Original

# Multicentric study on ${ }^{18}$ F-FDG-PET/CT breast incidental uptake in patients studied for non-breast malignant purposes 

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## A R T I C L E I N F O

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#### Abstract

Aim: Our study has aimed to establish the prevalence and pathological nature of fluorine-18fluorodeoxyglucose $\left({ }^{18} \mathrm{~F}\right.$-FDG) breast incidental uptake (BIU) in patients studied for non-malignant breast tumours and then to compare our data obtained in three Italian nuclear medicine centres with those available in literature. Material and methods: We retrospectively evaluated $42,927{ }^{18} \mathrm{~F}$-FDG-PET/CT scans performed on patients studied in three Italian Nuclear Medicine Centres. All patients underwent ${ }^{18} \mathrm{~F}-\mathrm{FDG}$-PET/CT for oncologic purposes not related to breast disease. Results: Among 42,927 scans, a BIU was identified in 79 ( $0.18 \%$ ) patients, 75 ( $95 \%$ ) female and 4 (5\%) male with an average age of $62 \pm 17$ years. Twenty-five out of 35 ( $71.5 \%$ ) BIUs were malignant and 10/35 (28.5\%) benign. Among the 25/35 incidentalomas that were malignant, 12/25 (48\%) were infiltrating ductal carcinoma, 5/25 (20\%) ductal carcinoma (infiltrating and in situ), 4/25 (16\%) lobular carcinoma, 2/25 ( $8 \%$ ) ductal carcinoma in situ and $2 / 25(8 \%)$ were metastases from the primary tumour under investigation. Of the 10 BIUs that were benign in the histological examination, after further investigations it was found that $9 / 10(90 \%)$ were fibroadenomas and $1 / 10(10 \%)$ was a benign lesion not better specified. The lesion to liver or to blood-pool SUVmax ratio in malignant lesions is significantly higher than in benign ones. Conclusions: Our multicenter study demonstrates that, although they are uncommon, BIUs show a high percentage of malignancy and therefore requires further research.


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## Estudio multicéntrico sobre la captación incidental en la mama con ${ }^{18}$ F-FDG-PET/TAC en pacientes evaluados con fines oncológicos no relacionados con la patología mamaria

## R E S U M E N

Objetivo: Objetivo de nuestro estudio fue establecer la prevalencia y el carácter patológico de la captación incidental en la mama (CIM) de ${ }^{18}$ F-FDG en pacientes evaluados para tumores malignos de origen nomamario y luego comparar nuestros datos obtenido en tres centros Italianos de Medicina Nuclear con los que están disponibles en literatura.
Material y métodos: Hemos evaluado retrospectivamente 42.927 estudios ${ }^{18}$ F-FDG-PET/TAC de pacientes en tres centros Italianos de Medicina Nuclear; todos los pacientes se han sometidos a una exploración ${ }^{18} \mathrm{~F}$-FDG-PET/TAC por fines oncológicos no relacionados con la patología mamaria.
Resultados: Entre 42.927 exploraciones, una CIM fue identificada en 79 ( $0.18 \%$ ) pacientes, 75 (95\%) mujeres y 4 (5\%) hombres, con una edad media de $62 \pm 17$ años. Veinticinco de 35 ( $71.5 \%$ ) CIM fueron malignas y 10/35 (28.5\%) benignas. Entre los incidentalomas malignos, $12 / 25$ ( $48 \%$ ) eran carcinomas ductales infiltrantes, $5 / 25(20 \%)$ carcinomas ductales (infiltrantes e in situ), 4/25 (16\%) carcinomas lobulares, $2 / 25$ ( $8 \%$ ) carcinomas ductales in situ y $2 / 25$ ( $8 \%$ ) eran metástasis de tumour primario objeto de investigación. Entre 10 CIM que fueron identificados como benignos en el examen histológico después de investigación adicional, 9/10 (90\%) fueron fibroadenomas y 1/10 (10\%) fue una lesión benigna no mejor especificada.

