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Research Article

Evaluation of Motion Effect on Dose Delivery in Tumor Tracking Based Stereotactic Body Radiotherapy of Abdominal Targets

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Abstract

Purpose: To evaluate the effects of respiratory motion on the delivered dose distribution in motion tracking-based stereotactic body radiotherapy of abdominal targets.

Methods: Eight patients with tumors in the abdominal region (three with pancreas tumors and five with liver tumors) were retrospectively selected; all of them received 4DCT during simulation. A3D plan was optimized on the end-expiration phase in the Cyber Knife Synchrony Multi Plan treatment planning system, with 40Gy prescribed in 5 fractions. A4D plan was then created using the Multi Plan 4D planning module. The other seven phases of the 4DCT were deformably registered to the end-expiration phase, and dose distribution in each phase was deformably mapped to the end-expiration phase for dose summation. Doses to the target and organs at risk, including duodenum, liver, spinal cord and both kidneys were compared between 3D and 4D plans for each patient.

Results: The target coverage in 4D plans which represent the real dose delivered could be compromised by up to 10.3% for some patients. Doses to organs varied depending on the location, with maximum dose differences observed up to 8.3Gy higher or 5.4Gy lower in 4D plans. Doses to the spinal cord and both kidneys were significantly different between 3D and 4D plans.

Conclusion: The delivered dose can be significantly different from the 3D planned dose for both target and organs at risk, which is caused by the patient anatomy changes while the radiation beams are chasing the moving target. This study suggests a 4D dose recalculation may be necessary to reliably assess the real doses delivered to patients in the stereotactic treatment of abdominal targets with tumor tracking strategy.

Keywords: Radiation dose; Motion management; Pancreas tumor; Liver tumor; Deformable registration

Abbreviations

4DCT: Four Dimensional Computed Tomography; DVH: Dose Volume Histogram; GTV: Gross Tumor Volume; ITV: Internal Target Volume; kV: Kilo Voltage; LED: Light Emitting Diode; MRI: Magnetic Resonance Imaging; MV: Megavoltage; OAR: Organs at Risk; PTV: Planning Target Volume; SBRT: Stereotactic Body Radiotherapy

Introduction

Treatment of tumors in lung or abdominal regions with stereotactic body radiotherapy (SBRT) can be challenging because of the respiration induced tumor motion. Motion management is critical for accurate dose delivery to the planning target volume (PTV) with satisfied coverage [1-5]. With the advance of imaging technology and incorporation of image guidance in patient setup and tumor localization, intrafraction motion, rather than interfraction motion, is more of a concern and this is particularly true in SBRT treatments [5]. There are several strategies of managing tumor motion during treatment [6-9]. One of them is tracking the tumor during treatment and then accounting for the tumor motion by chasing the tumor with radiation beams [10-15]. Cyber Knife Synchrony belongs to this category [14,15]. It uses serial orthogonal kilovoltage (kV) images to acquire tumor location, and then adjusts the beam directions in real time accounting for the tumor movement. Another intrafraction motion management strategy is restricting tumor motion, rather than tracking and accounting for it. The examples falling within this category are breath hold or active breathing control which temporally freezes the tumor position at the end of expiration or inspiration during radiation beam delivery [16-20]. Treatment with free breathing represents another alternative motion management strategy, and occasionally requires a large margin to compensate for tumor motion [21-24]. Radiation can be delivered either with full duty cycle such as in the internal target volume (ITV) motion management, or during a certain breathing phase such as in the respiration gating strategy.

