Stereotactic Body Radiation Therapy: The Report of AAPM Task Group 101

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ABSTRACT

Task group 101 of the AAPM has prepared this report for medical physicists, clinicians, and therapists in order to outline best-practice guidelines for the external-beam radiation therapy technique referred to as stereotactic body radiation therapy (SBRT). The task group report includes a review of the literature to identify reported clinical findings and expected outcomes for this treatment modality. Information is provided for establishing an SBRT program, including protocols, equipment, resources, and QA procedures. Additionally, suggestions for developing consistent documentation for prescribing, reporting, and recording SBRT treatment delivery is provided.

Keywords: Stereotactic body radiation therapy, SBRT, BED, Patient safety, 4DCT, immobilization, IGRT, hypo-fractionation

INTRODUCTION AND SCOPE

Stereotactic body radiation therapy (SBRT) refers to an emerging radiotherapy procedure that is highly effective in controlling early stage primary and oligometastatic cancers at locations throughout the abdominopelvic and thoracic cavities, and at spinal and paraspinal sites. The major feature that separates SBRT from conventional radiation treatment is the delivery of large doses in a few fractions which results in a high biological effective dose (BED). In order to minimize the normal tissue toxicity, conformation of high doses to the target and rapid fall off doses away from the target is critical. The practice of SBRT therefore requires a high-level of confidence in the accuracy of the entire treatment delivery process. *In SBRT confidence in this accuracy is accomplished by the integration of modern imaging, simulation, treatment planning and delivery technologies into all phases of the treatment process; from treatment simulation and planning and continuing throughout beam delivery*.

In addition to these major features, there are other characteristics that distinguish SBRT from conventional radiation therapy (Table 1). These include a general increase in the number of beams used for treatment, the frequent use of non-coplanar beam arrangements, small or no beam margins for penumbra, and the use of inhomogeneous dose distributions and dose-painting techniques (including IMRT). All of these technology improvements result in the highly conformal dose distribution that characterizes the SBRT technique.

HISTORY AND RATIONALE FOR SBRT

Over 4000 publications spanning several decades have affirmed the clinical usefulness of stereotactic radiosurgery (SRS) in the treatment of benign and malignant lesions [1-5] as well as functional disorders.[6, 7] The radiobiological rationale for SBRT is similar to that for SRS; delivering a few fractions of large dose in relatively short overall treatment time results in a more potent biological effect[8]. The clinical outcomes of SBRT for both primary and metastatic diseases compare favorably with surgery with minimal adverse effects. [9, 10] In addition, the limited number of treatment fractions makes SBRT more convenient for the patient, and a potentially more cost-effective treatment modality than traditional radiation therapy.

The specific argument for the application of SBRT to grossly evident sites of metastatic disease can be constructed in accordance with several conceptual theories:

- The "patterns of failure" concept combines systemic treatment with localized radiation therapy because of the expectation that sites of gross disease contain the highest number of clonogenic cells and are thus least likely to be eliminated by chemotherapy.[1, 11-13]
- The theory of oligometastases proposes a stage of disease that is at an intermediate point in its natural history, between completely absent and widely metastatic, and which might be cured if the limited numbers of metastatic sites are eradicated. [14-20]
- The Norton-Simon hypothesis suggests that the systemic burden of cancer cells increases from an initially low, undetectable level through a phase of exponential growth to a lethal plateau level. [21] A local intervention such as SBRT might aid in reducing the systemic burden of disease in a manner that could help prevent or delay as long as possible the condition of lethal tumor burden that is fatal to the patient.

- SBRT is now being explored within the broader concept of immunomodulation, whereby an effort is made to exploit the systemic anti-tumoral immune response generated in certain conditions of radiation-induced tumor cell death. [22-25]
- SBRT can offer a means of providing palliative treatment in certain settings, especially when there is a need to be particularly careful in the administration of treatment. For example, the added precision with SBRT might be advantageous when a tumor abuts or overlaps a previously irradiated region.

Because such dose intensification can also increase the risk of normal tissue toxicities, careful dose delivery and patient selection are of paramount importance. SBRT attempts to provide a clinical advantage relative to conventional radiation therapy by reducing dose to normal tissues and critical structures and maximizing tumor coverage through the use of accurate tumor localization, patient immobilization, specialized planning and image guidance techniques.

Clinical patient outcomes for SBRT were first published in 1995.[26] In Germany, investigators initially focused on the treatment of liver and lung lesions. [27-31] In the United States, the first publications described the treatment of lung tumors.[32, 33] Retrospective studies first described the safety and efficacy of SBRT for the treatment of lung and liver lesions.[28, 31, 34-39] Prospective Phase I and/or II trials were published in 2001 for the treatment of lung, and in 2003, for liver.[28, 30, 32, 33] The RTOG has completed enrollment of a Phase II study of SBRT for medically inoperable primary non small-cell lung cancer (NSCLC). Outcomes of retrospective series treating spinal lesions were first published in 2003.[40-44]

CURRENT STATUS OF SBRT – Patient Selection Criteria

The majority of patients treated with SBRT are those with lung, liver and spinal tumors. Most investigators limit eligibility to well-circumscribed tumors with a maximum cross-sectional diameter of up to 5 cm, although some centers have reported results for tumors are large as 7 cm. [32-34, 45-47] The use of SBRT as a boost in addition to regional nodal irradiation has been proposed. Even with the expectation that small volumes of adjacent organs at risk (OARs) will be irradiated during SBRT, an assessment of patient eligibility should include a careful evaluation of normal tissue function and dose distribution. Typically, pulmonary function and the volume of normal liver that is irradiated are the most immediate considerations.[32, 48-51] Tumors proximal to mainstem bronchi, trachea, esophagus, gastric wall, bowel, blood vessels, or spinal cord should be approached with great caution, or not at all, if the lack of spatial separation places them within the high-dose gradient region of treatment, which can lead to potentially devastating clinical outcomes.[18, 28, 32, 49, 52-54]

Recommendation: Since SBRT is still developing, the most effective way to further the radiation oncology community's SBRT knowledge base is through participation in formal group trials; whether single- or multi- institutional trials sponsored by the NCI or other sources, or through NCI-sponsored cooperative group trials such as those of the RTOG. Treating patients under such protocols guarantees that strict guidelines developed by experts are followed and is an effective way to further the radiation oncology community's SBRT knowledge base. When appropriate protocols are not available, clinicians wishing to develop a SBRT program must decide whether they will treat patients in accordance with published guidelines or develop new SBRT guidelines. At a minimum, an institutional treatment protocol or set of guidelines should be developed by radiation oncologists and physicists. If a decision is made to routinely employ

SBRT regimens that depart substantially from published experiences or to apply SBRT for indications not previously reported, it is best to structure the work as a formal prospective clinical trial to be reviewed, approved, and monitored by an institutional review board.

SIMULATION IMAGING AND TREATMENT PLANNING

The goal of imaging during SBRT simulation is to provide visualization of patient anatomy as it will appear during patient setup and throughout treatment. Treatment planning is concerned with the designation of target(s) and critical structure(s) as well as determining an optimal treatment delivery approach. The objective of reporting is to clearly communicate to the treatment team (physicists, radiation oncologists, dosimetrists, therapists, nurses, etc.) the vital specifics of the treatment, enable congruent and subsequent quality assurance, and evaluate treatment outcomes.

A. Simulation Imaging

SBRT requires precise delineation of patient anatomy, targets for planning, and clear visualization for localization during treatment delivery. Three-dimensional data sets assembled from CT or 4DCT for visualizations and dose calculation, and/or MRI and PET images assist in target and visualization for SBRT.

