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Abstract: The theme of this session was the production of isotopes. Papers detailing the production of both stable and radioactive isotopes were detailed.

Keywords: Sodium-22; Radioarsenic; Foils and targets; Accelerator physics; Molybdenum-99; Tc-99 or Ru-102 targets; isotopes production; Calultron; ^{13}C production

RADIOISOTOPE PRODUCTION AT THE LOS ALAMOS NATIONAL LABORATORY

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Summary: The Los Alamos National Laboratory has become a major supplier for bulk radioisotopes worldwide. Coordinated by the U.S. DoE Isotope Program, Los Alamos regularly produces radioisotopes for medical, industrial and research applications. Two production key facilities at Los Alamos are the linear accelerator bombardment station for 100 MeV protons and the Hot Cell Facility. Isotopes produced currently include ^{68}Ge, ^{82}Sr, ^{109m}Cd, ^{32}Si, ^{22}Na, ^{88}Y, $^{73,74}As$, ^{7}Be. Research and development on new isotopes and improved production methods are ongoing. Exemplarily, the chemical recovery details for large quantities of ^{7}Be, ^{82}Sr, ^{22}Na and radioarsenic are introduced.

Keywords: radioisotope production; 100 MeV protons; hot cells; strontium-82; sodium-22; radioarsenic; beryllium-7

Introduction: The Los Alamos National Laboratory is a large, multidisciplinary national security institution. With a yearly funding volume of roughly \$2.2 billion (FY06), a total workforce of 12,300, the Laboratory's site extends over $100\,km^2$ including 1,280 buildings and 14 operating nuclear facilities. The Laboratory's mission is to ensure the safety, security and reliability of the U.S. nuclear deterrents, to reduce threats of weapons of mass destruction, nuclear proliferation and terrorism. Los Alamos is also actively engaged in solving other emerging national problems in defense, energy, environment and infrastructure.

The Laboratory is a major supplier for bulk radioisotopes worldwide. The customer base consists of hospitals, research institutions and private sector companies like the pharmaceutical manufacturers GE Healthcare, Siemens and Sanders. The radioisotope program is supported by the Department of Energy, Office of Science, Nuclear Physics.

Radioisotope production at Los Alamos has a 30 year history. Isotopes were first produced in the 1970s at the beam stop at the Los Alamos Neutron Science Center (LANSCE), using an 800 MeV pulsed spallation neutron source. In 2004, the dedicated 100 MeV proton Isotope Production Facility, IPF, was commissioned. Los Alamos offers a unique cradle-to-grave capability; ranging from detailed irradiation planning and target design over radiochemical separation and shipment to customers down to final waste handling and disposal. Target irradiation at IPF allows for simultaneous multiple isotope production at different energies (Figure 1).

From 2005 until 2007, IPF irradiated over 169 targets including 109 targets of RbCl used to produce over 156 Ci of ^{82}Sr which, in turn, was used in radionuclide generators to produce ^{82}Rb. Rubidium-82 (ground state) has a half-life of 1.3 minutes. It is used to monitor heart function, replacing much longer and riskier tests, thereby increasing the number of lives saved. Imaging procedures with this live-saving tool are performed on thousands of patients each month. Potential patients treated each year based on production quantities accounting for decay to 60% of production value are 72,000 as of January 2009, 95,000 patients for 2007/2008 and 130,000 patients for 2006/2007. Moreover, 48 gallium targets were irradiated over that time period to produce ^{68}Ge along with several other critically needed radioisotopes.

Some notable radioisotope productions highlights in 2008 were related to large-scale ^{82}Sr production, the irradiation of new targets at a medium proton energy range (Se target for ^{73}As production; Hf target for ^{173}Lu production) and the gain of fundamental understanding of material and chemical properties associated with Nb clad Ga targets. Regarding large-scale ^{82}Sr production, the integrated beam on RbCl targets was increased from 10,000 μAh to 55,000 μAh. A high current test at 275 μA was successfully conducted. The regular production beam was increased from 150 μA to 250 μA which currently represents the highest beam current for a production facility at this energy range in the world.

Isotopes currently produced include ^{68}Ge, ^{82}Sr, ^{109m}Cd, ^{32}Si, ^{22}Na, ^{88}Y, ^{73,74}As and ^{7}Be. Research and development into new isotopes and improved production methods is ongoing.
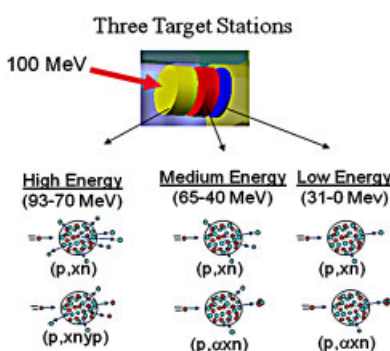

Figure 1. Proton beam target energy slots at the Los Alamos Isotope Production Facility.

Results and discussion: *General processing strategy*

Large scale radioisotope production at Los Alamos follows a general processing strategy. The target material is encapsulated in an appropriate canister material (usually Nb or inconel alloy). Encapsulated targets are exposed to a high energy proton beam at the Isotope Production Facility (IPF). Subsequent to irradiation, the target containment is punched, and the target material is dissolved using an appropriate, usually aqueous, reactant. Then, the main product isotope is chemically separated from both the target material and from radioactive byproducts, which often requires multiple steps and multiple approaches. Separation techniques may be ion exchange, solvent extraction, distillation and other chemical separation methods.

Beryllium-7 production: Beryllium-7 (half-life 53.1 d) is formed by light and medium mass nuclides in the process of complex particle emission with varying formation cross sections.[2] In the past, this radioisotope was recovered at Los Alamos as a secondary product from ZnO targets irradiated for Copper-67 production. Beryllium-7 was found among spallation products after 800 MeV proton bombardments. The isotope has been used to study berylliosis and as an environmental tracer.

Recently it was observed that significant quantities of ^{7}Be are formed in rubidium chloride (RbCl) targets irradiated with medium to high energy protons, and a prototype recovery procedure was developed. Initial steps of chemical Rb(p,x) product recovery include dissolving the target in water, then buffering to a pH between 9 and 10. This solution is filtered prior to passing through a Chelex column and the ^{7}Be is retained on the filter as a hydroxide precipitate. The precipitate is re-dissolved in hot 0.1 M HF and the resulting solution passed through an anion exchange column, followed by washes of the column with additional 0.1 M HF. Beryllium is retained while most other species pass through. The ^{7}Be activity is then stripped from the column with 0.1M HNO$_3$ and placed on a cation exchange column. This column is then washed with additional 0.1M HNO$_3$. The ^{7}Be is finally stripped from the column using 0.5 M HNO$_3$ collecting the activity in the center of the elution peak.

The resulting product has been free of radioisotope contaminants but part per million levels of Al and Fe have been measured.

