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ROLE OF NEW IMAGING MODALITIES OF BREAST CANCER RECURRENCE

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Abstract

The study of the breast after surgery has always been a challenge for breast radiologists. In patients with breast cancer surveillance strategies play an important role. The aims of any follow-up are to detect early local recurrence or contralateral breast cancer.

The complexity in the interpretation of radiological images causes many post-surgical alterations to be subject to misreading and recognized as malignant lesions.

There is currently no consensus on a protocol for imaging the postoperative breast. New imaging modalities, such as magnetic resonance imaging (MRI), ultrasound (US), and positron emission tomography (PET) are changing the way we image the postsurgical breast.

The role of functional imaging with nuclear medicine in breast cancer recurrence is well established and continues to expand rapidly.

Keywords: *Breast cancer, recurrence, us, mammography, mri, PET*

Introduction

The study of the breast after surgery has always been a challenge for breast radiologists.

The complexity in the interpretation of radiological images causes many post-surgical alterations to be subject to misreading and recognized as malignant lesions.

Considering that on average 6.3% of patients relapse during the median follow-up period of 5.3 years [1], a correct breast study is essential as well as knowledge of the normal developmental history of the imaging findings.

A recent study evaluated patients treated with mastectomy and adjuvant chemotherapy and found that the most common sites of recurrence were the chest wall and supraclavicular lymph nodes [2] and there is not significant difference when comparing the rates in patients who have undergone mastectomy versus breast reconstruction [3].

Breast cancer recurrence often presents as a palpable mass and we need to consider all the possible differential diagnosis.

They include a wide range of lesions in patients after mastectomy with or without reconstruction, such as seroma, hematoma, abscess, scar tissue, adipose necrosis, normal and abnormal lymph nodes, and of course recurrence of malignancy. [4]

Many of the common benign lesions seen after mastectomy have typically benign features in ultrasound imaging and can be diagnosed without additional investigations, as well as, malignant lesions often present with classic imaging features and biopsy is indicated without additional imaging methods. [5]

To disentangle the various possible diagnostic hypotheses, it is important to know the reparative and evolutionary processes after surgery.

Since the removal of a breast lesion, the normal scarring process of the tissues manifests a series of common alterations that include typical reliefs depending on the method of investigation.

Generally, in the initial phase we can observe focal cutaneous alterations of edemigenous significance, as a focal increase in the density of the mammary parenchyma and collections with fluid or fluid-gas content.

These findings show a variable evolutionary period, depending on the patient, from 3 to 6 years, beyond which frank involutionary changes are observed, from the presence of architectural distortions to scarring fibrosis and thickening of the skin associated with irregularities in its profile. In some cases, it's possible to notice the complete involution of the alterations seen in the early phase. [6]

Ultrasound

In the initial phase, the presence of seromas or hematomas can be detected as a liquid or liquid-gaseous collection communicating with the skin to indicate the exact path of the operating wound. [7] The presence of granulation tissue it is denoted by presence of signs florid vascularization with the color Doppler examination. [8] The skin can appear thickened with associated clear phenomena of imbibition of the peri-lesional subcutaneous soft tissues.

In the late stages, these findings undergo progressive resolution with reabsorption of the collections and signs of scarring like avascular tissue, about 5-6 months after the operation, and then the evolution in a fibrotic scar appears as a hypoechoic distortion area with dendritic offshoots. [9] Because of the overlaps of this findings with the recurrence of breast cancer, patient's medical history will help in the differential diagnosis. [10]

Many cancers in the post-mastectomy breast exhibit similar characteristics to the primary neoplasm and they may appear with classic imaging features of malignancy. [11]

Any solid mass with irregular shape, antiparallel orientation, spiked or indefinite margins, hypoechoic [12] or with complex echo pattern and posterior acoustic shadowing should be biopsied. If there are suspicious

sonographic features, no additional evaluation is required and it is imperative to proceed with a needle biopsy. [13]

Fig 1: US, hypoechoic lesion with irregular shape and posterior acoustic shadowing: Invasive ductal carcinoma (IDC) grade 2.

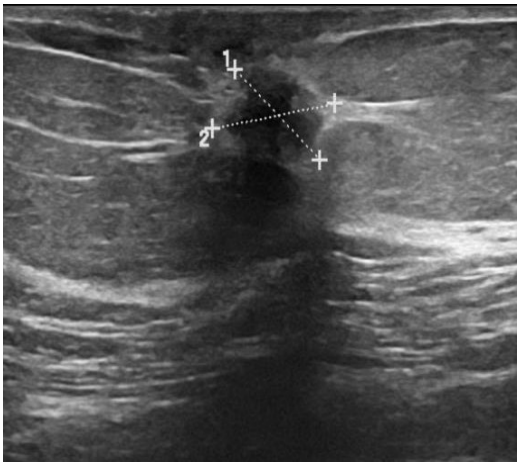

Fig 2: US, hypoechoic lesion with irregular shape, speculated margins and posterior acoustic shadowing: Invasive lobular carcinoma (ILC).

