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Liver cancer

Application of active breathing control in 3-dimensional conformal radiation therapy for hepatocellular carcinoma: The feasibility and benefit☆

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Abstract

***Background and purpose*: To investigate the feasibility and effectiveness of utilizing active breathing coordinator (ABC) in 3DCRT for HCC.**

***Materials and methods*: A dosimetric comparison between the free-breathing (FB) plan and ABC plan in HCC 3DCRT was performed. Set-up errors and reproducibility of diaphragm position using ABC were measured, and patients' acceptance was also recorded.**

***Results*: From April 2005 to February 2007, 28 HCC were irradiated with ABC and they tolerated ABC well. The mean dose to normal liver was reduced from 16.9 Gy in FB plan to 14.3 Gy in ABC plan. PTV for ABC and FB plans were 529 cm^3 and 781 cm^3, respectively, and V_{23} were reduced from 45% to 30%. The predicted incidences of radiation-induced liver disease by Lyman model were 1% and 2.5%, respectively, in favor of ABC plan. The systematic and random errors for the ABC and FB plans were 1.2 mm vs. 4.7 mm, 1.6 mm vs. 3.5 mm, and 1.8 mm vs. 2.7 mm, respectively, in cranio-caudal, anterior-posterior, and left-right directions. The average intrafraction reproducibility of diaphragm position in cranio-caudal direction was 1.6 mm, and the interfraction, 6.7 mm.**

***Conclusions*: The utilization of ABC in HCC 3DCRT is feasible, and can reduce liver irradiation.**

Keywords: Active breathing control; Hepatocellular carcinoma; 3-Dimensional conformal radiation therapy; Set-up error; Reproducibility; Dosimetric parameter

Three-dimensional conformal radiation therapy (3DCRT) has been increasingly used in the treatment for medically inoperable hepatocellular carcinoma (HCC). The efficacy of 3DCRT in regard to improving the quality of life and survival in unsectable or medically inoperable patients with HCC has been repeatedly suggested, although the number of publications is scarce [1–4]. One of the most pertinent issues during HCC irradiation is the target motion due to breathing, and it has been proven that breathing induced motion is mainly in cranio-caudal (CC) direction with a range between 1 and 3 cm [5–8]. To mitigate this effect, an extra margin is usually needed to ensure sufficient coverage of the clinical target volume (CTV) traditionally. As such, larger volume of normal liver would be irradiated, and the mean dose to liver parenchyma would be increased. Such planning strategy is usually associated with increased radiation-induced liver disease (RILD).

Techniques including respiratory gating system [9,10], real-time tumor tracking systems [11], and active breathing coordinator (ABC) [12] have been tested to reduce the negative impact of organ motion due to breathing in various cancers such as lung cancer. In the current study, we document a trial to evaluate the clinical feasibility and dosimetric parameters of ABC technique in the treatment of HCC using 3DCRT.

Materials and methods

Patients and treatments

All patients enrolled in the current study were derived from an IRB approved institutional phase I 3DCRT dose escalation trial for HCC patients. Written consent was obtained from all participating patients. The eligibility criteria

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included: (1) pathologically confirmed HCC; (2) surgically unsectable or medically inoperable diseases, or surgery declined by the patient; (3) solitary intrahepatic lesion; (4) associated with cirrhosis of Child–Pugh A; (5) Karnofsky performance status (KPS) of ⩾70; (6) normal renal function and adequate bone marrow reservation. In addition, all patients should be capable to hold breath for more than 30 s after deep inhalation, and the position of diaphragm should remain still with less than 3 mm movement during breath holding on verifying fluoroscopy observation.

All cases were treated with 2 cycles of transcatheter arterial chemoembolization (TACE) with 1-month interval between cycles, followed by 3DCRT. Radiation therapy was delivered one month after the completion of TACE using a dose escalation schedule in conventional fractionation (i.e., 2 Gy/daily fraction, 5 fractions per week). For tumors between 5 and 10 cm in their largest diameter, radiation dose escalation initiated from 42 Gy and ended at 62 Gy. For tumors larger than 10 cm in their largest diameter, radiation dose escalation initiated from 40 Gy and ended at 52 Gy. The increment dose was 4 Gy in both groups.