Strontium-82 production

Strontium-82 (half-life 25.5 d) is utilized in the Cardiogen-82 ^{82m}Rb radionuclide generator (Figure. 2). Production and recovery of ^{82}Sr have been described earlier [3]. The isotope is produced via (p,xn) reaction on natural Rb, which is introduced into a 100 MeV proton beam as either RbCl or the metal itself. Target material is dissolved (water in the case of chloride, *i*-PrOH if the metal is used), buffered (pH between 9 and 10), and contacted with a chelating resin (Biorad Chelex 100). Chelation allows the separation of ^{82}Sr (is retained) from the bulk of the dissolved target material Rb (elutes). Fine separation occurs via cation exchange (Biorad resin Ag 50Wx8), where ^{82}Sr is sorbed, while Rb isotopes and transition metal impurities elute using an HCl concentration gradient (ranging from 0.1 to 1.0 molL^{-1}). Stable isotope analysis (including specific activity determination) occurs via ICP.

Figure 2. Cardiogen-82 radionuclide generator.

Radioarsenic production

Arsenic has two particularly important longer lived radioisotopes: ^{73}As (half-life 80.3 d) and ^{74}As (17.7 d). While ^{73}As finds use as an environmental tracer for this toxic chemical element, ^{74}As has been suggested as a medical radioisotope. It emits both positrons (β^+) and negatrons (β^-) and is therefore suitable for both imaging (in-vivo PET tracer for long-term biological processes[4,5]) and therapy applications. Compared to β^+ emitting ^{124}I, which has been used in antibody labeling and appears to be susceptible to dehalogenation, As proved to form extremely stable covalent bonds, which is the key to achieving clear scans.

At Los Alamos, both isotopes are recovered from proton irradiated (incident energy < 50 MeV) Ge metal without the use of problematic hydrogen fluoride (HF) in the chemical recovery process. The following procedure is employed to separate arsenic (As) isotopes from the target matrix: after the Nb encapsulated Ge target is removed from the proton beam, Ge metal is mechanically removed from its encapsulation. It is then carefully dissolved in a slightly heated mixture of HNO_3/HCl (aqua regia). During this step, As is elevated to the non-volatile pentavalent state, while Ge is converted to volatile $GeCl_4$. Once the target is completely dissolved, the bulk of the Ge matrix is distilled off as tetrachloride and trapped in a water containing receiver.

The target residue is evaporated to dryness, and is subsequently taken up in HCl (12 molL^{-1}). Germanium traces are then removed via anion exchange (resin Biorad Ag1x8). Germanium is retained while As elutes. During the final purification step, As is reduced to the volatile trivalent chloride using hydrazinium chloride in an HCl (6 molL^{-1}) matrix. Arsenic distills as $AsCl_3$ and is then re-oxidized to H_3AsO_4 for storage. Typical batch yields are 240 μCi/μAh (^{73}As) and 230 μCi/μAh (^{74}As). Per ICP, typical ^{73,74}As specific activities are $\geqslant$ 7.1 E+14 Bqg^{-1} (19.1 kCig^{-1}) $\pm$ 27%. For comparison, the theoretical ^{73}As specific activity is 8.2 E+14 Bq$\cdot$g^{-1} (22.2 kCi$\cdot$g^{-1}).

Sodium-22 production

Sodium-22 can be produced via proton irradiation of Mg or Al. It is well suited as a radioactive tracer due to its relatively long half life (about 2.6 years) and its strong gamma ray emission (about 1275 KeV) with 99.9 percent abundance. The isotope's principal uses as a radioactive tracer are in biological and geological fields, e.g., as a radioactive tracer for logging data in subterranean formations such as oil wells. Additionally, high specific activity (HSA) ^{22}Na can be utilized as a β^+ source for various applications.

With Na being a ubiquitous element, HSA can only be achieved through extreme care along processing to minimize the introduction of Na traces during any step. Sodium-22 is generated via p induced (100 MeV$>$E$>$40 MeV) nuclear reaction on Al metal. Separation of Na from Al occurs via cation exchange on hydrated antimony pentoxide (HAP).[6] HAP is highly selective for Na, but sorption capacity is very limited (1 mg Na/g HAP). Typically, Na contamination of supplied HAP prohibits its use in the procedure. Thus, HAP is prepared on site via hydrolysis of $SbCl_5$. HAP precipitate is centrifuged off, dried (5 h at 270°C), crushed and sieved (first 80 mesh, then 60 mesh).

The proton irradiated Al target ($\sim$50 g) is dissolved in HCl (6 molL^{-1}), and contacted with a small HAP cation exchanger column (1.5 g), where ^{22}Na is retained on the solid, while Al elutes. The column is thoroughly washed with HCl (6 molL^{-1}), and subsequently digested in HCl (12 molL^{-1}) at 150°C utilizing a small autoclave. The resulting solution is diluted with water (to result in 2–3 molL^{-1} HCl), and is subjected to Sb electrodeposition (potential of 5V applied for several hours). Antimony solids are filtered off, and the filtrate is evaporated to dryness.

The dry residue is then reconstituted in HCl (0.5 molL^{-1}) and contacted with equilibrated anion exchanger Ag1x8 for fine purification. Antimony traces are retained while ^{22}Na elutes. It is evaporated to dryness and taken up in HCl (0.1 molL^{-1}) for storage. The ^{22}Na yield per batch typically amounts to 55.5 GBq (1500 mCi) with a specific activity of 8.92E+13 Bqg^{-1} (2410 Cig^{-1}). Due to the high HAP selectivity for Na, the sorption step introduced above can be used for ^{22}Na separation from many other target materials. One application of the strong Na/HAP sorption would be the study of charged particle or neutron induced ^{22}Na emission by medium mass and heavy target nuclei.[7]

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Conclusion: Radioisotopes provide the very basis for diagnostic and therapeutic nuclear medical applications. Moreover, they play an important role in both fundamental and application science. In space research, radioisotopes are used as alternative power sources and as sources for irradiation studies. Nuclear Physics has interests in reaction cross section measurements for the formation of radioisotopes. The Monte Carlo code MCNPX is partially based on experimental reaction cross sections and does thus benefit from empirical isotope research results. In astrophysics, studies of formation of instable nuclei are of significant importance for the interpretation of s-neutron capture processes.

In environmental science, tracer studies depend on medium and long–lived radioisotopes like ^{73}As (half-live 80 d) and ^{32}Si (160 a) for the determination of geological flow paths and hydrologic modeling. Radioisotopes find application in threat reduction, nuclear forensics and membrane permeability studies. In some defense programs, isotopes are utilized for fundamental property studies and for the improvement of nuclear material detection.

The U.S. Department of Energy's radioisotope program with its signature production and processing facilities at Los Alamos makes a major contribution to the national and international market availability of several medium-lived neutron deficient radioisotopes.

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MANIPULATING ISOTOPES FOR USE IN ACCELERATOR PHYSICS EXPERIMENTS

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Abstract: Within the field of low-energy nuclear physics, accelerator based research involves low emittance, isotopically pure beams which are used to induce nuclear reactions in enriched targets in order to create new isotopes and explore their structural stability and properties in detail. Stable beam and target combinations employing enriched isotopes across the periodic chart have been the mainstay of these studies for more than a half century. Over time, increasingly sophisticated detector systems such as the Argonne Fragment Mass Analyzer (FMA) and GAMMASPHERE deployed at the ATLAS superconducting linear accelerator have been built to collect data on very exotic isotopes produced from nuclear interactions at extremely low cross-sections, currently in the 10's of nanobarn regime. Obtaining and manipulating the rare isotopes into beams and foils demanded by the experimental requirements is often difficult and challenging. Continuous development of intense beams and target foils that can withstand the power deposition are required to reach new sensitivity levels. In addition, gamma and particle detectors need radioactive isotopes for calibration purposes. We present here some of these challenges taken from recent studies at Argonne.

