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Evaluation of Dosimetric Impact of Uncertainty of Measurement in Estimating External Radiotherapy Dose

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Abstract

Cancer is a major societal public health and economic problem, responsible for one in every six deaths. Radiotherapy is the main technique of treatment for more than half of cancer patients. To achieve a successful outcome, the radiation dose must be delivered accurately and precisely to the tumor, within ± 5% accuracy. Smaller uncertainties are required for better treatment outcome. The objective of the study is to investigate the uncertainty of measurement of external radiotherapy beam using a standard ionization chamber under reference conditions. Clinical farmers type ionization chamber measurement was compared against the National Reference standard, by exposing it in a beam ^{60}Co gamma source. The measurement set up was carried out according to IAEA TRS 498 protocol and uncertainty of measurement evaluated according to GUM TEDDOC-1585. Evaluation and analysis were done for the identified subjects of uncertainty contributors. The expanded uncertainty associated with 56 mGy/nC $N_{D,W}$ was found to be 0.9% corresponding to a confidence level of approximately 95% with a coverage factor of $k = 2$. The study established the impact of dosimetry uncertainty of measurement in estimating external radiotherapy dose. The investigation established that the largest contributor of uncertainty is the stability of the ionization chamber at 36%, followed by temperature at 22% and positioning of the chamber in the beam at 8%. The effect of pressure, electrometer, resolution, and reproducibility were found to be minimal to the overall uncertainty. The study indicate that there are flawless measurement, as there are many prospective sources of variation. Measurement results have component of unreliability and should be regarded as best estimates of the true value.

Keywords

Absorbed Dose to Water, Radiotherapy, Uncertainty of Measurement, Secondary Standards Dosimetry Laboratory, Ionizing Chamber

1. Introduction

Since the discovery of X-ray by Roentgen in 1895, radiotherapy has been used as treatment modality for cancer [1]. The innovation of Cobalt in early 1950s provided enormous increase in therapy treatment using higher photon energy [2]. Recent modernization and sophistication of linear accelerator has overshadowed Cobalt as the preferred source for radiotherapy around the world. Currently radiotherapy is the most applied technique for cancer treatment, benefiting approximately 60% of cancer patients [3]. Despite radiotherapy clear technological advantages with multimodality capabilities and more additional features, the accuracy of radiation dose delivery to the target volume is emerging as one of the major challenges to realize effective clinical outcome.

Radiotherapy is administered with considerably high dose, typically 60-80 Gy for curative cases. The dose delivered to the tumor should be approximately close to the prescribed dose, to yield the required treatment outcome [2]. Biological response of cells is highly non-linear, and therefore a small in the predicated dose may lead to errors in the prediction of biological response deviation. Hence, the quantitative concept of dosimetry is important in achieving the predicted associated biological response and in reproducing the clinical outcomes [1].

Essential key ingredients for radiotherapy quality measurement are traceability, accuracy and consistency [4]. The assessment of radiotherapy detectors is preferred to be carried out at the Secondary Standards Dosimetry Laboratory (SSDL) because of availability of reference conditions, international standard infrastructure appropriate for radiation measurement and quality management system [5]. **Figure 1** shows SSDL infrastructure with Cobalt 60 calibration system used in investigation.

The curative outcome of radiotherapy greatly depends on accuracy and uncertainty of dose delivery to the tumor. Measurements are not perfect and have many potential sources of variation. Any repeated radiation measurement will lead to different results, regardless of the method if the system is sufficiently sensitive. Results of measurement are therefore unreliable to certain extent and should be considered as best estimates of the true value. Radiation dose quantity measurement is subject to diverse sources of errors [6]. Measurement uncertainty provides an interval of values within which the true value is believed to lie with a stated probability [1]. Measurement uncertainty is therefore necessary to provide quantitative indication of the reliability of a measurement.

Figure 1. Cobalt-60 radiotherapy calibration system at Secondary Standards Calibration Laboratory (SSDL), Kenya Bureau of Standards (KEBS), Nairobi, Kenya.

Measurement uncertainty is of great importance for evaluating clinical methods suitability for medical use, or comparison of results of a similar type. It can be applied in verification of clinical methods and identifying opportunities for improvement [1]. Therefore, overall uncertainty is significant for curative treatment in order to deliver radiation dose within the determined accuracy to the patient. The clinical requirement is based on dose-response curves for tumor control probabilities (TCPs) and for normal-tissue complication probabilities (NTCPs). The TCPs and NTCP are directly related to the deviation between the prescribed dose and the actual absorbed dose, and hence the need for low uncertainties [7].

