REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY 22 (2017) 284–289

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Original research article

Evaluating the performance of TG-43 protocol in esophageal HDR brachytherapy viewpoint to trachea inhomogeneity

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ARTICLE INFO

Article history:
Received 5 November 2016
Received in revised form
24 February 2017
Accepted 18 April 2017
Available online 5 May 2017

Keywords:
Esophageal HDR brachytherapy
Trachea inhomogeneity
TG-43 protocol
Treatment planning
Film dosimetry

ABSTRACT

Aim: The aim of this study is to evaluate the effect of air within trachea on dose calculations of esophageal HDR brachytherapy treatment planning.

Background: Dose calculations in esophageal HDR brachytherapy treatment planning systems are greatly based on TG-43 protocol which in all materials are considered to be water equivalent.

Materials and methods: A cylindrical PMMA phantom with a tube in the center (neck equivalent phantom) accompanied by Flexitron HDR brachytherapy system was used in this study. Brachytherapy applicators with various diameters were placed inside the esophageal tube and EDR2 film was used for dosimetry. The absorbed dose by reference point of esophageal HDR brachytherapy and anterior wall of trachea were measured and compared with those calculated by Flexiplan treatment planning system.

Results: Based on the performed statistical analysis (t-test) with 95% confidence level (t-value >1.96), there was a meaningful difference between the results of film dosimetry and treatment planning at all of the points understudy.

Conclusion: The meaningful difference between the results of film dosimetry and treatment planning indicates that the trachea inhomogeneity has a considerable effect on dose calculations of Flexiplan treatment planning software featuring the TG-43 dose calculation algorithm. This mismatch can affect the accuracy of performed treatment plan and irradiation.

1. Background

Esophageal cancer is one of the most dangerous of today's cancers in the world. The common radiotherapy method for treatment of esophageal cancer is intraluminal high dose rate (HDR) brachytherapy.[1–8] HDR brachytherapy is an accepted technique[9] which has been well established over the past two decades.[10] In esophageal HDR brachytherapy, at first the applicator is entered to esophagus through the mouth and then a

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http://dx.doi.org/10.1016/j.rpor.2017.04.001

marker wire is put into it. Applicators with various diameters of 6, 8, 10, 12, 14, 16, 20 and 24 mm,[11] are available for this kind of brachytherapy technique. Then, the patient is transferred to a CT-scan room and acquired anatomic information is sent to the treatment planning system and the desired treatment plan is implemented by an associated treatment planning system. Finally, the applicator is connected to the remote afterloading irradiation system and the radioactive source is entered to the esophagus through the applicator and by stopping in different points, according to the implemented treatment plan, the prescribed dose is administered to the points of interest.[12,13] Because of high prescribed dose in each fraction and a few treatment sessions in this kind of brachytherapy, treatment planning errors must be kept as low as possible. Reliable performance of employed treatment planning system and accurate treatment planning procedure has an important role for the quality of clinical outcomes.[14,15]

One of the main treatment planning software for brachytherapy purposes is Flexiplan.[16] The function of this software is based on the AAPM TG-43 protocol in which all of the tissues are considered to be water equivalent.[17,18] On the other hand, the difference between mass absorption coefficient and electron density of different types of tissues and water[19] can introduce significant errors in the treatment planning procedure which will finally influence the accuracy of performed treatment.[20] One of the evident examples of this noncompliance is seen in esophageal brachytherapy. Since the trachea is located near the esophagus and considering the air inside it equivalent to water during the treatment planning procedure, some errors may occur in dose calculations using TG-43 protocol and finalizing the implemented treatment plan.

2. Aim

The aim of this study is to evaluate the effect of the air within trachea on absorbed dose in two main points of esophageal brachytherapy including reference point (the point which is 5 mm away from the applicator surface) and the anterior wall of the trachea. Finally, the accuracy of Flexiplan treatment planning software in esophageal HDR brachytherapy would be surveyed according to the obtained results.

