



Uncertainty Assessment: Relative versus Absolute Point Dose Measurement for Patient Specific Quality Assurance in EBRT

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Verification of dose distribution is an essential part of ensuring the treatment planning system's (TPS) calculated dose will achieve the desired outcome in radiation therapy. Each measurement have uncertainty associated with it. It is desirable to reduce the measurement uncertainty. A best approach is to reduce the uncertainty associated with each step of the process to keep the total uncertainty under acceptable limits. Point dose patient specific quality assurance (QA) is recommended by American Association of Medical Physicists (AAPM) and European Society for Radiotherapy and Oncology (ESTRO) for all the complex radiation therapy treatment techniques. Relative and absolute point dose measurement methods are used to verify the TPS computed dose. Relative and absolute point dose measurement techniques have a number of steps to measure the point dose which includes chamber cross calibration, electrometer reading, chamber calibration coefficient, beam quality correction factor, reference conditions, influences quantities, machine stability, nominal calibration factor (for relative method) and absolute dose calibration of machine. Keeping these parameters in mind, the estimated relative percentage uncertainty associated with the absolute point dose measurement is 2.1% ($k=1$). On the other hand, the relative percentage uncertainty associated with the relative point dose verification method is estimated to 1.0% ($k=1$). To compare both point dose measurement methods, 13 head and neck (H&N) IMRT patients were selected. A point dose for each patient was measured with both methods. The average percentage difference between TPS computed dose and measured absolute relative point dose was 1.4% and 1% respectively. The results of this comparative study show that while choosing the relative or absolute point dose measurement technique, both techniques can produce similar results for H&N IMRT treatment plans. There is no statistically significant difference between both point dose verification methods based upon the t-test for comparing two means.

Keywords: Uncertainty, EBRT, IMRT, Point dose, QA

Introduction

Uncertainty associated with each quality assurance (QA) procedure in external beam radiation therapy (EBRT) should individually be evaluated to minimise the overall uncertainty. The rationale is to minimise the uncertainty in

each QA procedure is to get a desirable clinical outcome, because normal tissue complication probability (NTCP) and tumour control probability (TCP) are directly related to the actual doses received by each organ at risk (OAR) and targets.¹⁾ The uncertainty associated with the actual delivered dose to the OARs and target volumes is the

reason for an increase or decrease in the variation of TCP and NTCP parameters depending on the slope of the dose response curve. The therapeutic ratio is based on the slope of the TCP and NTCP curve.^{2,6)}

Farmer type ionisation chambers are used as the local secondary standard for absolute dosimetry in many of clinical settings. Recently, a new FC23-C (volume 0.2cc) ionisation chamber (IBA Dosimetry Germany) became available to verify the point dose measurement for IMRT treatment plans. The chamber manufacturing company provides a secondary standard calibration laboratory (SSDL) chamber calibration coefficient in terms of absorbed dose in water (N_{D,w,Q_0}) at Cobalt 60 (^{60}Co) gamma ray beam quality. The calibration was performed at the IBA secondary standard calibration laboratory (SSDL) which is traceable to the primary standard dosimetry laboratory (PSDL). IBA uses the substitution method to measure the chamber calibration factor with an uncertainty of 2.2% at the 95% confidence level.⁷⁾

The 3D complexity of the dose in Intensity modulation radiation therapy (IMRT) treatment plan, along with the beam geometry and the resulting dose distribution, means that the QA of IMRT dose distributions needs to concentrate more on the cumulative delivered dose rather than on the QA of individual segments contributing to the overall dose delivered. Ezzell et al.⁸⁾ recommends performing a point dose measurement for IMRT treatment plans to verify the TPS computed point dose prior to patient treatment because of the complexity of the IMRT treatment plan. For point dose measurements, Low et al.⁹⁾ recommended, chamber should be made of tissue equivalent material.

