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EFFECT OF CONCENTRATION AND RINSING ON RESIDUAL RADIOACTIVITY OF LIQUID IODINE-131 IN SYRINGES DURING RADIOPHARMACEUTICAL PREPARATION

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ABSTRAK

Radioaktivitas residu pada spuit setelah penyiapan Iodium-131 cair dapat menyebabkan aktivitas yang dikeluarkan dari spuit lebih rendah daripada aktivitas yang disiapkan serta menambah sumber paparan dan limbah radioaktif. Penelitian ini mengevaluasi hubungan konsentrasi dan pembilasan dengan radioaktivitas residu Iodium-131 cair pada spuit. Penelitian eksperimental menggunakan konsentrasi 5, 10, dan 15 mCi/mL dengan aktivitas awal 2 mCi (n = 5). Aktivitas awal dan residu diukur menggunakan *dose calibrator*, sedangkan laju paparan radiasi diukur menggunakan *surveymeter* gamma pada jarak 100 cm. Pengujian pembilasan dilakukan pada 15 mCi/mL menggunakan tiga *aliquot* baru *water for injection* (WFI) atau NaCl 0,9% masing-masing 0,5 mL. Pada kondisi pengujian, konsentrasi yang lebih tinggi disertai volume pengisian yang lebih rendah dan berhubungan dengan peningkatan radioaktivitas residu: 12,90 ± 0,63%; 17,45 ± 1,08%; dan 20,97 ± 0,74%. Laju paparan masing-masing adalah 2,703 ± 0,102; 3,304 ± 0,100; dan 4,131 ± 0,237 µSv/jam. Pembilasan menurunkan radioaktivitas residu hingga 6,58 ± 0,43% dengan WFI dan 6,83 ± 0,44% dengan NaCl 0,9%. Tahap pembilasan berpengaruh bermakna ($p < 0,0001$), sedangkan jenis pembilas tidak berbeda bermakna ($p = 0,7134$). Pembilasan bertahap berhubungan dengan penurunan radioaktivitas residu, tetapi pengaruh konsentrasi tidak dapat dipisahkan sepenuhnya dari volume pengisian dan proporsi volume mati spuit.

Kata kunci: Iodium-131, radiofarmaka, radioaktivitas residu, spuit, pembilasan, keselamatan radiasi

ABSTRACT

Residual radioactivity in syringes after liquid Iodine-131 preparation may result in less activity being discharged than initially prepared and may increase radiation and

radioactive-waste burdens. This study evaluated the association of concentration and rinsing with residual radioactivity of liquid Iodine-131 in syringes. Experiments used concentrations of 5, 10, and 15 mCi/mL at an initial activity of 2 mCi (n = 5). Initial and residual activities were measured with a dose calibrator, and radiation exposure rates were measured with a gamma survey meter at 100 cm. The rinsing test at 15 mCi/mL used three fresh 0.5-mL aliquots of water for injection (WFI) or 0.9% NaCl. Under the tested conditions, higher concentrations were accompanied by lower fill volumes and were associated with higher residual radioactivity: 12.90 ± 0.63%, 17.45 ± 1.08%, and 20.97 ± 0.74%, respectively. Exposure rates were 2.703 ± 0.102, 3.304 ± 0.100, and 4.131 ± 0.237 μSv/h, respectively. Rinsing reduced residual radioactivity to 6.58 ± 0.43% with WFI and 6.83 ± 0.44% with 0.9% NaCl. The rinsing stage was significant ($p < 0.0001$), whereas rinsing solution was not ($p = 0.7134$). Sequential rinsing was associated with lower residual radioactivity; however, the concentration effect could not be fully separated from syringe fill volume and the relative contribution of dead space.