3. Materials and methods

3.1. *Phantom design and construction*

To achieve the aim of this research, at first we have to provide a phantom which is similar to the anatomic structure of the neck when esophageal applicator is placed into the body. The constructed phantom involves esophageal and tracheal tubes and has the ability to place various diameter applicators and intended dosimeters. Because of good accordance between the mass absorption coefficient and electron density of plexiglas and water,[21,22] plexiglas was considered for phantom construction.

The radius and height of constructed cylindrical phantom were 50 and 150 mm, respectively. A tube with 22 mm diameter was created in the middle of the phantom which was equivalent to the esophagus. In addition, a tube with 18 mm diameter was created at 24 mm distance from the center of the cylinder which plays the role of the trachea. The anatomical position of the esophagus and trachea inside the designed phantom is shown in Fig. 1.

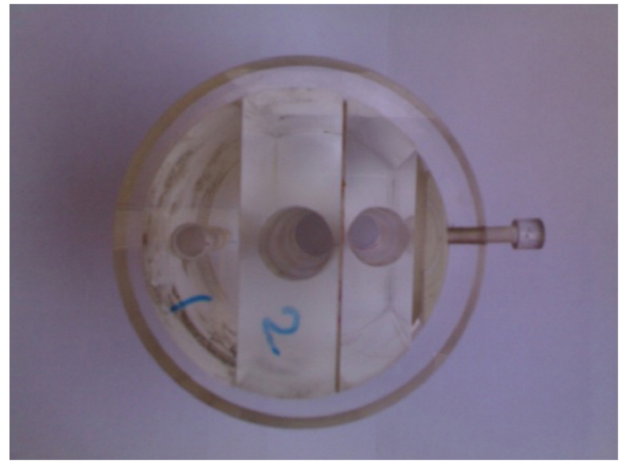

Fig. 1 – Anatomical position of esophageal and trachea inside the designed phantom.

Various parts of the employed phantom are also shown in Fig. 2.

To place the intended applicators into the phantom, some cylinders with external diameter of 20 mm were provided. A hole with the diameter that was equal to the external diameter of each employed applicator was created within it, so that the thickness of the thinnest part of the wall in each cylinder was equal to 1 mm. Four applicators with diameters of 6, 8, 10 and 20 mm were employed in this study. Each applicator was placed into the corresponding cylinders and the cylinder was placed inside the esophageal tube. The collection of these parts creates the anatomic state of the neck when esophageal applicator is placed into the body.

3.2. *Treatment planning*

Each of the above mentioned sizes of employed applicators with its specific cylinder and marker wire was placed into the phantom and transferred to the CT-scan room (Fig. 3).

Fig. 2 – Various parts of the employed phantom in this study.

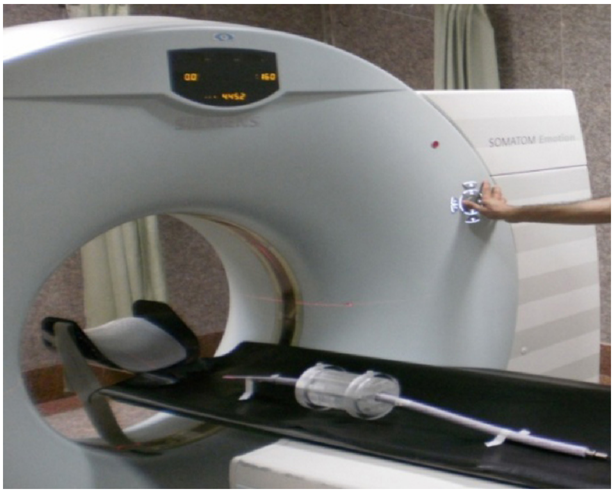

Fig. 3 – Positioning the applicator inside the phantom and acquiring the CT images for treatment planning.