Materials and Methods

1. Uncertainty with ion chamber measurement

All the components linked to measure the absolute or relative absorbed dose for patient specific QA needs to be analysed individually and estimate the standard uncertainty associated with each component. In this study, a rectangular distribution was assumed to estimate the type B uncertainties. A rectangular distribution to estimate the type B standard uncertainties is presented in Equation 1.

$$u_B = a / \sqrt{3} \quad (1)$$

Where u_B is the type B standard uncertainty and a is the maximum variation limits given by $\pm a$. To avoid the confusion, a coverage factor of $k=1$ is taken for each uncertainty value, corresponding to a confidence limit of 68.3% (One Standard deviation).

In this study, 13 H&N patients were selected. These patients were planned with the step and shoot IMRT treatment technique. Relative point dose measurement for these patients were already been measured in the CIRS H&N phantom using semiflex ionisation chamber (Serial #: 1976, Volume: 0.125 cc) with electrometer (PTW UnidosE, Serial # 090753). A sample calculation for point dose measurement using relative method for H&N IMRT treatment plans is presented in Appendix 1. To measure the absolute point dose measurement for these 13 patients, cross calibration of IBA FC23-C ionisation chamber was needed. As reported in TRS 398, if a field ionisation chamber is cross calibrated against the PSDL calibrated ionisation chamber, the uncertainty in the dose determination will increase by approximately 0.2%.¹⁰⁾ At Canberra hospital, clinical acceptable tolerance was chosen to be $\pm 3\%$ variation between the measured point dose and the TPS computed doses.

2. Absolute point dose measurement method

For absolute point dose measurements, a chamber calibration factor is required in term of the absorbed dose to water. The International Atomic Energy Agency (IAEA) technical report series (TRS) 398 dosimetry protocols was used to cross calibrate the field ionisation chamber.¹⁰⁾

1) Cross calibration of field chamber

The field ionisation chamber (IBA FC23-C, Serial number 2408) was cross calibrated with the local secondary standard ionisation chamber (NE 2571, Serial number 3036) using TRS 398. The reference chamber was calibrated (20 May 2016) at the APRANSA PSSDL. A solid water phantom (Gammex, Middleton, WI 53562, USA) was used to cross calibrate the field ionisation chamber because the reference chamber is not water proof.

Beam quality factor k_{Q,Q_0}^{field} for field chamber was obtained from Table 2 of IBA Doc-Id: P-Codes of Practice Absolute Dosimetry-510-001 01.¹¹⁾

2) Creation of the QA phantom in pinnacle TPS

The CIRS H&N phantom was scanned on a Toshiba Aquilion Large Bore CT (16 Slices) to create a QA phantom in the Pinnacle 9.8 TPS (Philips Radiation Oncology System, Fitchburg, WI) with the FC23-C ionisation chamber. The chamber sensitive volume was contoured during the creation of the QA phantom in the TPS and named as “sensitive volume”.

3) Treatment plan mapping on QA phantom

Before mapping the original treatment plans on the CIRS H&N QA phantom, the MUs of each treatment plan were recorded in the worksheet. After the plan mapping a few modifications were applied as listed below:

1. Remove the CT simulator couch,
2. Density of the sensitive volume overridden to 1 g/cm³,
3. Change the prescription to fixed MUs,
4. Set grid size (2 mm).

Couch was removed during the treatment plan mapping from the CIRS H&N phantom because the phantom was placed on the H&N extension board during the measurement of the point dose. Same setup was also used for the relative point dose measurement. To get a uniform dose distribution across the chamber sensitive volume the phantom position was adjusted in the TPS. This adjustment continued until the TPS computed standard deviation of chamber sensitive volume was $\leq 0.8\%$. Dose computation was computed using the collapsed cone convolution (CCC) algorithm.

