Empirical Validation Of Absorbed Dose To The Rectum In The Treatment Of Cervical Cancer Using High Dose Rate Brachytherapy

Justice Avevor, Joseph Amoako, George Amoako

Abstract: In brachytherapy treatment of the cervix, the tolerance of the normal tissue is often the limiting factor for the dose that can be delivered to the patient. The objective of this study is to determine the absorbed dose to the rectum in high dose rate brachytherapy of cervical cancer for empirical validation and system verification for patient treatment and safety. The dose distribution measurements were carried out in a locally constructed phantom. Gafchromic EBT3 films were used as a dosimeter for measuring doses to the rectum. The deviation between TPS dose and the film dose measured by the Gafchromic EBT3 film at the rectal point was 14.73%. This ranged from -47.22% - 51.06%. The doses predicted by TPS were higher than the doses measured by the film. At the rectal point 47% of the doses measured by the film were higher than the doses calculated by the TPS. For the rectum, the discrepancies between TPS dose and measured dose that were larger than 15% occurred in 64% of the entire treatment. Deviations at rectal point larger than 30% occurred in 6% of the entire measurements. In vivo dosimetry is the only practical way to check the delivered dose during treatment, because it provides the needed information which aids in assuring precise, targeted and conformal dose delivery.

Keywords: Brachytherapy, HDR, Gafchromic EBT3 Films, TPS, Rectal Dose

1 INTRODUCTION

Accuracy, careful planning and delivery are major requirements in treating cervix cancer using high dose rate brachytherapy (BT). This is crucial because a major part of the treatment site is in close proximity to critical organs and healthy tissues. It is important that the HDR used in the treatment performs very effectively and accurately to affect a series of planned source dwells treatment. Dose delivery accuracy depends on source positioning, because of the short distances between target and source, steep dose gradients and large inverse square law corrections for any geographic errors. In BT treatment, even small geometric uncertainties or errors may result in large dose discrepancies from the original treatment plan. These discrepancies may result in inadequate dose delivery to the target and/or increased dose to organs at risk and healthy tissues [1]. In-vivo dosimetry (IVD) is an important quality assurance technique for HDR BT for the cancer of the cervix. IVD is the only practical way to check the delivered dose during radiotherapy and BT. Through IVD, discrepancies in the dose delivered and the dose calculated using treatment planning system (TPS) may be determined. IVD supplies the needed information which aids in assuring precise, targeted and conformal dose delivery. Reports have proven that IVD is feasible and can be performed to predict dose delivery to the rectum and bladder during HDR BT also using Co-60 [2].

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The error types during BT treatments and their rates of occurrence are not well known. This knowledge gap is partially due to the absence of independent verification systems of the sequence in treatment in the clinical workflow routine. It is accepted that real time IVD can make available efficient error detection and treatment verification within the field of IVD. However, the non existence of high accuracy IVD systems that are straightforward for clinicians have hindered the widespread implementations of the systems [3]. Modern BT is growingly implementing the three-dimensional (3D) imaging, TPS based and remote afterloading [for HDT BT]. Due to these evolutions, the use of manual procedures has reduced, which are a common source of errors in radiotherapy (RT), [4], [5], [6], [7]. However, BT still typically involves more manual procedures during catheter/applicator insertion, treatment planning and treatment delivery than external beam RT (EBRT). Again, the verification of treatment delivery is not advanced in BT as it is in EBRT. This makes BT more susceptible to errors than EBRT. Application of 3D imaging in BT has enhanced the frequent implementation of individualized adaptive approaches via dose optimization and geometry of implants. The accuracy of dose delivery, conformality of dose to target and the reliability of the treatment flow are becoming very important. There is an improvement in understanding the correlation between dose and its effects on the patient and staff by the availability of the 3D dose distributions. This has paved way for an improved prospect to plan and direct treatments according to certain dose constraints in the balancing and prioritization between the target and organ-at-risk (OAR) doses. The effects of dose variations are more pronounced, particularly for patients with target and/or OAR doses close to constraint values, hence the need to control the precision of dose delivery [8]. There is a need to establish procedures for error detections and variations in future treatments verification so as to improve the overall accuracy of treatment delivery. This must be included in the context of high dose gradients in BT which makes treatments deliveries and precise dose measurements very challenging, because a small error or geometric discrepancy can result in large dose variation from the intended treatment plan. These discrepancies can result in inadequate dose delivered to the target and/or increased OAR doses. Errors in BT treatment are classified into human errors (e.g. incorrectly specified source strength, erroneously connected source transfer guide tubes and gross applicator reconstruction errors) or equipment malfunctions (e.g. defective afterloader stepping motor and flaws in the control software). There is limited information on these kinds of errors during treatment in BT and their rates of occurrence. Available sources of information addressing errors during RT include dedicated databases as reported by Chambrette et al. and Cunningham et al. [9], [10]. There is a possibility, however, that a significant portion of these errors are not known to the RT community since treatment centres are not subject to guidelines that demand public reporting when treatment errors are detected. Also, there are no control methods to monitor the flow of treatment in BT that are independent of the treatment delivery system; hence it is likely that these errors remain unknown in the entire treatment. In this paper, we determined the absorbed dose to the rectum in high dose rate BT of cervical cancer for empirical validation and system verification.

