THE AUTHOR'S REPLY: MECHANISM OF RADIOSTRONTIUM UPTAKE IN METASTASES FROM COLORECTAL CANCER

The observation that radiostrontium is localized in noncalcified extraosseous soft-tissue tumor is not infrequent. The exact mechanism of this phenomenon, however, still remains obscure. The incidence of radiostrontium (particularly ^{87m}Sr) deposition in the metastases from colorectal cancer is not uncommon. We observed significant accumulation of ^{87m}Sr in four cases of colorectal cancer metastases in soft tissue (three to the liver and one to the anterior abdominal wall). The histology of these metastatic lesions revealed well-differentiated adenocarcinoma of colorectal origin. In none of these cases was there any radiographic or macroscopic evidence of calcification. Even a Von Kossa stain failed to show microscopic calcification in these metastatic lesions. Since these patients were referred to us after the primary tumor had been resected, we did not have the opportunity to see whether or not in these cases the primary tumor per se would have taken up the radiostrontium. However, an uptake or excretion or both of ^{87m}Sr can also occur in normal colon, especially in the cecum (*1*). This would pose a problem in differentiating strontium uptake in primary colon cancer from normal colon unless the accumulation of strontium in the former significantly exceded that in the latter. In contrast, distant colon cancer metastases, with moderate uptake of ^{87m}Sr, can easily be identified in the scan because of the lack of interference of normal colonic activity in these metastatic areas. Interestingly enough, some lesions of this type have also been detected by ^{99m}Tc-polyphosphate scan (*2*).

Regarding ^{87m}Sr concentration in an apparently noncalcified extraosseous soft-tissue tumor, several mechanisms deserve consideration: (A) Since radiostrontium is actively concentrated and excreted by the normal colonic mucosa (*1,3*), it can be argued that ^{87m}Sr accumulation in metastatic sites from primary colon cancer could be due to metastatic cells retaining similar concentrating power. The more differentiated the cells are, the greater the chance of strontium accumulation in the lesion. In addition, tumor uptake of strontium varies significantly from one case to another depending upon various factors such as delivery of the nuclide to the tumor, residence time of the nuclide in the tumor, degree of fibrosis, and the number and strength of the binding sites available to a particular radiopharmaceutical. (B) Since strontium uptake in tumors (*4–6*) is not just limited to colorectal cancer, one might bring up Selkirk's (*7*) finding that certain tumor cells show an increased membrane-bound calcium (which is different from so-called calcification). If this is true for cancer cells in general, one may speculate that the mechanism of ^{87m}Sr uptake by cancer cells would be one of heteroionic exchange process. (C) It appears that one characteristic feature of malignant tumors is their greater uptake of proteins from the plasma (*8*). Therefore, the radiopharmaceuticals which can bind to the plasma proteins would be expected to preferentially enter the tumors along with the plasma proteins. Strontium can bind, like calcium, to these plasma proteins.

Samuels' theory (*5*) of citrate being responsible for strontium uptake in the tumors does not hold good in all cases as evidenced by the fact that certain tumors concentrate radiostrontium in both citrate as well as nitrate forms. We have also noted a case where a tumor with good ^{87m}Sr-citrate uptake failed to concentrate ^{67}Ga in citrate form (*2*).

Whatever the mechanism may be, well-differentiated colon cancer metastases seem to be avid for ^{87m}Sr and possibly for ^{99m}Tc-polyphosphate also. One often encounters patients having liver metastasis (demonstrated by colloid scan) with the primary site being unknown especially when usual routine workup failed to reveal the primary lesion. In such patients, ^{87m}Sr or ^{99m}Tc-polyphosphate scan may prove useful. An increased uptake of these radiopharmaceuticals in the liver metastasis may help the clinician in judging whether the colon is harboring an occult lesion and this may lead to a more meticulous search for the primary site in the colon.

The uptake of the aforementioned two radiopharmaceuticals occurs in varieties of other tumors. An elucidation of the specific mechanisms of uptake in the particular tumor requires further studies.

TAPAN K. CHAUDHURI
University of Iowa
Iowa City, Iowa

REFERENCES

1. CHAUDHURI TK: Uptake and excretion of ^{87m}Sr in normal colon. Unpublished data

2. CHAUDHURI TK, CHAUDHURI TK, CHRISTIE JH: Tumor uptake of ^{99m}Tc-polyphosphate—its similarity with ^{87m}Sr-citrate and dissimilarity with ^{67}Ga-citrate: to be published

3. CHARKES ND, SKLAROFF DM, YOUNG I: A critical analysis of strontium bone scanning for detection of metastatic cancer. *Am J Roentgenol Radium Ther Nucl Med* 96: 647–656, 1966

4. PAPAVASILIOU C, KOSTAMIS P, ANGELAKIS P, et al: Localization of ^{87m}Sr in extraosseous tumors. *J Nucl Med* 12: 265–268, 1971

5. SAMUELS LD: Detection and localization of extraskeletal malignant neoplasms of children with strontium

87m. *Am J Roentgenol Radium Ther Nucl Med* 115: 777–782, 1972

6. CHAUDHURI TK, CHAUDHURI TK, SUZUKI Y, et al: Splenic accumulation of ^{87m}Sr in a patient with Hodgkin's disease. *Radiology* 105: 617–618, 1972

7. SELKIRK JK, ELWOOD JC, MORRIS HP: Study on the proposed role of phospholipids in tumor cell membrane. *Cancer Res* 31: 27–31, 1971

8. GHOSE T, NAIRN RC, FOTHERGILL JE: Uptake of proteins by malignant cells. *Nature* 196: 1108–1109, 1962