Comparing to free breathing treatment, the advantage of tumor tracking is reduced PTV margin owing to the real time determination of target location and hence reduced normal tissue toxicity. In tumor tracking mode, radiation beams are delivered with full duty cycle and

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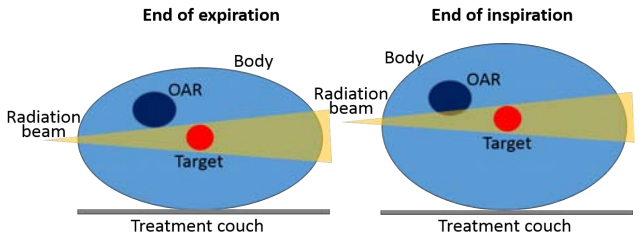

Figure 1: Illustration of motion induced dose difference from the treatment plan in the real dose delivery in tumor tracking based treatment. Usually a treatment plan with many radiation fields/beams was created on the end-expiration phase. During radiation delivery, dose to the organ at risk (OAR) may change when the radiation beams chase the target due to the change of relative position between the target and OAR. The dose to the target may also change due to the change of radiation beam path.

therefore treatment time is similar to that of free breathing treatment. Besides kV imaging, megavoltage (MV) [25,26] imaging and magnetic resonance imaging (MRI) [12,13] have also been implemented in real time tumor tracking. Due to the limited image contrast between tumor and its surrounding tissues in the abdominal region, KV and MV tumor tracking often necessitate fiducials implantation, an invasive procedure, to aid in tumor targeting [15,27].

In tumor tracking treatment, two factors can affect the real dose delivered to the PTV and critical structures. The main factor is the targeting accuracy of radiation beams to the PTV. CyberKnife Synchrony Respiratory Tracking system builds a tumor motion model for each individual patient by correlating the tumor or fiducials inside the tumor with external light emitting diode (LED) surrogates throughout respiratory cycles [14,15]. The surrogates are monitored in real-time with the synchrony camera array and radiation beams are immediately adjusted to account for tumor movement. The accuracy of tumor targeting for Synchrony is ~1.5mm [28-30] which can be readily accounted for in the PTV margin. Another factor is the altered radiation beam path due to target motion with respiration. The dose contribution to the target and critical structures from each radiation beam in reality is different from that calculated in treatment planning, as illustrated in Figure 1. This study investigated the effect of beam path change on target coverage and dose to organs at risk (OAR) in SBRT treatment of abdominal tumors, by comparing motion-accounted (4D) and motion-not-accounted (3D) treatment plans using CyberKnife Multi Plan treatment planning system. Treatment planning with ITV motion management was also performed to demonstrate the advantage of tumor tracking strategy in sparing of OARs.

Materials and Methods

A retrospective study was performed on eight patients with abdominal tumors, five with hepatic tumors and three with pancreatic tumors. This study was approved by the institutional review board. Patients were selected based on two criteria: (1) patients should be suitable for SBRT treatment with a single solid lesion < 5cm along the greatest dimension; (2) patients should undergo a 4D computed tomography (4DCT) study at the time of simulation. Two different plans were created in the Cyber Knife Multiplan treatment planning system (Accuracy, Sunnyvale, CA) for each patient: a 3D plan with Synchrony motion tracking (denoted as *3D plan*), and a 4D plan by subsequent recalculation of radiation doses in 4D mode (denoted as *4D plan*).

Planning for synchrony tumor tracking

The 4DCT study including eight breathing phases was sent to Cyber Knife Multiplan treatment planning system for contouring and planning. The gross tumor volume (GTV) and OAR were contoured on the end expiration phase of the 4DCT. The PTV was created by a 5mm isotropic expansion of the GTV. Multiplan sequential optimization algorithm was used to generate a 3D plan that covered at least 95% of the PTV with a prescription dose of 40Gy delivered in five fractions. OAR dose constraints applied during optimization were: the maximum dose D_{max} and D_{5cc} (dose to 5 cc on the dose volume histogram (DVH) curve) for duodenum; the maximum dose and $D_{0.25cc}$ for spinal cord; the D_{700cc} for liver and D_{200cc} for both kidneys.