4) Point dose measurement

To avoid the beam penetrating through the couch a carbon fiber head and neck extension board (Type-S FixatorTM Shoulder Suppression System by CIVCO) was used to treat the H&N IMRT patients. The CIRS H&N phantom was placed in net area of the H&N extension board because it has negligible transmission factor. This

area of H&N extension board was selected only for this experiment to reduce one variable which can effect on absolute point dose measurement due to attenuation of the radiation through the couch. A shift was applied to the phantom as recorded during the mapping of the treatment plan in TPS. Absolute dose of the LINAC was to correct for the day to day output variation of LINAC. Air density correction factors were calculated using measured temperature and air pressure as recommended in TRS 398. The phantom was exposed using the planned gantry and collimator angles. Absolute dose is calculated by using Equation 2. The measured point dose is corrected for the daily variation of the LINAC before comparing it with the TPS computed dose.

$$D_w = M^{field} \times N_{D,w,Q_0}^{field} \times k_{Q,Q_0}^{field} \times k_{pol}^{field} \times k_s^{field} \times k_{elec}^{field} \times k_p^{field} \quad (2)$$

3. Relative point dose measurement method

For relative dose measurement methods, the same steps were followed to measured cumulative charge of all the radiation beams for each IMRT treatment plan. To convert this cumulative charge reading to dose, a nominal calibration factor (NCF) of the chamber was carried out. Detail of nominal calibration is given below.

1) Chambers nominal calibration factor (NCF)

Before measuring the nominal calibration factor (NCF), leakage measurement test was performed. To calculate the NCF, chamber was exposed three times in water phantom with 6 MV for 200 MUs at calibration set up of the LINAC at 400 MU/min dose rate.

Similarly, the chamber was also exposed in the CIRS H&N phantom at Isocenter with 6 MV for 200 MUs at 400 MU/min dose rate (Fig. 1b) and record the electrometer reading. The detail calculation of the chamber nominal calibration factor (NCF) is explained in Appendix 1. A nominal calibration for semiflex ionisation chamber was carried out on 4 September, 2014. At each occasion, to account the LINAC output variation, the semiflex ionisation chamber was exposed to 200 MUs (Fig. 1b) before performing the relative point dose measurement for each H&N IMRT patient plan.

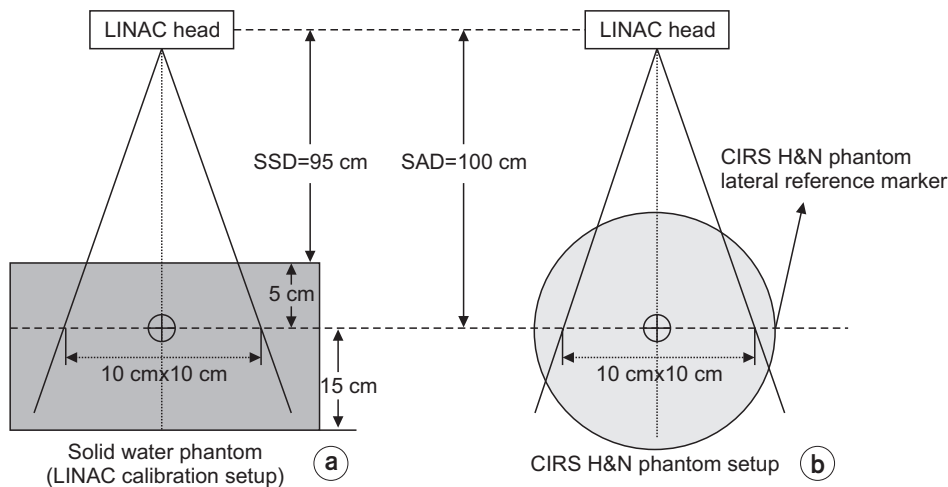


Fig. 1. Experimental setup to measure the nominal calibration factor. (a) LINAC calibration setup (solid water phantom), (b) The CIRS H&N phantom measurement setup.

Results

1. Uncertainty calculation in cross calibration

Several factors contribute to the uncertainty calculation in the cross calibration of the chamber using the TRS 398 dosimetry protocols. Each factor should be accounted for to calculate the total uncertainty associated with this process. The electrometer reading for reference and fields chambers are corrected for several factors like reading scale, polarity, air density, humidity, leakage, radiation background, distance and ionic recombination.