Unfortunately however, due to the loss of normal breast architecture, recurrence of malignancy in a patient with an autologous reconstruction or a post-mastectomy without reconstruction may exhibit unusual imaging features, like more typically benign sonographic features such as a parallel orientation, oval or round shape, hyperechoic or heterogeneous echo texture, and lack of posterior acoustic shadowing. [14]

In this context, any mass that does not have properly benign features should be biopsied. [15]

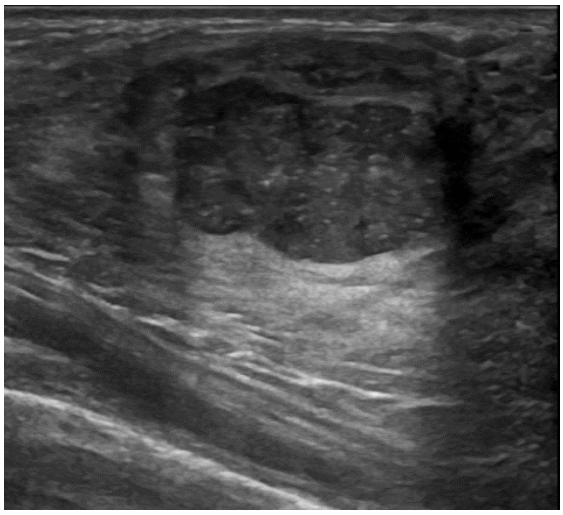

Fig 3: US, hypoechoic lesions with ovoid shape, circumscribed margins, microcalcifications and no posterior acoustic shadowing: Invasive ductal carcinoma (IDC) grade 1.

Mammography

Mammograms are rarely performed in the recent post-surgery period. [16-18]

Typically, they will show an area of increased density of the breast parenchyma, recognizable due to edema and hemorrhagic phenomena, possibly associated with the presence of a high density mass of variable morphology with the presence or absence of air, corresponding to collection. Thickening of the trabeculae of adipose tissue is associated. [19]

With the progress of time, we will observe resolution of the collection and edema phenomena with consequent scarring and fibrotic reaction, visible as an architectural distortion or spiculated mass and thickening and retraction of the skin with widespread mammary edema in probable actinic outcomes. [20,21]

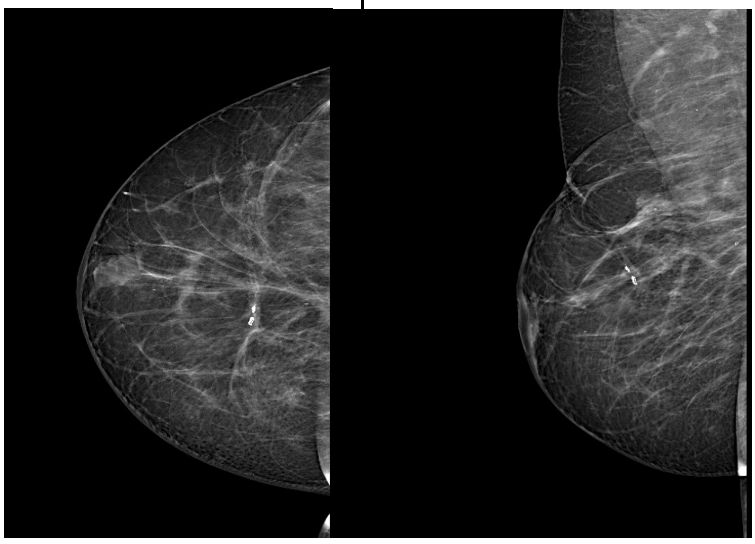

Fig 4: Mammography CC and MLO of right breast, architectural distortion in the upper quadrants after surgery.