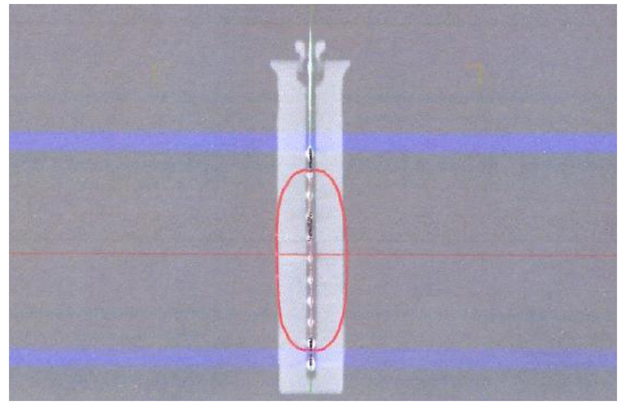

Fig. 4 – The implemented plan for irradiating the calibration films. As it can be seen, a uniform dose distribution exists at the outer wall of PMMA calibration phantom where the calibration films were attached.

The acquired CT images for each applicator were transferred to the Flexiplan treatment planning system. Then, the same treatment planning procedure was followed for all applicators, so that a specific dose was loaded at the reference point (14 mm away from the phantom center) and anterior wall of the trachea (33 mm away from the center of phantom) for each applicator.

3.3. *Dosimetry*

EDR2 film was used for practical dosimetry. This film is specifically designed for radiation oncology applications. Compared to most of other radiographic films, the response of this film is relatively independent from beam energy.[23] The dynamic range of this film is between 0.1 and 5 Gy[24] which was in accordance with the employed dose levels in this study. Due to the light sensitivity, the film should be handled with a black cover. The thickness of the film and its cover is about 1 mm that should be taken into account in phantom construction. To locate the employed films inside the phantom, a crack with 1 mm thickness (equal to the thickness of EDR2 film) was longitudinally created in two parts of the phantom. The first crack was created at the distance of 14 mm from the phantom center. This point was located at 5 mm distance from the surface of each applicator (reference point in esophageal HDR brachytherapy). The second crack was created at 33 mm distance from the phantom center (2 mm from the trachea anterior wall) to specify the absorbed dose in this point.

The employed films were calibrated using the Ir-192 radioactive source (Flexisource ^{192}Ir). Prior to calibration, the activity of the employed Ir-192 source was measured by a well type ion chamber. In order to calibrate the employed films, each calibration film was attached to the outer wall of a cylindrical PMMA phantom with a 2 cm radius. The Ir-192 source was put inside the PMMA phantom by inserting a hollow inside the calibration phantom and locating the corresponding applicator inside the hollow. It should be mentioned that the PMMA phantom was located in water to fully satisfy the backscatter condition. The films were covered by a very thin plastic to prevent the damage of films in water. Then, films were exposed to uniform dose levels of 0.5–2 Gy with 0.25 Gy increments by stopping the radiation source at specific predefined dwell positions. The considered plan for film calibration is shown in Fig. 4. The distance between the Ir-192 source and calibration films was equal to 2 cm.

Each irradiation in the calibration procedure was repeated three times. The irradiated films were uncovered in a dark room and placed into the film processor system for 3 minutes. Then, the processed films were scanned by the Microtek flatbed scanner (9800XL model) in the transmission mode and 16 bit per channel RGB mode. Then, the average pixel value (PV) of the central part of irradiated films ($1 \times 1\,cm^2$) was measured by the ImageJ software. Finally, the net optical density (net-OD) of scanned films was determined through the following equation[25,26]:

$$\text{Net Optical Density}\quad (\text{net-OD}) = \text{Log}_{10}\left(\frac{PV_{before}}{PV_{after}}\right) \tag{1}$$

Where PV_{before} and PV_{after} are the gray scale of unirradiated and irradiated films, respectively. It should be mentioned that the red channel response was considered for film dosimetry.

3.4. *Irradiation*

After treatment planning, EDR2 films were placed in embedded points within the phantom and applicator was connected to the Flexitron brachytherapy system.[16] Ir-192 source (Flexisource ^{192}Ir) was located into the phantom using the applicator and by stopping in dwell positions programmed by Flexiplan treatment planning system, prescribed dose was administrated to the points understudy. Each irradiation was repeated three times.