2 MATERIALS

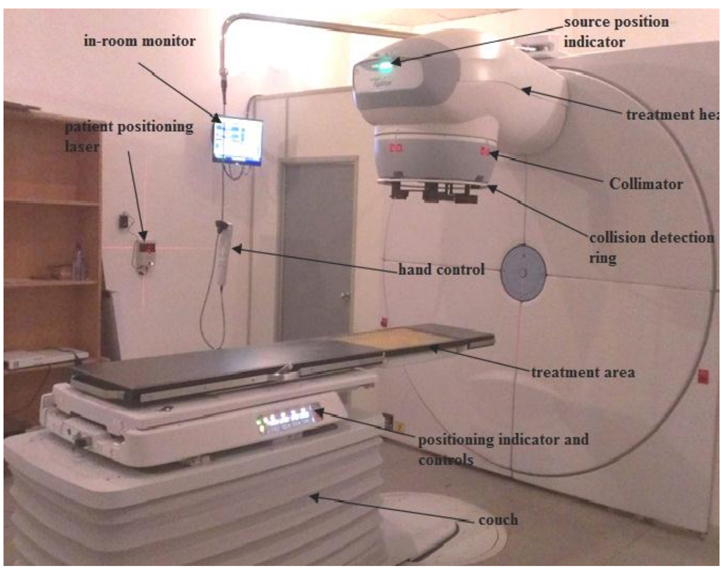

Fig 1: *Therathron Equinox 100 Cobalt - 60 Teletherapy Unit*

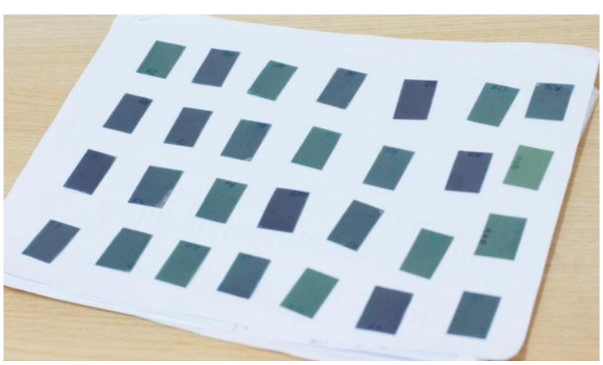

Fig 2: *Gafchromic EBT3 films*

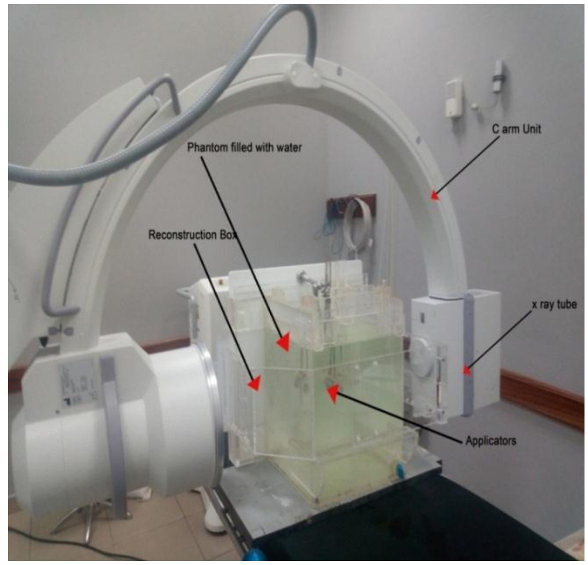

Fig 3: *C-arm fluoroscopic x-ray unit in an anterior-posterior position.*

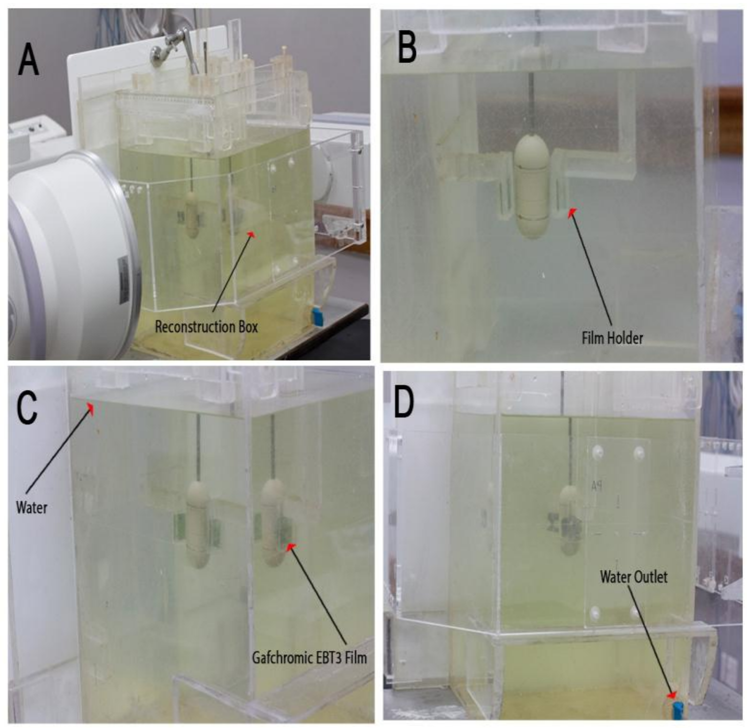

Fig 4: *Phantom filled with water for dose measurements showing (A) C-arm imager (B) Film holder (C) Gafchromic EBT3 film (D) Water Outlet*

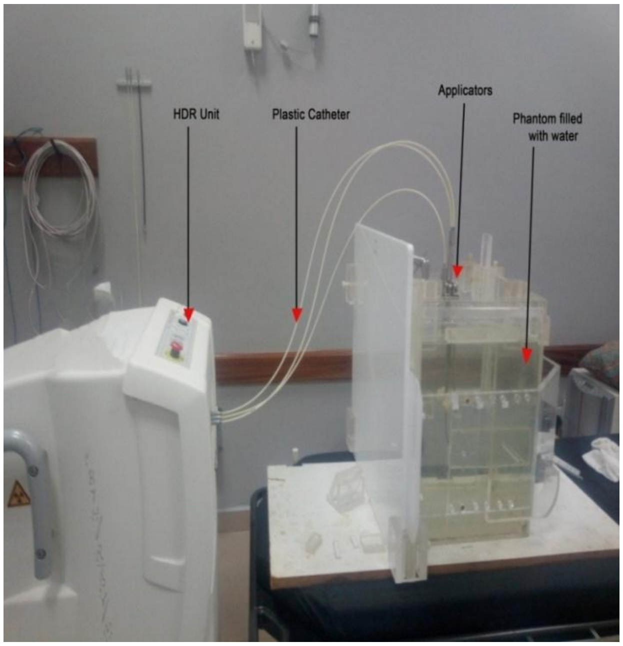

***Fig 5:** The experimental set up showing plastic catheters connected from the HDR treatment unit to the Fletcher suite of applicators in the locally constructed phantom filled with water.*

3 METHOD

3.1 Beam Output Measurement

The beam out measurement was determined using the equation 1 as proposed method by the IAEA [11].

$$D_{w,cal} = M \,.\, N_{d,w}\,(Gy\ /\ \min) \qquad (1)$$

$$M = M_l \bullet K_{TP} \bullet K_{pol} \bullet K_{ele} \bullet K_{sat} \qquad (2)$$

where, $M_l = \left(\frac{M_+}{\min}\right)$, is the uncorrected dosimeter reading in nC/min.)

$K_{TP} = \left(\frac{273.2 + T}{273.2 + T_O}\right) \times \frac{P_O}{P}$ is the room pressure and temperature of the air in the chamber cavity at the reference calibration conditions. P and T are the pressure and temperature measured during the experiment respectively.

$K_{pol} = \left(\frac{|M_+| + |M_-|}{2M}\right)$ is the polarity correction factor where M_+ and M_- are the

electrometer readings at the voltage $+V_1$ and $-V_1$ respectively; M is the absolute value of $M_+$for which voltage the chamber was calibrated. These readings are measured in nanocoulomb (nC).

K_{elec} is the dimensionless Electrometer calibration factor.

$K_{sat} = \left(\frac{\left(V_1/V_2\right)^2 - 1}{\left(V_1/V_2\right)^2 - \left(M_1/M_2\right)}\right)$, is the dimensionless recombination correction factor where

V_1 is the normal polarizing voltage, and V_2 is the reduced polarizing voltage.

$V_1 > V_2$, M_1 and M_2 are the readings at V_1 and V_2 respectively in (nC).