Sometimes we will be able to observe the presence of a radiolucent mass due to the adipose content with or without eggshell calcifications, all pathognomonic characteristics for adipose necrosis. [22-24]

The recurrence of malignancy in a breast with surgical procedure outcomes and therefore in a context of a distorting parenchymal texture can can show up as a high density mass, with variable morphology, with possibly spiculated margins, or as a cluster of amorphous, finely pleomorphic or linear microcalcifications in a suspicious distribution. [25-28]

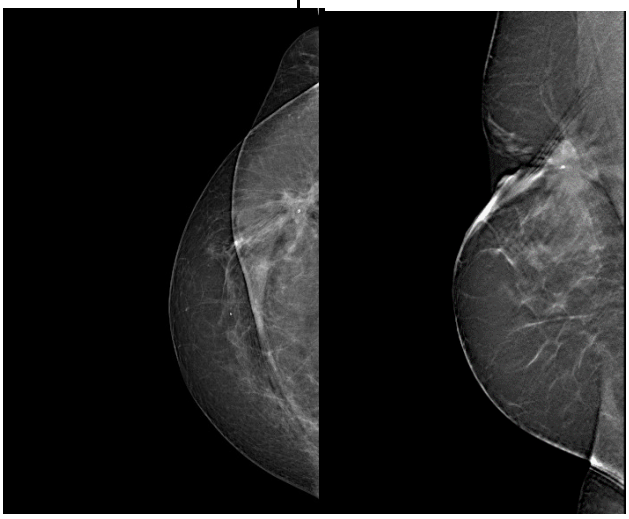

Fig 5: Mammography CC and MLO of right breast, irregular mass with spiculated margins in an area of architectural distortion in the upper outer quadrant after surgery, retraction and thickening of the skin.

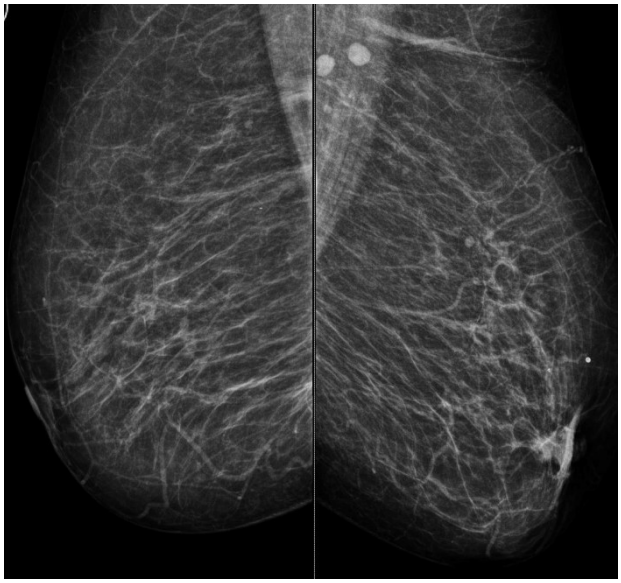

Fig 6: Mammography MLO of both breasts, ovoid mass with indistinct margins behind the nipple, retraction and thickening of the skin.

Breast MRI

Through this imaging modality, in the immediate post-surgery period the presence of a liquid signal collection can be noticed with enhancement of the neighboring tissue following the path of the surgical wound. The appearance of this lesion on MRI depends on the age of the hematoma with variable signal on T1 and T2 series. [29]

Up to about 6-9 months after surgery, the enhancement in the surgical wound may be appreciable, but after 10-18 months this will tend to a drastic reduction. [30]

Recurrence of the disease will appear with malignant characteristics, as a mass lesion, a space-occupying structure with convex-outward contour which may or not displace or otherwise affect the surrounding normal breast tissue, within or in close proximity to the surgical scar. [31]

It's characterized by suspicious enhancement, homogeneous or heterogeneous, with rapid wash-in with rapid wash-out or late plateau [32].

Otherwise it can appear as a non-mass lesion with focal, linear, segmental, regional, multiple regions, or diffuse distribution and characterized by homogeneous, heterogeneous, clumped, or clustered ring enhancement. [33,34]

Fig 7: Breast MRI, T1 and T2 series, mass lesion in the inferior inner quadrant.

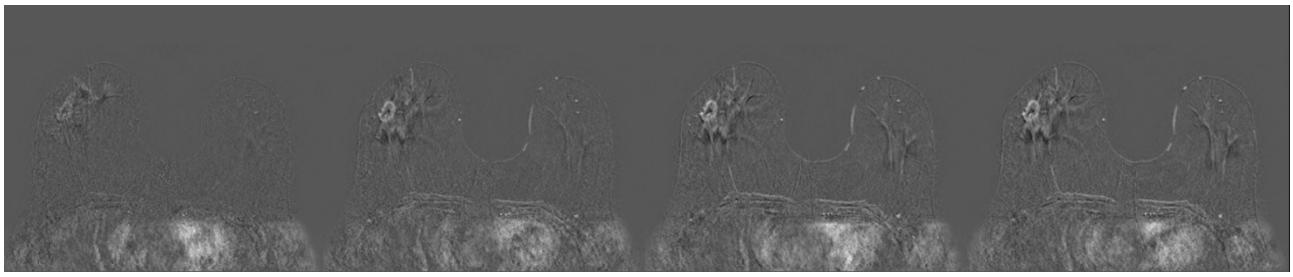

Fig 8: Breast MRI, axial subtracted image from the dynamic T1 weighted gradient-echo series, rim enhancement of mass lesion in the inferior inner quadrant

