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Review Article

Demystifying CyberKnife Stereotactic Body Radiation Therapy for Interventional Radiologists

Abstract

Stereotactic body radiation therapy (SBRT) using CyberKnife system is a relatively new radiation therapy that has demonstrated feasibility, safety, and efficacy with a high local control of various extracranial unresectable primary cancer and oligometastasis. It involves accurate delivery of very high dose of radiation to the target or tumor volume with high precision and conformity, while minimizing the radiation exposure of nontargeted tissue. Radiopaque fiducial markers (FMs) implantation in and around the tumors is required to track the selected tumor during CyberKnife SBRT, especially in those organs moving with respiration. They act as internal radiographic landmarks that maintain a fixed relationship within the tumor and with each other. Although their implantation can be technically demanding, it can be performed using various techniques with varying success; however, percutaneous implantation under image guidance by interventional radiologists is the most common method. Close collaboration between interventional radiologists and radiation oncologists with understanding of the technical aspects of CyberKnife SBRT and FMs implantation has important implications for optimal delivery of therapy and direct impact on the interventional radiology practice in selected patients proposed for CyberKnife SBRT.

Keywords: *CyberKnife, fiducial marker, stereotactic body radiation therapy*

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Introduction

With the relative outburst and development of novel technologies and innovative ablative therapeutic platforms, interventional radiology is facing challenges in adopting and responding to these new developments to maintain its integral role and maximize its potentials in the efficient management of patients with cancer. Such technological innovations induce transformation in the realm of medical practice expanding the therapeutic choices and approaches with great efficacy, efficiency, and value and improving the lives of cancer patients.

The field of radiation oncology primarily focuses on balancing the risks of normal tissue toxicity and the effectiveness of therapy. Stereotactic body radiation therapy (SBRT) is considered a relatively new paradigm in radiation therapy and representing a burgeoning accepted practice for radiotherapy of various extracranial tumors in selected sites.[1,2] Derived from the Greek term *stereo* meaning solid or three-dimensional (3D) and the Latin term *tact* meaning to touch, the concept of stereotactic radiation was evolved as a radiation technique that delivers high doses of radiation with exquisite accuracy to target lesions. This therapeutic concept was introduced first by the Swedish neurosurgeon Leksell in 1951 as stereotactic radiosurgery for the treatment of intracranial tumors,[3] with frame-based patient setup using external stereotactic coordinates. However, in 1991, a Swedish team at the Karolinska University Hospital in Stockholm was the first to propose and report the result expanding stereotactic radiotherapy approaches outside of the head to targets in the thoracic and abdominal cavities as SBRT with replacing the external coordinates by the internal coordinates of the image-guidance procedure based on improving stereotactic localization and internal motion management.[4,5]

Although SBRT was founded as a salvage/palliative option for locoregional and distant recurrences[6,7] for palliative conditions, its realm continues to widen. It has gained prominence recently as a curative treatment option in different oncological sites, such as lung,[8,9] kidney,[10] prostate,[11,12] and liver and pancreas.[13] However, as several

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studies have demonstrated that thoracic and abdominal tumors move during various phases of the respiratory cycle, respiratory motion tracking is essential to ensure that the entire target lesion is treated without requiring a substantial increase in the volume of tissue treated. Lesions located at the lung base can move up to 25 mm[14-16] while pancreatic and liver lesions can move up to 35 mm during respiratory cycles.[17-19] Therefore, respiratory motion is a challenge for CyberKnife SBRT in those extracranial sites.

This article will simply explain the principles and rationale of CyberKnife SBRT therapeutic platform with emphasis on the technical aspects relevant to the percutaneous placement of fiducial markers (FMs) by interventional radiologists for respiratory motion tracking.