After a 3D plan was created, a 4D plan was generated using Multiplan 4D planning module in the following manner. Briefly, all other seven 4DCT phases were rigidly registered to the end expiration phase by aligning corresponding surrogate markers in the lesion or anatomical features on/around the lesion. The radiation beams generated in the 3D plan were mapped to the remaining seven phases according to the rigid registration and dose was recalculated for each phase. Then each one of the seven phases was deformably registered to the end expiration phase and the 4D dose was summed according to the deformable registration. The deformable registration was performed using Multiplan 4D planning utility, and up to 20 anatomical landmarks were used as "locking points" to guide the deformation. The differences in target coverage and doses to OAR were recorded for analysis.

Planning for ITV motion management

GTVs were contoured in each phase of the 4DCT and combined to form an ITV, then a 5mm isotropic expansion of the ITV was performed to create the PTV. The ITV plan was optimized using the sequential optimization algorithm in Multiplan covering at least 95% of the PTV with the 40 Gy prescription dose. The same dose constraints for OAR in the previous tumor tracking planning were used in the ITV planning optimization. Dose comparison between the ITV plan and its 3D plan counterpart was performed. The PTV volume in the ITV plan was larger than its counterpart in the 3D plan; therefore we expect the achievable dose for OAR should be greater in the ITV plan.

Data analysis

Two-tail paired student t-tests were performed to compare the target coverage and doses to OAR between the 3D and 4D plans, and one-tail paired student t-tests performed to compare between the 3D and ITV plans, with the significance level determined at p value < 0.05. Maximum dose, dose to a fraction of OAR volume, and mean dose were used to evaluate the doses to OAR.

Results

Table 1 shows the dose coverage to PTV targets. There was no significant difference for target coverage between the 3D and 4D plans (95.5 ± 0.6 vs 93.6 ± 5.1, p = 0.32). The dose coverage for some patients was actually slightly better in the 4D plan. However,

Table 1: Target coverage for different plans.

Patients	3D plan (%)	4D plan (%)	ITV plan (%)	4D-3D (%)	ITV-3D (%)
P1	96.7	97.9	95.8	1.2	-0.9
P2	95	84.7	97.8	-10.3	2.8
P3	94.8	95.3	96.1	0.5	1.3
H1	95.1	86.2	94.9	-8.9	-0.2
H2	96	97	94.8	1	-1.2
H3	95.4	95.9	96.9	0.5	1.5
H4	95.2	96.8	96.1	1.6	0.9
H5	95.6	95.3	95.7	-0.3	0.1
Average	95.5	93.6	96	-1.8	0.5
St. Dev.	0.6	5.1	1	4.8	1.3
p value	NA	NA	NA	0.3	0.3

Note: *p* values are display here in the unit of 1 instead of %.

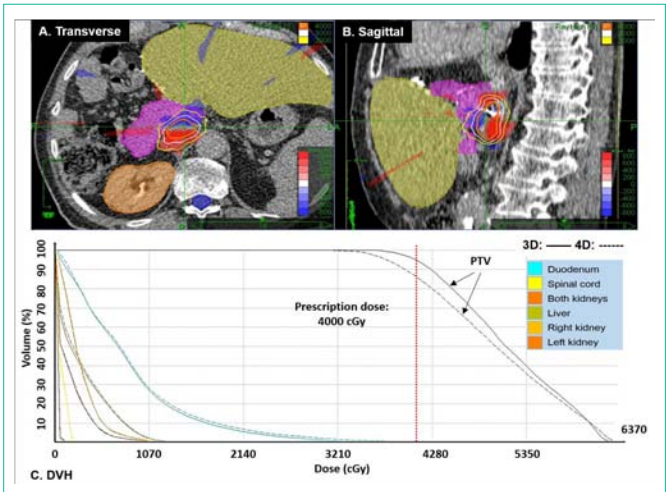

Figure 2: Dose difference between the 3D and 4D plan from a patient. Considerable dose discrepancy can be observed around the target in both the transverse (A) and sagittal (B) planes. Most dramatic differences occurred in the superior-inferior and anterior-posterior directions, concurring with the respiration induced motion directions. DVHs showed the PTV coverage was compromised by 10.3%, and maximum dose to the duodenum was 8.3Gy greater, although there was not much shift in the DVH curves for the OAR.

the target coverage for two patients was severely compromised in the 4D plan (84.7% vs 95.0% for patient P2, and 86.2% vs 95.1% for patient H1) with up to 10.3% decrease. Figure 2 demonstrates the difference in dose distribution between the 3D and 4D plans caused by motion for patient P2. The dramatic dose discrepancy occurred at the anterior-posterior and superior-inferior directions, with up to 8.3Gy difference in the structures near the PTV.

