Radiotherapy and Oncology xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

Dynamic tumor-tracking radiotherapy with real-time monitoring for liver tumors using a gimbal mounted linac

Yusuke Iizuka [a], Yukinori Matsuo [a,*], Yoshitomo Ishihara [a], Mami Akimoto [a], Hiroaki Tanabe [b], Kenji Takayama [b], Nami Ueki [a], Kenji Yokota [a], Takashi Mizowaki [a], Masaki Kokubo [b,c], Masahiro Hiraoka [a]

[a] Department of Radiation Oncology and Image-applied Therapy, Kyoto University Graduate School of Medicine; [b] Division of Radiation Oncology, Institute of Biomedical Research and Innovation, Kobe; and [c] Department of Radiation Oncology, Kobe City Medical Center General Hospital, Japan

ARTICLE INFO

Article history:
Received 12 February 2015
Received in revised form 24 August 2015
Accepted 30 August 2015
Available online xxxx

Keywords:
Dynamic tumor tracking
Real-time monitoring
Liver tumor

ABSTRACT

Purpose: Dynamic tumor-tracking stereotactic body radiotherapy (DTT-SBRT) for liver tumors with real-time monitoring was carried out using a gimbal-mounted linear accelerator and the efficacy of the system was determined. In addition, four-dimensional (4D) dose distribution, tumor-tracking accuracy, and tumor-marker positional variations were evaluated.

Materials and methods: A fiducial marker was implanted near the tumor prior to treatment planning. The prescription dose at the isocenter was 48–60 Gy, delivered in four or eight fractions. The 4D dose distributions were calculated with a Monte Carlo method and compared to the static SBRT plan. The intrafractional errors between the predicted target positions and the actual target positions were calculated.

Results: Eleven lesions from ten patients were treated successfully. DTT-SBRT allowed an average 16% reduction in the mean liver dose compared to static SBRT, without altering the target dose. The average 95th percentiles of the intrafractional prediction errors were 1.1, 2.3, and 1.7 mm in the left–right, cranio-caudal, and anterior–posterior directions, respectively. After a median follow-up of 11 months, the local control rate was 90%.

Conclusions: Our early experience demonstrated the dose reductions in normal tissues and high accuracy in tumor tracking, with good local control using DTT-SBRT with real-time monitoring in the treatment of liver tumors.

 Radiotherapy and Oncology xxx (2015) xxx–xxx

While hepatocellular carcinoma (HCC) is the most common primary liver cancer [1], the liver is also a frequent site of metastases from other tumors, especially those of the gastrointestinal tract. Clinical guidelines recommend surgical resection, liver transplantation or radiofrequency ablation (RFA) to treat localized HCC in patients with good hepatic function. However, only 10–30% of patients with HCC or liver metastases are candidates for tumor resection, mainly because of their poor hepatic function. Furthermore, RFA cannot be applied for primary or metastatic tumors larger than 3 cm, near vessels, the intestines, or the biliary system nor can it be used to treat tumors not reached under ultrasonography or computed tomography (CT) guidance [2,3].

Stereotactic body radiotherapy (SBRT) provides excellent local control of liver tumors and is thus recognized as an alternative therapy for patients with liver tumors not suitable for resection or RFA [4–8]. However, because the liver moves during the respiratory cycle, if respiratory motion is not appropriately managed, normal liver tissue will be unintentionally included in the irradiation field.

The American Association of Physicists in Medicine Task Group 76 proposed five methods to control motion: motion-encompassing, respiratory-gating, breath-hold, forced shallow breathing with abdominal compression, and real-time tumor-tracking [9]. Among these, real-time tumor-tracking is recognized as the optimum method of managing respiratory motion with respect to the normal tissue irradiation dose, treatment time, and patient compliance.

In this study, we applied dynamic tumor-tracking (DTT) SBRT to liver tumors and evaluated four-dimensional (4D) dose distribution, tumor-tracking accuracy, and positional variations between the tumor and the fiducial marker during the respiratory cycle.

* Corresponding author at: 54 Kawahara-cho, Shogoin Sakyo-ku, Kyoto 606-8507, Japan.
E-mail address: ymatsuo@kuhp.kyoto-u.ac.jp (Y. Matsuo).

http://dx.doi.org/10.1016/j.radonc.2015.08.033
0167-8140/

Materials and methods

Patients

Eligibility criteria for this study were as follows: (1) one or two liver tumors with a diameter ⩽50 mm, (2) patients medically unfit for surgical resection or percutaneous ablation, or who refused these therapies, (3) Eastern Cooperative Oncology Group performance status [10] of 0–2, (4) Child-Pugh score ⩽8, and (5) written informed consent. This study was carried out in Kyoto University Hospital (KU; Kyoto, Japan) and Institute of Biomedical Research and Innovation (IBRI; Kobe, Japan), and approved by our Institutional Review Boards.

Treatment system

We used the Vero4DRT system (formerly called MHI-TM2000; Mitsubishi Heavy Industries Tokyo, Japan, and BrainLab, Feldkirchen, Germany) v.3.1.6 for this study.

Mechanical details of the Vero4DRT system have been described [11].

Our tumor-tracking is based on a pre-built 4D model, which correlates the internal tumor position with an external respiratory signal. The internal tumor positions are determined via implanted fiducial marker detected with the kV X-ray imaging subsystems. The respiratory signals are acquired with an infra-red (IR) camera that monitors the IR markers on the patient's abdominal wall [12,13].

