# Clinical brain PET/CT scanning beyond FDG

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The most widely applied PET tracer is 2-[F-18]fluoro-2-deoxy-D-glucose (FDG) driven primarily by a demand in general oncology. In the brain this tracer can give important information in a range of clinical questions including brain tumours, and dementia.

**Brain tumours**

The most common indications for FDG in the work out in brain tumors are:

1. Evaluation of MR identified lesion. Is it neoplastic or benign?
2. Tumor grading.
3. Guide for optimal biopsy.
4. Malignant transformation.
5. Tumor recurrence/Treatment effects.
6. Treatment monitoring .

While the advantage FDG is its wide availability, the limitation is the unspecific qualities of the compound. FDG can be increased by regional epileptogenic activity, normal synaptic activity, and inflammation, and because the tumors are often infiltrative by nature it can be difficult to separate these effects. The ideal PET tracer is only taken up in the neoplastic process and nothing else. Further it would be preferable with a tracer with long-half life and a relative quick and easy production (1) .

There is no PET tracer that fit this description, however the aminoacid analogue [F18]-Fluoroethyl-L-Tyrosine (FET) has some of the characteristics. Even though FET does not show protein synthesis, but only increased tracer transport into the tumor, it is well suited to show the extent of viable tumor tissue, as uptake in normal brain tissue is low. Synthesis is relatively easy and can usually be produced in large enough quantities for transport to nearby PET scanners. It can be used for all the same indications as for FDG, and is superior for the evaluation of Tumor recurrence/Treatment effects, and is probably superior in biopsy planning and therapy monitoring (2-7). It is particularly well suited for tumor infiltration and can be used in the delineation of both low and high grade tumors. This is useful in radiation planning, where aminoacid PET shows the existence of tumor tissue outside the radiation margin in 1/3 of the patients (8). Further, an increased patient survival has been shown in brain tumor patients where the radiation field has been planned with aminoacid PET rather than MR alone (9).

**Dementia**

The number of patients with dementia will more than double in Europe over the next 30 years. In Denmark with a population of 5 mio there are 70.000 patients with dementia, and 15 000 new cases each year. The social budget is 100.000 Euro per year in direct care per patient. The overall direct costs, just on the social budget, is 1 billion Euro per year, but calculating the indirect costs of family support etc, the cost is more than 2 billion Euro. At the same time the patients are underdiagnosed. Only 1/3 of the patients receive additional investigation (MRI, PET, CSF). This impacts on the quality of diagnosis. A recent investigation involving a random sample of 200 patients with a diagnosis of dementia has shown that 14 % of the patients did not have dementia, and 2/3 had the wrong dementia subclassification (10, 11).

Brain FDG PET has become a supplementary diagnostic procedure as part of the new Alzheimer disease research criteria (12). The FDG uptake in the brain reflects the synaptic activity of the brain. This is progressively reduced during the development of neurodegenerative diseases giving rise to characteristic patterns that can be used to support the presence or absence of a dementing disorder. FDG PEThas been shown to add new information regarding the presence of neurodegenerative disorder and the subclassification (13-16). It has a high negative predictive value.

However, FDG PET primarily shows the effects of disease on the regional functions of the brain, not the cause. This can now be imaged using amyloid binding tracers for dementia (e.g. [11C]-PiB). There are three F18 labelled commercial compounds now under development for routine clinical use that are expected to be available within the next 3-5 years. This group of tracers will be important in diagnosing

early preclinical Alzheimers disease, particularly for selection of patients to the new targeted amyloid treatment, should these show clinical efficacy. Further they can have a role in differentiating dementia subtypes and in prediction conversion for early disease states (mild cognitive impairment, MCI) to overt Alzheimers disease.

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