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Table 1
Project type, population sizes and protocol prescriptions.

Project	Tracer	Sample size (n)	Uptake time	Dose (min-max)
A	FDG	5	Dual (1–3 h)	4 MBq/kg (200–400 MBq)
B	FDG	15	Dual (1–3 h)	4 MBq/kg (200–400 MBq)
	NaF	10	45 min	200 MBq
C	FDG	147	60 min	4 MBq/kg (200–400 MBq)
	FDG	3	Dual (1–3 h)	4 MBq/kg (200–400 MBq)
D	FDG	1	Dual (45–60 min)	4 MBq/kg (200–400 MBq)
E	FDG	11	60 min	4 MBq/kg (200–400 MBq)
	NaF	9	60 min	2 MBq/kg

FDG=2-deoxy-2-fluoro-D-glucose, NaF=sodium fluoride.

projects comprising a total of 201 patient studies (222 scans) and both [¹⁸F]-FDG-PET/CT of various protocols (single and dual time point scans) and [¹⁸F]-NaF-PET/CT for comparison. The projects and protocol details are listed in Table 1. No ethical approval was required for this type of study.

Although the department has no EU accreditation, all procedures followed the institutional standards mainly based on the European Association of Nuclear Medicine guidelines.^[27] As per routine, basic patient information was registered in individual handwritten record forms during patient preparation before tracer injection with the Intego system (MEDRAD, Inc.). Output prints of administered dose readings were included in the patient records. The same data were then typed for DICOM metadata entries at the scanner console before each scan, wherein acquisition commencement times were further noted in the patient record. Data and image quality were not checked by a core laboratory, whereas double reading was employed in diagnostic reporting.

2.1. Data extraction

For the patient studies included in this work, data registrations in the handwritten records were collected regarding basic patient data (weight, height, measured blood sugar level) as well as scan-related parameters: tracer type and dose, injection time (T_{inj}), and scan time (T). The corresponding typed DICOM metadata entries were looked up in the image files for comparison. Additional recording of variations from protocol prescriptions (Table 1) was carried out where applicable. In subsequent accounts of data entry inconsistencies, any whole number deviations were listed. Those relative to the protocol were further reworked, taking into consideration our institution’s guideline-based^[28] standard practical allowances of $\pm 10\%$ in dose and ± 5 minutes in tracer uptake time (ΔT).

2.2. Quantitation analysis

The impact of differing data entries used in quantitative analyses was evaluated in relation to common SUV calculations. SUVs were given as the tissue activity concentration, $C(T)$ [kBq/mL], normalized by a factor, Ω , which accounts for distribution volume, V , and injected dose, D_{inj} [MBq], corrected by a decay factor $f = e^{-\lambda \cdot t}$ with decay constant λ :

$$SUV = C(T) \cdot \Omega = C(T) \cdot \frac{V}{D_{inj} \cdot f} \quad (1)$$

where for the FDG distribution volume, patient body weight (BW) is mostly used, $V = BW$ [kg], or alternatively, the body surface area (BSA), calculated as $V = BSA_1$ [m^2]

BW [kg]^{0.425} · H [cm]^{0.725} · 0.007184 or $V = BSA_2$ [m^2] = $100 \sqrt{BW[kg] \cdot H[cm]} / 3600$,^[29] which includes patient height, H . From Eq. (1), variance estimates in calculated SUVs between deviating parameter entries (a, b) were found in terms of ratios:

$$\begin{aligned} \frac{SUV_a}{SUV_b} &= \frac{C(T_a) \cdot \Omega_a}{C(T_b) \cdot \Omega_b} \\ &= \frac{C_a}{C_b} \cdot \frac{V_a}{V_b} \cdot \frac{D_{inj,b}}{D_{inj,a}} \cdot \frac{e^{-\lambda \cdot \Delta T_b}}{e^{-\lambda \cdot \Delta T_a}} \\ &= U_C \cdot R_V \cdot R_{Dose} \cdot R_{\Delta T} \end{aligned} \quad (2)$$

which for a given time point scan (uptake ratio $U_C = 1$) amount to separate contributing factors of parameter ratios between discrepant entries of distribution volume, R_V , dose, R_{Dose} , and uptake time, $R_{\Delta T}$, respectively. In variations from protocol target levels, expected deviant concentrations ($U_C \neq 1$) would further impact SUV variance.