Beam output determination in this research was carried out using the Therathron Equinox Teletherapy Treatment Unit; at the field size of 10 for the reference field size of $10 \times 10\ cm^2$ at a depth of $5\ cm$ using the PTW 30001 ionization chamber with the mini water phantom. The ionization chamber's stability was checked using the strontium-90 check source kit provided by the manufacturer of the ionization chamber. The mini water phantom was filled with water and precautionary measures were taken to eliminate air bubbles that were trapped in the phantom. The phantom was filled with water to the brim and air bubbles were avoided. Special light field congruence and radiation tests were performed on the Therathron Equinox cobalt 60 machine using the MEDTEC iso-alighner and RT non-screen film to ensure the field size parameters are accurate and that of the radiation for the treatment machine. Source to surface (SSD) irradiation technique was employed during the beam calibration so that the SSD indicated by the optical distance measuring device on the gantry of the Therathron Equinox machine read $80\ cm$ on the surface of the manual water phantom. The manual water phantom was then carefully placed on the couch of the Therathron Equinox treatment unit and a digital spirit level was placed on the surface of the phantom to check its flatness. A slight adjustment was made to the phantom to ensure that the field size on the surface of the phantom corresponds with the light field of that of the Therathron Equinox treatment unit. The dose rate of the machine was then determined using the IAEA TRS 398 procedure [11] and verified with the TPS. A treatment plan was created such that it had the same configurations as the research set up with a dose of $2\ Gy$ being prescribed to the region of measurement and the treatment time was obtained. Using the TRS 398 formulas with manual calculations, the dose rate derived from the ion chamber was used to calculate the treatment time for the prescribed dose using equation 3.

$$Time = \left(\frac{Prescbribed\ Dose}{PDD/_{100}\ .\ Dose\ Rate.\ Decay\ factor}\right) - Shutter\ time \qquad (3)$$

The treatment time for the prescribed doses ranged from 0 – $1000\ cGy$ with a variation of $20\ cGy$ to a treatment depth of $5\ cm$ for SAD irradiation technique, using the iso-centre as the dose normalization point.

3.2 Calibration of Gafchromic EBT3 Films

Ten (10) strips of Gafchromic EBT3 films with the same lot number were cut to dimensions of $2.6\ cm \times 3.2\ cm$ and inserted in the manual water phantom. This was done such that the strip of film was at a depth of 5cm from the radioactive source within the phantom. The film was then inserted in perspex flab in the phantom. The phantom was aligned in a way that it was central to a field size of $10\ cm \times 10\ cm$ towards the direction of propagation of the beam whilst the gantry was kept at 0^{o}. The rest of the films were then exposed perpendicularly one after (0 cGy to 1000 cGy) the other to the cobalt 60 beam and the duration of exposure recorded (treatment time). The films were stored for 24 hrs to allow the colorization to reach its peak and also for the stabilization of post exposure density growth [20] before being scanned and analyzed. An EPSON scanner was used to scan all the irradiated films in a transmission mode. The films were arranged in the centre of the scanner and positioned in such a way that the longest side was perpendicular to the scanning direction according to the manufacturer's specification. The EBT3 films were split into (Red-Green –Blue Channels) (RGB). The images were then converted to a depth of 16 bits per color channel of spatial resolution of 72 dpi corresponding to a pixel size of $0.35 \times 0.35\ mm^2$ and saved in a Tagged Image File Format (TIFF). The scanned images of the film were then imported into the ImageJ software (National Institute of Health, USA) for analysis. In using the ImageJ the images were split into Red-Green-Blue Channels. Image measurements were performed on the point of interest which was the centre of each image of the irradiated film. Film intensity values were obtained from the ImageJ. The film intensities were then converted into net optical densities (OD) using the equation 4. A graph of prescribed dose as a function of optical density was plotted to determine the calibration curve or sensitometric curve of the Gafchromic EBT3 films for all three color channels (RGB). The best regression came from the green channel. The equation from the Green Channel was then used to calculate the optical density of the film to the absorbed dose measured by the film. A reproducibility test was performed on the EPSON Scanner. This was done by scanning a film repeatedly at different times. The film non-uniformity and film-to-film variations were determined from eight films selected randomly from the same film lot number using the method proposed by Saur et al [12] Using the method proposed by Van et al, 2008 [13], the overall accuracy of the Gafchromic EBT3 films was determined. This takes into consideration the most pronounced sources of uncertainties in dose determination when using the film (scanner, lateral correction, fit accuracy, intra-batch variation, background, intrinsic film inhomogeneity). An overall uncertainty was obtained using the error propagation analysis. The experimental set up for the beam calibration is shown in fig 6.

