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CONTRAST MEDIA

# The GREENWATER study: patients' green sensitivity and potential recovery of injected contrast agents

Moreno Zanardo[1*], Federico Ambrogi[2,3], Luigi Asmundo[4], Rosanna Cardani[5], Giulia Cirillo[1], Anna Colarieti[1], Andrea Cozzi[1], Massimo Cressoni[1], Isabella Dambra[1], Giovanni Di Leo[1], Caterina B. Monti[4], Leonardo Nicotera[6], Francesco Pomati[7], Laura V. Renna[5], Francesco Secchi[1,8], Marco Versuraro[5], Paolo Vitali[1,8] and Francesco Sardanelli[1,8]

## Abstract

**Objectives** The environmental footprint of iodinated contrast agents (ICAs) and gadolinium-based contrast agents (GBCAs) is noteworthy. This study assesses: (1) patients' "green sensitivity" as measured by their acceptance in a sustainability study and (2) the resulting potential reduction of contrast residuals in wastewater.

**Materials and methods** After ethical approval, participants scheduled for administration of ICAs or GBCAs for diagnostic purposes were enrolled in this prospective observational study from July 2022 to October 2023. They were asked to prolong their hospital stay by up to 60 min to collect their first urine in dedicated canisters, thereby measuring the recovery rates of ICAs and GBCAs as found/theoretical ratio of concentrations. Mann–Whitney *U*, $\chi^2$ tests, and multivariable regression analysis were used.

**Results** Patients scheduled for contrast-enhanced CT or MRI ($n = 455$) were screened; 422 (92.7%) accepted to participate. We enrolled 212 patients administered with ICAs and 210 administered with GBCAs. The median recovery rate was 51.2% (interquartile range 29.2–77.9%) for ICAs and 12.9% (9.0–19.3%) for GBCAs. At multivariable analysis, a significant effect of patient age (ICAs, $p = 0.001$; GBCAs, $p = 0.014$), urine volume ($p < 0.001$ for both), and time interval from contrast administration to urine collection ($p < 0.001$ for both) on recovery rates was found for both contrast agents; injected contrast volume ($p = 0.046$) and saline flushing usage ($p = 0.008$) showed a significant effect only for ICAs.

**Conclusion** The high patient enrollment compliance (93%) and potential recovery rates of 51% (ICAs) and 13% (GBCAs) play in favor of sustainable practices in reducing the environmental footprint of contrast agents.

## Key Points

***Question*** *How many patients are willing to extend their stay in radiology by up to 60 min to help reduce the environmental impact of contrast agents?*

***Findings*** *Over 90% of screened patients agreed to extend their stay by up to 60 min and collect their urine in dedicated containers.*

***Clinical relevance*** *Patients demonstrated a high willingness to cooperate in reducing the environmental impact of contrast agents, allowing for a potential recovery of approximately 51% for iodinated and 13% for gadolinium-based contrast agents.*

*Correspondence:
Moreno Zanardo
moreno.zanardo@grupposandonato.it
Full list of author information is available at the end of the article



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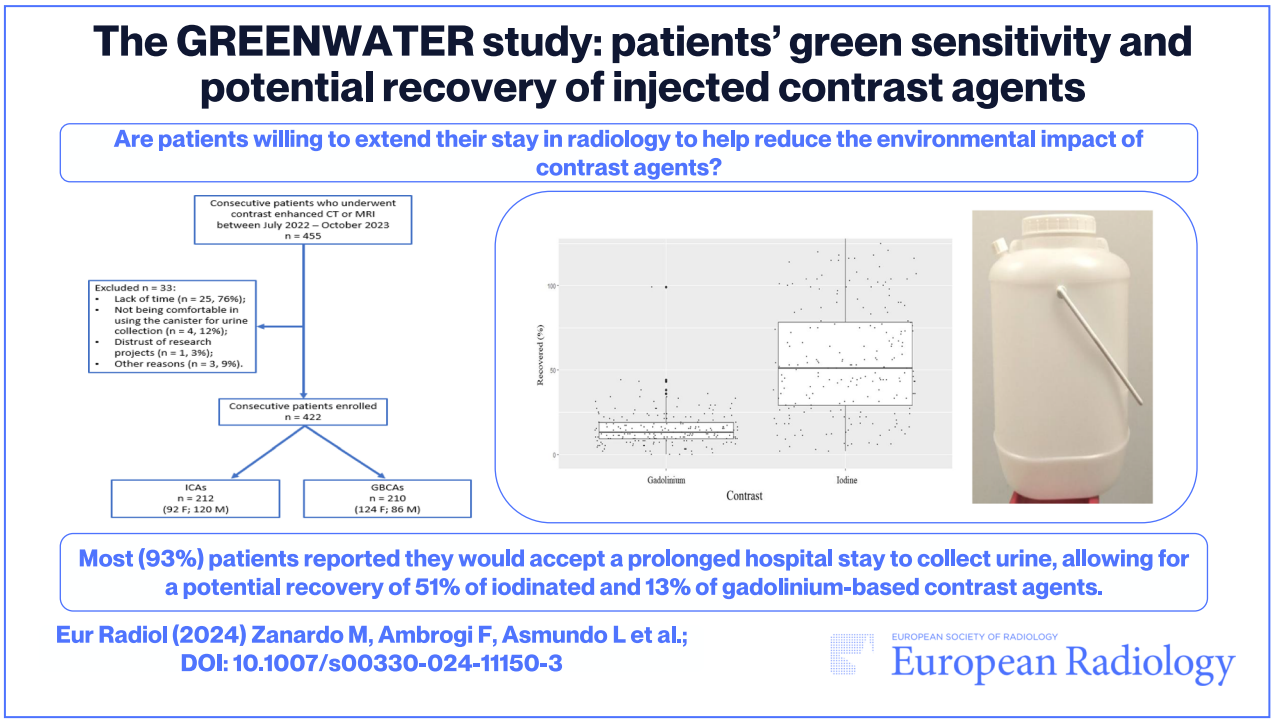
**Keywords** Contrast media, Sustainability, Environmental fate, Gadolinium-based contrast agents, Iodinated contrast agents