Differences in corresponding data registrations were graphically assessed by Bland-Altman plots. As neither raw nor log-transformed data were generally normally distributed, statistical tests for the null hypothesis were performed where relevant with 2-sided Wilcoxon signed-rank matched-pairs tests of entry differences and log ratios of SUV factors. Here, statistical significance was inferred at P value $< .05$. All data analyses were carried out in MATLAB 9.0 (MathWorks, Inc.).

3. Results

Three delayed time scans in dual point FDG were not performed for unspecified reasons and were disregarded in the listings. No missing data were otherwise found in the DICOM files, but some scan time entries were omitted in patient records (12/222 $\approx 5.4\%$). The error listings also excluded the often noncompulsory blood sugar measurements. Total accounts showed errors to be predominantly small, but with a few large discrepancies. In terms of whole number deviation, 41.8% (79/189, excluding missing entries) of the patient studies showed inconsistencies between patient records and DICOM entries. Moreover, 98.0% (197/201) differed from protocol targets, 50.7% (102/201) of which were noncompliant with allowed variations (dose $\pm 10\%$, $\Delta T \pm 5$ min). Manual misregistrations occurred to a lesser extent in routine FDG–60minutes (54/150 $\approx 36.0\%$) than in FDG–dual time (11/20 $\approx 55.0\%$), NaF–45 minutes (8/10 $\approx 80.0\%$) or NaF–60minutes (6/9 $\approx 66.7\%$) protocol studies. Meanwhile, the missing data entries only appeared in FDG studies.

Of individual entries, tracer dose and scan times were most prone to registration disparity. This was largely seen independently of study and tracer type (Figure 1). Differences tested

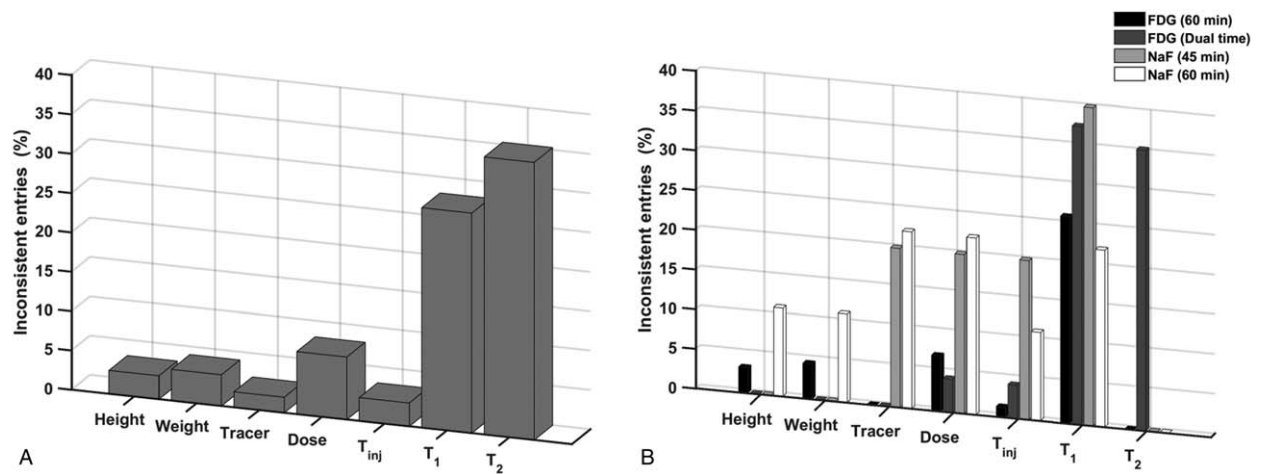


Figure 1. Bar diagrams of percentage inconsistent data registrations (excl. missing entries) between patient records and DICOM metadata for all studies (A) and individual study types (B) in entries of patient height and weight, tracer type and dose, tracer injection time (T_{inj}) as well as early (T_1) and late (T_2) scan times.