Definition and Principle of Stereotactic Body Radiation Therapy

National working groups in several different countries have reported their definitions of SBRT.[1,20] The definitions of SBRT provided by the American Association of Physics in Medicine Task Group 101;[21] the American Society for Therapeutic Radiology and Oncology and the American College of Radiology;[22] the Canadian Association of Radiation Oncology-SBRT;[23] and the National Radiotherapy Implementation Group of the UK.[1] All agree on the following items: SBRT is (1) a method of external beam radiotherapy that (2) accurately delivers a (3) high dose of irradiation in (4) one or few treatment fractions to an (5) extracranial target. Specifically, the components of SBRT definition are as follows:

- External beam radiotherapy using photon or particle with either traditional linear accelerators equipped with suitable image-guidance technology, accelerators specifically adapted for SBRT, or dedicated delivery systems
- Accurate delivery of highly conformal radiotherapy using sophisticated clinical and technical manners. Clinically, the treatment should be well indicated based on multidisciplinary discussion regarding disease staging, target site, and appropriate imaging for target site and organ at risk, active or passive motion management, and follow-up. Technically, the treatment requires system-specific end-to-end tests for both static and moving targets in addition to verification of the alignment of imaging and treatment isocenters before the treatment on a daily basis
- High dose of irradiation that is equal or more in intensity to radical dose in conventional radiotherapy
- One or few treatment fractions with a maximum of 10 fractions. The single-fraction dose and total dose to volume and location of the target should be adjusted appropriately
- Extracranial target is accurately localized using tumor site-specific imaging modalities to spatially separate organ at risk.

Radiobiological Mechanisms of Stereotactic Body Radiation Therapy

The tumor microenvironment comprised of extracellular matrix, carcinoma-associated fibroblasts, immune cells, and endothelial cells plays a critical role in tumor initiation, progression, and metastatic spread.[24] Changes in the tumor microenvironment have a marked impact on the therapeutic response in tumor cells which are more radiosensitive compared to normal cells.[25]

The energy of the radiation beam determines how deeply the radiation penetrates, whereas the amount of radiation absorbed (dose) determines the biologic effects. Available evidence strongly indicates that high-dose hypofractionated irradiation (8–10 Gy per fraction) leads to tumor cell death through:

- Direct breaking the double strand in DNA and killing the cells directly[26]
- Indirectly deteriorating the intratumor microenvironment through more specific robust endothelial apoptosis and microvascular dysfunction.[25-27]

Moreover, SBRT impacts disease outside the radiated target as the increase in the cell death releases massive amount of tumor antigens that stimulate antitumor T-cell immunity, leading to eradicating occult regional micrometastases and suppressing recurrence and metastatic tumor growth, the "abscopal effect."[26]

The short radiation time and high dose per fraction in SBRT have potential radiobiological therapeutic advantages compared with conventional fractionation, due to less proliferation of the surviving clonogenic tumor cells during a fractionated radiotherapy known as tumor repopulation in addition to less available time for cells to sense and repair radiation-induced DNA damage. The accurate and precise delivery of the radiation allows tumoricidal treatment sparing the organ at risk through the differences in radiosensitivity of normal and tumor tissue and through fractionation effects.[28]

Rationale and Indications of Stereotactic Body Radiation Therapy

SBRT is proposed in a multidisciplinary setting mainly for patients, in which other therapeutic means are counter indicated.[29] It has the potential to replace surgical resection or interventional ablative therapies with curative or palliative intent in many primary cancers and "oligo" (i.e., isolated) metastases associated with high risk due to comorbidities, poor organ function, or difficult sites. Patients selected for SBRT should have a limited number of demarcated tumors whose extent can be identified directly on treatment-planning image or reliably fused by image registration techniques.

The following issues need to be addressed when considering a patient for SBRT.

- Newly diagnosed/previously unirradiated tumor: Standard treatment options are preferred unless these are not feasible due to medical contraindications or poor general condition of patient; SBRT is considered even in exceptional circumstances
- Recurrent or second primary tumor in previously irradiated field: Surgical resection is preferred if it is possible otherwise the exact extent of the disease is determined and SBRT is considered for well-defined tumors not abutting, critical organs and structures such as major vessels
- Incurable metastatic tumors on systemic therapy: Current systemic therapy can be maintained or rather changed if only a few tumors are increasing and SBRT is considered for potentially improving or maintaining the quality of life.

SBRT is delivered on outpatient basis as a noninvasive therapy with shorter treatment times, generally completed within 1 or 2 weeks, allowing for little to no delays in systemic therapy and more convenience for patients.