The most appropriate imaging modality for a given clinical situation is driven by the characteristics of the tissues being imaged. In general, CT is the primary imaging modality for

SBRT and forms the basis for many treatment planning calculations. CT is helpful in identifying pulmonary nodules, parenchymal diseases, and chest-wall involvement for superior sulcus tumors and lung disease.[55, 56] Dynamic contrast-enhanced CT is the most sensitive study for the hepatic system.[57, 58]

MR is the gold standard for visualization of brain neoplasms and is increasingly used in SBRT applications including prostate, spinal tumors, chest, and solid abdominal tumors. [59-66]

^{18}F-fluorodeocyglucose (^{18}FDG) positron emission tomography (PET) greatly enhances the specificity and sensitivity in diagnosis and staging compared with CT.[67, 68] Combined PET-CT systems can reduce image registration/fusion uncertainties to less than 2 mm due to inherent co-registration achieved by acquiring both PET and CT images in a single acquisition session..[69] The CT image of the combined system is also used to correct the PET image for photon attenuation effects. However, the inherent limitations of spatial resolution in PET make that part of the system more useful for identification of sites of active disease rather than a source of imagery to be used for precise tumor delineation. Currently, PET/CT is widely used for lung cancer, head-and-neck tumors, colon cancer, liver cancer, melanoma, lymphoma and ovarian cancer.[70, 71]

Recommendation: Regardless of imaging modality, simulation of the patient should take place with the patient in the treatment position. The simulation study should cover the target and all organs at risk to obtain geometric and dosimetric information for the treatment setup. A typical scan length should extend at least 5-10 cm superior and inferior beyond the treatment field borders. For non-coplanar treatment techniques, the scan length may further be extended by ± 15 cm inferior/superior beyond the target borders to adequately model the patient. Along with the target, all organs of risk should be included and covered by the selected scan length so

they can be considered by the treatment planning system and evaluated with dose-volume histograms[72]. Scan parameters such as the slice thickness, inter-slice gap, and scan time per revolution, as well as the timescale of any underlying motion directly affect the size and appearance of tumor volumes in diagnostic and simulation studies. For SBRT applications, tomographic slice thickness of 1-3 mm though the tumor site is recommended for most clinical cases. [73-75]

B. Data acquisition for mobile tumors, patient-specific tumor-motion determination and respiratory motion management

Primary sources of organ/tumor motion during simulation imaging are respiration, cardiac function, peristaltic activity, and organ filling and emptying. For instance, it has been found that respiratory motion of lung tumors ranges up to 50 mm.[76] This motion can cause problems in traditional imaging techniques. For example, a study using real-time fluoroscopy of implanted fiducial markers in lung tumors showed that 3D tumor motion is complex, hysteretic, and difficult to visualize from the orthogonal views obtained with planar imaging.[77] PTVs deduced from radiographs at the extreme respiratory phases have been found to overestimate the actual volume.[78] Likewise, free-breathing fast spiral CT studies may not accurately represent the mean target position since each slice localizes the target positions at a different respiratory phase away from the actual mean position.[79, 80] Multi-slice scanners could take a snapshot of the entire tumor at a position that may not represent the mean, and in fact could be at an extreme position away from the mean. Thus, population-based margins to account for tumor motion may be incorrectly applied to a random position of the target (GTV/CTV) instead of its “true” mean

position, potentially resulting in undertreatment of the target and irradiation of unnecessary normal tissue.

The report of AAPM Task Group 76 describes the various tumor motion strategies in detail. Techniques to image moving targets include slow CT[50, 81-83], breath-hold techniques, [34, 84-94], gated approaches, 4D-CT used in conjunction with maximum-intensity projection (MIP),[95, 96] minimum-intensity projection (MinIP)[97], and respiration-correlated PET-CT[79].

C. Imaging Artifacts

One note of caution is that the same imaging characteristics that allow slower acquisitions to characterize the movement of the target can also lead to motion artifacts.[98] It is also possible to create artifacts due to high atomic number (Z) objects such as metal implants, prosthetics, and dental fillings. Motion-related artifacts may be improved by immobilization and patient cooperation. Barish and Jara have described some general clinical guidelines for motion control in body MR imaging.[99] Specific MR algorithms dealing with motion may be used to improve the quality of MR images.[100] In MR, practical imaging techniques, such as selection of the appropriate imaging plane and of the proper frequency encoding gradient axes can effectively reduce some of these artifacts.[101-103] The motion degradation of PET images can largely be minimized by respiratory-correlated gated or 4D PET techniques, as shown by Nehmeh et al.[104-107] A necessary step to minimize the effect of metal artifacts in CT-based treatment planning is to update the electron density conversion table to reflect the relative electron density values of the metals implanted in patients (For addressing the issues with metal implants, the report of AAPM Task Group 65 on tissue inhomogeneity corrections for megavoltage photon beams can be used as reference). One should verify that the treatment planning algorithm can account for these higher density materials in its calculation.

Recommendation: If target and radiosensitive critical structures cannot be localized on a sectional imaging modality with sufficient accuracy because of motion and/or metal artifacts, SBRT should not be pursued as a treatment option.

D. Treatment planning

Unlike conventional radiotherapy which is based on the delivery of a uniform prescription dose to the target volume, a paradigm of prescribing dose for SBRT is based on the following set of conditions:[26, 32, 49, 108-110]

1. A limited volume of tissue, containing the gross tumor and its close vicinity, is targeted for treatment through exposure to a very high dose per fraction, and hotspots within the target are often deemed to be acceptable. [111]
2. The volume of normal tissue receiving high doses outside the target should be minimized to limit the risk of treatment toxicity. Thus, the gradient describing the dose fall-off outside the target should be sharp.

The following sections describe how these conditions affect target definitions and treatment planning strategies.

SBRT, just as conventional radiation therapy, also makes use of the ICRU 50 and 62 definitions for Gross Tumor Volume (GTV), Clinical Target Volume (CTV), Planning Target Volume (PTV) and Organ at Risk (OAR).[112, 113] The need to keep the volume of normal tissues receiving high doses kept to a minimum requires that only well-defined targets can be considered for SBRT. In SBRT (especially for metastatic lung, liver, and paraspinal cases), the GTV and CTV are often considered to be identical. .[28, 31, 32, 41, 82] While there can be small volume

microscopic extension of tumor around the GTV in some settings [114], the typically very high reported local control rates after SBRT suggest that this component of tumor--if present--seems not to be a major source of recurrence, perhaps because it is still likely covered within a fairly high dose region as dose falls off around the PTV.

The variation of CTV size and position due to respiratory motion or organ filling is generally accounted for by an internal margin (IM) added to the CTV, resulting in the internal target volume (ITV).[113] The magnitude of this margin depends whether motion compensation is employed during delivery. The planning target volume (PTV) addresses all the possible geometrical variations by adding a variable margin for setup uncertainties, machine tolerances and intra-treatment variations to the CTV. . Typical SBRT margins for defining the minimal distance separating the CTV and PTV surfaces are 0.5 cm in the axial planes, and 1.0 cm in the inferior/superior directions, [32, 109, 115] for treatments that were performed in conditions that suppressed respiratory motion. Some centers are moving toward an isotropic expansion of the CTV when 4D imaging is used. In addition, some clinicians may include a 2-3 mm tissue margin surrounding the enhancing tumor for primary disease,[116-118]

Recommendation: At the current time it remains difficult to base target margins directly on clinical results. However the adequacy of the definitions of target margins (i.e. GTV, CTV, ITV, etc.) in SBRT should be based on an understanding of how the steep dose gradients and high fractional doses of SBRT effect the accuracy of traditional margin recipies[119] as well as the natural history of the tumor, the limitations of in-house localization capabilities to reduce random and systematic treatment uncertainty, and from information in the current literature. Simultaneously, centers should make systematic efforts to gather and analyze clinical results to improve margin design in the future.