Introduction: The availability of highly enriched separated isotope is a vital component in accelerator based nuclear physics research. Most experimental techniques involve isotopically pure beams impinging on enriched targets in order to induce the nuclear reactions of interest. Procuring isotopes and fabricating them into forms useful for beams and targets can be difficult. More recently, the development of intense beams require target foils capable of withstanding the high power deposition required for ever increasing levels of experimental sensitivity. We present here a few examples where isotope manipulation was needed for beams and targets taken from recent studies at Argonne. While this is not an exhaustive list, it does represent some of the challenges encountered working with isotopes in their available form. We have not here considered the enrichment techniques as these are covered elsewhere.

Availability of Stable Isotope: Within the US the responsibility for providing isotope to the community at large has come under the Department of Energy (DOE) with the main supplier of electromagnetically separated stable isotope being Oak Ridge National

Laboratory (ORNL). The DOE has just commissioned a study to assess the issue of isotope availability and released a report covering their findings.[1] In addition, there are several purveyors in the industry offering products originating from foreign laboratories which also include centrifugal separation techniques.

Gases: Noble gas elements are readily available as highly enriched species immediately amenable for introduction into, for example, an electron cyclotron resonance (ECR) ion source to produce accelerated beams directly. For target interactions, various schemes have been designed including, in our case, use within a confined gas cell requiring foil windows. This is not always ideal and therefore elaborate systems have been developed for differentially pumped windowless gas targets as well as cryogenic devices. For other isotopic gases, one can also find a suitable compound usable as targets for introduction into the beam.

The isotopes of hydrogen are often demanded for reaction studies as they play an important role in many crucial nuclear astrophysical experiments. In cases where a gas cell is not practical, compounds in solid form are sought out for these applications. The simplest hydrogen bearing materials used as accelerator targets are thin plastic films of polyethylene (CH_2) or longer polymer chain polypropylene. Commercially, these are obtained in a variety of thicknesses and may also be stretched thinner if necessary. For the next heavier isotope, deuterium, plastic films of CD_2 are easily cast from solutions of the polymer dissolved in xylene.[2] However, there are severe drawbacks in using plastic targets in that they cannot withstand appreciable beam currents. It is for this reason that we have recently turned to the metal compounds of titanium hydride and titanium deuteride for these experimental requirements. In this method, thin metal foils of Ti are prepared by evaporation or rolling and then reacted in a furnace at moderate temperatures under an atmosphere of hydrogen or deuterium.[3] Use of these foils also avoids interference from the carbon present in the plastic targets.

Other gases, such as nitrogen, oxygen and fluorine pose more complex issues in handling. To use these gaseous elements as accelerator targets, the quest is to find suitable solid compounds that can be easily manufactured into shapes suitable for this purpose. In the case of the nitrogen isotopes, a straightforward approach involves obtaining any number of commercially available labeled compounds, for instance, L-valine. This compound can be deposited onto a suitable carrier foil using a vacuum evaporator. Natural oxygen (mainly ^{16}O) readily combines with many elements and therefore can be easily fashioned into a target by first mounting the metal foil to be used then oxidizing it to create the compound.[4] This method can be further extended to the other isotopes of oxygen provided they are on hand as gases. There also exist a plentiful supply of $^{16,17,18}O$ labeled chemicals though many are organic solutions difficult to fabricate into anything useful. Fluorine, though mono-isotopic, is difficult to handle chemically. The most common fluorine targets are those made from lithium fluoride (LiF) which also works well for the isotopes of lithium.

Non-metals: The case for sulfur is set apart for a number of reasons. While isotopically enriched sulfur is available in its elemental form, it is difficult to work with due to its high vapor pressure and low melting point (115 C). Even for use in making ion beams it is usually preferred as a compound, e.g. FeS. Sulfur is requested often as a target as the nucleus ^{36}S is relatively neutron rich and ^{32}S is one of the heavier stable $A = Z$ nuclei which are important in the study of nuclear structure. The literature is abundant with sulfur compounds prepared as accelerator targets.[5] The issue then becomes the ability to bombard such compounds with intense heavy-ion beams. As the melting point for sulfur containing compounds are also rather low, target heating limits the amount of allowable beam. To reduce beam heating, a rotating target wheel was developed for use within GAMMASPHERE[6] to enable extended target lifetimes when dealing with low melting point materials. In addition, the choice of a sulfur compound is further complicated by possible interference from the other atoms present in the target.[7] Often one can prepare a compound of sulfur by reacting it with other metals such as Ag_2S, FeS, PbS and HgS, which is also a good preparation technique for obtaining Hg targets.

Similar approaches were devised for using both selenium and tellurium as accelerator targets as these isotopes are also routinely supplied in their elemental form. Both of these elements as isotope have been fabricated as target wheels for studies at GAMMASPHERE by deposition onto a supporting gold foil with the additional step of overcoating the Se or Te with a thin additional gold layer to prevent loss of material from sputtering. In the case of tellurium, a recent study[8] employed many of the Te isotopes as fixed targets on carbon backing foils using both the elemental form as well as the oxide compound.

Metals: Within the realm of low-energy, accelerator based nuclear physics experiments, the overwhelming requirements are for isotopically pure metals not only as feedstock in ion sources for the production of heavy ion accelerated beams but also for manufacture into target foils for beam interaction studies. Fortunately, the mono-isotopic elements as well as the stable isotope offerings already as metals cover a large portion of the periodic chart and provide a convenience in this regard. It then simply becomes a fabrication and handling problem to obtain the form necessary for these applications.

Oxide Conversions: Although it may be simple to procure the enriched isotope of interest, there are times when it cannot be supplied as the metal needed for producing targets. The common practice during the separation process is to provide the end product in the most chemically stable form. This is done to assure a long shelf life. This chemical dependence requires that the isotope be provided as nitrate or carbonate but mainly as an oxide. Over the years, methods have been devised for reducing the oxide to its metallic form. An excellent review is presented by Heagney and Heagney[9] as it relates to target preparation and is shown in Table I. Some examples of these reduction techniques are now given.

Hydrogen Reduction Furnace: There are several isotopic oxide compounds where a simple chemical reaction with hydrogen at elevated temperatures allows a reduction to the metal. Those metals in column IV A of the periodic chart–Ge, Sn, Pb as well as Fe can be easily reduced by this method. This has to do with the energy needed to break the oxygen bond. The apparatus usually employ consists of a tube furnace through which hydrogen gas may be passed[10]. A typical temperature range for these reactions are 600–1200°C. First, the isotope, as oxide, is placed within a carbon or quartz crucible within the furnace and then heated under an atmosphere of hydrogen until the reaction temperature is achieved. After cooling down, the final product may be weighed and the reaction checked for completion based on stoichiometry.