statistically among all entries or between deviating entries alone yielded the same results. They showed dose discrepancies to be generally significant, whereas uptake times were only so relative to protocol prescriptions ($P < .001$). DICOM metadata only differed significantly from patient records in weight by (mean \pm SD) 25.4 ± 40.3 kg ($P \approx .02$) and in dose by 4.1 ± 7.7 MBq ($P \approx .02$). Differences for all recorded data entries versus their mean are shown in Figure 2.

Discordances related to tracer type were not only more frequent but also generally larger in NaF studies than in FDG studies. Patient record and DICOM entry differences in FDG studies averaged in height: 36.4 ± 78.9 cm ($P \approx .44$); weight: 28.7 ± 42.3 kg ($P \approx .03$); dose: 3.3 ± 7.7 MBq ($P \approx .10$); T_{inj} : $-1.0 \pm$

3.5 minutes ($P = 1.0$); early scan time T_1 : -1.1 ± 8.9 minutes ($P \approx .93$); delayed scan time T_2 : -0.3 ± 5.3 minutes ($P \approx .78$); and related uptake times ΔT_1 : -1.3 ± 9.1 minutes ($P \approx .82$); ΔT_2 : -0.7 ± 5.2 minutes ($P = 1.0$). Corresponding entries in NaF studies had single errors in height and weight and deviations in dose: 6.5 ± 8.4 MBq ($P \approx .13$); T_{inj} : -4.7 ± 4.6 minutes ($P = .25$); T_1 : -2.3 ± 3.4 minutes ($P \approx .03$); and ΔT_1 : 0.0 ± 5.8 minutes ($P = 1.0$).

Departures from protocol prescriptions not only contributed predominantly to disparity counts but were typically also most significant. Figure 3 details the totals and magnitudes of the tallied inconsistencies. These were significant for dose and ΔT_1 ($P < .001$), but not ΔT_2 ($P \approx .45$). Again, overall smaller practical

