Journal of
Nuclear Medicine & Radiation Therapy

Zhang et al., J Nucl Med Radiat Ther 2012, S:6
DOI: 10.4172/2155-9619.S6-012

Review Article | Open Access

Motion Management in Stereotactic Body Radiotherapy

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Abstract

With the technologic advancements in image guidance and dose delivery, stereotactic body radiotherapy (SBRT) is being widely used for cancer treatment in various anatomical locations as a noninvasive alternative to surgery. To deliver ablative doses to tumors with limited normal tissue toxicity, SBRT requires high accuracy in treatment setup which requires taking tumor motion into account. Techniques are also applied in SBRT to minimize tumor motion during dose delivery. This paper reviews techniques for motion management in SBRT.

Keywords: Stereotactic body radiotherapy; Tumor motion management; Image-guided radiotherapy

Introduction

Stereotactic radiosurgery (SRS) and Stereotactic radiotherapy (SRT) are characterized by the delivery of a high radiation dose to a small volume in a short time interval with high accuracy as well as conformality. Intracranial SRS was first described by Lars Leksell using a stereotactic approach with a three dimensional Cartesian coordinate system to localize intracranial targets. The biologic effect of stereotactic irradiation rests on its ability of tumor ablation.

The great success of intracranial SRS has recently led to the development of similar techniques for the treatment of lesions outside the brain. Stereotactic body radiation therapy (SBRT), however, is much more complicated due to motion of targets and normal tissues. SBRT is used in the treatment of a wide range of tumor sites, including lung [1], liver [2], pancreas [3], prostate [4], spine [5], head-and-neck [6] and some other sites [7-12]. A variety of techniques have been reported to address this issue; these techniques for improvement of accuracy and precision can be classified into two broad categories: immobilization and motion reduction techniques, and image guidance. Immobilization with stereotactic body frames aims to optimize patient fixation, provide external reference system for stereotactic coordinates, and use a device to reduce breathing mobility. Image guidance technology allows the guidance of dose delivery with three-dimensional real-time information of target localization. These tools serve to reduce patient set-up errors and provide systematic assessment of organ motion and deformation during the course of treatment.

Different from the conventional radiotherapy, radiation dose is delivered in fewer fractions and higher fractional dose in SBRT [13]. For example, at our institution, if a patient with an early stage non-small-cell lung cancer is treated with SBRT, 50 Gy is delivered in 5 fractions, while, the conventional prescription would typically be 70 Gy in 35 fractions.

Treatment plans are usually generated based on patients' CT images and include either multiple non-coplanar fixed gantry beams or arcs. Multiple beams or large-angle arcs ensure sharp dose fall-off outside the target and help to reduce the skin dose which has a potential to cause serious injury [14]. The planning can be either forward (e.g., 3D conformal radiotherapy (3D-CRT)) or inverse intensity modulated radiotherapy (IMRT) or volumetric-modulated arc therapy (VMAT) [15,16]. The gross tumor volume (GTV) is contoured by a physician on the planning CT. The clinical target volume (CTV) is defined by a margin around GTV to include microscopic tumor extension. In lung SBRT, this expansion is often minimal, if any [17]. Another margin is then added to CTV to define the planning target volume (PTV), which takes account for daily setup error and tumor motion. The goal of a treatment plan is to cover the PTV with the prescribed radiation dose, and spare normal tissues surrounding PTV as much as possible at the same time. Unlike in conventional therapy, dose heterogeneity is allowed and even encouraged as long as the hot spots are confined to the PTV [13].

Because of the high fractional dose, it is extremely important that the treatment organ geometry is as close as possible to the planning CT data. Immobilization devices [18-21] or other inter-fractional motion management [22,23] is one way to move towards that goal [24]. The recent development in on-board imaging and cone beam CT technology greatly helps reducing the complexity of accurate patient setup [25].

During dose delivery, tumor motion due to respiration may vary the dose delivered to target volume and normal tissues [26,27]. Intra-fractional motion management, including abdominal compression [28], breath hold [29,30], respiratory gating [31,32], tumor tracking [33,34], is essential in SBRT to reduce the motion and/or its effect on dose coverage.