Nuclear Medicine Imaging

The role of functional imaging with nuclear medicine techniques oncology [35-38] (and in breast cancer recurrence [39]) is well established and continues to expand rapidly. [40] Nuclear medicine imaging techniques have an advantage, since they by principle are functional modalities, using radioactive pharmaceuticals to map physiological processes. [41] Moreover, changes in function often precede anatomical changes, thereby allowing for evaluation of biological changes in tissues on shorter timescales.[42] This is typically applied for evaluating the response of tumours to treatment. [43].

In breast cancer, functional techniques which do not depend on the anatomical appearances of the breast, like scintimammography, may have a role in this clinical setting, and could be an useful complement to radiological imaging.

The utilization of PET for prediction of treatment response to primary chemotherapy is an area of active research. [44]

In this diagnostic scenario, dominated by morphostructural techniques, radionuclide procedures play a secondary role both using gamma emitters, as Tc-99m sestamibi (MIBI), or Positron Emission Tomography (PET) with F-18 fluorodeoxyglucose (FDG) or other radiotracers beyond FDG. Compared to conventional imaging, FDG-PET has been shown to be more sensitive and specific in detecting distant metastatic disease. [45]

Above all, the new hybrid techniques such as PET/MRI, make it possible to obtain excellent information about neoplasms in order to planning the best possible treatment. [46]

In a single study that require a relatively short time, PET/MRI allows to create images with a high-resolution power that put together great information about both morphological and metabolic/physiologic aspects using different kind of labeled tracers. [47]

Bone scintigraphy is a very sensitive method for detecting skeletal metastases, although the specificity is often limited and abnormal findings require further evaluation e.g. via plain film radiographs. [48]

Radioguided surgery enables a surgeon to identify lesions or tissues that have been preoperatively marked with radioactive substances. [49,50] The Radioguided Occult Lesion Localization technique has been widely used to identify the sentinel lymph node and occult lesions in patients with breast cancer. Sentinel node biopsy has become accepted as a reliable method of predicting the status of the axilla in early stages of breast cancer.

FOLLOW UP

The initial phase of follow-up for patients presenting with a palpable lump is based on a thorough medical history including any post mastectomy procedures. [51]

After obtaining a full clinical history combined with an accurate physical examination, the analysis of palpable masses through imaging is indicated.

However, there is no solid scientific confirmation that materializes the benefit in the remaining patients who undergo follow-up [52].

From the analysis of the literature, it's evident that the accurate anamnestic collection and the clinical breast examination show a high rate of tumor recurrence detection.

After the end of therapy, the AIOM guidelines, following the recommendations of international scientific societies, suggest patient visits scheduled as follows: every 3-6 months in the first three years, every 6-12 months in the following two years, and every year thereafter. [53]

The role of breast ultrasound in the follow-up of the operated patient is not supported by strong scientific evidence.

Furthermore, the breast ultrasound supplementary to the mammography examination was associated with an increase in the rate of false positives [54]

Although there is a paucity in the literature on the use of breast ultrasound in the follow up of the breast after surgery, consecutive examinations at the site of surgery and ipsilateral axillary cavity in asymptomatic women, showed a cancer detection rate of 2.1% per patient. [55]

However, in some patients, especially in follow-up patients who present with a palpable nodule, the results of the ultrasound are often diriment and for this reason this is the imaging modality indicated ensuring in most patients a diagnosis without further investigation.

In fact, ultrasound is the initial step for evaluating palpable masses in most patients after mastectomy, as it has been shown to have a negative predictive value of 97%, it does not involve ionizing radiation, and it is more comfortable for patients than mammography; hence it is the initial imaging modality of choice.

In conclusion, although there are few studies about imaging modality recommended for patients with palpable masses after mastectomy, available studies generally suggest initial approach with ultrasound imaging [56]

The use of mammography examination in the follow-up of women with previous breast cancer is associated with a strong reduction in mortality. Mammography retains the advantage of being able to be performed after autologous reconstruction or prosthetic implantation.

It is in fact essential in the early diagnosis of both breast recurrence and secondary tumors.

In the surveillance program of patients in follow up for previous breast cancer, annual mammography reduces the risk of death.

Even if the guidelines suggest an annual mammography check-up at the end of treatment, there is no scientific evidence that defines the adequate interval between checks.

