Imaging of Brain Tumors with L-3-[^{123}I]Iodo-α-Methyl Tyrosine and SPECT

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Carbon-11-labeled amino acids have been successfully used to image brain tumors by PET. This study was undertaken to evaluate the potential of L-3-[^{123}I]-iodo-α-methyl tyrosine (^{123}IMT) for metabolic imaging of brain tumors. Ten patients (glioblastoma, oligodendroglioma, lymphoma, and metastases) had early and delayed brain SPECT with a rotating gamma camera after i.v.-injection of 200–300 MBq ^{123}IMT. In nine patients the tumors showed intense uptake of the radiotracer. Tumor-to-brain tissue ratios were between 1.4 and 2.6. ^{123}IMT shows potentials for monitoring the effects of brain tumor therapy.

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Compared with the brain tissue, many tumors have increased protein synthesis rates and consequently an increased uptake of amino acids which can be measured quantitatively by positron emission tomography (PET) using carbon-11- (^{11}C) labeled amino acids as radiopharmaceuticals (see, e.g., 1, 2, and references therein). This shows that there is a demand for iodine-123- (^{123}I) labeled analogs which might be used for single photon emission computed tomography (SPECT) of the brain. It had been previously reported that radioiodinated L-3-iodo-α-methyl tyrosine (IMT) is a radiopharmaceutical with high pancreatic specificity in mice (*3*) and it was applied for imaging of the pancreas of patients (*4*). It had also been shown in rodents that ^{131}IMT exhibited a high accumulation in melanomas (*5,6*). Later ocular melanoma could be detected with ^{123}IMT in patients using a special twin pinhole collimator (*7*). These first findings gave rise to the assumption that ^{123}IMT might also be a suitable agent for SPECT of brain tumors.

MATERIALS AND METHODS

Radiosynthesis of ^{123}IMT

Labeling of IMT (Fig. 1) was performed by direct electrophilic radioiodination based on previous procedures (*3,4,6*). Iodine-123 iodide (≥2 GBq) was oxidized in the presence of the substrate and 1 μg KI either with chloramine-T or KIO_3 in aqueous solution at pH 1 to achieve in situ iodination within 2 min at room temperature. ^{123}IMT was purified and isolated by means of isochratic high performance liquid chromatography (HPLC) (reverse phase RP-18 column 250 × 10 mm, LiChrosorb, Merck) with methanol:water:acetic acid (40:60:1) as eluant while monitoring uv and radioactivity. The specific activity obtained was ≥25 TBq/mmol with an isolated yield of ~65% after sterile filtration.

Patient SPECT studies

Ten patients (5× glioblastoma, 3× metastases, 1× lymphoma, 1× oligodendroglioma) had brain SPECT using a rotating gamma camera (APEX 409, Elscint, Gammatome T9000, CGR). Early (10 min) and delayed (60 min) brain SPECT with a high resolution, low-energy collimator was performed after injection of 200–300 MBq ^{123}IMT. During one 360° rotation 60 frames with a 4k (64 × 64) matrix were acquired within 20 min. Reorientated transverse slices were then reconstructed parallel to a line which passes through the lower pole of the frontal lobe and the cerebellum. This technique was useful to obtain identical slices for comparison of early and delayed brain SPECT. Using a region of interest technique, tumor-to-brain tissue ratios were calculated. Diagnosis of tumor was established by CT and—in four cases with primary brain tumor—by neurosurgical procedures.

All ten patients had planar sequential scintigraphy with time increments of 5 sec (first minute) or 10 sec (2.–5. minute), respectively, to evaluate the kinetics of IMT within the first 5 min after bolus injection.

RESULTS AND DISCUSSION

The time-activity curves of brain and tumor in all ten patients showed a first, perfusion-related peak fol-

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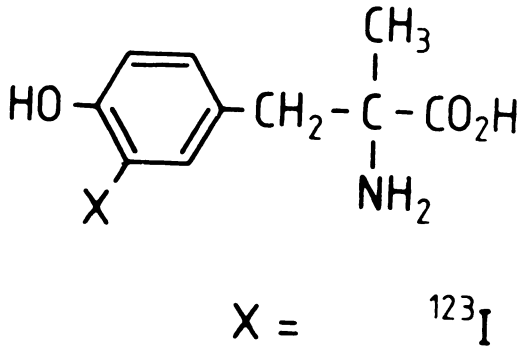

FIGURE 1
Chemical structure of ^{123}IMT.