Keywords: *Iodine-131, radiopharmaceutical, residual radioactivity, syringe, rinsing, radiation safety*

INTRODUCTION

Iodine-131 is used in nuclear medicine for the diagnosis and treatment of thyroid disorders, including hyperthyroidism and differentiated thyroid cancer (Haugen et al., 2016; Jirsa et al., 2017; Nguyen et al., 2024). Liquid Iodine-131 doses are commonly prepared in hospital radiopharmacy facilities, where activity measurement, contamination control, ventilation, shielding, and traceable preparation practices are required to support product quality and radiation protection (Badan Pengawas Obat dan Makanan Republik Indonesia, 2024, 2025; Gillings et al., 2021; Wadsley et al., 2023).

A portion of a radiopharmaceutical may remain in a syringe after its contents are discharged. This residual radioactivity may arise from liquid retained in the syringe dead space, a thin liquid film, or radioactivity associated with the syringe surface. Consequently, the activity leaving the syringe may be lower than the initially measured activity. The residual syringe may also contribute to occupational exposure and radioactive-waste activity, although the present study did not directly measure patient-delivered activity, environmental contamination, imaging quality, or total waste generation (Keskintepe & Özer, 2005; Stavrou et al., 2016).

Residual activity has been investigated mainly for Technetium-99m radiopharmaceuticals. Reported determinants include radiopharmaceutical formulation, concentration, contact time, syringe material, needle and syringe dead

space, and container-content interactions (Cambruzzi & Macfarlane, 2021; Galbraith et al., 2015; Kvaternik et al., 2020; Ladrière et al., 2024; Mushtaq et al., 2008; Swanson et al., 2013). Evidence concerning liquid therapeutic Iodine-131 and the effect of sequential syringe rinsing remains limited.

The concentrations of 5, 10, and 15 mCi/mL were selected to represent the range of liquid preparation conditions encountered in routine practice at the study facility while maintaining practical activity measurement and radiation-safety conditions. The novelty of this study was the evaluation of liquid Iodine-131 concentration and sequential rinsing in conventional polypropylene syringes, together with measurement of radiation exposure rate from the residual syringe. This study aimed to evaluate the association of concentration and rinsing with residual radioactivity of liquid Iodine-131 in syringes during radiopharmaceutical preparation.

METHODS

Study design and setting

This experimental study was conducted at the Radiotherapy and Nuclear Medicine Installation of Dr. Kariadi General Hospital, Semarang, Indonesia. The experiments did not involve patients, human specimens, or animals. All work involving radioactive material was performed by authorized personnel under institutional procedures for radiation protection, contamination control, and radioactive-waste management.

Materials and equipment

The materials were a bulk vial of liquid sodium iodide Iodine-131 (Curium), sterile water for injection (WFI; Otsu-WI), 0.9% sodium chloride solution (Widatra Bhakti), and 1-mL conventional polypropylene syringes (Terumo) fitted with 26-gauge needles. The same syringe size and needle configuration were used for all concentration and rinsing experiments, and the needle remained attached during initial and residual activity measurements. Equipment included a CRC-55TR dose calibrator (Capintec), an IT-09T area radiation monitor (Ecotest; serial number 1500328), an Inspector model 49052 gamma survey meter, and a dedicated radiopharmaceutical fume hood (Gaya Logam) with lead-lined walls, a lead-glass viewing window, and an exhaust system equipped with HEPA and activated-carbon filters.

Bulk-vial characterization

Before preparation, the bulk vial and external packaging were visually inspected. The activity was measured with the dose calibrator, and concentration was calculated from measured activity and labeled volume.

The direct surface-monitor reading from the external package was recorded in counts per second (cps). The initial exposure rate was measured at 100 cm.

Concentration test and residual-activity measurement

Liquid Iodine-131 samples were prepared at 5, 10, and 15 mCi/mL. Each syringe contained a target initial activity of 2 mCi, corresponding to fill volumes of approximately 0.40, 0.20, and 0.13 mL, respectively. Five independent syringes were evaluated in each concentration group. Initial activity was measured in the filled syringe with the 26-gauge needle attached. The sample was then held in the syringe for 2 h. This interval was selected to approximate the waiting period that may occur during routine radiopharmaceutical preparation at the study facility and was applied consistently to all groups. After 2 h, the sample was discharged into a receiving vial by fully depressing the plunger. The emptied syringe and attached needle were immediately remeasured with the same dose calibrator. Residual radioactivity was calculated as follows: residual radioactivity (%) = residual activity / initial activity × 100.