Furthermore there is no patient age threshold to suggest the possible suspension of surveillance breast imaging and prudently it is recommended for all surviving patients with a reasonable life expectancy.

Mammography can be extremely useful and indicated when the ultrasound examination is not conclusive.

For example, it is of particular importance when the ultrasound features suggest fat necrosis but are not so classic as to be certain.

While fat necrosis has variable ultrasound features, mammography findings are often diagnostic.

There is insufficient evidence to support mammography screening of the post-mastectomy side.

The controversy is that although some retrospective studies have shown that mammography increase cancer detection rate in post-mastectomy patients, other studies have shown no benefit.

Though mammography can be challenging in patients after mastectomy without reconstruction (implant, autologous or both), it is often still possible to perform full range views of a palpable area of concern.

Moreover, annual screening with mammography and sometimes with DBT mammography is recommended for the contralateral native breast.

The association of DBT, to integrate standard mammography images, helps in the study of the breast as it addresses some of the limitations encountered with standard 2D view of the mammography. In addition to standard images, DBT allows for the creation and the display of reconstructed thin-section images that can reduce masking effect of overlapping normal tissue to the lesion and reveal the true nature of it, reducing false positive results.

Therefore, when possible to be performed, mammography remains a valid ally in the examination of the breast in follow-up women, eventually integrated by DBT mammography.

There is no evidence about the benefits of the breast MRI study of the operated patient compared to the mammography study.

About the screening or follow-up, there is insufficient support in the literature to justify the use of MRI with or without the administration of intravenous contrast, particularly for post-mastectomy unreconstructed breast screening.

Therefore, in the patient's follow-up, breast magnetic resonance imaging is not recommended as a diagnostic modality, but it has a valid indication in some cases.

In fact, it can be integrative when there is a strong suspicion of recurrence from a clinical point of view not supported by other diagnostic investigations.

When the results of the ultrasound and mammography are not clear, magnetic resonance imaging can be a useful tool for problems solving.

Additionally, women with breast cancer risk factors, such as BRCA positive women or women with a strong family and personal history of breast cancer, age at cancer diagnosis, breast density, can undergo contrast-enhanced MRI of native breast for detection and the characterization of neoplasms and in this context, the post-surgery breast can be evaluated by magnetic resonance imaging [57].

The role of MRI in the evaluation of palpable masses in patients after mastectomy is also limited.

According to the practical guidelines of the American College of Radiology, the use of magnetic resonance imaging of the breast is recommended in the evaluation of recurrence when it is in addition to clinical or imaging findings and when the clinical, mammography and / or ultrasound modalities are inconclusive; also in the characterization of the lesions when other diagnostic imaging modalities are not diriment and therefore the biopsy cannot be performed; or in the evaluation of suspected cancer recurrence in patients with tissue transfer flaps.

Therefore, in a scenario where biopsy may be difficult in a patient with autologous reconstruction or prosthetic implant where the lesion is in a deep location or in the immediate vicinity of the implant, or if a lesion is difficult or inaccessible to ultrasound-guided biopsy and equivocal to ultrasound, the magnetic resonance could confirm the presence of the lesion, strengthen the radiological suspicion before surgery or excisional biopsy and help to determine the complete extent of the disease or even be a tool through which carry out the biopsy. However, the need for MRI in this context would be rare.

Conclusion

There is considerable overlap between the imaging features of recurrence disease and benign postoperative findings in patients with or without breast reconstruction. Disease recurrence in patients after mastectomy may have variable imaging findings, and it is essential that radiologists have a thorough understanding of the imaging features of benign and malignant masses after mastectomy.

In cases where the results from breast ultrasound are not classic, however, other ways of solving problems are useful, including mammography and magnetic resonance imaging.

In cases where results are not characteristic in multiple imaging modalities, biopsy may be warranted.

References

1. Samantha L. Heller, MD, PhDa, Ana P. Lourenco, MDb, Daymen S. Tuscano, MDn, Linda Moy, MD, et al. ACR Appropriateness Criteria Imaging After Mastectomy and BreastReconstruction, American College of Radiology 2020, 1546-1440/20
2. Katz A, Strom EA, Buchholz TA, et al. Locoregional recurrence patterns after mastectomy and doxorubicin-based chemotherapy: implications for postoperative irradiation. J Clin Oncol 2000;18(15):2817–2827.
3. Gieni M, Avram R, Dickson L, et al. Local breast cancer recurrence after mastectomy and immediate breast reconstruction for invasive cancer: a meta-analysis. Breast 2012;21(3):230–236.
4. Rissanen TJ, Mäkäräinen HP, Mattila SI, Lindholm EL, Heikkinen MI, Kiviniemi HO. Breast cancer recurrence after mastectomy: diagnosis with mammography and US. Radiology 1993;188(2):463–467.
5. Khatcheressian JL, Hurley P, Bantug E, et al. Breast cancer follow-up and management after primary treatment: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2013;31(7):961-5.
6. de Bock GH, Bonnema J, van der Hage J, et al. Effectiveness of routine visits and routine tests in detecting isolated locoregional recurrences after treatment for early-stage

invasive breast cancer: a meta-analysis and systematic review. J Clin Oncol. 2004; 22(19):4010-8.

