

Clinical Value of Generator Produced 87-M Strontium

R. L. Meckelnburg, M. D.¹

Wilmington, Delaware

Tracer methods in the study of bone were used as early as 1727 when Hales, by the use of metal markers, demonstrated the growth of bone by apposition. Bone scanning, begun by Treadwell and Associates in 1942, introduced strontium as a substitute for calcium as a metabolic tracer in scanning and turnover investigations. (1) Since that time, differences have been found to exist between calcium and strontium with regards to their metabolic turnover in the body. For example, the excretion rate is five times higher for strontium than it is for calcium. (2) However, there is enough similarity to allow semiquantitative analysis between the two, and more than enough similarity for clinical scanning purposes.

The objects of any scanning procedure are accuracy, reproducibility, safety to patient and laboratory personnel and simplicity of technique. I wish to emphasize the simplicity of the technique to be described. Strontium tracer studies have already shed new light on old theories. Wendeberg's serial studies in cases of delayed healing fractures or pseudoarthrosis have revealed no significant difference in isotope uptake in comparison with normal healing fractures. (3) This tends to negate the idea of poor blood supply as the basic defect in pseudoarthrosis. Higher isotope uptakes in immobilized extremities as compared to mobile limbs helps explain the changes in bone metabolism with stress.

Recently 87-M strontium has become available from the Oak Ridge National Laboratory in a yttrium-strontium generator. The 2.8 hour half-life of 87-M strontium, plus the absence of any betas and a 388 kev gamma-ray with 27 per cent internal conversion, make it ideally suited for collimation and scanning with commercial equipment. The "Generator-Milking System" is a means

¹Department of Isotopes and Endocrinology, Memorial Hospital, Wilmington, Delaware.

of separating a desired radioisotope from its parent and other contaminants. The relatively long-lived "parent" is fixed on a variable composition-ion-exchange column, from which its shorter lived "daughter" can be easily eluted. This system has the advantages of being simple to handle, operate and shield. It quickly gives a product of high purity in a chemical form suitable for use with little or no processing. The parent material remains in a form with which the process can be repeated. (4) Other practical milking systems using alumina derive ^{132}I from ^{132}Te , $^{99\text{m}}\text{Tc}$ from ^{99}Mo and ^{68}Ga from ^{68}Ge . The ^{132}I and $^{99\text{m}}\text{Tc}$ generators are made by adsorbing tellurite or molybdate on chromatographic alumina and eluting the product with 0.01 M NH_4OH and 0.1 M HNO_3 , respectively. Gallium is eluted from the ^{68}Ge generator with ethylene-diamine tetracetic acid (EDTA). Successful generators using cation-exchange resins have also been produced to obtain ^{140}La from ^{140}Ba , $^{137\text{m}}\text{Ba}$ from ^{137}Cs and $^{90\text{Y}}$ from ^{90}Sr .

PREPARATION OF GENERATOR

The 87 yttrium parent with an 80 hour $T_{1/2}$ was produced by the 87 strontium (PN) 87 yttrium reaction utilizing the 23 mev ORNL 86-inch Cyclotron. The target was 95.4 per cent enriched 87 strontium as the carbonate. Sufficient degradation of the cyclotron beam was accomplished to reduce the 88 yttrium production. An 8-hour irradiation of 100 mgm of strontium carbonate, yielded 53 mc yttrium activity. By chemical processing, the 87 yttrium was separated, carrier-free, from the strontium target and container with a yield estimated to be 95 per cent. Ammonium carbonate solution containing the 87 yttrium activity was then poured onto a BioRad AG-1, X-8 resin in an ion exchange column. The column was then rinsed with 25 ml of 0.01 M $(\text{NH}_4)_2\text{CO}_3$ and this first "milking" showed a slight trace of 87 yttrium activity, approximately 10^{-3} per cent of the 87-M strontium activity. On subsequent washings, less than 10^{-6} per cent of 87 yttrium was found in the 87-M strontium obtained from a generator containing 10 mc of 87 yttrium. (5) The generator can be replenished by slowly pouring ammonium carbonate-87 yttrium solution back on the ion exchange column and discarding the first elution. A picture of the ion exchange column in operation is shown in Fig. 1. Figure 2 shows the growth of 87-M strontium on a 87 yttrium generator.

