Technetium-99m sestamibi brain single-photon emission tomography for detection of recurrent gliomas after radiation therapy

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Abstract. Technetium-99m sestamibi (MIBI), an alternative radiopharmaceutical for myocardial perfusion imaging, has also been proposed for use as an imaging agent for various tumours, including breast cancer, lung cancer, lymphomas, melanomas and brain tumours. After routine radiation therapy, deteriorating clinical status or treatment failure may be due to either radiation-induced changes or recurrent tumour. Computed tomography and magnetic resonance imaging offer imperfect discrimination of tumour viability and radionecrosis. Against this background we undertook a retrospective study of 35 malignant glioma patients in whom clinical deterioration had occurred, in order to clarify the value of 99mTc-MIBI SPET in identifying tumour recurrence. SPET was performed 15 min after intravenous injection of 1110 MBq 99mTc-MIBI. The images were obtained with a dual-headed gamma camera using a fan-beam collimator. Transverse, coronal and sagittal views were reconstructed. Intense MIBI uptake was found in 31 patients. This uptake was correlated with tumour recurrence as proved by histology and/or rapid, fatal evolution of these cases. The statistical analysis performed on this population of patients with MIBI uptake revealed a group of patients with a long mean survival and a group with a short mean survival. Two subgroups were found within each of these groups, according to the functional index ratio (tumour uptake/pituitary gland uptake ratio). No MIBI uptake was found in four patients who are still alive and can be considered to be disease-free. In those cases showing MIBI uptake, death occurred an average of 6.69 months following brain SPET. According to our results, the specificity and sensitivity of 99mTc-MIBI brain SPET seem to be high. Moreover, this technique is more accurate than computed tomography or magnetic resonance imaging for discriminating between tumour recurrence and radionecrosis.

Key words: Gliomas – Tumour recurrence – Radionecrosis - Technetium-99m sestamibi – Brain single-photon emission tomography


Introduction

Primary tumours of the brain represent a challenge for clinicians and researchers. Malignant gliomas are generally considered to be among the most radioresistant of tumours [1], and are often not accessible to locoregional treatments such as surgery or radiotherapy. Despite oncological treatments such as combination radiation therapy and chemotherapy after surgery, the median survival of patients with malignant gliomas is generally less than 12 months and virtually no patient with glioblastoma multiforme (GBM) survives 5 years following treatment [2, 3]. For anaplastic astrocytomas, the prognosis after treatment is considered to be “better”, the median survival of these patients being approximately 2–3 years [1, 3]. With the development of aggressive therapeutic trials, an increasing number of patients are presenting after treatment with symptoms and signs that may be secondary to residual or recurrent tumour, or solely due to radiation-induced changes [4, 5]. Focal radiation effects on the brain may be associated with clinical deterioration, especially when high doses of radiotherapy are used [1, 4]. Surgery may prevent such a decline [1, 4, 5]. However, computed tomography (CT) and magnetic resonance imaging (MRI) offer imperfect discrimination of tumour viability and radionecrosis [4]; indeed, radiation necrosis and treated tumours have similar imaging char-
acteristics [4, 5]. A CT-guided biopsy of enhancing areas in the tumour bed may also be unreliable [4]. Functional imaging with positron emission tomography (PET) has been used to assess tumour viability and necrosis and has proved effective in differentiating recurrent glioma from radiation-induced changes [6–9]. However, this technology is available only in a limited number of institutions and is often cost-prohibitive. Thallium-201 brain single-photon emission tomography (SPET) is known to have a high sensitivity for detecting viable tumour, but its specificity is low [10–16] due to the poor definition of images obtained with $^{201}$TI. In order to improve the quality of scintigraphic images, a search for a new technetium-labelled agent was undertaken. $^{99m}$Tc-sestamibi (MIBI), an alternative radiopharmaceutical for myocardial perfusion studies, has also been proposed for use as an imaging agent for various tumours, including breast cancer, lung cancer, melanomas, lymphomas and primary brain tumours [17–24]. The difference between $^{99m}$Tc-MIBI and $^{201}$TI in terms of sensitivity could be explained by the fact that $^{99m}$Tc-MIBI images are superior in quality to $^{201}$TI images owing to the physical properties of $^{99m}$Tc (140 keV gamma-ray energy, higher photon flux, higher tumour to background ratio). In order to clarify the usefulness of $^{99m}$Tc-MIBI brain SPET for the identification of recurrent tumours, we undertook a retrospective study of 35 patients in whom clinical deterioration had occurred.

Materials and methods

Patient population. We studied 35 patients who were admitted in a clinically worse condition after radiation therapy for high-grade gliomas between October 1993 and December 1995. All tumours were supratentorial. According to Duhamas-Dupont’s histological classification, six cases were grade 3 and 29 grade 4. The 21 men and 14 women had a mean age of 57.65 years (range 32–73 years) and had previously undergone external beam radiation therapy; a few patients had also received adjuvant chemotherapy including a nitrosourea component. All patients were receiving corticosteroid therapy. Upon clinical deterioration, a CT scan and brain SPET were performed in each patient. The mean interval between diagnosis and the SPET analysis was 11.85 months (range 3–48 months), and the mean interval from completion of radiation therapy to brain SPET was 10.5 months (range 1–48 months).

Imaging protocol. Commercially available MIBI kits (Cardiolite, Dupont-Pharma, USA) were labelled with $^{99m}$Tc according to the manufacturer’s recommendations. Brain SPET was performed 15 min after an intravenous injection of 1110 MBq (30 mCi) of $^{99m}$Tc-MIBI in an antecubital vein. Images were acquired using a dual-headed gamma camera (Helix, Elscint), with a 128×128 matrix, 360° rotation, a 6° step-and-shoot technique and an acquisition time of 30 s per frame. Images were reconstructed in a 128×128 matrix using Butterworth filtered back-projection (cut off = 0.25× Nyquist frequency, order 5). On the one hand, $^{99m}$Tc-MIBI uptake was assessed visually. Transverse, coronal and sagittal views were generated and then qualitatively analysed by two experienced observers. On the other hand, a region of interest (ROI) was drawn on a transverse slice including the total repre-

![Fig. 1a–c. An example of a “whole-tumour” slice in the three projections, allowing calculation of the tumour volume](image-url)