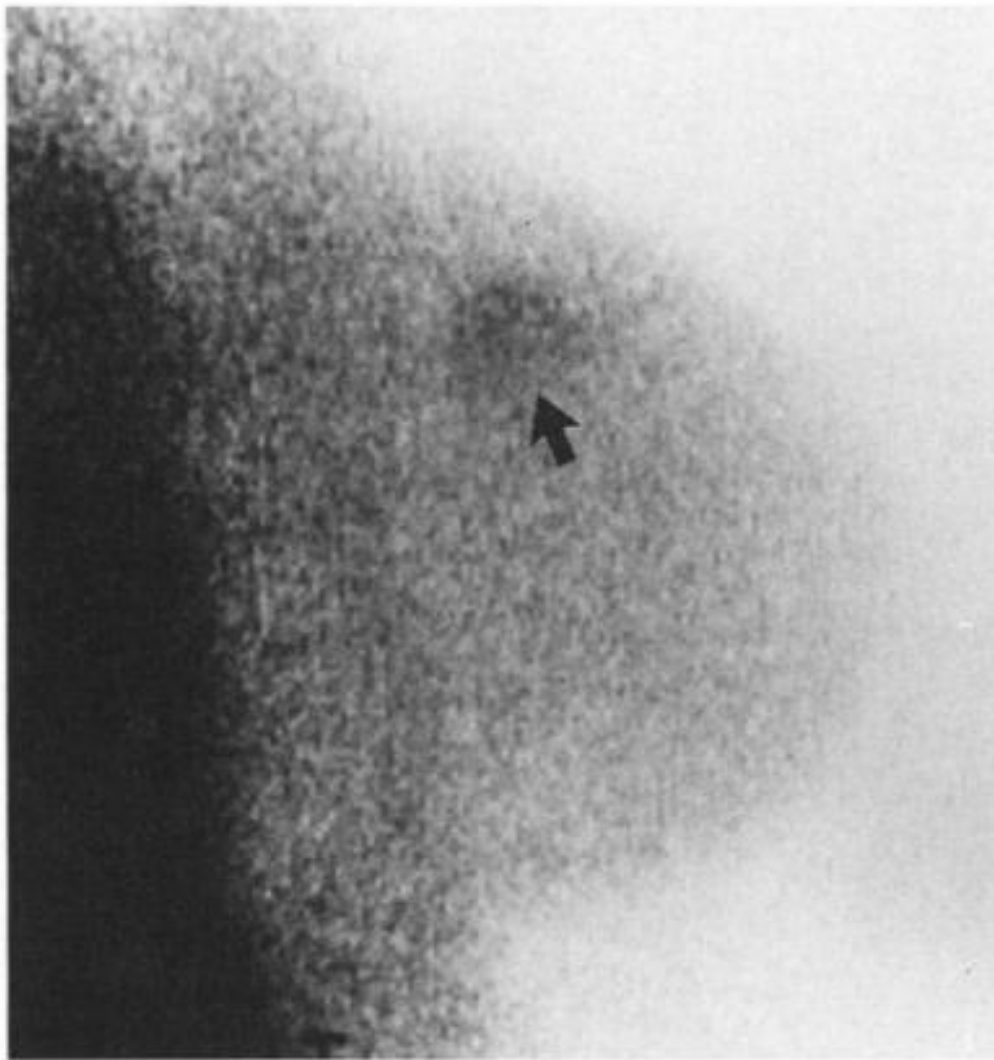


Fig 9. Scintimammography (right lateral prone view) performed 5 minutes after the injection of ^{99m}Tc -Methylenediphosphonate (MDP) in a patient with a primary breast carcinoma measuring 2.5 cm (arrow).



DETECCIÓN DE GANGLIO CENTINELA

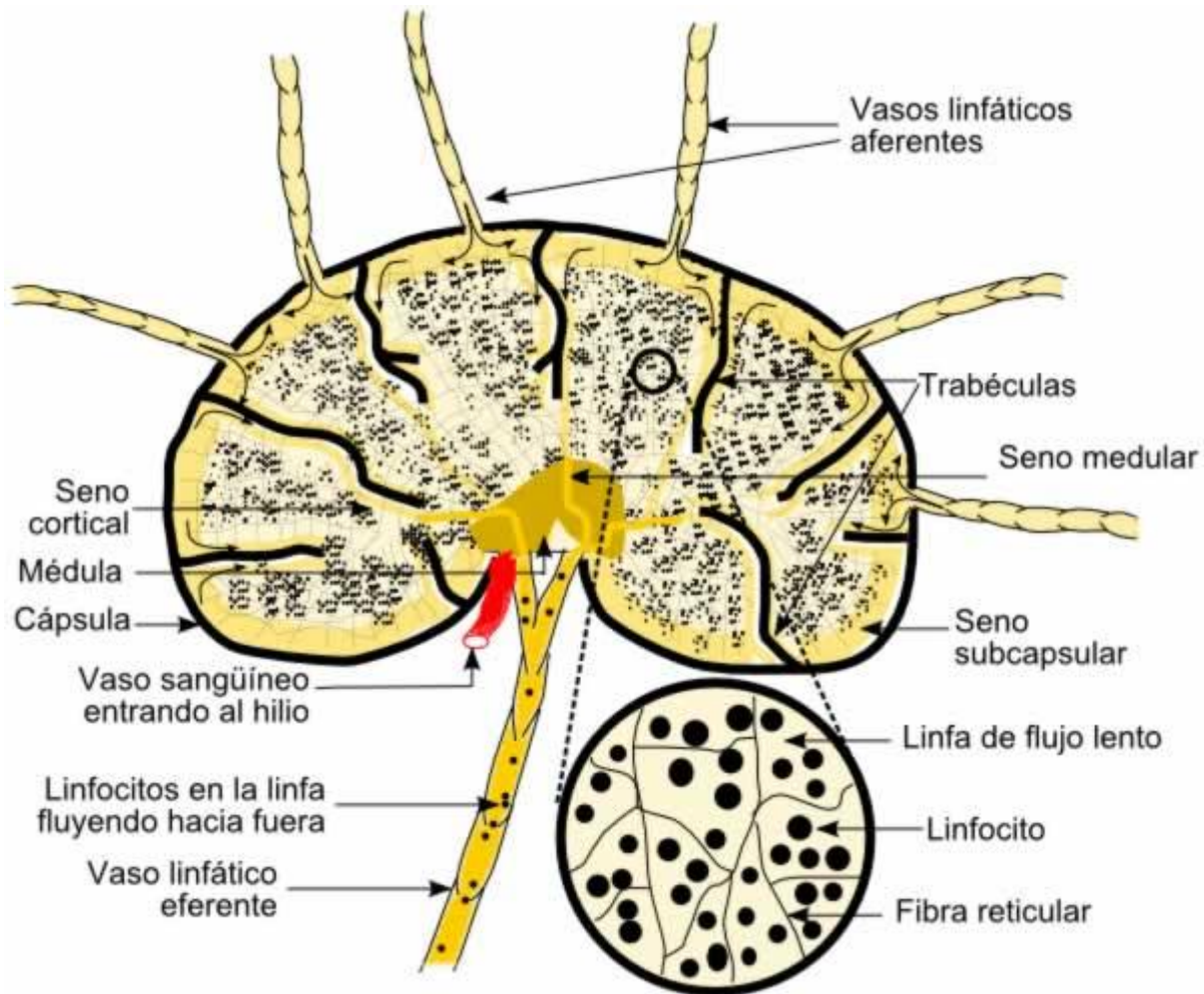
- La localización y biopsia del ganglio representa uno de los avances más importantes en cirugía y ya se han producido importantes cambios en el manejo de pacientes afectados por carcinoma de mama.
- La biopsia del ganglio (ganglio centinela) se aplicó por primera vez en el melanoma por Morton y sus colegas (Morton et al. 1992); inyectando colorante vital azul cerca de la lesión primaria.