Patient Immobilization

Vacuum cushions

A typical vacuum cushion consists of a flexible plastic bag filled with the tiny polystyrene beads. The bag is connected through a valve to a vacuum pump. When vacuum is drawn, the pillow forms a rigid cradle under the patient (Figure 1A). This rigid cradle formed at the time of simulation is capable of maintaining its shape throughout the entire treatment course. The impressions of the body on the vacuum cushion help to reproduce the patient's position during any treatment fraction.

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Received June 29, 2012; **Accepted** July 24, 2012; **Published** July 26, 2012

Citation: Zhang GG, Michael Yu HH, Stevens CW, Dilling TJ, Hoffe SE, et al (2012) Motion Management in Stereotactic Body Radiotherapy. J Nucl Med Radiat Ther S6:012. doi:10.4172/2155-9619.S6-012

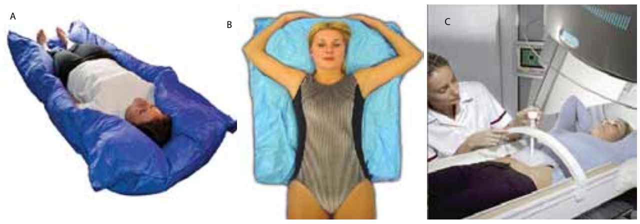

Figure 1: (A) Vacuum cushion, courtesy of Qfix.Systems. (B) Alpha cradle, courtesy of Smithers Medical Products. (C) Elekta stereotactic body frame, courtesy of Elekta Corp.

Vacuum cushions are commonly used in conventional 3-D conformal and intensity modulated radiotherapy (IMRT) treatments for patient positioning and immobilization. They are also an important piece of immobilization device in SBRT, used alone [22,35,36] or in combination with other immobilization devices [37,38].

Alpha cradles

Another type of the individualized external positioning device is made using Alpha Cradle™ (Smithers Medical Products, Inc., North Canton, OH) foaming agents. After the foaming agents are mixed and poured into a cradle frame, patient lies down on the cradle which is covered by a plastic sheet. About 15 minutes later, a foam cradle that follows patient's body contour is formed (Figure 1B). The cradle is then used during CT simulation and treatments for patient positioning and immobilization [39,40].

Thermoplastic masks

A clinical thermoplastic mask usually consists of a rigid frame that can be mounted to a treatment couch, and a piece of thermoplastic. The thermoplastic becomes soft and pliable when placed in a warm water bath. When the soft thermoplastic is pulled over a patient, it is molded to the patient's body contour. After cooling, a rigid replica of the patient's body contour is created, which can be used afterwards for patient repositioning before each treatment fraction.

Thermoplastic masks are sometimes used in SBRT, mostly together with vacuum cushions [37].

Body frame

Usually including an abdominal compression device (*vide infra*) and a vacuum cushion, stereotactic body frames are often used to reduce daily setup errors [2,21,38,41]. There are many different stereotactic body frames used clinically with the most commonly used developed by Elekta (Elekta Corp, Stockholm, Sweden, Figure 1C).

The stereotactic body frame is designed to be used with CT simulation for treatment planning and thereafter for each treatment fraction. The body frame has its own 3-D coordinate system, which can be read in CT images. The target volume and thus the treatment isocenter are defined using the body frame's coordinate system. The immobilization function is realized by the vacuum cushion inside the body frame. The abdominal compression device is used to reduce diaphragm motion (*vide infra*).

Before each treatment, a CT scan is taken with patient in the body frame. The tumor volume location is examined relative to the body frame's coordinate system. Isocenter adjustment is performed based on the CT examination.

When CT simulation is performed prior to each treatment to correct larger target deviations or set-up errors, the PTV margin of 5 mm is sufficient for lung, liver, abdominal, pelvic and bone cancers [21].