1) Chamber calibration factor (reference chamber)

Calibration factor (N_{D,w,Q_0}) of reference chamber was supplied by ADCL laboratory (ARPANSA) with expanded standard uncertainty 0.8% at a confidence level of approximately 95% ($k=2$).¹²⁾

2) Beam quality

In the TRS 398 dosimetry protocol, electron stopping powers for monoenergetic photon beam data is used which is presented in International Commissioning of Radiation Units and Measurements (ICRU) report 37, with the density effect model.¹³⁾ Beam quality factor (k_{Q,Q_0}) is a combination of different factors which are explained in detail in TRS 398.¹⁰⁾ These factors are derived from experiments and Monte Carlo (MC) simulation or other calculations. In the TRS 398 dosimetry protocol, for megavoltage photon energies, beam quality is specified by TPR_{20,10}. Besides

that, an additional factor involved in the determination of the beam quality is a linear interpolation of the table (Table 6III) to deduced the k_{Q,Q_0} .¹⁰⁾ The relative standard uncertainty in beam quality factor (k_{Q,Q_0}) is reported to be 1.0% in TRS 398 for cylindrical ionisation chambers.¹⁰⁾

3) Air density correction factor

Uncertainty associated with the air density correction factor depends on the thermometer and barometer resolution, calibration certificate and long term stability. The resolution of the thermometer and barometer used in this study are 0.1°C and 0.1 hPa respectively. Das et al.¹⁴⁾ also reported the affect of the temperature on chamber volume and its response; it should be taken into account if the temperature difference is higher than the normal calibration temperature. An estimated type B percentage standard uncertainty associated with the air density correction factor was reported by Castro et al.¹⁵⁾ 0.2%.

4) Polarity correction factor

Polarity effect depends on beam quality but cylindrical chambers do not have significantly dependency on beam quality.¹⁶⁾ The uncertainty associated with the polarity factor was estimated by accounting the machine reproducibility with the external monitor chamber. The standard deviation is 0.1% was calculated for both chambers with accounting the LINAC reproducibility. Total uncertainty was estimated 0.14% (associated with the user and standards laboratory).

5) Ion recombination factor

Ion recombination was calculated using a two voltage method.¹⁰⁾ The uncertainty associated with two voltage methods is based on the difference between expected value from the Boag theory and the value measured by two voltages method. The maximum deviation in polynomial fit error reported by Weinhou et al.¹⁷⁾ ⁶⁰Co beam quality was used to measure the ion recombination for reference ionisation chamber in standard laboratory. Similarly, two voltages method was used to calculate the ion recombination for reference ionisation chamber. The maximum difference 0.16% was reported between two voltage method and Zankowski et al.¹⁸⁾ model for cylindrical chambers. The combined estimated value of the ion recombination was 0.16% for field and reference chamber.

6) Humidity

No correction for humidity was needed because the calibration certificate was referred a relative humidity of 50% and this condition was also satisfied during our measurements.¹²⁾ If no correction is made for humidity effect, a maximum error of 0.3% is estimated in the range of 0% to 100% relative humidity.¹⁵⁾ Thus the uncertainty associated due to humidity is estimated 0.17% assuming the rectangular distribution.

7) Reference conditions

The reproducibility of reference conditions include the source to surface distance (SSD), depth of measurement (d), setting of the field size. The uncertainty associated with the reproducibility of the reference conditions was reported 0.4% in TRS 398.¹⁰⁾

8) Charge reading

The standard deviation of the charge reading of well-behaved therapy level chamber should not exceed 0.3%.¹⁹⁾ The variation in the charge reading depends on the following factors, reproducibility, display resolution, electrometer linearity, correct nulling of the electrometer and long term stability of the chamber. The uncertainty in the charge reading for both chambers (reference and field chamber) is estimated to 0.3%.

9) Electrometer calibration

In our case, the reference chamber and electrometer were calibrated as a system in a standard dosimetry laboratory. During the calibration, filed ionisation chamber and electrometer calibrated as a system. An electrometer calibration correction factor is applied only when the electrometer and chamber are calibrated separately.

Overall relative percentage uncertainty associated with reference and field chamber is estimated for each influenced quantity. Calculated combined total uncertainty in the chamber calibration coefficient is presented in Table 1.