**Graphical Abstract**




## Introduction

Intravenous contrast agents used in diagnostic imaging, such as iodinated contrast agents (ICAs) for CT scans and gadolinium-based contrast agents (GBCAs) for MRI, have significantly enhanced the ability to diagnose a broad spectrum of physiopathological conditions. They are eliminated via urinary excretion without being metabolized, mostly within 24 h after administration; ICAs have elimination half-lives of approximately 1.8–2.3 h, while those of GBCAs range from 1.3 to 1.8 h in patients with normal renal function [1–6]. Recently, the environmental footprint of hospital wastewater has come under scrutiny, including contrast agents spillage into aquatic ecosystems [7–10]. These substances often resist conventional wastewater treatment processes, being accumulated in water organisms with a potential impact on aquatic life [4, 9–13] and human health [14–16]. The chemical stability of ICAs and GBCAs is the reason for their documented presence in surface water, groundwater, and even drinking water, particularly near hospitals and locations with CT or MRI scanners. This has been extensively reported in the literature [4, 9, 10, 12, 13, 16–21].

The GREENWATER (reducinG contRast agEnts' rEsiduals iN hospital WAstewaTER) study [22] aimed to: (1) assess the patients' "green sensitivity", measured as their acceptance to have an additional waiting time before leaving the hospital and allow to collect urines containing contrast agents that would otherwise have been discarded in the environment, and (2) investigate the potential reduction of contrast agents' residuals in wastewater based on the first urinary excretion after administration.

## Materials and methods

This prospective monocentric observational study has been registered on Zenodo (https://zenodo.org/record/7800690), and the study protocol has been published in European Radiology Experimental [22]. The GREENWATER study has been approved by the local Ethics Committee (Comitato Etico Ospedale San Raffaele, then Comitato Etico Territoriale Lombardia 1, Milan, Italy; protocol number 53/INT/2022) on May 11, 2022, and emended on September 26, 2023. Enrollment was conducted at the Radiology Unit of IRCCS Policlinico San Donato (San Donato Milanese, Italy), aiming to obtain a

1:1 ratio between patients administered with ICAs and those administered with GBCAs. Patients were enrolled using the informed consent provided by the dedicated researchers, who were available for any questions. No information leaflets or videos were used.

The inclusion criteria comprised outpatients scheduled for contrast-enhanced MRI or CT scans, aged 18 years or older. Exclusion criteria were individuals unable to provide informed consent, those unwilling to extend their post-examination stay to up to 60 min, and patients with recent or ongoing infectious diseases. After having provided their written informed consent, patients proceeded with their scheduled CT or MRI scan without any deviation from usual clinical protocols. The type of contrast agent (molecule and concentration) was chosen by the attending radiologists based on the clinical question, the goal of the examination, and the patient's medical history, particularly in cases of hypersensitivity to the contrast agent molecule. The dose of contrast agent used adhered to clinical standards, and no modifications were made specifically for this study in terms of contrast agent type and dose.

After the examination, the usual observation time of approximately 30 min after contrast agent injection was extended up to 60 min, during which patients were requested to collect their urine into a dedicated canister (Fig. 1) to be delivered to the staff before leaving the hospital.

