PET/CT Imaging Beyond ^{18}F-FDG: ^{18}F and ^{68}Ga-labelled Tracers

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Fluorine-18 (^{18}F)-fluorodeoxyglucose (^{18}F-FDG) remains by far the most widely utilized tracer for PET imaging. Although the majority of ^{18}F-FDG PET imaging studies are performed in the field of oncology, a significant part of routine workload represent imaging studies in the field of neurology, infection and inflammation imaging and cardiology. Such broad use of the tracer reflects its polyvalent nature. However, polyvalence (and therefore non-specificity) can also be a disadvantage, preventing differentiation of malignant and infectious/inflammatory foci and/or physiological uptake in bodily tissues, localization of processes with inherently low glucose uptake and metabolism (such as well-differentiated neoplasms). Other ^{18}F and ^{68}Ga-labelled tracers are increasingly being used in clinical routine and investigational settings, aiming to evade shortcomings of ^{18}F-FDG.

^{18}F-fluorocholine (^{18}F-FCH) is a labelled phospholipid, reflecting cell membrane turnover. It is routinely used in patients with prostate cancer (PCA), which is mostly well-differentiated with poor ^{18}F-FDG uptake. Main indication for its use is biochemical recurrence of radically treated PCA; it is also used in initial staging of patients with high-risk PCA. Less common uses are in initial evaluation, staging and suspected relapse of hepatocellular carcinoma and brain tumours. Recently the radiopharmaceutical was introduced for parathyroid imaging.

^{18}F-fluoroethyltyrozine (^{18}F-FET) is an amino acid analog reflecting protein metabolism, well suited for imaging of brain neoplasms: its uses are initial evaluation, biopsy targeting, follow-up and suspected relapse after treatment. Its diagnostic performance is superior to ^{18}F-FDG and comparable to 11C-labelled amino acid tracers for the same indication.

^{18}F-fluorodeoxyphenylalanine (^{18}F-DOPA) is an amine precursor analog, taken up by tumours of neural crest origin. It is mostly used in initial evaluation, staging and suspected relapse of catecholamine-producing malignancies, such as pheochromocytoma and paraganglioma, as well as other neuroendocrine tumours (NETs), especially medullary thyroid cancer (MTC), and brain tumours. In addition, it reflects DOPA-decarboxylase activity and dopamine turnover in presynaptic neurons in basal ganglia, useful in evaluation of parkinsonian syndromes.

^{18}F-fluorotymidine (^{18}F-FLT) is a nucleotide analog reflecting DNA synthesis and therefore proliferation of tumour cells. Its main application is prediction and evaluation of response to therapy and prognosis, best explored in head and neck cancer, lung cancer and lymphomas. In spite of promising results, the tracer did not yet find broad or routine use.

^{18}F-sodium fluoride (^{18}F-NaF) is a revived tracer for bone imaging. It accumulates in remodeling, osteoblastically active bone tissue. In comparison to conventional bone scintigraphy, it was shown to be more sensitive for localization of bone metastases in prostate, breast and several other cancer types; experience in bone infection and inflammation is limited.

Gallium-68 (^{68}Ga) is a generator-produced radionuclide that allows synthesis of PET radiopharmaceuticals – various ^{68}Ga-labelled peptides – without an on-site cyclotron. Most commonly used ^{68}Ga-tracers are ^{68}Ga-labelled somatostatin analogs – DOTA-TOC, DOTA-TATE and DOTA-NOC, differing in the affinity for different somatostatin receptor (sstr) subtypes. They are used in initial evaluation, (re) staging, follow-up and treatment response, suspicion of relapse of NETs. As sstr analogs can also be labelled with a therapeutic radionuclide, yttrium-90 (^{90}Y) or lutetium-177 (^{177}Lu), imaging provides a unique opportunity for targeted peptide receptor radionuclide therapy (PRRT). ^{68}Ga-tracers for less common receptor subtypes, such as GLP-1 in insulinoma or CCK2 in MTC are being investigated.

In recent years, ^{68}Ga-labeled prostate-specific membrane antigen (^{68}Ga-PSMA) was introduced into prostate cancer imaging; superior accuracy in comparison to ^{18}F/^{11}C-choline was demonstrated in patients with biochemical relapse. In addition, first reports of advanced PCA theranostics using ^{68}Ga/^{177}Lu-PSMA have been published.

Several promising ^{68}Ga-labelled radiopharmaceuticals aimed at different targets (^{68}Ga-pentixafor, aimed at CXCR4 receptor, ^{6}8Ga-labelled RGD peptides, aimed at integrin receptors, etc.) are being investigated.

In summary, new ^{18}F and ^{68}Ga-labelled tracers significantly broaden the field of application of PET/CT in various oncological and non-oncological disorders.

References

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