



Incidental F18-FDG Breast Uptake: How to Consider and Manage

Francesco Bertagna*^a, Emanuela Orlando^b, Mattia Bertoli^a, Giorgio Treglia^c

^a Department of Nuclear Medicine, University of Brescia and Spedali Civili di Brescia, Brescia, Italy

^b 1st Division of Radiology, Spedali Civili di Brescia, Brescia, Italy

^c Department of Nuclear Medicine AND PET/CT Center, Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

Screening for breast cancer has been realised as a large-scale research in Europe and North America with effective diagnostic and clinical results.¹ The obvious reason for performing and encouraging screening is to reduce the incidence of mortality. Breast screening has been demonstrated to prolong lives; however, over-diagnosis is still a clinical problem.² Despite screening procedures, the available data reporting incidental breast uptake, revealed by F-18-fluoro-fluorodeoxygulose positron emission tomography/computed tomography (FDG-PET/CT) in patients studied for non breastrelated oncologic purposes, suggest that some lesions are still missed during traditional screening work-up. Breast incidentaloma could be defined as a breast lesion incidentally and newly detected by imaging techniques performed for an unrelated purpose and particularly not for oncologic breast diseases. Incidental focal FDG uptakes are relatively frequent and could involve prostate, thyroid, bowel and colon, and pituitary gland.³⁻⁹ It is generally accepted that whole-body FDG-PET/CT should not be recommended for primary breast cancer detection or early stage breast cancer evaluation, respectively, because of high falsenegative rates in presence of small lesions, and for cost-effectiveness concerns considering the low

Address for correspondence: Francesco Bertagna, M.D. Address: University of Brescia and Spedali Civili di Brescia, P.le Spedali Civili, 125123 Brescia, Italy Tel: +39 30 3995468 Fax: +39 30 3995420 Email: francesco.bertagna@spedalicivili.brescia.it francesco.bertagna@med.unibs.it probability of secondary lesions. In fact, it is of limited utility in the detection of small (less than 1cm) primary breast tumors. Newer-generation PET scanners with advanced crystal technologies have theoretically improved resolutions down to 3 mm at FWHM; however, these resolutions still do not match the spatial resolutions of the current screening techniques of mammography and ultrasonography or magnetic resonance. As a consequence, FDG-PET/CT is not appropriate as a screening procedure. However, the results derived from literature analysis give new insight on its possible role in detecting clinically unsuspected small lesions in an early stage.¹⁰ On the other hand, FDG-PET/CT shows a significant added value and can be an effective tool in the detection of loco-regional recurrence and metastases in locally advanced breast cancer.¹¹ Despite being statistically heterogeneous, many studies, considering a large number of patients, have analyzed clinical and diagnostic significance of breast incidental uptake (BIU) showing a pooled prevalence of BIU on all scans ranging from 0.11% to 0.83%, with pooled estimate of 0.40% (95%CI: 0.23-0.61%). The pooled prevalence of BIU on scans performed on female patients ranges from 0.36% to 1.84%, with pooled estimate of 0.82%(95%CI: 0.51-1.2%). The pooled malignancy risk of BIU that underwent further investigations ranges from 18% to 100%, with pooled estimate of 48% (95%CI: 38-58%). Moreover, the pooled malignancy risk of BIU that underwent histological examination (95%CI) ranges from 51% to 100%, with pooled estimate of 60% (95%CI: 53-66%). Finally, the most frequent malignancy detected in BIU is infiltrating ductal carcinoma.¹⁰ In patients



FDG uptake in breast

with known cancer traditional work-ups focus on the patient's primary disease, and coexistence of another primary malignant lesion can be missed, but its prevalence is not negligible. Dong et al. reported that 8.5% of 633,964 patients with known cancers were subsequently proven to have other and previously unrecognized primary cancer.¹² Ueno et al. reported that 5.2% of 24,498 cancer patients had multiple cancers.¹³ Clinical evaluation and imaging are therefore essential for evaluating the breast and it is well known that not all breast cancer histologies have similar glucose hypermetabolic potential. FDG uptake is significantly higher in ductal carcinoma than in lobular carcinoma and median SUV is markedly higher in infiltrating ductal carcinomas than in lobular one.¹⁴⁻¹⁶ In conclusion, although BIU is less frequent (about 0.4% of all scans) compared to other incidental PET or PET/CT findings, some important considerations could be: 1) it frequently signals the presence of an unsuspected subclinical lesion which differs from the indicated reason for which the patient was initially scanned; 2) the risk of malignancy is very high; 3) the most frequent histological type is ductal carcinoma; 4) further assessment of these lesions including second look mammogram and breast ultrasound with tissue sampling are absolutely justified. Finally, contrary to other imaging techniques which are usually limited to smaller body segments, FDG-PET/CT is a whole body imaging which provides information above and beyond that for which the scan was ordered.