Delivery Systems for Stereotactic Body Radiation Therapy

The landscape of SBRT consists of a myriad of platforms for radiation delivery with numerous technological approaches. The key components of any SBRT delivery system remain constant and include accurate immobilization, complex planning software capability, peritreatment image guidance ability, motion management, and robust quality assurance. There are many commercially available hardware facilities capable of SBRT.[30] The common feature among SBRT delivery systems uses linear accelerator with integrated advanced image-guidance systems, which incorporate either digital X-ray or tomographic imaging to assist in target localization and define tumor position in near real time. In addition, those systems allow integration of patient immobilization and respiratory control devices.

In our institution, we use the CyberKnife® system (Accuray, Sunnyvale, CA, USA) which was developed as a frameless SBRT system. It is composed of an integrated image-guidance and treatment delivery device that incorporates a computed-controlled robotic linear accelerator with two orthogonal kilovoltage X-ray tubes installed in the ceiling and flat panel detectors for near real-time image-guided radiation delivery. The CyberKnife® system tracks the tumor in real time during the treatment, and localization data are sent to a sophisticated software program that calculates and readjusts the position of the robotic arm to deliver the treatment. Its unique feature is that it does not require body frames or overly exquisite immobilization devices to ensure adequate delivery of the treatment. As a result, a key feature of the CyberKnife® system is that any positional changes of the patient or target are compensated for by adjustment of the robotic arm, rather than movement of the treatment couch, as is the case for conventional linear accelerators.

A multitude of specialized tracking systems has been developed. The most tracking systems used include as follows.

- Synchrony Respiratory Tracking System for tumors with respiratory motion such as those in the lung, liver, kidney, or pancreas. It couples motion tracking of internally implanted FMs placed in or around the tumor volume before treatment planning, with chest wall motion determined by an optical tracking system
- Xsight Systems for spinal lesions uses a hierarchical mesh tracking algorithm to track the bony anatomy for accurate treatment delivery.

Process of Stereotactic Body Radiation Therapy

Patient evaluation

It includes clinical history, physical examination, and review of relevant imaging studies, pathology and laboratory results in a multidisciplinary setting. In addition, it includes obtaining of inform consent with emphasis on the reason for choosing of such therapy and the potential risks and benefits associated with the placement of FMs in details.

Simulation

It includes fabrication and fashioning of immobilization device and imaging the patient in treatment position. Patient positioning should be comfortable over an entire session of SBRT (up to 1 h) and reproducible through all the treatment sessions. It is accomplished using a custom-molded cradle immobilization device which holds the patient comfortably, reliably, and securely in the treatment position. In addition, the device provides a precise, accurate correlation between the treatment machine and patient/target geometry, facilitating treatment planning and patient setup during treatment.

The avoidance of large safety margins around the target is very important to avoid toxicity to normal tissues. A high-resolution computed tomography (CT) scan is typically performed to image the patient and treatment target, providing the precise, quantitative location of target in space. The target is imaged with a 4D CT scan over the entire respiratory cycle in the case of mobile targets, such as a lung or liver lesion.[31] This CT technique allows as follows:

- Assessment of the range and nature of tumor motion
- Acquisition and binning of the respiratory cycle into the various phases
- Accuracy in defining the target so as to minimize margins.

Target motion information acquired through imaging requires time-based correlation of respiratory motion with the CT images. Respiratory signals are obtained

from surface-mounted or internal markers associated with respiration using one of the following techniques.

- Gating involves the monitoring of the respiratory cycle and the delivering of the treatment during one specific phase of the respiratory cycle, typically at the end of expiration, while the beam is turned off in the other phase of breathing
- Dampening involves abdominal compression or breath holding to reduce the cephalocaudal diaphragmatic excursion resulting in reducing target motion, especially in the lower lungs and the liver
- Tracking involves physically moving a beam of irradiation to coincide with tumor motion in the beam's eye view. Generally, FMs are used in tracking techniques to activate the beam delivery.

Although the surface marker is more popular because it is less invasive, the internal surrogates for respiratory motion, either anatomical structures or implanted FMs. are better correlated with the actual target motion than the surface markers and can be used for image-guided target verification in the treatment room.

