Radiotherapy and Oncology 107 (2013) 20–25

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Image guided brachytherapy

A multicentre comparison of the dosimetric impact of inter- and intra-fractional anatomical variations in fractionated cervix cancer brachytherapy

Nicole Nesvacil [a,*], Kari Tanderup [b], Taran P. Hellebust [c,d,e], Astrid De Leeuw [f], Stefan Lang [a], Sandy Mohamed [b,j], Swamidas V. Jamema [g], Clare Anderson [h], Richard Pötter [a,i], Christian Kirisits [a,i]

[a] Department of Radiotherapy and Oncology, Comprehensive Cancer Center, Medical University of Vienna, Austria; [b] Department of Oncology, Aarhus University Hospital, Denmark; [c] Department of Medical Physics, Oslo University Hospital; [d] Department for Radiation Protection and Nuclear Safety, Norwegian Radiation Protection Authority; [e] Department of Physics, University of Oslo, Norway; [f] Department of Radiation Oncology, University Medical Center Utrecht, The Netherlands; [g] Department of Medical Physics, Tata Memorial Hospital, Mumbai, India; [h] Clinical Physics Department, Mount Vernon Cancer Centre, UK; [i] Christian Doppler Laboratory for Medical Radiation Research for Radiation Oncology, Medical University of Vienna, Austria; [j] Department of Radiotherapy, NCI, Cairo University, Egypt

ARTICLE INFO

Article history:
Received 15 October 2012
Received in revised form 27 January 2013
Accepted 29 January 2013
Available online 18 April 2013

Keywords:
Image guided brachytherapy
Cervix cancer brachytherapy
Interfraction variations
Adaptive brachytherapy

ABSTRACT

Background and purpose: To compare the dosimetric impact of organ and target variations relative to the applicator for intracavitary brachytherapy by a multicentre analysis with different application techniques and fractionation schemes.

Material and methods: DVH data from 363 image/contour sets (120 patients, 6 institutions) were included for 1–6 fractions per patient, with imaging intervals ranging from several hours to ~20 days. Variations between images acquired within one (intra-application) or between consecutive applicator insertions (inter-application) were evaluated. Dose plans based on a reference MR or CT image series were superimposed onto subsequent image sets and D_{2cm^3} for the bladder, rectum and sigmoid and D_{90} for HR CTV were recorded.

Results: For the whole sample, the systematic dosimetric variations for all organs at risk, i.e. mean variations of D_{2cm^3}, were found to be minor (<5%), while random variations, i.e. standard deviations were found to be high due to large variations in individual cases. The D_{2cm^3} variations (mean ± 1SD) were 0.6 ± 19.5%, 4.1 ± 21.7% and 1.6 ± 26.8%, for the bladder, rectum and sigmoid. For HR CTV, the variations of *D*90 were found to be −1.1 ± 13.1% for the whole sample.

Grouping of the results by intra- and inter-application variations showed that random uncertainties for bladder and sigmoid were 3–7% larger when re-implanting the applicator for individual fractions. No statistically significant differences between the two groups were detected in dosimetric variations for the HR CTV.

Using 20% uncertainty of physical dose for OAR and 10% for HR CTV, the effects on total treatment dose for a 4 fraction HDR schedule at clinically relevant dose levels were found to be 4–8 Gy EQD2 for OAR and 3 Gy EQD2 for HR CTV.

Conclusions: Substantial variations occur in fractionated cervix cancer BT with higher impact close to clinical threshold levels. The treatment approach has to balance uncertainties for individual cases against the use of repetitive imaging, adaptive planning and dose delivery.

3D image guided brachytherapy (BT) of cervical cancer is becoming more and more used by centres with access to MRI or CT imaging facilities for BT planning. This technique allows delivery of high doses to target structures while doses to organs at risk can be reduced with the help of 3D images, which provide detailed information of the anatomical situation and applicator position at the time of BT planning. (e.g. [1]). Dose-effect relationships for cervix cancer BT have been previously reported for the bladder, rectum and sigmoid [2,3–5] and target [6]. When balancing target versus OAR dose, the dose levels are usually in the region of a steep dose-effect curve gradient. Therefore it seems necessary to report the applied dose with high precision, to identify systematic and random uncertainties and design treatment schedules and application techniques to reduce the uncertainties accordingly.

The present study focuses on the dosimetric impact of anatomical variations of target and organ structures in relation to the brachytherapy applicator as a fixed reference coordinate system.

The possibility of target and organ motion, i.e. changes in location relative to the applicator, variations of shape and/or filling

* Corresponding author. Address: Department of Radiotherapy and Oncology, Comprehensive Cancer Center, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria.
E-mail address: nicole.nesavcil@meduniwien.ac.at (N. Nesvacil).

0167-8140/$ - see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.radonc.2013.01.012

status of organs at risk (OAR), occurring between two individual BT fractions or within the time of delivery of one fraction, plays an important role in the assessment of total treatment doses for multi-fractional brachytherapy treatment and correlations with clinical outcome. This is especially the case when one treatment plan is used for multiple fractions, or when organ movement occurs in between imaging and dose delivery.

Dosimetric variations caused by such movement have been reported previously in various treatment planning studies. [7–16]. The majority of these studies focussed on the question whether or not a single treatment plan may be applied for a multi-fractionated BT treatment or whether repetitive imaging and, consequently, dose plan adaptation to modified OAR anatomy is generally required. Although it is commonly assumed that the relative position between the applicator and the target structure remains constant throughout the whole treatment, and little shrinkage of the target (HR CTV) will occur during BT, some studies have also analysed dosimetric changes for HR CTV. For all these studies repetitive 3D image series were obtained for a number of patients.