## Palabras clave:

PET/TAC
${ }^{18}$ F-FDG
Mama
Incidentaloma

[^0]El ratio del SUVmáx de la lesión en comparación con el hígado o con el pool vascular es significativamente mayor en las lesiones malignas que en las benignas.
Conclusiones: Nuestro estudio multicéntrico demuestra que, aunque son poco frecuentes, las CIM muestran un alto porcentaje de malignidad, por lo tanto las CIM necesitan investigación adicional.
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## Introduction

In Europe cancer is the second cause of death after cardiovascular disease, it accounts for about one-fifth of all deaths and breast cancer is the most frequent cancer in female patients. ${ }^{1}$ Screening for this cancer has either been implemented or is subject to large-scale research in order to reduce mortality and because it has been demonstrated to extend lives despite over-diagnosis is still a problem. ${ }^{2}$ Breast incidental uptake (BIU) of fluorine18 -fluorodeoxyglucose ( ${ }^{18} \mathrm{~F}$-FDG) is defined as a breast uptake incidentally and newly detected by positron emission tomography (PET) or PET/computed tomography (PET/CT) performed for an unrelated purpose and especially for non-breast disease. Incidental and unexpected focal ${ }^{18} \mathrm{~F}$-FDG uptakes in many organs are relatively frequent and could involve thyroid, ${ }^{3,4}$ prostate, ${ }^{5}$ bowel and colon, ${ }^{6,7}$ and pituitary gland. ${ }^{8}$ Despite screening procedures, the available data reporting BIU detected by ${ }^{18}$ F-FDG-PET or PET/CT suggest that some lesions are still missed during traditional screening work-up. ${ }^{9-22}$ When a BIU is detected, it creates for a management dilemma requiring further investigations. Overall, the prevalence of BIU on all scan ranges from $0.11 \%$ to $0.83 \%$, with pooled estimate of $0.40 \%$; the prevalence of BIU on scans performed on female patients only ranges from $0.36 \%$ to $1.84 \%$, with pooled estimate of $0.82 \%$; the pooled malignancy risk of BIU who undergo further investigations ranges from $18 \%$ to $100 \%$ with pooled estimate of $48 \%$; the pooled malignancy risk of BIU who undergo histological examination ranges from $51 \%$ to $100 \%$ with pooled estimate of $60 \%{ }^{9}$

## Aim

Aim of our study was to establish the prevalence and pathological nature of BIU in patients studied for oncologic purposes not breast-related and compare our data obtained in three Italian nuclear medicine centres with those available in literature.

## Material and methods

We have retrospectively evaluated 42,927 scans performed on patients studied in three Italian Nuclear Medicine Centres from August 2005 to October 2013; all patients underwent ${ }^{18} \mathrm{~F}$ -FDG-PET/CT for oncologic purposes not related to breast disease. ${ }^{18} \mathrm{~F}$-FDG-PET/CT was performed in the fasting state for at least 6 h and the glucose level lower than $200 \mathrm{mg} / \mathrm{dl}$ in centre N. 2 and N. 3 and lower than $150 \mathrm{mg} / \mathrm{dl}$ in the centre N.1. PET/CT studies were acquired with integrated PET/CT systems, a Discovery ST PET/CT or Discovery 690 tomograph (General Electric Company - GE ${ }^{\circledR}$ Milwaukee, WI, USA) in centre N.1, a Biograph 16 HT PET/CT scanner (Siemens Medical Solutions, Illinois, USA) in centre N.2, and an integrated PET/CT device (GEMINI GXL or GEMINI DUAL distributed by Philips Medical Systems) in centre N.3. Features of ${ }^{18}$ F-FDG-PET/CT included a whole body PET scans ( $6-8$ bed, $2-3$ min per bed) performed 60 min after radiopharmaceutical injection of $4.5 \mathrm{MBq} / \mathrm{Kg}$ in the centre $\mathrm{N} .1,250-400 \mathrm{MBq}$ in the centre N .2 and 370 MBq in the centre N .3 and co-registered low-dose CT WB scan ( $140 \mathrm{kV}, 80-120 \mathrm{~mA}$ ) without contrast enhancement. In all centres, patients were instructed to void before imaging, no oral or
intravenous contrast agents were administered or bowel preparation applied for any patient and a written consensus was obtained before studies in each centre. The readers had knowledge of the clinical history and every focal tracer uptake deviating from physiological distribution and background was considered as suggestive of BIU. No specific maximum standardized uptake value (SUVmax) cut-off was considered to discriminate focal incidental uptake or physiological activity but only the deviation from physiological distribution, background, blood-pool, liver uptake or from the normal tissue activity. Final diagnosis was obtained by cytological examination performed after ultrasonography guided fine needle aspiration or by histological examination after biopsy or surgery. Because SUVmax measurements of lesions obtained from the three different centres were not comparable, lesion to liver SUVmax ratio and lesion to blood pool SUVmax ratio were calculated (considering the SUVmax of the liver and the SUVmax of the blood-pool calculated at VIII hepatic segment and SUVmax of aortic arch using a region of interest not involving the vessel wall, respectively).

