On the stability of well-type ionization chamber source strength calibration coefficients

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Purpose: To investigate the variability and stability of brachytherapy source strength calibration coefficients for air-communicating and pressurized well-type ionization chambers among high-dose rate (HDR), low-dose rate (LDR), and electronic brachytherapy (EBT) source qualities. These qualities of an ionization chamber are important features to assess given their role in maintaining traceability to a primary national standards laboratory and facilitating efficacious patient care in brachytherapy.
Methods: The calibration records from the University of Wisconsin Accredited Dosimetry Calibration Laboratory (UWADCL) customer well-type ionization chamber database were retrospectively analyzed for calibrations performed between 1996 and 2019. A statistical analysis was performed and differentiated among calibration type to quantify the distribution of chamber calibration coefficients among several chamber models. Distributions were quantified based on their moments and by quantile analysis. For LDR calibrations, chamber response was further differentiated by seed type to study the variability in seed dependence within and across chamber models. In addition to these metrics, the calibration lineage at the UWADCL was used to assess the stability of these calibration coefficients among chamber model and source type based on the ratio of subsequent calibration coefficients.
Results: The distribution of brachytherapy source strength calibration coefficients for a particular chamber model is not necessarily normally distributed and is sensitive to changes in the machining tolerances or design of the chamber model. Calibration source quality also influenced the distributions of calibration coefficients for a chamber model; the air-kerma rate calibration coefficients for EBT sources were the most variable followed by LDR and then HDR source types. The stability of a chamber's source strength calibration coefficient exhibited a similar dependence on the source quality. Air-communicating and pressurized chambers exhibited an average stability between subsequent calibrations of 0.2% and 3.0%, respectively, for HDR calibrations, but could exhibit more than double this variability characteristic of their leptokurtic distributions. For LDR calibrations, the spread and stability in a model's calibration ratio toward another seed type is extensive and notable. For some seed types and chamber models exhibit variations of <0.5% while others exceeded 2.0%. Furthermore, the magnitude of this dependence is outside the variability of the source's source strength due to manufacturing, which was determined from the manufacturer and NIST source strength intercomparison records at the UWADCL. As a result, establishing and disseminating calibration conversion factors among different source and chamber models is not advised as it would substantially increase the uncertainty in a clinical user's determination of source strength.
Conclusions: The calibration of a well-type ionization chamber is unique to the chamber, source, and source holder. Attempting to generalize source strength calibration coefficients among chambers of the same model or source type is impractical given the variation in response observed across the calibration history of the UWADCL. Attempting to quantitate and transfer calibration coefficients in such a relative sense may significantly degrade the uncertainty relative to specifically calibrating a chamber for an individual source. [https://doi.org/10.1002/mp.14247]

Key words: brachytherapy, calibration, stability, well chamber

1. INTRODUCTION

Well-type ionization chambers are precise instruments that have been recommended by the American Association of Physicists in Medicine (AAPM) to disseminate the standard for brachytherapy sources.[1–3] Historically, the measurement of brachytherapy source strength has gone through extensive revisions from estimates of the apparent activity standards relative to a mass of radium to directly measurable quantities of dose rate in water for beta-emitting sources,[4] air-kerma rate for electronic brachytherapy sources, and air-kerma strength for gamma-emitting sources.[5] The preferred quantity to describe the strength of brachytherapy sources is air-kerma strength, S_K, as this metric reflects the differences in encapsulation material among sources. Air-kerma strength is strictly defined as the air-kerma rate a distance d from the source *in vacuo* due to photons of energy greater than δ multiplied by the square of the distance,[5]

$$S_K = \dot{K}_\delta(d)d^2, \quad (1)$$

and is described in units of U where $1\,\mathrm{U} = 1\,\mu\mathrm{Gy\,m^2\,h^{-1}}$. This parameter is the principal component in the general, two-dimensional (2D) dose-rate formalism presented in the original and revised AAPM Task Group 43 report for brachytherapy dosimetry protocols,[1,6]

$$\dot{D}(r,\theta) = S_K \cdot \Lambda \cdot \frac{G_L(r,\theta)}{G_L(r_0,\theta_0)} \cdot g_L(r) \cdot F(r,\theta), \quad (2)$$

where Λ is the dose-rate constant, G_L is the geometry function, g_L is the radial dose function, and F is the 2D anisotropy function. While initially proposed for gamma-emitting radioactive brachytherapy sources,[7] this formalism has been modified for electronic brachytherapy sources as well through the use of an air-kerma rate factor defined 50 cm from the source, $\dot{K}_{50\,\mathrm{cm}}$. The formalism also incorporates an applicator-specific dose-rate conversion coefficient, $\chi_i(1\mathrm{cm},\pi/2)$, in addition to applicator-specific geometry, radial, and anisotropy functions,[3]

$$\dot{D}(r,\theta) = \dot{K}_{50\mathrm{cm}} \cdot \chi_i(1\mathrm{cm},\pi/2) \cdot G_P(r,\theta) \cdot g_i(r) \cdot F_i(r,\theta), \quad (3)$$

where G_P, g_i, and F_i are the point source geometry function approximation, radial dose function, and anisotropy function indexed for applicator, i. Using consensus brachytherapy dosimetry, datasets can assist the clinical medical physicist in minimizing uncertainties in many of the aforementioned TG-43 parameters. However, source strength remains the responsibility of the physicist to measure and critically assess the associated uncertainty in delivering the prescribed dose to the intended region.[8] The AAPM has set forth a set of general recommendations to guide the practicing medical physicist in this endeavor.[9] However, the quality of these measurements reflect the precision and stability of the measurement device, which is the well-type ionization chamber.