Preparaciones de radiofármacos que se emplean comúnmente:

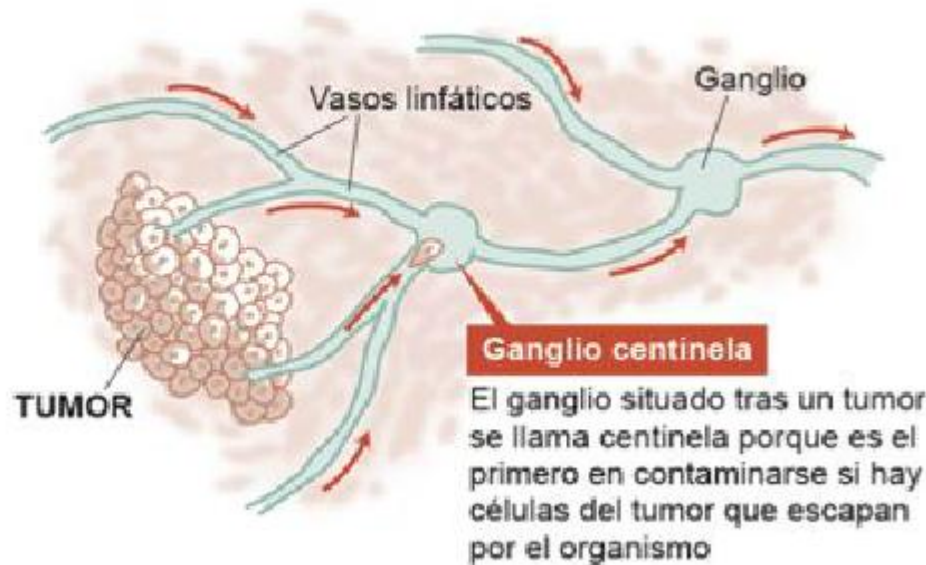
Colloid composition	Size range (nm)	Comments	References
Human serum albumin	7–23 ^a 3–16 ^a	Registered in different countries in Europe; not approved in USA	[2.59, 2.60]
Human serum albumin	100–600 ^b <100 ^b	Registered in different countries in Europe; not approved in USA	Refer to supplier brochures
Stannous/stannic hydroxide	30–200 ^a	Approved in some European countries	[2.60]
Rhenium sulphide	8–68 ^a	Registered in different countries in Europe	[2.61]
Sulphur colloid 0.1 µm filtered sulphur colloid	50–1000 ^c 30–50 ^c	Registered in USA	[2.50, 2.61]
Antimony trisulphide	2–16 ^d 17–23 ^a	Registered in Australia	[2.58]
Calcium phytate	150–200 ^a 150–1500 ^a	Mainly used in Japan; size depends on Ca ²⁺ concentration	[2.62]

Estructura del ganglio linfático



ANÁLISIS DEL GANGLIO CENTINELA

El sistema linfático está formado por una red de vasos y ganglios que drenan y limpian el organismo.

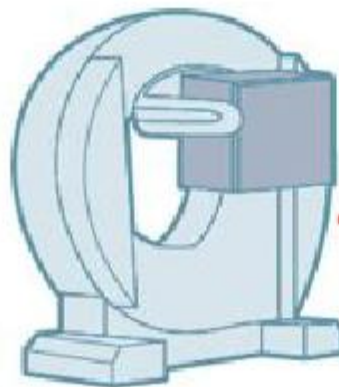


ANÁLISIS DEL GANGLIO CENTINELA

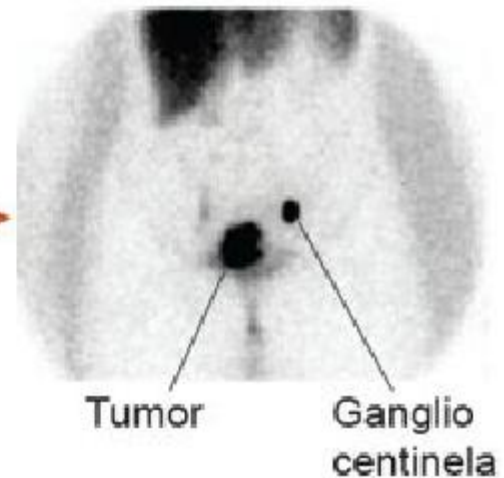
A la paciente se le inyecta un fármaco radiactivo en la proximidad del tumor.

Una gammacámara revela el ganglio centinela.

