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PICTORIAL ESSAY

Radioembolisation of Hepatocellular Carcinoma and Liver Metastases: Imaging Findings Using ^{90}Y Positron Emission Tomography/Computed Tomography and Bremsstrahlung Single Photon Emission Computed Tomography/Computed Tomography

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ABSTRACT

Radioembolisation with Yttrium-90 (^{90}Y)–labelled microspheres administered via the hepatic artery is currently used to treat primary and metastatic non-resectable liver tumours. ^{90}Y is a pure beta-particle emitter and its energetic beta particle has a range of about 4 mm in soft tissue, making it well suited for treatment of bulky tumours. Bremsstrahlung single photon emission computed tomography/computed tomography (SPECT/CT) is commonly performed to assess the biodistribution of ^{90}Y-labelled microspheres post-radioembolisation. Because ^{90}Y emits positrons in a small percentage of its decays, ^{90}Y positron emission tomography/computed tomography (PET/CT) has recently been used for this purpose, yielding higher-resolution visualisation of the distribution of the microspheres. This pictorial review presents, compares, and contrasts Bremsstrahlung SPECT/CT and PET/CT images post-radioembolisation in four patients treated with ^{90}Y-microspheres.

Key Words: *Hepatic artery; Liver neoplasms; Positron-emission tomography; Tomography, X-ray computed; Yttrium radioisotopes*

中文摘要

肝癌和肝轉移瘤的放療性栓塞：用^{90}Y正電子發射斷層掃描/CT和軔致輻射單光子發射電腦斷層/CT顯像結果

馬慧嫻、羅惠明、何偉然、黃廣權、吳楚儀、劉顯宇、曹偉權

經肝動脈內注入釔（^{90}Y）微球放療性栓塞目前用於治療無法手術切除的原發性和轉移性肝癌。^{90}Y是一個純β粒子發射器，其高能β粒子的射程在軟組織中約有4 mm，所以適合用於治療大體積的腫瘤。軔致輻射單光子發射電腦斷層/電腦斷層掃描（SPECT/CT）常用於評估放療栓塞後^{90}Y微球的分佈。由於^{90}Y衰變過程中會釋放少量正電子，^{90}Y正電子發射斷層掃描/電腦斷層掃描（PET/CT）最近應用於臨床以得出更高分辨率的微球分佈。本文比較分析四名接受^{90}Y微球放療性栓塞後病人的致輻射SPECT/CT和PET/CT的圖像結果。

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INTRODUCTION

In 2009, there were 1832 new liver cancer cases in Hong Kong, representing 14% of all new cancers in Hong Kong.[1] Surgical resection of tumours is considered to be the only curative treatment. Unfortunately, hepatocellular carcinoma may present late and may be non-resectable by the time the patient seeks medical attention. For such patients, there are other methods for disease control such as conformal radiotherapy, radiofrequency ablation, and transarterial chemoembolisation. The use of radioembolisation with Yttrium-90 (^{90}Y)–labelled microspheres has been applied as an alternative treatment method to inoperable primary liver tumours and liver metastases. ^{90}Y is a pure beta-particle emitter with a physical half-life of 64 hours and average path length in soft tissue of 4 mm, making it well suited for reasonably uniform irradiation of bulky tumours, while minimising the radiation dose to surrounding normal tissues. Two ^{90}Y products, TheraSphere (MDS Nordion, Ottawa, Canada) and SIR-Spheres (SIRTeX Medical, Lake Forest [IL], USA), have been approved by the US Food and Drug Administration in 1999 and 2002 for the treatment of unresectable hepatocellular carcinoma and colorectal metastases, respectively. ^{90}Y radioembolisation consists of intra-arterial injection of ^{90}Y-labelled microspheres, followed by Bremsstrahlung scintigraphy to confirm the distribution of ^{90}Y microspheres in the target. An important complication related to the treatment is extrahepatic deposition of ^{90}Y-labelled microspheres. For example, deposition of ^{90}Y microspheres in the lung parenchyma may result in radiation pneumonitis,[2] while radioembolisation to the gastrointestinal tract can induce gastrointestinal ulcer, gastritis, cholecystitis and pancreatitis.[3-5] In-vivo imaging of pure beta-particle emitters is generally problematic because of the very limited penetrability of beta particles through tissue. However, Bremsstrahlung, or "brake X-rays", are produced in small but imageable amounts by the higher-energy beta particles as they pass through matter and interact inelastically with atomic nuclei. The resulting X-ray energy spectrum is continuous, with a large proportion of the resulting X-rays having energies closer to zero, and progressively fewer X-rays having energies approaching the maximum, or end-point, energy of the beta particles. This broad distribution, skewed towards lower-energy X-rays, coupled with the small number of X-rays actually emitted (due to the small number of radioactive vs collisional energy-loss interactions) results in coarse energy and spatial resolution and, thus, limited detectability of small lesions by gamma