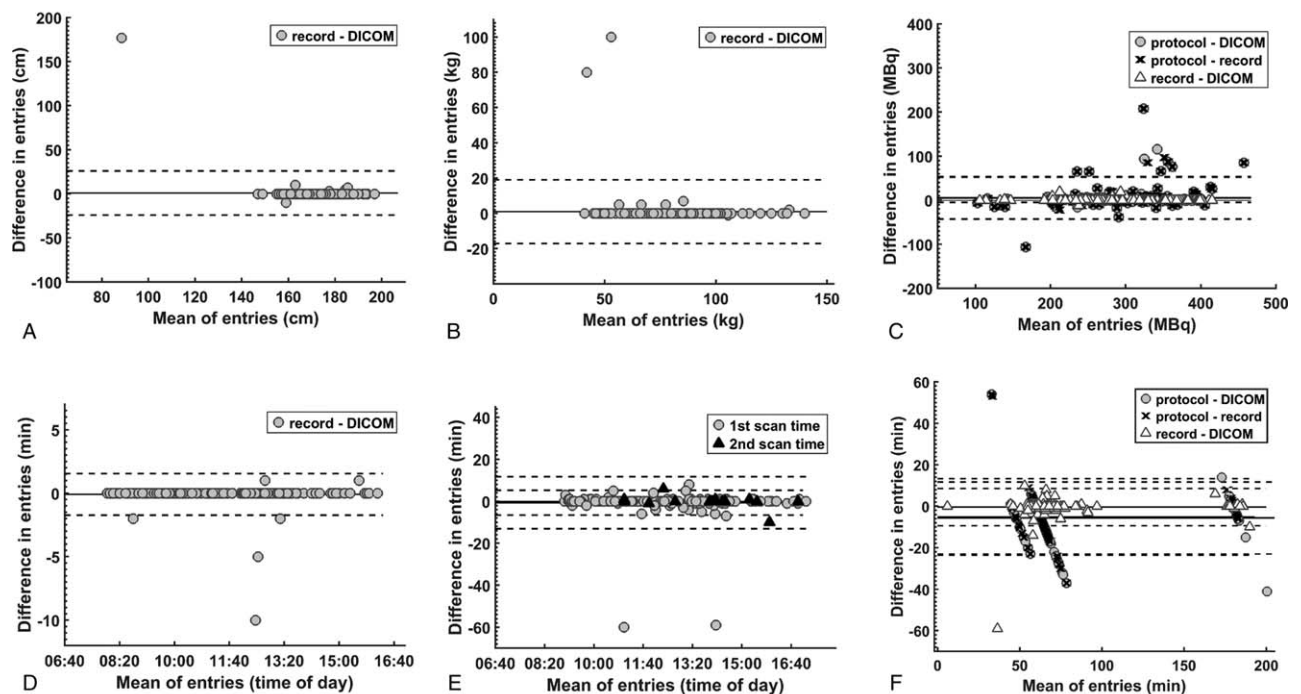


Figure 2. Bland-Altman plots of differences in all registered patient height (A), weight (B), tracer dose (C), injection time (D), scan times (E), and uptake times (F) between data entries in the patient records, image DICOM metadata, and study protocol prescriptions, respectively. Solid and dashed lines indicate mean \pm 2SD.

