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Supplement Article

Preliminary Results of a Comparison between High-tech External Beam and High-tech Brachytherapy for Cervix Carcinoma

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Introduction

Various technological developments have been evaluated in a clinical setting in order to improve external beam therapy (EBT) and brachytherapy (BT) during the past years. The most important are imaging tools, immobilization and tracking devices, treatment plan optimization, and the use of new beam qualities [3,5,6,8,9,11,15]. Stimulated by their new technological possibilities, EBT has tried to challenge BT and vice versa. Within this context several studies have been published, mostly treatment planning studies, but also small series clinical studies [1,10,12,14]. The conclusions drawn were rather biased because advanced EBT was predominantly compared with conventional BT. In addition, important concepts such as the need of margins in EBT to account for set-up (SM) and internal motion (IM) were not discussed in depth. Image guided and highly individualized BT has been developed and successfully implemented in clinics and cannot be neglected in such a comparison of (rival) treatment techniques. The aim of this study was to discuss and investigate a comparison of high-tech EBT vs. high-tech BT for cervix cancer patients.

When performing such a comparative treatment planning study a number of items need to be addressed and overcome. E.g. which PTV-CTV margin is appropriate for EBT based on latest technology? When considering recommendations to separate the margin in two components (SM+IM) they need to be combined in an appropriate manner to a total margin. Another set of questions arise from tolerance dose levels, i.e. which DVH parameters are important for EBT? As doses to larger amounts of the bladder (wall) or rectum (wall) are much smaller in BT, only high dose values are considered there. More specifically, clinical practice in image guided BT is based on $D_{0.1cc}$ and D_{2cc} which is representative for high dose regions in an organ or organ wall. Although correlations with clinical outcome are available for these DVH parameters, they cannot be simply transferred to EBT because of the very different overall dose gradient of the respective treatment techniques and resulting dose distribution in an organ at risk (OAR). It might therefore not be sufficient to compare D_{2cc} or ICRU point doses but also doses to larger volumes, e.g. D_{30cc}, D_{50cc}, or D_{10cc}. In general, when analyzing larger volumes, organ walls have to be contoured according to GEC ESTRO recommendations I and II [4,13]. Independent of contouring specific organs the total amount of irradiated volume has to be considered in addition as it has been demonstrated to correlate with morbidity.

Another class of open questions is related to target doses. What dose is needed to control the GTV? If using intracavitary brachytherapy, the dose to the GTV is automatically high due to the vicinity of the sources. D_{90} values of much more than 100 Gy (EQD_2) are observed. Such a high dose to the tumor is considered as one of the major reasons for the success of cervix brachytherapy. However, at the moment it remains unclear how high this dose has to be and if there is a certain dose limit which might be sufficient for EBT. Inverse planning algorithms for advanced EBT are designed to fulfill common ICRU standards for EBT, i.e. a homogeneous target dose. The finding that an inhomogenous dose prescription is more difficult to tackle with inverse planning is in agreement with previous studies in stereotactic body radiotherapy.

Materials and Methods

From regular cervix patients undergoing combined EBT and BT at the Department of Radiotherapy, three different groups were defined and from each group 2–3 patients were selected. Group a) consisted of FIGO stage IIB patients treated with intracavitary applicators only while group b) consisted of stage IIB patients treated with a combined intracavitary/interstitial approach. Group c) was defined as stage IIIB with complex interstitial implantations. For image guided BT the following target and organs at risk structures were used for individual treatment plan optimization: GTV, High Risk (HR) – CTV, Intermediate Risk (IR) – CTV, bladder, rectum and sigmoid. BT treatment planning was performed on a Plato system (Nucletron). For each patient MR image datasets and contours of one single brachytherapy fraction were transferred to the treatment planning system for EBT (XiO, CMS). If needed, additional contours were drawn or defined through Boolean algebra on the XiO system. The underlying EBT technique was based on seven to eleven intensity modulated fields. For EBT the same fractionation scheme as for BT was assumed but the BT CTV were expanded (3 mm and 5 mm) in order to account for set-up uncertainties and internal motion. As a starting point for inversely planned EBT, available DVH information in absolute volumes, i.e. cm^3, was utilized for OAR. Keeping maximum doses for D_{2cc} at a tolerable level, inversely planned IMRT with photons (IMXT) and protons (IMPT) was challenged to deliver the highest possible doses to GTV, HR-PTV, and IR-PTV.