The simulation CT images are frequently combined with magnetic resonance (MR), positron emission tomography (PET), and single-photon emission CT images. Such combination provides superior visualization of soft-tissue lesions in addition to biological/functional information. The diagnostic and planning image is then fused with rigid-body image registrations followed by exploring the image for any deformable image registration.

Treatment planning

This step is iterative and complex. It includes contouring the target and normal tissues, selection of appropriate technique, designing the treatment field, calculation of radiation dose, and critical review of dose distribution.

Contouring of the target volume and normal tissues is performed by drawing the outline of the image on each slice of the image set followed by combining these images using planning software to yield a 3D representation of the structure. The obtained images can be manipulated to define the margins of the treatment field based on imaging accuracy, SBRT system precision, possible universalized tumor extension, target motion, and possible setup error. This step is important for specifying dose constraints and dose distribution which the treatment plan will base on with taking into account the tissue inhomogeneity, especially for small field sizes. The proposed treatment plan depends on the size and shape of the target, the prescription dose, and the proximity and tolerance of organ at risk. The planned delivery positions are based upon a set of predefined source positions called "nodes," with a set of these nodes called a "path."

Treatment delivery

It includes positioning the patient in immobilization device, imaging the patient on treatment system, adjusting patient position or radiation beam isocenter, and managing the intrafraction motion and radiation delivery.

The patient is securely positioning the patient in immobilization device on the treatment table with roughly adjusting the position using markings on the device or patient. Imaging then is obtained with the orthogonal X-ray imager and compared with the image obtained at the planning treatment to adjust the patient position in the translational planes and rotational axes until the image sets exactly overlay one another in the region of interest.

The radiation is delivered at the planned delivery positions by the robotic arm-mounted linear accelerator which continuously moves and adjusts the position of the radiation beam to retarget according to the tumor localization as assessed by either Synchrony Respiratory Tracking or Xsight system depending on the position of external markers on the patient's surface or internally implanted FMs near the target.

Fiducial Markers

Devices

FMs are small, easily discernible radiopaque objects whose position relative to the target and/or normal tissues remains constant after implantation. FMs define a coordinate system that can be used to target the tumor, orient the treatment planning process, and ultimately guide the therapy conformally toward the intended location in the body without large expansions for organ motion and with limited toxicity from irradiating excessive normal tissue.

Numerous types of devices with various sizes and designs have been used as FMs. The specifically designed FMs for radiotherapy are typically made of a biologically inert metal with a high atomic number such as gold to be visible on planar X-ray images and fluoroscopy loops. The designs range from simple sections of gold wire or gold spheres to complex spiral gold shapes with segmented flexible titanium core, knurls, irregular surfaces, or a bendable structure to hook into the tissue and limit migration. Such dedicated devices are designed to increase convenience, so they are provided preloaded in needles or delivery device.

However, nonspecifically devices made of either biocompatible polymer-based materials or metals with lower atomic number such as nickel, stainless steel, or titanium or made of radio have been off-label used such embolic coils.[32]

Although we use gold FMs at our institution of 5 mm in length and 1 mm in diameter as specified in the CyberKnife software [Figures 1 and 2], we have also used off-label devices such as platinum coils [Figure 3]. Choice of FMs is generally based on design, cost, convenience, availability, preference, and the nature of imaging guidance modality in the SBRT system in the institution.

Principles of fiducial markers placement

The procedure of FMs placement can be tedious and technically demanding, adding complexity to the overall CyberKnife SBRT process and it can cause some inconvenience as it leads to a delay in treatment, especially when appointments are readily available.

FMs should be placed in proper distribution in relation to tumor geometry in a predictable way to move with the target volume rather than to define the extent of the tumor.

For optimal placement, the FMs should be identified by CyberKnife as separate and distinct points in the 45° orthogonal treatment imaging planes [Figure 4]. To accomplish such placement, the following recommendations should be considered for placement of FMs.