Intra-Fractional Motion Management

Patient motion during treatment includes respirations, cough, bowel peristalsis, etc., with the respiratory motion being most problematic for SBRT. Reducing respiratory motion and/or its dosimetric consequences is one of the major components of an SBRT Program. Different techniques have been suggested.

Abdominal compression

Minimizing respiratory motion with the application of abdominal pressure during pretreatment imaging and treatment delivery is a simple method to minimize respiratory-induced tumor mobility for both lung and liver lesions. Patients are forced to take shallow and fast breath when upper abdomen is pushed down by a pressure device, which limits diaphragm caudal excursion.

The pressure device built in a stereotactic body frame is usually controlled by a scaled screw which provides reproducible position of the compression plate for the entire treatment course [21]. Heinzerling et al. [27] reported a modification to this device: a pressure sensor is inserted under the plate so that the pressure can be quantitatively recorded and reproduced.

Breath hold

Another method to reduce tumor motion is breath-holding. This however requires patients who posses a relatively good respiratory function and are cooperative to follow systemic coaching. Residual mobility exists and should be accounted for.

Treatment planning is performed on a particular phase of a 4D CT scan. After the initial setup and tumor position verification, the radiation dose is delivered while the patient holds his breath at the planned respiratory phase, while the beam is put on hold (beam off) when the phase starts to deviate from the planned respiratory phase.

The breath cycle phase and/or the breath hold tidal volumes are often monitored by a spirometer. The reproducibility of organ position can be 5.1 ± 4.8 mm in the superior-inferior direction inter-fraction, and 4.0 ± 3.5 mm intra-fraction, at the end-inspiration phase. The end-expiration position is more stable, leading to a residual motion magnitude of about a half of that at the end-inspiration [30]. The study was conducted with 5 healthy volunteers. In another study of 20 patients without using a respiratory monitoring device [42], the intra-fractional mean maximum differences in deep inspiration were 2.2 and 3.1 mm in superior-inferior direction for self controlled (active) and following verbal command (passive) breath hold, respectively. The anterior-posterior differences were 1.4 and 2.4 mm and right-left 1.3 and 2.2 mm, respectively.

Radiation can be delivered at either expiration [43,44] or inspiration [45]. The advantage of using the expiration phase is better reproducibility [30], while the advantage of treating at inspiration is the potential for greater separation between the target and sensitive organs, with the resulting decrease in treatment toxicity [46]. In addition, for lung SBRT the irradiated lung volume is reduced when treated on inspiration [47] and it is easier for the patient to comply with. In abdominal cancer treatment, expiration breath hold is more preferred because it is more stable [29,30,48]. While the dosimetric advantages of expiration vs. inspiration breath hold were subject to debate [47,49], either one is preferable to free breathing. The maximum reduction in the lung volume irradiated to modest doses during lung SBRT associated with the deep inspiration breath hold is realized when the PTV margins are small (5 mm) [50] .

Respiratory gating

The idea of respiratory gating is similar to breath hold: radiation is delivered during a certain part of the respiratory cycle as defined in the treatment plan. The difference is that the patient can breathe freely and the radiation beam on/off state is controlled by a respiration monitor, with the beam being turned one periodically. The respiratory gating technique was introduced to conventional radiotherapy in late 1980s [51] and clinically implemented later on using linear accelerators especially for SBRT [52,53].

The respiratory gating process starts with the acquisition of a time-correlated (4D) CT scan. The patient breathing cycle is monitored and a quasi-periodic respiration trace curve is obtained. The breathing cycle is divided into multiple, typically 10, separate segments, either by phase or amplitude. Multiple gantry rotations are needed at each table position to capture the images corresponding to each respiratory phase. A properly sorted stack of images acquired at the same phase provides a 3D CT dataset for that phase. A full set of such 3D datasets for all respiratory phases constitutes a 4D CT dataset. The CT projections can be time (phase) stamped either through axial scanning with prospective binning [54] or helical scanning with retrospective binning [55]. 4D CT scans dramatically decrease respiratory motion artifacts prominent in conventional CT datasets. Ford et al. reported that reconstruction volumes match those expected on the phantom scans to 5% or less [56].

