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A planning study investigating dual-gated volumetric arc stereotactic treatment of primary renal cell carcinoma

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ABSTRACT

This is a planning study investigating the dosimetric advantages of gated volumetric-modulated arc therapy (VMAT) to the end-exhale and end-inhale breathing phases for patients undergoing stereotactic treatment of primary renal cell carcinoma. VMAT plans were developed from the end-inhale (VMATinh) and the end-exhale (VMATexh) phases of the breathing cycle as well as a VMAT plan and 3-dimensional conformal radiation therapy plan based on an internal target volume (ITV) (VMATitv). An additional VMAT plan was created by giving the respective gated VMAT plan a 50% weighting and summing the inhale and exhale plans together to create a summed gated plan. Dose to organs at risk (OARs) as well as comparison of intermediate and low-dose conformity was evaluated. There was no difference in the volume of healthy tissue receiving the prescribed dose for the planned target volume (PTV) (CI100%) for all the VMAT plans; however, the mean volume of healthy tissue receiving 50% of the prescribed dose for the PTV (CI50%) values were 4.7 (± 0.2), 4.6 (± 0.2), and 4.7 (± 0.6) for the VMATitv, VMATinh, and VMATexh plans, respectively. The VMAT plans based on the exhale and inhale breathing phases showed a 4.8% and 2.4% reduction in dose to 30 cm^3 of the small bowel, respectively, compared with that of the ITV-based VMAT plan. The summed gated VMAT plans showed a 6.2% reduction in dose to 30 cm^3 of the small bowel compared with that of the VMAT plans based on the ITV. Additionally, when compared with the inhale and the exhale VMAT plans, a 4% and 1.5%, respectively, reduction was observed. Gating VMAT was able to reduce the amount of prescribed, intermediate, and integral dose to healthy tissue when compared with VMAT plans based on an ITV. When summing the inhale and exhale plans together, dose to healthy tissue and OARs was optimized. However, gating VMAT plans would take longer to treat and is a factor that needs to be considered.

Introduction

For patients diagnosed with primary renal cell carcinoma (RCC), the primary form of treatment is surgical resection. However, because this disease occurs generally in an elderly population with multiple comorbidities, surgery is not always a viable option.[1,2] Alternative options include ablative therapies such as cryoablation and radiofrequency ablation.[2,3] These techniques are still invasive, delivered either laparoscopically or percutaneously, and as such carry associated risks and potential for morbidity.

Noninvasive ablative techniques using high-dose-per-fraction radiation have recently been investigated for the treatment of primary RCC. Historically, RCCs are considered radioresistant to conventional radiation therapy (RT), with RT typically being reserved for palliation only.[4] However, this notion has recently been challenged by the delivery of large-dose-per-fraction RT enabled by the advent of stereotactic ablative body radiotherapy (SABR). The potential toxicity of the large radiation doses involved is mitigated using image guidance, advanced planning techniques, and immobilization devices.[5] In the context of primary RCC, SABR has achieved local control rates in the order of 80% to 100%.[4]

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SABR treatment can be delivered via open fields 3-dimensional conformal RT (3DCRT) or dynamic multileaf collimator delivery, which includes intensity-modulated RT (IMRT) and volumetric-modulated arc therapy (VMAT). When compared with static dose delivery, the dynamic alternative can offer superior conformity of the prescription dose to the target with reduced dose to critical structures.[6,7] However, organs and tumors in the upper abdomen, such as the liver and the kidneys, can experience considerable motion caused by respiration, which limits the reduction of margins on the tumor.[8] This in turn causes greater amounts of healthy tissue to receive radiation and increases the risk of geographic miss of the target volume.[9]

Therefore, SABR treatment planning in the abdominal region requires motion management. There are a number of methods to take into account organ motion, including compression plates, breath-hold, and time-resolved 4D computed tomography (CT) scans.[10] A common planning method is to use the concept of the internal target volume (ITV), which provides treatment of the target throughout the breathing cycle.[11] Alternatively, gating is another technique used to account for motion by delivering treatment during a specific part of the breathing phase. The 4DCT-based gated planning study by Gabryś *et al.*,[12] in 2010, for liver tumors found a significant correlation between dose and volume reduction in the organs at risk (OARs). In addition, a preclinical evaluation of respiratory-gated delivery of VMAT by Nicolini *et al.*[13] concluded that there is potential for VMAT to be delivered in conjunction with respiratory gating.

The purpose of this study was to assess the dosimetric advantages of gated VMAT plans compared with that of VMAT plans based on ITVs. In addition, it was proposed that by combining both the end-exhale and end-inhale phases of a patient's breathing cycle into a "summed" plan dose to healthy tissue and OARs can be optimized further. Therefore, the secondary objective of this study was to investigate whether there were any dosimetric benefits to combining the gated plans for each patient into a "summed gated" VMAT plan. This would provide some insight into motion-adaptive RT.

Methods

Patient cohort

Patients enrolled into an ethics-approved pilot study of Focal Ablative Stereotactic Radiosurgery for Cancers of the Kidney (FASTRACK; clinical trials.gov ID NCT01676428) were the subjects of this study. FASTRACK is a pilot study investigating the feasibility of treatment of primary RCC using a stereotactic dose for treatment on a conventional linac. Patients with primary RCC < 5 cm in size were planned to receive a single fraction of SABR. A cohort of 5 sequentially treated patients with primary RCC who received a 26-Gy dose in a single fraction were identified and formed the basis of this planning study.