The yield of the generator is collected in a sterile beaker at the rate of approximately 1 ml per minute and evaporated to dryness for sterility. Ten ml of sterile isotonic saline is then added and takes up greater than 95 percent of the 87-M strontium activity. An aliquot is counted prior to intravenous injection via a millipore filter, adapted syringe. Efficiency of the well counter was interpolated for 87-M strontium from plots on standard reference sources.

DOSIMETRY

The radiation dose to the bone mass and the whole body can be calculated according to the following formula:

$$D_{\text{gamma}} = 0.0331 K P \bar{g} C T_{\text{eff}} \text{ rads. (6)}$$

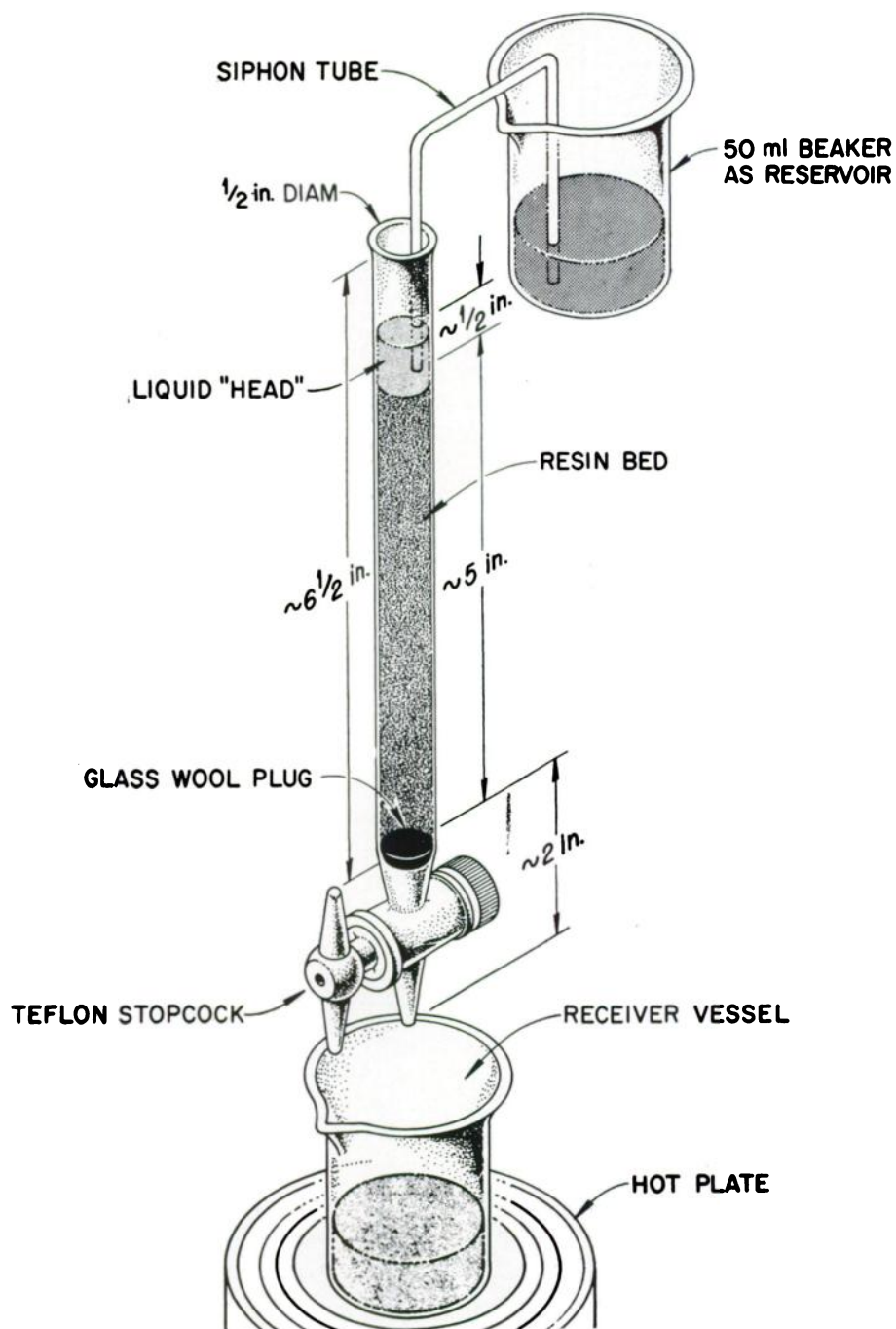


Fig. 1. Yttrium-Strontium Generator with ammonium carbonate being siphoned through Dowex column to carry off 87-M strontium.

