Editorial: Internally Administered Isotopes In the Treatment of Solid Malignancy

In the past decade, the use of internally administered isotopes in the treatment of patients with solid malignancies has had limited clinical application. The principal success of this modality has been in the treatment of subgroups of patients with well differentiated thyroid carcinoma by iodine-131 (^{131}I) (*1*). Investigative efforts are underway evaluating the potential efficacy of isotope conjugated monoclonal antibodies specific for tumor antigens in patients with a variety of solid tumors. The studies of Order et al. have demonstrated remissions of metastatic as well as primary hepatocellular carcinoma with ^{131}I-antiferritin and yttrium-90- (^{90}Y) antiferritin (*2*). Another recent investigative effort in the therapeutic use of internally administered isotopes has been treatment of patients with craniopharyngioma cysts by stereotactic puncture and installation of colloidal isotopes, particularly ^{90}Y and phosphorus-32 (^{32}P) (*3*).

Two studies in this issue of *The Journal of Nuclear Medicine* suggest additional applications of internally administered isotopes in the treatment of patients with solid malignancies. The study of Llaurado et al. evaluate the pathologic sequalae of radiosotopic pulmonary lobectomy in dogs with the extrapolation of this technique as treatment for patients with lung cancer (*4*). The work of Lattimer et al. studying the clinical, biochemical, and pathologic effects of samirium-153-EDTMP (^{153}Sm-EDTMP) in beagles suggest this compound as a potential treatment of patients with skeletal metastasis (*5*).

Carcinoma of the lung is a major cause of death in the United States and throughout the world. It is estimated that there will be 157,000 new cases of lung cancer in the United States in 1990. At the time of diagnosis, the disease has spread to regional nodes or distant sites in 70% of patients. As Llaurado et al. point out, curative surgical resection is possible in only one-fourth of all diagnosed non-small cell pulmonary cancers. For patients with localized but surgically unresectable non-small cell pulmonary carcinoma or for patients not resectable because of underlying medical illness, radiation therapy with and without chemotherapy has been the traditional treatment. Current results with modern and aggressive external beam radiation therapy indicate a 5-yr survival of 6% and 27%–48% failure rate within the irradiated volume depending on total radiation dose (*6*). Although the local failure rate is significant following external beam radiotherapy, 75%–80% of patients develop distant metastases following treatment. Although improvements in local control are needed, it is also clear that improvements in systemic treatment for lung carcinoma are required to result in meaningful improvements in survival. In search for an alterative treatment for inoperable cancer of the lung in humans, Llaurado et al. investigated in a canine model the effect of ^{32}P treated lobe and, based on this data, conclude that "this procedure may be useful in patients to destroy inoperable cancer of the lung." The difficulty with this conclusion is that although normal lung parenchyma is well perfused and vascularized, there is no evidence to suggest that lung carcinomas are adequately vascularized to allow uniform deposition of radioisotope labeled microspheres within the tumor. In fact, experimental as well as human data in many tumor systems have demonstrated the opposite—there is heterogeneity of blood flow within tumor both on a macroscopic as well as microscopic level (*7*). One of the explanations for the poor response to chemotherapy of many solid tumors is that portions of the tumor are not being exposed to drugs because of heterogeneous blood supply within tumors. Although the concept of selected infusion of radioisotopes for treatment of cancer is interesting, further investigation of this treatment in a canine lung cancer model is required prior to any consideration of human application.

The study of Lattimer et al. evaluate the acute toxicity, principally hematologic, of ^{153}Sm-EDTMP. The data from these experiments suggest that ^{153}Sm-EDTMP is a safe radiopharmaceutical in healthy beagles. This will obviously require evaluation in debilitated cancer patients exposed to myelosuppressive agents. It has been reported that ^{153}Sm-EDTMP localizes in bone and has a special avidity for bone that is involved by tumor. As Lattimer et al. note, there are ~125,000 new cases of skeletal cancer per year with the vast majority of cases being metastatic. Any improvement in palliation, quality of life, or survival for these patients by an innovative treatment would be an advance to current practice. The use of internally administered isotopes (^{89}Sr, ^{32}P, and ^{131}I) for skeletal metastases has had mixed results (*8*). Because of its more favorable physical characteristics—a beta emitter with a half-life of 46.27 hr and 103 keV gamma emission and its avidity for bone involved with cancer—it is hoped that ^{153}Sm will be more effective than prior

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radiopharmaceuticals. Estimation of radiation dose to metastases and to bone marrow for each patient appears possible with this agent. There is limited clinical experience with this radiopharmaceutical. However, a recent report by Turner et al. of a phase I study of ^{153}Sm-EDTMP for disseminated skeletal metastases is encouraging (*9*). Following a single administration of ^{153}Sm-EDTMP, pain was relieved in 22 of 34 evaluable patients (65%) for periods of 4 to 35 wk. In 15 of the 34 evaluable patients, there was evidence of radiologic stabilization or regression of skeletal metastases. It now appears that the next step in evaluation of ^{153}Sm-EDTMP will be in controlled clinical trials to determine response rates and optimal dosing and scheduling.

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