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Correlation Between CT/MRI and Bremsstrahlung SPECT of ³²P After Radioembolization of Hepatic Tumors

Background/Objective: Radioembolization (RE) is a minimally invasive transcatheter therapy through which radioactive microspheres are infused into the hepatic arteries and selectively implanted within the tumor arterioles. Some therapeutic agents are particles incorporating pure β emitter elements (⁹⁰Y, ³²P) and do not have gamma radiation. Bremsstrahlung imaging of these radiotherapeutic agents confirms distribution of the radiotracer in hepatic tumors or probable extrahepatic deposition of radiopharmaceuticals and helps the physician to predict the patient's response to RE therapy. The aim of this study was demonstration of ³²P images and its correlation with CT/MRI findings.

Patients and Methods: Ten patients with variable types of hepatic tumors treated with intra-arterial injection of ³²P were included in this study. 24-72 hours after radiotracer administration, bremsstrahlung SPECT imaging was performed in all patients with a single head gamma camera equipped with a medium energy collimator. Energy window setting of 100 keV \pm 25% was selected. Reconstructed images were evaluated by two nuclear medicine specialists and one radiologist, and based on compatibility of ³²P images with CT/MRI, a grading scale from 1 to 4 was used to express their correlations.

Results: By selecting optimized parameters for bremsstrahlung SPECT images of ³²P, we could obtain good quality images. In nine patients, ³²P distribution in the liver was correlated with anatomical findings of CT/MRI.

Conclusion: RE is appropriate to deliver high radiation doses to liver tumors with minimal accumulation in the normal liver tissue. Bremsstrahlung imaging is a useful method to confirm proper distribution of the radiotherapeutic agent, which has good correlation with anatomical findings.

Keywords: Radioembolization, Phosphorus Radioisotope, Bremsstrahlung Imaging, Liver Neoplasm

Introduction

In view of extremely high potential of beta emitting radionuclides for treatment of both malignant and non-malignant conditions, application of these radionuclides in clinical practice is increasing.¹ Brachytherapy, using colloidal ³²P, has been used as an accepted modality for treatment of various tumors in the pancreas, liver, brain, lung and the head and neck.²

Radioembolization, a form of intra-arterial brachytherapy, is a minimally invasive catheter-based therapy that delivers internal radiation via the arterial vessels feeding the tumors. "Radio" refers to the radiation that is imparted to tissues, and "embolization" refers to the microembolic effect and subsequent vessel occlusion.³ Since 2002, Food and Drug Administration (FDA) approved radioembolization (RE) with ⁹⁰Y for treatment of liver tumors. RE is based on the predominant arterial blood supply of the hepatic tumoral lesion by the hepatic artery as compared to the surrounding liver parenchyma which is mainly supplied by the portal vein. Therapeutic with proper size, incorporating the isotope emitting β agents are particles radiation (⁹⁰Y, ³²P).⁴⁻⁷

In this study, RE of hepatic tumors has been carried out for the first time in Iran with newly synthesized ^{32}P particles. ^{32}P is a suitable isotope because it is a pure beta emitter with an appropriate physical half-life of 14.3 days and mean beta particle energy of 0.695 Mev. ^{32}P has secondary photon emissions called bremsstrahlung radiation.⁸ Imaging of these photons confirms distribution of the radiotracer in hepatic tumors or probable extrahepatic deposition of radiopharmaceuticals and helps the physician to predict the patient's response to RE therapy. Imaging of bremsstrahlung has been reported by other investigators using the gamma camera.⁹⁻¹⁶ We report the results of bremsstrahlung imaging of 10 patients after RE with ^{32}P for treatment of hepatic tumors and correlation between CT/MRI findings and bremsstrahlung images.

Patients and Methods

Patients

Ten patients with unresectable hepatic or metastatic tumors of any origin were included in this study. Cross-sectional imaging with CT or MRI was performed in all patients to determine the size and location of lesions as numerical segments consistent with physiologic division of Couinaud.¹⁷

RE has been done in all patients by ^{32}P produced locally (IAEA, I.R. Iran) with the mean size of 50-150 μm .

Procedure

Radioembolization: Standard angiography method was performed through the femoral artery. Celiac and superior mesenteric arteries were catheterized by Simon I (Cordis, USA) catheter, and DSA angiography was prepared by C-Arm angiography unit (Siemens, Germany). Selective catheterization was done by 3F microcatheter (Cook, USA), ^{32}P particles were injected into the artery and post-embolization angiogram was obtained.

Bremsstrahlung Image Acquisition: 24-72 hours after radioembolization of hepatic tumors, bremsstrahlung imaging was performed in all patients. A single head SPECT gamma camera, e-cam (Siemens, Germany), equipped with a medium energy general pur-

pose (MEGP) collimator was applied for data acquisition. Energy window setting of $100\text{ keV}\pm 25\%$ was selected. SPECT images were acquired in 64×64 image matrix for 64 projections over 360° for 30 seconds per projection. Iterative reconstruction was used with the method of ordered subset (OSEM)¹⁸ with four iterations and two subsets.