Radiation exposure-rate measurement

After the 2-h contact period and discharge of the sample, the exposure rate from each residual syringe was measured with the gamma survey meter at a fixed source-to-detector distance of 100 cm. Measurements were performed without a syringe shield. Syringe position, detector position, and detector orientation were kept constant across groups. Background radiation was measured under the same geometry and subtracted from each reading. Results were expressed in μSv/h.

Syringe-rinsing test

The rinsing test was performed at 15 mCi/mL because this concentration produced the highest residual radioactivity and exposure rate in the concentration experiment. Each syringe initially contained 2 mCi in approximately 0.13 mL and underwent the same 2-h contact period before the sample was discharged into a receiving vial. The syringe was then rinsed sequentially three times with either WFI or 0.9% NaCl (n = 5 per solution). At each stage, a fresh 0.5-mL aliquot was aspirated through the attached 26-gauge needle. The plunger was not moved repeatedly, no additional contact interval was imposed between rinsing stages, and the rinsing solution was immediately and completely expelled into a receiving vial by fully depressing the plunger. The residual activity of the syringe and attached needle was measured after each stage.

Statistical analysis

Analyses were performed using

GraphPad Prism version 10 (GraphPad Software, Boston, MA, USA). Data are presented as mean ± standard deviation (SD). Normality was assessed using the Shapiro-Wilk test, and homogeneity of variance was assessed using the Brown-Forsythe test. Concentration groups were compared using ordinary one-way ANOVA followed by Tukey multiple-comparison tests; R^2 and 95% confidence intervals (CIs) were reported where available. Rinsing data were analyzed using a two-way mixed-design repeated-measures ANOVA, with rinsing stage as the within-syringe factor and rinsing solution as the between-syringe factor. Sphericity was not assumed, and the Greenhouse-Geisser correction was applied. Tukey tests were used for post hoc comparisons. A two-sided p value < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Initial characteristics of liquid Iodine-131

The bulk vial contained a measured activity of 102.6 mCi in 5 mL, corresponding to 20.52 mCi/mL. The packaging was intact and sealed, and no visible leakage was observed. Before the vial was opened, the direct surface-monitor reading from the external package was 18 cps. The initial exposure rate was 0.778 µSv/h at 100 cm.

Association of concentration with residual radioactivity and exposure rate

Residual radioactivity increased across the tested concentration groups (Table 1 and Figure 1).

Table 1. Residual radioactivity and radiation exposure rate at different liquid Iodine-131 concentrations

Conc. (mCi/mL)	n	Residual radioactivity (%)	Exposure rate (µSv/h)
5	5	12.90 ± 0.63	2.703 ± 0.102
10	5	17.45 ± 1.08	3.304 ± 0.100
15	5	20.97 ± 0.74	4.131 ± 0.237

Shapiro-Wilk p values were 0.6872, 0.4795, and 0.3368 for 5, 10, and 15 mCi/mL, respectively. Variances were homogeneous (Brown-Forsythe $F(2, 12) = 0.3031$, $p = 0.7440$). The one-way ANOVA was significant ($F(2, 12) = 116.9$, $p < 0.0001$, $R^2 = 0.9512$), and every pairwise comparison was significant after Tukey adjustment (all adjusted $p < 0.0001$). The mean differences (95% CI) were 4.548 percentage points (3.136-5.960) between 5 and 10 mCi/mL, 8.074 (6.662-9.486) between 5 and 15 mCi/mL, and 3.526 (2.114-4.938) between 10 and 15 mCi/mL.