As shown in Table 2, there was no significant difference for doses to the OAR near the target, i.e., duodenum and liver, all with p values > 0.05. Because the target is located inside the liver for the liver patients or very close to the duodenum for the pancreas patients, there could be considerable dose differences in the maximum dose to the liver or duodenum between 3D and 4D plans, due to the continuous adjustment of beam directions. The maximum dose was up to 8.3Gy different for the duodenum in one pancreas patient (P2), and 5.4Gy different for the liver in two liver patients (H1 and H5). All the maximum dose points appeared at the periphery of the PTV, and may be smeared out by the day to day patient setup variation and changes in breathing pattern. Doses to both kidneys and spinal cord were significantly different between the 3D and 4D plans. Specifically, the D200cc and mean dose for kidneys in 4D plans were significantly higher by 0.1 ± 0.1Gy (p = 0.05) and 0.2 ± 0.2Gy (p = 0.03), respectively; the D_{max} for spinal cord in 4D plans was significantly lower by 0.4 ± 0.5Gy (p = 0.04).

As shown in Table 1, there was no significant difference in the PTV coverage between the ITV and 3D plans (p = 0.3). But the doses to OAR were significantly greater for all OAR investigated in the ITV plans (all p values ≤ 0.05), as shown in Table 3. To maintain similar dose coverage to the PTV, the doses to the OAR have to be compromised in the ITV strategy due to the enlarged PTV margin accounting for the tumor motion. Therefore tumor tacking based motion management clearly demonstrated an advantage in terms of OAR dose sparing.

Discussion

Recalculating treatment plan dose in 4D mode will give a representation of the true dose delivered to the target and OAR since the dose distribution is adjusted accounting for the respiration motion. During treatment, the direction of radiation beams created in the 3D plan is adjusted in real-time as the patient breathes, to continuously follow the target through all phases of respiration and provide adequate dose coverage. Critical structures nearby, however, may remain static or move at a different pace as the target does, therefore the doses to critical structures achieved in treatment planning may differ significantly from those actually being delivered. Our study indicates that dose coverage can be compromised by ~10% for certain patients, and dose parameters to critical structures can significantly differ from those calculated in the 3D plan.

The change of dose parameters in 4D recalculation varies depending on the location of individual OAR. For example, the maximum dose to the spinal cord became lower, but mean dose to the kidneys became higher. Moreover, for the OAR in the vicinity of the target, dose parameters may change dramatically, such as the maximum dose to the duodenum in the pancreas cases and to the liver in the liver cases. Therefore, this study suggests that a 4D dose recalculation be necessary to reliably assess the real dose delivered to the target and OAR in tumor tracking based radiotherapy, especially when the OAR is close to the target. Moreover, we found the most dramatic dose discrepancies occurred in the superior-inferior and anterior-posterior directions, concurring with the most dramatic motions induced by respiration [31,32].

There are several drawbacks for this study. First, there were only a limited number of patients included. The conclusion could be more robust should more patients be included in future studies. Second, this is a retrospective study and most patients were not actually treated with Cyber Knife and did not have fiducials implanted. This may result in uncertainty in target alignment during 4D dose recalculation. To overcome this disadvantage, we identified as many landmarks and features as possible to assist the rigid alignment. This was also performed in the deformable registration to ensure a robust dose composite. Nonetheless, we were still able to draw meaningful conclusions that provide valuable guidance for the clinical practice.

Table 2: Differences in OAR doses between 4D and 3D plans (4D - 3D, unit: Gy).