**Fig. 1** Dedicated canister for urine collections

### Urine collection, storage, and chemical analysis

Collected urine was transferred to the institutional biobank (BioCor, IRCCS Policlinico San Donato, Italy) and processed according to the following operating procedures: measurement of the total volume of urine collected from each patient and centrifugation of 40 mL of urine at 2500 × *g* for 5 min at room temperature, then aliquoted and stored at −80 °C. All chemical analyses for the measurement of iodine or gadolinium concentration were performed at ArsChemica S.R.L. (Caselle Landi, Italy).

Quantification of urinary gadolinium and iodine was performed using a two-step procedure. The first step was microwave digestion in very hard oxidative conditions; the second was the analysis by inductively coupled plasma optical emission spectroscopy. The oxidation was carried out in a closed vessel microwave digester, dissolving 200 µL of urine in 10 mL of aqua regia. The same mineralization pathway was used regardless of the type of contrast agent. The sample was further diluted according to its initial concentration to fall within the calibration range. The quantitation range spanned linearly in the 0.25–10 mg/L concentration range; the calibration plot was calculated through a least squares model with five concentration levels, each one three times replicated. The preferred emission lines of the atomic elements were as follows: 335.047 nm and 310.050 nm for gadolinium and 178.276 nm and 183.038 nm for iodine. The matrix effect was studied with spiked urine samples at 0.5–1 mg/L; for both elements, spectral interferences were always under control. The iodine carry-over effect was reduced almost to zero by adding to the working standards a washing solution of ammonium hydroxide and 0.5% of 2-butanol; in these conditions, recovery is between 70% and 130% of the theoretical amount. This range is widely accepted in analytical works involving a complex biological matrix [23]. The method was devised to be repeatable within 5% [24].

For each sample, recovered iodine or gadolinium was provided in terms of percentage of the injected amount of contrast agent per unit volume of collected urine, representing the potential reduction of contrast residuals in wastewater.

### Statistical analysis

Data for continuous variables are given as median, interquartile range (IQR) and range (minimum–maximum). Data for categorical variables are given as counts and percentages. The acceptance rate was

calculated as the number of patients enrolled out of patients screened, investigating potential differences in age, sex, and contrast type; the Mann–Whitney *U* test was used for age and the $\chi^2$ test for sex and contrast type.

The study protocol initially planned to enroll 400 ICA and 400 GBCA patients (800 in total), limiting the individual analysis to the first 100 and 100, respectively. However, after analyzing these 200 cases, the study protocol was emended to expand the individual analysis to include 200 ICA and 200 GBCA patients, for a total target of 400 patients, to perform multivariable analysis on these individual data. The rule adopted was to have at least ten samples per predictor, based on simulation studies, to ensure a reliable model estimate [25].

For the enrolled patients, the association of patient-specific and imaging protocol covariates with the urinary excretion of contrast agents was investigated with multivariable regression analysis, performed on percentage recovered iodine and gadolinium as a function of injected contrast amount, age, sex, serum creatinine level, estimated glomerular filtration rate (eGFR) using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [26], interval time between contrast administration and urine collection, urine volume, and saline flushing.

Restricted cubic splines were used to model potential nonlinear effects of continuous covariates. To describe the association between the percentage of recovered contrast agent and continuous covariates, we used the difference in the percentage of recovered contrast agent between the third and the first covariate quartile.

## Results

### Sample characteristics

As shown in the study flowchart (Fig. 2), between July 21, 2022, and October 30, 2023, a total of 455 patients scheduled for contrast-enhanced CT or MRI were screened. Of them, 422 (92.7%) accepted to participate in the study. Enrollment occurred during weekdays from 7:30 a.m. to 4:45 p.m., capturing a diverse distribution across all seasons. Among the 33 patients who refused to be enrolled, no significant differences were found for age, sex, and type of contrast in comparison to the 422 enrolled patients ($p \geq 0.168$); the reasons for refusal were: lack of time ($n = 25$, 76%); not being comfortable in using the canister for urine collection ($n = 4$, 12%); distrust towards research projects ($n = 1$, 3%); other reasons ($n = 3$, 9%).

Patients receiving ICAs were 212/422 (50.2%), median 65 years of age (IQR 56–74 years; range 21–93 years), while those receiving GBCAs were 210/422 (49.8%), median 54 years of age (IQR 41–67 years; range 18–96 years) ($p < 0.001$). Of 422 patients, 216 were females