7. Montgomery DA, Krupa K, Cooke TG. Follow-up in breast cancer: does routine clinical examination improve outcome? A systematic review of the literature. Br J Cancer 2007;97(12):1632-41.
8. Di Grezia G., Somma F., Serra N., Reginelli A., Cappabianca S., Grassi R., Gatta G. Reducing costs of breast examination:Ultrasound performance and inter-observer variability of expert radiologists versus residents. Cancer Investigation (2016), 34(7),pp.355-360 doi 10.1080/07357907.2016.1201097
9. Reginelli A., Calvanese M., Ravo V., Di Franco R., Silvestro G., Gatta G., Squillaci E., Grassi R., Cappabianca S. Management of breast cancer in elderly patients. International Journal of Surgery (2014), 12(S2), pp.S187-S192 doi 10.1016/j.ijsu.2014.08.344
10. La Forgia D., Fausto A., Gatta G. Di Grezia G., Faggian A., Fanizzi A., Cutrignelli D., Dentamaro R., Didonna V., Lorusso V., Massafra R., Tangaro S., Mazzei M.A. Elite VABB 13G: A new ultrasound.guided wireless biopsy system for breast lesions. Technical characteristics and comparison with respect to traditional core-biopsy 14-16G systems.Diagnostics (2020), 10(5) art. N. diagnostics10050291 doi 10.3390/diagnostics10050291
11. Di Grezia G., Gatta G., Brunese L., Falco G. State of the art in integrated breast Imaging. BioMed Research International (2019), art. N. 7596059 doi 10.1155/2019/7596059
12. Falco G., mele S., Zizzo M., Di Grezia G., Cecinato P., Besutti G., Coiro S., Gatta G., Vacondio R., Ferrari G. Colonic metastasis from breast carcinoma detection by CESM and PET/CT. A case report. Medicine (US) (2018),97(21), art. N. e0888
13. Vestito A., Mangieri F.F., Gatta G., Moschetta M., Turi B., Ancona A. Breast carcinoma in elderly women. Our experience. Il Giornale di Chirurgia (2011), 32(10) pp. 411-416 ISSN:03919005
14. Di Grezia G., Romano T., De Francesco F., Somma F., Rea G., Grassi R. Gatta G. Breast ultrasound in the management of gynecomastia in Peutz-Jeghers syndrome in monozygotic twins: Two case reports. Journal of Medical Case Reports (2014) 8(1) art. N. 440 doi 10.1186/1752-1947-8-440
15. Schootman M, Jeffe DB, Lian M, et al. Surveillance mammography and the risk of death among elderly breast cancer patients. Breast Cancer Res Treat. 2008;111(3):489-96.
16. Lash TL, Fox MP, Silliman RA. Reduced mortality rate associated with annual mammograms after breast cancer therapy. Breast J. 2006;12(1):2-6.
17. Grunfeld E, Noorani H, McGahan L, et al. Surveillance mammography after treatment of primary breast cancer: a systematic review. Breast 2002;11(3):228-35.
18. Orel SG, Fowble BL, Solin LJ. Breast cancer recurrence after lumpectomy and radiation therapy for early- stage disease: prognostic significance of detection method. Radiology 1993;188(1):189-94.
19. Abner AL, Recht A, Eberlein T, et al. Prognosis following salvage mastectomy for recurrence in the breast after conservative surgery and radiation therapy for early-stage breast cancer. J Clin Oncol. 1993;11(1):44-8.
20. Montgomery DA, Krupa K, Jack WJ, et al. Changing pattern of the detection of locoregional relapse in breast cancer: the Edinburgh experience. Br J Cancer 2007;96(12):1802-7.
21. Houssami N, Abraham LA, Miglioretti DL, et al. Accuracy and outcomes of screening mammography in women with a personal history of early-stage breast cancer. JAMA 2011;305(8):790-9.
22. Mellink WA, Holland R, Hendriks JH, et al. The contribution of routine follow-up mammography to an early detection of

asynchronous contralateral breast cancer. Cancer 1991;67(7):1844-8.

