

exposure of several days. On the other hand, next slice of these sections were then stained using the hexatoxylin and eosin. From the observations of these autoradiogram and H·E stained slice, the following results were obtained.

It was concluded that concentration of ^{67}Ga , ^{111}In and ^{169}Yb was predominant in viable tumor tissue rather than in necrotic tumor tissue and concentration of these elements was predominant

in connective tissue (which contains inflammatory tissues) rather than in viable tumor tissue, regardless of time after the administration.

Considering the above-described facts, it is presumed that binding substance of these elements is acidic mucopolysaccharide, as there are large amount of acidic mucopolysaccharide in inflammatory tissues, which has many carboxy radical, sulfonic group in its structure.

Biological and Biochemical Studies on the Tumor Affinity of Gallium Element

S. OKUYAMA*, S. TAKEDA*, T. MATSUZAWA* and T. AWANO**

**Department of Radiology and Nuclear Medicine, The Research Institute for Tuber closis and Cancer, Tohoku University, Sendai, and **Fukushima Biomedical Institute of Environmental and Neoplastic Disease, Okuma, Fukushima*

^{67}Ga tumor scanning is useful in the diagnosis of cancer localization and rough estimation of therapeutic effectiveness and so on. Our interest was concentrated on the gallium affinity to tumors of different cancer biology of histopathology, negative membrane charge, cell growth and lysosomes. Various experimental rat and murine tumors as well as human malignancies were employed.

1) Histopathological difference of ^{67}Ga uptake: In vivo uptake of ^{67}Ga was greatest in undifferentiated cancer (Sato's lung cancer); adenocarcinomas (the ascitic hepatomas of AH 7974 and AH7974F), the next; melanoma and squamous cell carcinoma (WHT/Ht), and mucin-producing, slow-growing adenozarcinoma (R-1), the least.

2) ^{67}Ga in vitro uptake vs parameters of cancer biology

	Cellular membrane charge	Cellular doubling time	^{67}Ga in vitro uptake
FM3A (murine breast cancer)	μV^{-1} $\text{sec}^{-1} \text{ cm}$	hr	$\mu\text{Ci}/10^6$ cells
	-1.52 ± 0.24	12	0.26
C6 (human lymphosarcoma)	-0.64 ± 0.10	16.8	0.19
P3H (human Burkitt)	-0.60 ± 0.10	19.2	0.09

3) Extracellular-to-intracellular migration of ^{67}Ga : Fractionation studies at 3 and 48 hours of labeling revealed that ^{67}Ga localizes on the cell membrane during the initial hours and then gradually moves into the cell and localizes intracellularly.

4) Lysosomal fixation of ^{67}Ga : Ultracentrifugation studies and electron microscopic analysis confirmed that ^{67}Ga fixes in the lysosomes.

5) Gallium modification of cancer biology: When it was added to FM3A cell culture, cold, nonradioactive gallium produced (1) a temporary cessation of cell increase, (2) later reduction of cell growth, (3) marked reduction of saturation density, and (4) morphological acquisition of functioning cells such as macrophages, indicating "de-cataplasia" and "re-differentiation".

Gallium adheres to the cell membrane, then enters the cell rather gradually, and fixes specifically in the lysosomes. The element seems to take hold of cancer cells in such a way so as to modify their parameters of cancer biology.