As the authors themselves state, Berger and Johannssen have previously reported this method. In addition, the French National Blood Center was marketing in June of 1969 an O RH negative red cell labeled with technetium which had been pretreated with tin.

If one defines high efficiency of labeling and irreversibility of the label by in vitro saline washing of the tin treated pertechnetate labeled red cell, then this method is indeed acceptable. However, we have observed that 2 hr after the intravenous injection of labeled red cells there is: (1) high activity in plasma, (2) some uptake in the thyroid, and (3) activity in the bladder. These observations strongly suggest that pertechnetate is complexed to the red cell, and in vivo some undefined mechanism results in the release of radioactivity and the subsequent accumulation in the extravascular compartment.

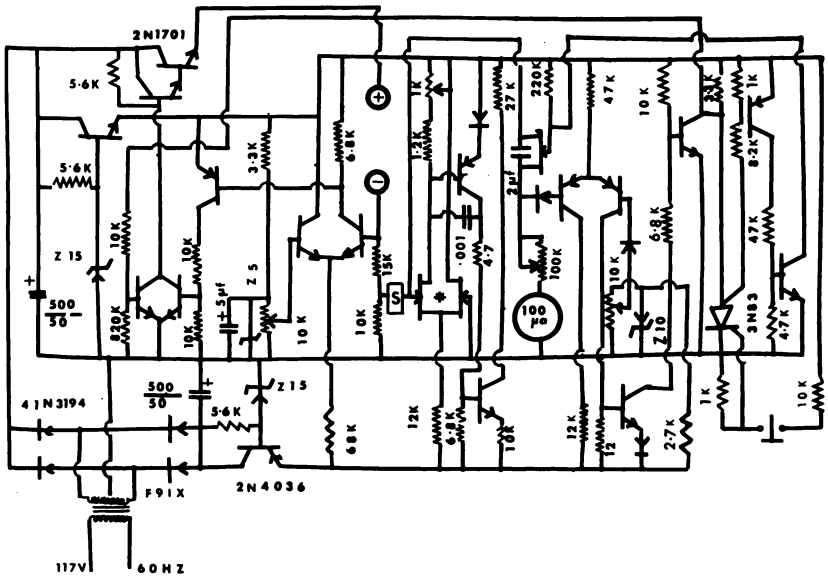
MORTON B. WEINSTEIN
University of Miami School of Medicine
Miami, Florida

SEMIAUTOMATED LABORATORY PRODUCTION OF ^{99m}Tc-ALBUMIN

Recently an electrolytic method of complexation of technetium with albumin through anodic dissolution of zirconium has been developed in our laboratory (*1–3*). For small-scale, routine production of ^{99m}Tc-labeled albumin by this process an apparatus can be designed which consists of the following:

1. **Power supply.** The primary requirement is the supply of a constant charge that will insure the minimum amount of dissolved zirconium for the maximum yield of labeled protein in a given volume of the electrolytic solution. Excess zirconium has to be avoided because: (A) zirconium must be well within clinically acceptable dose limits; (B) precipitation of large quantities of hydrous zirconia, on raising pH, is not desirable (it will block Millipore filtration of the final product for terminal sterilization); (C) possibilities of protein denaturation must be kept to a minimum.

The electronic circuit consists of a power supply with an adjustable current-controlled output, an integrator to measure the charge, and an automatic shut-off circuit to stop the current flow after the preset charge has been accumulated. So that the operation can be followed effectively, the integrator output is monitored by a meter which is calibrated in terms of the preset charge (0–100%). The desired charge can be preset by a two-decade digital switch that is calibrated directly in coulombs. The voltage range of this power supply is from 0 to 15 volts. Details of the circuit are shown in Fig. 1. The charge determining circuit was calibrated by measuring the current and time by standard instruments to an accuracy of 0.1%. The accuracy of the unit as used was limited to 1% because of the resistors in the decade switch.



* MATCHED PAIR
NPN TRANS 2N2270
PNP " 2N3638
FET " 2N3819
DIODES 1N4148

[S] DECADE SWITCH 50K PER STEP

FIG. 1. Circuit diagram of constant charge generator.

2. **The electrolytic cell.** A 15-ml zirconium crucible (Wa Chang Corp., Albany, Ore.) can serve conveniently as the anode. A micro platinum electrode with mercury for electrical contact (Sargent S-30420) attached to a synchronous rotator (Sargent S-76486) can be the cathode. With proper care the same electrodes may be used over and over again (*4*).

