Cyclotron produced lead-203

P. L. HORLOCK
L.R.I.C.M. L. THAKUR
M.Sc., Ph.D.I. A. WATSON
M.Sc.

MRC Cyclotron Unit, Hammersmith Hospital, Du Cane Road, London W12 0HS

Introduction

Radioactive isotopes of lead occur in the natural radioactive decay series and have been used as tracers since the early days of radiochemistry. These are ^{210}Pb ($t_{1/2}$ —20.4 y, radium D), ^{212}Pb ($t_{1/2}$ —10.6 h, thorium B) and ^{214}Pb ($t_{1/2}$ —26.8 m, radium B) all of which are separated from naturally occurring decay products of radium or thorium. There are in addition to these a number of other radioactive isotopes of lead which can be produced artificially with the aid of a nuclear reactor or a charge particle accelerator (Table 1).

There are at least three criteria in choosing the radioactive isotope for *in vitro* tracer studies. First, it should emit radiation which is easily detected. Secondly, it should have a half-life long enough to permit studies without excessive radioactive decay occurring but not so long that waste disposal creates a problem. Thirdly, it should be capable of being produced in a reasonable quantity at a moderate cost. For *in vivo* studies the characteristics of a radionuclide are of extreme importance. First, its half-life should not be so long that it persists in the body after the investigations have been carried out. Secondly, the radiation it emits should be such that it could cause only minimal radiation damage to the subject but be detected efficiently with existing devices such as a gamma camera or a rectilinear scanner.

So far as the half-life is concerned there are only three radionuclides of lead that can be considered. They are ^{212}Pb ($t_{1/2}$ —10.6 h), ^{200}Pb ($t_{1/2}$ —21.5 h) and ^{203}Pb ($t_{1/2}$ —52 h). The half-lives of the others are either too short (a few minutes) or too long (several years). Of the three, ^{212}Pb and ^{200}Pb have rather complex decay schemes including radioactive daughters. The energy of γ -photons and the absence of particle emission in the decay of ^{203}Pb makes it particularly suitable for certain *in vivo* (Stark *et al.*, 1972) and *in vitro* (Bartrop and Killala, 1967; Bartrop and Smith, 1971; Potter, McIntyre and Vattuone, 1971) applications.

TABLE 1. Isotopes of lead

Isotope	Half-life	Principal γ energy
^{194}Pb	11 m	*
^{195}Pb	17 m	*
^{196}Pb	37 m	*
^{197}Pb	42 m	*
$^{197}\text{Pb}^m$	42 m	*
^{198}Pb	2.4 h	*
$^{198}\text{Pb}^m$	25 m	*
^{199}Pb	90 m	*
$^{199}\text{Pb}^m$	12.2 m	*
^{200}Pb	21.5 h	** 0.109 to 0.605 (complex) (daughter radiations)
^{201}Pb	9.4 h	*
$^{201}\text{Pb}^m$	61 s	*
^{202}Pb	3×10^5 y	*** Tl X-rays, (daughter radiations)
$^{202}\text{Pb}^m$	3.62 h	*
^{203}Pb	52.1 h	** 0.279 (81%) 0.401 (5%) 0.680 (0.9%) (no daughter radiations)
$^{203}\text{Pb}^m$	6.1 s	*
^{204}Pb	stable	
$^{204}\text{Pb}^m$	66.9 m	*
^{205}Pb	3×10^7 y	*** Tl X-rays, no γ
^{206}Pb	Stable	
^{207}Pb	Stable	
$^{207}\text{Pb}^m$	0.825	*
^{208}Pb	Stable	
^{209}Pb	3.3 h	*
^{210}Pb (Ra D)	20.4 y	*** Bi X-rays, 0.047 (4%). (daughter radiations)
^{211}Pb (Ac B)	36.1 m	*
^{212}Pb (Th B)	10.6 h	*
		Bi X-rays, 0.239 (47%), 0.300 (3.2%) (daughter radiations)
^{213}Pb	10.2 m	*
^{214}Pb (Ra B)	26.8 m	*

* $t_{1/2}$ short *** $t_{1/2}$ long

Decay characteristics of lead-203

Lead-203 has a very simple decay scheme (Lederer, Hollander and Perlman, 1967, Fig. 1). It decays with a half-life of 52 hr by electron capture followed by emission of γ -photons of energies 279 keV (81%), 401 keV (5%) and 680 (0.9%), going to the ground state of stable thallium-203. Unlike some radionuclides of lead, lead-203 has no daughter radiations to cause any complication in its measurement. The

gamma ray spectrum taken using a 15 cm³ lithium drifted germanium detector is given in Fig. 2. This shows five well resolved peaks, three from lead-203 γ -photons and two from the 72 keV and 85 keV thallium X-rays (Waters, 1973). Gamma detectors, either thallium-activated sodium iodide crystals or the higher resolution lithium drifted germanium detectors, have higher detection efficiencies for the lower energy γ -photons. The 279 keV, principal γ -photon energy of lead-203 is in the middle of the optimum range for detection at high efficiency. As a result even a very small quantity of the radionuclide could be easily detected both *in vivo* and *in vitro*.