Gammacámara

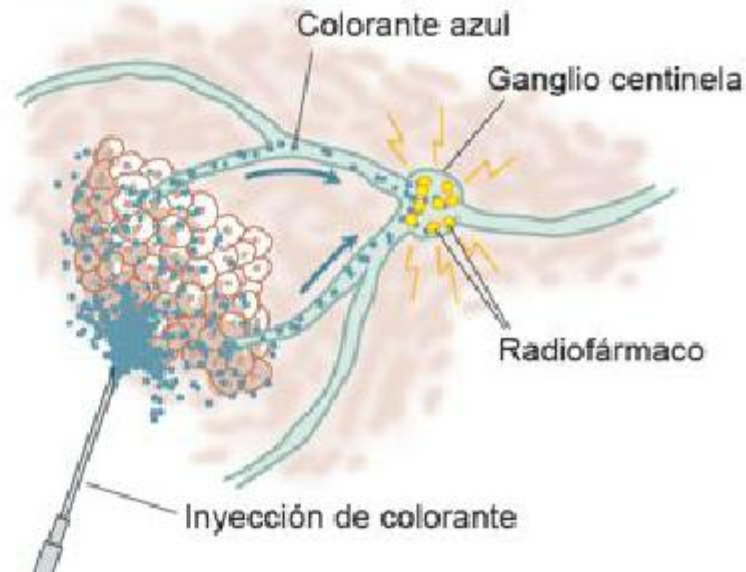


Linfogammagrafía



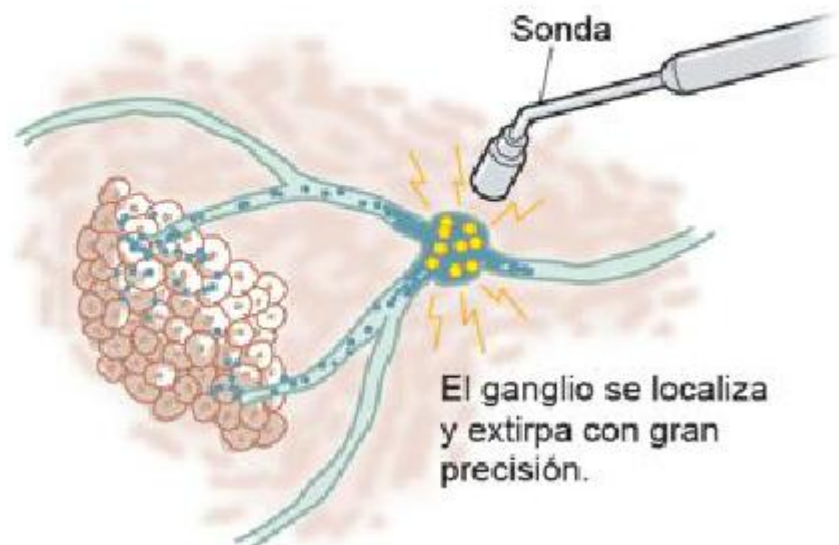
ANÁLISIS DEL GANGLIO CENTINELA

Antes de la operación se inyecta colorante azul cerca del tumor. El colorante viaja hasta el ganglio centinela y lo colorea.

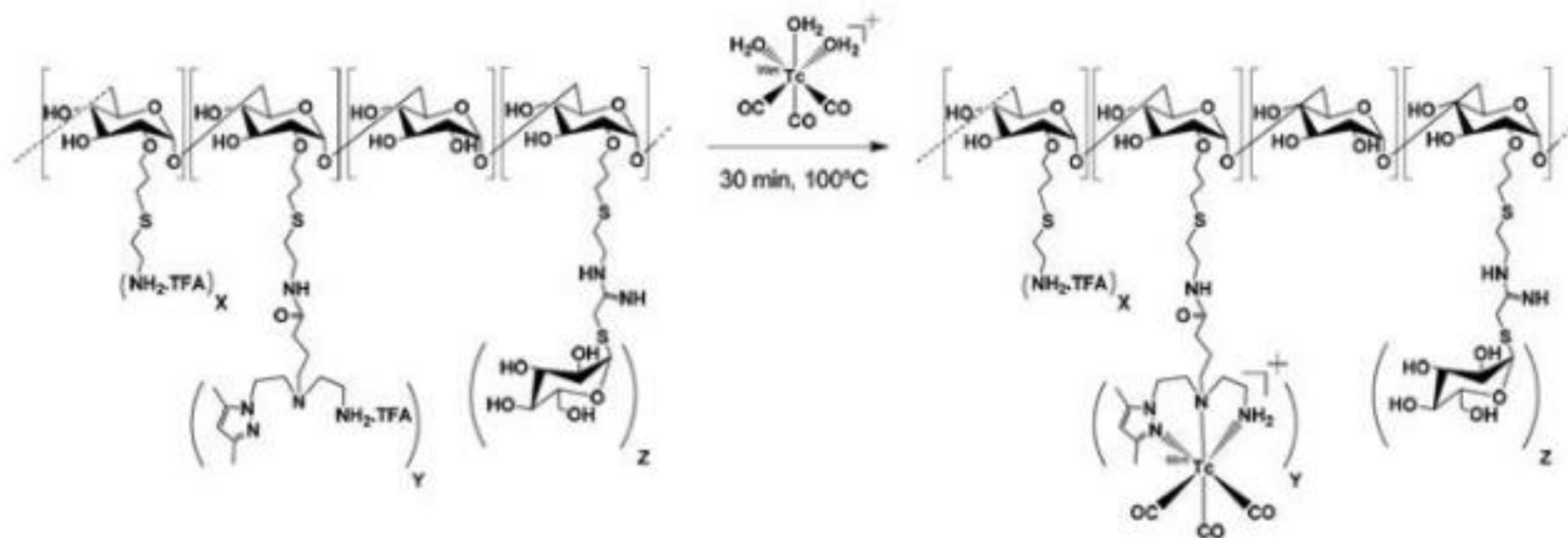


ANÁLISIS DEL GANGLIO CENTINELA

Una sonda detecta los rayos gamma del fármaco radiactivo, y el cirujano puede ver el colorante azul