Major commercial respiration monitoring systems include the Real-Time Position Management (RPM) Respiratory Gating System (Varian Medical Systems, Palo Alto, CA), ExacTrac™ (BrainLAB AG, Heimstetten, Germany) and air bellows belt adapted by Big Bore CT™ (Philips Medical Systems, Cleveland, OH), three-dimensional surface tracking GateCT™ and Gate RT™ (Vision RT Ltd, London, UK).

The RPM system uses a camera, infrared light sources and a reflector. The reflector is placed on patient's abdomen. The reflector box position, which is assumed to correlate to respiration phases, is obtained by the camera acquiring the reflected infrared light. The respiratory gating technology in ExacTrac system is conceptually similar to RPM, with the different reflectors and camera design. Three-dimensional (3-D) surface tracking is a newer optical based technology. The pattern of light is projected on the patient surface and its shape is constantly monitored by the two or three angled cameras. The respiratory phase is correlated to the reconstructed 3-D surface motion. The air bellows belt technique differs by using pressure sensor instead of optical technologies. An air bellows belt is placed around patient's abdomen. As the abdomen moves with respiration, the volume of the bellows changes, resulting in the pressure changes converted by the transducer into a pressure waveform from which the respiratory phase information is extracted.

Overall treatment time depends on the gating duty cycle (the ratio of the beam on time to the total elapsed time). A typical duty cycle used in respiratory gating is about 30%. The residual motion of the target volume also depends on the duty cycle [57]. The more phases are allowed for beam on, the higher is the duty cycle, but it obviously also allows for more residual motion. A compromise between treatment time and residual motion range needs to be made.

Tumor tracking

Ideally, radiation beams should follow the tumor. Technically, this is not easy to achieve due to the fact that real time tumor localization is still a difficult task with current technologies. However, periodical tumor motion monitoring is available in some commercial radiotherapy equipment, including Cyberknife (Accuray, Inc., Sunnyvale, CA). Differing from the other linear accelerators using a gantry rotating in a single plane, Cyberknife has its small linear accelerator mounted on a robotic arm, and is designed to deliver radiation beams from many possible angles. This flexibility provides tumor tracking capability. The in-room orthogonal x-ray system periodically takes x-ray images of radio-opaque fiducials inside or close to the tumor. The locations of the fiducials are calculated from the orthogonal images and compared to the reference locations. If the difference exceeds tolerance, the robotic linear accelerator adjusts its direction to aim at the new location of the target volume. A real-time respiratory motion tracking system, the Synchrony® respiratory tracking system, enables the Cyberknife beam to track the tumor based on the external breathing signal and the correlation model that relates the external breathing signal with the motion of the internal markers [58,59]. Usually, longer treatment times are associated with the robotic linear accelerator technology due to the small beam apertures.

Another passive tumor tracking technique has been employed with the conventional gantry-based linear accelerators. Using fluoroscopic tracking, the system triggers the linear accelerator to start and stop treatment only when the markers are located within a predetermined range. Ideally, four fiducial markers are needed to accurately detect tumor rotation and volumetric changes during treatment [60]. Limitations exist and include the feasibility and/or ability of inserting markers in tumors accurately and potential displacement or migration of the markers [61,62]. Available data demonstrated that migration of the markers was not a significant problem when treating liver and prostate lesions [63].

Breath hold technique may be used together with tumor tracking in order to ensure reproducibility [64].

Image Guidance Technology

The potent fractional dose in SBRT requires accurate delivery of radiation to target volume. Image guidance is an indispensable component in SBRT to guarantee accurate delivery [65]. Because of the advanced image guided radiotherapy (IGRT) technologies, frameless SBRT became feasible and popular [37,66-68].

