Video Article

Stereotactic Radiosurgery for Gynecologic Cancer

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Abstract

Stereotactic body radiotherapy (SBRT) distinguishes itself by necessitating more rigid patient immobilization, accounting for respiratory motion, intricate treatment planning, on-board imaging, and reduced number of ablative radiation doses to cancer targets usually refractory to chemotherapy and conventional radiation. Steep SBRT radiation dose drop-off permits narrow 'pencil beam' treatment fields to be used for ablative radiation treatment condensed into 1 to 3 treatments.

Treating physicians must appreciate that SBRT comes at a bigger danger of normal tissue injury and chance of geographic tumor miss. Both must be tackled by immobilization of cancer targets and by high-precision treatment delivery. Cancer target immobilization has been achieved through use of indexed customized Styrofoam casts, evacuated bean bags, or body-fix molds with patient-independent abdominal compression.[1-3] Intrafraction motion of cancer targets due to breathing now can be reduced by patient-responsive breath hold techniques,[4] patient mouthpiece active breathing coordination,[5] respiration-correlated computed tomography,[6] or image-guided tracking of fiducials implanted within and around a moving tumor.[7-9] The Cyberknife system (Accuray [Sunnyvale, CA]) utilizes a radiation linear accelerator mounted on a industrial robotic arm that accurately follows patient respiratory motion by a camera-tracked set of light-emitting diodes (LED) impregnated on a vest fitted to a patient.[10] Substantial reductions in radiation therapy margins can be achieved by motion tracking, ultimately rendering a smaller planning target volumes that are irradiated with submillimeter accuracy.[11-13]

Cancer targets treated by SBRT are irradiated by converging, tightly collimated beams. Resultant radiation dose to cancer target volume histograms have a more pronounced radiation "shoulder" indicating high percentage target coverage and a small high-dose radiation "tail." Thus, increased target conformality comes at the expense of decreased dose uniformity in the SBRT cancer target. This may have implications for both subsequent tumor control in the SBRT target and normal tissue tolerance of organs at-risk. Due to the sharp dose falloff in SBRT, the possibility of occult disease escaping ablative radiation dose occurs when cancer targets are not fully recognized and inadequate SBRT dose margins are applied. Clinical target volume (CTV) expansion by 0.5 cm, resulting in a larger planning target volume (PTV), is associated with increased target control without undue normal tissue injury.[7,8] Further reduction in the probability of geographic miss may be achieved by incorporation of 2-[^{18}F]fluoro-2-deoxy-D-glucose (^{18}F-FDG) positron emission tomography (PET).[8] Use of ^{18}F-FDG PET/CT in SBRT treatment planning is only the beginning of attempts to discover new imaging target molecular signatures for gynecologic cancers.

Video Link

The video component of this article can be found at https://www.jove.com/video/3793/

Protocol

1. Stereotactic Cyberknife Radiosurgery Consultation

1. **Describe Cyberknife radiosurgery treatment.** Cyberknife radiosurgery involves use of a linear accelerator mounted on an industrial robotic arm similar to machines used to make automobiles. The robotic arm moves the linear accelerator in three-dimensional space around a patient as it progresses through multiple treatment 'stops' for beam delivery. Cross-plane x-rays are obtained during treatment to verify the patient is in a correct treatment position. Since treatment beam delivery is not restricted to a two dimensional plane, this system further enhances the ability to deliver concentrated radiation doses to cancer targets while minimizing the radiation dose to critical skin and visceral organ structures.
2. **Discuss Cyberknife radiosurgery risks.** Cyberknife radiosurgery may result in possible tanning and reddening of skin, fatigue, infrequent nausea or diarrhea, rare visceral organ injury, muscle, nerve, and bone injury, and very small risk of second cancer.

2. Stereotactic Cyberknife Radiosurgery Fiducial Placement

1. **Describe fiducial placement.** Women being treated for persistent or recurrent gynecologic cancers undergo operative or CT-guided placement of *at least three* single 1.6 x 3 mm gold soft tissue fiducials (about the size of a grain of rice) within or near the cancer target. Surgical clips placed at the time of prior surgery are not of sufficient density to be used as radiosurgical fiducials. Surgical clips do not interfere with radiosurgical targeting because of the density discrepancy.
2. **Indicate fiducial positioning relative to radiosurgical target.** Fiducials are placed at varying tissue depths around the radiosurgical target and must be separated by two centimeters or more. Fiducials are positioned within 4 to 6 centimeters of the target.