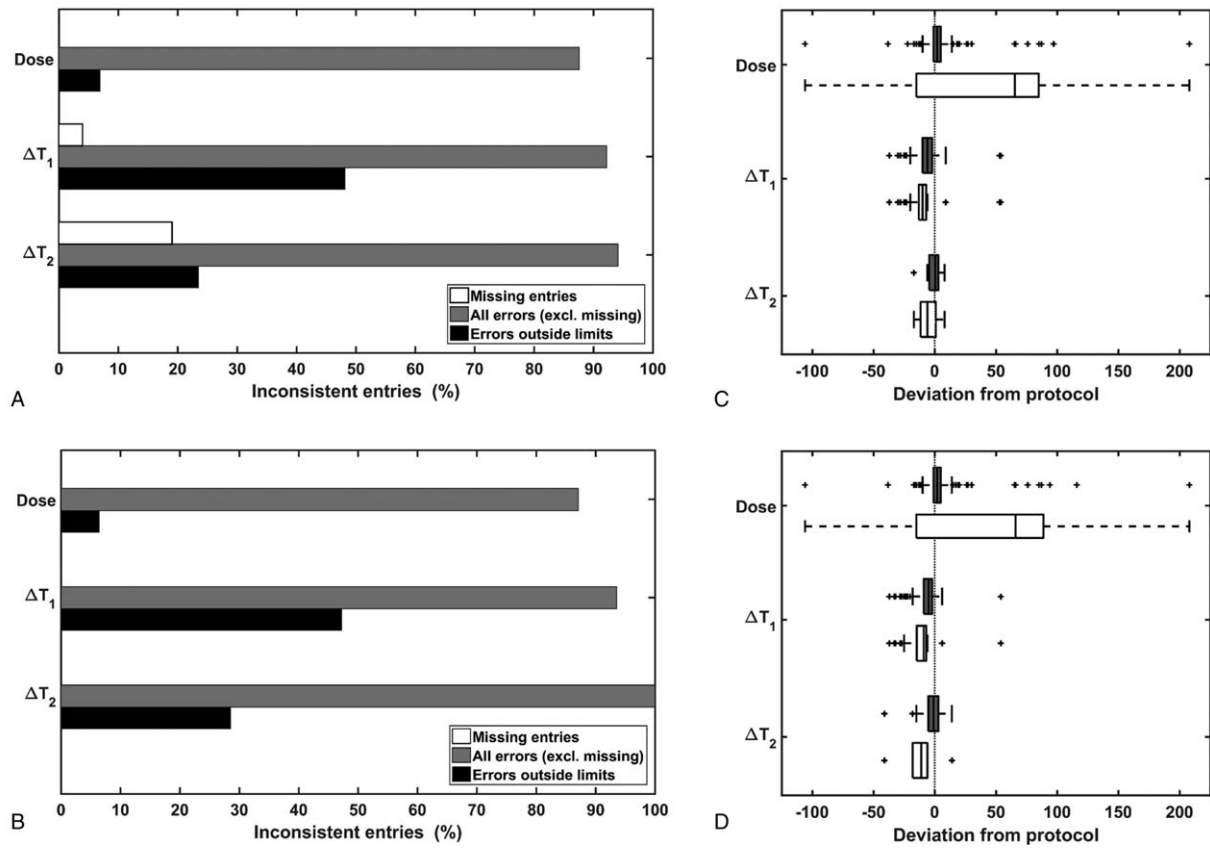


Figure 3. Number of entries noncompliant with protocol prescriptions shown as bar charts for patient record (A) and DICOM metadata (B) registrations, with and without deviations within allowed limits. Corresponding boxplots (C, D) of discrepancies, including (gray) and excluding (white) allowed deviations, display the range of variation in tracer dose [MBq] and uptake times [minutes] at early (ΔT_1) and late (ΔT_2) scans.

variations were seen for FDG studies than for NaF studies with deviations in dose: 5.6 ± 17.9 MBq ($P < .001$); ΔT_1 : -6.1 ± 9.1 minutes ($P < .001$); ΔT_2 : -2.1 ± 9.2 min ($P \approx .45$); and dose: 7.6 ± 58.5 MBq ($P \approx .22$); ΔT_1 : -9.4 ± 8.7 minutes ($P < .001$), respectively.

3.1. Quantitative impact

Variations in SUV normalization factors, Ω , calculated for deviant data entries can be seen in Figure 4A and B. For BW-based indices, SUV (BW), discrepant patient record and DICOM entries did not overall translate into significant SUV deviations ($P \approx .4$). There, only error contributions R_{Weight} and R_{Dose} signified a significant 0.72 ± 0.43 ($P \approx .02$) and 1.02 ± 0.03 ($P \approx .02$) times change in SUV, respectively.

Inconsistencies with the prescribed protocol were found to be generally significant ($P < .001$). This only applied for early T_1 but not late T_2 time scans when tested separately. Such differences in DICOM (*dic*) and protocol (*prot*) entry SUV levels were by a factor $R_{All} = \Omega_{dic} / \Omega_{prot}$ of 1.10 ± 0.25 ($P < .001$) for T_1 and 1.03 ± 0.10 ($P \approx .12$) for T_2 scans. Similar differences were seen for patient record entries (*rec*) by a factor $R_{All} = \Omega_{rec} / \Omega_{prot}$ of 1.10 ± 0.25 ($P < .001$) and 1.01 ± 0.06 ($P \approx .43$). In the extraction of compliance variation, clocked scan time DICOM entries were considered more reliable than those in patient records and inversely so for all other recordings yielding the Ω variances seen in Figure 4C. Mistyped data in DICOM files did not appear to confound actual compliance-related variance, as SUV_{dic} variation

overall reflected fluctuations in protocol adherence. Proportional differences were, on the whole, otherwise similar to those of separate FDG studies (Table 2).