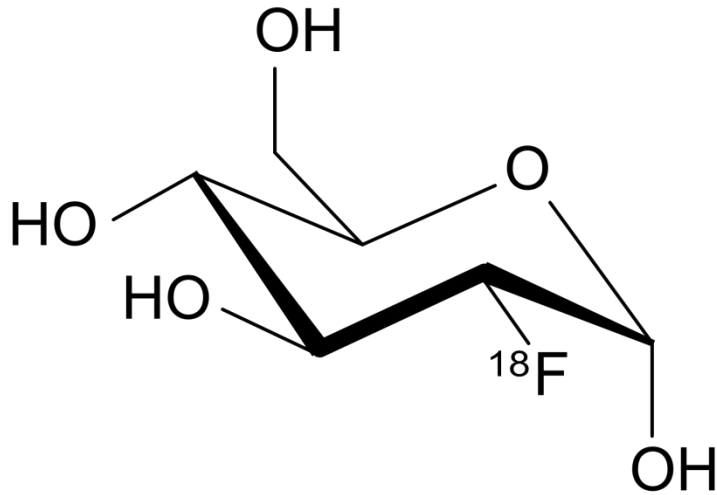


A NEW CLASS OF $^{99m}\text{Tc(I)}$ AGENTS FOR SLND: LABELLING AND QUALITY CONTROL



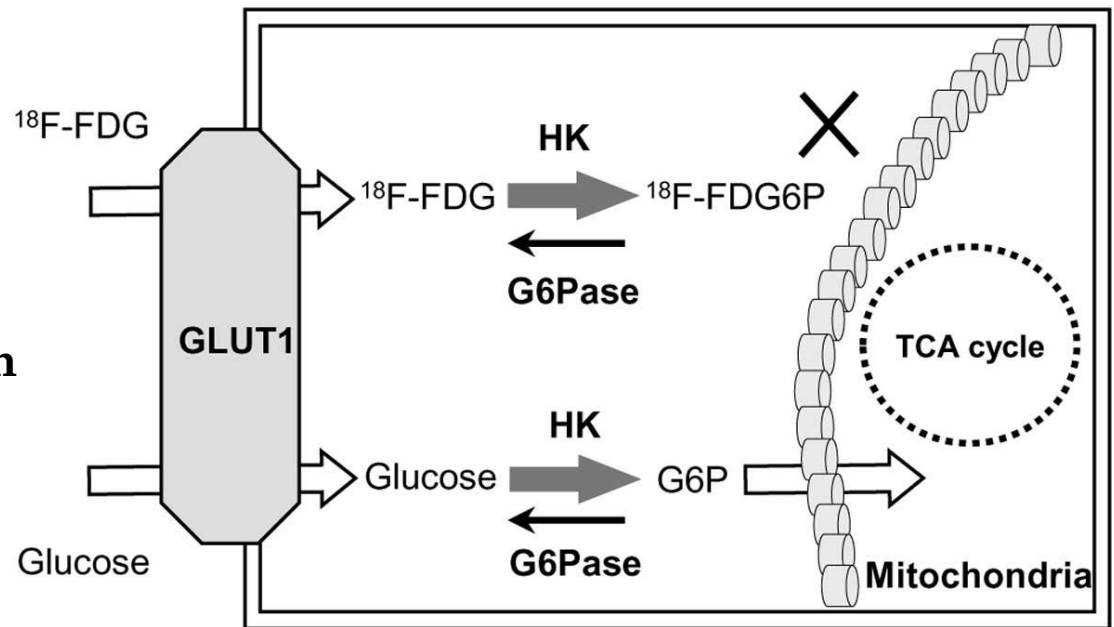
M. MORAIS, J.D.G. CORREIA, I., SANTOSM., PELECANOU, I. PIRMETTIS, M. PAPADOPOULOS. RADIOPHARMACEUTICALS FOR SENTINEL LYMPH NODE DETECTION. IAEA RADIOISOTOPES AND RADIOPHARMACEUTICALS SERIES No. 6