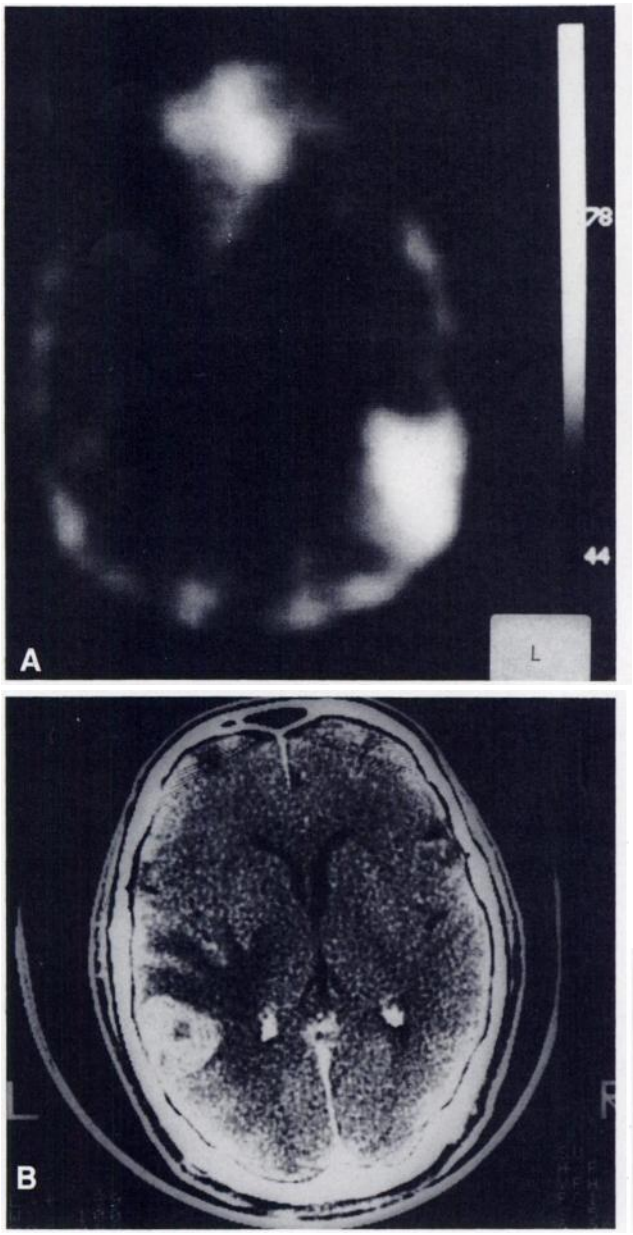

FIGURE 2
Brain-SPECT (^{123}IMT) (A) and CT (B) of a patient with glioblastoma of the left hemisphere.

lowed by a rapid decrease and after 30–60 sec by a plateau. All six patients with glioblastoma or oligodendroglioma and three patients with brain metastases of bronchogenic carcinoma had increased ^{123}IMT-uptake in the tumor (Figs. 2,3). The tumor-to-brain tissue ratio showed values between 1.4 and 2.6 and did not

