Radiolabelled Amino Acids for PET Imaging

P. Laverman (Nijmegen)

Background
The currently preferred imaging modality for positron emission tomography (PET) in oncology is 2-[18F]fluoro-deoxyglucose (FDG). Increased accumulation of this deoxyglucose analogue in tumour cells is based on elevated glucose metabolism by tumour cells and subsequent trapping in the cells. To further characterize tumours, radiolabelled amino acids have been widely studied. An amino acid tracer should preferably have similar high uptake in tumour cells but should have low aspecific uptake in any normal tissues or other pathology than tumour. In the past years, several amino acids have been labelled with either carbon-11 (1) or fluorine-18 (2).

Amino acid uptake mechanisms
The number of radiolabelled amino acids under investigation is increasing and one of the major points of discussion is the underlying mechanism of the tumour visualisation. Whereas it is shown for some amino acids that they can be used to measure the protein synthesis rate, others aim to measure solely the rate of uptake of the amino acid into the cell. The differences between measuring the amino acid transport (rate) and protein synthesis rate with 11C or 18F-labelled amino acids will be discussed.

Clinical studies with radiolabelled amino acids
The most widely studied fluorinated amino acids are tyrosine analogs. Whereas L-2-[18F]fluorotyrosine is incorporated into proteins, other analogs, such as L-3-[18F]fluoro-α-methyl tyrosine (FMT) and O-(2-[18F]fluoroethyl)-L-tyrosine (FET) are not incorporated and thus measuring amino acid transport rate rather then protein incorporation rate. Especially, FET has been widely studied in patients with several tumour types (3). The second widely used amino acid is 6-[18F]Fluoro-L-dihydroxyphenylalanine (18F-DOPA) (4). Besides imaging of the dopaminergic system, this tracer is increasingly used for PET imaging of neuroendocrine tumours. The most extensively studied carbon-11 labelled amino acid is 11C-methionine (Met) (5). This tracer has proven good potential in PET imaging of brain tumours.

Conclusions
Radiolabelled amino acids (or analogs) may have a potential role in tumour characterisation rather than tumour staging, i.e., measuring the elevated amino acid transport in tumour cells. Like glucose metabolism, cell proliferation, tumour hypoxia, protein synthesis rate and gene expression, amino acid transport is one of the parameters which can be used to monitor tumour response.

References