^{18}F -FDG

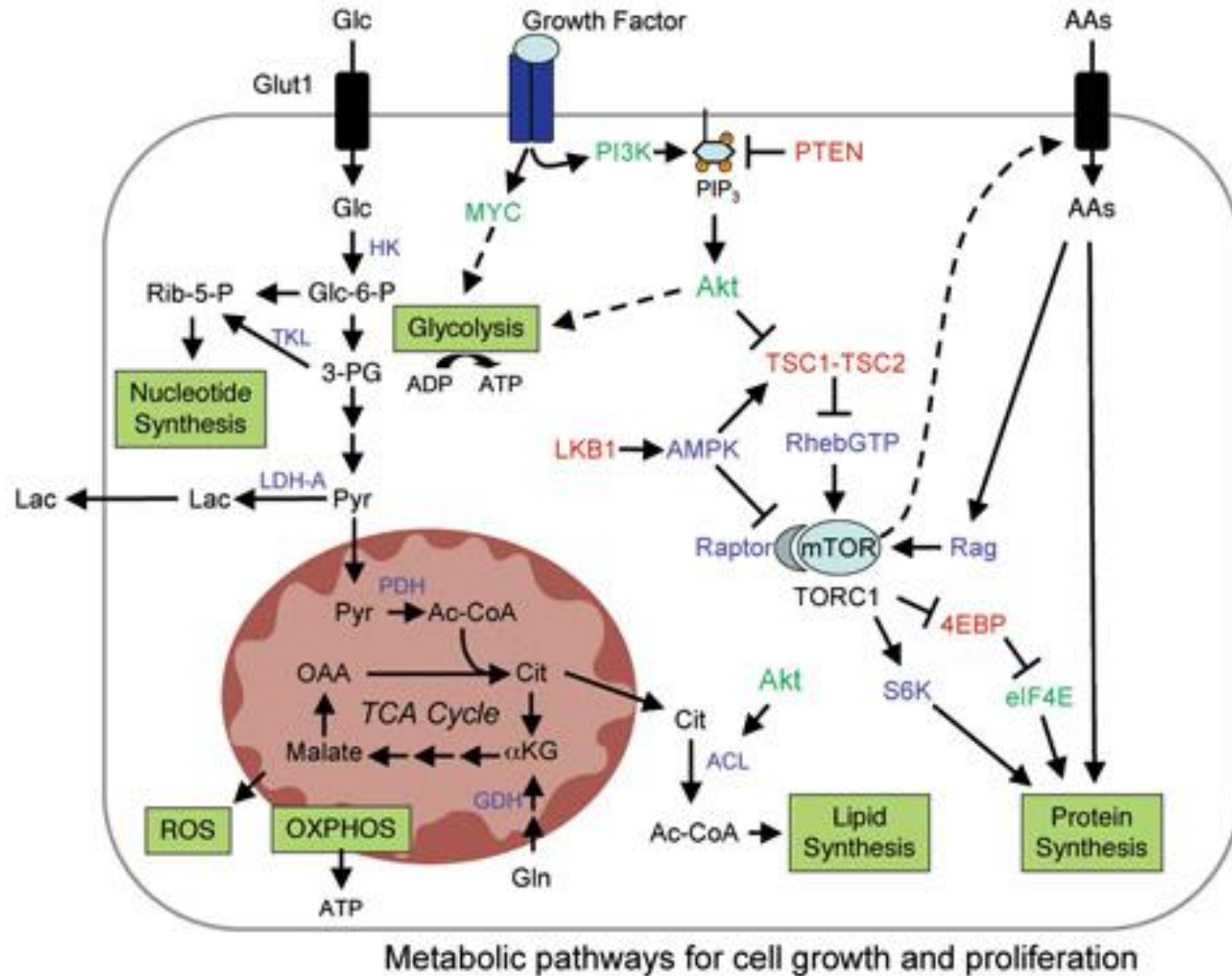


2-deoxy-2- (^{18}F) fluoro-D-glucose

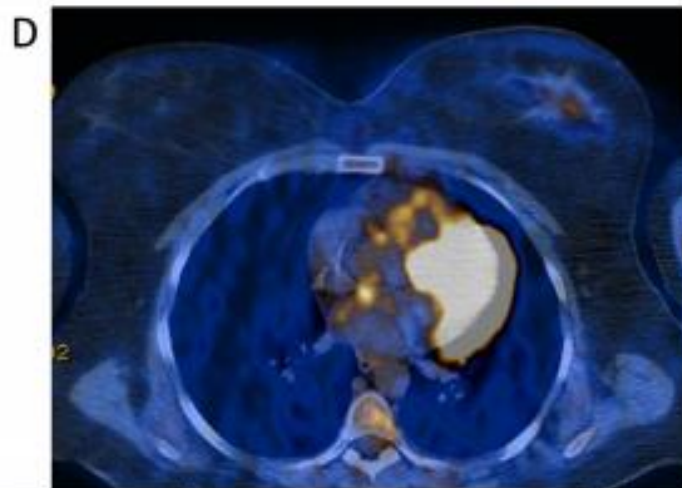
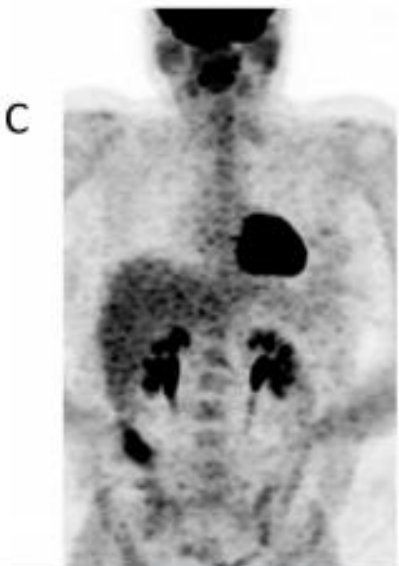
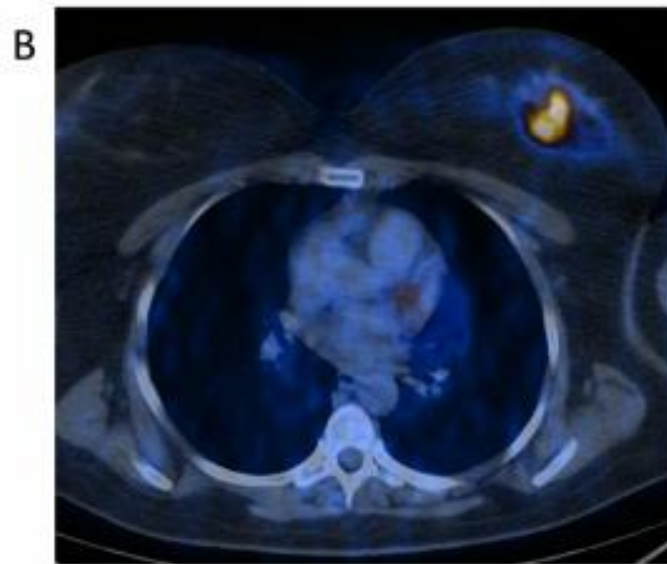
Mecanismo de captación



Fueling Cancer



Russell Jones. Assistant Professor Goodman Cancer Centre Department of Physiology McGill University. Canada



ORIGINAL ARTICLE

The Potential of F-18-FDG PET in Breast Cancer: Detection of Primary Lesions, Axillary Lymph Node Metastases, or Distant Metastases

Karl F. Hubner, MD¹, Gary T. Smith, MD¹, Joseph A. Thie, PhD¹,
John L. Bell, MD², Henry S. Nelson, Jr., MD², Wahid T. Hanna, MD³

Departments of ¹Radiology, ²Surgery, and ³Medicine,
University of Tennessee Medical Center, Knoxville, TN

Dan Med Bull. 2011 Jul;58(7):A4289.

Utility of 18FDG-PET/CT in breast cancer diagnostics--a systematic review.

Warning K¹, Hildebrandt MG, Kristensen B, Ewertz M.

Author information

¹Department of Oncology, Odense University Hospital, 5000 Odense, Denmark.

Abstract

18F-fluorodeoxyglucose-positron emission tomography/computed tomography (18FDG-PET/CT) is a non-invasive method for visualization of focally increased metabolism in the presence of discrete morphological changes. Based on a systematic review of current literature, PET/CT cannot be recommended as a primary diagnostic procedure in breast cancer; but it has the potential to be useful for the detection of distant metastases and for monitoring response to chemotherapy in breast cancer patients. PET/CT should still be regarded as a supplement to conventional diagnostic procedures such as CT and MRI.



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Médecine Nucléaire xxx (2016) xxx–xxx

**Médecine
Nucléaire**
Imagerie Fonctionnelle et Métabolique

General review

Impact of molecular and histological subtype of breast cancer on ^{18}F FDG-PET/CT imaging: Knowledge gained from recent studies

Impact du phénotype moléculaire et de l'histologie du cancer du sein sur l'imagerie TEP/TDM au ^{18}F FDG : données récentes

D. Groheux^{a,*}, D. Mankoff^c, C. Lemarignier^a, A. Cochet^{d,e}, O. Humbert^{d,e}, L. Champion^f,
J.-L. Alberini^{f,g}, E. Hindié^h

^a Department of nuclear medicine, Saint-Louis hospital, 1, avenue Claude-Vellefaux, 75475 Paris cedex 10, France

^b Inserm U944/CNRS UMR7212, university of Paris-Diderot, 75000 Paris, France

^c Department of radiology, university of Pennsylvania, Perelman school of medicine, Philadelphia, USA

^d Department of nuclear medicine, centre G.F. Leclerc, 21000 Dijon, France

^e UMR CNRS 6306, university of Burgundy, 21000 Dijon, France

^f Department of nuclear medicine, Institut Curie, Rene Huguenin Hospital, 92210 Saint-Cloud, France

^g University of Versailles–Saint-Quentin, 78190 Saint-Quentin-en-Yvelines, France

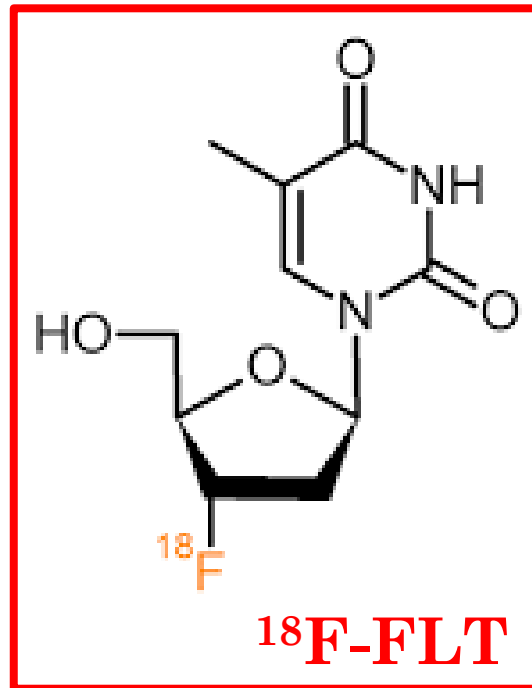
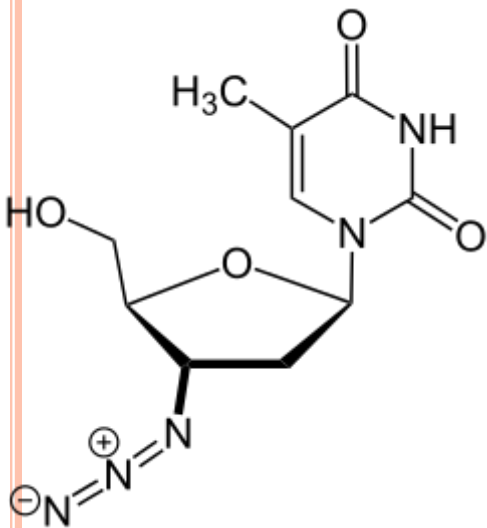
^h Department of nuclear medicine, Haut-Lévêque hospital, CHU de Bordeaux, university of Bordeaux, 33076 Bordeaux, France

¹⁸F-FLT

FLT (3'-deoxy-3'-fluorothymidine), tiene su origen en un compuesto testeado como retroviral para el HIV.