3. **Chemicals.** Chemicals used are 1 *N* hydrochloric acid, 25% human serum albumin, ^{99m}Tc-sodium pertechnetate in normal saline, and saturated sodium bicarbonate solution for final pH adjustments.

If various ingredients in the electrolytic solution are in the proportion 5 ml $NaTcO_4$ (saline), 0.5 ml 1 *N* HCl, and 0.05 ml 25% human serum albumin, the charge required for 90–100% labeling will be 4.2–4.3 coulombs. The estimated quantity of zirconium in the total volume of this preparation is approximately 1 mg, and the specific activity is usually in the range 2–10 mCi/ml depending upon the technetium generator. There is no toxicity at this level for several zirconium compounds administered to higher animals through different routes (*5–11*). The technetium activity remains bound to the protein for a wide range of pH (pH 1–8) and temperatures (0–100°C) so that micro- and macroaggregation can be effected by suitable pH adjustment and heat treatment.

Traces of oxidizing agents such as O_2^{2-}, ClO_4^-, MnO_4^-, ClO^-, etc. will inhibit this reaction. The presence of ReO_4^- seems to have no effect on the labeling efficiency.

ACKNOWLEDGMENTS

Encouragement from Mrs. Ivy Benjamin and from Gerald Bruno, Director, Radiopharmaceutical Research and Development, Squibb Institute of Medical Science, is greatly appreciated.

These studies were performed under the auspices of USAEC Contract No. W-31-109-Eng-78 and USPHS Grant No. CA-08034.

PHILIP P. BENJAMIN
WILLIAM H. VOELKER
HYMER L. FRIEDELL
Case Western Reserve University
Cleveland, Ohio

REFERENCES

1. BENJAMIN PP: A rapid and efficient method of preparing ^{99m}Tc human serum albumin: its clinical applications. *Int J Appl Radiat* 20: 187–194, 1969

2. BENJAMIN PP: Electrolytic complexation of technetium, inhibition by impurities and a recipe for routine preparation. *J Nucl Med* 11: 49–50, 1970

3. BENJAMIN PP, REJALI AM, FRIEDELL HL: Electrolytic complexation of technetium at constant current: its applications in nuclear medicine. *J Nucl Med* 11: 147–154, 1970

4. RICHET, GARDNER, GOODBODY: Effect of salts of Zr, Ti, and Mn on nutrition. *Compt Rend* 181: 1105–1106, 1925

5. BATES JI, LEWEY FH, REINERS CR: The reaction of cerebral tissue to Ag, Ta, and Zr—a discussion of the use of these metals for hemostatic brain clips. *J Neurosurg* 5: 349–353, 1948

6. HARRISON JWE, TRABIN B, MARTIN EW: The acute, chronic, and topical toxicity of zirconium carbonate. *J Pharmacol Exp Ther* 102: 179–184, 1951

7. SHUBERT J: An experimental study of the effect of zirconium and sodium citrate treatment of the metabolism of plutonium and radioyttrium. *J Lab Clin Med* 34: 313–325, 1949

8. DOBSON EL, GOFMAN JW, JONES HB, et al: Studies with colloids containing radioisotopes of yttrium, zirconium, columbium and lanthanum. *J Lab Clin Med* 34: 305–312, 1949

9. HARDING HE, DAVIES LTA: Experimental production of radiographic shadows by inhalation of industrial dust: Zircon, $ZrSiO_4$. *Brit J Industr Med* 9: 70–73, 1952

10. HARDING HE: Toxicology of Zircon—preliminary report. *Brit J Industr Med* 5: 75–76, 1948

11. BLUEMENTHAL WB, LEONARD CS: An investigation of the physiological and therapeutic properties of Zr compounds. *Report to the 12th International Congr Pure Appl Chem* 13: 1951

FISSURE SIGN IN LUNG PERFUSION SCINTIGRAMS*

Visualization of the region of interlobar fissures in perfusion pneumoscintigrams may indeed be a sign of pulmonary microembolization, as described by Eaton et al (*J Nucl Med* 10: 571–574, 1969), but their paper presents *no* factual data substantiating this conclusion. Since patients are referred for lung scintigraphy usually because of a clinical probability of embolization, it is obvious that any scan finding in this population will demonstrate the association described. This is not proof of a causal relationship. The statement regarding their two patients studied at autopsy is at best ambiguous. Apparently no microembolization was documented pathologically, and if larger emboli were found "in the region of perfusion defects," the fissure sign was diagnostically noncontributory and may have been due to other causes. Of the 200 scintigrams reviewed to April 1968, the number in which the authors en-

* Letter dated Sept. 26, 1969.