Image Interpretation and Correlation: The reconstructed images were reviewed by two nuclear medicine specialists and a radiologist, independently. Based on the compatibility of ^{32}P images with anatomical findings, a grading system was applied for each patient; as grade 4 for poor correlation, grade 3 for intermediate correlation, grade 2 for good correlation and grade 1 for perfect match. In the case of disagreement, the physicians discussed the case and a consensus was reached.

Statistical Analysis

The descriptive data were shown by mean \pm standard deviation and frequency. Variable comparison between different groups was performed by U-Mann Whitney test. All p values lower than 0.05 were considered as statistically significant.

Results

Ten patients, four men and six women, were included in this study; consisting of seven colon cancers, two breast cancers and one hepatocellular carcinoma (HCC). The mean age of patients was 59.7 ± 15.6 years (35-78).

The mean administered activity was 279.9 ± 89.3 (148-370) MBq in all patients; 203.3 ± 55.5 MBq in non-colorectal cancers and 312 ± 82.3 MBq in colorectal cancers ($p=0.67$) (Table 1).

Distribution of ^{32}P particles was recognized as focal or multifocal areas in the liver and their compatibility with CT/MRI were determined as correlation grading which is illustrated in Table 1. The mean correlation grade was 1.7 ± 0.95 (1-4). Totally, we had five patients (50%) with grade 1, four patients (40%) with grade 2 and one patient with grade 4. The mean correlation grade in non-colorectal cancers was 1.3 ± 0.58 and 1.9 ± 1.1 in colorectal cancers ($p=0.52$). Subsequently, in 90% of the patients (9 of 10 cases), bremsstrahlung

Table 1. Patients' Data and Comparative Results of ³²P Bremsstrahlung SPECT with CT/MRI

Patient	Age (Year)	Activity (MBq)	Tumoral Origin	Correlation Grading
1	64	155	Colon	2
2	76	370	Colon	2
3	43	277	Colon	1
4	66	370	Colon	4
5	57	370	Colon	2
6	67	277	Colon	1
7	78	370	Colon	1
8	35	148	Breast	1
9	39	203	Breast	2
10	72	259	HCC*	1

*Hepatocellular Carcinoma

SPECT of ³²P particles had good or perfect concordance with CT/MRI. Figure 1 shows an example of perfect correlation of bremsstrahlung images and CT

scan in the same patient.

Only in one patient, there was poor correlation between MRI and ³²P bremsstrahlung images. He was a colon cancer patient with multiple diffuse small metastases in the liver. Bremsstrahlung images could not localize these small lesions.

Photopenic regions visualized in bremsstrahlung imaging are interpreted as tumor necrotic areas, which are corresponding to CT/MRI images, as shown in Figure 2.

Extrahepatic activity as splenic uptake was also considered (Fig. 3).

Discussion

Pure beta emitting radionuclides (³²P, ⁹⁰Y, and ⁸⁹Sr)

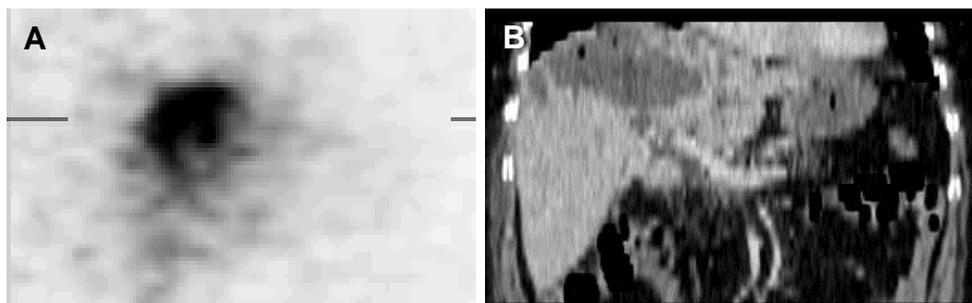


Fig. 1. An example of perfect correlation between MRI and ³²P in a patient with metastatic colon cancer treated with 277 MBq ³²P.

A. There is a large irregular area of ³²P uptake in segment 8 of the liver, shown in the coronal section of bremsstrahlung SPECT image.

B. CT scan of the liver.

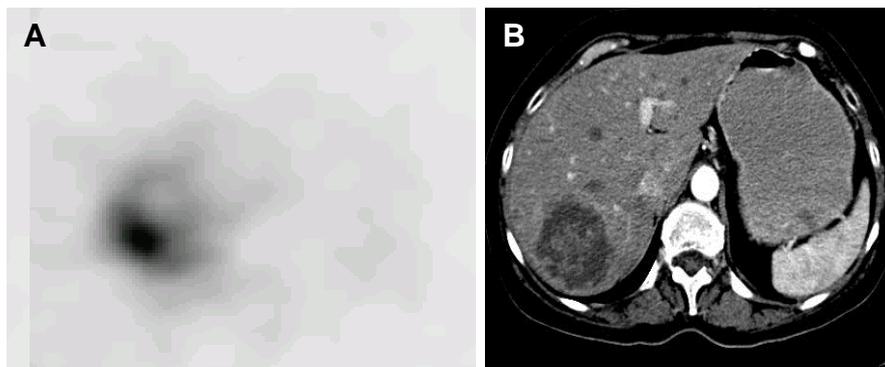


Fig. 2. A patient with metastatic colon cancer treated with 370 MBq ³²P particles.

