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Total reference air kerma can accurately predict isodose surface volumes in cervix cancer brachytherapy. A multicenter study

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ABSTRACT

PURPOSE: To demonstrate that V_{60} Gy, V_{75} Gy, and V_{85} Gy isodose surface volumes can be accurately estimated from total reference air kerma (TRAK) in cervix cancer MRI-guided brachytherapy (BT).

METHODS AND MATERIALS: 60 Gy, 75 Gy, and 85 Gy isodose surface volumes levels were obtained from treatment planning systems (V_{TPS}) for 239 EMBRACE study patients from five institutions treated with various dose rates, fractionation schedules and applicators. An equation for estimating V_{TPS} from TRAK was derived. Furthermore, a surrogate Point A dose (Point A*) was proposed and tested for correlation with V_{75} Gy.

RESULTS: Predicted volumes $V_{pred} = 4965\ (TRAK/dref)\ 3/2 + 170\ (TRAK/dref) - 1.5$ gave the best fit to V_{TPS}. The difference between V_{TPS} and predicted volumes was 0.0% ± 2.3%. All volumes were predicted within 10%. The prediction was valid for (*1*) high-dose rate and pulsed dose rate, (*2*) intracavitary vs. intracavitary/interstitial applicators, and (*3*) tandem-ring, tandem-ovoid, and mold. Point A* = 14 TRAK was converted to total EQD_2 and showed high correlation with V_{75} Gy.

CONCLUSIONS: TRAK derived Isodose surface volumes may become a tool for assessment of treatment intensity. Furthermore, surrogate Point A* doses can be applied for both intracavitary and intracavitary/interstitial BT and can be used to compare treatments across fractionation schedules.

Keywords: Cervical cancer; Treatment volumes; Image-guided brachytherapy; TRAK

Introduction

Image-guided brachytherapy (BT) in locally advanced cervical cancer has rapidly disseminated over the last decade and has changed clinical practice in a large number of institutions (1–4). The basic concepts for contouring and reporting in MRI-guided BT were developed by the Groupe Européen de Curiethérapie and European Society for Therapeutic Radiology and Oncology (GEC ESTRO) working group and published ~10 years ago (5, 6). Recently, the International Commission on Radiation Units (ICRU)/GEC ESTRO report 89 has further developed prescribing, recording, and reporting in cervix cancer BT (7). This harmonization has facilitated the exchange of treatment-related parameters and characteristics between radiation oncology centers and multicenter clinical trials. After the introduction of volumetric imaging, dose–volume histogram (DVH) parameters became the main parameters to describe the dose distributions within target volumes and organs at risk (OARs) (8, 9). Beyond knowing dose to each organ and contoured target, comprehensive and meaningful evaluation of absorbed dose distributions requires additional metrics like overall volumes irradiated to high and intermediate doses.

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There may be effects related to these volumes which are not directly controlled by dose–volume or point dose parameters for defined organ. This therefore necessities the need to report irradiated volumes to select doses in addition to target and OAR-related DVH parameters. The concept of reporting irradiated volumes is standard in external beam intensity-modulated radiotherapy and proton radiotherapy because treatment volumes are independent from contoured structures and uncertainties in contouring accuracy (10, 11). In addition, they may correlate with morbidity for all those side effects not directly controlled by dose–volume or point dose parameters for defined organs (12, 13).

The ICRU 89 report recommends the total reference air kerma rate (TRAK; $\mu Gy \times m^2 \times h^{-1}$) as an essential treatment parameter to be reported. TRAK is a simple and unambiguous quantity which is defined as the integral of the reference air kerma rate from all sources at a distance of 1 m from the source over the treatment duration (7). TRAK is directly related to the milligram-hour radium (mgh) concept which is defined as the product of radium mass and treatment duration (7). It is a physical parameter which is not directly associated with a given biological effect because TRAK does not take into account dose distribution, fraction size, and dose rate. For example, the same TRAK for a given treatment delivered with pulsed dose rate (PDR) causes lower biological effects compared with an equivalent treatment delivered with high-dose rate (HDR) especially in the region close to the applicator. The same considerations apply for a highly fractionated BT schedule vs. a schedule with fewer BT fractions. TRAK without any further radiobiological normalization can, therefore, be used only for comparisons among treatments with similar equieffective fractionation schedules.