2. Uncertainty calculation for point dose measurement methods

Uncertainty associated with each point dose measurement method is estimated and presented in the Table 2. Uncertainty associated with the nominal calibration factor for the relative point dose measurement method is estimated 0.7% including the setup reproducibility, beam monitor system, temperature change, charge reading and long term stability of the electrometer and chamber.

3. Cross calibration of field chamber

Results are presented in Table 1 for all the influence

Table 1. Percentage relative standard uncertainty of the each factor associated with the field and reference ionisation chamber.

Items	Percentage relative uncertainty	
	Reference chamber	Field chamber
$u(N_{D,w,Q_0})$	0.4	NA
$u(k_{Q,Q_0})$	1	1
$u(k_p)$	0.2	0.2
$u(k_p)$	0.1	0.1
$u(k_s)$	0.16	0.16
Humidity $u(k_h)$	0.17	0.17
Reproducibility of reference condition	0.4	0.4
$u(M)$	0.3	0.3
$u(MU)$	0.12	0.12
Percentage relative standard uncertainty ($k=1$)	1.24	1.18
Total uncertainty ($k=1$)	1.7%	
Extended uncertainty ($k=2$)	3.4%	

Table 2. Percentage relative standard uncertainty of the each factor associated with the absolute and relative point dose measurement methods and total percentage relative standard uncertainty and extended uncertainty.

Items	% Relative uncertainty (point dose measurement methods)	
	Relative	Absolute
$u(N_{D,w,Q_0})/u(NCF)$	0.7	1.7
$u(k_{Q,Q_0})$	NA	1
$u(k_t)$	0.4	0.4
Setup reproducibility	0.4	0.4
Long term dosimeter stability	0.3	0.3
Electrometer charge reading	0.3	0.3
$u(M)$		
Beam Monitor $u(MU)$	0.12	0.12
Percentage relative standard uncertainty ($k=1$)	1.00	2.07
Extended uncertainty ($k=2$)	2.0	4.2

quantities required for the cross calibration of the field chamber. Calibration factor of the reference ionisation chamber in terms of absorb dose in water at ^{60}Co beam quality was obtained from the PSDL calibration certificate.¹²⁾ The cross calibration coefficient of the field chamber was obtained by using TRS 398 dosimetry protocol.

$$N_{D,w,Q_0}^{field} = 13920 \text{ mGy} / nC \quad (3)$$

4. Point dose measurement

The measured absolute point dose difference was within $\pm 3\%$ as compared to the TPS computed point dose except patient 3. Results of the measured point dose with the relative method are also presented in Table 3.

The average percentage difference between the TPS computed dose and measured absolute and relative point dose was 1.4% and 1% respectively for all H&N IMRT treatment plans Fig. 2.

5. Statistic significance

Standard deviation of absolute and relative point dose measurement methods are 0.9% and 1.2% respectively. The standard deviation shows that the absolute point dose measurement method has relatively better reproducibility than the relative method.

Table 3. Percentage dose difference between measured dose (relative and absolute method) and TPS computed dose for H&N IMRT treatment plans.

Patients	Percentage Dose difference between measured and TPS computed dose	
	Relative method	Absolute method
1	-1.1	1.19
2	-0.1	0.40
3	1.38	3.45
4	1.2	1.08
5	2.2	0.06
6	2.5	1.93
7	1.35	1.36
8	0.0	1.42
9	1.5	2.19
10	1.40	1.40
11	1.40	1.56
12	-1.3	0.21
13	2.0	1.60
SD	1.2	0.9

Both methods were analysed statistically to see the difference. An independent samples t-test was conducted to compare the means of percentage point dose difference for absolute and relative methods. There was not a significant difference in the score of absolute ($M=1.37$, $SD=0.90$) and relative ($M=0.95$, $SD=1.20$) point dose measurement methods ($t(24)=-0.91$, $P=0.32$).