The safe and efficacious dissemination of brachytherapy sources in radiotherapy necessitates the traceability to a primary standard. In the United States, the primary standard for low-energy brachytherapy source air-kerma strength is the wide-angle free-air chamber (WAFAC) maintained at the National Institute of Standards and Technology (NIST).[10] The air-kerma rate primary standard for electronic brachytherapy sources is the NIST Lamperti free-air chamber, which was designed specifically for a broader range of photon energies.[11,12] NIST does not maintain an air-kerma strength measurement standard for HDR ^{192}Ir brachytherapy sources, but the AAPM recognizes interim standards that are maintained by the Accredited Dosimetry Calibration Laboratories (ADCLs).[13,14] These interim standards utilize an interpolated air-kerma calibration coefficient for an ionization chamber calibrated at ^{137}Cs and M250 x-ray beam qualities and has been used for numerous calibrations of HDR sources.[13–17] The ADCLs are responsible for disseminating the national standards from NIST to the clinic. This is achieved through a well-chamber calibration with a NIST-measured source and subsequent transfer calibration of a clinic's well chamber at an ADCL. A clinic's air-kerma strength calibration coefficient, N_{S_K}, is then supplied that relates the charge measured from the customer's ionization chamber to the known air-kerma strength for LDR and HDR sources as,

$$N_{S_K,\mathrm{user}} = \frac{M_{\mathrm{ref}}}{M_{\mathrm{user}}} N_{S_K,\mathrm{ref}}, \quad (4)$$

or an air-kerma rate calibration coefficient, $N_{\dot{K}_{\mathrm{airat50cm}}}$, for EBT sources as,

$$N_{\dot{K}_{\mathrm{airat50cm}},\mathrm{user}} = \frac{M_{\mathrm{ref}}}{M_{\mathrm{user}}} N_{\dot{K}_{\mathrm{airat50cm}},\mathrm{ref}}, \quad (5)$$

where the subscripts *user* and *ref* denote the source strength calibration coefficients for the user's and ADCL's reference chamber, respectively. The fully corrected charge reading from the user's and ADCL's reference chamber is provided as M_{user} and M_{ref}, respectively.

The calibration of a well-type ionization chamber is a redundant process that the AAPM recommends in their Task Group 56 report to complete every two years at an ADCL.[2] Careful consideration should be given to preserve the accuracy in the determination of the source strength while also maintaining NIST traceability.[18] However, both seed manufacturing changes and differences in the production of a chamber may lead to the variation of a chamber's calibration coefficient to a given brachytherapy source quality. This effect may be stochastic among similar chambers and seed models but may also drift over the lifetime of an instrument. Similar works have previously investigated the stability and distribution of absorbed dose-to-water calibration coefficients with reference-class ionization chambers to quantify chamber-to-chamber variability in their k_Q response.[19] In the same manner, it was the purpose of this study to present a retrospective analysis of customer well-type ionization chamber calibrations performed at an ADCL to investigate (a) variations in response among well-type ionization chambers of the same model, (b) variations in response among source quality, (c) stability and constancy among repeated source calibrations, and (d) the calibration stability among well-type ionization chambers with respect to LDR, HDR, and EBT sources.

In this report, source models and manufacturers are disclosed to provide both a historical and statistical context to the analysis. As a result, several of the brachytherapy sources and well-type ionization chambers presented in this work may no longer be in production. Brand names, manufacturers, and source qualities are given in this manuscript for identification purposes only. The authors do not endorse any of these commercial products nor recommend that the products are necessarily the best instruments available, nor superior to another, for any brachytherapy source measurements.

2. MATERIALS AND METHODS

2.A. Overview of sample well chamber calibration data

The well-type ionization chamber calibration records at the University of Wisconsin Accredited Dosimetry Calibration Laboratory (UWADCL) were retrospectively analyzed for several chamber models between the calibration dates of 1996–2019. The manufacturing dates for some of these well chambers may exceed the calibration date range. As a result, some of the chambers studied in this work may no longer be in production but still in use by a variety of clinics. The well chamber calibrations were organized into high-dose rate (HDR) ^{192}Ir, low-dose rate (LDR) interstitial, and electronic brachytherapy (EBT) source qualities. A list of the number of calibrations and well chambers considered in this study are provided in Table I.

While calibration data existed for additional chamber models, the criteria used for a chamber model to be included within this analysis was a minimum of five chambers within the calibration registry for a particular model. Several models of well-type ionization chambers are considered in this work, including air-communicating and pressurized chambers as denoted in Table I. The inclusion of a specified chamber was differentiated by a chamber's serial number, and the history of its own calibration at the UWADCL was monitored through the internal report identification number. A calibration was included within this manuscript only if it had been formally issued to the customer and followed an accredited calibration protocol. It is possible for a particular chamber to undergo more than one calibration with multiple source qualities. In these instances, the lineage of calibration was discriminated based on source type that is reflected on the report and calibration history of the chamber maintained at the UWADCL. A summary of the calibration histories investigated in this analysis are listed in Table II.

TABLE I. A list of well-type ionization chambers that have been analyzed in this study across the range of calibration dates.

Manufacturer	Chamber model	Number	Calibrations	Dates
Nucletron	077.091	11	27	1998–2018
Nucletron	077092	17	28	2010–2019
Standard Imaging	IVB1000	492	1773	2000-2019
Standard Imaging	HDR1000	149	541	1996–2019
Standard Imaging	HDR1000 Plus	3523	13864	1996–2019
PRM	WC-2	27	99	1996–2019
Sun Nuclear	1008	33	83	1996–2008
Sun Nuclear	100840	8	53	2001–2019
Atomlab	44D	111	547	1996–2019
Capintec	BTC/3007	9	23	2004–2019

Row entries are shaded for pressurized chambers.

TABLE II. A list of the number of well-type ionization chambers, regardless of model, and total number of calibrations performed for high-dose rate (HDR), low-dose rate (LDR), and electronic brachytherapy (EBT) source calibrations.

Source quality	Chambers	Calibrations	Dates
HDR	2831	8956	1996–2019
LDR	1805	9955	2001–2019
EBT	242	475	2014–2019

The total number of chambers or calibrations is listed for each model regardless of the type of calibration or air-communication. The dates represent the span of calibrations that are considered in this work.

2.B. Statistical methods of chamber model calibration analysis

All data compilation and statistical analyses were performed using MATLAB (version R2018a). The primary quantity studied in this work was the chamber's calibration coefficient distinguished by chamber model. For a given calibration type, the mean and standard deviation of the calibration coefficient ($\overline{N}_{S_K \text{or} K_{air}}$ and $\sigma_{S_K \text{or} K_{air}}$, respectively) were calculated from a population of all chambers (Cham) of the same model. Unless otherwise noted, the reported calibration (Cals) conditions were identical among all chambers. If a chamber underwent repeated calibrations (RCals) of the same type, then the average calibration coefficient among the chamber's reported calibrations was used as a single data point representing the particular chamber's calibration coefficient within the distribution of all calibration coefficients from chambers of that same model.

