Preface

PET/Computed Tomography-based Intervention

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Editor

PET/computed tomography (CT) plays an important role in staging, treatment response evaluation, restaging, and prognostication of various cancers. The synergistic use of structural and functional imaging provides excellent information regarding the disease. Changes at the molecular and cellular levels can be imaged effectively through specific radiopharmaceuticals using PET/CT for evaluating the effectiveness of chosen clinical treatment plans. Therefore, PET/CT allows the individualization of treatment for patients with cancer. These targeted therapies are aimed at various receptors, enzymes, or pathways, and hence, are less toxic and more specific than conventional chemoradiotherapies. Molecular imaging with PET can visualize such targets or biochemical processes and/or their dysfunction using specific radiopharmaceuticals. These radiopharmaceuticals help in identification of the presence or absence of various targets in cancer cells for directed therapy, and thus, can help in determining the suitability of patients for targeted therapy. Various such radiopharmaceuticals have been developed and explored in the last decade or so of which imaging of the somatostatin receptor using gallium-68-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (68Ga-DOTA) peptides has gained considerable popularity. Other popular molecular imaging agents used for targeted therapy include 68Ga-prostate-specific membrane antigen (PSMA) PET/CT in patients with prostate cancer (PCa), and 16 α -[18F]-fluoro-17 β -estradiol (18F-FES) PET/CT in patients with breast cancer. Various PET radiopharmaceuticals directed against tyrosine kinase

receptor, such as 64Cu/89Zr-trastuzumab63 for HER2 and 64Cu/86Y/89Zr-cetuximab and 64Cu/86Y/89Zrpanitumumab for EGFR, are also gaining popularity as molecular imaging probes for individualized targeted therapies.

This issue of *PET Clinics* has been prepared in the hope that it will help in the understanding of the role of PET/CT as a molecular imaging modality that can help in determining the suitability of patients for targeted therapy with different agents and the role of PET/CT in selecting patients with appropriate treatment and response.

Drs Pattison and Hofman describe the role of 2-fluoro-2-deoxy-D-glucose F18 (FDG) PET/CT in targeted radionuclide therapy of endocrine malignancies. FDG-PET/CT is the most powerful prognostic indicator in common endocrine malignancies (including gastroenteropancreatic neuroendocrine tumors [NETs] and differentiated thyroid cancer) facilitating risk stratification and optimization of personalized therapy. In these malignancies, increased FDG uptake represents dedifferentiated disease. However, in endocrine malignancy, intense FDG uptake does not always indicate dedifferentiated disease. In pseudohypoxic pheochromocytoma and paraganglioma and oncocytic thyroid tumors, intense FDG avidity is noted due to intrinsic mitochondrial dysfunction.

Drs Taïeb, Garrigue, Bardiès, Esmaeel, and Pacak show various application and dosimetric requirements for 68Ga-labeled somatostatin analogues in targeted radionuclide therapy for gastroenteropancreatic neuroendocrine tumors. PET/CT using gallium-68-labeled SSTa is a popular

PET-based theranostic approach that provides prognostic information, selecting good candidates for peptide receptor radionuclide therapy (PRRT) and enabling tumor response assessment for PRRT. PRRT using ^{177}Lu -labeled SSTa has also shown promise in the treatment of advanced progressive grade 1 and 2 NETs. Theranostics of gastroenteropancreatic NETs based on ^{68}Ga -labeled SSTa PET imaging and targeted therapy applying PRRT with ^{90}Y -labeled and/or ^{177}Lu -labeled SSTa have paved the way for personalized medicine.

Drs Ceci, Castellucci, Graziani, Schiavina, and Fanti review the role of PET/CT in the individualization of the treatment of PCa. Choline is a promising PET agent for imaging of PCa. PET/CT using choline in patients with relapsed PCa show the site of tumor recurrence earlier than other conventional imaging techniques. It also helps to guide personalized therapies in patients with oligometastatic disease. The addition of choline PET/CT as a diagnostic modality in patients with PCa may affect significantly treatment strategies and patient management.

Drs Sharma, Kumar, and Alavi summarize the individualized targeted therapies aimed at various receptors, enzymes, or pathways. Various such radiopharmaceuticals have been developed and explored in the last decade or so, including imaging of the somatostatin receptor using ^{68}Ga -DOTA peptides, ^{68}Ga -PSMA PET/CT in the patients with PCa, and ^{18}F -FES PET/CT in patients with breast cancer. Various PET radiopharmaceuticals directed against tyrosine kinase receptor, such as $^{64}\text{Cu}/^{89}\text{Zr}$ -trastuzumab63 for HER2, and $^{64}\text{Cu}/^{86}\text{Y}/^{89}\text{Zr}$ -cetuximab and $^{64}\text{Cu}/^{86}\text{Y}/^{89}\text{Zr}$ -panitumumab for EGFR, are also gaining popularity as molecular imaging probes for individualized targeted therapies.

Dr López describes the role of PET/CT in the evaluation of transarterial chemoembolization, which is a minimally invasive procedure that deprives the tumor of its blood supply and is especially used for the treatment of unresectable hepatocellular carcinoma. During chemoembolization, PET/CT is a useful tool for early recognition of incomplete tumor destruction. It also detects recurrence earlier than the conventional imaging modalities. Thus, FDG-PET/CT is one of the most useful imaging modalities in patients undergoing transarterial chemoembolization.

Drs Bonichon, Godbert, Gangi, Buy, and Palusière share their experience using PET/CT in thermoablation techniques. Thermal ablation is more frequently used in oncology for primary and secondary cancer but is also used to destroy benign tumors. PET/CT plays an important role in the

follow-up to detect residual viable tissue and early detection of a relapse that can be re-treated by thermal ablation or other means. Postablation aspects have to be well known by the specialist in charge of image interpretation. All studies done based on thermal ablation conclude that PET/CT is a useful tool for early recognition of incomplete tumor destruction after thermal ablation.

Drs Gill, Pai, McKenzie, and Beriwal review the utility of PET/CT for radiotherapy treatment planning. Development and accessibility of PET/CT have considerably changed patient management in oncology, allowing for more accurate clinical staging and target delineation for radiotherapy. Integration with radiotherapy planning, either at the time of simulation or with image fusion, has enabled adaptive planning and has become an additive tool to ensure accurate target delineation. Considerable work has been completed to demonstrate the value of PET/CT for radiotherapy planning, showing that in several malignancies like head and neck carcinoma, lung carcinoma, and gynecologic malignancy, this approach can lead to more accurate tumor targeting and can alter radiotherapy plans significantly. Continued research is needed to establish uniform contouring guidelines and evaluate the clinical impact of PET-based planning, with regard to both toxicity and disease control.

Drs Houshmand, Boursi, Salavati, Simone, and Alavi describe the FDG-PET/CT in the assessment and prediction of radiation therapy-related complications. Radiation pneumonitis is a life-threatening acute and subacute complication of radiation therapy happening in 4% to 30% of patients and manifesting 1 to 6 months after radiation. Detection of radiation pneumonitis, sometimes challenged by using other clinical criteria, might be aided by accurate and quantitative PET parameters before or after RT. FDG-PET/CT has also been shown to be feasible for the assessment of cardiovascular adverse events, such as vascular inflammation and cardiomyopathies. PET/CT is a valuable imaging modality to detect the effects of RT on the human body and the evolution of the short-term and long-term complications of RT and chemotherapy.

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