3.5. *Statistical analysis*

In order to statistically analyze the significance level of the difference between the film dosimetry and treatment planning results, an objective statistical test based on null

Table 1 – The results of film dosimetry at the points of interest for 6 mm diameter applicator.

Point of interest	Applicator diameter (mm)	Plan dose (Gy)	Measured dose (Gy)	(Film dosimetry – treatment planning) × 100 Film dosimetry
Reference point	6	1.34	1.255 ± 1.7%	−6.8%
Trachea anterior wall	6	0.19	0.22 ± 2%	13.6%

Table 2 – The results of film dosimetry at the points of interest for 8 mm diameter applicator.

Point of interest	Applicator diameter (mm)	Plan dose (Gy)	Measured dose (Gy)	(Film dosimetry – treatment planning) × 100 Film dosimetry
Reference point	8	1.53	1.475 ± 0.5%	−3.7%
Trachea anterior wall	8	0.23	0.26 ± 1.7%	11.5%

Table 3 – The results of film dosimetry at the points of interest for 10 mm diameter applicator.

Point of interest	Applicator diameter (mm)	Plan dose (Gy)	Measured dose (Gy)	(Film dosimetry – treatment planning) × 100 Film dosimetry
Reference point	10	1.63	1.575 ± 0.5%	−3.5%
Trachea anterior wall	10	0.30	0.32 ± 1.3%	6.3%

Table 4 – The results of film dosimetry at the points of interest for 20 mm diameter applicator.

Point of interest	Applicator diameter (mm)	Plan dose (Gy)	Measured dose (Gy)	(Film dosimetry – treatment planning) × 100 Film dosimetry
Reference point	20	1.52	1.490 ± 0.9%	−2%
Trachea anterior wall	20	0.32	0.36 ± 1%	11.1%

hypothesis was employed. The major outlines of employed statistical method are described bellow[27]:

At first, the associated standard deviation to the film dosimetry data was calculated (σ_{film}). Then, the standard deviation related to the difference between the results of film dosimetry and treatment planning (σ_{TPS}) was determined following the error propagation.[28]

$$\sigma_{diff} = \sqrt{\sigma_{film}^2 + \sigma_{TPS}^2} \quad (2)$$

Due to the fact that the expected dose from treatment planning system was always the same, σ_{TPS} was equal to zero.

Finally, based on the following equation, the difference between the film dosimetry results and treatment planning were scored as *t*-value:

$$t = \frac{|D_{film} - D_{TPS}|}{\sigma_{diff}} \quad (3)$$

The meaningful difference between the results was evaluated at the 95% confidence level ($t = 1.96$).[27] Tests with *t*-values >1.96 were scored as significant.

4. Results

The dose–response curve of EDR2 radiographic film at the range of 0.5–2 Gy is shown in Fig. 5.

Drawn error bars are corresponding to one standard deviation around average of netODs which are calculated by the error propagation formula.[28] The best fit for obtaining the film response curve was the first order polynomial fit (adjusted $R^2 > 0.99$). This finding was in accordance with the manufacturer claim (Carestream Health, Inc) about linear response of EDR2 film.[23]

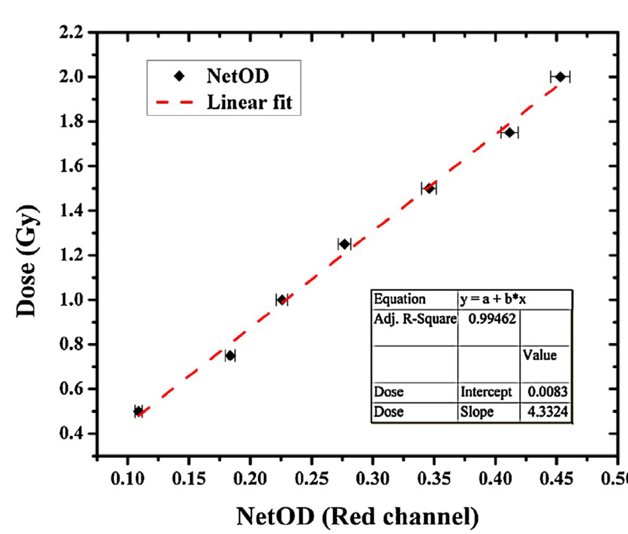

Fig. 5 – Dose–response curve of EDR2 radiographic film.