- Ideally, 3–6 FMs are placed in or in proximity to the tumor periphery with maximum of 5 cm from the target to move in synchrony with the tumor
- Minimum of 2 cm and maximum of 5 cm spacing between FMs
- Minimal angle of 15° between FMs, i.e., they must be noncollinear to allow the SBRT system to image and interpret each FM position accurately on the orthogonal X-ray systems in real time during treatment
- Approved FMs type should be used if possible based on counseling with the radiation oncologist
- Allow sufficient time for about 1 week between FMs insertion and planning scans to allow FMs to settle into stable position and the surrounding tissue to recover from possible potential complications related to the placement procedure such as hemorrhage or edema.

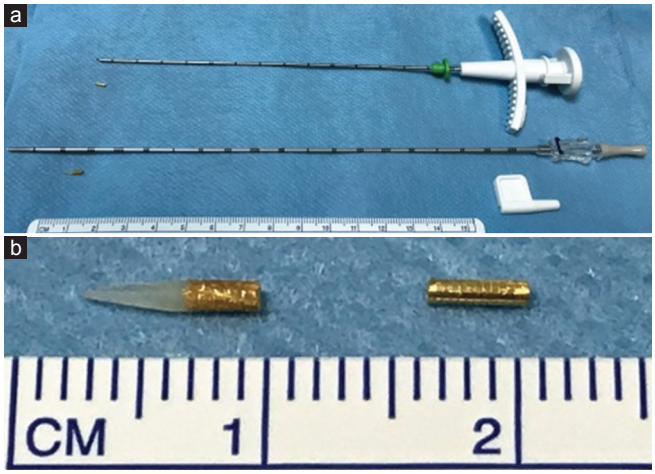

Figure 1: Gold fiducial markers devices. (a) Needles bearing fiducial marker with different mechanism of deployment. (b) Gold fiducial markers

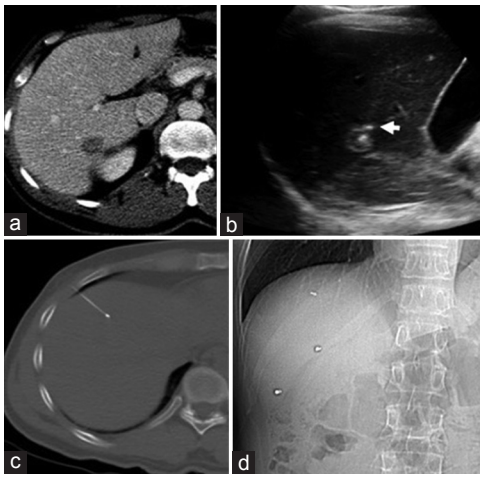

Figure 3: A 43-year-old male with metastatic colon cancer. (a) Three liver lesions were identified in segment VI, VII, and VIII on the cross-sectional imaging. Coils were placed under (b) ultrasound guidance as fiducial markers near the lesions in segment VI and VII (arrow) while coils was placed under (c) computed tomography guidance near the lesion in segment VIII. (d) Abdominal X-ray showing the three coils in the proposed locations

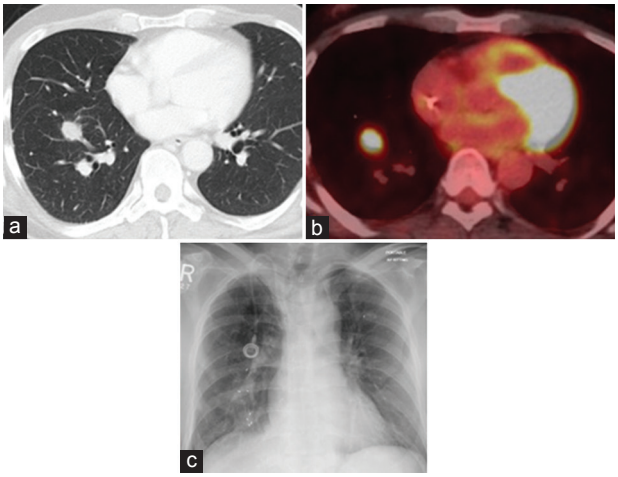

Figure 2: A 66-year-old female with a history of resected colon cancer with metastases to the lungs. (a) Metastatic lesions in the lung did not respond to chemotherapy. (b) Positron emission tomography/computed tomography showed uptake in right lung lesions. (c) Gold fiducial markers were placed under computed tomography guidance in the proper distribution in relation to geometry of lesions with high uptake on positron emission tomography/computed tomography images in a predictable target volume