Immobilization and simulation

All patients were immobilized with the BodyFIX whole-body double-vacuum system (Medical Intelligence, Schwabmünchen, Germany) and underwent a 4DCT on a Philips Brilliance Big Bore CT scanner (Philips Medical Systems, Cleveland, OH) and were positioned supine with their arms above their head. The 4DCT scans for each patient were reconstructed into 10 time bins, 0% to 90%, using respiratory phase binning and exported to a computer planning system (Eclipse v11.31; Varian Medical Systems, Palo Alto, CA). One of the patients had a deep-breathing 4D CT scan and a normal-breathing 4D scan, which are labeled accordingly. The deep-breathing scan was taken at the patient's own volition during the initial planning appointment without the knowledge of the planning therapist. A change in breathing amplitude was detected at a mock-up treatment session, and it was decided that a new 4D scan that was more representative of the patient's normal-breathing pattern was required. Therefore, both the scans were used for this study's purpose and were labeled accordingly.

Contouring

An ITV was contoured based on the 4D maximum-intensity projection data set. A 5-mm expansion around the ITV was used to generate the planning target volume (PTV). Maximum-inhale and maximum-exhale data sets were also selected based on the 10 time bins (generally 0% and 50%, respectively), and a gross tumor volume (GTV) was contoured based on each of these data sets and labeled GTV inhale (GTVinh) and GTV exhale (GTVexh). A 5-mm expansion was also placed around the GTVinh and GTVexh to generate the respective PTVs. Furthermore, OARs were contoured on the time-weighted average data set and on the maximum-inhale and maximum-exhale data sets independently; these organs included the small bowel, stomach, liver, skin, and spinal cord.

Planning technique and dose calculation

3-Dimensional conformal RT

3DCRT plans were created for each patient on the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA) and calculated using an Analytical Anisotropic Algorithm, v11.03. A minimum of 6 coplanar and a minimum of 2 noncoplanar fields with a combination of 6/18 MV were used with a prescription to the minimum surrounding isodose to ensure that 99% of the PTV received 100% of the dose. These plans were used clinically as part of the previously mentioned FASTRACK trial and have been included in the results as the clinically used plan but are not meant for comparison and are not the focus of this study.

VMAT plans

For each patient, 4 VMAT plans were developed and were labeled in relation to the relevant target volume. These plans include a plan based on an ITV (VMATitv), a plan based on the patient's maximum-inhale (VMATinh) breathing phase, and a plan based on the maximum-exhale (VMATexh) breathing phase. The VMATitv, VMATinh, and VMATexh plans were calculated independently on their associated data sets. The relevant volumes that were contoured on each of these data sets were then used to optimize the plan and report dose. In addition, a fourth VMAT plan was created, whereby the plans based on the inhale and exhale breathing phases were given a 50/50 weighting and summed together to create a summed gated plan (VMATsum). This plan was calculated using the time-weighted average data set, and the relevant dose for OARs from the VMATsum plan were reported from the contours based on the average data set.

As a separate analysis in the optimization of the summed gating technique, the inhale and exhale plans were summed with alternate weightings for the patient who showed the largest kidney motion. A 75/25 weighting was given to the exhale and inhale phases and vice versa, to assess the optimization of the summed gating plan. To simulate gating on both the inhale and the exhale phases, dose for the VMATsum plan was calculated on the time-weighted average scan. This method does not yield accurate dose information in the region of the target owing to dose inhomogeneities within, and steep dose gradients around, the PTV. As such, target doses were not reported for the VMATsum plan.

Plans were generated using the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA) based on 6-MV photon beams for Varian Clinac iX Linear Accelerator (Varian Medical Systems, Palo Alto, CA). The modulated arcs consisted of 359°, with a clockwise (CW) rotation for the VMATexh plans and counterclockwise (CCW) for the VMATinh plans. This was done to allow for "realistic" multiple-gated arc delivery. Collimators were placed on a 45° angle for the CW and 315° angle for the CCW rotation. Arc plans were optimized using Progressive Resolution Optimizer 3 (RapidArc Varian Medical Systems, Palo Alto). Dose calculations were performed with a grid resolution of 2.5 mm using Analytical Anisotropic Algorithm, v11.03 (Varian Medical Systems, Palo Alto, CA).

Dose prescription

The prescription dose was 26 Gy in a single fraction to the covering isodose, with 99% of the PTV receiving the full prescription dose with no limit on the maximum dose within the PTV. Optimization constraints were also placed on the following OARs: subcutaneous skin, spinal cord, liver, small bowel, and stomach; organ constraints are listed in Table 2.

Table 1
Patient descriptive

Patient	Sex	Age	Location	Centroid motion (cm)
1	M	74		
Normal			Left	0.3
Deep			Left	1.6
2	M	84	Left	1.3
3	M	82	Right	0.6
4	M	43	Left	0.4
5	F	74	Right	0.3

Centroid motion is the amount of craniocaudal motion of the center of the affected kidney.