Siemens CT-on-Rails™ has already been used clinically for quite a few years. The more recent IGRT technologies include Varian and Elekta on-board kilovoltage cone-beam CT (CBCT, Figure 2A). CBCT scans are taken prior to each treatment. The couch orientation does not need to change between the CT scan and treatment. Isocenter adjustments can be made remotely through table movements right after the CT

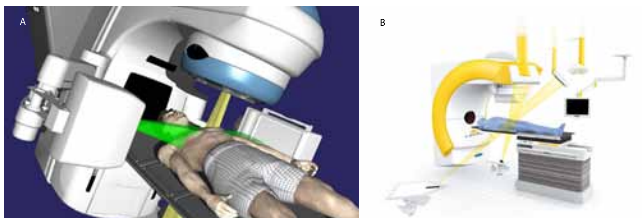

Figure 2: (A) Varian on-board imager that is capable of cone-beam CT imaging for treatment setup. Image provided courtesy of Varian Medical Systems. (B) Orthogonal x-ray system in Novalis for IGRT. Image provided courtesy of BrainLAB AG.

scan and the treatment is carried out immediately thereafter. Treatment tables or couches have traditionally provided three axis translations, but six-degree of freedom tables offering rotational adjustments (pitch, roll and yaw) are entering the market [69]. Another IGRT technique often used for SBRT is a kV image pair obtained from either an in-room x-ray system (Figure 2B) or on-board imager.

Radio-opaque fiducial markers are often surgically inserted into or near the target volume for better visualization. Usually, a pair of x-ray images is taken prior to treatment, and the fiducial marker or bony structure locations are compared with the digitally reconstructed radiograph (DRR) from the treatment planning CT. Isocenter adjustment, in 3D or 6D again can be made remotely immediately prior to treatment [31,43,70].

Treatment Improvement

Setup margin can be 5 mm or even smaller for lung SBRT irrespective of immobilization method when CBCT is used in IGRT [71-73]. The residual error however tends to increase as the treatment time increases, depending on the patient's performance status [74]. Without CBCT guidance, the typical CTV-PTV margin to account for motion and setup deviation in lung cancer IMRT treatment would be 11 mm in the transversal plane and 15 mm cranially and caudally [75].

Abdominal compression significantly reduces tumor motion range [19,28,76-78]. Normally, thoracic tumor motion ranges from 0 to 2 cm or even more [79,80]. With abdominal compression this range can be reduced to sub-centimeter, often to under than 5 mm. Tumor motion reduction using abdominal compression in liver was reported to be significant as well. For most patients, the motion amplitude was reduced to less than 5 mm in all directions [81]. However, another study showed that although abdominal compression reduced tumor motion in most patients, the magnitude of reduction was smaller than previously reported [82]. This difference may be due to the different compression forces. As reported by Heinzerling et al. motion range reduction varies with compression force [27]. With IGRT, CTV to PTV expansion margin in SBRT can be reduced, and thus large increases in the therapeutic ratio for the liver plans could be obtained [83].

In conventional radiotherapy, the local tumor control is historically poor for stage I Non-small-cell lung cancer (NSCLC) treatments, about 30% to 50% at 5 years, usually due to insufficient total dose to the target [84]. With escalation to a higher dose necessary for optimal tumor control, high risk of unacceptable lung toxicity exists [85]. In SBRT, the radiation dose to the normal tissue is minimized and the dose to the target is increased resulting in biologically equivalent doses up to twice as high as in conventional radiotherapy. This improves the local tumor control rates to higher than 90% at 3 years [86] and 73% at 5 years for stage I NSCLC, comparable to the rates after surgery [87]. Good quality of life, overall survival rate and low toxicity were also reported in addition to excellent local control [88,89]. Caution should be used when using SBRT to treat lung cancers near the central airways due to excessive toxicity [38]. Good local control and comparable toxicity was also achieved in liver [90], head and neck [91], and prostate [4] SBRT.

Conclusions

SBRT is a rapidly expanding non-invasive treatment modality for cancer management. Continuing advances in computing technologies and medical imaging will allow us to correct the inherent complex issue of organ motion and its implication on tumor target localization.

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This article was originally published in a special issue, **Cancer Radiation Therapy** handled by Editor(s). Dr. Xin Chen, University of Arkansas for Medical Sciences, USA