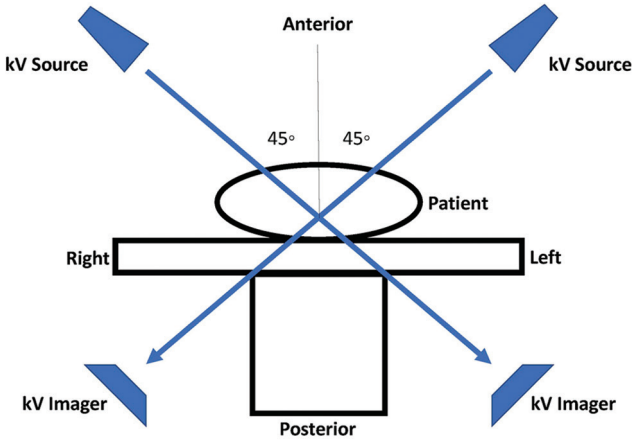

Figure 4: CyberKnife Schematic diagram shows two X-ray sources with 45° oblique angle and flat-panel detectors placed under the patient table. Fiducial markers should be placed noncollinearly for CyberKnife system to view them from 45° oblique angulation

Techniques of fiducial markers placement

Various techniques under different imaging guidance modalities have been proposed and found widespread acceptance for the placement of various types of FMs for CyberKnife SBRT.[30] They include percutaneous,[30,33-35] bronchoscopic,[36] endoscopic,[37] and endovascular[38-41] techniques. However, in our institution, FMs are implanted percutaneously under imaging guidance in a manner similar to that of percutaneous core biopsies.

Choice of the imaging guidance modality is determined by lesion characteristics on cross-sectional images such as size and location, availability of imaging systems, and local expertise and preference. However, randomized evidence suggests that the placement technique should be dropped in favor of image guidance where available on the basis of safety and technical easiness.

CT is the preferred and most common used guidance modality. It is the standard imaging modality for guidance in many institutions as it reveals the anatomic structures and characterizes the lesion. It permits planning a trajectory that minimizes risk passage through some structures and allows possible access to difficult sites [Figure 3c]. The recent advances in spiral CT and fluoroscopy CT[42] permit to access smaller lesion and perform the procedure more quickly, especially in less cooperative patients.

Ultrasound (US) is a safe with no radiation, quick, and low-cost modality. It allows real-time visualization with multiplanar capability of the needle advancement, allowing accurate placement of the needle and FMs placement. It should be used whenever possible and appropriate [Figure 3b]. However, US lacks spatial accuracy in three dimensions compared to CT scans which result in more failure in discriminating FMs, especially when placing more than three FMs.[34] Moreover, US cannot be used in many cases such lung lesions as US beam does not pass through air, previous surgery, multiple lesions, and/or body habitus.

Yet, two techniques are used for insertion of needles bearing FMs; coaxial and noncoaxial. Each technique has certain advantages compared to the other. However, there is no proof that any type of technique is superior to other types in terms of complication rate. Using the coaxial technique, an introducer needle will be inserted allowing manipulation and placement of multiple FMs from a single puncture and that may help in reducing of complications associated with multiple punctures, especially with using smaller diameter introducer needle. In addition, the coaxial technique provides more stability when advancing the needle bearing the FMs to the target. In contrary, the advantage of the single puncture for each needle is that it is more flexible and it may help in guiding the needle to the precise location.

Procedure of fiducial markers placement

Planning

A baseline cross-sectional imaging (CT or MR imaging) not older than 2 weeks is required before placement of FMs.[42] It is carefully reviewed with the radiation oncologist to determine the lesion depth and its relation to other structures and to plan a placement route and technique based on the size and location of the lesion, availability of imaging systems, and local expertise. The needle path is chosen considering straight pathway from the skin to target. Ideally, the pathway should avoid risky transversal of structures.

Patient positioning

Patient position is an important factor in improving the accuracy and safety of FMs placement and in reducing both patient movement and anxiety. Consideration of position should be made during placement planning as the patient should maintain the same position during the procedure.