The investigation focused on the uncertainty evaluation of absorbed dose to water associated with measurement of clinical farmers ionization chamber against National Reference Standard for external-beam radiotherapy [7]. The overall results are subject to measuring system, procedure used, skill of the operator, environmental conditions, conversion factors among others. The uncertainty associated with the measurement is considered as the parameter that characterizes the dispersion of the values and could reasonably be attributed to the measurand. The aim is to estimate lack of exact knowledge in measurement, after all recognized systematic effects have been eliminated by applying appropriate corrections [1].

Similar studies done by [8], concluded that accuracy and traceability of absorbed dose to water measurement of radiotherapy beam is so critical in achieving curative outcome. Investigation done by [9] outlined that uncertainties for LINAC treatment must be taken into consideration during treatment planning stages. Hence, the study builds on these recommendation to quantify the overall uncertainty and analyze each measurement contributor. Additionally, study done by [10] on quantification of the uncertainties within the radiotherapy dosimetry chain and its impact on tumor control, indicated great variation in dose delivery to target volume as a result errors in calibration. Kenyatta National Hospital being the oldest hospital in Kenya and with radiotherapy treatment of

over 120 cancer patients on daily basis [11], there is need to investigate the effect of uncertainty of measurement on its reference ionization chamber used for treatment.

2. Materials and Methods

2.1. Measurement and Procedure

Measurement was carried out by positioning the ionization chamber at the reference point in a water phantom. The National Reference and clinical ionization chambers were set up according to Figure 2, in a water phantom, at a distance of 100 m from the source, at a depth of 5 cm^2 and then exposed to gamma beam. The chamber orientation was aligned at a mark on the stem towards the source for both the reference and user ionization chamber, as guided by [5] protocol. Before measurement, leakage current of the reference standard dosimeter was obtained before exposure.

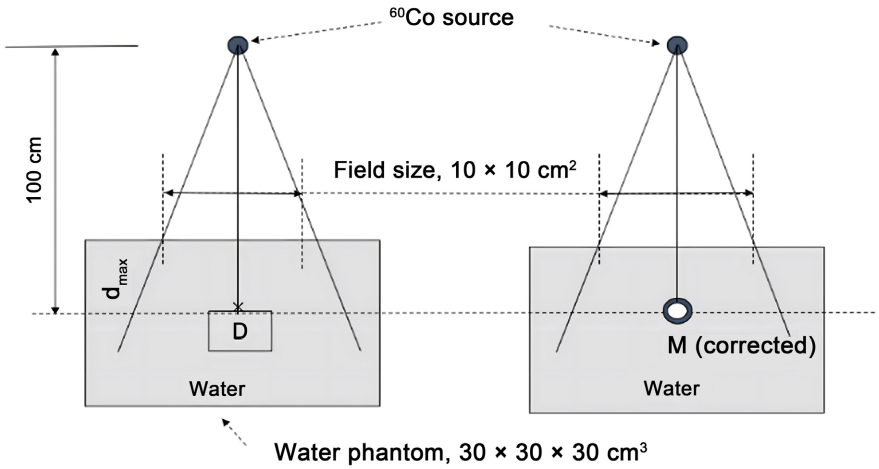

Figure 2. Measurement setup for absorbed dose to water by exposing ionization chamber in Co-60 beam, at Secondary Standards Dosimetry Laboratory (SSDL).

Figure 3. Reference ionization chamber used for calibration of hospital radiotherapy detectors.

The measurement was then carried out under defined reference conditions as outlined in IAEA protocol [12]. The equipment used for measurement are

ionization chamber, electrometer, water phantom, barometer, thermometer, cobalt 60 source and calibration system. Ionization chambers was preferred for measurement because of its high accuracy and traceability to primary standards.

Measurement was performed in terms of absorbed dose to water in a water phantom [5] and using the ionization chamber as shown in **Figure 3**. The water phantom was positioned on the central axis beam aligned to Cobalt calibration source. The measurement technique was carried out by substitution method, where the reference point of each chamber was placed successively at the same measurement point [1]. Constant environmental conditions was maintained throughout the measurement period for both clinical and SSDL ionization chambers.