AZT –

el primer fármaco para el tratamiento del VIH

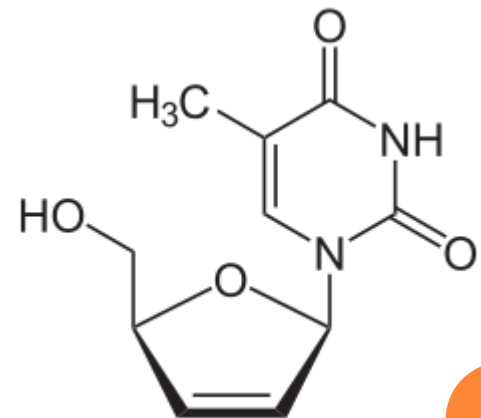


Estavudina –

Marca comercial: **Zerit**

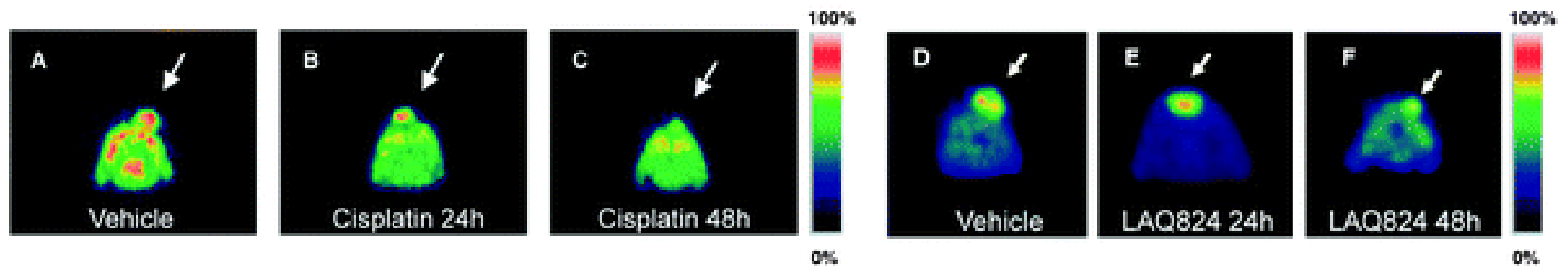
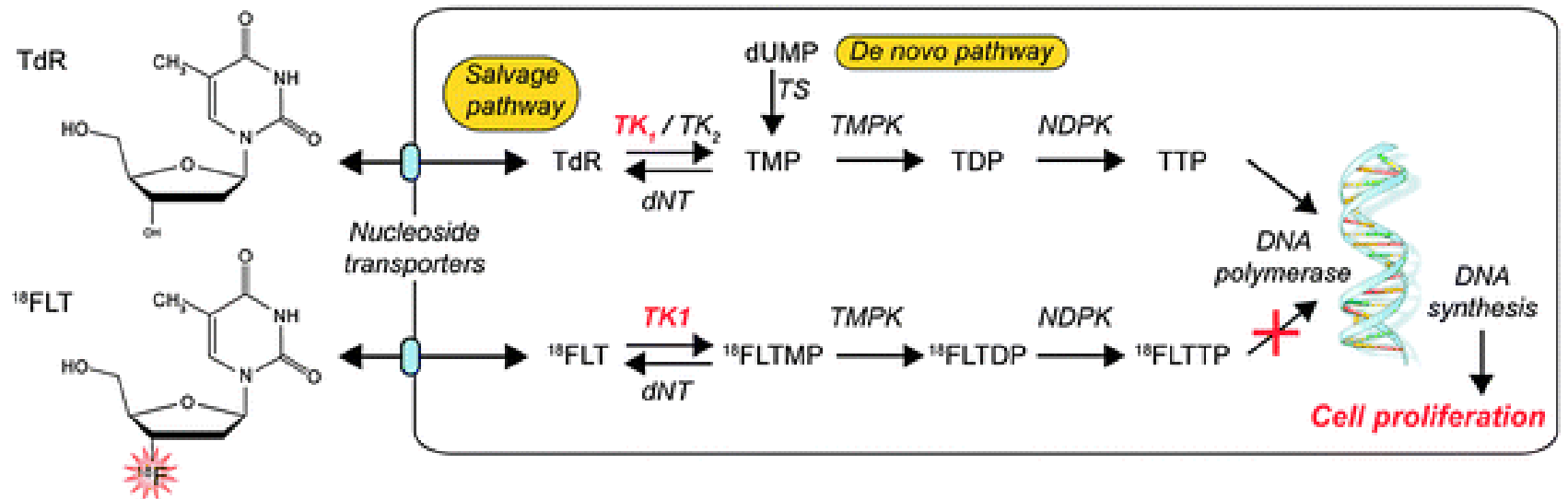
Otro(s) nombre(s): BMY- 27857, d4T

Clase de medicamento: Inhibidor de la transcriptasa inversa
análogo de los nucleósidos
Uso aprobado: Infección por el VIH



NATURE MEDICINE • VOLUME 4 • NUMBER 11 • NOVEMBER 1998. Imaging proliferation in vivo with [F-18]FLT and positron emission tomography ANTHONY F. SHIELDS¹, JOHN R. GRIERSON², BERNHARD M. DOHMEN³, H.-JUERGEN MACHULLA³, JOSEPH C. STAYANOFF¹, JAWANA M. LAWHORN-CREWS¹, JOYCE E. OBRADOVICH⁴, OTTO MUZIK¹ & THOMAS J. MANGNER¹
¹ Karmanos Cancer Institute, Departments of Medicine and Radiology, Wayne State University, Detroit Medical Center, 5 Hudson, 3990 John R Street, Detroit, MI 48301, USA

Mecanismo de captación



Phase II Study of Fluorine-18 3'-Deoxy-3'-Fluorothymidine (F-18-FLT) in Invasive Breast Cancer. NCI.

Purpose

This phase II trial studies how well 3'-deoxy-3'-18F fluorothymidine (18F-FLT) positron emission tomography (PET)/computed tomography (CT) works in predicting response in patients receiving chemotherapy and undergoing surgery for breast cancer that has spread from where it started to nearby tissue or lymph nodes. Diagnostic procedures, such as 18F-FLT PET/CT, may help in learning how well chemotherapy works to kill breast cancer cells before surgery and help doctors plan the best treatment.

