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The Relationship Between Different Doses and Effects After Injection of P-32-GTMS and Y-90-GTMS into the Cancer

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Purpose: By intratumoral injection of different doses of P-32-GTMS or Y-90-GTMS, we try to clarify the biological effect and distribution of the radiopharmaceuty, in order to bring up some information for the clinical trial. **Methods:** Kunming rats were inoculated subcutaneously with S180 tumor cells. After 7-10 days, solid tumors grew at the injection site. 84 rats bearing tumor were divided into 3 groups; 12 rats as a control group, and 72 rats with 2 treated subgroups. The P-32-GTMS or Y-90-GTMS were injected into the tumor center of the subgroups with the doses of 37, 74, and 148 MBq, respectively. On 7th, 14th, 21th, 28th days after the injection, rats were killed for tumor measurement and pathological examination. The fatal radiuses of the tumors were calculated by measuring the diameter of necrosis on the slice. **Results:** A significant tumor regression and cell killing effect were observed for both of P-32-GTMS or Y-90-GTMS. Two weeks after the injection, the tumor shrinkage was found in all test groups, some tumors even disappeared. The pathological result showed that the tumor cell lethality in the test groups was much higher than the control group. When the source dose increased from 37 to 148 MBq, the irradiation time increased from 14 to 28 days, the fatal radius in all the test groups was 7-8 mm for P-32-GTMG and 10 mm for Y-90-GTMS, but it has no relationship with the source dose. Thus, it was observed that the fatal radius of P-32-GTMS was 3.5-4 mm and of Y-90-GTMS was 5 mm, which does not increase with the dose of source. Most of the P-32-GTMS and Y-90-GTMS remained locally, no obvious distribution was noted from the injection site to the other organs of the body, such as liver, kidney or bone. **Conclusion:** The largest killing radius did not increase with the increase of injected doses. 37 MBq P-32-GTMS or Y-90-GTMS is enough to necrotize the tumor cells for a tumor of 1 cm in diameter, and it is more suitable increasing of the injection points than increasing the source dose for a larger tumor. The results of the study will provide the scientific basis for treatment of malignant tumor in the administration and dose of the radiopharmacon.

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In Vivo Image of Radioiodinated IVDU and IVFRU in HSV-TK Gene Tranduced Hepatocellular Carcinoma Bearing Buffalo Rat

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Objectives The extent of gene delivery and expression in gene therapy with suicide genes such as herpes simplex virus thymidine kinase (HSV-tk) is assessed with measurement of selective localization of radioiodinated HSV-tk substrates in HSV-tk expressing tumor. we compared in vitro uptake of ^{125}I -IVDU, IVFRU and in vivo image of HSV-tk gene tranduced hepatocellular carcinoma model. **Methods** Using H_2O_2(hydrogen peroxide), IVDU and IVFRU was radiolabeled as carrier free form. The uptake of ^{125}I-IVDU, IVFRU was determined with increasing incubation periods in MCA-tk and MCA cell line(1×10^6 cell/flask). The cell harvested and counted after incubation of 15, 30, 60, 120, 240, 480 minutes. For estimating accumulation of radiolabelled IVDU, IVFRU in HSV-tk expressing tumor, MCA-tk cells($1\times10^6/100\mu l$) injected intramuscularly into right thigh of buffalo rats. To determine selective localization of radiolabelled IVDU, IVFRU in HSV-tk expressing hepatocellular carcinoma bearing buffalo rats, MCA-tk cells(1×10^7 cell/$100\mu l$) were injected subcutaneously into both shoulders of buffalo rats. Established tumor mass implanted into liver of buffalo rats using intra-hepatic tumor injection. Two weeks later, ^{123}I labelled IVDU, IVFRU(7.4×10^7Bq/$200\mu l$) injected intravenously into tail veins of each buffalo rats. Gamma camera used as revealing localization of ^{123}I-IVDU, IVFRU in MCA-tk cells grafts rats and in vivo image was taken 2 hrs, 24 hrs after injection. **Results** radioiodinated IVDU, IVFRU were radiolabeled with ^{123}I as labeling yield 70%, ^{125}I as 84%. Two compounds showed minimal uptake in MCA cell line. but, in MCA-tk cell line, increased uptake was observed. The ratio of MCA-tk to MCA was upto 116-fold in ^{125}I-IVDU, upto 37-fold in ^{125}I-IVFRU at 480 min. The uptake of IVDU was 4 times higher than IVFRU in MCA-tk cells. Gamma camera images of HSV-tk gene tranduced MCA tumor showed accumulation of ^{123}I-IVDU and ^{123}I-IVFRU to clearly defined images. In hepatocellular carcinoma bearing buffalo rats, selective localization of ^{123}I-IVFRU observed. **Conclusions** Both compounds could be used as imaging HSV-tk gene expression for gene therapy monitoring in MCA-tk tumor model. In HSV-tk tranduced hepatocellular carcinoma bearing buffalo rat model, IVFRU could be used as prognostic marker.