Discussion

The estimation of the type B uncertainties is partly based on subjective consideration and published literature. The components associated with the cross calibration factor have been shown to be able to considerably change the uncertainty in the chamber calibration coefficient due to beam quality correction factor. In this study, beam quality correction factor is based on the theoretical calculation and it does not consider chamber to chamber disparity. The uncertainty in chamber calibration coefficient will increase if the ionisation chamber is cross calibrated with the primary standard for photon beam due to this additional step of cross calibration. According to TRS-398 dosimetry protocol, the uncertainty in dose determination increases by approximately 0.2% if the field ionisation chamber is used to determine the absolute dose.¹⁰⁾

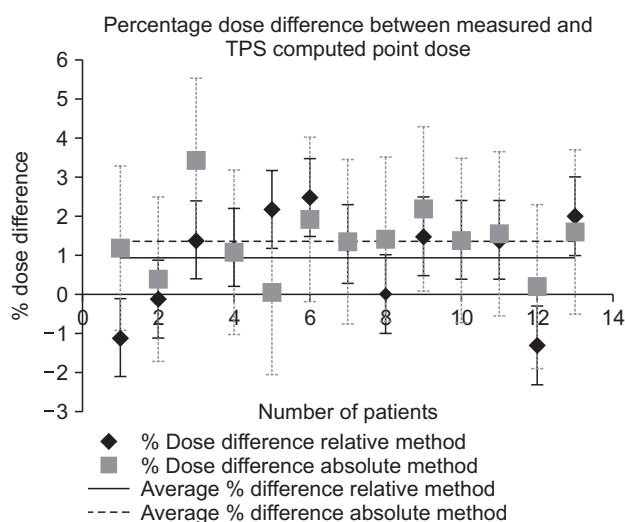


Fig. 2. Comparison between measured point dose (relative and absolute method) with TPS computed dose.

The uncertainty associated with this cross calibration (FC23-C ionisation chamber) was estimated 1.7% ($k=1$). This cross calibration factor was used to determine the absolute point dose for H&N IMRT treatment plans. The measured absolute point dose difference was found within $\pm 3\%$ as compared to TPS computed point dose except for one patient (3.45%). The difference is most likely due to the high standard deviation (1.5%) in the TPS computed dose to chamber sensitive volume resulting from the highly modulated dose distribution. To reduce the standard deviation in the TPS computed dose, the chamber position was shifted multiple times but it was not possible to reduce the standard deviation to below 1.5%. For absolute method, the measured dose is higher than the TPS computed dose by 1.4% on average of 13 patients. For relative method, the measured point dose was higher than TPS computed dose by $\sim 1\%$ on average. Average percentage difference between these two point dose measurement methods is approximately 0.5%. In Fig. 2, it can be seen that the average value of both point dose measurement methods are laying in the positive axis of the percentage dose difference. Most of the commercial TPS has limitation to model the MLC leakage precisely which may cause this difference as reported by Gareth et al.²⁰⁾ Another possible reason may be MLC transmission, which increases with the field size, but most of commercial TPS use only a single value for it.²¹⁾ Semiflex ionisation chamber was used for

relative point dose measurement method which has small sensitive volume as compared to the FC23-C ionisation chamber. In Varian LINACs, independent jaws open to the maximum field size during the step and shoot IMRT delivery and jaws do not conform to each segment. Those segments which are quite far from the chamber sensitive volume, also contribute to the chamber signal due to MLC transmission, intraleaf leakage and interbank leakage. It is also reported that stem effect of the chamber will increase with the increase the exposed length of stem.²²⁾

The estimated extended uncertainty ($k=2$) associated with the absolute point dose measurement method is almost double the relative point dose measurement method. The major contribution in the estimated uncertainty associated with the absolute point dose measurement method is coming from the chamber cross calibration coefficient and beam quality correction factor (k_{Q,Q_0}). The difference in the mean value of these measurement methods is $0.5\% \pm 2.1\%$. The difference in the mean value of 0.5% is not significant when compared to the percentage standard uncertainty of 2.1%.