A. Bremsstrahlung SPECT images obtained 48 hours after radioembolization of hepatic tumor. There is a photopenic region in the central part of the lesion, which is compatible with necrotic tissue in CT scan (**B**).

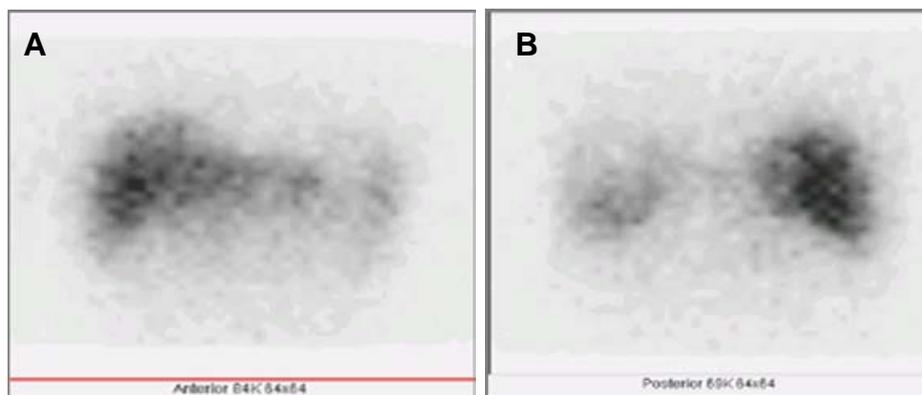


Fig. 3. Faint splenic uptake is seen in anterior (**A**) and posterior planar images (**B**) of ³²P bremsstrahlung radiation.

have been widely used for therapy to deliver a high dose radiation to the target tissue. Although there is no gamma ray for imaging, these elements have secondary photon emissions called bremsstrahlung radiations, as a result of interaction between beta particle and the surrounding tissues.¹⁹ Imaging of these photons is possible with gamma camera which has been reported by some researchers.^{9,11-16,20} Optimal parameters for bremsstrahlung imaging of ³²P particles has been noticed in this study with a good correlation to patients' lesions identified by CT/MRI.

The most critical determinant of the clinical effectiveness of therapy with beta emitters is the degree of targeting of the radiopharmaceutical to the tumor. Negligible uptake of the radiotracer in normal parenchymal liver and prominent retention of the radiotherapeutic agent in hepatic tumors confirms predominant arterial blood supply of the tumoral lesions.⁴ This leads to minimal radiation-absorbed dose to the surrounding normal tissue which is a potential advantage of RE over external radiotherapy.²¹ On the other hand, an important factor for predicting the patient's response to therapy is proper localization and quantification of incorporated beta emitters. Mansberg et al.¹² presented a patient with metastatic liver disease who had been treated with ⁹⁰Y labeled SIR spheres and bremsstrahlung images, which showed anatomic correlation with sites of maximum tumor density. Similarly, Tehranipour et al.¹⁶ reported a patient with concordant findings of ¹⁸F-FDG PET and ⁹⁰Y bremsstrahlung scans after radioembolization of the hepatic tumor with ⁹⁰Y microspheres. Our study showed a relatively good correlation (grade 1 and 2) between SPECT images and CT/MRI in 90% of the patients (Table 1). This grading system has been proposed by Boan et al.²² which used ^{99m}Tc-MAA to correlate with CT/MRI images for pre-treatment planning of RE therapy. Our study revealed that bremsstrahlung SPECT imaging has acceptable resolution for post-treatment matching with CT/MRI images. Good and perfect correlation confirms technically appropriate localization of radiopharmaceuticals and could predict potential good responses to therapy. Conversely, poor correlation could be due to small diffuse metastatic lesions, which are not seen in bremsstrahlung imaging because of inherent low spatial resolution of images. In

addition, bremsstrahlung images are a snapshot of ³²P particle distribution during intra-arterial injection of the tracer that could be affected by vessel selection, flow in a selected vessel and the size and amount of injected particles. Technical error during RE or poor vascularized lesions lead to accumulation of the radiotracer in the normal parenchyma.^{14,20} Clinical application of an anticipated grading system is being evaluated in an ongoing study.

As expected in nuclear medicine studies, the potential advantage of ³²P scintigraphy is its ability to depict tumor cells perfusion rather than non-viable necrotic tissue of a tumor mass (Fig. 2). So, bremsstrahlung imaging of ³²P after RE of hepatic tumors may be reflective of viable and vascularized tumoral tissues.¹⁴

Bremsstrahlung imaging is useful for determination of unexpected deposition of the radiotracer, which leads to inadequate radiation burden to the target and probable complications of other organs.^{11,12,15,19}

In conclusion, intra-arterial injection of labeled microspheres is appropriate to deliver a high radiation dose to liver tumors with minimal accumulation in the normal liver tissue. Bremsstrahlung imaging is a useful method to confirm proper distribution of the radiotherapeutic agent, which has good correlation with anatomical findings of CT scan and MRI.

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