1. Dose heterogeneity, gradient and fall-off, and beam geometry

Dose prescriptions in SBRT are often specified at low isodoses (e.g. 80% isoodse) and with small or no margins for beam penumbra at the target edge, as compared to traditional radiation therapy. The rationale is to improve dose falloff outside of the targeted volume and help to spare nearby organs at risk. This practice increases dose hetereogeneity within the target. [27, 109] However, in contrast to conventionally fractionated radiotherapy, dose heterogeneities within the target for SBRT are acceptable for targets not involving functional normal tissue. Hot spots within the target volumes are generally viewed to be clinically desirable, as long as there is no spillage into normal tissue. It has been hypothesized that hotspots within the central region of a tumor might offer a special advantage in eradicating radio-resistant hypoxic cells that might be more likely located there. [120] While the locations of hypoxic sub-regions in solid tumors might not be stable[121], regardless the observed dose-response for tumor control after SBRT supports an effort to administer the highest safely achievable dose. [122]

The use of multiple non-overlapping beams is the primary means of achieving a sharp dose fall-off in SBRT, similar to that in intracranial radiosurgery. This optimally requires that radiation should converge on the target as concentrically as possible from many directions. Provided that OARs (serially functioning organs such as spinal cord or sensitive mucosa)are sufficiently spaced from the target, the gradient of dose distribution outside the target should be ideally isotropic, with dose falling-off uniformly away from the surface of the target.[123]

Other parameters that affect the dose fall-off are beam energy and the resolution of beam shaping (*e.g.*, multileaf collimator [MLC] leaf width). For small beams such as those commonly used in SBRT, the higher the beam energy, the larger the beam penumbra due to lateral electron

transport in medium. In a low-density medium, such as lung tissue, this effect becomes more significant. A 6-MV photon beam, available on most modern treatment machines, provides a reasonable compromise between the beam penetration and penumbra characteristics for SBRT lung applications. Additionally, most SBRT applications use MLC collimation. While the finer MLC collimation resolution improves the conformity of target dose distribution, this improvement is limited by characteristic blurring caused by the finite source size and lateral range of secondary electrons. The commonly available 5 mm MLC leaf width has been found to be adequate for most applications, with negligible improvements using the 3-mm leaf width MLC for all but the smallest lesions (< 3 cm in diameter).[124-127]

2. Beam selection and beam geometry

In determining beam direction in SBRT, the avoidance of sensitive organs, mechanical constraints imposed by the equipment[123, 128], and short beam paths for most beams must all be considered. In general, a greater number of beams yields better target dose conformity and dose fall-off away from the target, and when the number of beams is sufficiently high, the choice of beam direction becomes less significant. However, for practical reasons it may be preferable to limit the number of beams or arcs. Restricting the entrance dose of individual beams to less than 30% of the cumulative dose and avoiding beam overlaps are desirable. This will help to prevent acute skin reactions and maintain the isotropic fall-off of dose gradients. Use of beam arrangements employing 5-8 coplanar or non-coplanar static conformal beams shaped by 5-10 mm MLCs for targets in the thorax and abdomen have been reported.[29-31, 116-118, 129] Mechanisms for optimizing SBRT beam angles to minimize normal tissue dose have been also reported[123, 128]. Recent developments in volumetric modulated arc techniques have the potential to create conformal dose distributions, achieve the required level of normal tissue sparing, and reduce

treatment times, as compared to their static field counterparts. [130] In most cases an isotopic dose gradient is desirable, though in cases where critical structures are in close proximity to the target volume it may be preferable to increase the dose gradient between the target and the critical structure. For example, SBRT of paraspinal tumors usually require the irradiation of a vertebral bone and/or an attached soft tissue tumor growth, with a special consideration to the spinal cord a few millimeters away. An isotropically sharp dose fall-off all around the tumor may result in an unacceptable dose to the spinal cord for such a case. Nine to eleven posterior and posterior-oblique beams equally-spaced at 18-20° apart have been shown to generate a sharp dose gradient of up to 12%/mm between the target and cord, adequately sparing the cord while delivering better than 90% of the prescription dose to the target volume.[131] Specific IMRT planning strategies for paraspinal cases involve the delineation and manipulation of anatomical and optimization volumes and constraints.[132]

3. Calculation grid size

The calculation grid resolution used in the treatment planning system (TPS) affects the accuracy of the dose distribution calculated. It has been reported in the literature that a 2.5-mm isotropic grid produces an accuracy of about 1% in the high-dose region of an IMRT plan consisting of multiple fields.[133] Another report indicated an accuracy of +/- 5% for an isotropic grid resolution of 4 mm.[134] Chung et al. find a dose difference of 2.3% of the prescribed dose for 2 mm calculation grids as compared to 1.5 mm grids, rising to 5.6% for 4mm grids. Their conclusion is that 2mm grids are required for IMRT procedures, especially in high dose gradient areas. [135]

Recommendation: SBRT commonly includes extremely high dose-gradients near the boundary of the target and often makes use of IMRT techniques. This report recommends the use of an isotropic grid size of 2 mm or finer. The use of grid sizes greater than 3 mm is discouraged for SBRT.

4. Bio-effect–based treatment planning and SBRT

SBRT involves the application of high fractional doses in a range not studied in prior decades. It is unlikely that normal tissue tolerance doses derived from the study of conventionally fractionated radiation therapy will apply in the context of SBRT. One way to evaluate the possible biological effect of an SBRT treatment plan in terms of its potential local tumor control and its potential normal tissue effects is to convert its associated physical dose distribution to a biologically normalized dose distribution. Using the biologically normalized dose distribution, bioeffect measures can then be calculated to rank and compare the SBRT treatment plan with others. Examples of such bioeffect measures are the biologically effective dose (BED) concept, the normalized total dose (NTD) concept, and the equivalent uniform dose (EUD) concept[136-141].

These bioeffect measures can be used in the evaluation of the effectiveness and safety of an SBRT dose distribution. In particular, the EUD concept can be used to rank competing treatment plans in terms of their expected tumor effect while the BED and NTD concepts can be used to evaluate the biological effectiveness of different dose fraction schemes. It must be understood that a physical dose distribution, giving a total dose of 60 Gy, has different biological effects both in terms of expected normal tissue complications and tumor effects, depending upon which fractionation schedule is employed (cf.[120], [142], and [51] for a detailed discussion).

For example, NTD is defined as the total dose given in 2-Gy fractions that has the same biological effect as the actual dose fractionation schedule under consideration. Essentially, the NTD concept simply converts BED values back to biologically equi-effective doses delivered at the standard dose per fraction of 2 Gy, generating numbers that can be more easily compared with the dose levels of standard treatment schedules. Table 2 summarizes the NTD for several dose fractionation schemes. Note the biological dose equivalents are very high due to the large dose per fraction. The Progression-free survival of patients with NSCLC at 30 months was estimated from Martel et al. [143] for the schedules marked with a * and from Fowler et al. [120] when rapid re-proliferation can be neglected.