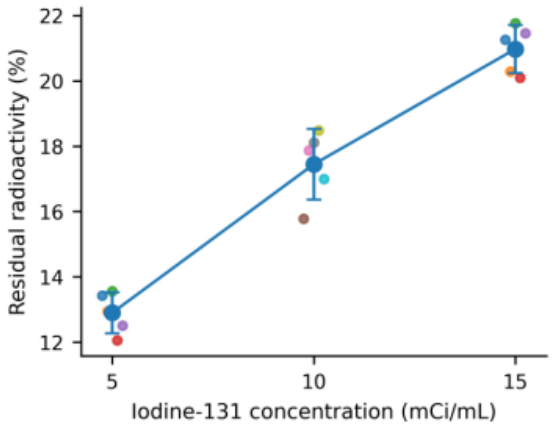


Figure 1. Residual radioactivity at different liquid Iodine-131 concentrations. Points represent individual measurements; symbols and error bars represent mean ± SD (n = 5 per group)

Exposure rates also increased across groups (Table 1 and Figure 2).

Shapiro-Wilk p values were 0.7260, 0.8144, and 0.8222. Variances were homogeneous (Brown-Forsythe $F(2, 12) = 1.882$, $p = 0.1945$). The one-way ANOVA was significant ($F(2, 12) = 100.6$, $p < 0.0001$, $R^2 = 0.9437$). Tukey-adjusted p values were 0.0002 for 5 versus 10 mCi/mL and < 0.0001 for the other comparisons. Mean differences (95% CI) were 0.601 µSv/h (0.332-0.871), 1.428 µSv/h (1.159-1.698), and 0.827 µSv/h (0.557-1.097), respectively.

The findings demonstrate an association rather than an isolated concentration effect. All syringes contained the same target activity of 2 mCi; therefore, increasing concentration necessarily reduced the fill volume from approximately 0.40 to 0.13 mL. With a conventional syringe and attached needle, a relatively fixed dead-space volume would represent a larger proportion of a smaller fill volume. Liquid films and source geometry may also vary with fill volume. Accordingly, the observed increase in percentage of residual radioactivity and exposure rate may reflect concentration, lower fill volume, the increasing relative contribution of syringe and needle dead space, or a combination of these factors. These mechanisms cannot be separated by the present design. This interpretation is consistent with evidence that dead space, container material, formulation, concentration, and container-content interactions can influence residual radiopharmaceutical activity (Cambruzzi & Macfarlane, 2021; Galbraith et al., 2015; Kvaternik et al., 2020; Ladrière et al., 2024; Swanson et al., 2013).

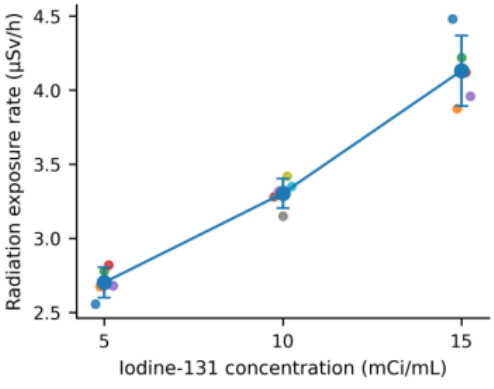


Figure 2. Radiation exposure rate from residual syringes at different liquid Iodine-131 concentrations. Points represent individual measurements; symbols and error bars represent mean ± SD (n = 5 per group)

Effect of sequential rinsing

Sequential rinsing substantially

reduced residual radioactivity in both groups (Table 2 and Figure 3). In the two-way mixed-design repeated-measures ANOVA, sphericity was not assumed (Greenhouse-Geisser ε = 0.8139). Rinsing stage was significant ($F(2.442, 19.53) = 1661$, $p < 0.0001$), whereas rinsing solution was not ($F(1, 8) = 0.1449$, $p = 0.7134$), and the stage-by-solution interaction was not significant ($F(2.442, 19.53) = 0.4698$, $p = 0.6692$). The overall difference between WFI and 0.9% NaCl was -0.044 percentage points (95% CI, -0.3106 to 0.2226). For WFI, sequential comparisons were significant for baseline versus rinse 1 ($p < 0.0001$), rinse 1 versus rinse 2 ($p = 0.0181$), and rinse 2 versus rinse 3 ($p = 0.0247$). Corresponding p values for 0.9% NaCl were < 0.0001, 0.0077, and 0.0335.

