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## Use of Amino Acids for Tumour Detection

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**Introduction:** Radioactively labelled amino acids (AA) have been used for the characterization of brain tumours for more than 20 years. Early studies employed  $^{11}\text{C}$ -methionine as a tracer for AA metabolism. Lately, fluorine-18-labelled AAs have been introduced and evaluated<sup>3</sup>.

**Most common available AAs:** Most studies so far have been performed with  $^{11}\text{C}$ -methionine. The most commonly used AA tracer for SPECT-imaging is Iod- $\square$ -Methyltyrosin (IMT), which is labeled with 123-Iodine. Recently, a number of studies have been published using [ $^{18}\text{F}$ ]fluoroethyltyrosine (FET). This AA can be produced with high radiochemical yield. Owing to the Fluorine-18-label, the tracer can be distributed to PET-centers without onsite cyclotron<sup>3</sup>.

**Mechanism of uptake:** Although most fluorine or iodine labelled AAs are not incorporated into proteins, comparative studies have shown an identical intratumoural distribution of e.g. methionine, FET and IMT. During the time of acquisition, incorporation into proteins is negligible even for methionine. The crucial step of AA incorporation is AA transport, with membrane bound, specific transporters, which facilitate the incorporation of AAs. Since AA uptake in normal cortex and subcortical brain tissue is lower, the increased expression of AA transporters in gliomas can be used to image tumours with high contrast<sup>3</sup>.

**Glioma characterization:** All AAs have been shown to delineate the tumour extent most accurately when compared to magnetic resonance tomography (MRI) or computed tomography (CT). Uptake distribution differs significantly from contrast media enhancement in CT and MRI or signal alterations in FLAIR or T2-weighted MRI images. The accurate identification and delineation of tumour with AAs can be used to determine the site of biopsy or to plan computer assisted surgery or radiotherapy<sup>3</sup>. The role of AAs in grading tumours is less evident<sup>7</sup>. In the follow up of gliomas, AAs help to differentiate radionecrosis from recurrent tumours<sup>2,5</sup>. In the differential diagnosis of unclear brain lesions, AAs show some potential for the differentiation of tumour and inflammation although some uptake in inflammatory lesions may be present.

**Inflammatory CNS lesions:** Inflammatory processes play an important role in many CNS disorders. Ring-enhancing brain lesions are a special diagnostic challenge. The differentiation of central necrotic glioma (in most cases high-grade glioma) and a brain abscess may be difficult. It has been shown, that although uptake in brain tumours is significantly higher, considerable AA uptake may be present in brain abscesses too<sup>1,6</sup>. Multiple sclerosis may also cause tumour-like lesions. In those cases AAs may be used for the differential diagnosis, but biopsy cannot always be avoided. In radionecrosis both vascular and inflammatory changes are discussed as underlying mechanisms. The role of AAs for the differentiation of recurrent tumour and radionecrosis has been discussed above.

**AAs in extracerebral tumours:** AAs have been studied for diagnosis of head and neck tumours (HNT). In a comparative study of FET-PET, FDG-PET and CT in HNT patients, FET showed lower accumulation in inflammatory lesions<sup>4</sup>. Owing to a slightly higher sensitivity of FDG in HNT, FET however is not likely to replace FDG in staging HNT.

**Conclusion:** AAs play an important role in molecular imaging of brain tumours. The extent of tumours and the optimal site of biopsy can be determined. In the differential diagnosis of tumour versus inflammation, the intensity of AA uptake is useful but it is unlikely that AA PET will replace biopsies in all cases.

### References

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