23. Ancona A., Capodieci M., Galiano A., Mangieri F., Lorusso V., Gatta G. Vacuum-assisted biopsy diagnosis of atypical ductal hyperplasia and patient management. Radiologia Medica (2011), 116(2), pp.276-291 doi 10.1007/s11547-011-0626-9

24. Sardu C.,Gatta G.,Pieretti G., Viola L., Sacra C., Di Grezia G., Musto L., Minelli S., La Forgia D., Capodieci M., Galiano A., Vestito A., De Lisio A., Pafundi P.C., Sasso F.C., Cappabianca S., Nicoletti G., Paolisso G., Marfella R. Pre-menopausal breast fat density might predict MACE during 10 years of follow up:The BRECARD Study. JACC Cardiovascular Imaging (2021), 14 (2), pp.426-438 doi 10.1016/j.jcmg.2020.08.028

25. La Forgia D., Catino A., Fausto A., Cutrignelli D., Fanizzi A., Gatta G., Losurdo L., Maiorella A., Moschetta M., Ressa C., Scattone A., Portincasa A. Diagnostic challenges and potential early indicators of breast periprosthetic anaplastic large cell lymphoma. A case report. Medicine (2020), 99 (30)

26. La Forgia D., Catino A., Dentamaro R., Galetta D., Gatta G., Losurdo L., Massafra R., Scattone A., Tangaro S.,Fanizzi A.Role of the contrast-enhanced spectral mammography for the diagnosis of breast metastases from extramammary neoplasms. Journal of B.U.O.N., (2019), 24(4), pp. 1360-1366 ISSN:11070625

27. Gatta G., Di Grezia G., Ancona A., Capodieci M., Coppolino F., Rossi C., Feragalli B., Iacomino A., Cappabianca S.,Grassi R. Underestimation of atypical lobular hyperplasia and lobular carcinoma in situ at stereotaxic 11-gauge vacuum-assisted breast biopsy. European Journal of Inflammation (2013), 11(3) pp.825-835

28. Ferraro G.A., Romano T., De Francesco F., Grandone A., D'Andrea F., Giudice E.M.D., Cataldo C., Gatta G., Di Grezia G. Perrone L., Nicoletti G. Management of prepubertal gynecomaastia in two monozygotic twins with Peutz-Jeghers syndrome: from aromatase inhibitors to subcutaneous mastectomy. Aesthetic Plastic Surgery (2013), 37(5), pp.1012-1022.

29. Quinn EM, Coveney AP, Redmond HP. Use of magnetic resonance imaging in detection of breast cancer recurrence: a systematic review. Ann Surg Oncol. 2012;19(9):3035-41.SEP23.

30. Berg WA, Zhang Z, Lehrer D, et al. Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. JAMA 2012;307(13):1394- 404.

31. Yilmaz MH, Esen G, Ayarcan Y, et al. The role of US and MR imaging in detecting local chest wall tumor recurrence after mastectomy. Diagn Interv Radiol 2007;13:13-8.

32. Peng C, Chang CB, Tso HH, Flowers CI, Hylton NM, Joe BN. MRI appearance of tumor recurrence in myocutaneous flap reconstruction after mastectomy. AJR Am J Roentgenol 2011;196(4):W471–W475.

33. Moy L, Elias K, Patel V, et al. Is breast MRI helpful in the evaluation of inconclusive mammographic findings? AJR Am J Roentgenol 2009;193(4):986–993.

34. Devon RK, Rosen MA, Mies C, Orel SG. Breast reconstruction with a transverse rectus abdominis myocutaneous flap: spectrum of normal and abnormal MR imaging findings. Radiographics 2004;24(5):1287–1299.

35. Cuccurullo V, Di Stasio GD, Cascini GL. PET/CT in thyroid cancer - the importance of BRAF mutations. Nucl Med Rev Cent East Eur. 2020;23(2):97-102.

36. Briganti V, Cuccurullo V, Berti V, Di Stasio GD, Linguanti F, Mungai F, Mansi L. 99mTc-EDDA/HYNIC-TOC is a New Opportunity in Neuroendocrine Tumors of the Lung (and in other Malignant and Benign Pulmonary

Diseases). Curr Radiopharm. 2020;13(3):166-176.