The ICRU/GEC ESTRO report 89 also introduces the concept of isodose surface volumes, which is the volume, enclosed by a specific isodose in terms of a physical dose or an biological equivalent dose in 2 Gy fractions (EQD2) dose level (7). The isodose surface volume is independent from the contoured volumes but related to the dwell times, source strength, and implant geometry. The isodose surface volumes are in principle based on the idea of the ICRU 38 reference volumes (14), however instead of being limited to one fixed dose value (60 Gy), became more flexible to report the total prescribed dose distribution for different dose values related to total external beam radiotherapy (EBRT) and BT EQD_2 dose (e.g., 60 $Gy_{\alpha/\beta=10}$, 75 $Gy_{\alpha/\beta=10}$, and 85 $Gy_{\alpha/\beta=10}$).

Current three-dimensional (3D) treatment planning systems can calculate treatment volumes enclosed by any isodose level. However, routine recording and reporting of reference isodose surface volume is not a standard practice in many BT departments and has been shown to be low historically (15). In addition, treatment plans are typically archived after a certain period of time, and departmental treatment planning systems are upgraded or changed. This emphasizes the need for an alternative and simple method to retrospectively calculate isodose surface volume, specifically in retrospective and prospective studies where there are large amounts of data available with reporting of TRAK, but not isodose surface volumes.

Various authors have demonstrated that a simple mathematical equation relates TRAK to the volume contained within an isodose surface in intracavitary (IC) BT (16–19). These studies considered the relation between TRAK and the isodose surface volumes contained within a given physical BT dose, whereas comparison of isodose surface volumes between departments and patients requires a terminology which is based on total EBRT and BT EQD_2 dose. Furthermore, it is not known if the simple relation between TRAK and volume is also valid for different applicators including combined intracavitary-interstitial (IC/IS) BT.

Another parameter that the ICRU 89 report still recommends as mandatory for reporting IC BT is Point A dose. Point A dose has been the most widely used parameter for dose reporting in IC BT (15, 20). It has limitations but also clear advantages: (*1*) it is straightforwardly defined, (*2*) it can be converted to equieffective dose, (*3*) it is related to the intensity of a given treatment, and (*4*) it is linked with most of the clinical experience accumulated over the last decades. Reporting of the dose to Point A is not dependent on target-volume contouring, and furthermore, Point A can be converted into equieffective dose. Point A is therefore a key parameter that allows a direct comparison of equieffective dose delivered to different patients in different departments with different fractionation schedules and absorbed-dose rates. However, reporting of Point A is not meaningful for combined IC/IS BT when needles are in close proximity to Point A (21). For IC/IS, TRAK is presently the only parameter which quantifies the intensity of a given treatment without dependence on target volume delineation, however with the inherent limitation that it cannot be converted to equieffective dose.

The purpose of this work was to investigate whether TRAK can be used to determine 60 $Gy_{\alpha/\beta=10}$, 75 $Gy_{\alpha/\beta=10}$, and 85 $Gy_{\alpha/\beta=10}$ isodose surface volumes in patients treated with various EBRT treatment protocols followed by IC only or IC/IS image-guided adaptive cervical cancer BT (IGABT) using either HDR or PDR and various applicator types. Furthermore, a new TRAK-based metric is proposed (Point A*) and tested as a surrogate Point A dose which can be applied for both IC and IC/IS BT. Point A* has the quality, that it can be converted to EQD_2, and it is hypothesized that Point A* EQD_2 represents the biological intensity of a given treatment in terms of total volume irradiated.

Methods and materials

Patients

The EMBRACE study is a prospective observational multicenter study on MRI-guided BT in locally advanced cervical cancer with patient accrual from 2008 to 2015. A detailed description of the EMBRACE protocol can be