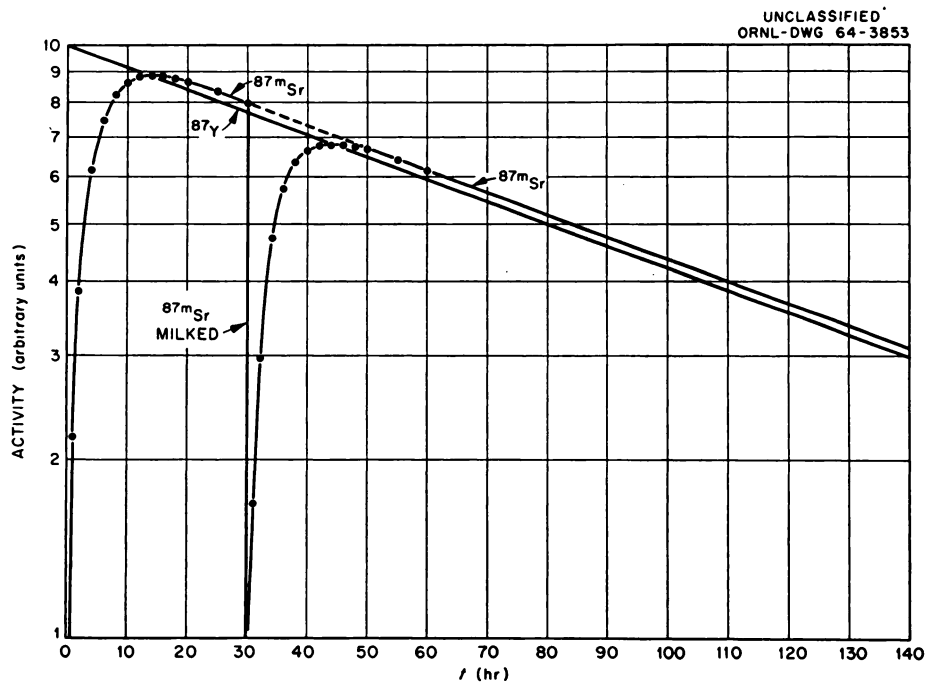


Fig. 2. As shown on graph, generator may be "milked" each day with maximal recovery of 87-M strontium produced. The useful life of the generator would depend upon the amount of yttrium contained.

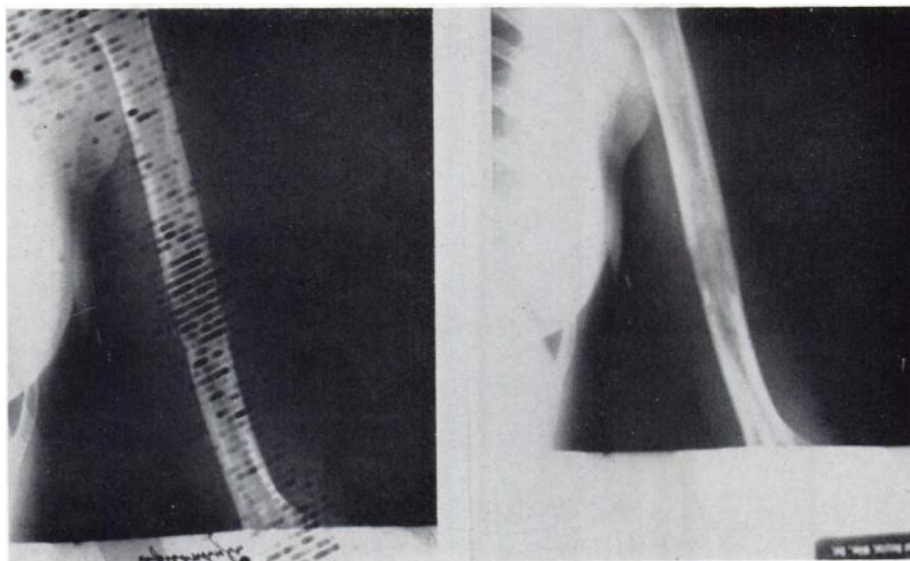


Fig. 3. Osteolytic metastatic adenocarcinoma of breast to shaft of left humerus is shown. A. 87-M strontium scan superimposed on roentgenogram. B. Plain roentgenogram of lytic lesion.