A chamber's stability was also quantified by how subsequent calibration coefficients fluctuate for a specific chamber undergoing repeated calibrations. Only well chambers that underwent a minimum of three repeated calibrations were included in this analysis, and a chamber model was included only if there were at least three chambers that underwent three multiple calibrations. The mean, $\overline{R}_{rep}$, and standard deviation, $\sigma_{R_{rep}}$, from the mean was calculated from the distribution of a chamber model's repeated calibration ratio defined as,

$$R_{rep} = \frac{(N_{S_K \text{ or } K_{air}})_{new}}{(N_{S_K \text{ or } K_{air}})_{previous}}. \quad (6)$$

Additionally, the average that a chamber would deviate from its own mean, $\overline{\sigma}_{R_{rep}}$, was determined on an individual basis and averaged among all chambers of the same model.

2.C. Extended investigations for LDR calibrations

Unlike HDR or EBT well chamber calibrations specific to one source type, LDR calibrations encompass several seed models and nuclear isotopes. Separate chamber calibration coefficient distribution analyses were performed uniquely to each chamber model and LDR seed type. Additional filtering criteria were instituted given the potential variability in its calibration including the seed orientation and seed holder that were used during calibration. In addition to the statistical analysis used to quantify chamber model response variation and stability, the variation and stability of chamber model-averaged calibration coefficients among multiple seed models was quantified relative to a common ^{131}Cs seed calibration. However, the total variation in a chamber's response among multiple calibrations is a result of the chamber's intrinsic variability and the manufacturing tolerances of the brachytherapy seeds. Seed variability was quantified from intercomparisons of multiple seed models between the NIST primary standard and the UWADCL reference standard.

3. RESULTS

3.A. HDR Ir-192 well chamber calibrations

Eight models of well-type ionization chambers were investigated spanning 23 yr of HDR ^{192}Ir calibrations. These calibrations have been performed utilizing several ^{192}Ir sources and afterloader units.[14] However, the data were not differentiated by ^{192}Ir source model, but analyzed cohesively as the UWADCL offers a single calibration representing the average source model standard chamber response.[14] Instead, the small amount of variability between source models is included within the expanded uncertainty of the well chamber calibration.

Table III lists the analyzed statistics from the ^{192}Ir well chamber N_{S_K}'s among several chambers. A chamber model was only included within the HDR analysis if there were at least five chambers that underwent recalibration as determined from the UWADCL calibration records. In addition to the basic statistical quantities determined from the calibration data, the 95% quantile for a chamber's N_{S_K} reproducibility among repeated calibrations, denoted as $Q_{95\%}$, was determined.

The lineage of a chamber model's manufacturing process may also influence the variability in the determined N_{S_K}'s of a specific chamber model. It is hypothesized that these differences include an external component of variability outside of the calibration process, specifically manufacturing differences among chambers of the same model. Figure 1 illustrates the distribution of measured N_{S_K}'s among 47 44D and 2548 HDR1000 Plus well-type ionization chambers. Quantile–quantile (Q-Q) plots were then generated from these histogram distributions to investigate the normality of the chamber's N_{S_K} distributions. In each plot, the calculated quantile from the data sample is mapped to that of a theoretical normal distribution with the same mean and standard deviation, which is plotted in a dashed red line for reference.

Given the large amount of HDR1000 Plus well chamber data, an additional Q-Q plot was generated from chambers manufactured on or after 2010. The relationship between the lineage of a chamber model and the respective N_{S_K}'s were assessed by plotting the median-normalized N_{S_K}'s as a function of the chamber's serial number. For the case of the HDR1000 Plus well chamber, the serial number was converted to the year of production as the serial numbers follow similarly to the International Organization for Standardization date format. However, the same relationship was not known for the 44D chamber model, and it was simply assumed that an increasing serial number resulted in an increasing manufacturing year.

Air-kerma strength calibration coefficient variability was quantitated using Eq. (6) for each chamber that underwent at least three recalibrations. The average of each chamber's N_{S_K} recalibration ratio with its prior calibration was assessed for a given well chamber model in addition to the average that a single chamber would vary about its own mean N_{S_K}. The distribution of this variability for the HDR1000 Plus well-type ionization chamber is shown in Fig. 2. A chamber's stability was quantified based on its 95% quantile in addition to the standard deviation. All quantiles and standard deviations are provided in percent of the mean.

TABLE III. Statistical results of archived HDR ^{192}Ir air-kerma strength calibrations for well-type ionization chambers sorted by their air-communication status. Row entries are shaded for pressurized chambers. The average N_{S_K}'s for all chambers are normalized to the mean N_{S_K} determined for the HDR1000 Plus well chambers. The response of the HDR1000 Plus chamber has also been subanalyzed discriminating chambers based on their manufacturing date.

	Number of								
Model	Cham	Cals	RCals	$\overline{N}_{S_K}$	$\sigma_{N_{S_K}}$(%)	$\overline{R}_{rep}$	$\sigma_{R_{rep}}$(%)	$\overline{\sigma}_{R_{rep}}$(%)	$Q_{95\%}$(%)
077.091	11	26	5	1.986	0.53	0.9996	0.17	0.14	0.50
077092	17	27	6	2.016	1.86	1.0002	0.15	0.09	0.27
HDR1000	120	430	66	1.076	3.31	0.9997	0.27	0.13	0.44
HDR1000 Plus	2548	7885	1278	1.000	1.72	1.0001	0.25	0.15	0.42
HDR1000 Plus	Post 2005[a]		905	0.997	0.56	1.0001	0.13	0.13	0.36
HDR1000 Plus	Post 2010[a]		287	0.997	0.37	0.9998	0.12	0.08	0.27
IVB1000	100	324	64	0.962	0.54	1.0004	0.71	0.19	0.59
1008	14	24	5	0.302	3.32	0.9986	0.89	2.95	5.26
100840	5	31	5	0.319	7.32	1.0024	2.04	2.40	4.18
44D	47	166	32	0.312	8.43	1.0105	1.13	1.51	3.40

Chambers included in this entry were manufactured after the specified date.