3. Stereotactic Cyberknife Radiosurgery Treatment Planning

1. **Discuss radiosurgical treatment planning.** *At least one week* after fiducial placement (i.e., so that healing has occurred and fiducial movement is minimized), patients undergo CT-guided SBRT treatment simulation. In our program, two-pin localized evacuated vacuum-bag pelvic immobilization is used.
2. **Indicate patient positioning on the treatment table.** Women are treated in a supine treatment position on the Cyberknife radiosurgical flat tabletop.
3. **Discuss target and patient immobilization.** Patient may undergo evacuated vacuum-bag immobilization to reduce intrafraction motion during radiation dose delivery. Once immobilized, women undergo non-contrasted contiguous axial CT high-resolution imaging (1 to 1 pitch, 1.0 mm slice thickness, voltage 120 kVp, 450 mAs).
4. **Discuss use of advanced imaging for target localization.** After CT imaging, women undergo *preferably* conventional ^{18}F-FDG PET/CT imaging in the same SBRT treatment position. Alternatively, women may undergo conventional contrasted pelvic magnetic resonance imaging.
5. **Describe image co-registration for radiosurgical treatment planning.** Images from high-resolution CT and ^{18}F-FDG PET/CT are imported for inverse radiation treatment planning on the MultiPlan 3.5.2 Treatment Planning System (Accuray).
6. **Describe team approach to radiosurgical treatment planning.** For treatment planning, both a radiation oncologist and gynecologic oncologist contour cancer target clinical target volumes (CTVs). Other disease at-risk tissue is contoured and is included in CTVs. Nearby normal tissue structures such as the small bowel, rectum, bladder, liver, kidneys, lungs, bilateral proximal femurs, vagina, and sacral nerve roots are contoured by the radiation oncologist.
7. **Describe radiation dose prescription.** A radiation prescription dose of 3 × 800 cGy = 2400 cGy (commonly to the 70% isodose line) has been selected. In a 200 cGy biological equivalent dose calculation, nearly 6170 cGy are delivered with this prescription assuming an "α/β" ratio of 10 for tumor. The radiation emitted from a SBRT linear accelerator is collimated either by using one of 12 fixed tungsten circular collimators (5 to 60 mm) or by using a tungsten-copper alloy segmented hexagon IRIS collimator.[14] Normal organs have a tolerance of radiation and use of dose-volume histogram parameters for normal tissue constraint during ablative stereotactic radiosurgery are listed in **Table 1**.

4. Stereotactic Cyberknife Radiosurgery Treatment Delivery

1. **Perform cross-plane image verification.** During Cyberknife SBRT, soft-tissue fiducials (or in some cases rigid anatomical landmarks such as the skull for intracranial lesions and the spine for spine lesions) are tracked by cross-plane radiographic imaging and confirmed to be in the expected target location by the target localizing system (TLS) subsystem.
2. **Verify target positioning.** Fiducials are tracked in three and up to six degrees of freedom (i.e., x, y, z, pitch, roll, and yaw). Images generated by the TLS are automatically registered and compared with digitally reconstructed radiographs (DRRs) generated from the initial treatment planning CT scan.
3. **Verify target positioning.** If results of automatic registration indicate that fiducials have shifted beyond predefined tolerances in any one of the six degrees of freedom (x, y, z, pitch, roll, and yaw), treatment is automatically paused. Patient repositioning then occurs.
4. **Consider target motion.** Targets that move with respiratory motion are treated utilizing the Synchrony Respiratory Tracking subsystem (Synchrony). With the use of a camera mounted in the treatment room, the system continuously tracks the patient's breathing pattern (i.e., obtain external position data) with the use of light-emitting diodes (LEDs) affixed to a vest around the patient's thorax.[10] Together with the fiducial location information (internal position data) obtained from cross-plane x-rays, the Synchrony system builds a correlation model with the external data and the internal data. This correlation model allows the robotic arm to follow any respiratory-induced motion of the target while during the delivery of any and all treatment beams.
5. Treatment may entail 100-150 deliverable treatment positions of the robotic arm. Treatments may last 30 to 90 minutes.

