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Comparative Study of ^{82}Sr Purification Procedures Used at Brookhaven National Laboratory and ARRONAX

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1. Introduction

Nuclear imaging is one of the most powerful means available for non-invasive diagnosis and management of poorly perfused myocardial region resulting from coronary epicardial vascular disease [1]. Several radionuclides are available for myocardial perfusion imaging. The most validated radionuclides for the measurement of cardiac blood flow are: ^{13}N, ^{15}O, ^{201}Tl and ^{82}Rb. ^{13}N, ^{15}O and ^{201}Tl require the presence of an on-site cyclotron, whereas, ^{82}Rb requires only a generator [2].

Rubidium (Rb), an alkali metal ion, acts biologically like potassium, and accumulates in myocardial tissue. Rb has rapid blood clearance profile which allows the use of ^{82}Rb with an ultra-short physical half-life of 75 s for non-invasive evaluation of regional myocardial blood flow [3]. There are several advantages of ^{82}Rb over other radionuclides. An ultra-short half-life significantly reduces the radiation dose to the patient and offers the possibility of repeatable injections to investigate the effects of medical intervention. As a positron emitter, use of ^{82}Rb allows the full advantages of positron emission tomography (PET) such as image quantification with superior sensitivity [4].

^{82}Rb can be produced from a generator system by decay of its 25-day half-life parent ^{82}Sr. However, the ^{82}Sr parent is difficult to prepare, because in routine generator production, certain purity is required to meet the specification of the product. Recently reported result from ARRONAX research group showed that a Chelex-100 column is sufficient for this purpose and no additional column is necessary [5]. While Brookhaven National Laboratory (BNL) method includes three ion exchange column separation, including Chelex-100 column [6]. Currently, since no ^{82}Sr production site is available in Korea, Korea Atomic Energy Research Institute (KAERI) has plan to produce ^{82}Sr with certain purity. We compared ^{82}Sr purification methods reported from ARRONAX and BNL to investigate the most suitable method for future reference.

2. Methods and Results

2.1 Preparation of a cold stock solution for comparison of purification procedures

Mass of cold Sr for test of purification procedure can be calculated using the following equation:

Calculation of the total number of atoms and total mass of ^{82}Sr present in 24.2 GBq (654 mCi) ^{82}Sr ($t_{1/2}$ = 25.6 days)

$$\lambda \text{ for } ^{82}\text{Sr} = \frac{0.693}{25.6 \times 24 \times 60 \times 60} = 3.1 \times 10^{-7}\,\text{sec}^{-1} \quad (1)$$

$$A = 654 \times 3.7 \times 10^{7} = 2.4 \times 10^{10}\,\text{dps} \quad (2)$$

$$N = \frac{A}{\lambda} = \frac{2.4 \times 10^{10}}{3.1 \times 10^{-7}} = 0.77 \times 10^{14}\,\text{atoms} \quad (3)$$

Since 1 g·atom ^{82}Sr = 82 g ^{82}Sr = 6.02 x 10^{23} atoms of ^{82}Sr (Avogadro's number)

$$\text{Mass of } ^{82}\text{Sr in } 654\,\text{mCi } (24.2\,\text{GBq}) = \frac{0.77 \times 10^{14} \times 82}{6.02 \times 10^{23}}$$
$$= 10.49 \times 10^{-6}\,\text{g}$$
$$= 10.49\,\mu\text{g} \quad (4)$$

Where λ is the decay constant and N is the number of atoms.

Because in BNL paper, up to 24.2 GBq of ^{82}Sr has been produced in a 35 g RbCl target, a cold stock solution was prepared by considering both RbCl target mass and produced ^{82}Sr activity to mass. In addition, the generated impurities during ^{82}Sr production such as Fe, Be and Se were mixed with the same amount of Sr.

2.2 Optimization of Chelex-100 resin column chromatography procedure

Before comparison of purification methods between ARRONAX and BNL, Chelex-100 resin column chromatography procedure was optimized. First, we tested the proper amount of Chelex-100 resin (Bio-Rad laboratories, France) to separate Sr from bulk RbCl. Second, pH of loading buffer mixed with stock solution was confirmed by using three pH buffers like 9.05, 9.50 and 9.92. Finally, we varied loading time of the sample for the reaction of the loading sample with resin. Results are shown in Fig. 1.