Table 2. Residual radioactivity during sequential syringe rinsing

Rinsing stage	n	WFI (%)	0.9% NaCl (%)
Baseline	5	20.58 ± 0.55	20.33 ± 0.62
Rinse 1	5	9.61 ± 0.36	9.74 ± 0.50
Rinse 2	5	7.76 ± 0.45	7.81 ± 0.15
Rinse 3	5	6.58 ± 0.44	6.83 ± 0.45

The largest reduction occurred after the first rinse, followed by smaller but statistically significant incremental reductions. The residual activity may represent a combination of remaining liquid in the syringe and needle dead space and radioactivity associated with the syringe surface.

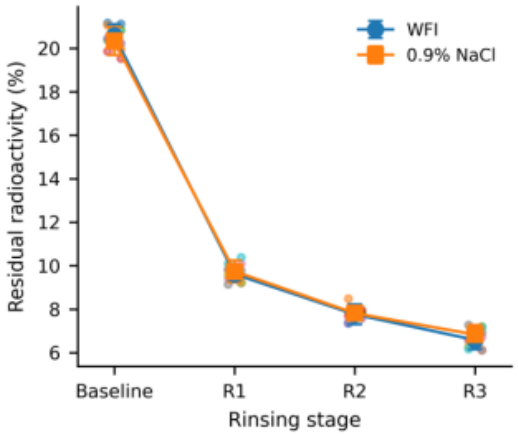


Figure 3. Residual radioactivity during sequential rinsing with WFI or 0.9% NaCl. R1-R3 denotes rinses 1-3. Points represent individual measurements; symbols and error bars represent mean ± SD (n = 5 per solution)

Because no procedure was used to separate these components, the results should not be interpreted as a direct measurement of adsorption. The similar profiles for WFI and 0.9% NaCl indicate that, under the tested conditions, the mechanical process and number of rinses were more influential than the selected rinsing solution.

After the third rinse, mean residual radioactivity remained 6.58% with WFI and 6.83% with 0.9% NaCl. The present experiment did not establish an operational or clinical acceptance threshold for this residual level. Additional rinsing might further decrease residual activity, but the incremental gain diminished after the first rinse and must be balanced against additional handling, occupational exposure

opportunities, preparation time, and the increased volume of liquid radioactive waste. Therefore, the number of rinses should not be generalized as a universal procedure; it requires facility-specific validation, compatibility assessment, radiation-safety review, and incorporation into an approved standard operating procedure.

From a pharmaceutical-quality perspective, monitoring residual radioactivity supports traceability of the activity leaving the preparation device. From a radiation-protection perspective, reducing residual activity may lower the source strength of discarded syringes. These are plausible process and safety implications; however, the study did not directly measure the activity delivered to patients, patient imaging outcomes, environmental contamination, occupational dose, or total radioactive-waste generation.

Study limitations

This study used one brand and one configuration of a conventional 1-mL polypropylene syringe, with five replicates per group and a single target initial activity of 2 mCi. Concentration was intrinsically linked to fill volume, preventing separation of concentration, source geometry, and relative dead-space effects. Only one 2-h contact period was evaluated. The measurements did not distinguish retained liquid from surface-associated radioactivity, did not quantify actual patient-delivered activity, and did not evaluate operator-to-operator variability. The findings therefore apply to the tested materials, geometry, and experimental conditions and should be validated before implementation at another facility.

CONCLUSION

Under the experimental conditions used in this study, higher liquid Iodine-131 concentrations, accompanied by lower syringe fill volumes, were associated with higher residual radioactivity and higher measured exposure rates from residual syringes. Three sequential rinses significantly reduced residual radioactivity, with the largest reduction after the first rinse; WFI and 0.9% NaCl showed comparable performance. The concentration association cannot be separated from fill volume and dead-space effects. These findings support facility-specific evaluation of syringe configuration and standardized rinsing as part of radiopharmaceutical process control and radiation-safety optimization.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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