The comparisons in Table 2 are offered only as an example of how one particular model can be applied to SBRT, and they should be viewed with certain caveats in mind. First, they compare only nominal prescription dose and do not take into account differences in prescription isodose line covering the PTV or dose calculation algorithm used. Second, clinical outcome reports of local control after a given dose-fractionation regimen are always the definitive measure of a treatment regimen's potency, not a model-based prediction. Finally, while there are reports showing higher control rates above certain BED cutoff levels [144-146], it should be appreciated that BED, NTD, and EUD are all ultimately derived starting from the linear-quadratic model, which may not describe tissue effects in hypofractionated dose regimens. [147] As more clinical data become available, these models will have to be refined and updated. In addition, alternative approaches to radiation effect modeling have been developed and require further investigation before their validity and predictability can be fully evaluated [148-150].

5. Normal Tissue Dose Tolerance

Normal tissue dose limits for SBRT are considerably different from conventional radiotherapy due to extreme dose-fractionation schemes and are still quite immature. Thus normal tissue dose limits for SBRT should not be directly extrapolated from conventional radiotherapy data. Likewise, data on intermediate-level doses, especially in organs that show partial-volume effects (lung, kidneys, etc.) are currently immature and should be treated with care.

Particular attention should be paid to fraction size, total dose, time between fractions, and overall treatment time, which are important radiobiological factors that need to be maintained within clinically established parameters where available in the SBRT literature. This becomes increasingly important for new hypofractionated schedules and trials for which there is no reliable mechanism to estimate their radiobiological effects. Therefore, in a clinical trial situation, not only the fraction size but also the frequency and overall treatment time should be maintained throughout the entire trial for all patients to obtain reliable outcome data.

Scenarios in which re-treatment is under consideration can be quite complicated, with (currently) sparse literature to guide treatment decisions. In re-treatment situations composite dose distributions across all treatments should be assessed when deciding if additional treatment is possible.

Table 3 summarizes tolerance doses from the University of Texas Southwestern[8] and the University of Virginia.[151] The doses are mostly unvalidated, and while most are based on toxicity observation and theory, there is a measure of educated guessing involved as well (R. Timmerman, 10/26/09, pers. comm.). Additional information may be found in several published reports, including Indiana University's lung SBRT experience, Karolinska Hospital's SBRT

experience, and a recent report from Stanford University. [18, 152-154] Because of the sparseness of long-term followup for SBRT it should be recognized that the data in both Table 3 and the published reports represent at best a first approximation of normal tissue tolerance. When proceeding in areas where there is a lack of published literature for toxicity and complications, this report recommends that formal institutional guidelines and prospective trials be implemented.

Recommendation: Normal tissue dose tolerances in the context of SBRT are still evolving, and only a limited experience exists from which to draw recommendations. Except in the setting of IRB approved Phase 1 protocols, critical organ tolerance doses based on the SBRT experience in the evolving peer-reviewed literature must be respected.

E. Treatment Plan Reporting

SBRT treatment plans often use a large numbers of beams, unconventional dose fractionations and delivery frequencies, and more comprehensive image guidance data and information. It is critical to accurately communicate the details of the treatment plan and its execution to the treatment team.

The quality of planned dose distributions for SBRT can be evaluated from parameters characterizing target coverage, dose homogeneity, dose outside of the target definition, and volumes of normal tissue exposed to lower doses. Simple methods of articulating these parameters may rely on combinations of DVHs for different organs and tables representing dose allocation in different subvolumes of these organs. Metrics that have been reported at some centers include:

- Prescription dose
- Prescription ICRU reference point or dose/volume (e.g. isodose covering PTV to a particular percentage)
- Number of treatment fractions
- Total treatment delivery period
- Target coverage
- Plan conformity (example: ratio of prescription isodose volume (PIV) to PTV, or a conformity index (CI) such as proposed by Hazard et al.[155])
- Dose falloff outside the target (example: ratio of the volume of the 50% of prescription isodose curve to PTV)
- Heterogeneity index *(e.g. the ratio of highest dose received by 5% of PTV to lowest dose received by 95% of PTV)*
- Notable areas of high or low dose outside of the PTV.
- Dose to organs at risk (dose to 1% and 5% volumes and mean doses)

PATIENT POSITIONING, IMMOBILIZATION, TARGET LOCALIZATION, AND DELIVERY

Ideally, the delivered dose would exactly match the planned dose distribution. This is seldom achieved in practice. However, in practice there are a number of considerations that can result in the dose delivered to the patient differing from the planned distribution (e.g. limits to beam modeling precision, treatment machine limitations, etc.). One of the most important potential sources of variation is positional changes of the target or surrounding tissue; for example, the patient's position in the immobilization system at treatment will likely not be exactly what it was at the time of CT simulation; and their soft tissue anatomy may have altered

in shape and position. This may be especially true during the long treatment times associated with SBRT that result from hypofractionated doses delivered through small treatment fields.

Historically, in order to minimize many of these potential variations, the developers of SBRT [109] scanned the patient in a body frame with an integral coordinate system that could be visualized in the CT image. Fortunately, the current availability of IGRT has made this older body frame/fiducial based system obsolete. The setup error of a stationary target can now be corrected to within the imaging and positioning accuracy of the system for each treatment. Residual translations of less than 2 mm are achievable for bony targets. [156] Robotic couches, when used in conjunction with stereotactic X-ray or volumetric imaging, have made it possible to also correct (up to 3–4° for roll and pitch and 10° for yaw) for the small rotational errors that can occur. [157, 158] However, soft tissue targets require volumetric imaging such as CBCT or CT on rail to achieve the necessary setup precision required. [159]

Recommendation: For SBRT, image guided localization techniques shall be used to guarantee the spatial accuracy of the delivered dose distribution with a high confidence level. Body frames and associated fiducial systems may be used for immobilization and coarse localization; however they shall not be used as a sole localization technique. In addition, it is crucial to maintain the spatial accuracy throughout the treatment delivery through either integrated image-based monitoring systems or through aggressive immobilization of appropriate targets, such as the spine.

F. Immobilization

The degree of required immobilization for SBRT is largely influenced by the ability of the dose delivery system to both detect and correct for the changes in patient position that may

occur during treatment. Even current image-guided positioning systems reduce but do not eliminate the need for proper immobilization.

Table 2 summarizes historical immobilization strategies and their associated localization errors. Stereotactic body frames (e.g. Elekta, Medical Intelligence Body Fix, Leibinger, Yenice, Lech Papiez, etc.) serve both to immobilize the patient physically and provide an initial approximate target localization, which is subsequently refined by in-room image-guided techniques. Body frames typically make use of vacuum cushions for immobilization. Stereotactic localization and targeting can be facilitated by a localizer arch which can be affixed to the body frame or to the Linac couch top and defines the reference coordinate system of body frame fiducials. Some body frame systems also include equipment for abdominal compression which can be used to minimize respiratory motion. [88, 160, 161]

G. Image-Guided Localization

Image guidance provides the finest level of localization and is used to reduce the spatial uncertainty in the positioning of targets and possibly critical structures prior to radiation delivery. In its more advanced implementations, image guidance is also used to monitor the position of the target or a surrogate during radiation delivery.