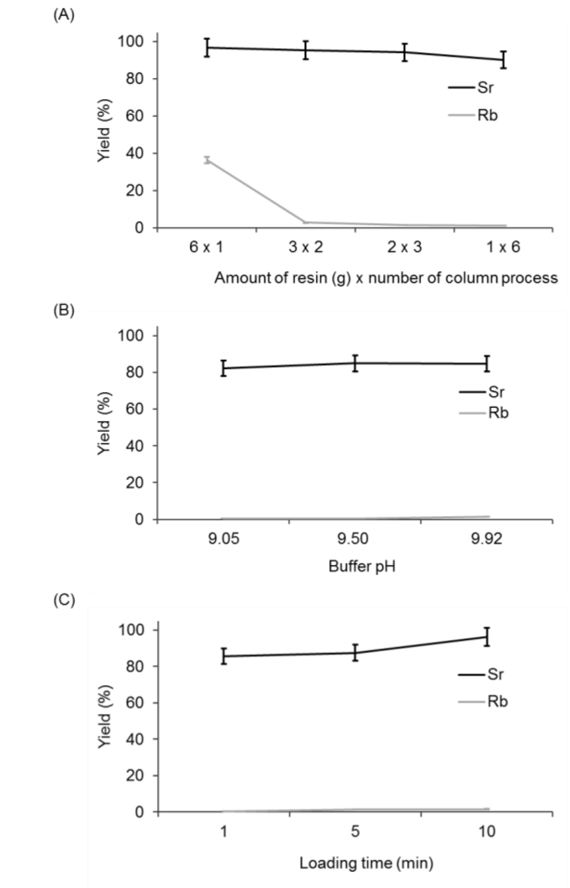

Fig. 1. Recovery yield of Sr and Rb in eluate measured by ICP-MS as a function of (A) the amount of resin, (B) buffer pH and (C) the sample loading time.

When large amount of resin was used, not only higher recovery yield of Sr occurs but also higher concentration of Rb impurity in the eluate was observed. On the other hand, the recovery yield resulting from use of less amount of resin and many process of column chromatography showed decreasing pattern in both Sr and Rb in the eluate (Fig. 1A). Effect of buffer pH was negligible (Fig. 1B), whereas effect of the sample loading time was found to be the most important factor for Sr separation. Sufficient time for reaction of the loading sample with resin is necessary (Fig. 1C).

2.3 Comparison on the final yield of Sr purified by BNL and ARRONAX procedures

ARRONAX reported that only Chelex-100 resin column process was enough for the final Sr solution within specifications. While BNL proceeded three ion exchange column separation such as Chelex-100, AG50W-X8 (cation exchange resin) and AG1-X8 (anion exchange resin). We performed both purification methods and compared the results to decide the suitable method of our research environment. Comparison result on Sr, Rb, Se, Be as well as Fe is presented in Table I.

Table I: Comparison results on the final yield of Sr and other impurities purified by BNL and ARRONAX procedures.

		Final yield (%)
Sr	BNL	33.6
	ARRONAX	97.57
Rb	BNL	0.002
	ARRONAX	0.77
Se	BNL	4.23
	ARRONAX	32.39
Be	BNL	1.20
	ARRONAX	89.47
Fe	BNL	1.09
	ARRONAX	47.57

To meet specification requirements for final Sr product, only Chelex-100 column was not sufficient. Superior recovery yield of Sr and the low concentration of Rb are satisfied. However, other impurities such as Se, Be and Fe were also included in the final Sr solution. While the final Sr solution separated by BNL procedure included much lower amount of impurities including Rb, Se, Be and Fe than that purified by ARRONAX procedure. Only the low recovery yield of Sr was a problem. Currently, we found the reason of the low recovery yield of Sr. So we are trying to increase the recovery yield to satisfy the specification of the final product.

3. Conclusions

In order to produce certain purity of ^{82}Sr, the most suitable procedure for our facility was investigated by comparing the well-known methods from BNL and ARRONAX. As compared to both procedures, it has been found that in our environment, a Chelex-100 column is not sufficient and additional ion exchange column is necessary to remove contaminations of stable elements like Se, Be, Fe, etc.

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