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METHODS OF PRODUCING RADIOIRON, PARTICULARLY HIGH SPECIFIC ACTIVITY Fe\textsuperscript{59}

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November 30, 1951

Berkeley, California
METHODS OF PRODUCING RADIOIRON,
PARTICULARLY HIGH SPECIFIC ACTIVITY Fe\textsuperscript{59}

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November 30, 1951

ABSTRACT

Possible methods of production of radioiron, as well as methods in actual use are discussed together with a detailed description of the procedure employed for the preparation of high specific activity Fe\textsuperscript{59} by the cyclotron (d,2p) reaction. Included are procedures for the purification and electroplating of cobalt, preparation of the probe target, removal of the radioactive material from the target after bombardment, radiochemical separation of the iron from cobalt, and preparation of the purified material for medical use. Quantitative data are given on the yields and specific activities of samples from various sources, and from several cyclotron bombardments. The (d,2p) reaction produces about 0.07 μc per μa hr. of 20 Mev deuterons in the 60-inch Berkeley cyclotron. The specific activity of the product is of the order of 3 to 10 μc per μg; the maximum achievable specific activity is estimated to be around 100 μc per μg with a 100-hour bombardment at beam currents of 200 μa.

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Introduction

Of the four known radioisotopes of iron\(^{(1)}\) only two are important from the standpoint of ease of production and length of half-life; namely, 2.91 year Fe\(^{55}\)\(^{(2)}\) and 46 day Fe\(^{59}\)\(^{(3)}\). Both of these radionuclides are simultaneously produced by deuteron bombardment of iron in the cyclotron or by neutron capture in the uranium pile.\(^{(4,5,6)}\) The production of each of these two radioisotopes, free of the other, may only be accomplished by a transmutation; i.e., Fe\(^{59}\) is produced from cobalt,\(^{(11,13,14,17)}\) or copper\(^{(15)}\) and Fe\(^{55}\) from manganese.\(^{(16,17)}\) A deuteron beam is needed for these three transformations, and the reactions may therefore be accomplished only in a cyclotron. Fast neutrons, produced by bombardment of beryllium with deuterons, will also yield Fe\(^{59}\) from cobalt;\(^{(17,18)}\) pile-produced fast neutrons induce the same reaction.\(^{(19)}\)

The Production of Radioiron from Iron.

Reported cyclotron yields of Fe\(^{59}\) by the Fe\(^{58}\) (d,p) Fe\(^{59}\) reaction are 0.03 and 0.05 μC per μA hr. with 14\(^*\) and 12 Mev deuterons, respectively.\(^{(14,6)}\) In the later case, the specific activity was about 1.3 μC per mg of iron after long bombardment, and when some 100 mg per square centimeter were milled from the surface of the target. No recent quantitative information is available on radioiron production from iron targets by cyclotron bombardment, but with higher energies, such as the 20 Mev beam of the 60-inch Berkeley cyclotron, one might expect perhaps as high as 0.1 μC per μA hr. The stationary probe used in this cyclotron will take a beam of 200 to 250 μA, if the piece of target metal is 0.010 in. to 0.020 in. thick, and is

\* Originally published as 16 Mev, this value was remeasured, at a later date, and found to be 14 Mev. The present 20 Mev energy is a maximum, during operation it is known to vary between 19 and 20.
properly fixed to the water-cooled copper probe block with silver solder. By careful selection of the hottest area of the 1-1/2 in. by 2-1/2 in. surface, one might remove iron to a depth of 0.005 in. from, for instance, 10 of the total 24 square centimeters, and obtain an estimated yield of some 20 μc of Fe$^{59}$ for each hour of bombardment, per gram of iron, or 2 μc per mg after 100 hours. This compares favorably with the Oak Ridge Fe irradiation unit which has an Fe$^{59}$ specific activity of only 0.06 μc per mg mixed with an Fe$^{55}$ activity of 0.05 μc per mg. (10) There are no data on Fe$^{55}$ activity levels produced in cyclotron iron targets.

By increasing the time of Oak Ridge irradiation to 92 days, or two half lives, one should be able to increase the specific activity to 0.15 μc per mg; and with either pile or cyclotron production, the specific activity can be improved nearly 130-fold through the use of iron enriched in Fe$^{58}$. (12) However, at the present time would not be practical, because of the waste of the electromagnetically processed iron which would be left on the cyclotron probe, to use such material for other than pile irradiations.

Oak Ridge Fe$^{59}$ Unit 26-PX, prepared from iron enriched in Fe$^{58}$, is listed as having a specific activity of greater than 0.5 mc per mg (500 mc/g of Fe). (9) Three such samples received at this laboratory, as assayed at Oak Ridge, has Fe$^{59}$ activities of 1.2, 1.8, and 5 (estimated) mc per mg of iron, with accompanying Fe$^{55}$ activities of 0.14, 0.22, and 0.2 (estimated) mc per mg of iron, respectively, at time of shipment. No report on total iron accompanied the third listed sample; the values were estimated from the reported total solids.