Table 5 – The results of significance test for employed applicators.

Applicator diameter (mm)	t-value (reference point)	t-value (trachea anterior wall)
6	3.98[a]	6.82[a]
8	7.46[a]	6.79[a]
10	6.98[a]	4.81[a]
20	2.24[a]	11.11[a]

[a] Significant difference between the results of film dosimetry and treatment planning.

The results of film dosimetry at the points of interest for various applicator diameters of 6, 8, 10 and 20 mm are reported in Tables 1–4, respectively. The corresponding loaded doses during the treatment planning procedure are also separately reported in each presented table.

As can be seen from the presented Tables, the results of film dosimetry are considerably different from those expected by implemented treatment plan. Significance level of difference between the dosimetry and plan results is shown in Table 5.

As reported by Table 5, the difference between the results is significant and cannot be assigned to the systematic errors of measurement tools or statistic errors that are associated with a stochastic nature of measurement.

Absorbed dose at 14 mm distance from the phantom center (reference point in esophageal HDR brachytherapy) was on average 4% lower than the calculated dose by Flexiplan treatment planning software. Due to the decreased backscatter radiation in air relative to water, the radiation intensity would be reduced in comparison with the treatment planning calculations. As a consequence, it is expected that the film dosimetry results at the reference point would be lower than those calculated by Flexiplan treatment planning software.

Absorbed dose at 33 mm distance from the phantom center (trachea anterior wall) was on average 11% higher than the expected dose by Flexiplan treatment planning software. Due to the lower attenuation coefficient of air relative to water, the radiation intensity at the trachea anterior wall is more than the supposed condition in treatment planning procedure and, therefore, the absorbed dose would be higher than the calculated dose during the treatment planning procedure.

The effect of patient inhomogeneity in esophageal HDR brachytherapy has been studied by Anagnostopoulos et al. through Monte Carlo simulation.[29] The results of this study showed that there is no meaningful difference between the results of Monte Carlo simulation and employed treatment planning system in planning target volume (PTV). But regarding the organs at risks (OARs) exposure, the results of TG-43 based treatment planning were considerably different from those obtained by Monte Carlo simulation (up to 15%).

The impact of different inhomogeneities in brachytherapy dose calculations is also investigated by Poon et al.[30] In this study the effect of some inhomogeneities, like air, on absorbed dose in different regions was calculated by PTRAN Monte Carlo code and compared with those estimated by TG-43 protocol. The results of mentioned study showed that the TG-43 based dose calculation underestimates the absorbed dose at the points behind the air cavities with respect to the Monte Carlo simulation. The results of our study are in accordance with those reported by Poon et al.

5. Conclusion

The effect of trachea air inhomogeneity on dose calculations of a commercially available brachytherapy treatment planning software (Flexiplan) was investigated through film dosimetry by EDR2 radiographic film and inside a specially designed esophageal phantom. The results showed that the accuracy of Flexiplan treatment planning software in esophageal brachytherapy is affected by anatomic position of the trachea and associated air inhomogeneity. This finding was in accordance with the Monte Carlo based results reported by other studies.[29,30]

The absorbed dose by the trachea, which is considered as an organ at risk (OAR) in esophageal brachytherapy, was found to be higher than that of calculated by TG-43 dosimetry formalism. To overcome the unnecessary administered dose to the trachea, the air inside trachea should be taken into account during dose calculations. This may be performed through employing the Monte Carlo simulation as a complementary part to the TG-43 dose calculation algorithm, or direct measurement of air inhomogeneity effect through in vitro dosimetry and further correction of the TG-43 based calculated results.

Furthermore, the designed esophageal phantom can be considered as a useful tool for quality assurance in esophageal and tracheal HDR brachytherapy and applying further corrections, if needed.

Conflict of interest

None declared.

Financial disclosure

None declared.

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