Inclusion of brain in FDG PET/CT scanning techniques in cancer patients: Does it obviate the need for dedicated brain imaging?

Metastases to the brain can affect about 10-20% cancer patients.[1] Rising incidence of brain metastases in recent years is related to improved survival rates as a result of advances in cancer therapy and development of more sensitive diagnostic imaging techniques.[2] In patients with extracranial malignancies detection of brain metastases is very important in deciding further diagnostic procedures, planning therapeutic strategies and also to ascertain prognosis. Computerized tomography (CT) and magnetic resonance imaging (MRI) are the modalities which have been traditionally used to assess metastatic disease to the central nervous system. It is generally accepted that MRI (contrast enhanced) is superior to CT scan (contrast enhanced) in the diagnosis of brain metastases. An inherently better soft tissue contrast resolution, stronger contrast enhancement, lack of bone artifacts and partial volume effects and direct multiplanar imaging enables MRI to pick up smaller sized as well as more number of metastases than a CT scan.[3,4]

Positron emission tomography (PET) using 18 F-Flurodeoxyglucose (FDG) has been used for staging and restaging of several cancers. With the advent of combined PET/CT the accuracy of the modality has been further improved due to the combination of anatomic and functional information in one single study. The growth of PET/CT in oncology has been so rapid in the last decade that it has been recommended as the first line imaging modality in staging, restaging and response assessment of different cancers.[5] In oncology a whole body PET/CT is typically performed from the skull base to upper thigh, often referred as eyes -to -thighs or lips- to- hips.[6] The popularity of PET/CT is primarily due to its whole body imaging capability which enables metastatic screening of a large part of the body. However the term whole body is misleading as several parts of the body are left out including the brain in majority of whole body PET/CT protocols. One of the important reasons for excluding brain is the relatively lower sensitivity of FDG for brain metastases, due to limited spatial resolution of PET scanners and the intense FDG distribution normally seen in the brain tissue.[7] Brain metastases are identified on PET as discrete hypermetabolic or hypometabolic foci relative to the FDG uptake in the grey matter [Figure 1].The role of FDG PET in the detection of brain metastasis has been often questioned in literature and found to be limited owing to its low sensitivity. Out of the total number of metastatic lesions detected by MRI, PET was able to detect only 61-68 % lesions according to some reports,[8,9] emphasizing the superior ability of MRI to diagnose brain metastases [Figure 2]. The primary reason for the poor sensitivity of PET mentioned in these studies was the small size of the brain lesions (<1cms), exactly the situation where MRI outperforms other modalities. In a study of more than thousand patients with various malignancies, unsuspected brain metastases were detected in only 0.4% patients using FDG PET.[10] A study of 500 patients evaluating the incremental value of an extended whole body PET/CT protocol (including the brain), detected only 1 patient with asymptomatic brain metastases.[11]

Excluding brain from the PET field of view (FOV) during screening of asymptomatic cancer patients may not be necessarily harmful, since the detection rate of unsuspected brain metastases has been reported to be very low according to a large study by Ludwig *et al*,[10] which evaluated the role of FDG in incidentally detected brain lesions in patients with body malignancies. Owing to the overwhelming evidence in literature which questions the ability of FDG PET to detect brain metastases; its use was and has been majorly restricted in this clinical setting. However, with the introduction of intravenous contrast in several PET/CT protocols, entire body coverage (including head) due to availability of the faster scanners, the CT component of the PET/CT study can actually function as an independent CT scan of the brain and it has the potential to obviate the need for a dedicated diagnostic Brain CT.[12] When such an IV contrast extended PET/CT protocol is used, the overall yield of the combined study in detecting brain metastasis will be certainly higher when compared to the reported low sensitivity of a PET alone study. However, it will still pale in comparison to the superior lesion detectability and characterisation of MRI. Since MRI has been proven to be more accurate when compared individually with CT Brain and also PET[3,4,8,9] for detection of brain metastases, it is but natural that it will continue to maintain that superiority even over a contrast PET/CT. This has been conclusively proven in a recent study on lung cancer patients where addition of Brain MRI to PET/CT resulted in the detection of brain metastases in additional 7% (32/442) patients.[13] Thus the incremental benefit

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due to the addition of benefits of a contrast CT in a PET study should be viewed with caution. The dangers of a false sense of security arising due to negative PET/PET/CT results should be avoided and the referring physician should be educated about the limitations of the study so as to avoid errors in treatment due to potentially misleading PET/PET/CT results.

Brain metastases are commonly seen in primary tumors of the lung, kidney, breast, skin (melanoma) and GI tract. Amongst these, the frequency of brain metastases is highest in lung cancer.[2,14,15] Since up to 10% patients with small cell lung cancer can have brain metastases at the time of diagnosis,[16] except for small cell lung cancer routine screening for brain metastases has