The Fe$^{55}$ simultaneously produced in both cyclotron and pile irradiations has not been particularly useful in contributing to the overall activity of the bombarded material. This is by reason of the fact that whereas the
short-lived isotope decays with the production of $\beta^+$'s of 0.26 and 0.46 Mev, and $\gamma$'s of 1.10 and 1.30 Mev, the longer-lived produces only manganese K-capture x-rays of 5.9 kev, with possibly a very small percentage of weak gammas. Detection of radiation from the Fe$^{55}$, therefore, is not so readily accomplished. Most useful for radioassay of such weak emitters is the gas-flow proportional counter, furthermore, with the considerable improvement in gamma-sensitive scintillation counters, and increase in x-ray counting efficiency may also be achieved. Increased counting efficiency for Fe$^{55}$ should greatly enhance the usefulness of this isotope for tracer applications, allowing full advantage to be taken of its longer half-life.*

**Limitations in the Use of Mixed Fe$^{55}$ and Fe$^{59}$.**

The presence of the long-lived isotope in material which is to be used as a tracer in in-vivo medical research is frequently undesirable, since it remains as a source of ionizing radiation long after the Fe$^{59}$ has been eliminated by decay. For this reason, samples of mixed radioactivity, which are supplied by the AEC, may not at the present time be used as tracers in any medical investigations involving normal individuals.

**Transmutation Reactions and the Production of Carrier-Free Samples.**

The term "carrier-free" is applied to the products of all or nearly all transmutation reactions. While it is theoretically possible to obtain samples in which the radionuclide is the sole isotope of the element which is present, and the sample is then truly carrier-free, this condition is

*It should be noted that measurements of Fe$^{55}$ x-ray activity, such as are reported in this paper, do not represent actual decay rates, as defined by the "curie", but are merely expressions of equivalent or apparent activities.*
seldom if ever achieved in actual purifications. However, for all practical purposes, a condition approaching carrier-free may be accomplished, and it is in this less restrictive sense that the term is generally used; i.e., a very small but detectable amount of the stable isotope or isotopes of the element accompany the radioisotope in the product. Furthermore, if the sample contains only one species of radioisotope, it is said to be radiochemically pure. This term is itself only relative, since, for instance, in bombardments with deuterons, the transmuted product may very well be accompanied by measurable amounts of other radionuclides of the same element, the latter being simultaneously produced by (d,p) reactions on stable isotopes of the desired radioisotope which were originally present as an impurity.

In order to approach the carrier-free condition it is essential that the bombarded or activated material be highly purified insofar as the product isotope is concerned, that precautions be taken to prevent external contamination of the sample with this element, that all reagents employed in the radiochemical separation be purified before use, and that the glassware, etc., be thoroughly cleaned.

In tracer studies, particularly in the fields of biology and medicine, it is exceedingly important to have samples which are carrier-free, or at least have very high specific activities. However, in practical applications it is very difficult to purify the bombarded or activated sample in the complete absence of carrier, so that a balance must be maintained which is compatible with the chemistry involved and with the end usage of the product.
The Production of Fe$^{55}$ from Manganese.

The Mn$^{55}$ (d,2n) Fe$^{55}$ reaction, originally investigated by Hamilton,\(^{(16)}\) has also been successfully applied by Evans for the production of useful amounts of this radioisotope.\(^{(17)}\) Bombardments in the 60-inch Berkeley cyclotron were estimated to produce 0.02 $\mu$C per $\mu$A hr with 20 Mev deuterons;\(^{(24)}\) the activity level of the product was obtained by comparison with a radioactive standard, using a Lauritsen electroscope. The target material was manganese dioxide, packed under a thin tantalum foil; this chemical compound, and bombardment arrangement, are naturally not conducive to production of the best yields. The MIT cyclotron bombardments were made with 14 Mev deuterons, using a 90 percent manganese alloy target and a beam of 100 $\mu$A.\(^{(17)}\) The yield was reported as approximately $2/3$ $\mu$C per $\mu$A hr. The activity level of the purified product was estimated in this case by means of a beryllium-window counter tube. No specific activity data were given by these authors; however, the use of a ferric hydroxide precipitation step in the purification procedure and the addition of 1 to 10 mg of carrier, "if needed," would indicate that a 10 hour bombardment should produce a specific activity of not less than 0.07 mc per mg.

The use of a proton beam for production of this isotope by the Mn$^{55}$ (p,n) Fe$^{55}$ reaction has been investigated,\(^{(25)}\) but yield data are not available. In view of the higher energies of deuteron beams over proton beams, bombardments with the latter are unlikely to give greater yields, and this method is therefore not so important.

Higher Energy Deuteron Production of Fe$^{59}$ from Copper.

Production of Fe$^{59}$ from copper by 190 Mev deuterons in the 184-inch Berkeley cyclotron has been reported, and is listed as occurring,
effectively, as a Cu$^{65}$(A-6,Z-3)Fe$^{59}$ reaction.\(^{(15)}\) Although of interest, such bombardments are not considered practical, for production purposes, because of the small beam currents obtainable at these energies.

A test was made, however, in order to ascertain whether useful amounts of this radioisotope could be so obtained, the copper target was a current-testing probe which had received an unknown total amount of intermittent bombardment over an unknown period, followed by a cooling-off period of about one month. A reasonable estimate of the activity level at the time of assay would be about one-tenth of the maximum or saturation value. Based upon this estimate and upon the assay data, it was determined that, at best, a recovery of 0.1 mc could be obtained from 10 to 20 g of copper target material, but that the specific activity would not be better than 10-15 µc per mg of iron, due to impurities in the copper. In consequence, further work with these targets was not undertaken.