For BSA-based measures, height and weight misregistrations seen in about 6.5% (13/201) of all studies amounted to concomitantly significant BSA and SUV (BSA) deviations (Figure 4D). These errors gave DICOM-based $SUV(BSA_1)$ levels an average 0.79 ± 0.37 times those with patient record entries ($P \approx .01$) and a corresponding factor of 0.78 ± 0.38 ($P \approx .003$) in $SUV(BSA_2)$. Although the deviations pertaining to FDG studies remained significant (BSA_1 : 0.75 ± 0.40 , $P \approx .02$; BSA_2 : 0.74 ± 0.41 , $P \approx .01$), those in NaF studies generally did not (BSA_1 : 0.98 ± 0.03 , $P = .5$; BSA_2 : 0.98 ± 0.02 , $P = .5$). Between all corresponding DICOM and patient record entries, SUV (BSA) discordances overall, as well as among deviating entries only, were not significant ($P \approx .8$) in this sample.

4. Discussion

The present study confirms that data registration errors are somewhat common, as implied in the literature.^[5,25] Furthermore, the high frequency of protocol nonconformity seen is also in line with other studies.^[25,26,30,31] However, we found manual misregistrations to be predominantly minor, with few significant discrepancies. Although no similar studies have been found to verify the generality of this finding, there is support in the literature. For instance, 0.8% to 7.4% of weight entries in patient reports deviated from actual values by $> \pm 10\%$ in one study.^[20]