Condition	Intervention	Phase
Stage IIB Breast Cancer Stage IIIA Breast Cancer Stage IIIB Breast Cancer Stage IIIC Breast Cancer	Procedure: CT Drug: 18F-FLT Procedure: PET	Phase 2

Study Type: Interventional
Study Design: Endpoint Classification: Efficacy Study
 Intervention Model: Single Group Assignment
 Masking: Open Label
 Primary Purpose: Diagnostic

Official Title: 3'-Deoxy-3'-18F Fluorothymidine PET/CT in Predicting Response To Chemotherapy Before Surgery in Patients With Locally Advanced Breast Cancer

Radiofármacos para receptores de estrógenos

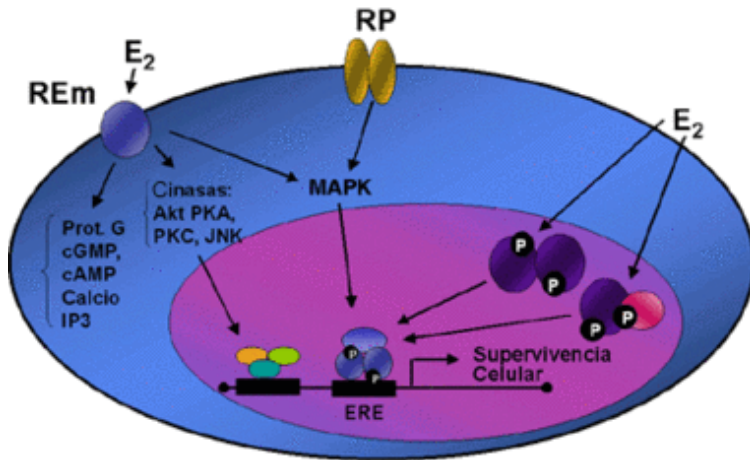
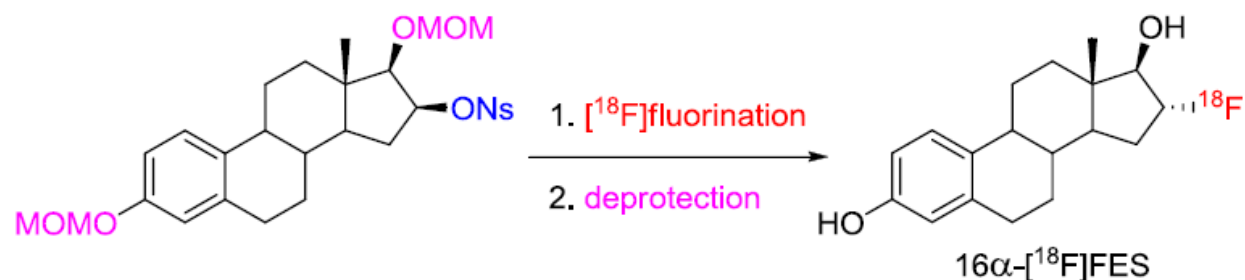
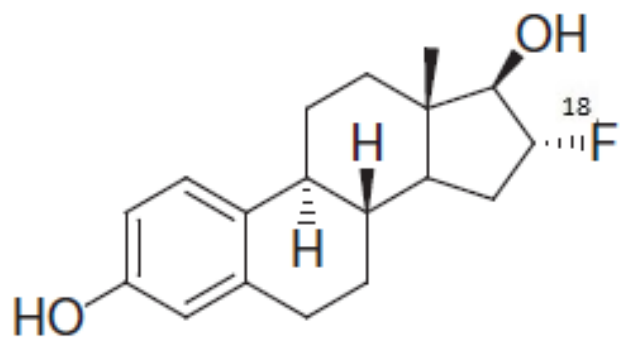


Figura 5.

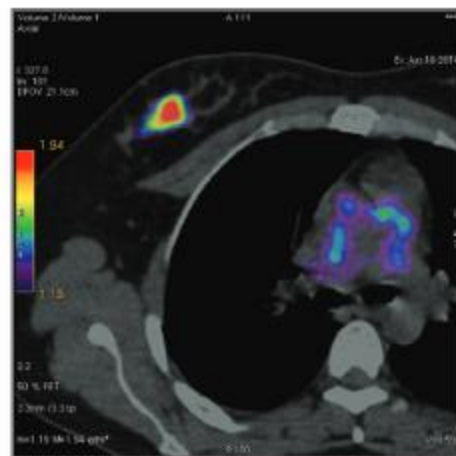
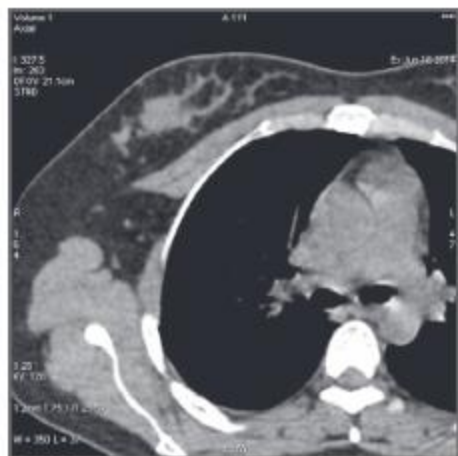
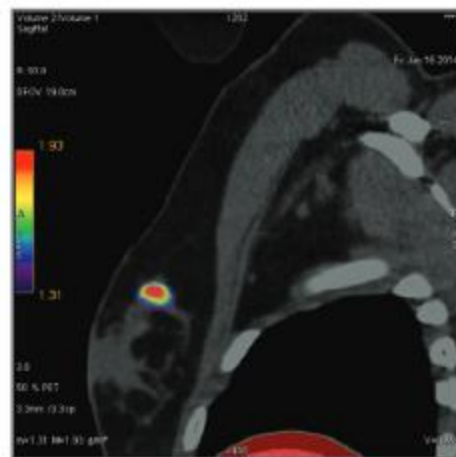
Efectos "No Genómicos" del Receptor de Estrógeno de Membrana. El estradiol 17- β (E_2) se une a receptores de membrana (REm) y activa diferentes cascadas de señales que pueden directa o por comunicación cruzada estimular la activación de mecanismos genómicos. Entre los efectos mediados por el receptor de membrana están la activación de canales de Ca^{2+} , proteínas G, interacción con receptores de péptidos (RP), activación de quinasas, etc.