**The Production of Fe$^{59}$ from Cobalt.**

The use of fast neutrons for Fe$^{59}$ production from cobalt by the (n,p) reaction, as employed by Evans, is reported to give yields of 0.023 µc per µa hr.\(^{(17)}\) Although the specific activity is not given, it cannot have been very high, inasmuch as the cobalt which backed against the beryllium, and throughout which the radioiron was formed, weighed 40 g. At best, this much metallic cobalt would contain not less than 10-15 mg of iron, unless previously purified.

The above method of production may be profitably employed, however, if cobalt low in iron is used for the target. It is the only satisfactory method for use with cyclotrons having deuteron beam energies of less than 18 Mev.
The exposure of highly purified cobalt to fast neutrons, in the pile, offers the possibility of producing this radioisotope in good yield.\(^{(19)}\) So far as can be ascertained however, quantitative data are not available. This source of produces should be investigated further.

Cyclotron production of Fe\(^{59}\) from cobalt by the Co\(^{59}(d,2p)Fe^{59}\) reaction, first investigated by Tobias, is the only convenient means of obtaining the isotope free from Fe\(^{55}\), and in an approximately carrier free condition. The energy threshold for this reaction, as determined by Tobias, is somewhere in the neighborhood of 18 Mev.\(^{(13)}\)

Some fifteen samples have been prepared from cobalt in the 60-inch cyclotron at the University of California Radiation Laboratory. The procedures which have been followed and are herewith described are satisfactory but still need improvement, as pointed out below. Due to the expense involved in these bombardments, they were only undertaken at infrequent intervals, as dictated by the needs of the medical group. Further experimental work on procedures was discontinued late in 1950, due to a transfer of personnel, and no further experimental work is contemplated at the present time. The methods outlined are sufficiently reliable, however, to serve as a basis in meeting the growing needs for high specific activity Fe\(^{59}\).

**Preparation of Cobalt Chloride of Low Iron Content.**

The iron content of all cobalt solutions was reduced by ether extraction, followed originally by conversion of the chloride to sulfate for electroplating. Later experiments indicated that a better result could be obtained with a chloride electroplating solution, so this conversion has been omitted in the procedure which is outlined below.
A saturated solution of CoCl₂ in 8 N HCl contains slightly less than 1.2 moles per liter at room temperature, by rough determination. In order to prevent the salt from crystallizing out if the laboratory temperature drops during the night, the solution should be prepared for extraction by dissolving not more than 1 mole of CoCl₂·6H₂O in sufficient 8 N HCl to make 1 liter.

In view of the wider range of acid concentration, i.e., 6 to 8 N, in which isopropyl ether will give almost quantitative extraction of iron, and for reasons of safety, this ether is recommended in preference to the ethyl. It is prepared for use by extracting two or three times each with equal volumes of 8 N HCl and of water, ending with the latter.

A batchwise or a continuous extraction of the cobaltous chloride solution may be employed, but the latter is much to be preferred. It is the only method for which quantitative data were obtained in this work. A convenient standard-taper joint extraction apparatus may be assembled using a flat-bottomed round flask, such as Ace #6895, into which is fitted adapter #5040, the side-arm of which is fitted into adapter #5075, and the latter into a round-bottomed distilling flask such as #6885. Between the top joint of #5040 and the bottom of the condenser a straight adapter is needed that will fix the condenser drip-tip above the side-arm at a distance which is equal to about one and one-half times the distance below this point. The condenser itself, of Liebig or Allihn type, should be not less than 250-300 mm in length, or as dictated by the rate of ether vaporization. About 1 cm below the drip-tip and running all the way to the bottom of the acid chloride solution is a straight glass tube, 6 to 8 mm in diameter, funneled at the tope and with a Corning #39533 coarse porosity dispersion tube at the bottom. In order to minimize the volume of
isopropyl ether, it is recommended that the extraction flask size be such that it will be about nine-tenths filled with the cobalt solution to be extracted. Also, the funneled top of the dispersion tube should be large enough to catch the condensed ether while still fitting through a 29/42 joint, but not so large as to block the upward passage of vapor. It is also recommended that all joints be size 29/42 or larger. The size of the boiling flask should be one liter, and this flask should be provided with a hemispherical Glasscol heating mantle and glass beads.

The cobalt solution is introduced into the extraction flask and the complete apparatus is then assembled. The charge of washed ether is introduced through the top of the condenser until it overflows 200 to 300 ml into the boiling flask. Due to the distance which the vapor travels before reaching the condenser, an insulating layer of asbestos tape, around these tubes, is desirable. Otherwise a large portion of the ether merely refluxes without passing through the aqueous solution.

No determinations of minimum extraction time were made, nor was the liquid ether flow rate measured. However, satisfactory results were obtained by extracting for 4 hours with the ether boiling at a maximum rate obtainable with a 380 watt Glasscol heating mantle, followed by a further two-hour period after addition of 1 to 5 ml. of 30 percent hydrogen peroxide. The latter is for the purpose of oxidizing any ferrous iron which remains and would not otherwise be extracted.

Upon completion of extraction, the condenser, extension, and dispersion tubes are removed, and, by tipping, as much ether is poured through the extraction flask side arm to the boiling flask, as is convenient. The remaining ether is almost completely removed with a pipette. It is recommended that the extracted solution be washed by shaking with several
small volumes of the purified ether, in order to free it of small amounts of organic decomposition products which might have been formed during the six hours of extraction. Following these operations, the sample is at all times carefully protected from contamination with iron. It is evaporated initially under a hood, and finally in an oven at 70°C, until dry and free from HCl.