Data for measurement was obtained from electrometer exposed to a Co-60 beam in water phantom, in form of charge. The air kerma rate for the reference instrument was determined by:

$$K_a = N_k^{ref} M_{corr}^{ref} k_{Q,Q_0} \tag{1}$$

Calibration factor of the instrument used for radiotherapy derived by:

$$N_k^{User} = \frac{k_a \cdot k_{source}}{M_{corr}^{user}} \tag{2}$$

where:

N_k^{ref} is the air kerma calibration coefficient of the refence instrument, in a reference quality Q_0.

N_k^{user} is the air kerma calibration coefficient of the user instrument in the calibration quality Q.

K_a is the air kerma rate determined with the reference instrument.

K_{source} is the correction for the effect of a change in source positioning.

K_{Q,Q_0} is the correction effect for difference between qualities of the beams for KNH and SSDL.

2.2. Method of Analysis of Uncertainty

The objective of measurement uncertainty is to express the statistical dispersion of values attributed to radiation measurand. Uncertainty of measurement is expressed as relative standard uncertainty and evaluation classified into type A and type B [6]. Type A are those that arise from random effect, while type B are those that arises from systematic effect. The method for evaluation of type A standard uncertainties is by statistical analysis of a series of observations, whereas evaluation of type B standard uncertainties is through non-statistical techniques [5]. Type B is based on scientific judgement using scientific information available including manufacturer manual, calibration certificate, previous records among others.

The best estimate of absorbed dose to water quantity is given by arithmetic mean $\dot{x}$ in a series of measurement n with observed values x_i

$$\dot{x} = \frac{1}{n}\sum_{i=1}^{n} x_i \tag{3}$$

where

$\dot{x}$ is the arithmetic mean.

x_i is the observed values.

n series of measurement.

Standard deviation $s(x_i)$ is given by:

$$s(x_i) = \sqrt{\frac{1}{n-1}\sum_{i=1}^{n}(x_i - \dot{x})^2} \tag{4}$$

where

n is the number of measured values.

$s^2(x_i)$ is the sample variance.

The standard deviation of the mean value $s(\dot{x}_i)$ is given by:

$$s(\dot{x}_i) = \frac{s(x_i)}{\sqrt{n}} \tag{5}$$

The standard uncertainty of type A, denoted u_A, is identified with the standard deviation of the mean value:

$$u_A = s(\dot{x}) \tag{6}$$

For type B standard uncertainty u_B for rectangular probability is given by

$$u_B = \frac{M}{\sqrt{3}} \tag{7}$$

where M is the given limits obtained from the literature.

The combined standard uncertainty quantity u_c for type A and type B is given by:

$$u_c = \sqrt{u_A^2 + u_B^2} \tag{8}$$

where

u_A combined uncertainty for type A.

u_B combined uncertainty for type B.

u_c overall combined uncertainty.

The expanded uncertainty, U is given by:

$$U = k \cdot u_c(y) \tag{9}$$

where k is the coverage factor and is obtained from a student-t distribution table based on the required level of confidence.

2.3. Uncertainty Budget and Evaluation Technique

Uncertainty budget provides itemized table of components that contribute to the uncertainty of the measurement results [6]. Uncertainty budget present information that identifies, quantifies, and characterizes each of the independent variable contributors in a structured manner, so as to allow validation of results [5].

Influence quantities are regarded as parameters that are not subject to meas-

urement but affect the measurement of ionization chamber readings. The influence quantities identified were air pressure, ageing, zero drift, beam quality, dose rate and field size [1]. The corresponding effects and their impact on the results were considered in the final analysis of results [13].

Several sources of contributors to dose determination of uncertainties were considered from different physical quantities, procedures, and environment conditions. Evaluation was carried out for the uncertainties due to the calibration of the user ionization chamber $N_{D,w}$ at the SSDL [14]. This was followed by analysis of uncertainties measurement due to ^{60}Co beam and uncertainties associated with the measurements at the reference point in a water phantom and k_Q values.

3. Results and Discussion

Results of Evaluation of Uncertainty Budget

Table 1 shows how different uncertainty source and contributors that affect dosimetry measurement were identified and analyzed. Some of the contributors identified include calibration of standards, pressure, temperature, position of the chamber, stability of the chamber, electrometer of the chamber, resolution, and reproducibility. The best estimate of arithmetic mean was determined according to Equation (3), standard deviation according to Equation (4), combined standard uncertainty according to Equation (8) and expanded uncertainty according to Equation (9).