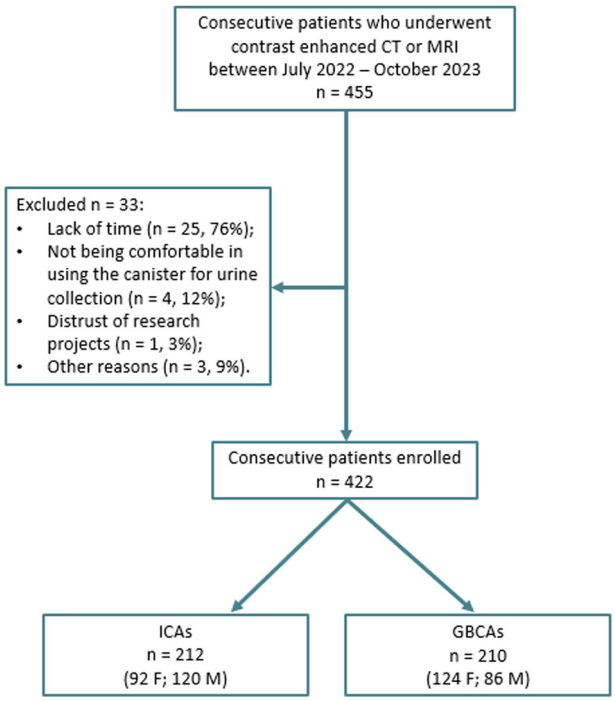



**Fig. 2** Study flowchart

(51.2%; 92 receiving ICAs, 124 GBCAs), while 206 were males (48.8%; 120 receiving ICAs, 86 GBCAs). Iodixanol, Iohexol, Iomeprol, and Iopamidol were the ICAs used, varying in concentration from 320 to 400 mgI/mL, with a median injected volume of 65 mL (IQR 60–80 mL). Gadobenate dimeglumine, Gadobutrol, Gadoterate meglumine and Gadoteridol were the GBCAs used, with a median injected volume of 12 mL (IQR 10–14 mL). Approximately 20 mL of saline flushing was used in 171/212 ICA patients (80.7%) and in 62/210 GBCA patients (29.5%) ($p < 0.001$).

Median serum creatinine level was 0.92 mg/dL (IQR 0.78–1.04 mg/dL) for patients receiving ICAs and 0.83 mg/dL (IQR 0.72–0.94 mg/dL) for patients receiving GBCAs ($p < 0.001$), with an eGFR of 96 mL/min/1.73 m² (IQR 88–107 mL/min/1.73 m²) and 108 mL/min/1.73 m² (IQR 94–123 mL/min/1.73 m²) ($p < 0.001$). Median time interval from contrast administration to urine collection was 25 min (IQR 15–33 min; range 5–70 min) for patients receiving ICAs, while it was 24 min (IQR 17–35 min; 4–132 min) for patients receiving GBCAs ($p = 0.320$). Median collected urine volumes were 124 mL (IQR 79–186 mL; range 4–660 mL) for patients receiving ICAs and 115 mL (IQR 72–166 mL; range 5–1200 mL) for patients receiving GBCAs ($p = 0.269$). The main characteristics of the two patient groups receiving ICAs or GBCAs are reported and compared in Table 1.

**Table 1** Main characteristics of the two patient groups receiving ICAs or GBCAs

| Variable | ICAs ($n = 212$) | GBCAs ($n = 210$) | *p*-value |
|---|---|---|---|
| Sex | 92 F (43%); 120 M (57%) | 124 F (59%); 86 M (41%) | 0.001* |
| Age (years) | 65 [56–74; 21–93] | 54 [41–67], min 18 max 96 | 0.001 |
| Serum creatinine level (mg/dL) | 0.92 [0.78–1.04], min 0.47 max 1.58 | 0.83 [0.72–0.94], min 0.53 max 1.77 | < 0.001 |
| eGFR (mL/min/1.73 $m^2$) | 96 [88–107], min 59 max 158 | 108 [94–123], min 42 max 163 | < 0.001 |
| Contrast agent volume (mL) | 65 [60–80], min 20 max 190 | 12 mL [10–14], min 6 max 26 | 0.001 |
| Saline flushing usage (~20 mL) | 171 (81%) | 62 (30%) | 0.001 |
| Time interval between contrast administration and urine collection (min) | 25 [15–33], min 5 max 70 | 24 [17–35], min 4 max 132 | 0.320 |
| Urine volume (mL) | 124 [79–186], min 4 max 660 | 115 [72–166], min 5 max 1200 | 0.269 |

Data are reported as median [interquartile range; minimum–maximum range]
*ICAs* iodinated contrast agents, *GBCAs* gadolinium-based contrast agents, *F* females, *M* males, *eGFR* estimated glomerular filtration rate
* $\chi^2$ test