**Determination of Iron Extraction Efficiency.**

One batch of 3.5 moles of reagent grade CoCl₂·6H₂O was processed by a modification of the above procedure which permitted the obtaining of data regarding the completeness of iron extraction. Instead of a separate adapter with side arm, as noted above, the apparatus was actually prepared by joining a side arm to a long-necked 3-liter flat-bottomed flask having an outer 29/42 $\varnothing$ joint at the top. Otherwise the apparatus was as described.

The solution volume was 3.3 liters, which filled the extraction flask up to the neck. As noted above, a smaller volume should have been used, allowing a better separation of ether and aqueous droplets between the top of the cobalt solution and the side arm. As it was, a small amount of cobalt chloride solution was carried over with the ether but this did not effect the results, and might, indeed, have happened anyway.

After a five-hour extraction period, the apparatus was disassembled, the ether charge removed, and the boiling flask cleaned for reuse.*

* The ether from the first extraction was straw colored after removal of the iron, indicating decomposition, but that from the second was clear. These results would appear to show that formation of colored decomposition product or products upon heating, is catalyzed by iron, since this phenomena is not observed in cold batch extractions. Furthermore, the oxidizing action due to undecomposed hydrogen peroxide, would be of too short duration for completely decolorizing these compounds if continuously formed during the second four hour period. These results indicate the possible need for washing the aqueous solution with fresh ether after extraction and before evaporation.
second four hour extraction was then made with fresh ether after adding \( \text{H}_2\text{O}_2 \), and this charge was also removed as above. A back extraction of the ether with several small portions of water was performed on both of these batches, and iron analyses were run on the aqueous solutions. The iron in the first extract was 59 mg, with less than 0.1 mg in the second.

Two pieces of reagent grade iron wire of approximately the same mass as the iron extracted, were cut off and weighed. Each was dissolved in HCl, and the first solution, containing 61.2 mg of iron, was added to the cobalt solution, together with 2.0 ml of a tracer Fe\(^{59}\) solution, and thoroughly mixed. The tracer solution assayed 18,160 counts per minute, neglecting coincidence correction. This counting rate was determined in a scintillation counter having reproducible geometry; the 2 ml of solution were contained in a sample vial which was placed above the sodium iodide crystal. After counting, the contents of the container were transferred quantitatively to the cobalt solution.

The added normal and radioactive iron were then extracted for 4 hours, plus 2 more after the addition of 1 ml of \( \text{H}_2\text{O}_2 \). The ether charge was again removed and the boiling flask cleaned for reuse.

The second iron solution, containing 60.0 mg of iron was then added to the cobalt solution and thoroughly mixed. The same extraction procedure was again followed. The ether was then removed and back extracted with water. The latter, containing the iron, was evaporated to small volume, transferred quantitatively to a sample vial, diluted to 2.0 ml and counted. Likewise, the used ether was evaporated and counted. The iron solution assayed 572 counts per minute; the ether residue activity was essentially at background. The original activity, corrected for decay, would have been
17,100 counts per minute at the time the second assay was made. As a first approximation, therefore, the unextracted iron was $61.2 \times \frac{572}{17,100}$, or close to 2 mg. This amount in 3.5 moles of cobalt solution is equivalent to some 10 μg of iron per gram of cobalt.

The Electroplating Apparatus.

An apparatus for this work will consist of a variable d.c. power supply, a glass container to serve as an electroplating bath, a holder for the cathode, the cathode itself, a platinum anode, an electric stirrer, hot plate, water-cooled condenser, and a cover to enclose the bath. The assembly of this equipment may be made more or less to suit the convenience of the operator. However, the apparatus as used and described below, needs to be improved insofar as the stirring and anode-cathode arrangements are concerned, in order to eliminate completely the collection of precipitated material on the surface of the cathode. The simple expedient of mounting the cathode vertically does not solve this problem, since, in this position, the evolved hydrogen prevents the production of a smooth plate.

The electroplating cell consists of a heavy-walled pyrex jar about 93 mm in inside diameter and 150 mm high. The beaded lip is ground flat in order to provide a seal for the 1/2 in. lucite top, the lower face of which is 92 mm in diameter, and machined to fit about 8 mm down into the beaker. The o.d. at the top is 100 to 110 mm, thus providing a flange for resting the cover on the rim of the beaker. This top is drilled with three 1 in. holes in line, one of which is in the center, and the other two with centers 1-1/8 in. on each side. It is recommended that Teflon stoppers be provided for these holes, since small amounts of iron may be introduced from rubber stoppers. The latter may be used however, if carefully cleaned...
and protected, preferably with a cover of thin polyethylene sheet. The stopper for the center hole is drilled to take a 5 mm diameter glass tube. Sealed into the lower end of this tube, with connecting wire leading up through the center, is a flat spiral of 0.051 in. diameter platinum wire, 5 in. long. Two 9/32 in. diameter holes are also drilled 1-1/2 in. from the center on a line at right angles from the line of the larger holes, and into one of these is inserted a thermometer. One of the larger holes serves for the introduction, through a stopper, of a vertical 15 mm glass tube which is bent to about 45° from the vertical 5 or 6 cm above the stopper. This tube has an outer 19/38 joint at the top, to which a 350 mm condenser is attached for the prevention of excessive evaporation losses during plating. A small glass propeller fixed in a variable speed electric stirrer is introduced through a stopper in the remaining large hole, and a 7 mm glass tube, extending a few centimeters above and nearly to the bottom of the beaker, is inserted through the other small hole. The latter serves to bring out the cathode connection wire.