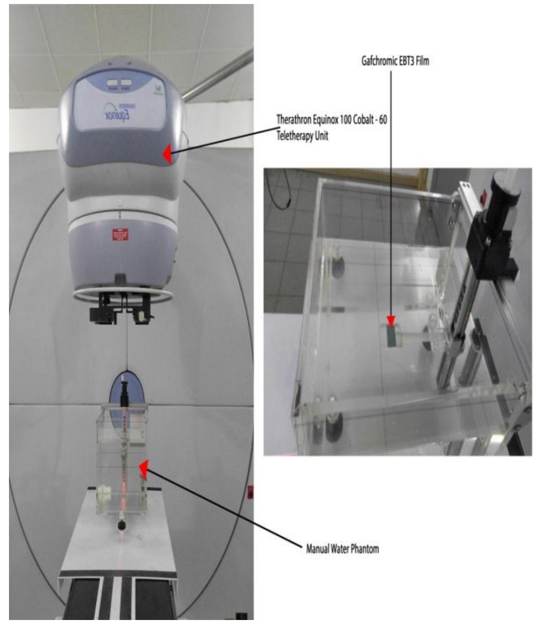

Fig 6: *A set-up for Beam Output measurement and Calibration of the Gafchromic EBT3 Film.*

3.3 Measurement of dose to the Rectum.

The applicators were inserted into the phantom as shown in fig 3 and carefully tightened and held in place by a metallic knot to minimize applicator movements. The applicators were positioned such that they lied close to the rectal compartment created inside the phantom. The phantom was then filled with water and the applicators held in their respective positions. The Siemens C-arm fluoroscopic x-ray machine as shown in fig 3 was used in taking orthogonal images of the applicators held in place inside the phantom. During each insertion of the applicators, two orthogonal images were taken; the lateral view as shown in figs 7 and 8 for Fletcher suite of applicators and anterior – posterior view as shown in figs 9 and 10 for cylinders only. For insertions that included the Fletcher suites of applicators (applicators involving tandems with the ovoids), doses were prescribed to point A, however, for insertions involving only cylinders, doses were prescribed to the surface of the voids at a depth of $0.5\ cm$ from the surface of the ovoids. This is in accordance with BT treatment protocol.

3.4 Treatment Planning

The orthogonal radiographs taken were then imported into the TPS (HDR-Plus) via a diacom transfer for planning. On the TPS the acquired images were reconstructed using the reconstruction box (i.e. determination of magnification and orientation of the images). The applicators used were selected from the applicator library and superimposed on the system. Then the dose to point A was defined as well as dose to the rectum. The dwell positions of the cobalt-60 sources are selected on both the tandem and the ovoids. The prescribed dose was then normalized to point A and calculated. Fig 11 depicts the TPS planning window for insertion involving Fletcher suites of applicators. For insertions where only the cylinders were used as shown in fig 12, the doses were prescribed at $0.5\ cm$ to the surface of the cylinder. The prescribed doses were then normalized and calculated. After the calculation the TPS generates a dose control point report indicating the Point A dose, minimum dose, average dose and maximum dose for the rectum. Ninety five (95) different clinical insertions were performed on the locally constructed phantom. Different applicator configurations that were used in the treatment of patients at the center were used in the insertions. Gafchromic EBT3 films with Lot#04201601 that had already been calibrated were cut to $2.6 \times 2.7\ cm^2$ to and inserted into the compartment designed in the phantom which mimics the rectum. This was done cautiously to avoid the movement of the applicators. The films were placed inside the phantom as shown in fig 4C after the orthogonal images were taken. Catheters were used in connecting the applicators to the respective channels on the HDR BT treatment unit as shown in fig 5. After these connections the doors are locked and the treatment was initiated with the HDR brachytherapy treatment unit from the monitor in the control room. The Cameras installed in the treatment room enabled the monitoring of the entire treatment process. For each treatment, the overall time was noted and this ranged from 10 mins to 45 minutes depending on the prescribed dose and the type of applicators used. The films were labelled after each irradiation and were scanned after 24 hours to allow the colorization to reach its peak. Fig 2 shows strips of the irradiated films. An EPSON scanner was used to scan all the irradiated films in a transmission mode. The films were arranged in the centre of the scanner and positioned in such a way that the longest side was perpendicular to the scanning direction. Films that were not irradiated (unexposed) were placed at the end of the irradiated ones. ImageJ software was used to determine the intensities of the irradiated films (I) and the intensities of the films that were not irradiated (I_O) to serve as a control. The film intensities were then converted to optical density (OD) using equation 4.

$$Optical\ Density = \log_{10}\left(\frac{I_O}{I}\right) \qquad (4)$$

Where I_o is the intensity of the exposed film and I is the intensity of the exposed film (irradiated)

The optical densities obtained were converted to doses using equation 5 obtained from the sensitometric curve.