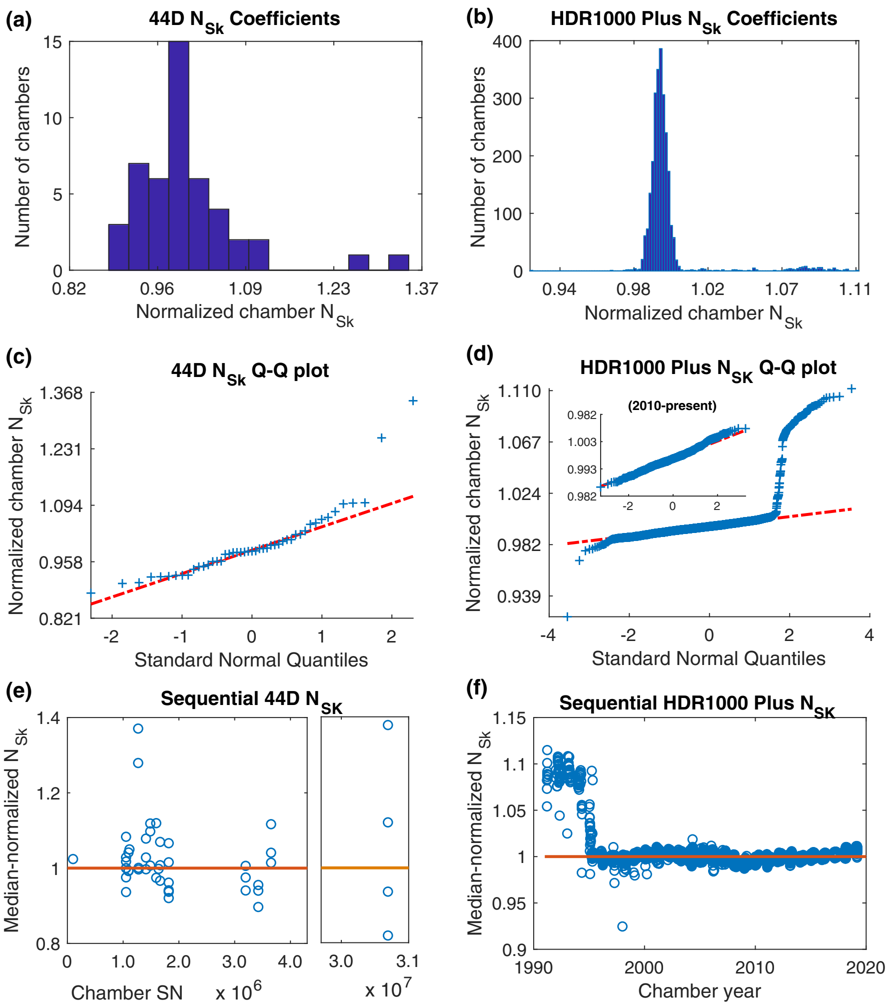

FIG. 1. Histogram distributions of chamber ^{192}Ir air-kerma strength calibration coefficients, N_{S_K}, for the pressurized 44D (plot a) and air-communicating HDR1000 Plus (plot b) well-type ionization chambers, normalized to their median value, measured for several 44D (plot a) and HDR1000 Plus (plot b) well chambers at the UWADCL. The normality is assessed using quantile–quantile plots for the 44D (plot c) and HDR1000 Plus (plot d) chambers. The chamber models were also assessed chronologically in order of their serial number (44D, plot e) or production date (HDR1000 Plus, plot f) relative to the model's median ^{192}Ir air-kerma strength calibration coefficient. [Color figure can be viewed at wileyonlinelibrary.com]

3.B. LDR well chamber calibrations

The LDR air-kerma strength calibration data were analyzed from calibration records following the 1999–2000 NIST revisions.[20] The data included calibration records among several seed types and manufacturers across several different chamber models. Chamber and seed calibration combinations are reported only if there were five or more chambers for a given model that underwent repeated calibrations with the same seed. The same N_{S_K} distribution metrics were computed for each reported chamber and seed combination as done for the ^{192}Ir well chamber calibration analysis. Table IV lists the chambers, seed types, N_{S_K} and stability values for this work.

Well-type ionization chamber source strength calibrations are holder- and seed orientation dependent. Any differences among the population of chamber calibrations for a given seed and chamber model were differentiated based on their calibration methods. For the calibrations studied in this work, each of the calibrations followed the UWADCL calibration protocols. Most calibrations were performed with a standard seed holder, which included a 50 mm plug for HDR1000 Plus and IVB1000 chambers. A linear tube source holder was used for ^{137}Cs sources, and a modified loop holder for LDR ^{192}Ir seeds in ribbon.

In addition to chamber construction and gas volume, variation among seeds of the same model and isotope can also lead to changes in a chamber's N_{S_K}. Consistency in the calibration coefficient is therefore contingent on the stability of seed manufacturing. As recommended by the AAPM Task Group report 43, intercomparisons among the manufacturers, NIST, and secondary standards laboratories should be completed annually for current sources distributed clinically throughout the United States.1 While the acquisition of this data has a large historical motivation, it also serves in this work to examine how the variation among seeds may impact chamber response for the same seed model. Table V lists the recorded intercomparisons between the NIST WAFAC primary standard and the UWADCL secondary standard well chamber for several seed models studied in this work. The