The aim of the current study is to compare the dosimetric impact of target and OAR variations by a multicentre analysis based on pooled data from different institutions with different application techniques and fractionation schemes, introducing a common method for reporting such variations.

As no general recommendations for the reporting of dosimetric variations caused by relative motions between structures and applicators during cervix cancer BT exist up to this date, we propose a general method to report dosimetric uncertainties in percentage of planned dose of a reference image set. By doing so, it becomes possible to compare variations observed at different centres with different treatment strategies, independent of the absolute dose values obtained. Derived uncertainties could thus be converted to different treatment schedules and expected ranges of true delivered doses could be calculated.

The results of our study could help to uncover systematic correlations of time between image acquisitions and dosimetric variations, and to identify which of the critical organs is affected most by motions occurring during BT treatment.

Materials and methods

Six participants in the GEC ESTRO GYN network performed repeated imaging for the analysis of dosimetric changes caused by anatomical variations during cervix cancer BT. (Medical University of Vienna (MUV), Mount Vernon Cancer Center (MVCC), University Medical Center Utrecht (UMCU), Oslo University Hospital (OUH), Tata Memorial Hospital (TMH), Aarhus University Hospital (AUH)). These centres were invited to submit their raw data and to participate in a direct comparison of their individually reported observations with other institutions.

Table 1 gives an overview of centre-specific treatment details and available image data. Details about the imaging protocols, application techniques, patient selection, contouring and treatment planning were reported in the individual publications listed in Table 1. Four of the participants in the current study (MUV, UMCU, OUH, AUH) have previously published mono-institutional data for variations due to anatomical changes during BT treatment. For centres MVCC and TMH, additional unpublished data were included in this study. Detailed descriptions of their clinical imaging and treatment protocols have been reported by Wills et al. and Mahantshetty et al. [17,18].

For the present study each centre contributed a set of DVH data generated with similar workflows as described hereafter. An overview of the data included in this study is given in Table 1. At every institution cervix cancer patients were treated with intracavitary (ic) applicators (tandem/ring (5) or tandem/ovoid (1)) with or without interstitial (is) needles. Two of the centres treated patients with PDR BT, four centres used HDR treatment schedules in addition to EBRT treatment of 45–50 Gy. Data for 120 patients (363 image/contour sets, 308 MRI, 55 CT) were included in this study. For each patient at least two 3D image sets (MRI (5) or CT (1)) were acquired over the course of BT [19]. In four centres 2–6 image series were analysed for each patient. Three centres analysed images obtained during the same applicator insertion (intra-application variations) while the other three analysed DVH parameters based on images acquired for subsequent applicator insertions (inter-application variations). Time intervals between two images for one patient spanned a large range between 3 and 5 h within one applicator insertion and up to three weeks between different insertions. For bladder filling protocols the centres used: constant bladder filling procedures before imaging and before dose delivery, empty bladders, or open catheters.

HR CTV and OAR were contoured for each image series according to GEC ESTRO recommendations [20,21] in five centres. For centre OUH, CT based contours of bladder wall and rectal wall had been included in their original analysis and DVH data included in the present study are based on these contours. For all centres a treatment plan generated on the basis of images taken at the beginning of BT with applicator in place was transferred to consecutive images of the same patient and DVH parameters (D_{90} for target and D_{2cm^3} for OAR) were reported for HR CTV, bladder, rectum and sigmoid for all image sets available. The original CT based data from centre OUH allowed only to investigate minimum doses to 5% of the bladder and rectum walls, instead of the D_{2cm^3} nowadays used for OAR dose reporting. Given the volumes of bladder wall ($61.5 \pm 21.0\ cm^3$, mean ± 1SD) and rectum wall $51.4 \pm 18.8\ cm^3$) contours these parameters translate to $\sim D_{3cm^3}$. It was therefore considered that these parameters were comparable to the D_{2cm^3} used for analysis by other centres, especially since the current study is focussed on investigating relative changes between DVH parameters at different time points during BT, rather than comparing absolute DVH values between centres.

For assessment of dosimetric changes due to variations of shape, position or volume of the delineated structures, the relative difference between the doses calculated for the reference image and a subsequent image was calculated as $\Delta D = (D_i - D_{ref})/D_{ref}$ [%].

Table 1
Overview of participating centres and the data submitted to this study. Intra-application means that the applicators stayed in place between two image acquisitions, while inter-application means that applicators were removed and reinserted between image acquisitions. References for detailed descriptions of the individual study setups and/or individual centre's standard practice are given in the last column.

Centre	No. of patients	Treatment type	Applicator type	Time between image acquisitions	Image type	No. of image sets	Variation type analysed	References
MUV	21	HDR	T/R (ic ± is)	12–16 h	MRI	84	Intra-application	[9,10]
MVCC	21	HDR	T/R (ic ± is)	5 h (average)	MRI	72	Intra-application	[17]
UMCU	9	PDR	O (ic + is)	22 h (average)	MRI	36	Intra-aplication	[11]
OUH	11	HDR	T/R (ic)	1–20 days	CT	55	Inter-application	[12]
TMH	27	HDR	T/R (ic ± is)	7–10 days	MRI	54	Inter-application	[18]
AUH	31	PDR	T/R (ic)	7 days	MRI	62	Inter-application	[7,8]