Metallothermic Reduction Techniques: For the alkali earths, these monoxides are tightly bound making simple hydrogen reduction no longer an option. In these cases as well as for the rare earth oxides, a different approach is necessary. A metallothermic reduction is performed which makes use of a reducing agent resulting in low vapor pressure oxide having similar thermochemical

properties. For instance, one can combine calcium or magnesium with a stoichiometric quantity of zirconium as the reductant and heat this under vacuum in a closed 'pinhole' boat. The reaction proceeds based on the enthalpies of the resulting compound and the free energy needed for the breaking of the oxygen bond. This resulting reduction-distillation process creates a vapor stream of the calcium or magnesium within the evaporator, leaving behind the much higher melting point zirconium oxide. In this way targets of these elements may be deposited directly starting from the oxide. The case for the rare-earth oxides is very similar[11] and detailed calculations have been carried out for the thermochemical properties on several candidate reducing agents.[12]

Chemical and Electrochemical Reductions: Finally, there are isotopic oxides that are not amenable to either of these thermal techniques. For these elements the only avenue for reduction to the metal is through a chemical reaction, in most instances, while in solution. To reduce the oxide of the column IV B elements such as titanium, one first combines the titanium oxide with a stoichiometric amount of CaH and heats it to the reaction temperature. Afterwards the Ti may be precipitated out in a solution of acetic acid.[13] There are many such procedures, not all of which are easily accomplished (Zr, Hf). Another method employs electrochemistry where, for example, the monoxides of Zn and Cd can be reduced to metal.[14] First the oxide is dissolved into a solution of glacial acetic acid, placed in an electrochemical cell and when voltage is applied the reduced metal collects at the cathode. Plating chromium, osmium and ruthenium is similarly accomplished though the solution chemistry is more difficult.

Compounds and Special Handling: As mentioned earlier, gaseous elements can be employed as accelerator targets but with severe restrictions in their use. The densities encountered in gas targets are orders of magnitude lower than those obtained with solids. The density can be improved somewhat with higher pressures using cells containing windows and further with additional cryogenic cooling. Clearly, finding chemical compounds containing these elements would aid greatly in increasing the atom density of these isotopes as encountered by the beam. While not directly amenable to producing thin foils, these compounds may be deposited on carrier foils and nevertheless prepared as targets. The issues of target purity and conflicts arising from the other elements present need to be overcome.

Finally, while obtaining the metallic form of the element or isotope helps with the experimental demands, the resulting metal often will react again with air or moisture once produced. Special handling techniques have been developed in order to preserve the metallic form in ways that do not adversely restrict their experimental properties. We provide below examples of such applications.

Reactive Metals: The alkali elements and, hence, their isotopes if available in the form of a metal pose a problem of handling and storage as they can be quite reactive. This is certainly true for ^{6,7}Li. But for the most part, with Li and the remaining heavier alkalis, the isotopic form provided usually consists of a fluorine or chlorine salt which is fairly inert. Also, as discussed earlier the alkali earth and rare earth isotopes can be readily reduced to metal from the available oxides. Once obtained, the metal then has a tendency to react again with the surrounding air or moisture. For these reasons clever handling techniques have been devised to prevent reoxidation from occurring while transporting reactive foil targets from the preparation laboratory for use at the accelerator.[15] At Argonne, a vacuum transport cell capable of attaching both to the evaporator as well as the experimental target chamber developed for just such applications was employed recently for a study involving Li metal targets.[16[Another remedy is to provide a coating of gold acting as an oxygen barrier to both sides of the metal foil. This is routinely applied to isotopic targets of calcium and well as the rare earths.

Conclusion: In conclusion, the continued availability of stable, separated isotope remains vital to the low-energy accelerator physics community for use in the study of nuclear properties. Unfortunately, these isotopes are not always provided in a state useful for these purposes. Manipulating them into forms and foils useful for experimental work becomes a necessity at these widely used accelerator installations. These have been but a few examples of one can expect to encounter using isotopes in these instances. Fortunately, abundant literature exists in the field for a highly skilled technical staff to take full advantage of.

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MOLYBDENUM-99 PRODUCTION WITH HIGH SPECIFIC ACTIVITY USING MEDIUM ENERGY NEUTRONS ON TECHNETIUM OR RUTHENIUM TARGETS

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Abstract: Calculations have been made showing that high specific activity ^{99}Mo can be very effectively produced using medium energy neutrons (10–20 MeV) and ^{99}Tc or ^{102}Ru targets. Suitable 'Compact Neutron Generators' are being developed, employing charged particle accelerator mini-fusion systems, which can deliver sufficiently high fluxes of these neutrons ($>10^{14}$ cm^{-2}s^{-1}). For example, consider the ^{99}Mo that would be produced after a 7 day irradiation with 14 MeV neutrons on ^{99}Tc. The calculation made take into account all the reactions ((n,p),(n,d),(n,alpha), etc.) producing stable molybdenum isotopes and ^{99}Mo. Monte Carlo (MCNPX) calculations were made to determine flux levels in a 1000 g ^{99}Tc target. Using calculated neutron cross sections (Empire-18) for ^{99}Tc, the calculated activity at discharge of the ^{99}Mo for a 7 day irradiation was 200 Ci. The resulting very high specific activity product is 80,500 Ci/g on discharge (which is even higher than that typically obtained from fission product ^{99}Mo). Subject to ongoing experimental confirmation, this could open the possibility for future local/'in-house' production of Mo-99.

Keywords: Molybdenum-99; Neutrons; Tc-99 or Ru-102 Target; High Specific Activity; Commercial Production

Introduction: Over the past years, recurring problems and shortages in Mo-99 production have become increasingly critical. Aging reactors with chronic maintenance and repair issues have become a serious issue. The lack of reliability and increasing prices are getting to the point where using alternate isotopes are now being seriously considered. To address this need, several new projects are underway in an attempt to achieve a reliable long-term supply of Mo-99, particularly for US domestic use. Plans are underway to build or extend reactors to produce 'fission Mo' by conventional means while others are attempting to use accelerator-based technology. All of these methods are designed to produce hundreds to thousands of curies of Mo-99 per week in order to fill the need in the existing supply base. Unfortunately, most of these methods will also take several years to achieve this goal. Meanwhile, hospitals and patients will likely suffer with shortfalls in Mo-99/Tc-99m supply for imaging procedures resulting in problems such as poor or late diagnosis of urgent medical conditions.

An alternative approach towards filling the Mo-99 supply need might be achieved without reactor or U-235 based technology. Thermal neutron capture on Mo-98 is routinely used in many parts of the world but this method suffers from low specific activity and correspondingly bulkier generator systems that are deemed undesirable in the major Mo-99 consuming countries. Other similar reactions employing photons, protons and even alpha particles have also been considered. These may produce the required specific activities but generally do not produce significant quantities for clinical applications.

This paper addresses a possible candidate method(s) for producing generator quantities of high specific activity Mo-99 with relatively simple technology and without the use of U-235. Medium energy neutrons, available from an increasing number of available generators, can be used to convert Tc-99 or Ru-102 to moderate quantities of high specific activity Mo-99. In-house or local production of a few generators per week is feasible from single production units. The advantages of simple operation and lack of U-235 in these methods should speed up the time to market.