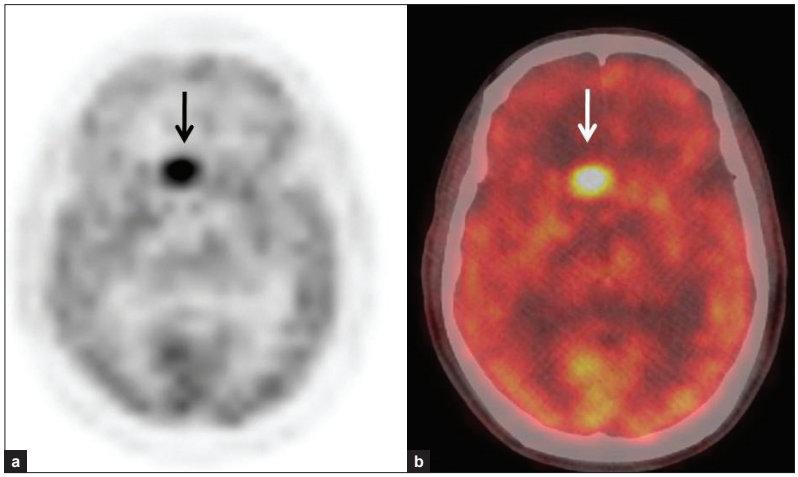

Figure 1: Treated case of melanoma of the toe. Focus of intense FDG uptake is seen in the midline anterior to the third ventricle on axial PET (a) and fused PET/CT images (b) suggesting the diagnosis of cerebral metastasis

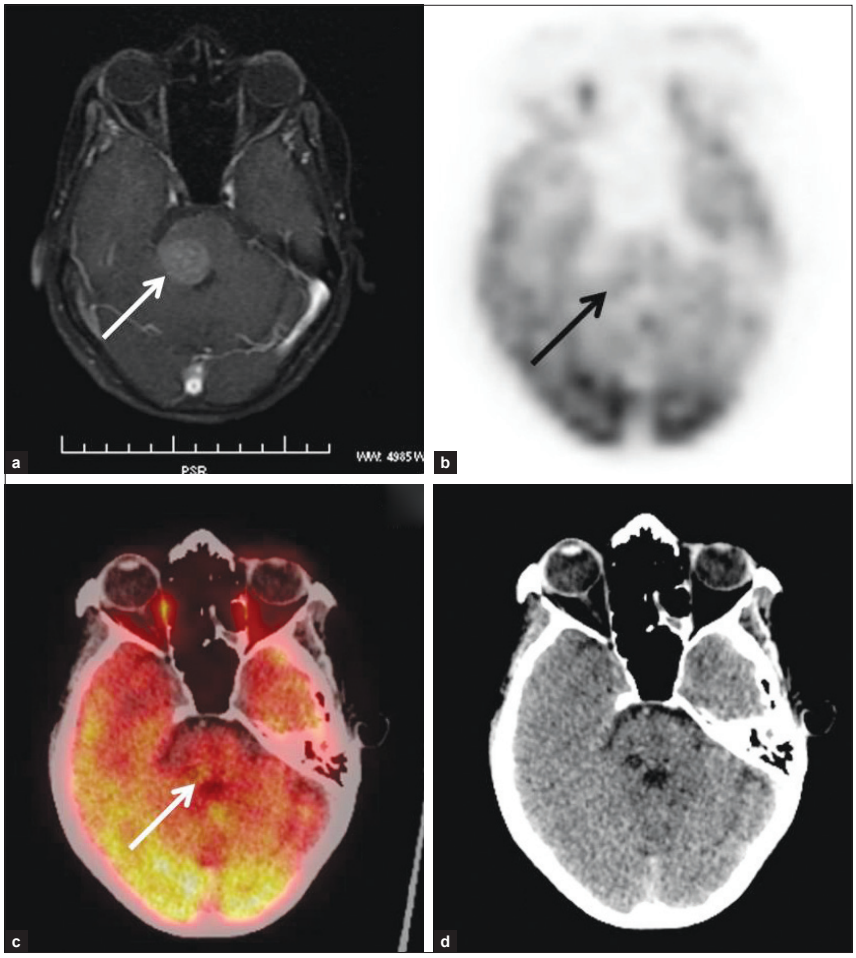

Figure 2: Operable case of lung cancer for preoperative staging for brain metastases. Contrast enhanced T1 W axial MRI (a) shows a well-defined enhancing metastatic lesion in the pons (arrow). Lesion is not appreciated on axial PET and fused PET/CT images (b and c)

not been recommended across all cancer subtypes. For non-small cell lung cancers, though there is no definite consensus, brain imaging is used more effectively in patients with neurological symptoms, or prior to treatment with a curative intent for early tumors. Irrespective of the negative result on FDG PET/CT, an MRI of the brain is necessary if: a) the patient has CNS symptoms, whatever the type of cancer; b) if the patient is staged for carcinoma of the lung (which has a high propensity for brain metastases) and a potentially curative therapy is planned based on standard imaging; c) in a patient with brain metastasis where an optimum therapeutic approach has to be decided as regards the decision to operate or primarily irradiate.

As the evidence in favour of PET/CT increases in literature and with more widespread availability of PET/CT scanners, there will be more pressure from the clinical fraternity towards the use of PET/CT as a single stop shop metastatic imaging modality. Though this trend is encouraging, beneficial to patients and evidence based in most situations, when it comes to imaging of brain metastases the clinician should be educated and informed about the possible pitfalls of PET interpretation and at the same time judicious use of standard brain imaging techniques needs to be encouraged.

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Nilendu C Purandare

Bio-Imaging Unit, Tata Memorial Hospital, Parel,
Mumbai 400 012, Maharashtra, India.
E-mail: nilpurandare@gmail.com

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