Production of Lead-203

Lead-203 can only be produced with charged particle bombardments of either mercury or thallium. Natural mercury has six stable isotopes and if this were to be bombarded with either helium-3 or helium-4 particles several radionuclides of both lead and thallium would be produced. This would result in a very complex chemical and radionuclidic system. Enriched mercury as a target material would partially solve this problem but it would of course be very expensive.

FIG. 1. Decay scheme for Pb-203 (Lederer *et al.*, 1967). Observed gamma emission: 279 keV-81%; 401 keV-5%; 608 keV-0.9%.

FIG. 2. Gamma ray spectrum of ²⁰³Pb (smoothed data). 15 cm; Ge(Li) detector; energies in keV.

The preferred target material for the production of lead-203, therefore, is thallium. Natural thallium contains 29.5% thallium-203 and 70.5% thallium-205. The possible charge particle nuclear reactions and their threshold energies to produce ²⁰³Pb from thallium are listed in Table 2. Also listed are some production yields, in $\mu\text{Ci } \mu\text{Ah}^{-1}$ at certain energies, which have been reported in the literature.

It can be seen from the table that proton and deuteron bombardment of thallium will produce

TABLE 2. Reactions producing ²⁰³Pb from natural thallium; ²⁰³Tl (29.5%), ²⁰⁵Tl (70.5%)

Reaction	Threshold energy MeV	Reported yields† μCi μAhr ⁻¹ at E.O.B.
²⁰³ Tl(d, 2n) ²⁰³ Pb	11*	75 (15 MeV)‡ 241 (22.7 MeV)
²⁰⁵ Tl(d, 4n) ²⁰³ Pb	18	
²⁰³ Tl(p, n) ²⁰³ Pb	11.5*	67 (12.5 MeV) 50 (16.2 MeV) 70 (20 MeV) 2000 (28 MeV)§
²⁰⁵ Tl(p, 3n) ²⁰³ Pb	15.8	2 (46 MeV)
²⁰³ Tl(α, 4n) ²⁰³ Bi	54	
²⁰³ Tl(³ He, 3n) ²⁰³ Bi		
<div> <div>11.8h</div> <div>→</div> <div>²⁰³Pb</div> </div>		
	22*	7.5 (29 MeV)

* Threshold determined by Coulomb barrier.

† Merrill *et al.* (1973).

‡ Yield on M.R.C. cyclotron.

§ Acerbi *et al.* (1973).

^{203}Pb directly and helium-3 and helium-4 bombardments will produce ^{203}Bi which then decays to ^{203}Pb with a half-life of 11.8 h. This latter approach was investigated by Chackett, Chackett and Welborn (1971) at Birmingham. However, possibly owing to the high threshold energies of the ^{203}Tl (α , 4n) and ^{203}Tl (^3He , 3n) reactions, and the high probabilities of other competing nuclear reactions taking place, the yields are disappointingly low, making this route undesirable. Much higher yields are obtained by bombardment of thallium with relatively low energy (28 MeV) protons which produce in excess of 2 mCi μAh^{-1} (Acerbi *et al.*, 1973). The yields from bombardment with deuterons in the energy range up to 23 MeV are again adequate. With 22.7 MeV deuterons, yields of more than 240 μCi μAh^{-1} are reported (Merill, Lambrecht and Wolf, 1973).

The only beams available from the MRC cyclotron are 32 MeV ^4He , 15 MeV deuteron and 8 MeV protons. We can see from the table that the only reaction we can use which will give a reasonable yield of ^{203}Pb is ^{203}Tl (d, 2n) ^{203}Pb . We regularly obtain yields of about 75 μCi μAh^{-1} , after chemical separation, from this reaction.

Target design

Thallic oxide, the most stable compound of thallium, was chosen as the target material. Two to three grams of the powder is evenly spread on a 3 mm thick $\times 19\text{ cm} \times 5\text{ cm}$ grooved copper plate. The powder is held in place during irradiation with a 0.12 mm thick copper foil which is stuck on to the copper plate by means of double-sided adhesive tape. The target plate is then held in an assembly (Fig. 3) and placed on the external beam of the

cyclotron for irradiation. Forty-five microamperes of the 15 MeV deuteron beam is uniformly spread over an area of about $12\text{ cm} \times 2.5\text{ cm}$ and the bombardment is carried out for 3–4 hr. During this time the back of the target plate is cooled with circulating water and the front of the foil with an air blast. Along with lead-203 a large quantity of $^{204}\text{Pb}^m$ ($t_{1/2}$ —66.9 m) is produced from the ^{203}Tl (d, n) and ^{205}Tl (d, 3n) reactions. The target is left overnight for the $^{205}\text{Pb}^m$ to decay before starting the chemical processing.

