is at present no outstanding Tc-99m radiopharmaceutical for the imaging of various malignant tumors. A need exists for such agents.

Hoping to find good radiotracers for tumors, we prepared Tc-99m complexes of substances which were expected to have affinity for tumor tissues such as amino acids, peptides, and porphyrins and studied the scintigraphic behaviors in experimental animals bearing spontaneous or transplanted tumors.

In the course of the study, we found that S-containing amino acids and peptides were complexed with Tc-99m in high yield, and the images of transplanted Ehrlich tumors in mice were visualized with the complexes of cysteine, S-carboxymethylcysteine, and glutathione. Recently the Tc-99m complex of ethylenediamine-N,N-diacetic acid (EDDA) was found to give much more satisfactory scintigrams of Ehrlich tumor in mice. Sequential scintigrams show that the image of the tumor was recognized in 1 hr and visualized very clearly 2–5 hr after the i.v. administration of Tc-99m complex of EDDA. The radioactivity was not accumulated in any specific organ other than the tumor and excreted through kidneys. The Tc-99m EDDA complex was also effective for scintigraphic visualization of other malignant tumors in experimental animals.

A number of chelating ligands structurally related to EDDA were examined for Tc-99m labeled radiotracers for tumors. Among the Tc-99m complexes examined, those of ethylenediamine-N,N′-diacetic acid, N-hydroxyethyliminodiacetic acid, and propylene-1,3-diamine-N,N-diacetic acid achieved clear visualization of Ehrlich tumors.

Studies on the scintigraphic visualization of human tumors and on the mechanism of the concentration in the tumor tissues of the Tc-99m complexes are in progress in our laboratories.

V3

Technetium in Biology and Medicine

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Ever since the availability on a large scale [1] of technetium-99m and its application in science and technology [2], followed by an increasing use of technetium-99m in non-invasive diagnostic nuclear medicine [3], there has been great interest in the biological behaviour of this element in animals and humans [4]. Formerly the use of technetium-99m in functional imaging of different organs and tissues was based on its very favourable physical properties: pure gamma emission of 140 Kev, and short half-life of 6 h, ideal for external imaging, with low radiation risk both to the patient and to the nuclear medicine department personnel. During the past 20 years since its first use in nuclear medicine, it has been increasingly realized that for the synthesis of new technetium-99m radiopharmaceuticals and for evaluations of their biological behaviour a rigorous knowledge of the aqueous solution chemistry of technetium-99m in its various oxidation states, from −1 to +7, is needed. For pertechnetate-99m ion, now widely used for the imaging of the thyroid glands, brain, stomach and salivary glands, and also forming the starting material for the synthesis of other technetium-99m radiopharmaceuticals, little solution chemistry and consequently biological behaviour is known [5]. We have shown that the presence of a small amount (~4 ppm) of free aluminum in the generator-produced pertechnetate-99m eluate not only gives false images of the thyroid gland, but also produces impure technetium-99m radiopharmaceuticals [4–6]. These inconveniences are easily avoided by chromatographic quality control of generator-produced pertechnetate-99m eluate before its administration for radionuclidic imaging, or before its use for the preparation of other radiopharmaceuticals. The results we have explained by complexation of the pertechnetate-99m ion with free Al^{3+} present in the generator column. These conclusions are supported by the chromatographic and electrophoretic examinations of all eluates during the useful life of the generator. Chromatography and electrophoresis are the only techniques which lend themselves to the study of solution chemistry of technetium-99m at the radiopharmaceutical concentration level (which is of the order of nanomolar).

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