The 1-1/2 in. by 2-1/2 in. cathode is made of copper, 1/4 in. thick. Although thinner copper probably would also be satisfactory, too thin a piece is warped during plating, producing a concave deposit. The preparation of the copper surface for electroplating is quite important; the smoother it is made, the less chance there is for production of pin-holes due to continuing evaluation of hydrogen at fixed locations. However, if too smooth, the deposit will break loose after several hours and will be useless. The best results are obtained by polishing one side with successively finer pieces of emery paper, ending with wet polishing using number 400. Before plating, the copper is washed with detergent, rinsed, and dried.
In order to prevent electroplating of cobalt on the sides and bottom, and to minimize the "edge effect," the copper block is fitted into a square glass holder, 1/2 in. deep, having a clearance of 0.002 in. to 0.004 in. between the sides and metal. The bottom of this holder is drilled through with two holes 5/8 in. in diameter centered about 1-1/2 in. apart. These serve for easing the block out of the holder after plating, and one hole is used to bring out the cathode connection.

The copper block is drilled and tapped 1/8 in. deep for a small brass screw at a position corresponding to the center of one of the holes in the holder. A thin glass-insulated copper wire is attached to this screw, and a length of small diameter polyethylene tubing is slipped over the wire ending against the block. Before placing the block in the holder, a small hole is punched on the center line, about 1-1/4 in. from the short side, of a 3 in. by 4 in. piece of thin polyethylene sheet. The enclosed cathode wire is then pulled through the hole, and the sheet is held against the back of the block while the latter is dropped into the holder. The excess polyethylene is then trimmed off close to the surface of the copper, using a scalpel, but without touching the block, so as not to introduce iron in excess of that which is already present as an impurity in the copper. The plastic sheet serves as a gasket, preventing, in some measure, attack of the copper by the hot solution during plating, with consequent increase in the iron content.

Two 4-5 cm lengths of 5 or 6 mm diameter glass rod are placed in the bottom of the electroplating breaker, and the copper and glass cathode assembly is placed upon them. This arrangement provides a quiescent area under the block where precipitated solids can collect during plating.
The condenser, stirrer, anode, and the cathode lead are fitted through the cover plate, the assembly placed on a hot plate, and the unit is then ready for introduction of the cobalt solution. The electrolysis current may be obtained from a 6 volt storage battery or two batteries connected in parallel, with a variable resistance in series for controlling the current, or preferably from a 5-amp, 10 volt rectifier unit with a Variac input.

The Electroplate Solution.

The standard electroplate procedure for cobalt uses a cobalt sulfate and boric acid bath, and employs, preferably, a cobalt anode.\(^{27,28,29}\) Since no such anode is available which is sufficiently low in iron, electroplating was originally performed using spectroscopically pure aluminum anodes. Although fairly satisfactory pieces of cobalt of sufficient thickness were thus obtained, the difficulty and uncertainty of overcoming the passivity of the aluminum surface made this an unreliable procedure, and the details are therefore not included.

The latest electroplating procedure employs the flat spiral platinum anode in a solution of cobalt chloride, sodium chloride, and boric acid. This procedure needs considerable improvement, since consistently satisfactory results are not obtainable. The reasons for this were not determined, because of discontinuance of work on the problem.

An approximately 80 percent saturated solution of reagent grade boric acid is prepared and freed of iron by passing it through a 3 cm i.d. column of hydrogen-form 50-100 mesh Dowex-50 resin, 40 cm long, at a rate of about 0.3 liter per hour.\(^*\) The dimensions of the column are not critical, but

\(^*\) This manner of purification was tested by ascertaining that a tracer amount of radioactive iron, placed at the top of a similar column was completely retained at the top after passage of several liters of boric acid solution.
the flow-rate should be adjusted in accordance with the size adopted. A more saturated solution may just as well be used, provided that its temperature does not decrease, thus crystallizing out some solid acid which would clog the resin bed.

The reagent grade sodium chloride was not repurified before use, since the amount of iron impurity in this salt was deemed to be sufficiently low that it would not be greater than the amount introduced with the cobalt. However, it is probably safer to use a batch ether extraction of a nearly saturated solution of the salt in 8N HCl, and to prepare the purified dry salt in the same manner as with the cobalt.

About one-sixth mole each of the purified cobaltous chloride and of reagent grade sodium chloride are dissolved in 500 ml of the purified 4-5 percent boric acid solution, and the pH is adjusted to around 3. The solution is placed in the electroplating breaker, the hot plate turned on, and the stirrer set to slow speed. This speed adjustment is more or less a matter of trial and error. The rate should be such that precipitated material will not remain on the cathode surface, but will collect under the cathode assembly. With fast stirring an uneven deposit is obtained which usually shows a pattern due to the motion of the liquid.

The anode should be fixed at a maximum distance from the cathode, but sufficiently below the surface so that it will remain in the solution if the volume of the latter decreases due to electrolysis and evaporation. When the temperature reaches 60°C, the current is turned on and set to about 0.5 amp at 4 to 5 volts. The current must not be interrupted until plating is completed, and the temperature should be maintained between 60 and 70°C.
Under the conditions outlined, plating efficiency is low. Deposition may or may not be complete after 24 hours, but if incomplete, the solution pH and salt concentration will have changed sufficiently so that no further deposition will be obtained and the cathode should therefore be removed. No additional plating occurs, apparently, after the pH has dropped to or below 2.5.