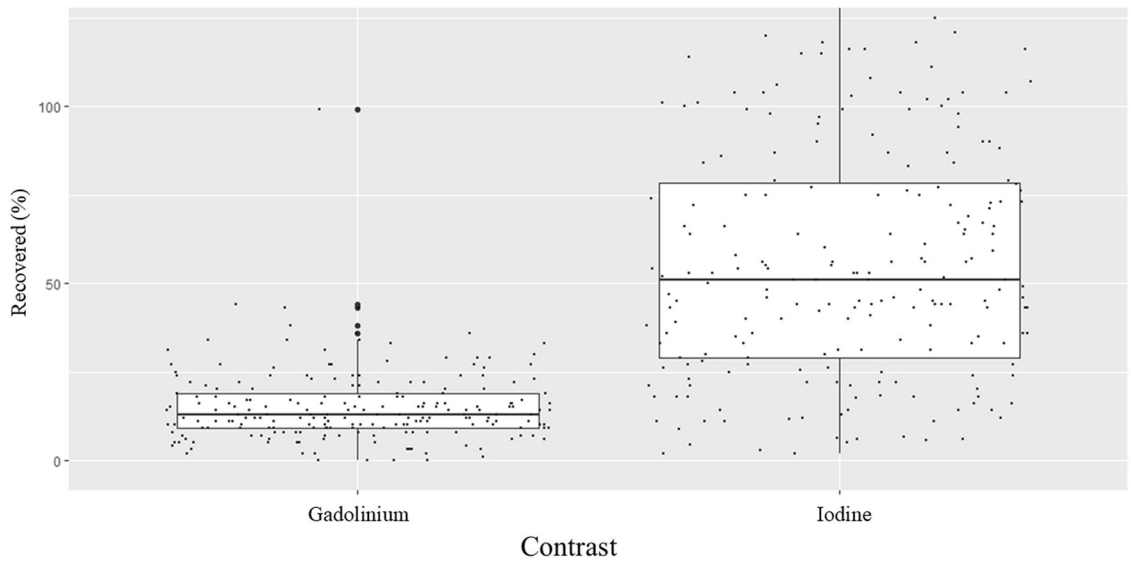



**Fig. 3** Box plot showing the distribution of percentage recovery for ICAs and GBCAs. A high degree of diversity is notable, resulting from multiple factors, including patient age, renal function, hydration status, and the time interval between contrast administration and urine collection, among others. Additionally, individual factors such as heart rate or blood pressure may also have an impact

### Contrast agent recovery

Chemical analysis demonstrated a median recovery of 51.2% (IQR 29.2–77.9%) of administered ICAs and a median of 12.9% (IQR 9.0–19.3%) of administered GBCAs (Fig. 3) ($p < 0.001$).

When exploring the associations between patient characteristics (age, sex, eGFR) and other variables (time interval between contrast administration and urine collection, urine collected volume, contrast injected volume, and saline flushing) with the contrast recovery rate, the following results were obtained: older age, shorter time interval between contrast administration and urine collection, and lower amount of urine collected volume correlated with decreased recovery rates. In particular: age (ICAs, $p = 0.001$; GBCAs, $p = 0.014$); time interval between contrast administration and urine collection ($p < 0.001$ for both); urine collected volume ($p < 0.001$ for both). For ICAs only, lower injected contrast volume ($p = 0.046$) and absence of saline flushing ($p = 0.008$) were associated with higher recovery rates. The contribution of each variable to the outcome is reported in Tables 2 and 3. Scatter plots of recovery rates over the waiting time before urination for ICAs and GBCAs are shown in the Supplementary material.

**Table 2** Multivariable regression results for the associations between patient characteristics (age, sex, eGFR) and other variables (time interval between contrast administration and urine collection, urine collected volume, contrast injected volume, and saline flushing) with the contrast recovery rate for iodinated contrast agents

| Covariate | Comparison | | Difference | Effect on recovery rate (%) | | | *p*-value |
|---|---|---|---|---|---|---|---|
| | | | | Absolute value | Standard error | 95% confidence interval | |
| Age (years) | Q3 = 74 | Q1 = 56 | 18 | −12.30 | 3.30 | −18.80, −5.80 | 0.001 |
| eGFR (mL/min/1.73 $m^2$) | Q3 = 107 | Q1 = 88 | 19 | 3.52 | 2.80 | −2.01, 9.04 | 0.213 |
| Time interval between contrast administration and urine collection (min) | Q3 = 34 | Q1 = 15 | 19 | 21.75 | 3.33 | 15.18, 28.31 | < 0.001 |
| Collected urine volume (mL) | Q3 = 186 | Q1 = 80 | 106 | 20.74 | 3.08 | 14.67, 26.80 | < 0.001 |
| Contrast injected volume (mL) | Q3 = 80 | Q1 = 60 | 20 | −6.37 | 2.74 | −11.76, −0.97 | 0.046 |
| Sex | Females | Males (ref) | NA | −1.68 | 4.46 | −10.48, 7.12 | 0.707 |
| Contrast concentration (mgI/mL) | 320 | 350 (ref) | NA | 5.34 | 5.18 | −4.88, 15.56 | 0.481 |
| | 370 | 350 (ref) | NA | 8.62 | 5.66 | −2.55, 19.77 | |
| | 400 | 350 (ref) | NA | 4.64 | 5.86 | −6.93, 16.19 | |
| Saline flushing | No | Yes (ref) | NA | 13.77 | 5.10 | 3.70, 23.83 | 0.008 |