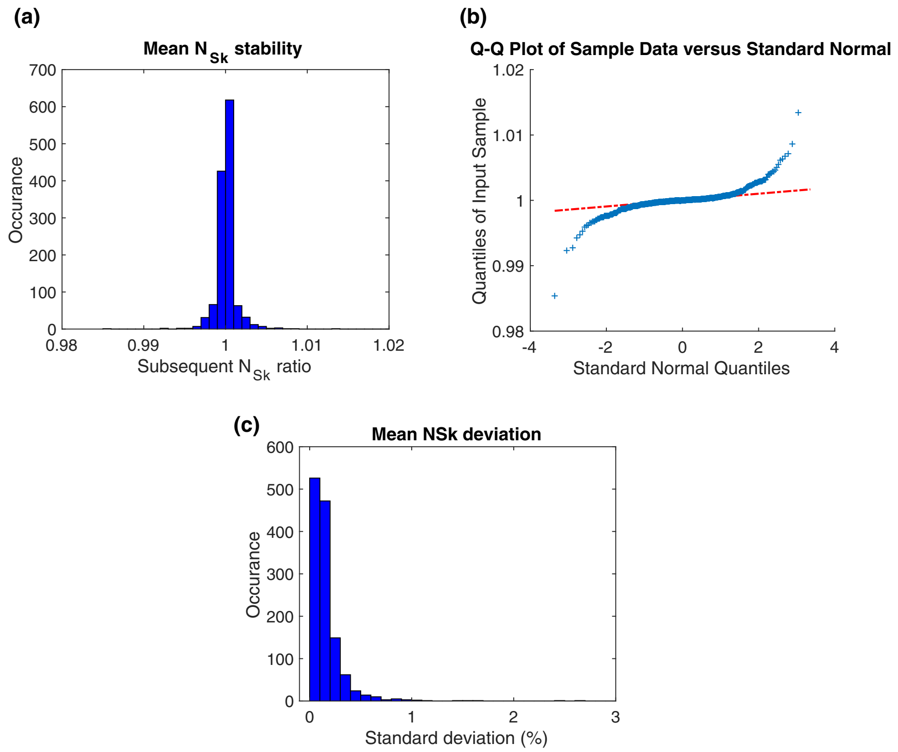

FIG. 2. Histogram distribution of the subsequent N_{S_K} ratios representing the distribution of chamber stabilities for the HDR1000 Plus (plot a). The quantile–quantile distribution plot testing the normality of the chamber stability distribution in plot a (plot b). The sampled histogram distribution that shows the average variability expected for a single chamber around its own mean N_{S_K} (plot c). [Color figure can be viewed at wileyonlinelibrary.com]

root-mean-squared difference in the measured air-kerma strength from NIST was compared to the air-kerma strength measured using the UWADCL's standard reference ionization chamber that is used to transfer the NIST standard to customer chambers.

The response of a well chamber among different LDR seed models was investigated from the archived UWADCL customer well chamber LDR calibration records. Chamber response was characterized by the ratio of N_{S_K}'s between a given seed model referenced to a ^{137}Cs source. Therefore, all chambers included in this analysis were limited to those that had a recorded ^{137}Cs source calibration in addition to any other LDR chamber N_{S_K} calibrations by source. Subsequent chambers undergoing repeated calibrations were further limited to tandem calibrations of both the test source and ^{137}Cs source. There was only enough data present within the UWADCL LDR calibration records for the HDR1000 Plus and IVB1000 well chamber models to be included in this portion of the analysis among a few seed models due to the specific criteria necessary for aforementioned analysis. The results are listed in Table VI.

3.C. EBT well chamber calibrations

The UWADCL has provided EBT air kerma rate calibration coefficients defined 50 cm from the source, $N_{\dot{K}_{air}}$, for the Xoft Axxent source since 2014. So far, only the HDR1000 Plus well chamber has been calibrated at the UWADCL. In each of these calibrations, a custom Axxent source holder is used during the calibration that is unique to each chamber calibrated specified by a source holder serial number. Table VII lists the analyzed statistics from the EBT well chamber air-kerma rate calibrations among several chambers. In addition to the basic statistical quantities determined from the calibration data, the 95% quantile for a chamber's calibration coefficient reproducibility among repeated calibrations, denoted as the $Q_{95\%}$, was determined.

4. DISCUSSION

4.A. HDR ^{192}Ir calibrations

The distributions of calibration coefficients can provide insight into the intra- and intervariability that exists within a specific chamber model and are listed for several chamber models in Table III. The spread of a model's N_{S_K} about their average highlights the manufacturing tolerances; a chamber's N_{S_K} relative to another will largely depend on the geometric consistency between two chambers. While this may also be true due to ^{192}Ir source manufacturing differences, HDR ^{192}Ir well chamber calibrations are source independent within the calibration uncertainty, as it has been shown to minimally influence the overall response of a chamber.[14] Intersource variability is assumed as a 0.96% type B component within the calibration uncertainty provided by the ADCL. For this work, the reported calibration uncertainty for an HDR ^{192}Ir well chamber transfer calibration is 2.75% at

TABLE IV. Statistical results from the LDR well-type ionization chamber N_{S_K} calibrations including the 44D (pressurized), HDR1000 Plus (air-communicating), and the IVB1000 (air-communicating) well chambers. The $\overline{N}_{S_K}$ for a given chamber model has been normalized to its $\overline{N}_{S_K}$ for a ^{137}Cs seed.