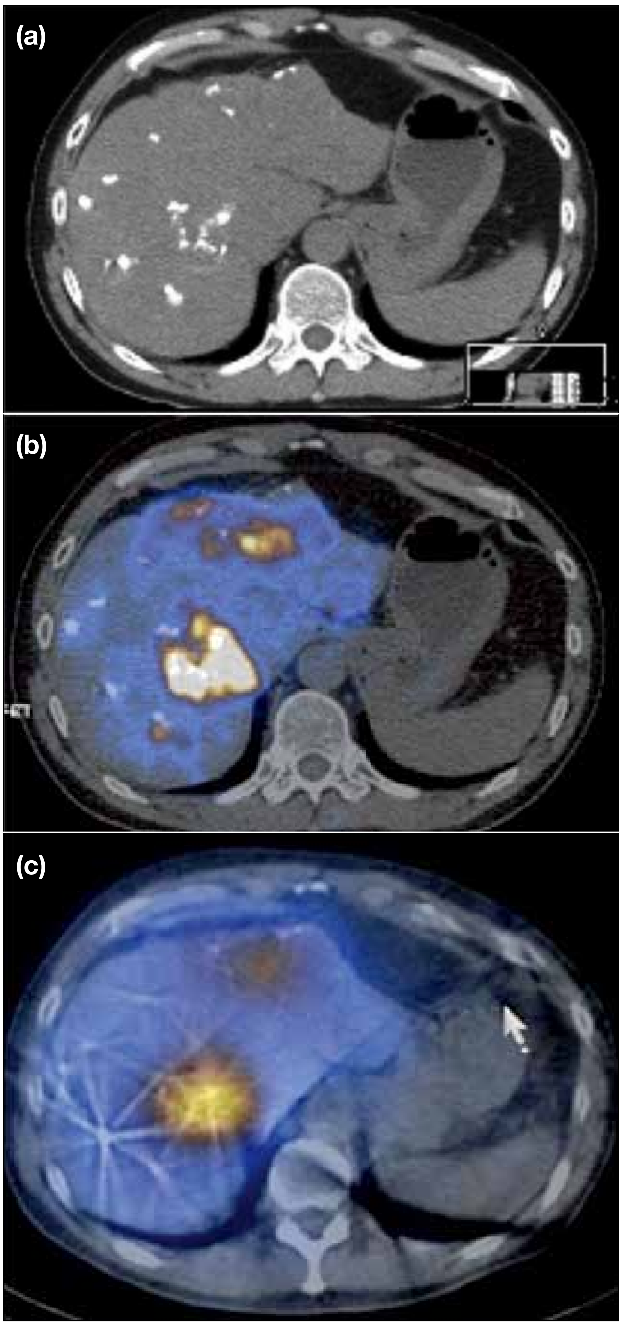

Figure 1. Comparison between positron emission tomography/computed tomography (PET/CT) and single photon emission computed tomography/computed tomography (SPECT/CT) images of a 45-year-old man who had multifocal hepatocellular carcinoma. The patient had been treated with left lateral segmentectomy, radiofrequency ablation to segment V and chemotherapy. An activity of 1.3 GBq ^{90}Y microspheres to both hepatic lobes was administered via hepatic proper artery. (a) A CT image obtained immediately after the radioembolisation shows the contrast (Lipiodol)-enhanced liver. (b) Fused transaxial ^{90}Y PET/CT image demonstrates multifocal uptake of the microspheres in both lobes with higher uptake in segment VII/VIII. (c) Bremsstrahlung SPECT/CT image shows a concordant distribution of the microspheres but non-visualisation of the small satellite lesions in the left hepatic lobe, presumably due to the coarser spatial resolution of this modality.

camera imaging of Bremsstrahlung. Nevertheless, post-radioembolisation ^{90}Y Bremsstrahlung single photon emission computed tomography/computed tomography (SPECT/CT) has been used to determine the technical success for radioembolisation.[6] For sufficiently high activity depositions, ^{90}Y positron emission tomography/computed tomography (PET/CT) can provide higher-resolution,[7] more quantitatively accurate images of the microsphere distribution, despite the very low positron branching ratio of ^{90}Y (31.86 ± 0.47 ppm).[8]