Patient immobilization

All patients were immobilized using customized vacuum lock in supine position with arms placed on their forehead. The immobilization device was used during planning CT, observation of diaphragm motion under fluoroscopy, and each radiation session.

ABC technique and patients' training

The device of ABC used in this study was manufactured by Elekta Oncology System (Crawley, UK). The components and procedures of ABC were described previously [12]. In the current study, all patients were required to hold breath after a deep inhalation at approximately 70–80% of their total lung capacity. Training was essential for patients' cooperation to ABC, and the repeated exercises were required in all patients prior to the start of radiation. Inhaled threshold volume and the breath-holding time were recorded, and a patient-specific ABC data file was created for CT simulation and radiation for each patient.

Observation of liver motion with free-breathing (FB), and measurement of intrafraction reproducibility and stability of liver/diaphragm position with ABC

The liver movements were observed under fluoroscopy of a conventional simulator in both FB and ABC breathing pattern after patients' training. In FB, the tumor and liver movement was measured in CC direction using the deposited iodine in the TACE treatment. In cases iodine was not observed, the dome of the diaphragm as surrogate of tumor was observed and its position measured. The distance between the most superior and inferior positions was used to determine the margins of CTV to internal target volume (ITV). During ABC, patients were asked to have breath holding after deep inhalation and to hold breath for the predetermined holding time length in evaluating both reproducibility (intrafraction) and stability of liver/diaphragm position by comparing the level of the lesion/diaphragm and bony structures. The observation would be repeated for five times to get standard deviations. Photoshop 7.0 (Adobe System, San Jose, CA) was used to establish the relative positions of deposited iodine or the dome of diaphragm to isocenter on the anterior-posterior (AP) fields.

Treatment planning

All patients underwent CT simulation for planning. Helical CT scan was performed with 5 mm thickness and a pitch of 1.1. Two sets of CT images from 3 to 4 cm above the dome of diaphragm to the level below right kidney were taken both in FB and breath-holding status with ABC. Two 3DCRT plans in FB and ABC were then generated.

Organs at risk (OAR) contoured included liver, kidneys, spinal cord, stomach and duodenum. Gross tumor volume (GTV) was delineated with the aid of iodinated-oil deposited in lesions by TACE. Whereas, for cases, whose iodinated-oil deposit was poorly, or not, found in the tumor, fusion of MRI or diagnostic CT with contract to the planning CT was required. Eight-mm margin was added uniformly to the GTV to form CTV, and the ITV was determined according to the motion of the tumor or liver seen in fluoroscopic observation in FB, or diagram reproducibility when ABC was used. An addition 6 mm margin was added to ITV to form the planning tumor volume (PTV).

Multiple co-planar or non-coplanar fields were designed. Dose was prescribed at isocenter from 40 to 62 Gy according to the dose escalation schedule. Mean dose to normal liver (MDTNL) (normal liver volume = total liver volume − PTV) was limited to 23 Gy or less, and the dose volume histogram (DVH) of the normal liver was in the tolerable area according to our previous experience [13]. Both FB and ABC plans were designed using the same beam numbers, and were optimized in the same method; however, minor adjustment of beam angles was made to assure dose to OARs within tolerance.

Measurement of set-up error and interfraction reproducibility

Patients' positions were verified weekly by electronic portal imaging device (EPID) at 0 and 270 to measure the set-up errors. Dose of 2-MU was needed for EPI acquisition. Anterior and left-lateral edges of the vertebral column and diaphragm dome seen on EPI were compared and matched to digital reconstruction radiography (DRR) by template-matching software (Iview GT, Elekta Oncology Systems, Crawley, UK). The software automatically generated position offsets in CC, left-right (LR) and anterior-posterior (AP) directions after comparisons. Patient reposition was required when displacement was more than 5 mm in any direction. The offset of diaphragm dome relative to the vertebral bodies in CC direction was used to calculate interfraction reproducibility of the diaphragm.

Radiation delivery

After the patients were placed on the identical position as that for CT simulation, one radiation therapist gave instruction to the patient and monitored his/her breath pattern. Radiation was initiated immediately once the ABC advice triggered breath hold. Irradiation dose of one field could be delivered in one or two periods of breath holding,