		Number of							
Seed	Model	Cham	Cals	RCals	$\overline{N}_{S_K}$	$\sigma_{N_{S_K}}$(%)	$\overline{R}_{rep}$	$\sigma_{R_{rep}}$(%)	$\overline{\sigma}_{R_{rep}}$(%)
Cs-137	HDR1000 Plus	267	676	112	1.000	2.83	1.0012	0.61	0.44
I-125(125SH)	HDR1000 Plus	102	182	21	0.492	2.81	1.0070	1.16	1.95
I-125(2301)	HDR1000 Plus	114	300	43	0.403	1.85	1.0002	0.44	0.98
I-125(2301)	HDR1000 Plus	114	300	43	0.403	1.85	1.0002	0.44	0.98
−125 (3500)	HDR1000 Plus	29	46	6	0.432	2.11	1.0038	0.84	1.00
I-125(3631A/M)	HDR1000 Plus	102	171	19	0.409	2.01	0.9981	0.37	1.27
I-125(6711)	HDR1000 Plus	530	1228	203	0.461	1.69	1.0020	0.36	0.93
I-125(6733)	HDR1000 Plus	35	53	5	0.457	1.66	1.0017	1.20	1.74
I-125(9011)	HDR1000 Plus	16	23	3	0.464	1.68	1.0011	0.04	0.49
I-125(Advantage)	HDR1000 Plus	156	310	51	0.446	1.84	1.0019	0.44	0.82
I-125(AgX100)	HDR1000 Plus	139	243	36	0.453	1.44	1.0018	0.25	0.77
I-125(I125.S06)	HDR1000 Plus	52	73	3	0.414	2.14	0.9983	0.65	1.87
I-125(LS-1)	HDR1000 Plus	23	35	3	0.428	1.41	0.9927	0.90	0.73
I-125(STM1251)	HDR1000 Plus	290	770	148	0.402	1.80	1.0019	0.30	0.92
I-125(SelectSeed)	HDR1000 Plus	27	52	10	0.451	2.04	0.9986	0.29	0.79
Ir-192(Best)	HDR1000 Plus[a]	26	45	7	0.889	3.58	1.0015	0.28	0.25
Ir-192(Best)	HDR1000 Plus[c]	108	333	68	0.884	2.91	1.0005	0.18	0.51
Pd-103(2335)	HDR1000 Plus	74	165	24	0.886	1.57	1.0041	0.42	1.16
Pd-103(CivaDot)	HDR1000 Plus	25	41	3	1.579	1.47	1.0010	0.09	0.10
Pd-103(IAPd-103A)	HDR1000 Plus	46	73	6	0.927	3.89	1.0043	0.54	1.27
Pd-103(MED3633)	HDR1000 Plus	84	127	13	0.879	1.47	1.0053	0.37	0.83
Pd-103(TheraSeed 200)	HDR1000 Plus	424	1203	212	0.899	1.66	1.0014	0.41	0.98
Cs-137	IVB1000	45	95	16	1.000	0.49	1.0025	0.22	0.51
I-125(125SH)	IVB1000	17	35	5	0.518	2.88	1.0023	0.31	1.46
I-125(2301)	IVB1000	31	58	6	0.420	1.43	1.0027	0.15	0.76
II-125(6711)	IVB1000	60	128	16	0.484	1.22	1.0039	0.64	1.01
I-125(Advantage)	IVB1000	28	69	12	0.468	0.94	1.0008	0.24	1.27
I-125(AgX100)	IVB1000	23	43	6	0.474	0.89	1.0058	0.52	0.88
I-125(STM1251)	IVB1000	51	135	24	0.420	3.06	1.0012	0.33	0.95
Ir-192(Best)	IVB1000	13	38	9	0.876	0.42	1.0006	0.29	0.63
Pd-103(2335)	IVB1000	25	41	5	0.917	1.73	1.0033	0.81	1.27
Pd-103(TheraSeed 200)	IVB1000	65	183	35	0.928	1.09	1.0027	0.52	1.15
Cs-137	44D	33	70	10	1.000	8.35	1.0192	1.77	2.25
I-125(6711)	44D	37	71	10	0.203	8.85	1.0242	0.89	1.04
Ir-192(Best)	44D[a]	13	26	3	0.861	11.67	1.0026	2.12	4.09
Ir-192(Best)	44D[b]	13	25	3	0.880	12.71	1.0170	0.43	0.61
Pd-103(TheraSeed 200)	44D	40	92	16	0.729	11.49	1.0157	1.47	1.98

[a]Subset of chamber calibration data performed with the standard seed holder and plug.
[b]Subset of chamber calibration data performed with the standard loop holder.
[c]Subset of chamber calibration data performed with a modified loop holder.

the k = 2 confidence level, which allows the ADCL to provide a single calibration for several source models.[14,17]

Most of the air-communicating chambers' HDR ^{192}Ir N_{S_K}'s varied within the estimated variability assumed from specific source models in addition to the expanded uncertainty of a customer calibration. The largest variability among N_{S_K}'s were observed for pressurized well chamber models. Since the N_{S_K} is unique to a given chamber, its deviation among other chambers of the same model indicates the machining and Argon gas fill tolerances established by the manufacturer. Any systematic change in the mean N_{S_K} outside this variation over time, or serial number, can infer changes to the manufacturing process. This effect is observed in Fig. 1 for the HDR1000 Plus well chamber as the variability and magnitude of the calibration coefficient sharply changes around 1996, which is coincidental to a significant

TABLE V. NIST intercomparison of LDR brachytherapy seed measured air-kerma strength with the UWADCL decay-corrected to the NIST measurement date. The reported RMS comparison is differentiated between intercomparison before and after 2010.

Seed	model	Number (post 1999)	RMS(%) NIST vs UW	Number (post 2010)	RMS(%) NIST vs UW
Cs-131	CS-1	15	1.80	0	
Cs-131	CS-1, Rev 2	27	0.66	15	0.54
I-125	125SH	36	4.04	9	0.32
I-125	2301	26	1.24	11	0.40
I-125	3500	13	1.96	0	
I-125	3631A/M	34	1.32	0	
I-125	6711	38	2.07	14	1.06
I-125	6733	15	0.80	0	
I-125	9011	12	1.02	11	1.01
I-125	Advantage	30	1.36	15	0.87
I-125	AgX100	12	0.38	12	0.38
I-125	I25.S06	36	1.50	6	0.18
I-125	STM1251	30	1.21	15	0.84
I-125	SelectSeed	36	1.50	15	0.98
Pd-103	1031L	9	5.13	0	
Pd-103	200	80	2.87	12	0.30
Pd-103	2335	29	1.80	12	0.28
Pd-103	IAPd-103A	21	1.09	15	0.60
Pd-103	MED3633	39	1.64	0	
Pd-103	CivaDot	5	1.13	5	1.13

manufacturing change confirmed with the manufacturer. Systematic changes also occur with pressurized chambers. Chambers such as the 44D studied in this work have been found to drift toward decreased sensitivity over time, as much as 1.0% per year.[21] Therefore, these systematic changes may not be indicative of manufacturing variability but are instead a result of the fill gas slowly leaking from pressurized chambers.