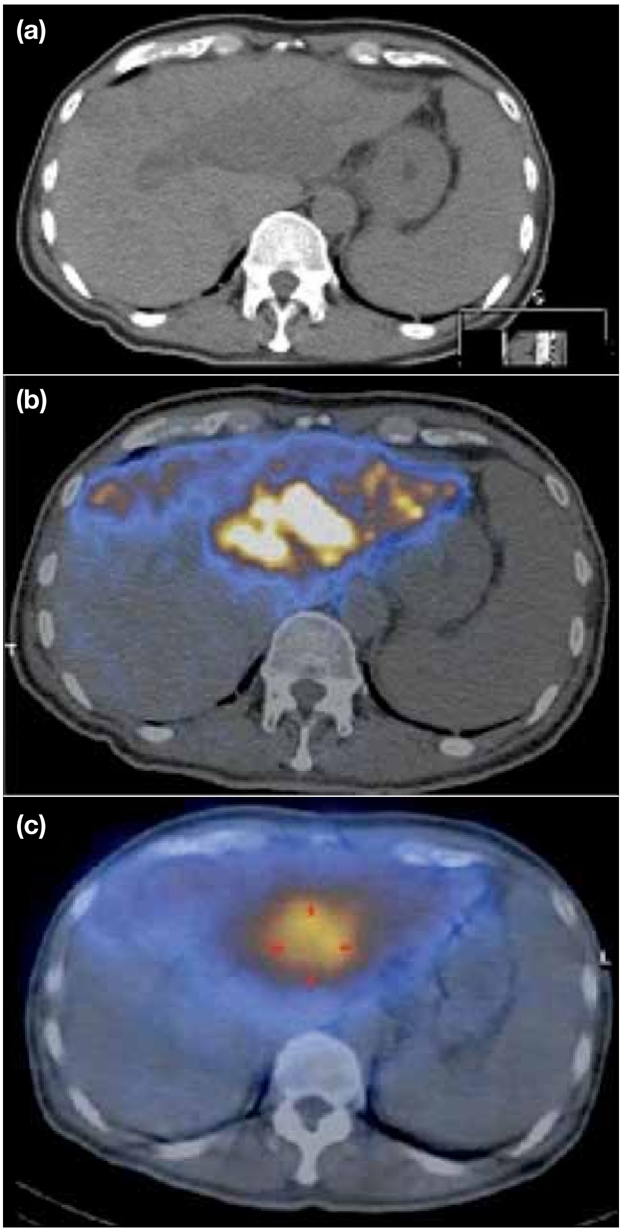

Figure 2. ^{90}Y positron emission tomography/computed tomography (PET/CT) and Bremsstrahlung images of a 56-year-old man with a clinical history of hepatitis B viral cirrhosis complicated with hepatocellular carcinoma. Radiofrequency ablation to segment VII/VIII lesion was performed. However, there was tumour recurrence in segments VIII, VI, and II/III. The patient was administered 1.2 GBq ^{90}Y microspheres via the hepatic proper artery. (a) Axial CT and (b) axial fused ^{90}Y PET/CT scintigraphy show microsphere localisation in the main tumour bulk in segment II/III. (c) ^{90}Y PET/CT scintigraphy also demonstrates adjacent satellite nodules in subcapsular region which are not visualised in Bremsstrahlung single photon emission computed tomography scintigraphy.

The aim of this pictorial review was to demonstrate: (1) the superiority of PET/CT to Bremsstrahlung SPECT/CT after ^{90}Y radioembolisation in terms of improved spatial resolution and tumour localisation, and (2) the potential error in the interpretation of PET/CT images in lesions with low activity concentrations.