The traditional approach has been the use of 2D MV electronic portal imaging (EPID). This approach, used in conjunction with implanted fiducial hardware, has been used to deliver SBRT treatments to spinal sites while keeping the target within 2 mm of its planned position.[162]

Volumetric image-guidance allows for the precise localization of bone and soft tissue targets.[131, 163] This is achieved using MV [164] or kV [165-167] cone beam scanning, an MV fan beam

using a tomographic acquisition [168], and in-the-vault CT systems [131, 163]. Dual[169, 170] or multiple[171] room mounted kV imaging systems are used to provide rapid 3D localization of targets or implanted markers using pairs of 2D radiographs for both patient setup and intra-fractional monitoring. Treatment machines with gantry mounted kV units capable of fluoroscopy, radiographic localization, and cone beam imaging (especially for soft tissue targets) are being widely adopted. This has had a profound effect on SBRT. On board imaging when integrated with image registration software makes accurate target positioning and verification for SBRT readily available. Ideally, IGRT systems would be capable of visualizing the actual target volume directly. In practice, the imaging system available may not be able to image the target, especially if it is soft tissue. A well established approach is to implant radiopaque markers in the vicinity of the tumor and use them as surrogates in localizing targets such as prostate[172-174], liver[175], and lung[33, 176-179], and spine[180-182]. Implanting fiducials percutaneously in to the lung poses a high risk of pneumothorax. [183, 184] Ultrasound (US) is effective for imaging soft tissue structures and tumors in the pelvis and abdomen. The probe is tracked in 3D using a stereoscopic infrared camera system installed in the treatment room, allowing the reconstructed volumetric images to be referenced to the machine isocenter. The use of US in SBRT for a variety of sites has been described by Meeks et al.,[185] Fuss[186], and reviewed by Kuban and coworkers. [187]

Finally, a technique that relies on radiofrequency tracking rather than imaging is that used by the Calypso system (Calypso Medical Technologies, Seattle, WA), which can continuously (at 10 Hz) report the 3D position of a target throughout a procedure, even during radiation delivery. [188]

With any localization methodology, a careful assessment of the random and systematic errors of the imaging system and a quality assurance program are necessary for a successful SBRT program.

H. Localization, Tumor-Tracking, and Gating Techniques for Respiratory Motion Management

The respiratory motion assessment of targets in the thorax and abdomen and its management strategies are described in detail in the Report of AAPM Task Group 76: "The Management of Respiratory Motion in Radiation Oncology".[189] They are mentioned here briefly for the sake of completeness.

1. Image-Guided Techniques

Image-guided techniques such as fluoroscopy, gated radiographs, and cone beam imaging of soft tissue can be used to localize targets moving during treatment due to respiratory motion.[190, 191]. A few problems remain, however; for example during the respiratory cycle the target may move with respect to nearby critical structures which themselves may not be tracked. Therefore, though a delivery may reduce dose to a volume of critical structures, it may not lessen the uncertainty in the doses to them.[192]

Cone beam imaging is increasingly being used for localization of lung tumors.[193-195] Cone beam scans can have an acquisition time 60 seconds or more and therefore have the advantage of capturing the average tumor position over 15 or more breathing cycles, which may correspond well to the planning internal target volume (ITV)[113] as obtained from 4DCT. [196, 197] In contrast, the use of fast CT either during simulation or during image guidance at the time of treatment is

less ideal because the tumor and/or critical structure position captured could be random due to motion.

Cone beam scans can be used to resolve the respiratory motion in lung tumors using a respiration correlated approach. A large number of projections are acquired during a slow (on the order of 4 minutes) scan. The projections are sorted into phase bins, then each phase bin is reconstructed, thus the tumor position at each phase bin can be determined. The technique can be used to verify that the target motion amplitude is within the planned limits, and can be acquired just before treatment delivery, reducing the chance of a systematic error due to patient setup changes between imaging and treatment delivery.[198] While not yet available commercially at the time of this report, the ability to record tumor position at each respiratory phase may be advantageous for respiratory motion management as compared to the average of a 4DCT scan.

2. Optical Tracking Techniques

After localization, some kind of monitoring is desirable to track patient breathing and monitor patient positioning during the treatment. Two optical technologies, stereoscopic infra-red cameras and video photogrammetry are used to track the 3D coordinates of points on the patient's skin in real time.

Infra-red tracking systems use either active infrared light emitting diodes (IRLED) or passive markers that reflect the infrared light emitted from an external source. These are temporarily attached to the patient's skin. In a stereoscopic system, two infra-red cameras are used to track the IRLEDs or reflectors in 3D during treatment.[199] Several optical tracking systems have been developed for stereotactic radiation therapy.[111, 200-205] Video photogrammetry systems use several video cameras and speckle-textured light projectors to acquire a 3D surface without the need to attach any markers to the patient's skin. [206] Finally, some systems combine

in-room optical systems with kV imaging to detect changes in the correspondence between the external markers and the tumor over the course of treatment. These report RMS positioning errors as low as 2mm in certain situations. [207-209]

A critical assumption of these monitoring techniques is that the external marker motion correlates with the internal tumor/organ motion. In certain instances this assumption has been called into question, especially for lung tumors[210]. Careful consideration should be given to the clinical situation when a decision is taken to use optical tracking technologies in order to ensure an appropriate level of confidence in the correlation.

3. Respiratory Gating Techniques

The localization and tracking techniques described above are often used in conjunction with respiratory gating, where dose is delivered only in particular phases of the respiratory cycle with the goal of reducing the probability of delivering dose to normal tissue and underdosing the target.[211-213] The efficacy of respiratory gating is affected by the reproducibility of a patient's breathing patterns from cycle-to-cycle and day-to-day. Respiratory gating increases treatment time as compared to non-gated treatments; published duty cycles (ratio of beam on to total beam delivery time) range from 30-50%.[214-216] Increasing the dose rate, if possible, would counteract the increase in treatment time. Another consideration is the amplitude of the respiratory motion. Several reports have shown that the benefit of gated beam delivery is minimal and does not outweigh the increase in treatment time and complexity for patients with motion amplitudes smaller than 2 cm. [119, 211, 217]

Recommendation: For all SBRT patients with targets in the thorax or abdomen, a patient specific tumor motion assessment is recommended. This serves to quantify the motion expected during the respiratory cycle. This data may then be used to:

A. Determine if the patient's treatment would likely benefit from techniques such as respiratory gating.

B. to quantify the residual motion expected during the respiratory gated delivery if such delivery is used,

C. to design margins for treatment planning and

D. to quantify and account for any phase shift between the tumor motion and the respiratory signal.

If external markers are used for motion tracking, it is recommended that their suitability as a surrogate for tumor motion be verified.

Repeat motion assessment for each SBRT treatment is recommended in order to verify and if necessary correct the treatment if changes in the motion patterns, magnitude or correlation with the respiratory signal are observed.

I. Delivery data reporting

It is important that an SBRT program has an established quality assurance process and proper documentation for accurate treatment delivery. The treatment delivery report should indicate that a quality assurance process is in use and adherence to quality assurance is documented.

Quantitative information regarding daily image registration and calculated shifts and verification of treatment ports with respect to bony anatomy and the target should be recorded.

Action levels should be defined for residual target positions and patient rotations, which if exceeded, should trigger repositioning of the patient. Action levels should also be defined for internal anatomic variation. These action levels are likely to be less than the various treatment margins defined for the treatment, and may vary according to institution, equipment, technique, and treatment site. Any significant internal organ variations or changes in the target volume that cannot be accommodated by treatment margins should be noted and their consequences, such as re-simulation and re-planning should be indicated.

The patient position should be monitored during the entire treatment, and any deviations in treatment/target position as assessed from available visual, optical and radiographic tools (such as repeat imaging) should be recorded for the entire treatment duration. Tolerance values for such deviations consistent with the applied treatment margins should be indicated. In addition, any treatment interruptions or deviations from the fractionation time interval should be recorded.