A precipitate of what is presumably cobaltic oxide usually occurs shortly after the start of electroplating, which may or may not clear up at a later time. The conditions which are necessary to prevent formation of this precipitate were not determined. Although additions of hydroxylamine and of hydrogen peroxide will redissolve the precipitate, they will not prevent its formation. Furthermore, if these reagents are initially present they have a deleterious effect on the deposit. The most satisfactory conditions of temperature, salt concentration, pH, stirring rate, anode-cathode distance, etc., have not been ascertained. As mentioned above, consistently good results are not obtained, although several excellent plates weighing between 7.5 and 9 grams were produced in this manner. Spectrographic analysis showed less than 20 p.p.m. of iron in these pieces of cobalt. Further experiment work on this procedure is definitely indicated.

Preparation of the Probe Block.

Water-cooled probes are standard equipment for cyclotron targets, and are frequently rotated during bombardment in order to distribute the heavy heat load which must be dissipated. These probes are tangentially introduced into the cyclotron tank at the outermost periphery of the beam orbit, thus permitting the use of far greater bombardment currents than may be
obtained if the beam must be brought through a window to an external target.

Details of the 1-1/2 in. x 2-1/2 in. x 1/2 in. probe block actually used are not included here, since this particular block is limited to use in the 60-inch Berkeley cyclotron, and, furthermore, is supplied by this laboratory as part of the bombardment service. Unfortunately, there is no provision for rotating the probe in this cyclotron, so that full advantage may not be taken of the maximum beam which is available; namely, some 600 μa.

The method of fixing the cobalt target metal to the probe may be used with any cyclotron probe block, and with many other electroplated metals as well. The surface of the electroplated metal is usually uneven; infrequently it is also quite rough. The cobalt itself is dense and massive, and between 0.008 in. and 0.010 in. thick in the center. The depressions on this surface are not readily cleaned with acid without dissolving appreciable amounts of the exposed metal, so that the best method of obtaining a satisfactory surface, which will be almost completely wetted by the solder, is by use of a high-speed cloth wheel. Both the cleaned cobalt surface and the face of the copper probe block are tinned with Easyflo silver solder before being placed in contact, leaving an excess on each. The tinned surfaces are then placed in contact and firmly pressed together while being heated with a torch. After cooling, the four sides are roughly squared on a belt sander, thus removing the excess solder and providing better surfaces for subsequent machining operations.

The 1/4 in. copper electroplating block is next milled away, or infrequently, may be pried off. The milling operation should be stopped, however, when the cobalt surface is just reached, and the final removal of
the copper plus the first one or two thousandths of an inch of cobalt should be accomplished with a surface grinder. Since the surface of the cobalt in contact with the original copper cathode will not usually be exactly parallel with the back of the probe block after soldering, the first cuts with the grinder should be across the thickest part of the remaining copper. Following this either the copper may be ground away in a stepwise manner, or the block should be relocated so that the wheel will grind off the copper with only a minimum of cobalt.

After finishing the cobalt surface, and before use, the whole block should be thoroughly cleaned by immersion in boiling water. Otherwise small amounts of sodium salts from the soldering flux will remain with the target, producing during bombardment considerably greater amounts of contaminating radioactivity than are obtained from both the iron and cobalt together. Finally, the block, and particularly the cobalt surface, should be cleaned with hydrochloric acid for the removal of external iron, and the cobalt should additionally be etched to a depth of about 0.001 in. with nitric acid for the removal of iron which may have been embedded from the grinding wheel.

Removal of Activity after Bombardment.

Manipulations with the activated block are carried out behind lead shields according to standard procedures for handling radioactive materials.

Originally, the method for removing activity from the cobalt surface was to mill it off, using a milling machine exclusively devoted to the handling of hot targets. However, the alignment of the target surface in order that maximum recovery could be obtained with minimum cobalt was exceedingly difficult, and involved excessive exposures of personnel to
radiation. This procedure was consequently abandoned in favor of one which is considered to be considerably superior, and which involves far less exposure to radiation.

Since this \((d,2p)\) reaction occurs only at or above beam energies in the neighborhood of 18 Mev, and since the incidence of beam to the target is about 10° from grazing, the \(\text{Fe}^{59}\) will only be produced at or close to the surface of the cobalt. It is therefore necessary merely to remove cobalt to a depth of about 0.001 in. in order to effect complete, or nearly complete, recovery of the radioactive iron.

A thickness of 0.001 in., dissolved from an area of 1-1/2 in. by 2-1/2 in., yields about 1 g of cobalt. Since 50 ml of 1 N nitric acid will dissolve the stoichiometric amount of cobalt i.e., about 1.1 g from this amount of surface if left in contact for a sufficient time, this procedure was adopted for removal of the active surface layer. Unfortunately, there is no way of checking to make sure that the cobalt surface is not selectively attacked by the acid. One target was actually treated twice with acid and the activity in the second fraction was estimated by its radiation level to be about one-tenth of the first, but this sample was inadvertently discarded before a radioactivity assay could be made on it. It must be assumed that the area which actually receives the maximum beam is attacked by the acid at a rate which is not less than the rate of attack in other areas, and this assumption is probably valid.

The container in which the cobalt is to be dissolved is a specially made breaker about 3 in. to 3-1/4 in. in inside diameter with beaded lip and without a pouring spout. It should be provided inside with a rubber pad of nearly the same diameter, and, like all equipment with which the
cobalt solution must be in contact, both should be clean and free of iron.