Calculations: Medium energy neutrons (10–20 MeV) and Tc-99 or Ru-102 targets can be employed to produce Mo-99 by the following reactions:

$$Tc-99(n,p)Mo-99 \tag{1}$$

$$Ru-102(n,\alpha)Mo-99 \tag{2}$$

Figures 1 and 2 show the measured cross-section data for these reactions. Additionally, the predictions of a computer modeling code (EMPIRE18 [1]) are plotted for comparison.

Existing sources of medium energy neutrons include the Berkeley compact fusion systems that include the D(T,n)He-4 reaction which produces 14 MeV neutrons. They claim that fluxes of up to 10^{15} n/s/cm^2 are possible with their system. Other possible neutron sources include systems being developed using the Be-9(d,n)B-10 reaction. For present calculation purposes we have used the Berkeley parameters but expect that future developments could further improve on these.

MCNPX [2] model calculations employing typical neutron fluxes (above) and various target designs have been made to estimate the yields that would be available. Spherical shell targets encompassing the neutron source were used to predict the maximum yields possible as a function of target thickness. Realistic yields were calculated using a beam on cylindrical target model. Experimental data and model calculations were both used to cover the complete energy range of the neutrons as they degraded through the target. Scattering losses, in-target decay and losses due to other reactions were also accounted for in MCNPX. In this model, the targets were irradiated for about 150 hrs to evaluate the weekly production rate. A wide range of target thicknesses and geometries were investigated resulting in a range of realistic yields.
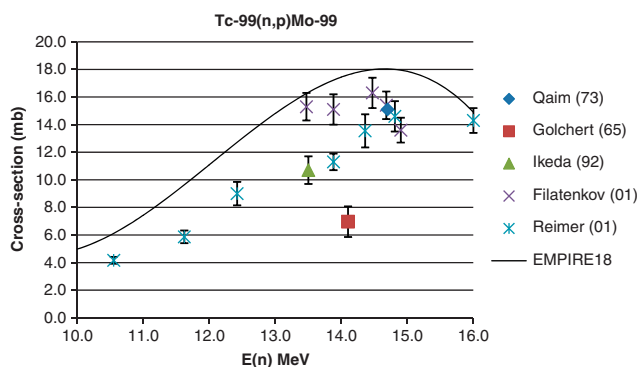
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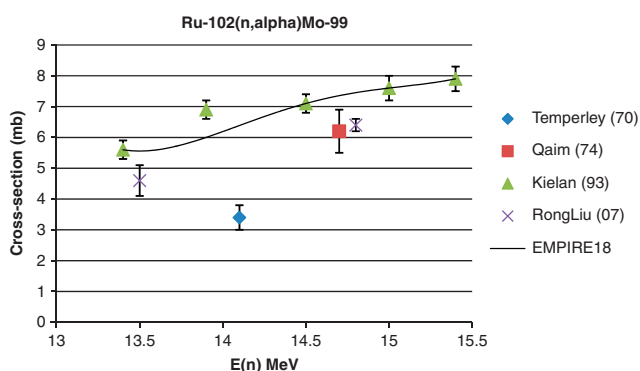
Figure 1. ^{99}Tc(n,p)^{99}Mo cross-sections

Figure 2. ^{102}Ru(n,α)^{99}Mo cross-sections

Results: Typical results are shown in Table 1 which should be understood to only be 'ballpark' values at present. 'Max Yield' refers to results from a spherical shell model surrounding the neutron source and represents the maximum yield possible. 'Yield' refers to realistic quantities extracted from a cylindrical/cone target of varying dimensions. These numbers include reasonable processing losses and refer to the quantity of Mo-99 loaded onto generators at the time of shipment. The very high specific activity implies that this product can readily be integrated into existing fission-Mo generator designs (c.f. is carrier-free $\sim$480,000 Ci/g). '6-Day Ci' is the industry standard measure and refers to the quantity of Mo-99 remaining on the generator(s) six days later. Although these numbers are only a guideline they do indicate that clinically significant quantities of Mo-99 can be produced for in-house or local supply.

Table 1. Predicted ^{99}Mo Yields			
Target	Max Yield (Ci/week)	Yield (Ci/week)	'6-Day Ci' (Ci/week)	Spec. Activity (Ci/g)
Tc-99	$\sim$300	$\sim$20–100	$\sim$4–20	80,500
Ru-102	$\sim$180	$\sim$12–60	$\sim$2–12	c.f.
Nat-Ru	$\sim$60	$\sim$4–20	$\sim$1–4	$\sim$c.f.

Conclusions: Advantages of this approach include:

(a) U-235 use is avoided thus reducing regulatory concerns. This would considerably speed up time to market.
(b) The moderate yield makes this a candidate for limited supply, e.g., 'in-house' or local demands. As higher neutron flux devices are designed this method will scale.
(c) The very high specific activity makes it a good candidate to substitute for fission-Mo.
(d) Product can likely be loaded onto existing Mo-99 generator systems.
(e) Small footprint and simplicity of operation lends itself to use in commercial units.
(f) Employs Tc-99 which is a fission 'waste' by-product.
(g) Ru-102 method potentially makes carrier-free Mo-99 and will be easier to handle.
(h) Ability to quickly turn-on and turn-off.

Remaining Questions:

(a) Are yields high enough for practical use locally or 'in-house'?
(b) Advantages/Disadvantages of Tc-99 and Ru-102 production routes (byproducts, chemical purification, etc.)?
(c) Process handling issues with Tc-99?
(d) Issues with enrichment of Tc-99 and Ru-102? Can we just use natural Ru?
(e) Can practical commercial equipment be devised to employ these production routes in hospitals or regional production sites?
(f) How much external shielding is required?
(g) Are these methods economical? Can they compete with existing and planned commercial sources of Mo-99?
(h) Can this method be scaled up to supply a significant portion of the US demand?

Future Plans:

1. Further detailed modeling and calculations will be used to design a prototype system. Test irradiations will be used to confirm the yields. Chemical methods will be designed to extract the Mo-99 for loading onto conventional generators.
2. Thereafter, a commercial production unit that can supply local Mo-99 to hospitals, pharmacies, etc. will be designed, built and installed.
3. Efforts will be made with regard to scaling up the method (higher neutron sources, improved targetry, multiple units, etc.) to better secure the Mo-99 supply within the US.

The lack of secure sources of Mo-99 in the nuclear medicine industry is becoming increasingly critical. This method could compliment other larger-scale methods being considered at this time. In view of some proliferation concerns, the lack of U-235 in this production method makes it particularly attractive, quick to market and could help secure the supply of Mo-99 in the nuclear medicine community.