Doses computed by the TPS were compared with doses measured using the Gafchromic EBT3 films and the percentage difference was determined using equation 5

$$\%\ difference = \frac{TPS\ Dose - Film\ Dose}{TPS\ Dose} \times 100 \quad (5)$$

where TPS Dose is the dose calculated by the TPS.

Fig 7: *An anterior – posterior radiograph (AP) of the Fletcher suite of applicator insertions obtained from one of the experimental set-ups.*

Fig 8: *Lateral (LAT) radiograph of the Fletcher suite of applicator insertions obtained from the experimental set-up.*

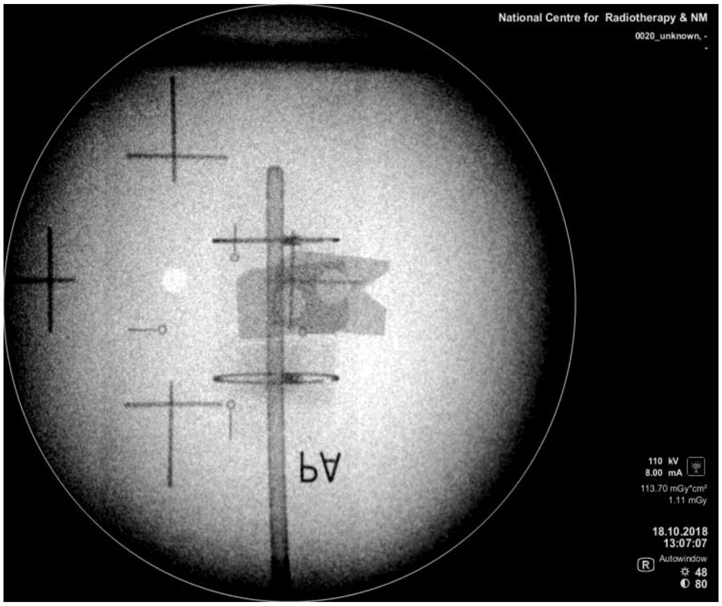

Fig 9: *An Anterior – Posterior (AP) radiograph of the applicator (cylinder only) insertions obtained from the experimental set-up.*

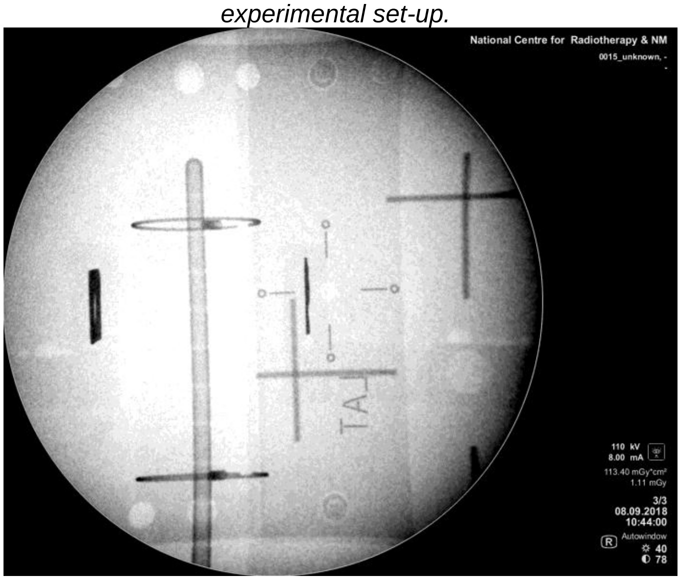

Fig 10: *Lateral radiograph (LAT) of the applicator (cylinder only) insertions. obtained from the experimental set-up.*

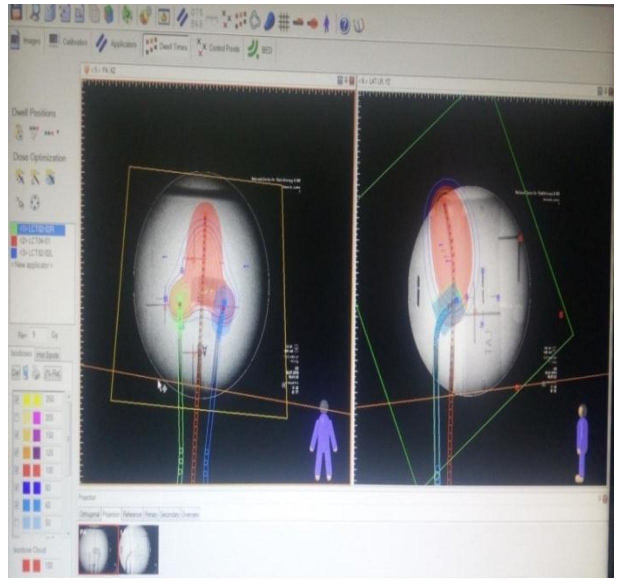

Fig 11: *TPS window showing treatment plan for dose calculation for Fletcher suite of applicators.*