5. Representative Results

Stereotactic body radiation therapy (SBRT) may involve many individual radiation beams (blue vectors) all converging on single or multiple closely associated clinical radiation targets, as shown in **Figure 1A**. A representative good radiosurgical planning outcome gives a deliverable SBRT treatment with high radiation dose cancer target volume coverage and cancer target conformality. **Figures 1B-D** show 131 beams were used to treat on a pelvic relapse of a chemorefractory ovarian cancer target over 42 minutes. SBRT prescribed to the 80% isodose line rendered 100% clinical target volume coverage with a conformality index of 1.94 for a total dose of 2400 cGy in three daily 800 cGy fractions. The dose-volume histograms for the clinical target (red) and for the critical structures of rectum (brown), bladder (yellow), small bowel (light blue) sacral nerves (tan) and hips (orange) are depicted in **Figure 2**.

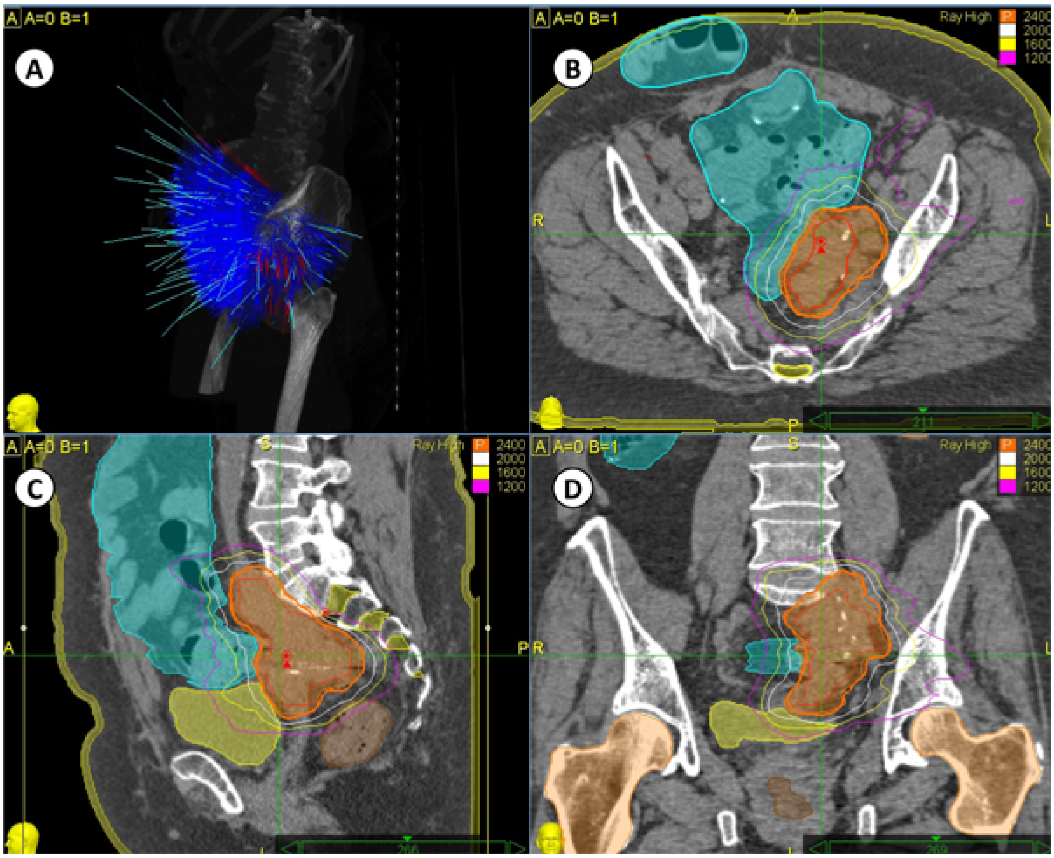

Figure 1. **Click here to view larger figure.**

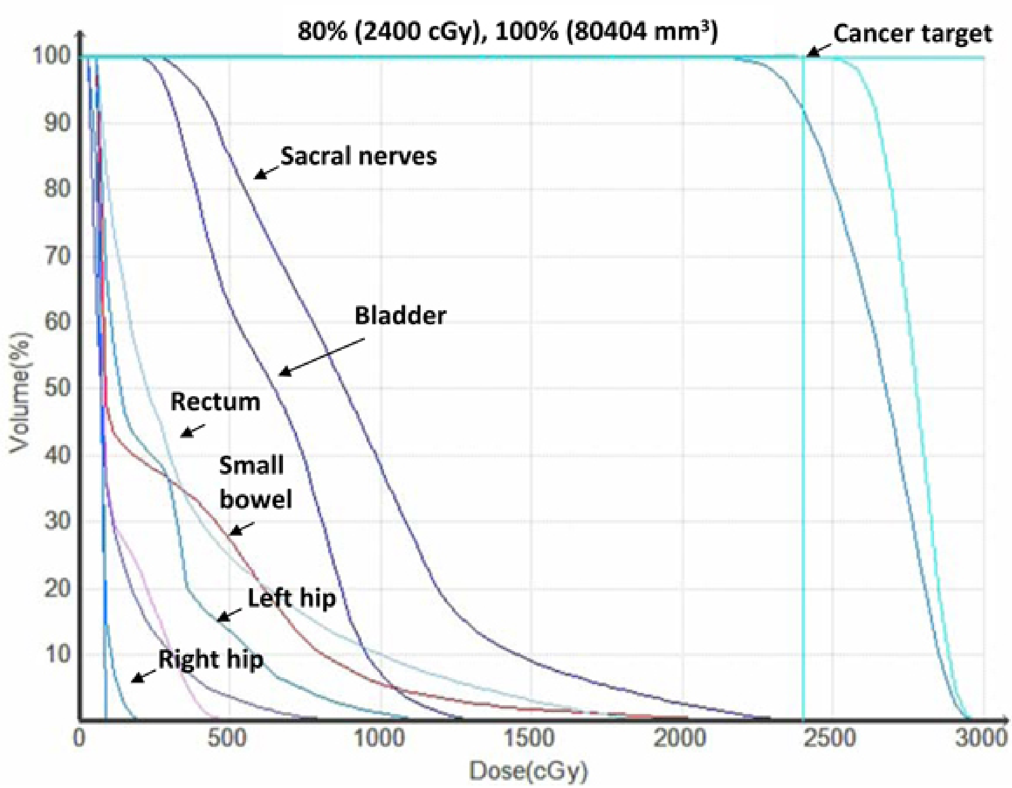

Figure 2. Dose-volume histograms for the clinical target (red) and for the critical structures of rectum (brown), bladder (yellow), small bowel (light blue) sacral nerves (tan) and hips (orange).

Discussion

Encouraging early SBRT outcomes have fueled clinical investigation of radiosurgery for treatment of persistent or recurrent gynecological cancers.[7, 8, 15] Data question radiobiological effects and mode of cell death resulting from SBRT. Small clinical studies have shown that ablative radiation doses provided by SBRT produce targeted disease control rates exceeding 90%. Unlike with conventional radiation, it has been challenging to combine SBRT with radiosensitizing and cytotoxic/cytostatic chemotherapies. Better cancer targeting through increased planning treatment volume expansions and through inclusion of ^{18}F-FDG PET/CT images has improved clinical outcomes. While it is imperative to look into other methods of delivering dose-escalated radiation with high precision, it remains undecided whether SBRT can provide equivalent therapeutic effectiveness as low and high dose-rate brachytherapy. Indeed, brachytherapy is the more commonly and validated technique to achieve radiation dose escalation in gynecologic cancer targets. As such, both enthusiasm and prudence are appropriate in reading available SBRT data for treatment of gynecologic cancers.

Disclosures

We (CAK, JMB, RD) have nothing to disclose.

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