## Results

Among 42,927 scans a BIU was identified in 79 ( $0.18 \%$; Table 1) patients, 75 females ( $95 \%$ ) and 4 males ( $5 \%$ ); the average age was $62 \pm 17$ years. Considering all BIUs 41 ( $52 \%$ ) were in the right breast and 38 ( $48 \%$ ) in the left one. Twenty-one BIUs ( $26.6 \%$ ) were in the upper outer quadrant, 15 (19\%) in the upper inner quadrant, 11 $(13.9 \%)$ in the equatorial outer quadrant, $8(10.1 \%)$ in the lower outer quadrant, 7 (8.9\%) in the lower inner quadrant, 6 (7.6\%) lower central quadrant, $6(7.6 \%)$ in the retro-areolar region, and 5 (6.3\%) in the upper central quadrant. Out of 79 BIUs, 35 (44\%) underwent further investigation to determine the nature of the nodules while $44(56 \%)$ were lost at follow-up ( $n=19$ ) or did not undergo further evaluation because of the clinical condition and stage of the primary oncologic disease $(n=25)$. The average size of the corresponding nodule at CT was $15.95 \pm 7.8 \mathrm{~mm}$. Twenty-five out of 35 ( $71.5 \%$ ) BIUs were malignant (Fig. 1) while 10/35 (28.5\%) benign (Fig. 2); of 25/35 incidentalomas which resulted malignant, 12/25 (48\%) were infiltrating ductal carcinoma, 5/25 (20\%) ductal carcinoma (with an infiltrating and in situ component), 4/25(16\%) lobular carcinoma, 2/25 (8\%) ductal carcinoma in situ and $2 / 25$ ( $8 \%$ ) were metastases from the primary tumour under investigation; conversely, out of 10 benign BIUs, $9 / 10(90 \%)$ were fibroadenomas, and $1 / 10(10 \%)$ a benign lesion not better specified (Table 2). Moreover, a centrebased evaluation was performed to analyse lesion to liver SUVmax ratio and lesion to blood-pool SUVmax ratio; in fact a global analysis on the SUVmax of the entire population was not performed in each centre due to different methodologies, technology equipments and software that disable the possibility to compare semi-quantitative parameters. The average of the lesion to liver SUVmax ratio was $1.2 \pm 1$ while the average of lesion to blood-pool SUVmax ratio was $1.6 \pm 1.2$. Considering malignant lesions, the average of the lesion to liver SUVmax ratio was $1.5 \pm 1$ while the average lesion to bloodpool SUVmax ratio was $1.8 \pm 1.1$. Considering benign lesions, the average lesion to liver SUVmax ratio was $0.8 \pm 1$ while the average lesion to blood-pool SUVmax ratio was $0.4 \pm 0.6$. The median value of lesion to liver SUVmax ratio of malignant and benign lesions was 1.2 and 0.7 respectively; the median value of lesion to blood-pool

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