Uptake and Binding of Gallium and Selen in Malignant Tumors

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Many clinical investigations on the uptake of gallium in malignant tumor have been performed since the first report of Hayes and Edwards in 1969, and the evaluation on its applicability and on its limit have been well recognized. However, no fundamental mechanism of its uptake has been understood as yet. In this presentation the results on experimental approach by way of solid experimental tumor of rat and mouse are reported.

The uptake of gallium by solid Yoshida sarcoma of rat increases rapidly and gets its highest value 12-20 hrs after intraperitoneal injection, and the visualization by scintillation camera is possible at this point where higher radioactivity was found in tumor as well as in liver and spleen, in contrast to brain and muscle which contained little radioactivity. By subcellular fractionation radioactivity was distributed mainly in 105,000g supernatant in tumor as well as in normal tissue, and no specific localization of radioactivity was found in tumor tissue. In supernatant fraction gallium-protein binding of different intensity was found by Sephadex column chromatography eluted with 4M KCI and 6M urea, which revealed the presence of a gallium-protein binding not ionic, non hydrogen-bond in nature, i.e., no radioactivity was released from the peak. In respect to the relationship of gallium uptake and tumor growth, uptake by solid tumor treated with nitrogen mustard-N-oxide was compared with that of control, and it was found that no decrease in its uptake was observed in treated tumors. X-irradiated tumor gave the same results. These findings, togather with the results obtained in regenerating rat liver (no increase of uptake after partial hepatectomy) suggests that the uptake of gallium by tumor may be independent on tumor growth processes. Selen-selenite, in contrast to gallium, does not concentrate to tumor as gallium does, and the biological half life is relatively long. This fact may not favor its use as a scanning agent. In virto study of gallium and selen is in progress.

Comparative Study of the Distribution of ^{67}Ga-Citrate, ^{111}In-Chloride and ^{75}Se-Selenite in Tumor Bearing Mice Using a Semiconductor Detector

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Numerous recent reports have indicated that ^{67}Ga-citrate is readily taken up by malignant tissues. In addition there has been recent evidence that ^{111}In-chloride and ^{75}Se-selenite are also preferentially incorporated into tumors. In order to evaluate the above findings, the authors have studied the uptake of these isotopes by Ehrlich's tumor bearing mice. Because of the difficulty inherent in detecting these three isotopes with a conventional Nal (Tl) detector, the experiments were performed with a Ge (Li) semicondutcor detector.

The experimental animals were mice (DDN-strain) 14 days after transplantation of Ehrlich's tumor cell into the femoral region. Standard solutions was produced by mixing 10 μCi of each of the 3 radioisotopes such as ^{67}Ga-citrate (carrier-free), ^{111}In-chloride (carrier-free) and ^{75}Se-selenite (specific activity: 50 mCi/mg) 0.2 cc of standard solution was injected into the abdominal cavity of each tumor bearing mouse. The mice were sacrified 48 hours after injection, and the tumor, liver, kidney, lungs, stomach, intestines and vertebrae (containing the bone marrow) were excised. The photo-peaks of the 3 radioisotopes in each organ were measured with a 200-channel multianalyser attached to a Ge (Li) semiconductor detector. The photo-peaks of ^{67}Ga, ^{111}In and ^{75}Se were measured at 182 KeV, 172 KeV and 136 KeV respectively. The uptakes of ^{67}Ga, ^{111} In and ^{75}Se by each organ were measured in comparison to the photo-peaks fo the standard solutions. The following results were obtained A) ^{67}Ga-citrate is most readily incorporated into the tumor with ^{111}In-chloride and ^{75}Se-selenite having similar but lower uptakes, B) ^{67}Ga-citrate had the lowest kidney uptake. C) ^{67}Ga-citrate uptake by the bone (containingk the bone marrow) was high whereas, uptake of the other isotopes was low. D) The other organs studied had similar uptakes for all three isotopes. The use of a Ge (Li) semiconductor detector made it possible to detect uptakes of ^{67}Ga-citrate, ^{111}In-chloride and ^{75}Se-selenite into the same tumor bearing mouse at the same time.

Radiolymphadenography in Patients with Malignant Lmphoma Using ^{67}Ga-Citrate and ^{99m}Tc-Sulfur-Colloid

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^{67}Ga has been shown to have a high uptake in many soft tissue tumor, but it has, also rather high uptake in some normal organ and tissues. Scintiphotograph of abdomen, therefore, often presents difficult problems in interpretation.

Gelatin stabilized ^{99m}Tc-Sulfur-Colloid, following subcutaneous injection in the back of the feet, has been shown to give image of pelvic-abdominal lymphnodes.

In this report, we used both nuclides and compared both scintiphotoes.

Materials and Methods:

Scintiphotoes with ^{67}Ga-citrate 1-2 mCi were taken 48-72 hours after intravenous injection with Pho-Gamma III.

Scintiphotoes with ^{99m}Tc-Sulfur-Colloid, 2-3 mCi were also taken 2-4 hours after subcutaneous injection with local anesthesia.

Results:

Remarkable uptakes of ^{67}Ga were shown in lymphnodes of neck, mediastinum and axilla, in patients with malignant lymphoma.

Lymphnodes in pelves and abdomen, however, could be rather hardly visulized, because of ^{67}Ga-activities of abdominal organs' and bowel, even in patients with malignant lymphoma.

Markedly decreased uptakes were seen after chemotherapy and or radiotherapy, and successfully, abnormal uptake was not seen.

Radiolymphadenography using ^{99m}Tc-sulfur-Colloid in normal case shows lymphnodes of inguinal area, pelves, and para-aortic area, in the shape of inverted "Y" and this images well correspond to the lymphography with lipiodol.

In patients with malignant lymphoma, their scintiphoto varies according to the group of nodes involved and degree of involvement, such as absence or interruption, marked asymmetry, abnormal collateral lymphpathways and enlargement.

After treatment by drugs and/or radiation, normalizations on scintiphotoes were seen.

Normalization with both nuclides on scinti-