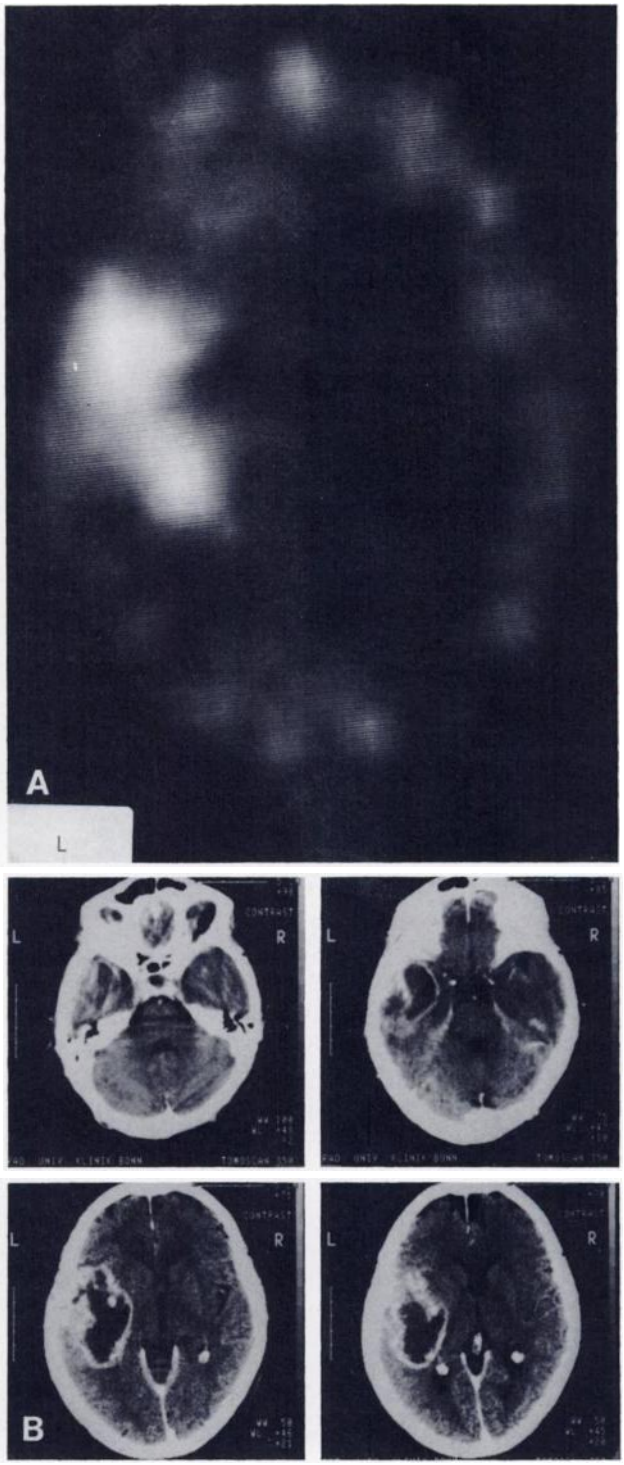

FIGURE 3
Brain-SPECT (^{123}IMT) (A) and CT (B) of a patient with glioblastoma of the left hemisphere.

TABLE 1
Tumor/Brain Tissue Ratios of ^{123}IMT in a Variety of Brain Tumors

Tumor	Tumor/background ratio Early*	Delayed†
Glioblastoma		
Case 1	1.55	1.40
Case 2	1.42	1.34
Case 3	–(‡)	1.60
Case 4	2.33	2.64
Case 5	1.36	–(‡)
	1.64 + 0.35	1.75 + 0.53
	N.S.	
Lymphoma		
Case 1	No visualization	
Oligodendroglioma		
Case 1	1.61	1.37
Brain metastases		
Case 1	1.53	–(‡)
Case 2	1.49	1.58
Case 3	1.21	1.19
	1.41 + 0.14	1.39
	N.S.	

* Aquisition time 10–30 min p.i.
† Aquisition time 60–80 min p.i.
‡ Study not completed due to motion artifacts.

change with time (Table 1). One patient with a very small lymphoma (~1 cm in diameter) was false negative.

These data make it evident that ^{123}IMT is accumulated in brain tumors like ^{11}C-labeled amino acids being used for PET studies (*1,2*). The incorporation rates of ^{123}IMT in normal tissue are much lower compared to those obtained in rats with L-[^{14}C]-leucine and L-[^{11}C] methionine 40 min p.i. [85% and 62%, respectively (*8*)]. The tumor uptake, however, of the radioiodinated amino acid is comparable to that of their ^{11}C-analogs. Further, the tumor-to-brain tissue ratios are in agreement with the PET-findings of Schober et al. (*2*) who have found a high tumor-to-brain tissue ratio (2.6) in astrocytoma i.v. using PET and [^{11}C]methionine. L-α-Methylthyrosine is an enzyme inhibitor, and it might therefore be possible that there is also a trapping mechanism for the iodinated analog via enzyme inhibition.

It has also been suggested that IMT can be used to measure aminoacid transport (*9*). Strong arguments against a blood-brain barrier mediated uptake (like with pertechnetate) are the rapid uptake of the radiopharmaceutical in the tumors as well as the constant tumor-to-brain tissue ratio with time. ^{123}IMT shows potentials to evaluate therapeutic procedures (irradiation, cytotoxic therapy) in brain tumors and might thus have widespread clinical application as a SPECT radiopharmaceutical.

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