Sedation

Sedation and intravenous analgesic medications are usually not required with the liberal use of local anesthetic. The pain associated with the procedure is usually limited and momentary and arises from administration of the local anesthetic and violation of the tissue with the needle. The burning sensation resulting from the administration of local anesthetic can be reduced with adding sodium bicarbonate to raise the pH of local anesthetic. However, the patients differ in their ability to tolerate the procedure without sedation which may lower the patient's level of cooperation. Sedation and analgesia are primarily used for anxious and uncooperative patients; some selected elderly people who have osteoarthritis or degenerative joint disease and cannot maintain certain positions through the procedure.

Computed tomography scan parameters

The parameters are related to the choice of mA and slice thickness. Generally, the lowest dose that allows for evaluation of the needle in relation to the target is required. Most of modern CT scanners allow a routine low-dose axial scan with 120 kVp with 40 mA or lower per slice. Radiation dose reduction is important because it is often necessary to perform multiple images through the same tissue volume during the procedure.

Procedure process

After appropriate patient positioning, a radiopaque marker or grid is placed on the patient's skin over the area of interest. During suspended respiration, a short CT scan of the region of interest is obtained, followed by choosing the appropriate table position and needle trajectory as previously planned. The depth from the skin entry site to the lesion is then measured.

With the use of the gantry laser light to delineate the Z-axis position, and the radiopaque skin marker to

reference the X-axis position, the needle entry site is marked with indelible ink on the patient's skin. The skin site is prepped and draped using sterile technique, followed by administration of local anesthesia into the skin, subcutaneous tissues, and muscles.

In our institute, the standard practice is to use coaxial technique whenever it is possible for the advantage explained before taking into consideration the possible potential risks. We use an introducer needle as guidance with appropriate length depending on the depth of target lesion.

All needle movements and manipulations should be performed with patient's respiration suspended. When advancing the introducer needle, it is important to maintain the same trajectory with each movement, as even slight deviations of the needle at the skin or within the subcutaneous tissues will produce marked deviation at a deeper level. In addition, the patient is instructed to breathe quietly, remain motionless, and repeat a breath hold of a similar size during needle manipulations throughout the procedure. The needle should be allowed to sway to-and-fro with respiratory motion, not be held or fixed during respiration, as this will lacerate the tissue passing through with each breath.

As needle insertion is considered a dynamic process from skin to the target area; a short-segment CT should be performed always to verify the needle angle and tip position based on the last scan (a sequential technique). The needle is then advanced in one motion to the prescribed depth. The needle-bearing FM is passed through the lumen of the larger introducer needle and into the target. The entire needle shaft should be within the scan plane. If not, additional images above or below the entry site must be obtained. The key to recognizing the true tip of the needle is the identification of an abrupt square tip with a black shadowing artifact arising from in. After needle tip position as close as possible to the periphery of the lesion is confirmed and documented, the FM is deployed during suspended respiration as per the manufacturer's instructions for the used FMs.

It is important when using coaxial technique to leave always the inner stylet inside the entry needle, especially when approaching lesion in the lung to prevent devastating air embolism if the tip was in a small branch of a pulmonary vein.

Postprocedure care

After the placement of the FMs is complete, a short CT scan is performed to confirm the location of FMs and to evaluate for immediate complications. If the scan is normal with no significant new findings, the patient is transported to the recovery area for vital signs and oxygen saturations monitoring by the assigned medical staff. The patient should remain recumbent throughout the monitoring period. Follow-up expiratory chest radiographs are obtained with sitting upright at 1–2 h after the procedure when placing FMs in the thorax. If the chest radiograph shows no new changes, the patient discharges. On discharge, the patient is asked to abstain from strenuous or weight-bearing activities for 3 days. In addition, anticoagulants, antiplatelets, and nonsteroidal anti-inflammatory drugs are not allowed.

Complications

Complications of the FMs placement procedures are classified according to the Society of Interventional Radiology Standard of Practice Committee classification of complications by outcome.[15] The reported overall major complication rate is 5%,[35] which is within the reported range for percutaneous biopsies.[43] Most complications occur immediately or within the first few hours after completion of the procedure. Majority of them are self-limiting and can be treated conservatively, often on an outpatient basis, or may require minor care or some prolonged hospitalization.