Patients	Duodenum			Liver			Kidney			Spinal cord		
	D_{max}	D_{5cc}	Mean dose	D_{max}	D_{700cc}	Mean dose	D_{max}	D_{200cc}	Mean dose	D_{max}	$D_{0.25cc}$	Mean dose
P1	6.5	0.1	0.2	-0.5	0	-0.1	-0.2	-0.6	0	-0.5	-0.3	0
P2	8.3	2.1	0.4	1	0.3	0.1	0	0	0	-0.3	0	0
P3	-2.5	-0.4	0.2	0.3	-0.5	-0.3	2.5	-0.1	0.5	-0.6	-0.4	0.1
H1	-3	-0.8	-0.2	-5.4	-0.1	-0.1	2.2	-0.3	0.4	0	0	0.1
H2	0.4	-0.2	0.1	1	0.3	0.6	-1.7	-0.1	0.5	-1.4	-1.2	-0.1
H3	0.2	0	0	2	0.1	0.2	-0.1	-0.1	0	0.1	0.1	0
H4	-0.1	-0.1	0	0.4	0.1	0.2	-1.5	-0.3	0	-0.4	-0.4	0
H5	2.5	1.5	0.1	5.4	0.8	0.8	0.3	-0.5	0.3	-0.1	-0.1	0.1
Average	1.5	0.3	0.1	0.5	0.1	0.2	0.2	-0.2	0.2	-0.4	-0.3	0
St. Dev.	4	1	0.2	3	0.4	0.4	1.5	0.2	0.2	0.5	0.4	0.1
P value	0.3	0.44	0.17	0.64	0.36	0.26	0.74	0.02	0.03	0.04	0.09	0.55

Table 3: Differences in OAR doses between ITV and 3D plans (ITV-3D, unit: Gy).

Patients	Duodenum			Liver			Kidney			Spinal cord		
	D_{max}	D_{5cc}	Mean dose	D_{max}	D_{700cc}	Mean dose	D_{max}	D_{200cc}	Mean dose	D_{max}	$D_{0.25cc}$	Mean dose
P1	5.1	2.7	2.4	0.5	0.2	0.7	3.2	0.6	0.6	1.1	1	0.3
P2	14.4	14	4.4	4.8	1.1	1.1	4.3	0	0.1	0.2	1.1	0.5
P3	7.4	1.9	1.5	1.3	0.7	0.8	0.5	0.3	0.3	1.6	2.1	0.4
H1	6.7	3.2	1.9	14.3	1.8	2.2	1.1	0.4	0.5	2.4	1.9	0.7
H2	1.6	0.8	0	9.1	1.2	1.3	1.2	0.3	0	0.3	0.1	0.2
H3	-6	-2.1	-0.1	2.6	0.8	1.8	1.4	0.1	0.5	-0.7	-0.4	0.3
H4	0.8	0.3	0.5	2.1	1.3	1.9	4.3	0.2	1.1	2.4	2.4	0.7
H5	6.8	4.7	0.7	1.9	2.3	2.7	1.1	0.7	0.7	1.7	1.7	0.6
Average	4.6	3.2	1.4	4.6	1.2	1.6	2.1	0.3	0.5	1.1	1.2	0.5
St. Dev.	6	4.8	1.5	4.8	0.7	0.7	1.5	0.2	0.4	1.1	1	0.2
P value	0.03	0.05	0.02	0.02	<0.01	<0.01	<0.01	<0.01	<0.01	0.01	<0.01	<0.01

Conclusion

Although it is an invasive option with the need of gold fiducial implantation in or near the target, using tumor tracking to treat abdominal targets can be of great benefit. It minimizes the dose to OAR because of the reduced PTV volume, unlike the ITV strategy which includes an ITV margin to account for the respiratory motion. Our study suggests a 4D dose calculation may be necessary in order to assess the real doses delivered to the target and OAR. Dose change varies in the 4D plan depending on the location of OAR, therefore dose parameters to an OAR should be examined individually.

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