Chemical separation

The chemical separation of lead from the thallium target material is based on the chemistry described in a monogram published by the U.S. Atomic Energy Commission (Gibson, 1961). The copper foil is carefully peeled off the target plate and the thallic oxide powder is slurried with a known volume of water into a beaker. To this is added concentrated nitric acid so that the strength of the acid is about 6 mol/l. This is boiled on a hotplate until the thallic oxide is dissolved. Sulphur dioxide gas is then bubbled in the solution to reduce Tl^{3+} ions to Tl^{+} . The solution is allowed to cool when the bulk of thallic nitrate is precipitated. This is eliminated by centrifugation and any remaining thallic ions in the supernatant are reduced again. The precipitation step is repeated and greater than 95% of the thallium is eliminated from the solution. The loss of lead activity is less than 5% at this stage. To the solution is then added about 5 mg of ferric chloride. This is precipitated as $\text{Fe}(\text{OH})_3$ by addition of concentrated ammonium hydroxide. The $\text{Fe}(\text{OH})_3$ co-precipitates the radioactive lead quantitatively

FIG. 3. 1, target carrier; 2, target plate and a foil; 3, water flow spoiler; 4, target head; 5, support tube with water connector.

leaving any copper there may be as cuproammonium complex in the solution. The ferric hydroxide is twice redissolved in dilute nitric acid, re-precipitated and finally washed with ammoniacal water. The excess of ammonia is then expelled by heating the residue under a gentle stream of nitrogen and finally dissolved in 8 mol/l HCl previously equilibrated with di-iso-propyl ether. The iron is then extracted into di-iso-propyl ether equilibrated with 8 mol/l HCl. The HCl containing the lead activity is boiled to dryness and the residue is dissolved in isotonic saline solution. At no stage in the separation is lead carrier added keeping the product 'carrier free'.

An aliquot is withdrawn for chemical and radiochemical assay. Thallium, iron, and any lead (as an impurity in the thallic oxide), is determined polarographically using 0.1 mol/l sodium hydroxide as an electrolyte. The lower detection limit of this method is 0.5 μg of each element per millilitre of the solution. Occasionally as much as 25 μg of lead in the total target material has been detected. The thallium content of the final solution is less than 50 $\mu\text{g ml}^{-1}$ and iron is less than 25 $\mu\text{g ml}^{-1}$. No detectable radioactive impurities have been observed in the solution of ^{203}Pb which is assayed using the full 279 keV (81%) energy peak. The total separation time is 2–3 hr and the chemical efficiency is 80–90%. Ten to 12 mCi of ^{203}Pb are obtained after chemistry, from a 3.5–4 hr bombardment. All the separation procedure is carried out by hand behind a lead wall and the radiation dose to the hands is less than 100 mrad.

Lead-203 has been prepared using the MRC

cyclotron for several years now. Owing to its attractive characteristics it proved itself sufficiently promising for us to increase its production rate from a few μCi every 2 months to several mCi every other week. This has led to a variety of interesting applications some of which we are looking forward to hearing more about today.

References

- ACERBI, E., BIRATTARI, C., CASTIGLIONI, M., RESMINI, F. & SPAVERI, G. (1973) Survey of applied physics experiments at the Milan AVF Cyclotron. *10th European Cyclotron Progress Meeting* September, 1973, Gronigen.
- BARLTROP, D. & KILLALA, N.J.P. (1967) Faecal extraction of lead by children. *Lancet*, ii, 1017.
- BARLTROP, D. & SMITH, A. (1971) Interaction of lead with erythrocytes. *Separation Experimenta*, 27, 92.
- CHACKETT, G.A., CHACKETT, K.F. & WELBORN, J.B. (1971) The preparation of carrier free lead-203 for medical use. *The International Journal of Applied Radiation and Isotopes*, 22, 715.
- GIBSON, W.M. (1961) The radiochemistry of lead. *National Academy of Sciences, National Research Council U.S.A. Nuclear Science Series—3040*, 127.
- LEDERER, C.M., HOLLANDER, J.M. & PERLMAN, I. (1967) *Table of Isotopes*. Wiley, New York.
- MERRILL, J.C., LAMBRECHT, R.M. & WOLF, A.P. (1973) Cyclotron production of lead-203 for radiopharmaceutical applications. *The International Journal of Applied Radiation and Isotopes*, 24, 701.
- POTTER, G.D., MCINTYRE, D.R. & VATTUONE, G.M. (1971) The fate and implication of lead-203 ingestion in a dairy cow and calf. *Health Physics*, 20, 650.
- STARK, V.J., HARPER, V.S., LATHROP, K.A., KRIZEK, H., ROWED, D.W., LAMBARES, N., & HOFFER, P.B. (1972) Evaluation of lead-203 as an imaging agent for cisternography. *Journal of Nuclear Medicine*, 13, 468.
- WATERS, S.L. (1973) Personal Communication.