Age, eGFR, time interval between contrast administration and urine collection, urine collected volume and contrast injected volume were modeled with restricted cubic spline with three knots (placed at 10, 50 and 90 percentiles). Association of these covariates with contrast recovery rate was reported according to the difference in recovery rate between the third and the first quartiles
*Q3* third quartile, *Q1* first quartile, *eGFR* estimated glomerular filtration rate

**Table 3** Multivariable regression results for the associations between patient characteristics (age, sex, eGFR) and other variables (time interval between contrast administration and urine collection, urine collected volume, contrast injected volume, and saline flushing) with the contrast recovery rate for gadolinium-based contrast agents

| Covariate | Comparison | | Difference | Effect on recovery rate (%) | | | *p*-value |
|---|---|---|---|---|---|---|---|
| | | | | Absolute value | Standard error | 95% confidence interval | |
| Age (years) | Q3 = 66 | Q1 = 41 | 25 | −3.50 | 1.21 | −5.89, −1.11 | 0.014 |
| eGFR (mL/min/1.73 $m^2$) | Q3 = 123 | Q1 = 94 | 29 | 0.62 | 1.38 | −2.10, 3.34 | 0.200 |
| Time interval between contrast administration and urine collection (min) | Q3 = 35 | Q1 = 17 | 18 | 4.63 | 0.94 | 2.77, 6.49 | < 0.001 |
| Collected urine volume (mL) | Q3 = 169 | Q1 = 72 | 97 | 4.31 | 0.87 | 2.60, 6.03 | < 0.001 |
| Contrast injected volume (mL) | Q3 = 14 | Q1 = 10 | 4 | −1.60 | 0.89 | −3.35, 0.15 | 0.198 |
| Sex | Females | Males (ref) | NA | −1.84 | 1.40 | −4.60, 0.91 | 0.188 |
| Saline flushing | No | Yes (ref) | NA | −0.27 | 1.20 | −2.63, 2.088 | 0.820 |

Age, eGFR, time interval between contrast administration and urine collection, urine collected volume and contrast injected volume were modeled with restricted cubic spline with three knots (placed at 10, 50 and 90 percentiles). Association of these covariates with contrast recovery rate was reported according to the difference in recovery rate between the third and the first quartiles
*Q3* third quartile, *Q1* first quartile, *eGFR* estimated glomerular filtration rate

## Discussion

This study showed two main results. First, of 455 patients screened for prolonged stay in the radiology department for up to 60 min to allow urine collection after contrast-enhanced CT or MRI, 422 (92.7%) accepted the proposal. Second, a median recovery rate of 51.2% for ICAs and 12.9% for GBCAs was observed.

Considering the rapid renal excretion of ICAs and GBCAs, as well as the results of previous studies investigating the compliance of patients with different urine collection methods [13], this is—to the best of our knowledge—the only study targeting the first urinary excretion after contrast-enhanced CT or MRI.

The patient compliance (more than nine out of every ten patients) was certainly higher than that expected when the protocol was planned (30%), which considered time constraints thought to be relevant for a patient population coming from a large metropolitan area [22]. This result

plays in favor of a high "green awareness" among patients, showing a strong willingness to cooperate with healthcare personnel for environment protection, recently even more relevant [27]. No significant differences in age, sex, and type of administered contrast were found between the 33 patients who refused to be enrolled and the 422 who accepted. The main reason for refusal was the lack of time (25/33, 76%), not easily counteracted, while discomfort in using the canister for urine collection (4/33, 12%) could be overcome by providing dedicated devices in the radiology bathrooms.

The significantly younger median age of patients administered with GBCAs (54 years) compared to those administered with ICAs (65 years) was relatively expected due to the different clinical conditions of patients undergoing contrast-enhanced CT or MRI. This aligns with the observation that ICAs tend to be administered to an older demographic, reflecting the concerns with renal safety among older patients, as noted in the study by Gorelik et al [28]. Meanwhile, patients receiving GBCAs are generally younger, as reported by McDonald et al [29] in a single-center retrospective study of 281,945 injections, finding a median age of 55 years (IQR, 40–67 years). The males-to-females ratio of patients enrolled was about 1:1, but a higher prevalence of females in GBCA-enhanced exams (59.0%) than in ICA-enhanced exams (43.4%) was observed, probably due to the main cardiovascular focus of our center, implying a higher prevalence of males for CT scans.

