Radiopharmacy

Discrepancies in Dose Calibrator Assays for Various Forms of Therapeutic Iodine-131

Geoffrey Levine*†, Balwinder Malhi†, and Lloyd Struttman‡

**University of Pittsburgh, †Presbyterian-University Hospital, Pittsburgh, Pennsylvania*
‡Mallinckrodt, Inc., St. Louis, Missouri

Differences in product packaging have the potential to yield differences in assays for the same quantity of radioactivity. We report on the assay variance between packaging of sodium iodide I-131 in capsules and in solutions. We have observed differences of sufficient magnitude that, under certain circumstances, could result in reports of misadministrations to the Nuclear Regulatory Commission when in fact, none has occurred. Establishment of appropriate calibration factors and development of separate dose calibrator potentiometer settings for liquid and capsule dosage forms can minimize the problem.

Radioactivity assay discrepancies resulting from differences in packaging of differing dosage forms of radiopharmaceuticals can lead to reporting a misadministration when, in fact, none has occurred. For therapeutic administrations, if more than a 10% variance from the prescribed dose or dosage range occurs, the NRC requires immediate notification (within 24 hr) by telephone, and in writing within 15 days. The referring physician and patient (or relative or guardian) must also be notified (*1,2*). We report on the assay variance between packaging of capsule and solution dosage forms of sodium iodide I-131.

Materials and Methods

Sodium iodide I-131 in liquid (n = 11) and in capsule (n = 15) (Mallinckrodt) was assayed in a dose calibrator (Capintec CRC-6A). The measured assay was compared with the assay stated on the product label, or calculated from the product label using decay correction. Deviation from the product label assay was noted. Mean, standard deviation, and standard error of the mean were calculated along with the ratio of capsule-to-solution deviation. Pentuplicate measurements of capsule and solution at positions laterally across the radioisotope dose calibrator chamber were made, as were assays of the capsule upright and on its side. Geometric variance due to source height was determined by adding increasing quantities of sterile water for injection to the capsule and solution (2,4,6,8, and 10 ml). Capsule measurements were made in original plastic vials and then transferred to glass vials used for shipping solution. Three random individual capsule assays (specific capsule assays) were requested at the manufacturer site; these assays were compared to the labeled assay. Hospital measurements were compared to the manufacturer's labeled assay and to the manufacturer's specific capsule assay. Dose calibrator potentiometer settings were empirically determined to bring our measured results into accord with the manufacturer's label assay and the manufacturer's specific assay for sodium iodide I-131 capsules.

TABLE 1. Assay of Sodium Iodide I-131 Capsules in Original Plastic Vials

N	Label assay (mCi)	Measured assay (mCi)	% Deviation
1	8.0	9.1	13.8
2	22.0	24.2	10.0
3	10.0	10.9	9.1
4	26.0	29.0	11.5
5	8.0	8.6	8.9
6	9.1	10.5	15.4
7	2.8	3.0	6.1
8	3.0	3.1	3.3
9	15.5	17.1	10.3
10	2.8	3.0	6.1
11	20.7	23.0	11.1
12	12.8	14.2	10.9
13	27.0	30.0	11.1
14	17.8	19.7	10.6
15	9.9	10.7	8.1

N = 15; range = 3.3–15.4; mean percent over labeled quantity = 9.8%; SD = 3.15; and SEM = 0.81.

For reprints contact: Geoffrey Levine, Dept. of Nuclear Medicine, Presbyterian-University Hospital, Pittsburgh, PA 15213.

Results

We have found that sodium iodide I-131 capsules (when measured in our Capintec radioisotope dose calibrator) read about 10% higher than the labeled radioactivity. The liquid, however, is in very close agreement with the radioactivity specified on the package label (Tables 1 and 2). We have observed this variance for both Mallinckrodt and Squibb products. The 15 most recent capsule assays were between 3.3 and 15.4% above the radioactivity specified on the Mallinckrodt label (mean = 9.84%; SEM = 0.81%). The most recent 11 assays of liquid were 2.8% below to 8.2% above the radioactivity specified on the Mallinckrodt label (mean = 1.72%; SEM = 1.10%). Because of different dose calibrators and reference standards, measured radioactivity in liquid and capsule forms of I-131 is likely to be different at other institutions, and will thus bear a different relationship to the quantity stated on the label. The measurement ratio of capsule-to-liquid is calibrator independent. At our hospital and in our experience, this ratio is 1.08.

TABLE 2. Assay of Sodium Iodide I-131 Therapeutic Solution in Original Glass Vials

N	Label assay (mCi)	Measured assay (mCi)	% Deviation
1	97.0	97.1	+0.1
2	97.0	105.0	+8.2
3	141.1	144.0	+2.1
4	105.8	108.7	+2.7
5	141.1	151.6	+7.4
6	105.1	105.7	+0.6
7	141.1	137.0	−2.8
8	141.1	138.4	−1.9
9	109.0	114.0	+4.5
10	35.3	34.9	−1.1
11	141.1	140.0	−0.8

N = 11; range = −2.8–8.2; mean percent over labeled activity = 1.72%; SD = 3.67; and SEM = 1.11.

TABLE 3. Sodium Iodide I-131 Capsule Measurements: Geometric Variance Due To Source Displacement From Long Axis of Dose Calibrator Chamber

Pentuplicate Assay of a Sodium Iodide I-131 Capsule* in Dose Calibrator

	Position (mCi)				
Trial	Left Wall	Mid Left	Center	Mid Right	Right Wall
1	22.0	21.7	21.2	21.7	21.9
2	21.8	21.7	21.2	21.7	21.9
3	21.9	21.7	21.2	21.6	21.9
4	21.8	21.6	21.2	21.6	21.9
5	21.9	21.7	21.2	21.7	21.9
Mean	21.88	21.68	21.20	21.66	21.90

Note: $\frac{21.89}{21.20} = 1.033 = 3.3\%$.