Most reported complications occurred with FMs placement in lung lesions with higher rate than that reported in the literature and above the suggested threshold of 10%.[43] The reason of the higher rate may likely due to the poor lung reserve/function in those patient population and the need for more needle manipulation or punctures. However, the overall complication rate could potentially be reduced with using a coaxial technique (single puncture) with a needle size smaller than 18-gauge for placement of multiple FMs.[42,44]

Migration of FMs has been reported[34,45] to be minor or major via venous system.[46] It may depend on the shape, size, and material of FMs. It results in high rate of reimplantation of more FMs.[34]

Tumor seeding is another risk associated with placement of FMs due to possible violation of the tumor. It can be avoided by sandwich placement of FMs without penetrating the tumor.[47]

In our institution, we have one unreported case of migration to the heart after placement of platinum coil as FM in the lung in addition to another unreported one of tumor seeding along the needle tract after US-guided placement of gold FM in the liver. The seeding was confirmed with PET/CT scan performed after 2 weeks.

New Trends and Future Directions

Image-guided percutaneous placement of FMs is technically performed by interventional radiologists. However, a robust multidisciplinary approach, including medical and radiation oncologists, radiologists, pathologists, oncologic surgeons, and medical physicists, is required on a local or institutional level to standardize protocols for using of FMs with regard to the placement technique and the number and type of FMs taking into consideration following the

institutional policies and relevant safety measures. Such a multidisciplinary collaboration should be adopted whenever possible as it will help to fulfill emerging requirements for the design and set-up of SBRT program, avoid unnecessary costs, limit patient stress, risk, and uncertainties surrounding FMs placement, ensure safe and efficient treatment, and optimize patient care.[1] Moreover, it will facilitate building local database and inclusion of patients in specific clinical trials.

The availability of C arm cone-beam CT with a flat-panel detector system, in which a cone-beam X-ray tube and a flat-panel detector are integrated with a C arm gantry, may add new image guidance modality to use by interventional radiologist for placement of FMs. This system has both CT and fluoroscopy image capabilities and offers greater flexibility in orientating the detector around the patient than closed CT gantry systems in addition to advanced real-time fluoroscopic and 3D CT capabilities. This image-guided system can be utilized for placement of FMs as it allows identification of the correct trajectory of the needle to the target area under real-time fluoroscopic capability and verification of the exact location of the needle tip near the target lesion using the CT capability of the system.

Going forward, major advances and improvements in engineering and computing have been made in the field of radiation therapy.[48] As FMs are placed as inert biomaterials in the vicinity of tumors with only function of ensuring geometric accuracy during SBRT, there is a compelling rationale for upgrading their function to be multifunctional or "smart" biomaterials that can deliver additional therapeutic or treatment-enhancing benefits. One proposal is to us FMs loaded with radiosensitizing drugs that could be activated by the tumor microenvironment during postimplantation period to sustainably deliver a specific drug directly into the tumor area.[49] Furthermore, gold nanoparticles can also act as radiosensitizers and they have been investigated as payloads loaded into FMs to enhance efficacy of radiation therapy.[50] However, the use of FMs loaded with smart biomaterials is not straight forward and still needs further research to be included into treatment algorithms.

Conclusion

With the demonstration of feasibility, safety, and efficacy for local control of various extracranial unresectable primary cancer and oligometastasis, CyberKnife SBRT has risen and will continue growing as a complementary option added to the arsenal of ablative options and as a safer and more alternative to effective alternative to conventional radiation therapy by enabling delivery of more potent doses to target tumor tissue, while minimizing normal tissue injury. However, CyberKnife SBRT requires precise placement of FMs for tumor localization in nonstationary anatomical sites for safe and accurate delivery of the intended dose to the target. Such requirements have potentially expanded the role of interventional radiologists conducting placement of FMs under imaging guidance. Well-understanding of CyberKnife SBRT concept and process and responding to its increasing demands are essential for optimal delivery of the therapy in close collaboration with the radiation oncologists on multidisciplinary setting basis.

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Conflicts of interest

There are no conflicts of interest.

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