Results and Discussion

The mean HR-CTV and IR-CTV were 43,6 ± 30,8 cm^3 and 93,8 ± 40,3 cm^3; and HR-PTV and IR-PTV were 84,4 ± 43,0 cm^3 and 159,0 ± 48,5 cm^3 for the patients investigated. Figure 1 illustrates a typical isodose distribution for an IMRT and image guided brachytherapy plan, based on combined intracavitary and interstitial BT.

Results of this study point out that if IMXT plans are limited to similar D2cc and D1cc values as advanced BT, D90 for the HR-PTV

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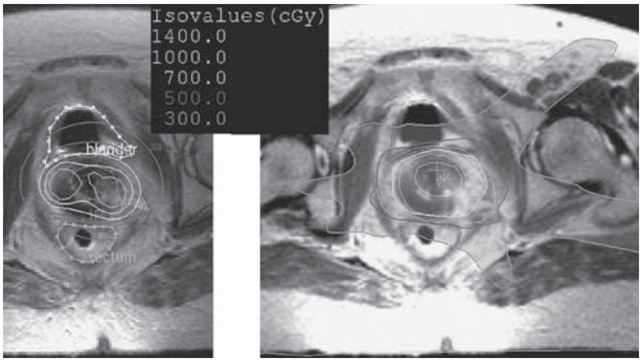

Figure 1. Example of a typical isodose distribution of an IMRT treatment plan and the respective image guided brachytherapy plan for a patient with an advanced cervix carcinoma.

and IR-PTV was lower depending on treatment margin and patient specific anatomy. For plans with 3 mm margin, the D90 for the HR-PTV was in 5 out of 8 cases by 10–40% lower than the dose given to HR-CTV with image guided BT. For 5 mm margin this patient ratio was 6/8. For 4 patients the desired minimum IR-PTV dose of 3.5 Gy was not achieved when applying a 5 mm margin, and for 3 patients for the 3 mm margin. D90 values for the various treatment techniques are summarized in table 1. This dose limit for HR-CTV was, however, depending on patient anatomy (thickness) and tumor shape. The treatment margin applied in EBT had a negligible influence. The overall volume receiving 60Gy (in EQD_2) was substantially higher when using IMRT. The mean volumes were 516 ± 193 cm^3 for a 5 mm margin and 494 ± 184 cm^3 for IMRT when applying a 3-mm margin. Corresponding values for advanced brachytherapy were 325 ± 83 cm^3. Such a comparison is impaired by the fact that for BT a large part of this volume is even located within the applicator and the packing. It has been pointed out that large volume in the pelvic region receiving more than 60 Gy correlate to side-effects [2].

Within the field of particle beam therapy Carbon ion beams have been already applied as an alternative to brachytherapy [7]. Initial results of a comparison between image guided BT, IMRT with photon and proton beam therapy based on scanning technology show a reduction of this 60 Gy volume while keeping the same dose constraints of OAR as in BT.

If advanced BT techniques are used for benchmarking advanced EBT, previous reports on the superiority of IMXT over BT need to be taken with precaution. Although the current results for advanced EBT techniques for gynecological applications are encouraging, more detailed studies on practical aspects of precision dose delivery need to be performed, e.g. on MR verification

Table 1. Summary of D_{90} [Gy] values for image guided brachytherapy and IMXT treatment plans.

		Dose in 90% of Volume [Gy]							
Patient No. →		# 1	# 2	# 3	# 4	# 5	# 6	# 7	# 8
BT	HR-CTV	7,2	7,9	7,8	9,7	10,1	6,5	9,3	6,6
	IR-CTV	5,4	6,1	4,6	6,3	5,4	3,5	5,5	NA
IMXT	HR-PTV	7,3	7,1	6,4	7,2	6,1	6,7	8,0	6,5
(3 mm)	IR-PTV	5,7	5,4	3,9	4,6	2,8	4,8	3,2	5,7
IMXT	HR-PTV	7,2	6,9	6,0	6,9	5,8	5,7	8,0	6,2
(5 mm)	IR-PTV	5,5	5,3	3,1	4,4	2,6	4,6	3,1	5,4

possibilities of patient set-up, target and patient immobilization, or options for "on-line" or adaptive treatment planning.

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