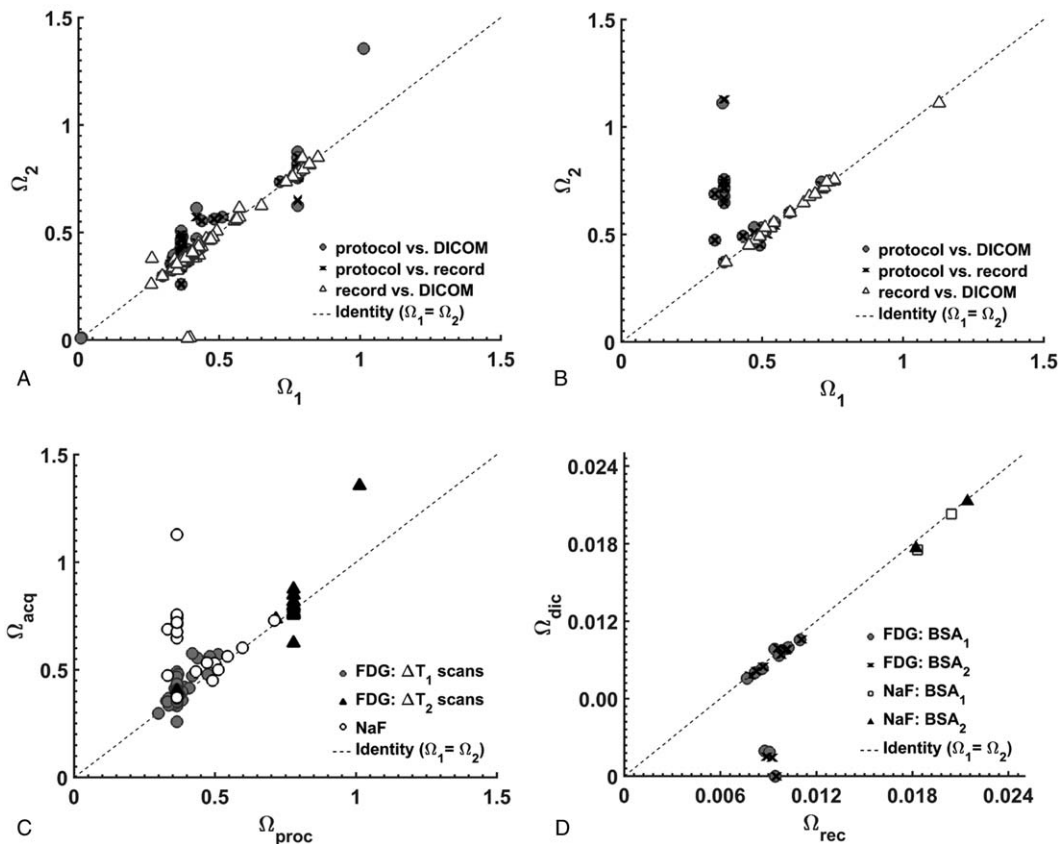


Figure 4. Variation in normalization factors, Ω , for SUV (BW) calculations with deviating parameters in FDG (A) and NaF (B) studies as well as (C) between entries most representative of true levels in acquired scans (Ω_{acq}) vs. protocol targets (Ω_{proc}), indicating parameter compliance variance. Similar plots for SUV (BSA) between discrepant patient record (Ω_{rec}) and DICOM (Ω_{dic}) entries of height and/or weight (D). BSA=body surface area, FDG=2-deoxy-2-fluoro-D-glucose, NaF=sodium fluoride, SUV=standardized uptake value.

In the present study, this level of error was seen in 1.0% of the deviations between DICOM entries and measured weights noted in patient records. In contrast, mistyped dose in DICOM entries appears widely undocumented. The 8.0% occurrence we observed (all errors were <10%) was also low relative to reported weight error rates. Although manual scan time misrecordings, having the highest observed rate, also lack reporting, one study did note misregistered times between transmittal forms and DICOM data from 11 sites, giving 31.4% discrepant uptake times (>1 min, max. difference 1 hour 4

minutes).^[25] In our listings, the analogous error count would total 10.5% (max. difference 59 minutes).

Our single-center error recordings thus appear generally lower than reported levels. Still, comparison with reports is limited and primarily involves intersite rather than intrasite accounts. Protocol adherence evaluation is likewise primarily reported in cross-center longitudinal variability^[22,25,26] and test-retest repeatability^[21,30] studies. These have typically small per-site sample sizes ($n \lesssim 20$). No direct account is thus given of in-center compliance variation across any study population, as is provided here.

Table 2
SUV (BW) parameter error ratios, R , between listed entries individually and collectively.

Study type	Ratio	R_{Weight}	R_{Dose}	$R_{\Delta T1}$	$R_{\Delta T2}$	R_{All}
FDG	$\frac{SUV_{dic}}{SUV_{rec}}$	$0.68 \pm 0.45^*$ (0.02–1.01)	1.01 ± 0.03 (0.95–1.07)	1.01 ± 0.07 (0.95–1.45)	1.00 ± 0.03 (0.96–1.07)	0.98 ± 0.18 (0.02–1.45)
	$\frac{SUV_{rec}}{SUV_{prot}}$	—	$1.02 \pm 0.05^\dagger$ (0.88–1.32)	$1.04 \pm 0.06^\dagger$ (0.71–1.26)	1.01 ± 0.04 (0.95–1.11)	$1.05 \pm 0.08^\dagger$ (0.71–1.36)
	$\frac{SUV_{dic}}{SUV_{prot}}$	—	$1.02 \pm 0.06^\dagger$ (0.88–1.41)	$1.04 \pm 0.05^\dagger$ (0.71–1.26)	1.02 ± 0.08 (0.92–1.30)	$1.05 \pm 0.08^\dagger$ (0.71–1.46)
NaF	$\frac{SUV_{dic}}{SUV_{rec}}$	0.99 ± 0.00 (—)	1.03 ± 0.04 (1.01–1.09)	1.00 ± 0.04 (0.94–1.05)	—	1.01 ± 0.02 (0.99–1.05)
	$\frac{SUV_{rec}}{SUV_{prot}}$	—	1.03 ± 0.28 (0.52–1.95)	$1.06 \pm 0.06^\dagger$ (0.98–1.17)	—	$1.55 \pm 0.60^\dagger$ (0.92–3.09)
	$\frac{SUV_{dic}}{SUV_{prot}}$	—	1.03 ± 0.27 (0.52–1.95)	$1.06 \pm 0.06^\dagger$ (0.98–1.17)	—	$1.56 \pm 0.59^\dagger$ (0.92–3.09)

BW=body weight, FDG=2-deoxy-2-fluoro-D-glucose, NaF=sodium fluoride, SUV=standardized uptake value. Numbers are mean \pm SD (range) for SUV ratios between patient record registrations (SUV_{rec}), DICOM entries (SUV_{dic}), and protocol prescriptions (SUV_{prot}). Statistical significance.