IMAGING

Our patients underwent both ^{90}Y PET/CT imaging within

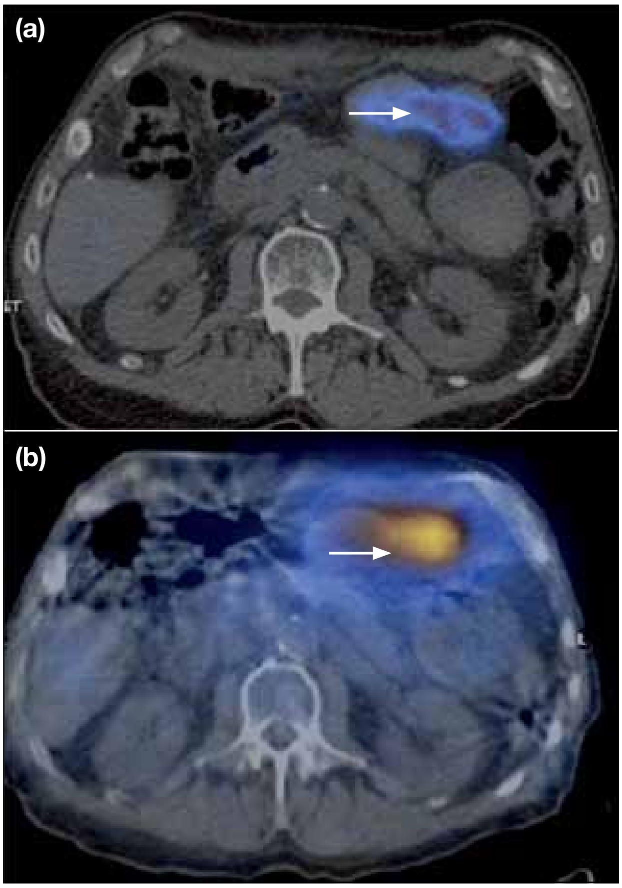

Figure 3. ^{90}Y positron emission tomography/computed tomography (PET/CT) and Bremsstrahlung scans after radioembolisation of a 72-year-old man suffering from liver metastases from carcinoma of sigmoid colon. The patient had been treated with chemotherapy and anterior liver resection before therapeutic ^{90}Y radioembolisation was considered. (a) The post-^{90}Y radioembolisation fused PET/CT image and (b) Bremsstrahlung image show intrahepatic confinement of the radiolabelled microspheres, demonstrating successful selective embolisation to the left hepatic lobe (arrows). There is no evidence of extrahepatic radioactivity uptake by both imaging methods.

