POSITRON-SCANNING WITH COPPER-64 IN THE DIAGNOSIS OF INTRACRANIAL LESIONS

PARTITION OF COPPER-64 VERSENATE IN, AND EXCRETION FROM, THE BODY*

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The development of apparatus for automatic coincidence scanning for localization of brain tumors by means of a positron-emitting isotope (described by Brownell and Sweet;² Sweet and Brownell;¹¹ Aronow and Brownell³) has enabled us to study the suitability of several such isotopes. The technique used and results obtained using Copper-64 in the localization of intracranial lesions will be described and compared with those following the use of Arsenic-74, and the experimentally determined distribution and excretion of Copper-64 both in normal and neoplastic tissues have been studied and constitute the basis of this report.

Wrenn et al.¹⁴ employed Copper-64, injected as a phthalocyanate for the localization of brain tumors. In the present series the great majority of patients received Copper-64 as a versenate—Copper-64 ethylene-diamino tetra-acetic acid (EDTA). In a few instances the copper ammonium complex ion has been given as the nitrate [Cu(NH₃)₄(NO₃)₂].

METHODS

1. Preparation and Administration of the Isotope

Copper-64 can be produced in high specific activity either by cyclotron bombardment (d-p) of copper foil, or by pile irradiation (n-γ) of copper wire.⁴ Copper-64 decays, emitting gamma radiation of 1.34 Mev. with 19 per cent β⁺ emission: 42 per cent K-capture and 39 per cent β⁻ emission. Its half life is 12.8 hours. By the time of injection its specific activity is usually less than 1 mc./mg. of copper.

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¶ We are now obtaining Copper-64 at very high specific activity from Abbott Laboratories at Oak Ridge produced by a Szilard-Chalmers reaction.
(a) A chelated form of Copper-64 is prepared by dissolving the copper wire in (N/3) nitric acid and adding 10 per cent sodium carbonate until a stable blue precipitate is formed. After filtration the calcium salt of versene (EDTA) is added in excess, at least 100 mg. of versene being used for every mg. of copper. The pH of the solution is about 7.2 after autoclaving and it may then be administered intravenously. The dosage is 2.0 mc. per 70 kg. body weight and this contains about 60 mg. of versenate and 3 mg. of copper. In no case has any untoward effect been noticed even in cases in which this chemical dosage was exceeded by a factor of three.

An alternative and simpler method used only in the latest patients is to dissolve the Copper-64 wire in 6N nitric acid and to adjust the pH of the solution with a mixture of Na2CO3—versene. The resulting solution is transferred to a vial and is ready for administration after autoclaving. This method of H. B. Carter, Jr. of the Physics Research Laboratory, Massachusetts General Hospital, is carried out as follows:

**Copper Scheme** (see Fig. 1).
1. Dissolve copper wire in 3 ml. of 6N HNO3.
2. Raise pH of solution to 6.5–7. Add 15 ml. of Na2CO3 versene mixture (620 ml. of a 10 per cent Na2CO3 sol. + 380 ml. versene).
3. Transfer solution to vial via vacuum.

(b) Ionic copper is produced by dissolving the irradiated wire in nitric acid and neutralizing with ammonium hydroxide, just enough excess being added to convert the solution to the copper ammonium complex ion, this being necessary to keep the Copper-64 in solution at body pH. The solution is then autoclaved.

2. **Scanning Procedure**

Almost immediately following intravenous injection of the Copper-64 versenate, automatic coincidence scanning was commenced. One must give a greater amount of radioactivity as Copper-64 than as Arsenic-74 to achieve scans of similar density with the two isotopes (the latter is the isotope generally and routinely used in this laboratory). Scans have been carried out at varying intervals after the injection in order to determine the optimal time for the procedure. Although the pictures at 3 hours showed perhaps a little better definition, such a delay in the use of this isotope with its relatively short half life was not practicable in terms of the maximal number of scans with each shipment of Copper-64. In fact, as we shall see later, the