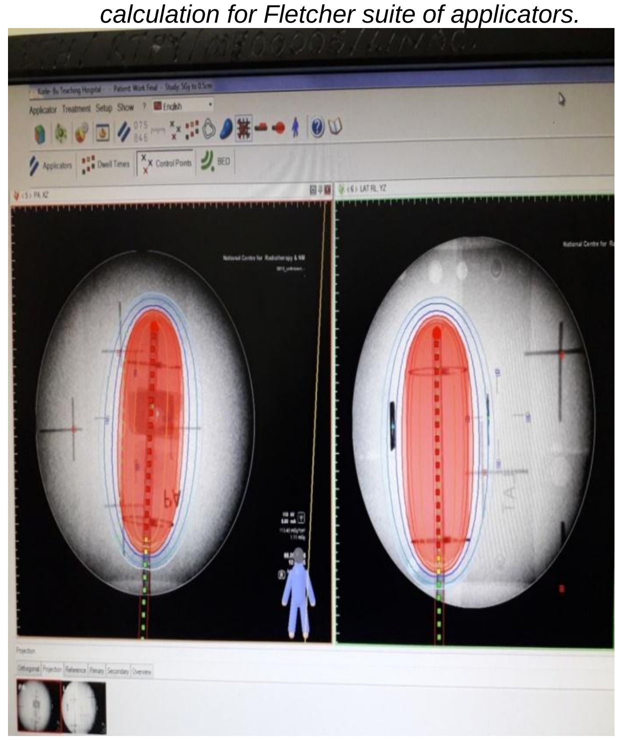

Fig 12: *TPS window showing treatment plan for dose calculation for cylinders only.*

4 RESULTS

The beam output measurement was determined using the IAEA calibration protocol (TRS 398). The results of the parameters of the TRS 398 have been shown in table 1. A calibration curve was plotted to show the variation of the optical density with the dose. In fig 13, a plot of dose as a function of optical density is shown for the Gafchromic EBT3 film. The Regression equation and the correlation coefficient R^2 are presented above the curve. After the irradiation of the gafchromic films, a good linear correlation was obtained between the absorbed dose and the optical density of the film. The correlation coefficient R^2 = 0.998, is very close to unity and this signifies that the regression equation can be used to predict the absorbed dose of the film using its optical density (OD). Microsoft excel was used to obtain the regression equation and this is given as:

$$y = 5718.6\times^{3} - 94.833\times^{2} + 1388.7\times - 3.9103 \quad (6)$$

where x is the optical density and y is the measured dose (dependent parameter). The optical densities of each irradiated Gafchromic EBT3 film in this research were converted to dose using the equation 6 from the calibration curve (fig 13).

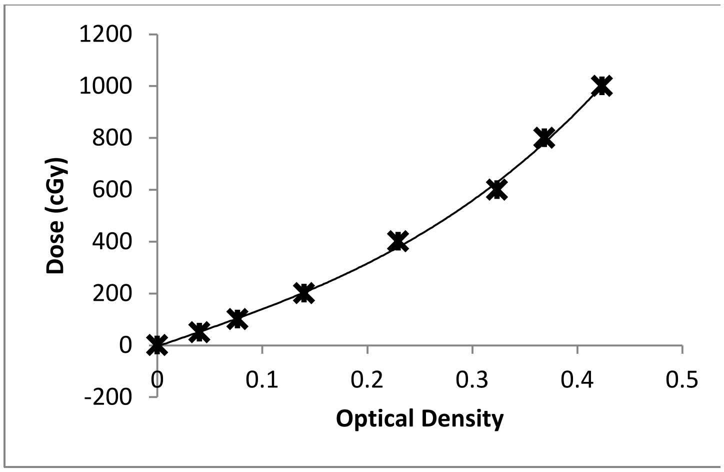

Figure 13: *Calibration curve for the green channel.*

Table 1: *TRS 398 and treatment time Parameters for absorbed dose to water determination.*

Parameter	Value
$N_{d,w}(Gy/C)$	5.402×10^7
K_{TP}	1.029054832
K_{pol}	1.000547945
K_{ele}	1.0000
K_{sat}	1.000182782
$Dw(5cm)$	1.01525
$Dplastic(5cm)$	1.00408225
$Dw(Zmax)\,cGy/min$	126.30
Scaling factor	0.998
Shutter time	-0.01
Decay factor	0.9153
$PDD/100$	0.804

4.1 Film Readings

The intensities of the films were measured after they had been exposed to radiation dose. The film intensities were converted to optical densities using the equation 4. The optical densities were inserted into the calibration equation 6 to obtain the doses measured by the Gafchromic EBT3 film. The deviations between the TPS doses and the film doses were expressed as percentage difference of the TPS dose using equation 5.