Table 1. Expanded uncertainty budget for absorbed dose to water using reference ionization chamber exposed in cobalt 60 beam.

No	Contributor	Type	Probability Distribution	Uncertainty Estimate (±)	Divisor	Standard uncertainty $u(x_i)$	Sensitivity coefficient c_i	Uncertainty contributor $u(y_i) = c_i * u(x_i)$	Significance %	$u(y_i)^2$	$u(y_i)^4$
	Contribution of reference ionization chamber										
1	Calibration of standard	B	Normal (95.45%)	0.13	2	0.07	1	0.07	2.4%	0.004	1.8E−05
2	Pressure	B	Rectangular	0.005	2	0.002	1	0.002	0.01%	5.3E−06	2.8E−11
3	Temperature	B	Rectangular	0.34	1.73	0.2	1	0.2	22.3%	0.039	0.002
4	Positioning of chamber	B	Rectangular	0.2	1.73	0.12	1	0.12	7.7%	0.013	0.0002
5	Stability of Chamber (Drift)	A	Normal	0.5	2	0.3	1	0.3	35.9%	0.07	0.004
6	Electrometer Calibration	A	Normal	0.0995	2	0.05	1	0.05	1.4%	0.003	6.2E−06
	Contribution of chamber under test										
7	Pressure	B	Normal	0.005	2	0.002	1	0.002	0.01%	5.3E−06	2.8E−11
8	Temperature	B	Rectangular	0.34	1.7	0.2	1	0.2	22.33%	0.039	0.002
9	Positioning the chamber	B	Rectangular	0.2	1.7	0.12	1	0.12	7.67%	0.0133	0.0002
10	Resolution	B	Normal	0.001	1.7	0.0006	1	0.0006	0.01%	3.3E−07	1.1E−13
11	Reproducibility	A	Normal	0.02	1	0.02	1	0.02	0.18%	0.00032	9.9E−08
	Combined standard uncertainty, $u_c(y)$							0.42		0.17	0.0073

Uncertainty contribution $u(y_i)$ is estimated by multiplying the standard uncertainty $u(x_i)$ with the sensitivity coefficient. The resulting uncertainty contribution, standard deviation, is the same unit as the measurand and is scaled according to its influence on the measurand by

$$u(y_i) = c_i \cdot u(x_i) \tag{10}$$

Using the central limit theorem to combine all the uncertainty contributors in order to have a single value representing the standard deviation of the measurement system:

$$U_c(y) = \sum_{i=1}^{n} u(y_i)^2 \tag{11}$$

Using information from Table 1,

$$\begin{aligned} u(y_i)^2 &= 0.004 + (5.3\text{E}-06) + 0.04 + 0.07 + 0.003 + (5.3\text{E}-06) \\ &\quad + 0.039 + 0.0133 + (3.3\text{E}-07) + 0.0003 \\ &= 0.17 \end{aligned}$$

$$\begin{aligned} u(y_i)^4 &= (1.8\text{E}-05) + (2.8\text{E}-11) + 0.002 + 0.0002 + 0.004 + (6.2\text{E}-06) \\ &\quad + (2.8\text{E}-11) + 0.002 + 0.0002 + (1.1\text{E}-13) + (9.9\text{E}-08) \end{aligned}$$

$$u(y_i)^4 = 0.0073$$

Combined uncertainty

$$u_c(y) = \sqrt{u(y_i)^2} = \sqrt{0.17} = 0.42 \tag{12}$$

Effective degree of freedom calculated from Welch-Satterthwaite formula, in order to weighs the degree of freedom for each uncertainty by its uncertainty contribution:

$$v_{eff} = \frac{\{u_c(y)\}^4}{\frac{u(y_i)^4}{V_i}} = 6.1 \times 10^5 \tag{13}$$

Taking Level of Confidence to be 95.45%, which translate to a coverage factor of $K = 2$,

$$\text{Expanded Uncertainty} = u_c(y) \times 2.0 = 0.42 \times 2 = 0.84\% \tag{14}$$

In this regard, the overall expanded uncertainty was found to be 0.8% associated with ND,W of 57 mGy/nC, with a coverage factor of 2 and at level of confidence of 95.45%. This illustrates that the dispersion of results of data obtained from the radiation measurement can be described approximately by a Gaussian or normal probability distribution, with 95.45% of the results falling within ±2 standard deviations of the average value. This is because uncertainty of measurement is for specific beam quality and ionization chamber. The investigation therefore outlined the importance of measurement of uncertainty in analyzing the quality of radiation radiotherapy beam thereby building on work done by Bulinski [9].

