Patient Dose Estimates After Lactated Ringer's Related Breakthrough of a Rubidium-82 Generator

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Purpose

Retrospective patient dose estimates were calculated for eight Rb-82 cardiac rest/stress patients imaged over three days with PET/CT. Lactated Ringers' (LR) solution was mistakenly used for infusion on the first day instead of 0.9% sodium chloride, causing elevated levels of Sr-82 and Sr-85 to be administered. The event was discovered on the third day and use of the generator stopped. Dose estimates were calculated two weeks after the incident.

Methods

QC vials from three days were used to determine strontium levels. Four vials were not dated but were assumed to be the vials from the first day because of their long half-life material and their location near the labeled vials from the second and third days. All vials were assayed independently two weeks after the incident using a Rb-82 dose calibrator setting. The highest vial from each day was selected to represent a potential maximum breakthrough amount. This is only a mildly conservative assumption as the other vials from each day were within 10-20%. After initially performing these calculations, we were informed that the most radioactive unlabeled QC vial may be a repeated calibration vial from the second day. While we consider this plausible and potentially the most likely explanation, we have no way to verify this idea. We have thus included calculations for the two patients from the first day using both the highest of the four unlabeled vials (which may actually be from the second day and is the more likely scenario) and with the highest of the remaining three vials.

To determine the amount of Sr-82 two weeks later, the assayed amounts were divided by the Divisor from Bracco-supplied Generator Data Sheet on the day of assay. Those readings were then decay corrected to the day of elution using the half-life of Sr-82.

Sr-85 activity was determined using measured ratios of Sr-85/Sr-82 from a radiochemistry lab. The lab analyzed four samples representing all three days. The average Sr-85/Sr-82 ratio from the four samples was determined to be 0.82 two weeks after the incident, about 10% less than the Bracco provided value for that date of 0.91. The measured ratio was multiplied by the Sr-82 activity after two weeks to determine the amount of Sr-85 after two weeks. The Sr-85 activity was then decay corrected to the day of elution using the half-life of Sr-85. Strontium ratios in units of µCi/mCi on the day of elution were then calculated.

Our initial dose calculations assumed the amount of strontium injected was dependent on the total activity of rubidium injected. This is also the method suggested by the Bracco quality control process. But the reported rubidium activity at the end of infusion is over-estimated because of the presence of strontium in the elution. If we assume uniform deposition of strontium and strontium-calcium exchange within the generator, then strontium contamination may be logically described as a volume-dependent process. We therefore also calculated breakthrough ratios in units of µCi/ml. Breakthrough concentrations are shown for activity based and volume based calculations in Figure 1.

Breakthrough Ratios (Activity Based)			Breakthrough Ratios (Volume Based)		
	Sr-82 µCi/mCi	Sr-85 µCi/mCi		Sr-82 µCi/ml	Sr-85 µCi/ml
1st Day*	6.46	4.22	1st Day*	4.74	3.10
1st Day**	22.58	14.77	1st Day**	16.58	10.84
2nd Day	23.04	15.34	2nd Day	17.61	11.72
3rd Day	16.99	11.51	3rd Day	12.07	8.17

Figure 1 Breakthrough Ratios calculated both per mCi of Rb-82 and per ml of elution
*** More likely scenario with highest vial attributed to the second day**
****Potential maximum breakthrough**

			Activity Based Calculation			Volume Based Calculation		
	Total Rb-82 activity (mCi)	Total volume (ml)	Total Sr-82 (µCi)	Total Sr-85 (µCi)	Total Dose (mSv)	Total Sr-82 (µCi)	Total Sr-85 (µCi)	Total Dose (mSv)
P1*	74.8	100	483	355	131	474	310	127
P2*	90	78	581	346	154	370	242	101
P1**	74.8	100	1689	1241	449	1658	1172	439
P2**	90	78	2074	1211	538	1293	846	341
P3	84.3	89	1943	966	498	1567	965	410
P4	77.7	100	1791	890	459	1761	817	449
P5	66.1	100	1123	679	293	1207	1172	333
P6	63.2	100	1074	633	280	1207	1172	333
P7	60.4	100	1026	748	273	1207	1172	332
P8	63.6	100	1081	771	287	1207	1172	333

Figure 2 Activity of Rb-82 and volume administered, Sr-82 and Sr-85 doses computed with activity and volume based ratios, and total dose in mSv
*** More likely scenario with highest vial attributed to the second day**
****Potential maximum breakthrough**

Methods (cont.)

Multiplying the ratios in Figure 1 by the total amount of Rb-82 injected or total volume during both rest and stress, we obtained the total amounts of Sr-82 and Sr-85 infused for each scenario. Bracco's Cardiogen package insert provides dose conversion coefficients of 4.74 mrem/mCi for Rb-82, 23.4 mrem/µCi for Sr-82, and 4.03 mrem/µCi for Sr-85. Note that strontium coefficients are per µCi and the rubidium coefficient is per mCi. The dose conversion factors were used to calculate dose per isotope and summed to give the total dose.

Total administered activity for all three radionuclides and total dose for both activity-based and volume-based methods are summarized in Figure 2.

Results

Ten days after the incident, the highest measured patient dose rate at 1m was 0.2 mR/hr. Exposure rates decreased slowly as expected due to the long half-life of both strontium isotopes.

Sr-82 breakthrough over three days ranged from 6.5 to 23.0 µCi/mCi and 4.7 to 17.6 µCi/ml. Sr-85 breakthrough ranged from 4.2 to 15.3 µCi/mCi and 3.1 to 11.7 µCi/ml . Total contaminant activities ranged from 474 to 2074 µCi Sr-82 and 310 to 1241 µCi Sr-85. Effective doses ranged from 101 to 538 mSv.

Conclusion

The ion-exchange breakthrough seen in this case caused elevated levels of strontium at least two days after returning to sodium chloride elution. Breakthrough peaked on the second day, after the LR had overnight contact-time with the generator and then fell somewhat on day three, but was still many orders of magnitude above allowable limits.

Experimental measurement of the Sr-85/Sr-82 ratio generally agreed with the included generator value. Questions remain about distribution of the strontium isotopes within the generator. If strontium is not uniformly distributed, the reported ratio may not be correct once ion-exchange based breakdown has occurred.

While Rb-82 generator manufacturers have repeatedly warned users of the risk of mistakenly using LR solution, this work is thought to be the first published patient dose estimate for that scenario. The long half-lives of Sr-82 and Sr-85 and biological behavior lead to substantial doses from µCi activity levels. These results also indicate the importance of daily QC testing as mandated by the manufacturer. In this case, QC vials were being eluted properly but incorrectly analyzed.