The results of the chamber calibration response have been normalized to the chamber model's mean calibration coefficient. However, chamber manufacturing changes may not be normally distributed. This has been shown for two well chamber models, 44D and HDR1000 Plus, using Q-Q plots. Over the course of a model's manufacturing history, systematic changes may occur as observed for the HDR1000 Plus well chamber that significantly shift the average calibration coefficient. A student's two-sided *T*-test performed on the distribution of all HDR1000 Plus chambers produced post-2010 in Table III show statistical difference ($P \ll 0.001$) with the population of all chambers, but no statistical difference with the population of chambers produced after 2005 ($P = 0.228$). The larger standard deviation for all HDR1000 Plus chambers is therefore dominated by chambers produced before 2005. While these changes can be distinguished at the level of secondary standard laboratories, they may not be detectable by an end user. Thus, it is inappropriate to assume an average N_{S_K} value for chambers of the same model as doing so would substantially increase the uncertainty in the measured source strength.

A wide spread in calibration coefficients among chambers of the same model does not necessarily suggest that a chamber is not a precise instrument. While a chamber's accuracy is maintained through a NIST-traceable calibration, its precision is a factor of the chamber's measurement and calibration repeatability. The well-type ionization chambers studied in this work all showed an average stability to between 0.01% and 1.05% of their repeated calibration coefficients, but the spread about these average values depended on the chamber type; the N_{S_K}'s for pressurized chambers showed greater variance between subsequent calibrations than air-communicating chambers. A retrospective analysis on the historical account of a well chamber's repeated calibrations show that their stability deviates within 0.2% and 3.0% for air-communicating and pressurized chambers, respectively, at the $k = 1$ confidence level. However, the histograms and quantile analysis plotted in Fig. 2 suggests that the stability of the chambers for a model are also not normally distributed.

While the stability around unity for the HDR1000 Plus well chamber is leptokurtic, resulting in a standard deviation within 0.15% the expected stability, the tails of this distribution are broader and indicate that 5% of customer chambers' N_{S_K}'s may deviate up towards 0.42% between calibrations. Thus, assuming that all well chambers retain their calibration coefficients over several years may not necessarily be true and should not be generalized from an instance of a single chamber's behavior, which has been the focus and scope of some works.[22] This is further exacerbated for pressurized chambers that are susceptible to a slow but steady loss of fill-gas pressure over time. A drift common to all air-communicating chamber's response over time, apart from damage or repair, may also be due to fluctuations in impurities in the air built up on the electrodes over time or electrostatic changes

TABLE VI. LDR seed chamber air-kerma strength calibration intercomparison. All chamber responses are normalized to the chamber's ^{137}Cs N_{S_K} calibration coefficient. Only chamber-seed model comparisons that had at least five chambers undergo multiple calibrations with both the test seed and ^{137}Cs seed are included.

Models		Number of				
Chamber	Seed	Chambers	Cals	$(N_{S_K})^{test}_{^{137}Cs}$	$\sigma_{R_{rep}}(\%)$	$\overline{\sigma}_{R_{rep}}(\%)$
HDR1000 Plus	Cs-137	151	602	1.000	0.00	0.00
HDR1000 Plus	Cs (Cs-1)	12	33	0.358	1.25	0.41
HDR1000 Plus	I-125 (125SH)	6	17	0.483	1.72	1.07
HDR1000 Plus	I-125 (2301)	13	46	0.406	0.49	0.55
HDR1000 Plus	I-125 (3500)	5	12	0.432	1.56	0.53
HDR1000 Plus	I-125 (3631A/M)	5	13	0.410	0.90	0.71
HDR1000 Plus	I-125 (6711)	70	232	0.462	1.81	0.63
HDR1000 Plus	I-125 (6733)	3	8	0.460	1.14	0.90
HDR1000 Plus	I-125(Advantage)	12	32	0.447	1.35	0.62
HDR1000 Plus	I-125(AgX100)	2	4	0.457	0.78	0.90
HDR1000 Plus	I-125(I125.S06)	3	6	0.411	1.43	1.27
HDR1000 Plus	I-125(STM1251)	31	111	0.402	1.84	0.61
HDR1000 Plus	I-125(SelectSeed)	5	11	0.453	1.23	0.38
HDR1000 Plus	Ir-192(A-O)	3	6	0.926	0.47	0.42
HDR1000 Plus	Ir-192(Best)	65	254	0.883	1.02	0.51
HDR1000 Plus	Pd-103(2335)	7	21	0.899	1.04	0.67
HDR1000 Plus	Pd-103(IAPd-103A)	2	5	0.913	2.51	0.61
HDR1000 Plus	Pd-103(MED3633)	2	4	0.889	0.47	1.79
HDR1000 Plus	Pd-103(TheraSeed 200)	58	217	0.898	2.20	0.68
IVB1000	Cs-137	24	77	1.000	0.00	0.00
IVB1000	I-125(2301)	2	4	0.420	0.97	0.37
IVB1000	I-125 (6711)	7	21	0.482	0.30	0.42
IVB1000	I-125(STM1251)	6	18	0.420	0.92	0.49
IVB1000	Ir-192(Best)	4	16	0.874	0.08	0.33
IVB1000	Pd-103(2335)	2	5	0.917	0.05	1.79
IVB1000	Pd-103(TheraSeed 200)	7	20	0.929	0.58	0.48

TABLE VII. Statistical results of archived EBT air-kerma rate calibrations for well-type ionization chambers. The response of the HDR1000 Plus chamber has also been subanalyzed discriminating chambers based on their manufacturing date. The air-kerma rate calibration coefficient has been normalized to the chamber's LDR ^{137}Cs air-kerma strength calibration coefficient.

	Number of								
Model	Cham	Cals	RCals	$\overline{N}_{S_K}$	$\sigma_{N_{S_K}}(\%)$	$\overline{R}_{rep}$	$\sigma_{R_{rep}}(\%)$	$\overline{\sigma}_{R_{rep}}(\%)$	$Q_{95\%}(\%)$
HDR1000 Plus	242	475	63	0.202	2.13	1.0026	0.45	0.67	1.43
HDR1000 Plus[a]	161	303	41	0.204	1.74	1.0028	0.28	0.61	1.26
HDR1000 Plus[b]	69	129	21	0.204	1.47	1.0038	0.19	0.61	1.17

[a]Chambers included in this entry were manufactured after 2010.
[b]Chambers included in this entry were manufactured after 2015.

in the electric field due to small physical changes in the components' alignment.