SPECIAL DOSIMETRY CONSIDERATIONS

J. Problems associated with dosimetry of small/narrow field geometry

SBRT and IMRT routinely use small fields and beamlets of less than 10 mm in diameter in order to achieve the desired, highly-focused and precisely modulated dose distribution.

Measurement of small photon beams is complicated by the loss of lateral electronic equilibrium,[218] volume averaging,[218-221] detector-interface artifacts, collimator effects,[222-225] and detector position-orientation effects.[94, 221, 226]

Recommendation: Due to the small dimensions and steep dose gradients of photon beams used in SRS/SRT and IMRT, an appropriate dosimeter with a spatial resolution of approximately 1 mm or better (stereotactic detectors) is required to measure the basic dosimetry data, *e.g.*, the total scatter factor (SF, or relative output factor), tissue-maximum ratio (TMR), and off-axis ratios (OARs). Even with stereotactic detectors, careful detector-phantom setup, and detailed dose corrections, one might still find more than 10% discrepancies among the measurements of very small fields (< 10 mm in diameter).[219, 227-229] MLC-shaped fields have more geometry and dosimetry uncertainties than those of the circular cones. Li *et al.*[230] demonstrate that large errors are often caused by a small setup error or measuring point displacement from the central ray of the beam. For small MLC fields, the collimator leaf-edge effect is almost independent of the depth but is closely related to the field size and type of MLC. The volume effect becomes significant when the detector diameter is comparable to the half size of the small fields.

For the profile (off-axis ratio) measurement of the small photon beams, Higgins *et al.*[231] demonstrated a simple approach to unfolding the chamber size artifact from measured small-beam profiles using typical cylindrical chambers by de-convolving the detector-response artifact from each point in the profiles.

Recommendation: the maximum inner diameter of a detector should be less than half the FWHM of the smallest beam measured in order for the deconvolution of the detector-size effect to work properly.

K. Problems associated with small-field heterogeneity calculations

Head-and-neck and lung tumors are often situated at air–tissue interfaces. The effects of transient electronic disequilibrium and increased lateral electron range in air will result in an important reduction of the central-axis dose beyond the cavity and potentially an underdosage of the tumor.[232-234] Heterogeneity correction becomes extremely important in situations where the target is surrounded by low-density tissue such as the lungs. Some dose-calculation algorithms which do not account for lateral electron scattering can yield incorrect results.

Most treatment planning systems used for SBRT make use of one of a variety of advanced photon dose-calculation methods based on Monte Carlo (MC) pre-calculated dose-spread kernels and employing convolution/superposition techniques. Unlike conventional, approximation-based treatment planning methods which consider only photon transport, these newer algorithms consider recoil electron transport, however the inhomogeneity corrections are still approximate. For example, dose calculation using pencil-beam superposition will not account for increased electron scattering in lower-density material. For methods using point dose-spread kernels, density scaling is performed for the distance between the interaction point and the calculation point, thereby assuming that electrons travel in a straight line along this direction.

Several studies have described the validity of inhomogeneity corrections in small field situations[233, 235]. The Radiological Physics Center conducted a study comparing various dose calculation regimes used by institutions participating in the RTOG 0236 protocol for lung tumors using an anthropomorphic thorax phantom. Convolution/superposition and Clarkson/pencil beam algorithms matched well at the center of the target PTV (embedded in the phantom); however there were significant differences in the target periphery. [236]

AAPM task group 65 on tissue inhomogeneity corrections for megavoltage photon beams reviewed the literature extensively and recommended that inhomogeneity corrections be used for patient dose calculations, while they cautioned the user of potential pitfalls for various clinical conditions with several commercially available heterogeneity correction algorithms.[237] Task group 65 also reported that while the dose calculation estimations are not accurate in certain situations, they are often closer to the actual values than calculations with no inhomogeneity corrections at all. It should be noted that Task Group 65[237] specifically disallows the use of pencil-beam algorithms for the situation of a target surrounded by low-density tissue as this class of algorithms does not account for lateral scattering in the small field sizes used in SBRT. **Recommendation**: Algorithms that account for 3D scatter integration such as convolution / superposition have been found (including by the RPC study) to perform adequately in most clinical situations, including (in many cases) for circumstances where there is a loss of electronic equilibrium such as the lung tissue interface or tumor margin in low density medium. Calculation algorithms accounting for better photon and electron transport such as Monte Carlo would be ideal for the most demanding circumstances, such as a small lesion entirely surrounded by a low density medium. However, at the time of this publication, Monte Carlo calculations are not yet widely available in the clinic. Pencil beam algorithms accounting for only 1D scatter corrections are not recommended for accurate estimate of the dose in such tumors and in general for any lung tumors.[238] For site specific recommendations, the clinical user should refer to Report 85 of Task group 65.[237]

CLINICAL IMPLEMENTATION OF SBRT

The high dose delivery and precision targeting requirements of SBRT demands stringent procedures and tools in order to guarantee that the accuracy of the system is achieved for each treatment and each fraction. The critical steps for initiating a clinical SBRT program involve:

1. Establish the scope of the SBRT program including a selection of treatment sites and the clinical goal(s) for each site.
2. Determine a treatment modality, dose/fractionation scheme, and treatment planning goals (target definition, target coverage, conformity index, etc.) for that support the clinical goals for each treatment site.
3. For each treatment modality and treatment scheme, determine the equipment requirements for patient positioning, treatment delivery and verification.
4. Determine personnel needs for SBRT implementation and maintenance
5. Establish and perform acceptance and commissioning test procedures for the SBRT equipment
6. Establishing SBRT simulation, treatment planning, delivery and verification guidelines, reporting methodology, and routine QA procedures, and action levels
7. Conducting personnel training

L. Establishing the scope and clinical goals of the SBRT program

The clinical rationale and historical perspective for the use of SBRT in primary and metastatic disease have been outlined previously. The clinical physics team plays an essential

role in determining the limitations of available technology for patient immobilization, localization, treatment planning and treatment delivery for a given treatment site. Strategies for addressing these issues must be thoroughly discussed with the clinical team. Outside of a formal prospective clinical trial approved by an institutional review board, clinical guidelines from national protocols and/or published literature should be used to determine the parameters for best individualized patient treatment. Also critical is the role the physics team plays in evaluating the adequacy of space and personnel resources for SBRT. A thorough feasibility analysis of existing resources to achieve the clinical and technical goals of the proposed SBRT must be performed and discussed with the medical center administration. The role and responsibility of each individual team member should be clearly laid out along the recommendations of ASTRO/ACR Practice Guidelines for SBRT.[239]

1. Equipment considerations

The primary technical issues for SBRT equipment selection are the adequacy of physical space and the ability to integrate the new equipment with the existing technology including the treatment planning and record and verify systems. In most facilities, existing linear accelerators with image guidance capability may be adequate to perform SBRT procedures. It is also important to make sure that the Treatment Planning System (TPS) has the capability of accurately calculating the sophisticated plans needed for SBRT and handling multimodality imaging (registration and fusion) and image guidance technology. However, as noted earlier and in Task Group Report 85[237], the use of pencil beam algorithms is not recommended for lung SBRT applications..