Pre-planning procedures

Before treatment planning, a gold coil marker (Visicoil, IBA dosimetry, Louvain-la-neuve, Belgium) was inserted near the tumor [14]. Planning CTs were acquired 1 week after insertion of the marker.

Two sets of 4DCT (non-contrast and contrast-enhanced) and two or three sets of breath-hold CT at exhale were acquired for treatment planning using a 16-slice CT scanner. The non-contrast 4DCT images were used to calculate the monitor units (MUs), to avoid an influence of contrast medium, and the contrast-enhanced 4DCT images were used for delineation of target volumes. After CT scanning, a 4D model was built to evaluate mean and standard deviation (SD) in errors between detection and prediction from the 4D model, and to evaluate tumor motion amplitude using the ExacTrac subsystem. The detailed protocols for the Visicoil insertion and CT acquisition are described in the Supplementary materials section.

Treatment planning

The non-contrast breath-hold CT and the end-exhale phase from the non-contrast 4DCT were used as a reference CT at IBRI and KU, respectively. Gross tumor volumes (GTVs) were delineated on the contrast-enhanced breath-hold CT scans and on the 10-phase images from the contrast-enhanced 4DCT scans using iPlan RT image (v4.1; BrainLab). When the tumors were difficult to identify on the planning CTs, the images were fused with diagnostic CT or magnetic resonance images (MRI) based on anatomical landmarks. An internal target volume for tumor-tracking ($ITV_{tracking}$) was defined as a composite of the GTVs from the breath-hold CT and the ten-phase images from 4DCT that were superimposed onto the reference CT, with translation of the mid-point of the Visicoil to be matched. The $ITV_{tracking}$ was supposed to compensate influence of tumor deformation, positional error due to the fiducial marker rotation, and uncertainty in the positional relationship between the tumor and fiducial marker during respiration. The planning target volume for tumor-tracking ($PTV_{tracking}$) was defined as the $ITV_{tracking}$ plus additional margins of 5 mm or larger in each direction. The additional margins were defined individually for each patient. An offset vector between the tumor and the mid-point of the Visicoil was determined on the reference CT, which was transferred to ExacTrac system. The offset vector was assumed to be constant and was applied to all treatment fractions. A static SBRT plan, based on the motion-encompassing method, was prepared as a backup in case tracking irradiation could not be applied. ITV for the motion-encompassing method (ITV_{backup}) was defined as a simple composite of GTVs from the breath-hold CT and the 4DCT without CT center translation. For the PTV for static irradiation (PTV_{backup}), a 5-mm margin expansion was applied to the ITV_{backup} in each direction. We describe and illustrate the definition of these targets in detail in the Supplementary material section.

The reference CT image set was used for dose calculation in the tracking plan, and an average image from the 4DCT was used for the static plan. The dose distributions were calculated using the X-ray voxel Monte Carlo algorithm in iPlan RT dose (v4.5; BrainLab).

The prescribed dose was 48–60 Gy, delivered in 4–8 fractions at the isocenter in both the DTT and the static plans. The multi-leaf collimator was shaped to the PTV plus 0- to 5-mm and adjusted manually to fit the 80% isodose line to the PTV edge and follow dose constrains of the liver or other organs at risk (OARs). The dose constraints in our hospitals are shown in Table 1. Seven to nine static non-coplanar ports of the 6-MV beam were arranged, with a dose rate of 500 MU/min. Intensity modulated radiotherapy (IMRT) was not used in this study.

An in-house-developed software was used to compare dose distributions between the DTT and the static plans. The software can calculate dose distribution based on a Monte Carlo simulation and by considering the gimbal head rotation which was determined by the offset vector and the position of fiducial marker [15,16]. Doses were calculated for each phase from the non-contrast 4DCT in the both plans without dose accumulation and evaluated statistically by paired *t*-test, after these values were assured to follow a normal distribution. The target and OAR volumes were transferred from the contrast-enhanced 4DCT and modified manually. When the dose–volume metrics in the DTT plan were better than those in the static plan, we decided to apply the DTT irradiation to the patient.

Beam delivery and evaluation of accuracy

The patient was placed in supine position on the vacuum pillow and set-up error was corrected. Then, a 4D model was built for the treatment fraction. During irradiation, the position of the Visicoil was monitored visually using the kV X-ray imagers every second through the console display to ascertain the irradiation was performed accurately (Supplementary Fig. 2) [17].

The evaluation of intrafractional prediction error and positional variation was carried out after the treatment was finished in each patient in the same way as in the lung tumor [18,19]. The details are described in the Supplementary material section.

Table 1
Dose constraints for organs at risk in our hospitals.

Organ	Dose constraint
Liver	V_{20} < 25%, spared V_{15} > 700 cm^3 (if possible)
Spinal cord	Max dose 25 Gy/4 fr, 33.5 Gy/8 fr
Kidneys	V_{20} < 30%
Stomach, colon	V_{35} < 1 cm^3 (4 fr), V_{40} < 1 cm^3 (8 fr)
Duodenum	V_{28} < 1 cm^3 (4 fr), V_{35} < 1 cm^3 (8 fr)

Spared V_{15} means the volume receiving ⩽15 Gy; V_n: organ volume that receives a dose of *n* Gy or less; D_n: dose received by *n*% of organ volume.

Please cite this article in press as: Iizuka Y et al. Dynamic tumor-tracking radiotherapy with real-time monitoring for liver tumors using a gimbal mounted linac. Radiother Oncol (2015), http://dx.doi.org/10.1016/j.radonc.2015.08.033