The observed median recovery rates were distant from 100% for both ICAs and GBCAs, as expected. In fact, the contrast excretion in the first hour after administration is known to be limited by the physiological kidney function [30]. Interestingly, ICAs showed a significantly higher median recovery rate (51.2%) than that of GBCAs (12.9%). The distinct chemical properties and pharmacokinetics of ICAs compared to GBCAs may have played a role. ICAs, due to their relatively larger molecular-sized agents, are less efficiently reabsorbed by renal tubules, leading to a higher excretion rate [31]. Conversely, GBCAs have different molecular structures and excretion patterns compared to ICAs, and these differences might explain the lower recovery rates observed in clinical settings [32].

Multivariable analysis showed that a number of other factors were associated with the recovery rates of ICAs and GBCAs, to be added to the different chemico-physical characteristics of contrast agents discussed above.

The observed median time of 25 min for ICAs and 24 min for GBCAs from contrast injection to urination, despite asking patients to stay up to 60 min, can be explained by several factors. Many patients may have felt the need to urinate sooner, as an effect of hydration status and physiological response to the contrast agent. Moreover, some patients might have preferred to urinate as soon as they felt comfortable doing so, rather than waiting the full 60 min. Additionally, some patients may have experienced a psychological state following the anxiety or agitation associated with the diagnostic exam: a sense of relaxation prompted them to leave the hospital as soon as possible. These waiting times are due to the natural variation in individual patients and the clinical workflow. In any case, patients could not be compelled to hold their urine beyond their capacity, and they had the discretion to wait up to 60 min. This is evidenced by the patient who urinated at 4 min after GBCA administration and another one who waited up to 132 min after GBCA administration before urinating.

Regarding ICAs, age and injected contrast volume were negatively associated with recovery rate with an effect equal to −12.30% and −6.37%, respectively. While the role of age was expected, taking into account the well-known decrease of renal function with age [30], we interpret the effect of contrast injected volume as the amount of contrast to be excreted in a short time interval (up to 60 min); however, we note that the $p$-value was only borderline significant ($p = 0.046$) [33]. Conversely, a positive association with recovery rate was found for time interval between contrast administration and urine collection (+ 21.75%), collected urine volume (+ 20.74%), and no usage of saline flushing (+ 13.77%). While the positive association of the first two covariates with recovery rate is expected (as more time allows for more urine to be excreted), the negative association of saline flushing with recovery rate lacks a clear explanation and warrants further investigation. It is noteworthy that this effect was not observed for GBCAs.

Regarding GBCAs, we observed, similarly to ICAs, a negative association with recovery rate by age, apparently less impacting (−3.50%) compared to ICAs (−12.30%). In fact, if these absolute values are referred to the recovery rates of the two types of contrast agents, similar proportions are obtained: 27.1% (3.5/12.9) for GBCAs and 24.0% (12.3/51.2) for ICAs. On the other hand, the limited median GBCA injected volume (12 mL), with only a 4-mL IQR to be compared with 65 mL and 20-mL IQR for ICAs, did not act as a covariate significantly associated with GBCAs recovery rate. The larger median volume and IQR of administered ICAs allowed the association with recovery rate to be observed at multivariable analysis. Finally, similarly for ICAs, a positive association with GBCAs recovery rate was found for time interval between contrast administration and urine collection (+ 4.63%) and collected urine volume (+ 4.31%). Of course, due to the much lower recovery rate of GBCAs, the absolute effects of those covariates were lower, even though the relative proportion was not so distant. The use of saline

flushing (limited to only 30% of patients receiving GBCAs) was associated with a small effect (−0.27%) on the recovery rate, possibly due to the better kidney function of patients receiving GBCAs compared to patients receiving ICAs (median eGFR 108 versus 96 mL/min/1.73 m², respectively) who were also younger (54 versus 65 years, respectively). Moreover, the lack of significance for eGFR in the multivariate analysis for both contrast agents could result from interactions with other covariates such as age and time interval between contrast administration and urine collection might have more direct or pronounced effects on the CAs recovery rates, overshadowing the influence of kidney function.