2. Time and personnel considerations

The complexity of SBRT requires an increased level of physicist involvement in every aspect of the process including the initial commissioning of immobilization and stereotactic localization system, small field measurements and verifications, and continued quality assurance. Additional physics resources will be needed to implement and maintain an SBRT program for most centers. Physics staffing requirements can be derived by referencing the 2008 ABT study[240, 241] (Medical Physicist Work Values for Radiation Oncology Physics Services). The study defines work as a product of time and intensity (Work = Time * Intensity), where intensity is a measure of mental effort, emotional stress, and the complexity of the technique. The study reports a median work estimate for a special medical physics consultation (CPT code 77370) relative to a continuing physics consultation (the defined baseline CPT code of 77336) of 13.94. For procedures within CPT 77370; SBRT, single-fraction SRS, IMRT, and IGRT have time estimates of 4.0, 6.0, 4.0, and 1,0 hours respectively, vs. 2.0 hours for a routine 77370 procedure. Likewise, median intensity estimates are reported as 4.0, 5.0, 4.5, and 4.5 vs. 2.0 for the routine 33730 procedure.

Recommendation: The 2008 ABT report suggests that an SBRT procedure requires a total effort which is approximately equal to that required for IMRT and significantly greater that that required for a standard 3D conformal procedure. The guidelines published by ASTRO/ACR [239] includes provisions for SBRT personnel, and clearly specifies that that qualified radiation oncology staff, therapists, dosimetrists, physicists, and physicians, are required to maintain a high quality SBRT Program. In this report we underscore the commitment by everyone involved in an SBRT program to continually update the training of staff and physicians with regard to any new developments.

M. Acceptance, commissioning, and quality assurance

Acceptance test procedures provided by the vendor are typically designed to verify contractual system specifications for performance characteristics of the system. Commissioning tests should be developed by the institution's physics team to explore in detail every aspect of the system with the goal of developing a comprehensive baseline characterization of the performance of the system. A rigorous, continuing process of periodic and treatment-specific quality assurance is vital for minimizing systematic errors that can result in less than optimal treatments. Specific tests should be developed to look at all aspects of the system both individually and in an integrated fashion. These tests should be including but not limited to: integrity of the simulation imaging data, dose calculation algorithms, MLC leaf sequencing, MU calculation algorithms, leaf speed, machine dose rates used for SBRT and accuracy of calibration at these dose rates, delivery precision at small MUs, patient positioning and localization, motion tracking and gating, etc[242, 243]. While in many cases the specific tests used are similar for acceptance, commissioning, and quality assurance, it is important to remember that the intent of each activity is different.

A variety of task groups and reports are available which provide guidance on best practices for performing commissioning and quality assurance of delivery devices (including TG-40 and TG-45) [244, 245], imaging equipment[244, 246, 247], treatment planning systems (TG-53[248]), and IMRT[249]. TG-142 provides an update to TG-40 and includes specific recommendations for SBRT.[243] In addition, a recent QA supplement published in the International Journal of Radiation Oncology Biology Physics[250] suggests a set of annual, monthly and daily QA activities and tolerances which allow verification of the overall accuracy of various aspects of the IGRT/SBRT treatment process (summarized in Table 5).

For SBRT, the imperative need for accuracy requires special consideration when

designing acceptance, commissioning, and quality assurance tests. For instance, it is paramount to verify that the radiation isocenter coincides with the mechanical isocenter, including couch rotation, and that the lasers are aligned to the radiation isocenter. An elaborate method of system accuracy determination has been published for intracranial applications using the BRW head frame by Lutz et al [251]. The integral use of on-board imaging in SBRT makes it critical to also verify the coincidence of the imaging isocenter. [252] Non-isocentric modalities such as the Cyberknife have tests similar to the Winston-Lutz test which can verify overall geometric accuracy. [169]

Redundancy tests should be introduced to check the integrity of the process of localization in CT and treatment rooms. If a technique for motion management is used, treatment delivery must be evaluated in a manner consistent with clinical use.

The individual components of the SBRT process (imaging, localization, treatment delivery, etc) each have associated error. However even if each of these individual errors are small by themselves, cumulative system accuracy for the procedure can be significant and needs to be characterized through an end-to-end test using phantoms with measurement detectors and imaging. The best way to accomplish this is to employ a test that uses the image guidance system to position a phantom with internal fiducial markers at isocenter then and image those markers with the treatment beam. This test demonstrates the agreement between the image-guidance system's positioning and beam delivery at isocenter.[253, 254]. The phantom should be positioned with known error and then the IGRT system is used to correct them. A simulation CT scan of the phantom is used to position the fields that irradiate the targets in the phantom. In situations where it is not easy to take an image with a detector behind the phantom, an alternative such as radiochromic film within the phantom may be used. Moving phantoms can be employed to

simulate respiratory motion effects. Multiple fiducial markers placed in the test phantoms can be used to evaluate rotational errors when investigating 6 degree-of-freedom tables.

Finally, it should be recognized that system accuracies determined from well defined targets in idealized phantom geometries represent only the upper limit of targeting accuracy for ideal conditions. The actual patient targeting accuracy will likely suffer from pervasive dynamic conditions at patient setup as well as decreased image quality with the patient anatomy. Therefore, treatment-specific and patient-specific QA procedures should be established to govern both the treatment planning and delivery process as a whole as well as to provide sanity checks of the setup for individual patient fractions. The former would include institutional protocols for imaging, segmentation, normal tissue dose constraints, dose coverage criteria, motion suppression and tracking strategies, treatment verification, and treatment documentation. Patient-specific quality control would include procedures for validation of treatment plans, data integrity, beam configuration, patient-setup and target localization (including specific action levels that would trigger a review of patient setup), and patient safety.

N. Patient safety and the medical physicist

There are several patient safety issues that must be addressed on an ongoing basis in a SBRT program. These include: verification of correct patient, correct patient plan, correct isocenter, correct and properly configured immobilization devices, collision with patient or patient accessories, interference of patient arm, elbow, chin or accessories with the beam, redundancy check with MV orthogonal port films in addition to more sophisticated image guidance, treatment plan verification with second MU calculation or measurements, pretreatment verification of appropriate treatment machine parameters and accessories including lasers, monitoring for patient movement during treatment, etc. The large intra-fractional doses

delivered in SBRT mean that a mistake in any of these steps could easily lead to patient harm, and would be difficult to compensate for in subsequent fractions.

Recommendation: For these reasons it is recommended that at least one qualified physicist be present from the beginning to end of the first treatment fraction. For subsequent fractions, it is recommended that a qualified physicist be available (e.g. in his office or available by pager and within minutes of the machine), particularly for patient setup in order to verify immobilization, imaging, registration, gating, and setup correction. It is important that the radiation therapist be well-trained in SBRT procedures. It is also recommended that a radiation oncologist approve the result of the image guidance and verify the port films before every fraction of the SBRT treatment.

O. Quality Process Improvement: Vigilance in the error reduction process in the treatment planning and delivery process.

The complexity, variation in individual practice patterns, and continued evolution of SBRT-related technology can render a static, prescriptive QA paradigm insufficient over time.

Recommendation: A vital component of any comprehensive QA strategy should be to regularly review existing QA procedures with the objective to assess and critique the current QA practice in the context of current and proposed equipment. For some institutions, it may be useful to introduce tools which have proved effective in systems engineering, such as formalized process mapping and fault analysis[255].