Figure 4 illustrates that Type B had greater impact on the overall uncertainty

contribution compared to Type A. In this case, 62% of the contribution was from Type B compared to 38% of Type B, using data obtained from Table 1. This illustrates that external factor contribution of measurement had a more significant impact on the overall uncertainty contribution. Therefore, information obtained through measurement is limited and must be supplemented with information obtained from non-statistical means, which in this case include calibration certificates, manufacturer manuals, publications, historical data among others.

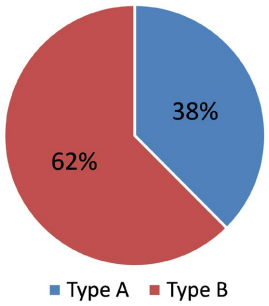

Figure 4. Type A and Type B contributions to the overall uncertainties.

Figure 5 illustrates the magnitude of each identified contributor to the overall uncertainty. This follows analysis of different components that contribute to uncertainty of measurement including environmental conditions, stability of the chamber, ionization chamber under test (UUT), resolution, reproducibility of measurement, positioning of the chamber and electrometer. The largest contribution was from stability of the standard ionization chamber, followed by temperature contribution standard chamber (STD) and clinical chamber (UUT).

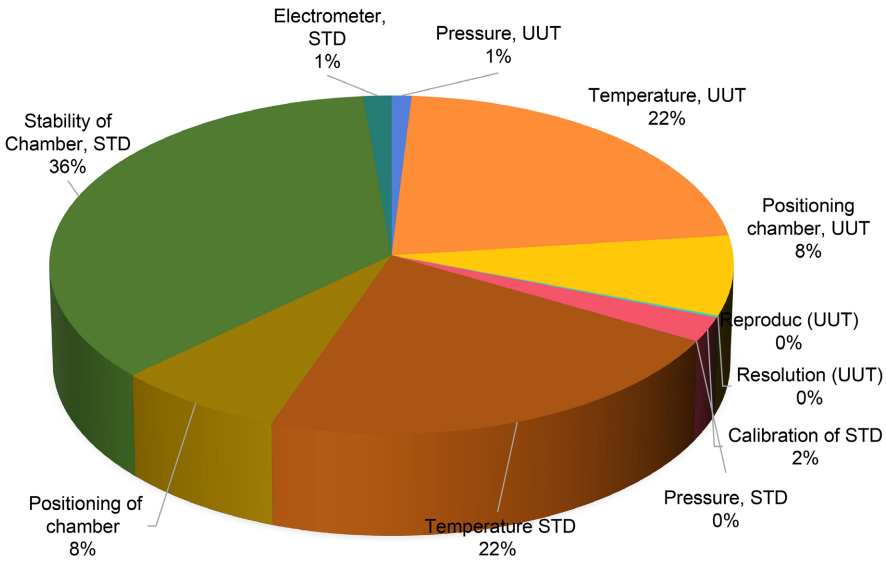

Figure 5. Analysis results for each contributor.

During analysis of uncertainty, not all the factors were available for considera-

tion including information about the geometry of the chamber and software. Furthermore, the calibration factor was obtained from calibration certificate and is prone to change due to use in a different environment.

4. Conclusion

The study established the impact of uncertainty of measurement in estimating radiotherapy dose. The investigation demonstrates that uncertainty of measurement can be used as a tool to judge the quality of beam used for radiotherapy treatment, through statistical analysis attributed to each measurand. The overall expanded uncertainty associated with 57 mGy/nC $N_{D,W}$ was found to be 0.8% corresponding to a confidence level of approximately 95% with a coverage factor of $k = 2$. The largest contributor of uncertainty of measurement was the stability of the reference ionization chamber at 36%. This was followed by temperature at 22% and positioning of the chamber from the source at 8%. The contribution of temperature and positioning of chamber was from both clinical and reference ionization chambers. Hence the equipment selected for radiotherapy measurement must be judiciously determined with good stability to reduce impactful contribution to the overall uncertainty. On the other hand, the uncertainty contribution from pressure, resolution and reproducibility was found to be less than 1%. Therefore, a good clinical radiotherapy outcome can be achieved by minimizing uncertainties by improving ionization chamber stability and controlling environmental condition.

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Conflicts of Interest

There was no conflict of interest in this study.

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