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PRODUCTION OF HIGH ENRICHED ^{176}LU USING THE SU20 CALUTRON

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Abstract: Low β energy ^{177}Lu has become an important RIT (Radio-immunotherapy) for the treatment of various inoperable tumors. As this isotope has moved from the research stages to the treatment phase for many cancers including endocrine, prostate and lung, the need for higher purity precursor material has been required. This is primarily owing to the fact that production methodologies involve neutron activation. The high relative cross section of other rare earth impurities in the target material can have a significant impact on the cost and processing of the finished product. Regardless of modality of manufacture, ^{176}Lu (n,γ) for cost effective production of large quantities of non carrier free product, or ^{176}Yb (n,p) for the production of high specific activity material, precursor materials need to be refined to the highest order to eliminate these impurities. While similar in processing to Yb, this paper will only focus on the production of ^{176}Lu. Given that Lutetium is the scarcest of the rare earth's elements, at some 0.8 grams per Mt of ore[1] and separation difficult, elemental Lu is one of the most expensive element on the periodic table at some 6 times the price of Au[2]. Further compounding the cost of enrichment of ^{176}Lu is the low natural abundance 2.61%[3] and proximity to the other stable sister isotope ^{175}Lu. These challenges have been met and exceeded through many successful production campaigns at the SU20 calutron at Electrokhimprebor of Lesnoy Russia. Earlier batch runs in the 70's typically achieved enrichments of only 40% with impurity levels as high as 5% making this precursor unattractive for ^{177}Lu applications. In addressing these issues, recent campaigns have provided for an average enrichment of over 82% with total impurity levels of less than 100 ppm making this an ideal candidate for ^{177}Lu via the n,γ production method.

Keywords: 176Lu–isotope production–calutron–177Lu precursors

Introduction: The bone seeking element of Lutetium has become and important nuclide for researchers in recent years. In particular the radiochemical properties of ^{177}Lu are ideally suited for many radio-immunotherapies (RIT's) in the treatment of a host of tumors. Moreover, the bonding characteristics are ideal for many monoclonal labels and with a low relative β energy and 6.7[4] day half-life, ^{177}Lu is quickly becoming a key element in patient treatment. As an additional benefit there are also two production modalities for this nuclide. For large scale production of ^{177}Lu the preferred route is via the ^{176}Lu (n,γ) reaction. Given the cross section of ~2000 Barns[5] this method is ideally suited for mass production via this technique. The only draw back with this route is the high cost of the precursor

isotope, ^{176}Lu and the simultaneous production of the relatively long-lived ^{177m}Lu. Aside from bone-palliation applications the 160^6 day half life can prove extremely problematic for many other needs. Applications requiring the labeling a many available ligands, such at DOTA or TETA, require carrier free ^{177}Lu. This is achieved via the ^{176}Yb (n,p) production method. While yields are relatively low, improvements in rare element separation have lead to the commercialization of this isotope in recent months via this methodology.

With either modality, historically produced isotopic target material has been unsuitable for use given low isotopic enrichment and high contamination levels. Original production campaigns of ^{176}Lu typically yielded enrichments in the range of 65% to 70% and impurity levels were as high as 5%. These impurities were either other rare earths or a host of other high cross section elements. Once irradiated, these impurities render radio pure material an impossibility due to low specific activity, and hence bonding efficiencies were extremely low to highly irregular at best. These challenges were also compounded with the fact that of all the bi-isotopic stable elements, ^{175}Lu and ^{176}Lu have the lowest mass difference ratio of 0.56%. This makes production very time consuming and extremely costly.

Elemental Lu is also the scarcest of all rare earth isotopes with a natural abundance of some 8 grams per ton of ore. Prices of Lu have been comparable to that of Au over the last 30 years due to natural scarcity and isolation costs. A major benefit in recent times however, is that feedstock purity levels have increased substantially and often 99.99% chemical elemental enrichment is available. With the mass ratio mentioned above and the non-existent nature of suitable gaseous compounds for centrifuge separation only calutron^7 separation is possible. With improvements in feedstock purity, ion source modifications and chemistry techniques, production yields however are still in the range of 0.08%. Campaigns lasting months and requiring kilograms of elemental Lu only provide a few grams of enriched ^{176}Lu which is suitable for ^{177}Lu production.

With these challenges in consideration, the separation of Lu isotopes was undertaken at Electrokhimprebor with a new set of parameters.

Processing: Since calutron separation is the only suitable technology for the isolation and enrichment of rare earth elements, new feed stocks had to be acquired and a new set of handling and processing procedures had to be developed.

Earlier production campaigns in the 1970's did not place specifications on the in-bound feedstock material namely LuCl$_3$. This was a critical step in producing higher quality finished products. While the isolation process does a small amount of purification via elemental plasma differentials the actual chemical extraction from the collection pockets is fraught with sources of contamination. Obtaining the highest purity product from the outset is thus desirable.

A typical 'run' time is a function of the life of the calutron ion source which on average has a useful run time of some 25 hours. During this period a typical yield of 2.35 mg/hr of finished product is achieved. A total campaign of runs typically last as a along as 6 months in order to ensure sufficient stocks are available and often create inventories of only 5–6 grams of finished product. Despite the improvements in technology, and calutron efficiency, Lu remains as one of the least efficient separations with a nominal effectiveness of some 0.08% as a function of feedstock vs. final yield.

Materials and Methods: Elemental Lu (as the salt LuCl$_3$), is obtained from the company, ChimSyntes' of Yekaterinburg Russia. Once validated the material is heated to near dryness in an Ar furnace then placed into the ion source crucible. The LuCl$_3$ is then introduced into the ion source for processing in to a plasma for isotope separation in the calutron. Once a 'run' is completed and the collection pocket is removed from the calutron the Lu goes thru a series of 'pickling' steps, or etching, to extract the Lu from the Cu lined pockets.

The pockets are processed with layers of gauze swabs that have been dampened with HCl in order to loosen or dissolve the enriched isotope. This process is repeated several times until the pocket contains virtually no Lu product. The gauze swabs are then processed whereby the Lu is removed to a solution of HCl. The major impurity of Cu (pocket composition material) is extracted via several steps with ammonium precipitation whereby Lutetium hydroxide is formed. Once as the hydroxide Pb and other like metals are extracted using hydrogen sulfide. Finally the end product is made using a calcination method to form the oxide.

Once in the oxide form the material is then analyzed using an ICP-MS, model (ELAN-6000 PE SCIEX ICP-MS), manufacturer Perkin Elmer. Typical protocols using 0.5–1 mg of Lu are used for isotopic analysis and a semi-quantatative method using 3–10 mgs is used for spectral chemical analysis.

In previous production campaigns no specifications were given for the use of any acids or dedicated glassware for Lu processing. It was determined that HPLC grade, low conductivity acids, were required and dedicated glassware for each processing are needed to avoid cross contamination. Several processing steps had to be repeated when it was learned that improper washing of glassware resulted in the introduction of various elemental impurities.

Results: From the comparisons noted in Tables 1 and 2 below, the changes in protocol and in handling procedures have proven effective in increasing overall product quality. On average isotopic purity has increased on average by 11% and chemical purity has increased from 95% to over 99.9%.