- Al momento del diagnóstico, el 70% de los pacientes con cáncer de mama tienen tumores positivos para receptores de hormonas.
- La determinación de estos receptores es muy importante no solo en la identificación de los procesos tumorales, sino que también la eficacia del
- Las directrices de la Comisión Nacional del Cáncer (NCCN) de Estados Unidos y la Sociedad Europea de Oncología Médica (ESMO) indican que la evaluación de la respuesta a los receptores estrogénicos, es un factor importante en la predicción de la respuesta frente al tratamiento

^{18}F -FES



New ^{18}F FES precursor, 3,17 β -*O*-bis(methoxymethyl)-16 β -*O*-*p*-nitrobenzenesulfonylestriol has been developed for the synthesis of 16 α - ^{18}F fluoroestradiol (^{18}F FES).



¹⁸F-FES. La hipercaptación en cuadrante superointerno de mama derecha permite visualizar en esta paciente con antecedente de cáncer de mama receptores de estrógeno positivos.



Clinical production, stability studies and PET imaging with 16- α -[^{18}F]fluoroestradiol ([^{18}F]FES) in ER positive breast cancer patients.

Kumar P¹, Mercer J, Doerkson C, Tonkin K, McEwan AJ.

Author information

¹Department of Oncologic Imaging, Cross Cancer Institute, 11560 University Avenue, Edmonton, Alberta, Canada T6G 1Z2.
piyushku@cancerboard.ab.ca



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Médecine Nucléaire 39 (2015) 64–70

**Médecine
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Imagerie Fonctionnelle et Métabolique

General review

16 α -[^{18}F]-fluoro-17 β -oestradiol ([^{18}F]FES): A biomarker for imaging oestrogen receptor expression with positron emission tomography (PET)

16 α -[^{18}F]-fluoro-17 β -œstradiol ([^{18}F]FES) : un biomarqueur de l'expression des récepteurs aux œstrogènes pour l'imagerie par émission de positons (TEP)

C. Lefebvre-Lacœuille^{a,b}, F. Lacœuille^{a,d}, C. Rousseau^c, F. Courbon^e,
F. Benard^f, O.-F. Couturier^{a,d,*}

^a LUNAM Université, Inserm UMR-S 1066, Micro- et nanomédecine biomimétiques, 4, rue Larrey, 49933 Angers Cedex 09, France

^b Gynecology and Obstetrical Department, University Hospital – Angers, 4, rue Larrey, 49933 Angers Cedex 09, France

^c Nuclear Medicine Department, ICO Saint-Herblain, France

^d Nuclear Medicine Department, University Hospital – Angers, 4, rue Larrey, 49933 Angers Cedex 09, France

^e Nuclear Medicine Department, Institut Universitaire du Cancer, Oncopole, Toulouse, France

^f Nuclear Medicine Department, Vancouver, Canada

Received 8 January 2015; accepted 20 January 2015

Available online 6 March 2015

ARTICLE IN PRESS

PET/Computed Tomography in Breast Cancer

Can It Aid in Developing a Personalized Treatment Design?

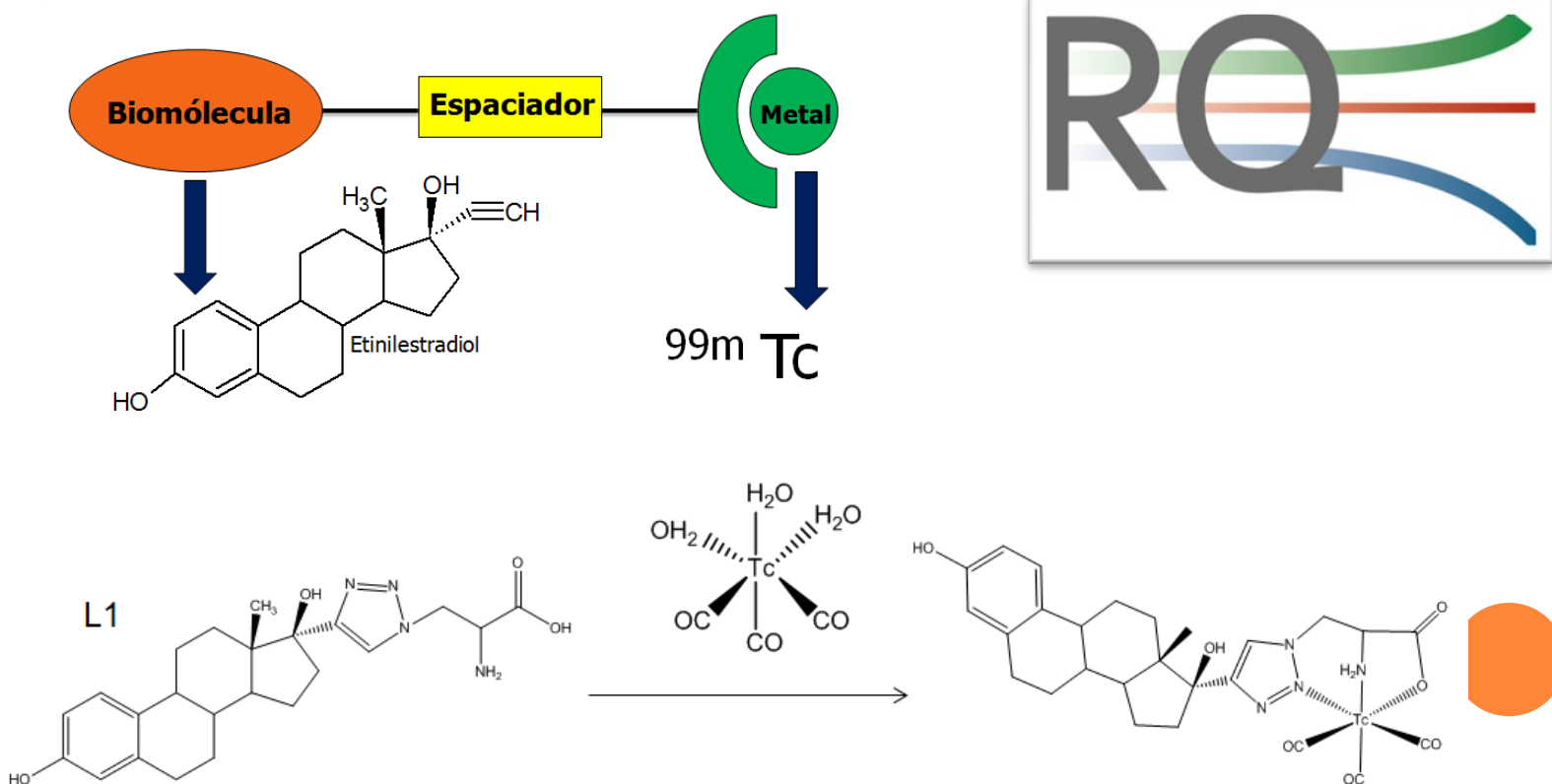
Sumeet Suresh Malapure, MD^a, Kalpa Jyoti Das, MD^b,
Rakesh Kumar, MD, PhD^{b,*}



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Emilia Tejería, Javier Giglio, Ana Rey





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