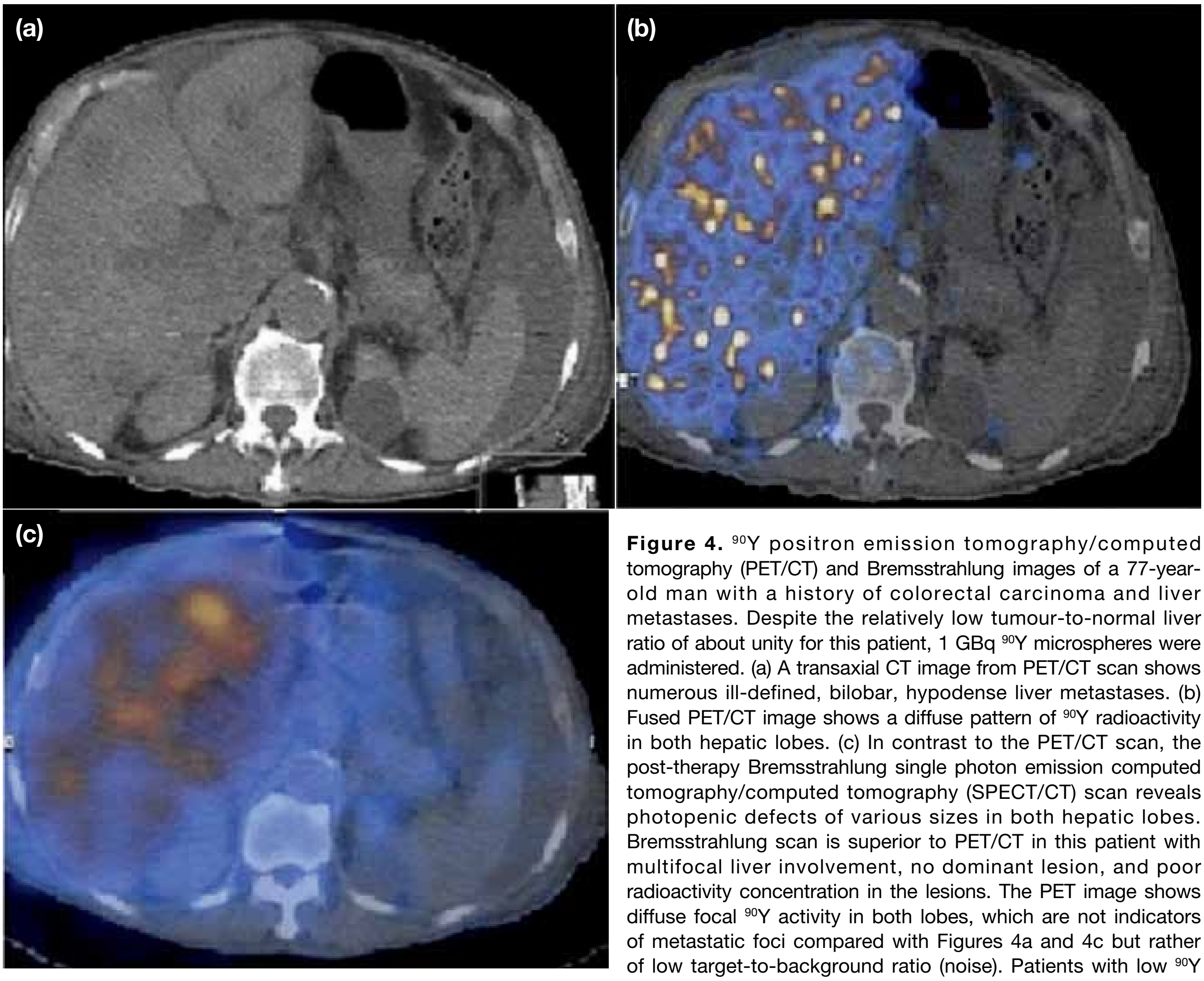

Figure 4. ^{90}Y positron emission tomography/computed tomography (PET/CT) and Bremsstrahlung images of a 77-year-old man with a history of colorectal carcinoma and liver metastases. Despite the relatively low tumour-to-normal liver ratio of about unity for this patient, 1 GBq ^{90}Y microspheres were administered. (a) A transaxial CT image from PET/CT scan shows numerous ill-defined, bilobar, hypodense liver metastases. (b) Fused PET/CT image shows a diffuse pattern of ^{90}Y radioactivity in both hepatic lobes. (c) In contrast to the PET/CT scan, the post-therapy Bremsstrahlung single photon emission computed tomography/computed tomography (SPECT/CT) scan reveals photopenic defects of various sizes in both hepatic lobes. Bremsstrahlung scan is superior to PET/CT in this patient with multifocal liver involvement, no dominant lesion, and poor radioactivity concentration in the lesions. The PET image shows diffuse focal ^{90}Y activity in both lobes, which are not indicators of metastatic foci compared with Figures 4a and 4c but rather of low target-to-background ratio (noise). Patients with low ^{90}Y uptake in lesions may not benefit from PET/CT imaging as a post-radioembolisation scan. Bremsstrahlung SPECT/CT imaging may be a better choice for this subgroup of patients.

6 hours after ^{90}Y radioembolisation and Bremsstrahlung imaging at 2 days after radioembolisation (Figures 1 to 4). ^{90}Y PET/CT was performed with a hybrid PET/CT scanner (Discovery VCT; GE Medical, USA). The CT images were obtained with 120 kVp; 300-500 mA, unenhanced; field of view 50 cm^2, pixel size 0.98 x 0.98 mm; helical CT pitch 0.516:1, interval 2.5 mm, and gantry rotation speed 0.5 second. PET was performed with 2 beds position and 15 minutes per bed position. PET data with CT images were reconstructed with an ordered-subset expectation maximisation iterative algorithm (14 subsets, 2 iterations). Bremsstrahlung SPECT/CT images were read via electronic patient record (ePR) and the ^{90}Y PET/CT images were viewed side-by-side on a separate screen. PET/CT system was able to provide accurate anatomical detail of the distribution of ^{90}Y microspheres in the target. Because of the better spatial resolution in PET, small lesions that are identified by ^{90}Y PET/CT may not be visualised by Bremsstrahlung SPECT/CT system (Hawkeye 4; GE Medical, USA).[9] In cases where there is non-target extrahepatic uptake in close proximity to the liver, the coregistered PET/CT images will enhance the diagnostic confidence in image interpretation.

CONCLUSION

Bremsstrahlung SPECT/CT scintigraphy is used currently for visualisation of intraphepatic distribution of the ^{90}Y microspheres. ^{90}Y PET/CT images have better image quality than Bremsstrahlung scintigraphy, except in cases of tumours with low ^{90}Y concentration. ^{90}Y PET/CT imaging allows precise localisation of extrahepatic uptake and immediate prophylactic treatment for foreseeable complications.

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