Substituting the appropriate figures for the gamma ray dose constant, density of tissue, geometrical factor, initial concentration and effective half life, the following equations are obtained:

87M strontium—per 100 μ c

$$\text{Dose to bone} = 0.0331 \cdot 1.65 \cdot 41.6 \cdot 1 \cdot \frac{100}{7000} \cdot 0.125 = 40.5 \text{ mrad}$$

$$\text{Dose to whole body} = 0.0331 \cdot 1.65 \cdot 126 \cdot 1 \cdot \frac{100}{70,000} \cdot 0.125 = 1.2 \text{ mrad}$$

85 strontium—per 100 μ c

$$\text{Dose to bone} = 0.0331 \cdot 3.0 \cdot 41.6 \cdot 1 \cdot \frac{100}{7000} \cdot 64 = 3.7 \text{ rads}$$

$$\text{Dose to whole body} = 0.0331 \cdot 3.0 \cdot 126 \cdot 1 \cdot \frac{100}{70,000} \cdot 64 = 1.1 \text{ rads}$$

Dosage calculations of Charkes and Sklaroff (7) were somewhat lower while those of Fleming were higher. (8) Variations in these calculations seemed to be due to the use of different effective half-lives and geometrical factors.

CLINICAL OBSERVATIONS

Representative scans of malignant metastatic bone lesions are shown in Figs. 3 & 4. The increased uptake of 87-M strontium in the lesions is apparent. Scans were made approximately 1 to 2 hours after intravenous injection of the isotope, utilizing a commercial photoscanner with background cut off and contrast enhancement. Over areas of increased uptake, counts from 180 to 500 cpm above background were usually obtained. Amounts of isotope varying from 200 to 1000 μ c were injected into the patients.

Of interest in Fig. 5 is the posterior scan of the bony thorax of a patient with metastatic bronchogenic cancer. Although various sites of increased uptake can be seen in the several vertebral bodies, increased uptake is also seen in the left apical lobe area which is opacified on the chest x-ray by primary tumor. Bone involvement in this area was not seen on the roentgenogram. This may help explain why metastases to bone can be seen with calcium and strontium isotopes prior to any x-ray evidence of involvement. The uptake in these tumor bearing areas is probably due to increased blood supply and this phenomena in an area of bony metastasis may precede bone destruction by many months. (3) Also in Fig. 5, the outline of both kidneys is seen at the time of the one hour scan. A prominent renal accumulation of the isotope is occurring and studies of urinary specimens obtained at varying intervals after injection showed very low levels of excretion of strontium in the first six hours.

SUMMARY

The findings of this investigative procedure have shown the usefulness of the yttrium-strontium generator for making a short-lived isotope available to

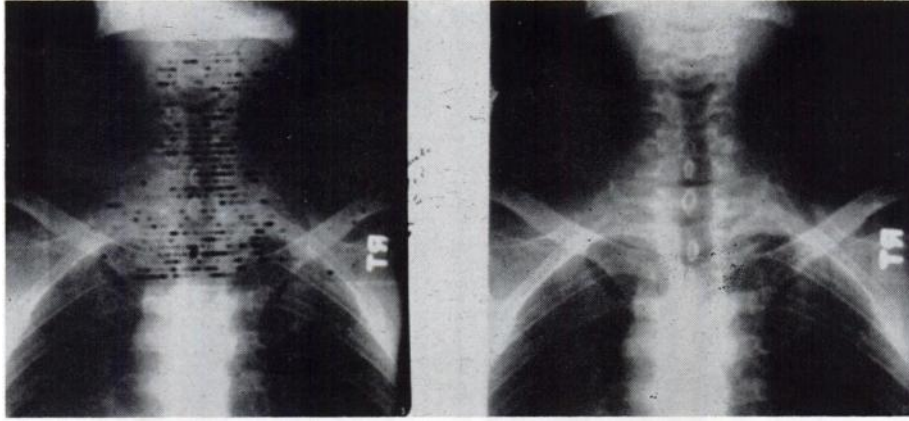


Fig. 4. Osteolytic metastatic bronchogenic carcinoma involving cervical vertebrae 3, 4 and 5. A. Cervical vertebrae roentgenogram with superimposed 87-M strontium scan. B. Plain P-A view of cervical vertebrae.