* $P < .05$.

† $P < .003$.

Our finding from our audit of practical procedures over a year that non-compliance was the most generally significant of errors is in line with reports of low protocol adherence^[25] and high practical variability.^[30] Especially uptake time variation is acknowledged as an enduring problem in oncological PET,^[32] with considerable deviations noted in one single-center study.^[30] Yet, our account of a 52.7% and 71.4% compliance (within $\Delta T \pm 5$ minutes) for early and late scans, respectively, was comparatively better than reported multisite compliances of 31.4%^[25] and 35.0%^[26] (both for $\Delta T \pm 5$ minutes). Higher-dose compliance of 93.0% (within dose $\pm 10\%$) was also seen, compared to a reported 79% to 86% for FDG dose $\pm 25\%$ and [¹⁸F]-deoxythymidine (FLT) dose $\pm 10\%$.^[22]

The above might suggest a perhaps expected higher variability in multicenter than in single-center settings. It also would imply highly variable intracenter error rates, which in some sites can be greater than what we found. The generally seen higher compliance in dose rather than uptake times is likely because of a reduction in error resulting from widely replacing manual with automated tracer administration.^[33] However, retrospective compliance evaluation like this relies on correct parameter recordings without validation against true values. A prospective study would better assess this.

As SUV calculation with commercial analysis software generally uses parameters extracted from DICOM metadata, we evaluated variation in DICOM based SUV_{dic} against patient record-based SUV_{rec} as a ground truth proxy. Although entry errors caused largely insignificant SUV variability, instances of a -98% to 45% factor different SUV_{dic} can be consequential in clinical applications. Variability naturally becomes more broadly significant in measures additionally reliant on height entries, as seen in SUV (BSA) as an example. Moreover, the translation of noncompliant dose and ΔT_1 into overall significant SUV error factors can compromise comparability. The generally greatest ΔT_1 error contribution is also reported by others.^[21]

Thus frequent data entry inconsistencies can indeed cause sizeable errors in quantitative analyses. This warrants parameter checks as part of data processing. Overlooked errors can affect patient management and SUV variability weakens the power of clinical trials.^[34] Data loss from lacking parameter registration further reduces statistical power. Whereas missing DICOM entries were not among our findings, a 5.4% to 32% loss has been reported.^[20,26,31] Also, noncompliance has caused high data decimation in multicenter settings.^[21,25,26] Our observations substantiate a general significance of such parameter inconsistency. Hence, protocol standardization alone does not suffice for reliable translational trials. Intracenter quantification variability by human error in data registration and compliance is an underlying limiting factor to intercenter harmonization. It must be integrally assessed for any such case. A greater transparency regarding reports of such variances is equally called for.

This first evaluation hence revealed a potentially significant clinical impact of data entry inconsistency and particularly non-conform practices. Moving forward, ongoing work-flow optimization beyond staff training is therefore needed. Besides persistent emphasis on correct data registration generally, data checks, for example, peer-based, should be worked into practices. Greater awareness of protocol adherence is imperative. Special reminders and attention are required for less common protocols, as errors were often linked to nonroutine practices, independent of the time of day, wherein especially changed ΔT targets (NaF vs. FDG studies) increased SUV variability. Prospective quality

control^[21] and developments to automate procedures can also promote reproducibility in clinical studies.

Author contributions

Conceptualization: Tram Nguyen.

Data curation: Christina Baun.

Formal analysis: Tram Nguyen.

Writing – original draft: Tram Nguyen.

Writing – review & editing: Christina Baun, Poul Flemming Høilund-Carlsen.

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