This study has limitations. First, we asked the patients to prolong the hospital stay up to 60 min only; therefore, we do not know what recovery rate could have been obtained by asking them to wait more. Of course, this requested longer hospital stay could have impacted on the enrollment rate. Second, patients collected the first urine during the hospital stay after injection (the median time was about 25 min for both contrast agents): we did not ask for a specific minimum waiting time before urination. This is an option that could be explored in further studies. Third, a word of caution is necessary regarding potential measurement errors related to the analytical methods used, which may have led to an overestimation of the recovery rate. Specifically, the observed 51% recovery rate for ICAs seems to be higher than expected, considering their estimated elimination half-lives of approximately 2 h [6]. Future studies are needed to provide further insights into methods for estimating contrast agent recovery from both inpatients' and outpatients' urine in clinical practice. Fourth, in terms of the generalizability of results, we should note that the study was conducted at the IRCCS Research Hospital Policlinico San Donato, taking advantage of a specific context that probably increased the patients' acceptance to participate. On the one hand, we emphasize the role of two researchers (M.Z. and L.A.) who were highly committed to patient enrollment. On the other hand, the hospital's location in a major European metropolitan area may have contributed to a strong attitude toward environmental awareness. In fact, the study was conducted in the Po Valley—one of the most polluted areas in Europe (https://atmosphere.copernicus.eu/extreme-episode-particulate-matter-air-pollution-across-italys-po-valley). Patient willingness to participate in protocols like this could vary based on demographic, cultural, and local factors. We defined patients' "green sensitivity" as their willingness to extend their hospital stay to participate in an environmentally sustainable practice research study. While it is true that we did not administer a dedicated questionnaire to directly assess the patients' environmental attitudes or motivations, their high compliance rate (92.7%) in agreeing to participate in a sustainability study with no direct clinical benefit for the patients (e.g., no urine exams or any other benefit) indirectly suggests a significant level of "environmental awareness and willingness to contribute to sustainability efforts". We acknowledge the absence of a direct measure of patients' environmental attitudes or motivations, which should be addressed in future research by integrating a specific questionnaire to assess these factors.

Early treatment of hospital wastewater could extend potential benefits in the overall sustainability of contrast agents, also improving economic efficiency and global resource management through recycling iodine and gadolinium, especially in light of the scarcity of ICAs [34–36] and gadolinium reserves and the environmental footprint of GBCAs production [37, 38]. Looking forward, the disparities in recovery rates and the significance of various covariates underscore the need for innovative approaches to the management of contrast agents' waste. Recycling contrast agents, while challenging, emerges as a compelling prospect. However, this requires careful consideration of the costs associated with recycling processes, the ownership of the recycled material, and the implications for industrial practices. Developing models for recycling contrast agents used in hospital settings, similar to existing models for managing other pharmaceutical wastes in sewage systems, such as those used in Nuclear Medicine departments with radiopharmaceutical tracers, could provide a sustainable path forward. These models must account for the financial implications of recycling processes, balancing environmental benefits against operational costs.

In conclusion, we showed that 93% of patients asked to prolong their stay in the radiology department up to 60 min to allow urine collection after contrast-enhanced CT or MRI accepted the proposal. In addition, a median potential recovery rate of 51% for ICAs and of 13% for GBCAs was observed. As the healthcare services continue to address their environmental responsibilities, the insights presented in this article provide guidance for future research and innovations focused on minimizing the ecological footprint of diagnostic imaging.

**Abbreviations**

| | |
|---|---|
| eGFR | Estimated glomerular filtration rate |
| GBCAs | Gadolinium-based contrast agents |
| ICAs | Iodinated contrast agents |
| IQR | Interquartile range |

## Supplementary information

The online version contains supplementary material available at https://doi.org/10.1007/s00330-024-11150-3.

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## Compliance with ethical standards

**Guarantor**
The scientific guarantor of this publication is F.S.

**Conflict of interest**
The authors of this manuscript declare relationships with the following companies: F.S. has received research grants from Bracco, Bayer, GE. F.P. is an employee of ArsChemica S.R.L. The other authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

**Statistics and biometry**
Professor Federico Ambrogi, Full Professor of Medical Statistcs at the University of Milan, kindly provided statistical advice for this manuscript.

**Informed consent**
Written informed consent was obtained from all subjects enrolled in this study.

**Ethical approval**
The GREENWATER study has been approved by the local Ethics committee (Comitato Etico Ospedale San Raffaele, then Comitato Etico Territoriale Lombardia 1, Milan, Italy; protocol number 53/INT/2022) on May 11, 2022, and emended on September 26, 2023.

**Study subjects or cohorts overlap**
None.

**Methodology**

- Prospective
- Cross-sectional study/observational
- Performed at one institution

**Author details**
[1]Radiology Unit, IRCCS Policlinico San Donato, San Donato Milanese, Italy. [2]Laboratory of Biostatistics and Data Management, Scientific Directorate, IRCCS Policlinico San Donato, San Donato Milanese, Italy. [3]Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy. [4]Postgraduation School in Radiodiagnostics, Università degli Studi di Milano, Milan, Italy. [5]Biobank BioCor, IRCCS Policlinico San Donato, San Donato Milanese, Italy. [6]Department of Radiology, ASST Santi Paolo e Carlo, Milan, Italy. [7]ArsChemica S.R.L., Caselle Landi, Italy. [8]Department of Biomedical Sciences for Health, Università degli Studi di Milano, Milan, Italy.

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