The probe block is introduced face up into the beaker and placed or carefully dropped on the rubber pad. A heavy lead block about 4 in. in length with a 1-1/2 in. x 2-1/2 in. face on one end and a long handle on the other, is provided with a 1-1/2 in. x 2-1/2 in. soft rubber pad which is glued to and covers the face. Since this assembly is difficult to clean, and later to decontaminate, the lead block is placed face down on a piece of clean polyethylene sheet, and the latter is then carefully folded up so that no creases occur on the face and fastened to the handle or upper part of the block with Scotch tape. Although polyethylene was actually used, it is recommended that some other plastics be tried, since paraffin sticks rather tightly to this material, making the following operations somewhat difficult.

The plastic-covered rubber face is next placed against the cobalt surface and aligned as well as is possible by observation in the mirrors behind the shield. Molten paraffin from an electrically heated pouring pot is then introduced through a funnel made of heavy waxed paper. The bottom of the funnel should be placed in such a position that the liquid will pour on the rubber pad at the bottom of the beaker, or against the wall of the beaker near the bottom, rather than on the plastic-covered block, and should be above the level of the cobalt so that it will not be embedded in the paraffin when the latter solidifies. The embedding material should be quite hot so that it will flow evenly around the cold copper, and a sufficient amount of it should be added to bring the level a slight distance above the surface of the cobalt.

Before removing the protecting block, the paraffin should be allowed to cool to room temperature, since, if still warm and pliable, it may pull
away from the edges of the probe block during this operation, particularly if the paraffin sticks to the plastic which is used as a cover for the block.

Upon completion of the embedding, 50 ml of 1 N nitric acid are introduced, and the beaker is fitted with a glass stirrer introduced through a small hole drilled in the center of a solid watch glass. The glass stirrer is fixed in the chuck of an electric motor, and the latter is rotated at a speed which is just sufficient to keep the solution gently agitated. The acid should be allowed to react completely, which requires several hours. It is usually left in contact overnight.

The solution is removed from the beaker, together with a few milliliters of wash, and evaporated to dryness in a 200 ml tall-form beaker using a ribbed watch glass cover. After cooling, the dry salt is carefully treated with 10 ml of iron-free concentrated hydrochloric acid and again taken to dryness. Although care must be exercised when adding the HCl in order to prevent spattering, and the hot plate temperature should not be too high, the beaker need not be cooled completely before adding each of the subsequent three or four 10 ml portions of acid. The completion of conversion to chloride may be determined by noting the presence or absence of the brown fumes reaction after each HCl addition to the warm dry salt. Additions should be continued until two are obtained from which no NO₂ evolutions are observed.

The cobaltous chloride is next dissolved in 25 ml of iron-free 8 N HCl and transferred to the 6 unit ether extraction apparatus, one cell of which is shown in Fig. 1. The assembled apparatus with six cells in series is shown in Fig. 2.
of glass, has been modified and considerably improved by W. G. Ruehle of the U.C.R.L. Health Chemistry Division. The use of specially designed Teflon valves at top and bottom have eliminated the leakage which developed with the glass stopcocks when they were subjected to pressure during extraction.

The assembled apparatus is designed to fit in a standard glove-box, together with a variable capacity Teflon-lined diaphragm pump. Drawings of the latter, which was designed by L. Dickard, also of the Health Chemistry group, are not available for inclusion here.

Before introducing the radioactive solution, the six units are mounted and connected as shown, and the Teflon stopper-valves are closed at the bottom but left open at the top. The 6 stoppers are removed from the upper sidearms and 20-25 ml of iron-free 8 N HCl are introduced through these openings into cells 2, 3, and 6, counting from left to right. A like amount of distilled water is placed in cells 4 and 5. Following these additions, sufficient washed isopropyl ether is individually introduced into these five cells to fill each to a level which is slightly above the effluent side arms on the right, and approximately the same volume of ether is placed in cell number 1. The stoppers are placed in the side-arms and clamped, as shown, omitting number one, and the upper valves are closed. The radioactive solution is then introduced into the first cell, and this cell is then stoppered and the valve closed. Additional ether is introduced, if needed to prime the pump, through the side arm of cell 6.

The pump diaphragm vibrates with small displacement at a rate of about 45 pulses per minute. The internal pump volume is between 1 and 2 ml, and the small Teflon flutter valves are loaded by means of a tempered platinum wire spring. The throughput is about 3 ml per minute, but has not been accurately measured.
In operation, the effluent ether from cell 6 travels out through the side arm at the right side and through the connecting tube leading from this cell directly to the pump. The holdup in this pump is negligible, since the internal volume is less than 2 ml, so that the flow is effectively direct from cell 6 to cell 1. Each of these extraction cells, as shown in Fig. 1, is so constructed that the influent ether is introduced at the bottom of the cell through a sintered dispersion tube. In passing upward through the aqueous layer it mixes and extracts, then passes on to the next cell.

The ferric chloride is progressively removed from the first cell, the ether is washed to remove entrained and/or extracted cobalt and other inorganic salts in cells two and three, and the iron is back extracted into water, principally in cell 4 but some in cell 5. Due to the variation in salt and acid concentration between cells, there is a constant transfer of water from the back-extraction cells to the CoCl$_2$, thus diluting the latter and decreasing the efficiency of the extraction. In order to minimize this transfer, 8 N HCl is placed in cell 6, but this expedient is only partly successful.