References

- 1. Bretthauer M, Kalager M. Principles, effectiveness and caveats in screening for cancer. Br J Surg 2013; 100(1): 55-65.
- 2. The benefits and harms of breast cancer screening: an independent review. Lancet 2012; 380(9855): 1778-86.
- Hwang I, Chong A, Jung SI, Hwang EC, Kim SO, Kang TW, et al. Is further evaluation needed for incidental focal uptake in the prostate in 18 fluoro-2-deoxyglucose positron emission tomography-computed tomography images? Ann Nucl Med 2013; 27(2): 140-5.
- 4. Bertagna F, Treglia G, Piccardo A, Giovannini E, Bosio G, Biasiotto G, *et al.* F18-FDG-PET/CT thyroid incidentalomas: a wide retrospective analysis in three Italian centres on the significance of focal uptake and SUV value. Endocrine 2013; 43(3): 678-85.
- Bertagna F, Treglia G, Piccardo A, Giubbini R. Diagnostic and clinical significance of F-18-FDGPET/ CT thyroid incidentalomas. J Clin Endocrinol Metab 2012; 97(11): 3866-75.
- Chopra A, Ford A, De Noronha R, Matthews S. Incidental findings on positron emission tomography/CT scans performed in the investigation of lung cancer. Br J Radiol 2012;

85(1015): e229-e237.

- Gill RS, Perry T, Abele JT, Bedard EL, Schiller D. The clinical significance of incidental intra abdominal findings on positron emission tomography performed to investigate pulmonary nodules. World J Surg Oncol 2012; 10:25.
- Treglia G, Calcagni ML, Rufini V, Leccisotti L, Meduri GM, Spitilli MG, *et al.* Clinical significance of incidental focal colorectal (18)Ffluorodeoxyglucose uptake: our experience and a review of the literature. Colorectal Dis 2012; 14(2): 174-80.0
- 9. Hyun SH, Choi JY, Lee KH, Choe YS, Kim BT. Incidental focal 18F-FDG uptake in the pituitary gland: clinical significance and differential diagnostic criteria. J Nucl Med 2011; 52(4): 547 50.
- Bertagna F, Treglia G, Orlando E, Dognini L, Giovanella L, Sadeghi R, *et al.* Prevalence and clinical significance of incidental F18-FDG breast uptake: a systematic review and metaanalysis. Jpn J Radiol 2014; 32(2): 59-68.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) [Online]. [cited 2011]; Available from: URL: http://www.nccn.org/professionals/physician_ ls/f_guidelines.asp/
- 12.Dong C, Hemminki K. Second primary neoplasmsamong 53 159 haematolymphoproliferative malignancy patients in Sweden, 1958-1996: a search for common mechanisms. Br J Cancer 2001; 85(7): 997-1005.
- 13. Ueno M, Muto T, Oya M, Ota H, Azekura K, Yamaguchi T. Multiple primary cancer: an experience at the Cancer Institute Hospital with special reference to colorectal cancer. Int J Clin Oncol 2003; 8(3): 162-7.
- 14. Avril N, Menzel M, Dose J, Schelling M, Weber W, Janicke F, *et al.* Glucose metabolism of breast cancer assessed by 18F-FDG PET: histologic and immunohistochemical tissue analysis. J Nucl Med 2001; 42(1): 9-16.
- 15. Buck A, Schirrmeister H, Kuhn T, Shen C, Kalker T, Kotzerke J, *et al.* FDG uptake in breast cancer: correlation with biological and clinical prognostic parameters. Eur J Nucl Med Mol Imaging 2002; 29(10): 1317-23.
- 16. Crippa F, Seregni E, Agresti R, Chiesa C, Pascali C, Bogni A, *et al.* Association between [18F] fluorodeoxyglucose uptake and postoperative histopathology, hormone receptor status, thymidine labelling index and p53 in primary breast cancer: a preliminary observation. Eur J Nucl Med 1998; 25(10): 1429-34.