4.B. LDR calibrations

A comparison between Tables III and IV highlights the differences among chamber models and seed types. Air-kerma strength calibrations for LDR well chambers show more variability than observed for HDR ^{192}Ir calibrations with the pressurized chamber exhibiting the largest variability in their calibration coefficients and stability. A notable difference between LDR and HDR well-type chamber calibrations is the signal stability; lower activity LDR sources provide less signal than HDR sources. Chamber response also varies widely by seed type, which includes both the source encapsulation material and the contained isotope. It does not appear that the increase in a model's spread of chamber air-kerma strength calibration coefficients or the stability is due to the seed energy. Both higher energy seeds, such as ^{131}Cs and LDR ^{192}Ir seeds, and lower energy seed models exhibit spreads in their model-average calibration coefficients greater than 1%, which is much larger than observed for the same model chamber with the HDR ^{192}Ir calibrations. Instead, the variability appears to be from chamber-specific qualities such as the source holder as it directs the alignment of the seed in the well chamber. A 2.30% difference in the N_{S_K}'s was observed for two macroscopically different ^{192}Ir source holders for the 44D well chamber, and it is possible that intravariability of the same model of holder and well chamber could be responsible for the increased spread in both the average chamber's LDR calibration coefficient. This is in contrast to the minimal dependence source holders have been found to have with HDR ^{192}Ir well-type ionization chamber calibrations.[17]

Multiple materials and isotopes are used to produce brachytherapy sources, which has also motivated the sole metric of air-kerma strength to be used in place of contained activity, as it is more sensitive to changes in the seed manufacturing. The observed differences in a chamber's stability over repeated calibrations in addition to the spread in a chamber's model average calibration coefficient may be influenced by the manufacturing tolerances of the seed model over time.[5] The reported RMS in Table V between NIST and the UWADCL's standard reference chamber across the entire history of seed intercomparisons show a general regime of 1%–2% from 1999, with a few seeds having RMS values greater than 4%. However, the RMS for the majority of seed models with intercomparisons between the NIST and the UWADCL performed after 2010 are within 1%.

The reproducibility of a chamber's calibration coefficient among different seed models is dependent on several factors including the chamber's stability toward each seed model independently and the manufacturing tolerance of the seed. Each of these variations that exist across the history of a chamber's calibration will impact the ability to precisely quantitate the expected ratio of one calibration coefficient to another, ultimately increasing the uncertainty beyond calibrating a chamber specifically for an intended seed. The summary provided in Table VI highlights the variability in multiple calibration coefficients over the course of a chamber's calibration history. It should be emphasized that data used to generate Table VI maintains continuity of each chamber with respect to its own calibration; the distributions presented are an average of the calibration ratios between different seed models that have been calibrated with the same chamber multiple times. The distributions shown in Table IV are averages of the nominal calibration coefficients of any chamber that has undergone an air-kerma strength calibration with a particular seed.

The change in repeatability of a chamber's calibration coefficient can vary substantially. For some seed models, the variation may be <0.5% but may be over 2.0% for others. The spread in a model's calibration ratio between different seeds is notable, with most seed-chamber model combinations having a 1.0% or more spread about an average ratio. The ratio in a chamber's response to a common seed quality, such as ^{137}Cs, can vary among seeds sharing the same isotope. The calibration coefficient ratios summarized in Table VI for the HDR1000 Plus well chamber are all significantly different at the 95% confidence level for ^{125}I seed models analyzed using a two-sided, two-sample *T*-test with most of the intercompared ratios having differences outside each other's standard deviation. As shown from this analysis, well chamber calibrations with different seed models of the same therapeutic radioisotope share no common distribution of calibration coefficients and are distinct from one another; calibration coefficients should be treated as chamber, seed, and seed-holder dependent. Furthermore, the relative response of a well chamber to different seed models relative to other chambers of the same model appears to vary in the order of the calibration uncertainty itself. The reported expanded $k = 2$ calibration uncertainty for LDR calibrations at the UWADCL is 2.41%, but if a chamber has a calibration coefficient change over 2% it is considered out-of-tolerance. Expanding the observed variations between all chambers of the same model and the intrachamber variability among the majority of seed models would result in an additional chamber uncertainty surpassing these recommended limits.

4.C. EBT calibrations

The UWADCL only contains calibration data for HDR1000 Plus well chambers that have undergone air-kerma rate calibration with the Xoft Axxent EBT source. Each of these calibrations is specific to a unique user source holder that has been designed to filter out the clinically insignificant low-energy photons. The spread of $N_{\dot{K}_{air}}$s for the HDR1000 Plus EBT calibrations is larger than observed for the HDR1000 Plus HDR ^{192}Ir source strength calibrations. Given the low-energy spectrum resulting from these EBT sources, chamber manufacturing tolerances and interholder variability are the largest contributors to the observed increase in the air-kerma rate calibration coefficient variability for the same model chamber. The stability of the air-kerma rate calibration coefficient has also shown to vary more than observed for an HDR1000 Plus well-type ionization chamber counterpart HDR ^{192}Ir or LDR source strength calibrations. It should also be noted that EBT source strength measurements with air-communicating chambers require an altitude effect correction similar to LDR source measurements.

5. CONCLUSIONS

A retrospective analysis was performed on the archived HDR, LDR, and EBT source strength calibrations at the UWADCL. For each of these calibration qualities, the variability of calibration coefficients was quantified for specific chamber models, and the stability of a single chamber's calibration over the course of its calibration lineage was studied. The distribution of calibration coefficients for well-type ionization chambers are not necessarily normally distributed; changes in source or chamber manufacturing can cause notable changes in the calibration coefficients across the lineage of a chamber model. Machining tolerances may also influence the range of calibration coefficients for a chamber model, which may also influence the constancy a chamber's response toward a particular source quality. Overall, the calibration coefficients were observed to vary the least between subsequent HDR ^{192}Ir air-kerma strength calibrations and the most for EBT air-kerma rate calibrations. However, it is important to note that the distribution of calibration coefficients does not indicate the quality of a chamber within the presence of routine calibration by a primary or secondary standards laboratories, and it does not appear safe nor practical to assume an expected behavior of a chamber without substantially compromising its reliability to accurately determine source strength.

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CONFLICT OF INTEREST

Dr. Larry A. DeWerd has a partial interest in Standard Imaging. The other authors have nothing to disclose.

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