Present procedure calls for two or three four-hour extractions, depending upon the amount of total iron, with a change of the water in cells 4 and 5 between extractions. Completeness of extraction is determined by monitoring the several extraction cells, except the first, after each period. Little quantitative data are available to serve as a guide, and completion time of the process is therefore more or less up to the judgment of the operator. It should be judged on the basis of the activity of each of the removed water fractions.

A test run was made with the original all-glass apparatus, using
reagent grade CoCl$_2$ in the first cell together with a tracer amount of Fe$^{59}$, 8 N HCl in the next three cells, and water in the last two. The diaphragm pump in this test was set to circulate ether at about 7 ml per minute. After one hour of extraction, some 99 percent of the activity was removed from the cobalt and an estimated 95 percent was recovered from the combined acid and water cells. This extraction was discontinued after the one hour period due to failure of the pump, but the cobalt solution was saved for subsequent tests, since it was considered to be nearly completely freed of its original iron impurity.

Subsequent tests with known amounts of normal iron and tracer added to the cobalt solution and a flow rate of 4 ml per minute gave results indicating recoveries as high as 96 percent with 0.7 mg of carrier, down to about 90 percent with 0.4 mg, when two extractions of 2 and 3 hours each were performed, with the water replaced between extractions. Recovery data are for the combined water fractions.

Further quantitative data were not obtained before this apparatus was placed into use, and no test data were obtained with the modified apparatus and pump described and actually in use at the present time. A fair estimate of recovery from the latest runs is between 80 and 90 percent.

It should be pointed out that this apparatus would not successfully recover the radioactive iron if the amount of carrier were actually as low as indicated by the amount in the purified cobalt solution; i.e., 10 µg from 1 g of dissolved target cobalt. When originally designed, it was not known that the amount of impurity could be lowered to this extent. At later dates, when using targets prepared from the highly purified cobalt, a sufficient amount of iron was always introduced at unknown times and from unknown sources, which permitted successful extractions.
Although a satisfactory performance has been obtained with the above apparatus, it is recommended that either a new design be attempted which would allow the use of much smaller volumes during extraction, or that a new procedure be devised. This should be accomplished in anticipation of the time when full advantage may be taken of the ultimate carrier level which is achievable, as pointed out above.

A straightforward approach to such a separation has been developed by Gile,\(^{(30)}\) who used a cobalt target which had previously been treated as described above so that only small amounts of Fe\(^{59}\) still remained. The metal surface was etched with 12 N HCl to remove approximately 100 mg of cobalt, the solution centrifuged, and the supernatant removed. The solution was then neutralized with 15 N NH\(_4\)OH to pH 9, and slowly drawn through Whatman No.50 filter paper. The iron is stated to be quantitatively recovered on the filter paper and to be carrier-free.

Preparation of the Product for Medical Use.

The final solution containing the Fe\(^{59}\) plus small amounts of acid and ether has been processed by a variety of procedures, none of which could safely be applied if the total iron content were actually at the ultimate minimum, i.e., 10 \(\mu\)g. In the presence of 0.1 mg or more of carrier, it is satisfactory to evaporate the solution to small volume, but not to dryness, transfer it to a 10 ml centrifuge cone with the aid of a few drops of concentrated HCl as a beaker wash, and to precipitate the iron from not more than 5-6 ml of solution with concentrated ammonium hydroxide, which frees it of the major portion of the non-volatile ether residues. The precipitated ferric hydroxide may be redissolved and re-precipitated as desired, and finally taken up in ammonium citrate for
dilution, sterilization, and injection.

If lesser amounts of carrier are present, it is suggested that the solution free of cobalt and other radioisotopes, be neutralized to a pH of 2.5 to 3.0 and the iron then absorbed batchwise on one or two 1 g portions of 250-500 mesh Dowex-50 H-form cation resin. It should be noted that this resin is initially fairly high in iron; this iron must be removed with hydrochloric acid before use. After washing with water, the active material may be eluted from the resin with small volumes of 6 N HCl, or may be removed directly into a complexing solution such as ammonium citrate, from which dilutions may be made directly for medical usages.

With most of the high specific activity samples, the ferric hydroxide precipitation method has been used, but the relatively small amounts of iron have permitted the resulting ferric chloride to be combined directly with globulin fraction IV - 7, after neutralization to pH 3.\(^{(31)}\)

Fe\(^{59}\) Yields and Specific Activities.

Four of the best runs made during the past year produced total yields of 1.8, 0.8, 1.5 and 0.5 mc. The respective specific activities were 11, 1.1, 3.1, and 3.9 μc per μg, and the corresponding total iron assays showed 0.16, 0.71, 0.38, and 0.17 mg. The bombardment efficiencies for the first three were 0.11, 0.07, 0.07 μc per μa hr. The probe current data for the fourth sample are not available.

The radioassay data were collected using either an end-window counter or a scintillation counter with reproducible geometry. Both counters were standardized against radioiron samples previously calibrated in a coincidence counter. The iron content of these samples was determined
colorimetrically, by the α-α, diphyridyl method.

From these data, the 60-inch cyclotron yield of Fe$^{59}$ is estimated to be equal or greater than 0.07 μC per μA hr. of 20 Mev deuterons. The yield after 100 hours at 200-250 μA should be between 1.5 and 2 mc; and the maximum specific activity may be as high as 100 μC per μg of iron.

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Fig. 1