*Capsule was labeled as 20 mCi at calibration. Capsule measurements were made at noon on day of calibration.

TABLE 4. Sodium Iodide I-131 Therapeutic Solution Measurement: Geometric Variance Due to Source Displacement From Long Axis of Dose Calibrator

Pentuplicate Assay of Sodium Iodide I-131 Solution* in Dose Calibrator

	Position (mCi)				
Trial	Left Wall	Mid Left	Center	Mid Right	Right Wall
1	50.6	49.9	49.7	50.1	50.6
2	50.5	49.8	49.7	50.0	50.7
3	50.5	49.9	49.7	50.1	50.6
4	50.5	49.9	49.7	50.3	50.7
5	50.5	50.0	49.6	50.2	50.6
Mean	50.52	49.90	49.68	50.14	50.66

Note: $\frac{(50.52 + 50.66) \div 2}{49.68} = 1.018 = 1.8\%$.

*Sodium iodide I-131 therapeutic solution was labeled as 50 mCi at calibration. Measurements were made at noon on day of calibration.

TABLE 5. Pentuplicate Assay of a Sodium Iodide I-131 Capsule* Measured Upright and on Its Side in Capsule Vial

Trial	Upright (mCi)	On Side (mCi)
1	21.2	21.3
2	21.3	21.3
3	21.2	21.2
4	21.2	21.2
5	21.3	21.4
Mean	21.24	21.28

Note: $\frac{21.26}{20.00} = 1.063$.

*Capsule was labeled as 20 mCi at calibration. Measurement made at noon on day of calibration.

Discussion

When the measured radioactivity exceeds ±10% of the value stated on the product label for a therapeutic administration, the difference is of sufficient magnitude that under certain circumstances these findings become reportable to the NRC. Certainly the causes for these discrepancies, low photon absorption and sample configuration, have long been known to the nuclear medicine community (*3,4*).

One can account for the observed difference as being due primarily to attenuation and geometric factors resulting from differences in radiopharmaceutical packaging. If the capsule (shipped in plastic) is placed in the French square glass container used to ship liquid, our readings are very close to the radioactivity stated on the label. The Mallinckrodt French

TABLE 6. Alteration In Assay Due to Geometric Variance Resulting From Change in Source Height

Added volume (ml)	20-mCi capsule in glass vial*	50-mCi solution in glass vial*†
0	19.9	49.5
2	19.8	49.5
4	19.6	49.4
6	19.7	49.3
8	19.6	49.4
10	19.5	49.5

*Pentuplicate measurement at noon on day of calibration
†After venting

about 8% higher than a similarly labeled solution. Thus a sodium iodide I-131 solution labeled as 20 mCi would assay at about 20.3 mCi, but a capsule labeled as 20 mCi would be expected to assay as 20.3 × 1.08 or 22.0 mCi. An alternative method of handling this problem is to have separate dial calibration settings on the dose calibrator for liquid and capsule (Table 7). One must be careful to recognize the individual variation in capsule activities associated with acceptable limits of product specifications. The fact that three random specific request capsule assays required three different settings speaks to this point (Table 7).

Zimmer et al. (*5–7*) have previously used the technique of varying the dose calibrator potentiometer setting in order to establish agreement with the manufacturer's stated assay. Gels et al. (*8*) have developed a correction factor for Xe-133 vials for use with a dose calibrator.

TABLE 7. Sodium I-131 Capsule Measurements: Determination of Dose Calibrator Setting

Measured activity (mCi)			Dose calibrator setting used to read	
Labeled capsule activity	Specific assay*	Measurement‡§	Specific assay	Label assay
5	5.07	5.38 (1.061)†	166	170
12	12.38	12.69 (1.025)	158	166
17	17.19	17.89 (1.041)	161	163

*The specific assay is a special request manufacturer's assay recognizing the slight variation associated within acceptable limits of product specifications.
†The number in parenthesis is the ratio of the hospital assay to the Mallinckrodt assay.
‡A potentiometer setting of 151 is used for the Capintec model CRC-6A dose calibrator.
§Measurements made at noon on date of calibration.

One risk is that capsules could conceivably be prescribed or ordered 8–10% low (below reading in our case) in order to have agreement in readings between liquid and capsule in the dose calibrator. This could result in a theoretically reportable underdose and more importantly have an effect on treatment outcome. A physician could prescribe an underdose if he or she was unaware of the problem described above.

We suggest that dose calibrators should be standardized with the NBS reference source in each of the categorically different types of containers.

square glass vial is molded with a nonuniform glass wall thickness, especially at the bottom. It is square in cross-section, which presents an effective mean wall thickness greater than the actual thickness. The National Bureau of Standards (NBS) I-131 reference sources and the plastic shipping containers for the capsule have relatively uniform wall thicknesses by comparison, and are considerably thinner; and in the case of the latter, considerably less dense. The circular vials have cross-sections that present effective mean wall thicknesses closer to their actual thickness. One would expect that the attenuation and spectral (energy) distribution of photons emerging from these vials would be quite different due to different internal scattering angles and effective mean wall thicknesses. Second, measurement of discrepancies can result from capsule displacement from the long axis of the ionization chamber. The measured value will tend to increase as the capsule is moved nearer to the wall at the bottom of the chamber (Tables 3–6).

There are two relatively easy methods to correct this problem. The first method is to apply a packaging correction factor when recording the radioactivity assay of the sodium iodide I-131 capsule. At our hospital, we find that the capsule reads

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