

Letter to the Editor

Indirect evidences of functionality of insulinoma on FDG-PET: The 'whole body-metabolism' advantage and its clinical implications

Sir,

The diagnosis and localization of functioning insulinoma is frequently a clinical challenge to physicians, surgeons, and radiologists alike. An early accurate diagnosis is of pivotal importance in preventing disease-related complications and morbidity. Several tracers have been utilized to explore their potential in this area including 4-Dihydroxy-6-fluoro-Dlphenylalanine (F-DOPA), ^{68}Ga -DOTA-Dphe-1-Tyr-3-octreotide (^{68}Ga -DOTATOC) and ^{11}C -5-hydroxy-L-tryptophan (C-5-HTP), as FDG-PET imaging for insulinomas are not very promising, which is

likely related to the low proliferate index of these tumor cells. While these tracers produce very good tumor visibility and can be used for the examination of both the thorax and abdomen, we herein describe the indirect clues on FDG-PET study that can give excellent information about the functionality of this group of tumors because of its unique ability to explore glucose metabolism in the whole body. The FDG-PET images of a known case of insulinoma are described. The FDG-PET image demonstrates relatively intense uptake in the heart and skeletal muscle [Figure 1]. A similar picture can be observed with respect to muscle and cardiac FDG uptake in patients of diabetes mellitus who had taken insulin along with the early morning breakfast. A patient of metastatic gastrointestinal tumor, who had such a history, is depicted in [Figure 2].

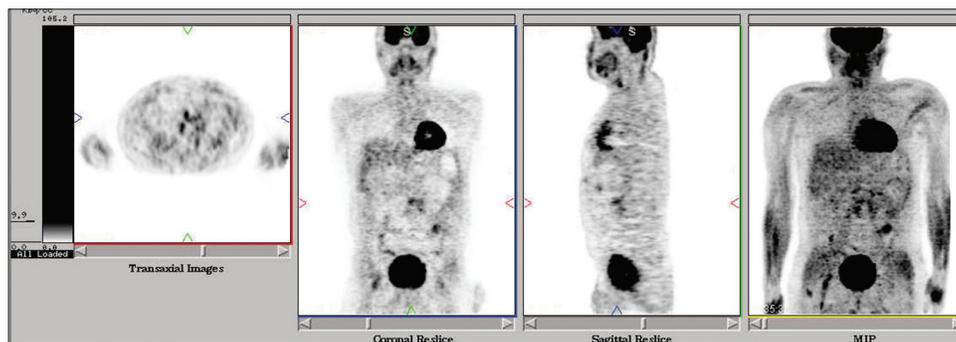


Figure 1: In this diagnosed patient of insulinoma, the FDG-PET image demonstrates relatively intense uptake in the heart and skeletal muscle, whereas the primary tumor is not visualized

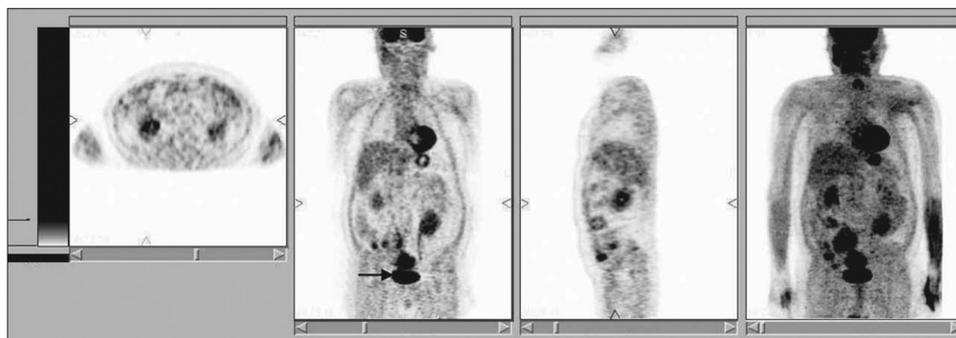


Figure 2: A 67-year-old male patient, a diabetic on insulin (who had his early morning dose of insulin around 6 hours back) and a diagnosed case of peritoneal GIST, who had a history of multiple surgeries previously and had been put on imatinib (3 months before) in view of multiple recurrent abdominal masses. The computed tomography (CT) scan of abdomen done 3 months previously demonstrated multiple soft tissue masses (prominent among them were a nodular mass measuring 6.7 × 6 cm just below the aortic bifurcation and another solid cystic mass measuring 5.1 × 3 cm in the pelvis along the right internal iliac chain Fluorodeoxyglucose (FDG)-PET (after 3 months of imatinib) in a patient of gastrointestinal stromal tumor demonstrating persistent avid FDG uptake in the abdominal masses indicating treatment failure. Note the FDG uptake in the skeletal muscles and heart, which is related to the insulin-dependent GLUT IV receptor activation in these tissues. The figure is reproduced with permission^[2]

Pancreatic endocrine tumors are clinically categorized into functioning or non-functioning according to the presence of symptoms of hormone hypersecretion. The two important characteristics of FDG-PET scans in the setting of functioning insulinoma are increased FDG uptake in the muscles and the myocardium.^[1,2] Myocardial glucose kinetics is related with feeding state, insulin, and free fatty acid levels and heart work. Glucose enters muscle through *insulin-dependent* glucose transporter 4 (GLUT4). It is important to recognize that different mechanisms work for enhanced GLUT 4 receptors in the patients of insulinoma and insufficient oxygen availability or energy compromise. While in the former, insulin increases GLUT 4 exocytosis through phosphatidylinositol 3-kinase and serine/threonine protein kinase (Akt) pathway, in the latter, energy deprivation retards GLUT 4 endocytosis through 5'-adenosine monophosphate-activated protein kinase (AMPK) and calcium inputs.

While tumor FDG uptake (if present in the baseline scan) can be used for monitoring therapeutic efficacy, the uptake in both these additional sites (esp. muscles) can be utilized for monitoring functionality of the tumor, particularly when medical therapy like diazoxide or mTOR inhibitor everolimus has been administered. In a recent study, it has been observed that everolimus reduced tumor and muscle ¹⁸F-FDG uptake after 2 weeks by, respectively, 26 ± 14% and 19 ± 41% and after 5 months by 31 ± 13% and 27 ± 41%.^[1] While cardiac FDG uptake is usually variable,

but in an identical internal metabolic milieu (i.e., when identical patient preparation schedule is maintained among the scans) in a particular patient, this also can form an additional complementary parameter for monitoring therapeutic efficacy. This, however, requires to be examined further in prospective setting.

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