

pool.

Further improvement will be achieved by

pursuing investigation in the same category.

## Studies on the Accumulation Mechanism of Radioisotopes Used for Tumor Diagnostic [ $^{67}\text{Ga}$ -citrate, $^{169}\text{Yb}$ -citrate and $^{51}\text{Cr}$ -Bleomycin]

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As reported previously [H. Orie; Tumor scanning with Ga-67 and its mechanism studied on rats. *Strahlentherapie* 144 192-200 (1972)], the accumulation of Ga-67 citrate in the rat experimental tumor was not influenced by the tumor growth rate. Also the incorporation of Ga in regenerating rat liver after partial hepatectomy was not increased. Further it was observed that the rate of Ga incorporation in the tumor remained fairly unchanged after the treatment with chemotherapeutic agent and X-irradiation. However, when human patients are treated in the same way, a decrease in scan-image was observed when treated effectively.

The author pointed out that even when the uptake per unit mass of the tumor remains unchanged after treatment, the discrepancy may result from the difference in the assessment, i.e., cpm/g of animal experiments v. scan density expressing cpm/g  $\times$  depth. As to the mechanism of Ga transport in the blood, the author and T. Hishizawa found that Ga binds transferrin, as indicated by the fractionation study of  $^{59}\text{FeCl}_3$  and  $^{67}\text{Ga}$  labelled (*in vitro*) mouse serum on Sephadex G-200.

Ga-protein binding *in vivo* of liver supernatant and blood serum was found very labile, and when filtered through Sephadex G-50 repeatedly, a dissociation of Ga from protein was observed.

The lability of the binding may influence the localization study of Ga in the cell, in which most radioactivity was shifted in 105,000 g supernatant fraction during centrifugation, as a result of its

dissociation from the protein, and the absence of a firmly bound Ga-protein complex in liver supernatant may indicate the absence of the much discussed Ga-specific protein receptor in cells as well as in the tumor.

The alternative hypothesis of Ga localization in tumor, the adsorption of Ga to bone matrix (hydroxyapatite) as proposed by Anghileri (1971), was in turn examined by *in vitro* adsorption experiment and expressed in adsorption isotherm, which indicated that no more affinity exist between Ga/Yb and hydroxyapatite as compared to other non-tumoraffin radionuclides (Cr, Fe, Sr, Hg,  $\text{PO}_4$  and  $\text{TcO}_4$ ).

The tumor localization of radionuclide by way of tumor-specific chemotherapeutic agent was investigated on  $^{51}\text{Cr}$ -labelled Bleomycin. The preparation of  $^{51}\text{Cr}(\text{III})$ -Bleomycin was carried out in acid range with excess of ligand and the chelated ligand was separated on Sephadex G-10. The preparation was identified on TLC by Umezawa's method.

Tumor localization by this agent was studied *in vivo* on rabbits inoculated with Dr. Rous' V 2 squamous cell carcinoma and on mice inoculated with Ehrlich's carcinoma. A positive scan was obtained in rabbits within 60 min after intravenous injection of 200  $\mu\text{Ci}$  of  $^{51}\text{Cr}$ -Bleomycin and the positive image persisted for 48 hrs. In mice higher radioactivity was found in solid tumor and bone. Our further study on  $^{169}\text{Yb}$ - and  $^{85}\text{Sr}$ -Bleomycin is in progress.