37. Cuccurullo V, Di Stasio GD, Mansi L. Physiopathological Premises to Nuclear Medicine Imaging of Pancreatic Neuroendocrine Tumours. Curr Radiopharm. 2019;12(2):98-106.
38. Briganti V, Cuccurullo V, Di Stasio GD, Mansi L. Gamma Emitters in Pancreatic Endocrine Tumors Imaging in the PET Era: Is there a Clinical Space for 99mTc-peptides? Curr Radiopharm. 2019;12(2):156-170.
39. Cuccurullo V, Cascini GL, Mansi L. Structural, pathophysiological and clinical aspects of diagnostic imaging in breast recurrence: the breast after treatment. Q J Nucl Med Mol Imaging. 2013 Dec;57(4):322-31.
40. Cuccurullo V, Faggiano A, Scialpi M, Cascini GL, Piunno A, Catalano O, et Al.Questions and answers: what can be said by diagnostic imaging in neuroendocrine tumors? Minerva Endocrinol. 2012 Dec;37(4):367-77.
41. Cuccurullo V, Di Stasio GD, Cascini GL, Gatta G, Bianco C. The Molecular Effects of Ionizing Radiations on Brain Cells: Radiation Necrosis vs. Tumor Recurrence.Diagnostics (Basel). 2019 Sep 24;9(4):127.
42. Cuccurullo V, Di Stasio GD, Prisco MR, Mansi L. Is there a clinical usefulness for radiolabeled somatostatin analogues beyond the consolidated role in NETs? Indian J Radiol Imaging. 2017 Oct-Dec;27(4):509-516.
43. Cuccurullo V, Prisco MR, Di Stasio GD, Mansi L. Nuclear Medicine in Patients with NET: Radiolabeled Somatostatin Analogues and their Brothers. Curr Radiopharm. 2017;10(2):74-84.
44. Kitson SL, Cuccurullo V, Ciarmiello A, Mansi L. Targeted Therapy Towards Cancer-A Perspective. Anticancer Agents Med Chem. 2017;17(3):311-317.
45. Cuccurullo V, Di Stasio GD, Schillirò ML, Mansi L. Small-Animal Molecular Imaging for Preclinical Cancer Research: PET and SPECT. Curr Radiopharm. 2016;9(2):102-13.
46. Mansi L, Cuccurullo V, Ciarmiello A. From Homo sapiens to Homo in nexu (connected man): could functional imaging redefine the brain of a "new human species"? Eur J Nucl Med Mol Imaging. 2014 Jul;41(7):1385-7.
47. Mansi L, Ciarmiello A, Cuccurullo V. PET/MRI and the revolution of the third eye. Eur J Nucl Med Mol Imaging. 2012 Oct;39(10):1519-24.
48. Cuccurullo V, Cascini GL, Tamburrini O, Rotondo A, Mansi L. Bone metastases radiopharmaceuticals: an overview. Curr Radiopharm. 2013 Mar;6(1):41-7.
49. Parmeggiani D, Gambardella C, Patrone R, Polistena A, De Falco M, Ruggiero R, et Al. Radioguided thyroidectomy for follicular tumors: Multicentric experience. Int J Surg. 2017 May;41 Suppl 1:S75-S81.
50. Cuccurullo V, Di Stasio GD, Mansi L. Radioguided surgery with radiolabeled somatostatin analogs: not only in GEP-NETs. Nucl Med Rev Cent East Eur. 2017;20(1):49-56.
51. Henry NL, Hayes DF, Ramsey SD, et al. Promoting quality and evidence-based care in early-stage breast cancer follow-up. J Natl Cancer Inst. 2014;106(4):1-7.
52. Schreve RH, Terpstra OT, Ausema L, et al. Detection of liver metastases. A prospective study comparing liver enzymes, scintigraphy, ultrasonography and computed tomography. Br J Surg 1984;71(12):947-9.
53. Cherah Pryce, DO1,and Wendi Owen, MD1 Palpable Masses after Mastectomy: Differentiating Benign Postoperative Findings from Recurrent Disease. Society of Breast Imaging 2020, Vol. 2, Issue 5, 501–510
54. Rissanen TJ, Makarainen HP, Mattila SI, Lindholm EL, Heikkinen MI, Kiviniemi HO. Breast cancer recurrence after mastectomy: diagnosis with mammography and US. Radiology 1993;188:463-7.

55. Dashevsky BZ, Hayward JH, Woodard GA, Joe BN, Lee AY. Utility and outcomes of imaging evaluation for palpable lumps in the postmastectomy patient. AJR Am J Roentgenol 2019;213(2):464–472.

56. Rissanen TJ, Mäkäräinen HP, Mattila SI, Lindholm EL, Heikkinen MI, Kiviniemi HO. Breast cancer recurrence after mastectomy: diagnosis with mammography and US. Radiology 1993;188(2):463–467.

57. Fajardo LL, Roberts CC, Hunt KR. Mammographic surveillance of breast cancer patients: should the mastectomy site be imaged? AJR Am J Roentgenol 1993;161:953-5.