4.2 Summary of Results

Comparison of TPS Dose with Film Dose for the Rectum has been shown in Table 1.

Table 2: *Summary of comparison of TPS Dose with Film Dose for the Rectum.*

nth insertions	Rectal Dose (Gy)
	% Deviation
Mean	14.73
MIN	-47.22
MAX	51.06

5 DISCUSSION

The discrepancy between the optimised dose from the TPS and the measured dose by the film has been summarised in Table 2. The difference between doses calculated by the TPS and the doses measured by the Gafchromic EBT3 film at the rectum point was 14.73% ranging from -47.22% - 51.06%. The AAPM TG-46 has proposed ±15% (for dose measurements in phantom) deviation of prescribed dose delivery for intracavitary BT [14]. Comparing the 14.73% deviation of the rectum to the acceptable limit of ±15% indicates that these deviations are within the range of deviations documented by the AAPM TG 46. The phantom used in this study is a homogenous one however the dose distribution measurement carried out by Hanson et al, was done with a phantom that had homogenous and heterogenous component [14]. This could account for some level of variations in measurement done in this work. Gholami, Mirzaei, & Meigooni investigated the source of errors in Treatment Planning of HDR brachytherapy using a phantom with Gafchromic films; they reported a ±23.4% of dose deviation between the TPS and measured dose [15]. It can therefore be established that the deviations reported in this study compares well with other investigations. There are numerous reports that show that deviations in clinical measurements could be as high as 50% [16]. From the study, the maximum percentage difference between dose calculated by the TPS and dose measured by the Gafchromic EBT3 film was 51.06%, while the minimum percentage was -47%. It was observed from the study that the film does not respond appreciably and quite accurately at low energy of the photon. This is due to the energy dependence characteristic of the film. Dose measurement in very low energy range gave higher deviations. This is because the film's response in these low energy range is low. Many investigators have researched the energy dependence of the films in several applications [17]. The degree of energy dependence can affect the dosimetry properties of the film when an unknown spectrum of radiation energies is present. Most of these films under-respond at very low energies. Sayeg et al. have suggested that the lower response of the film is due to the larger carbon content in the film relative to that in soft tissues [17]. The TPS used in this study employs the algorithm of AAPM TG 43 dosimetry protocol for calculation of dose. The TG 43 formalism assumes that the entire human body or any medium used as a patient is entirely water equivalent. However, this is not the case during this research or even during patient treatment. The Gafchromic EBT3 film in the phantom during measurements generates an inhomogeneous condition. This is due to the fact that the effective atomic number (Z_{eff}) for the film is 6.84 but the effective atomic number of water is 7.42. The implication is that the dose from the TPS will not correspond entirely with the dose measured by the film. Reports from Uniyal et al indicates that the TPS that is commercially available and used by hospitals for treatment uses dose calculation algorithms that do not account for the impact of the heterogeneities encountered in the film or the patient [18]. Another factor responsible for the discrepancies between TPS dose and measured dose is the tungsten shields provided in the rectal and bladder compartment of the Fletcher suite of applicators used in this study. The shielding in the applicators minimize dose to the critical organs. During BT of the cervix, clinical complications do result from high doses received by OAR. Reports from Meli have also shown that dose deviations as a result of the shielding at some points in these applicators could be as high as 25% [19]. The deviations at the points of measurement in this study are due to the shielding. The study has shown that shields in the applicators have a significant impact on the dose delivery during treatment. The algorithms used by commercially available TPS do not take into account the effect of the shielding provided in these applicators on dose delivery [20]. Further study can be done to account for the shielding in these applicators and inculcate it into the algorithm of the TPS.

6 CONCLUSIONS

In this work, the doses calculated by the TPS were compared to the doses measured by the Gafchromic EBT3 films for the rectum. The deviation between the doses was 14.73%. This deviation is within the proposed dose variations ±15% in phantom measurements by the AAPM TG 46 [6].

7 ACKNOWLEDGEMENTS

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