In order to demonstrate if there is a significant difference between the methods, the subtraction of the mean on one against the other can be performed and compared to the uncertainty involved. This uncertainty can be assumed to follow the summation of the individual errors in quadrature.

Conclusion

It can also be concluded from the results that absolute point dose measurement method does not produce results different from the relative point dose measurement method for head and neck IMRT treatment plans.

Conflicts of Interest

The authors have nothing to disclose.

Availability of Data and Materials

All relevant data are within the paper and its Supporting Information files.

Ethics Approval and Consent to Participate

The study was approved by the institutional review board (IRB approval number; ETHLR.17.044).

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<Appendix 1>

Nominal Calibration Factor (NCF)

Setup to measure the NCF is shown in Fig. 2. NCF is obtained by dividing the electrometer reading in solid water phantom to the CIRS H&N phantom for 200 MUs. Electrometer reading was not corrected for temperature and pressure because the temperature and pressure was remained constant during the measurement.

NCF for 6 MV (Semiflex)

Electrometer reading in Solid water phantom at LINAC calibration Setup for 200 MUs	(X)=6.784 nC
Electrometer reading in the CIRS H&N Phantom (setup in Fig. 1b) for 200 MUs	(Y)=6.146 nC
NCF	(X)/(Y)=1.104

Nominal Dose for 6 MV in the CIRS H&N Phantom (Semiflex)

Nominal dose (ND) in the CIRS H&N phantom was calculated by dividing the total MUs (200 MU) delivered in the CIRS H&N phantom at LINAC calibration setup (Fig. 1b) by the NCF. A sample calculation of ND for semiflex ionisation chamber in the CIRS H&N phantom for 6 MV is given below. LINAC calibration set up (field size=10 cm×10 cm, SSD=95 cm, Depth=5 cm, Dose per MU=0.01 Gy/MU) is shown in the Fig. 1a.

$$\begin{aligned}
 \text{ND (Gy) per 200 MU in the CIRS H\&N phantom} &= ((\text{LINAC Calibration (Gy/MU)} \times (\text{Total delivered MUs}))/(\text{NCF})) \\
 &= (0.01 \text{ Gy/MU} \times 200 \text{ MU}) / (1.104) \\
 &= 1.812 \text{ Gy}
 \end{aligned}$$

Sample calculation of point dose measurement

A step by step example of how to calculate the relative point dose for H&N IMRT treatment plans is presented below. In this example the TPS computed mean dose was 76.3 Gy in 35 fractions to the chamber sensitive volume. To account the daily variation of the LINAC, the semiflex chamber was exposed three times in the H&N CIRS phantom (average reading was 5.546 nC) and set up information is tabulated in Table 4. After that the predetermined position of the phantom was adjusted as recoded during the treatment plan mapping on the CIRS H&N phantom. The cumulative charge was 5.969 nC was recorded for all the radiation beams of the treatment plan.

Table 4. Setup information to expose the semiflex ionisation chamber in the CIRS H&N phantom to account the daily variation of LINAC output.

Parameters	Values	Parameters	Values
Field Size	(10 cm×10 cm)	Gantry angle	0°
Collimator angle	0°	Energy	6 MV
MUs	200	Dose rate	400 MU/min

Point dose calculation

Total TPS computed dose for all fractions to chamber sensitive volume

$$(A)=67.40 \text{ Gy}$$

Total number of fractions

$$(B)=35$$

TPS computed dose per fraction (Gy)

$$(C)=(A)/(B) \\ = 1.926 \text{ Gy}$$

Average electrometer reading at reference setup in the CIRS H&N Phantom for 200 MU

$$(D)=5.546 \text{ nC}$$

LINAC daily variation correction (Gy/nC)

$$(G)=(ND)/(D) \\ =0.327 \text{ Gy/nC}$$

Total charge collected for all IMRT beams (nC)

$$(H)=5.969 \text{ nC}$$

Measured dose (Gy)

$$(H)=(G) \times (H) \\ = 1.952 \text{ Gy}$$

Percentage dose difference between TPS and measured point dose

$$=[1 - \{(H)/(C)\}] \times 100 \\ =1.35\%$$