Table 1. Lu impurity specifications

Element	Symbol	1970's Production ppm	2008 Production ppm	% Change
Aluminum	Al	5	5	0
Cerium	Ce	37	6	84
Erbium	Er	17	1	94
Gadolinium	Gd	6	3	50
Lanthanum	La	66	3	95
Lead	Pb	87	22	75
Samarium	Sm	2	1	50
Ytterbium	Yb	13	12	8
Zinc	Zn	22	3	87

While seemingly minor in overall enrichment, the increase in isotopic purity from a high of 74.1% in early campaigns to consistently over 82% has had a tremendous impact on cost effectiveness and purity of the final product production of [177]Lu. This has been achieved by reducing the 'slit' entrance to the pocket collectors by a few millimeters. While decreasing overall production efficiency, it has allowed for an overall increase in product quality and thus making [176]Lu a suitable precursor candidate for the production of [177]Lu.

Table 2. Lu isotopic enrichments

Isotope	175 (1970's)	176 (1970's)	175 (2008)	176 (2008)	% Change
Enrichment (%)	25.9	74.1	17.2	82.8	11%

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[4] Table of Isotopes–Seventh Edition, Pg. 1105.
[5] Table of Isotopes–Seventh Edition, Pg. 1097.
[6] Table of Isotopes–Seventh Edition, Pg. 1107.
[7] Calutron - Is a type of mass spectrometer, whereby a vaporized sample is bombarded with high energy electrons, which cause the sample components to become positively charged ions (plasma). The plasma is then accelerated and subsequently deflected by a magnetic field, whereby the particles are bent due to their mass ratio. Ions of the different isotopes have the same electric charge but different masses, the heavier isotopes are bent less by the magnetic field, causing the beam of particles to separate out into several beams. Once the paths are sufficiently separated by a distance of a few centimeters the plasma goes thru a 'slit' or window entrance into a collector pocket.

RESEARCH ON THE MASS PRODUCTION OF [13]C

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Abstract: A carbon monoxide cryogenic distillation pilot plant was built up in China in order to develop low-cost production technology. After six months running smoothly, it confirmed that the experimental column met the requirements of ^{13}C enrichment and the production capability of the plant was significantly higher than conventional production facilities applying random packing. The column was studied by computational simulation, and ideal conditions were evaluated at different pressures, F-factors, and reflux rations. Finally, an annual production capacity of 100 kilograms ^{13}C industrial mass production plant was designed after uniform experiment design and computer simulation. Liquid nitrogen refrigeration cycle was utilized in this industrial plant in order to save energy consumption, and an ideal cascade transmission without rotary machine was exploited according to hydrodynamic principles. The total height of industrial plant was below 30 meters, and the production efficiency could be greatly improved. Through energy efficiency analysis, it was concluded that the newly designed industrial plant could decrease about 50% of the production cost compared to traditional devices, which provided a solid foundation for ^{13}C-breath test becomes a routine physical examination.

Keywords: [13]C production; cryogenic distillation; optimization design; computer simulation

Introduction: Stable isotope carbon-13 is widely used in chemical, biochemical, biological, pharmacological, medical, and genetic researches. Especially it has been used in clinical diagnosis of Helicobacter pylori in recent years, which promotes the need for the cheap production of [13]C. Traditional methods have the disadvantages of difficulty in scaling up, too long of columns, low production capacity, and high production costs,[1–5] which largely restrict the application of ^{13}C-breath test in clinical diagnosis. Particularly in developing countries, the expensive price of ^{13}C can't compete with the cheap price of [14]C. The price of special ^{13}C-breath test mass spectrographs and ^{13}C-infrared spectrograms is decreasing markedly. It became a keen problem to develop cheap mass production technologies. In China, There were about 19 million ^{14}C-urea breath tests in 2008, and it would require nearly 300 kilograms of ^{13}C to replace the ^{14}C-urea breath test; but it is a pity that there were only 500 thousand persons using the ^{13}C-urea breath test. That provides a power for engineers to industrialize mass production of [13]C. A pilot plant by carbon monoxide (CO) cryogenic distillation was set up, and a new kind of structured packing PACK-^{13}C was developed.[6] PACK-^{13}C worked with good performances in mass transfer and hydrodynamics, which met well the requirements of isotope

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separation through distillation. The ideal operation conditions were carried out through computational simulations. At last, an optimized mass production plant with annual capacity of 100 kg was designed by way of CO cryogenic distillation. The factory was organized elaborately in energy utilization process. According to economic evaluation, a newly developed technique could save about 50% of the production cost vs. traditional methods, which would establish a solid foundation for ^{13}C-breath test becomes a routine physical examination.

Experimental column: An experimental pilot plant was set up in the Shanghai Research Institute of Chemical Industry for CO cryogenic distillation.[7] Packing height of the column was 17.5 meters, with 15.5 meters in rectification section and 2.5 meters in extraction section. Diameter of the column was 45 mm. The column was thermally isolated by vacuum multilayer materials, and the whole of the assembly is settled in a steel vacuum cover for better thermal isolation. The experimental column was shown in Figure 1. A new structured packing was developed to resolve the difficulty of scaling up, and it worked eminently in the tests. The pilot plant has a capacity to produce 600 grams 15% [13]C a year. CO gas was bought in industrial steel bottles with a purity of 99.95%. After the removal of oxygen by catalytic reaction, water by molecular sieves, oxygen, water, and carbon dioxide were all bellow 1ppm. Purified CO gas flowed into the column at a feeding point through a regulator valve. Extracted gas was pumped out at the top of the column, and concentrated [13]CO was drawn out at bottom of the column. The column was installed above the ground. The condenser was made of aluminum alloy plate-fin heat exchanger, and the reboiler was made of electric stick with a power of 250 watts. CO was condensed by liquid of nitrogen supplied from a 5 m^3 liquid tank on the ground. The pilot plant consumed 500 liters liquid nitrogen each day. About 300 liters was lost by heat exchange in the liquid transfer pipes and liquid tank. Pressure in the condenser was maintained stably by vacuum pumps.
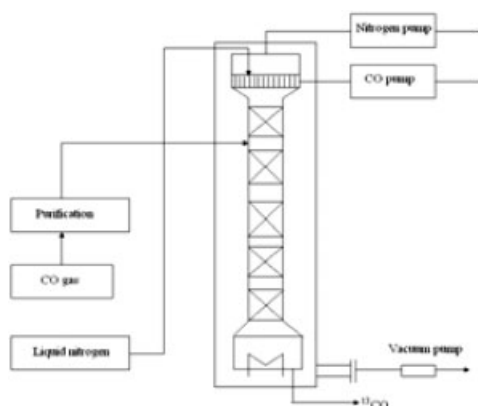

Figure 1. [13]C cryogenic distillation column.

Evaluation of the experimental column: For the sake of optimization, a uniform design experimentation table was adopted on the basis of the pilot plant test results, shown in Table 1. By way of uniform design experimentation, three factors including pressure, F-factor, and reflux ration and seven levels were put into consideration by the computer simulation. In order to obtain good separation efficiency, it is necessary to achieve separation factor as high as possible, which requires reduced operation pressure of the column, namely, vacuum distillation. Drawbacks of this are increase of energy consumption, decrease of production efficiency for unit equipment volume, and high requirements of air tightness for instruments, equipments and valves. Even more, the ^{13}C separation column is run at low temperature, and thus the equipment must operate at low temperature and high vacuum. In addition, there are lots of difficulties for ^{13}C cryogenic distillation resulting from its micro-flow cryogenic fluid's insulation, control, and safe longtime operation. In this study, different conditions were evaluated by computational simulation in order to obtain optimal conditions for industrial design.