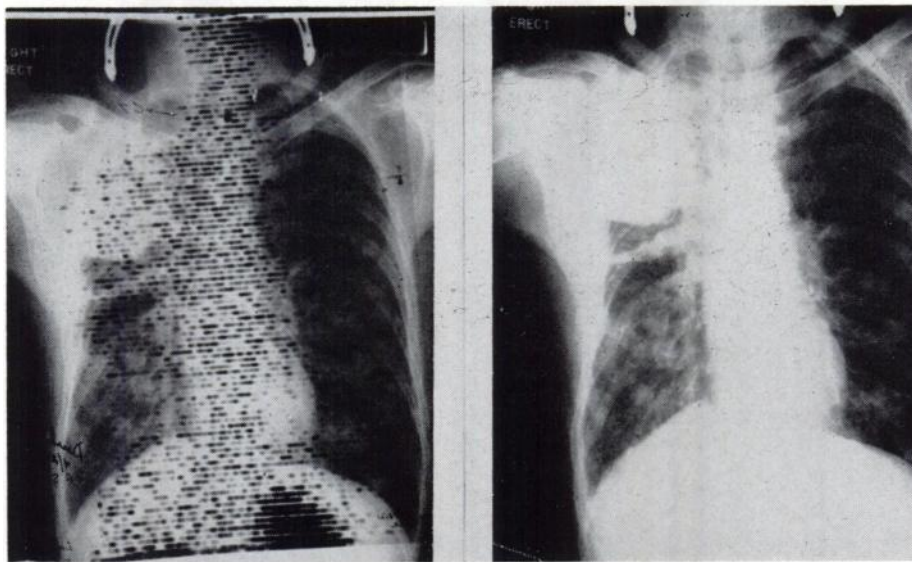


Fig. 5. Extensive bronchogenic carcinoma. A. Superimposed 87-M strontium scan showing increased uptake in area of tumor in right upper lobe. Accumulation of strontium in kidneys is readily seen. B. Plain chest roentgenogram showing extent of tumor involvement.

laboratories remote from the production facility. The present technique demonstrates the simplicity of the process required for the use of 87-M strontium in patients. The low radiation exposure makes this particular isotope suitable for study of other nonmalignant conditions, such as fractures, infections and osteopenic states. Even studies in children can be performed without undue exposure. Because of the short half-life, repeat studies of bone metastasis can be made to measure the effectiveness of different forms of therapy. The large doses possible with 87-M strontium improve counting statistics and thereby enhance resolution, gaining better definition and shorter scanning times.

ACKNOWLEDGEMENT

I am indebted to Dr. M. F. Nelson of Atlas Chemical Industries and Dr. J. J. Pinajian and J. F. Allen of the Oak Ridge National Laboratory for their help and interest in the study. Technical assistance was provided by Mrs. N. Thomas and Miss M. Quashne of the Memorial Hospital Isotope Laboratory.

REFERENCES

1. TREADWELL, A. DE G.; LOW-BEER, B. V. A.; FRIEDEL, H. L. AND LAWRENCE, J. H.: Metabolic studies on neoplasm of bone with aid of radioactive Strontium. *American J.M.S.* **204**: 521, 1942.
2. BAUER, G. C. H.: Strontium 85 and Ca47, in the study of bone. *Radioisotopes and Bone*, F. A. Davis Co., Philadelphia, 1962, p. 103.
3. BAUER, G. C. H. AND WENDEBERG, B.: External Counting of Ca47 and Strontium 85 in studies of localized skeletal lesions in man. *J. Bone and Joint Surgery*, **41B**:558, 1959.
4. GREENE, M. W.; DOERING, R. F. AND HILLMAN, M.: Milking Systems: Status of the Art. *Isotopes and Radiation Technology* **1**:152, 1964.
5. PINAJIAN, J. J. AND ALLEN, J. F.: Oak Ridge National Laboratory, Personal Communication.
6. JOHNS, H. E.: *The Physics of Radiology*. Charles C Thomas, Springfield, Ill., 1961, P. 557.
7. CHARKES, N. D.; SKLAROFF, D. M. AND BIERLY, J.: Detection of Metastasis to Bone by Strontium 87-M. *American J. Roentgenol., Rad Therapy and Nuclear Medicine*, **91**:1121, 1964.
8. FLEMING, W. H.; MCLLRAITH, J. D. AND KING, E. R.: Photoscanning of bone lesions utilizing Strontium 85. *Radiology* **77**:635, 1961.