Table 1. Evaluation of the experimental column by uniform design experimentation

Test number	Pressure, kPa	Reflux Ration	P, mol/day	Pxp/W	Pxp/F	OC, RMB/day
1	45	83	7	0.00112	0.00566	62.6
2	90	62	6	0.00104	0.00416	73.5
3	15	97	5	0.00106	0.00642	55.9
4	60	76	4	0.00090	0.00449	63.4
5	105	55	3	0.00075	0.00282	77.1
6	30	90	2	0.00073	0.00445	55.7
7	75	69	1	0.00042	0.00203	64.7

*In the table: F, P, and W are feeding, product, and extraction respectively, mol/day; X_p is ^{13}C abundance at the bottom of column; OC is operation cost including boiling power, liquid nitrogen and feeding gas, RMB/day.

From the results of the uniform design experimentation, it showed the more product removed the higher the energy consumption saved. However, total operation costs tended to decrease with lower pressure with the cost of equipment's size increasing. Unexpectedly, reflux ratio did not play a key role on operating costs, which might be related to the small scale of the test column.

Design of mass production plant: There needs to be nearly 2000 theoretical plates for ^{13}C isotope enrichment from the natural abundance of 1.1% to 99%. In order to design an ideal production plant, engineers must keep a balance between heights and diameters of columns.

Two factors and seven levels of uniform experiment design scheme is listed in Table 2 to approach optimal operation parameters. Mass flow, isotope concentration, and parameters of columns for the seven schemes were developed by computer simulation. Optimization objects were total mass flow and total volume of the colums. The smaller total flow, the smaller overall consumption, and the smaller total volume the larger investment saved.

Table 2. Results of uniform design experimentation for 100 kg 99% ^{13}C factory

	Design scheme						
	1	2	3	4	5	6	7
Pressure/kPa	40	47	54	61	68	75	82
Reflux Ration	76	64	84	72	60	80	68
Total flow/kgday^{-1}	15 182	14 196	16 770	14 776	15 776	16 314	16 472
Total volume/m^{-3}	9.1	8.3	9.0	7.4	7.6	7.6	7.3

As seen by the simulation results in Table 2, when the pressure is 61 kPa, reflux ratio is 72, total flow and total volume are relatively small. We selected parameters of the fourth design scheme for the industrial design.
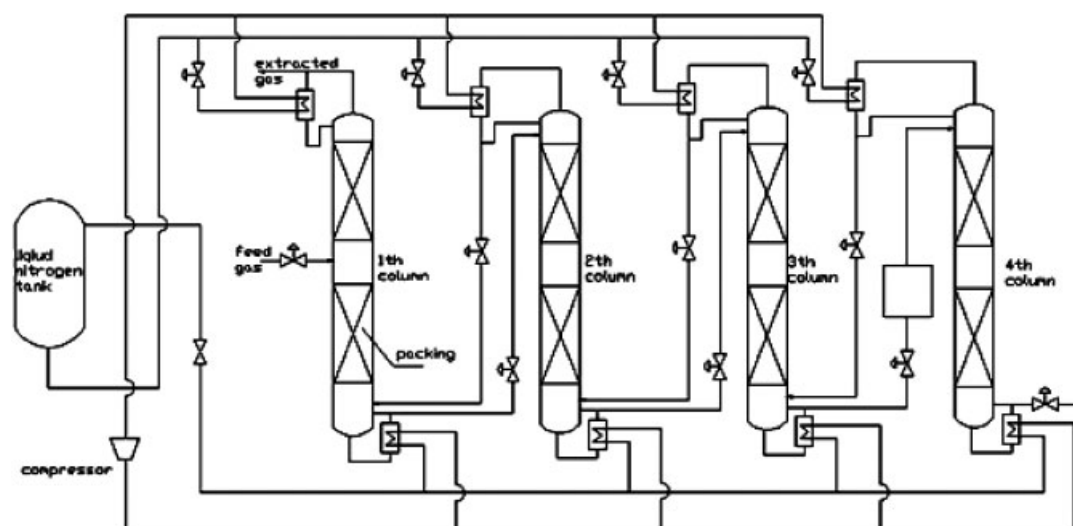

Figure 2. Flow sheet of annual 100 kg 99% ^{13}C factory.

An annual production capacity of 100 kg 99% ^{13}C production factory was designed on the basis of the experimental pilot plant, as seen in Figure 2. The facility consisted of four columns, laid on the ground end to end, of 30 meters. Transmission between the cascades is pump free. Steams at the bottom of former column flow to the top of back column by driving force of pressure drop, and condensates from back column flow to the bottom of former column by gravity. Thus the system could run stably without rotary equipment. In the interest of further reducing energy consumption, the liquid nitrogen refrigeration recycling process was applied. The CO gas is extracted from industrial synthesis gas, by which the cost of materials is greatly reduced. After economic analysis, the newly developed mass production factory could save about 50% energy consumption compared to that of traditional plants. Parameters of the designed plant are shown in Table 3. The distribution of isotopes in different columns was simulated by computer, as seen in Figure 3.

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Table 3. Parameters of annual 100 kg 99% ^{13}C factory

	1th column	2th column	3th column	4th column
Diameter, mm	390	200	90	45
Height, m	30	30	30	30
Packing	PACK-^{13}C	PACK-^{13}C	PACK-^{13}C	PACK-^{13}C
Steam flow rate, mol/d	437940	134860	26040	13760
Spraying density, $m^3 m^{-2} h^{-1}$	3.75	3.75	3.75	2.25
Liquid flow, L/d	15520	4760	920	480
F-factor	0.5	0.5	0.5	0.5
Top concentration, %	0.7	5	43	92
Bottom concentration, %	5	43	92	99
Boiling power, kW	30.8	9.4	1.8	1.0
Material consumption	Feeding CO gas: 6366 mol/day; product: 25.76 mol/day; Compressor power: 50 kW			
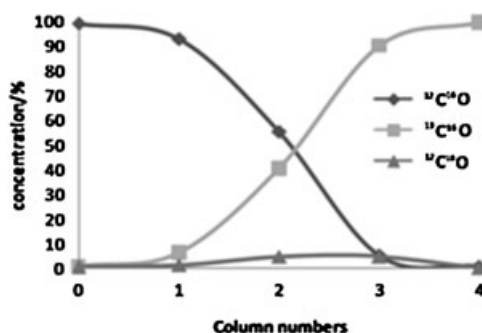
Figure 3. Isotopes concentration in different columns.

Conclusion: A mass production factory with an annual capacity of 100 kg 99% ^{13}C was designed after test and computational simulation of a pilot plant. Through innovation of packing, utilization of a new process, and development of energy organization, the designed factory shows excellent character with low consumption, which saves about 50% of the ^{13}C production cost compared to that of traditional ^{13}C plants. It is feasible for ^{13}C-breath test becomes a routine physical examination by mass production to decrease diagnostic costs.

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