FUTURE DIRECTIONS

While the development of SBRT has made great strides, many issues remain investigational, and there is clearly room for future research and development. This Task Group recommends in particular the following areas for future investigation:

1. Incorporation of strategies for the adaptive conformation of treatment fields. These may include deformable image segmentation and registration strategies, probability-based dose distribution optimization that can predict tissue response over time.
2. Incorporation of bio-effect knowledge into the treatment process.
3. Incorporation of improvements in small-field dosimetry performance in clinical treatment planning systems.
4. Incorporation of strategies for adjuvant chemotherapies in patients undergoing SBRT and timing radiation- and chemo-therapy in a way that can enhance the tumoricidal effect.
5. Incorporation of molecular imaging and its applications for enhanced tumor identification, predictive oncology, and as a metric for treatment effectiveness.
6. Incorporation of (residual) tumor motion effects into the treatment planning and the methods of evaluation for the delivered SBRT dose to a dynamic target.
7. Volumetric modulated arc therapy to deliver conformal SBRT doses while substantially shortening delivery times.
8. Proton and heavy ion therapies which can take advantage of minimal or no exit dose and a potentially lower integral dose.

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TABLES

Table 1

Characteristic	3D/IMRT	SBRT
Dose / Fraction	1.8 – 3 Gy	6 – 30 Gy
# Fractions	10 – 30	1-5
Target definition	CTV / PTV (gross disease + clinical extension): tumor may not have a sharp boundary.	GTV / CTV / ITV/ PTV (well-defined tumors: GTV=CTV)
Margin	Centimeters	Millimeters
Physics / dosimetry monitoring	Indirect	Direct
Required setup accuracy	TG40, TG142	TG40, TG142
Primary imaging modalities used for treatment planning	CT	Multi-modality: CT/MR/PET-CT
Redundancy in geometric verification	No	Yes
Maintenance of high spatial targeting accuracy for the entire treatment	Moderately enforced (moderate patient position control and monitoring)	Strictly enforced (sufficient immobilization and high frequency position monitoring through integrated image guidance)
Need for respiratory motion management	Moderate – must be at least considered	Highest
Staff training	Highest	Highest + special SBRT training
Technology implementation	Highest	Highest
Radiobiological understanding	Moderately well understood	Poorly understood
Interaction with systemic therapies	Yes	Yes

Table 2

Total Physical Dose (Gy)	Reference	NTD_{10} (Gy)	Log_{10} Cell Kill	Estimated 30-mo. Local Progression-Free Survival[#]	NTD_3 (Gy)
30 x 2 = 60[*] in 6 weeks	Estimated from Martel, 1999[143]; Fowler 2004[120]	65	9.9	17.7 % * with repop	60
35 x 2 = 70[*] in 7 weeks	Estimated from Martel, 1999[143]; Fowler 2004[120]	72	10.9	28.4 % * " "	70
4 x 12 = 48	Nagata, 2002[37]	83	12.6	78.9 % no repop	144
3 x 15 = 45	Nyman, 2006[256]	94	14.2	90.8 % " "	162
5 x 12 = 60	Hodge, 2006[257]	110	16.7	97.1 % " "	180
3 x 20 = 60	McGarry, 2005[49]; Timmerman 2003[32]	150	22.7	>99% " "	276
3 x 22 = 66	McGarry, 2005[49]; Timmerman 2003[32]	176	26.7	>99% " "	330

[#]Progression-Free Survival at 30 months has been estimated using the following dose response model: $LPF_{30m} = \frac{1}{1+\left(NTD_{10}^{50}/NTD_{10}\right)^{4\gamma_{50}}}$ using the following parameter values: $NTD_{10}^{50} = 84Gy;\ \gamma_{50} = 1.5$ (cf. Ref. [143]) when repopulation is included and $NTD_{10}^{50} = 70Gy;\ \gamma_{50} = 1.94$ (cf. Ref. [120]) when repopulation is not included.

The Progression-free survival of patients with NSCLC at 30 months was estimated from Martel et al. [143] for the schedules marked with a * and from Fowler et al. [120] when rapid re-proliferation can be neglected.

1 Table 3

		One Fraction		Three Fractions		Five Fractions		
Serial Tissue	**Max critical volume above threshold**	**Threshold dose (Gy)**	**Max point dose (Gy)****	**Threshold dose (Gy)**	**Max point dose (Gy)****	**Threshold dose (Gy)**	**Max point dose (Gy)****	**Endpoint (≥Grade 3)**
Optic Pathway	<0.2 cc	8 Gy	10 Gy	15.3 Gy (5.1 Gy/fx)	17.4 Gy (5.8 Gy/fx)	23 Gy (4.6 Gy/fx)	25 Gy (5 Gy/fx)	neuritis
Cochlea			9 Gy		17.1 Gy (5.7 Gy/fx)		25 Gy (5 Gy/fx)	hearing loss
Brainstem (not medulla)	<0.5 cc	10 Gy	15 Gy	18 Gy (6 Gy/fx)	23.1 Gy (7.7 Gy/fx)	23 Gy (4.6 Gy/fx)	31 Gy (6.2 Gy/fx)	cranial neuropathy
Spinal Cord and medulla	<0.35 cc <1.2 cc	10 Gy 7 Gy	14 Gy	18 Gy (6 Gy/fx) 12.3 Gy (4.1 Gy/fx)	21.9 Gy (7.3 Gy/fx)	23 Gy (4.6 Gy/fx) 14.5 Gy (2.9 Gy/fx)	30 Gy (6 Gy/fx)	myelitis
Spinal Cord Subvolume (5-6 mm above and below level treated per Ryu)	<10% of subvolume	10 Gy	14 Gy	18 Gy (6 Gy/fx)	21.9 Gy (7.3 Gy/fx)	23 Gy (4.6 Gy/fx)	30 Gy (6 Gy/fx)	myelitis
Cauda Equina	<5 cc	14 Gy	16 Gy	21.9 Gy (7.3 Gy/fx)	24 Gy (8 Gy/fx)	30 Gy (6 Gy/fx)	32 Gy (6.4 Gy/fx)	neuritis
Sacral Plexus	<5 cc	14.4 Gy	16 Gy	22.5 Gy (7.5 Gy/fx)	24 Gy (8 Gy/fx)	30 Gy (6 Gy/fx)	32 Gy (6.4 Gy/fx)	neuropathy
Esophagus*	<5 cc	11.9 Gy	15.4 Gy	17.7 Gy (5.9 Gy/fx)	25.2 Gy (8.4 Gy/fx)	19.5 Gy (3.9 Gy/fx)	35 Gy (7 Gy/fx)	stenosis/fistula
Brachial Plexus	<3 cc	14 Gy	17.5 Gy	20.4 Gy (6.8 Gy/fx)	24 Gy (8 Gy/fx)	27 Gy (5.4	30.5 Gy (6.1 Gy/fx)	neuropathy

						Gy/fx)		
Heart/Pericardium	<15 cc	16 Gy	22 Gy	24 Gy (8 Gy/fx)	30 Gy (10 Gy/fx)	32 Gy (6.4 Gy/fx)	38 Gy (7.6 Gy/fx)	pericarditis
Great vessels	<10 cc	31 Gy	37 Gy	39 Gy (13 Gy/fx)	45 Gy (15 Gy/fx)	47 Gy (9.4 Gy/fx)	53 Gy (10.6 Gy/fx)	aneurysm
Trachea and Large Bronchus*	<4 cc	10.5 Gy	20.2 Gy	15 Gy (5 Gy/fx)	30 Gy (10 Gy/fx)	16.5 Gy (3.3 Gy/fx)	40 Gy (8 Gy/fx)	stenosis/fistula
Bronchus- smaller airways	<0.5 cc	12.4 Gy	13.3 Gy	18.9 Gy (6.3 Gy/fx)	23.1 Gy (7.7 Gy/fx)	21 Gy (4.2 Gy/fx)	33 Gy (6.6 Gy/fx)	stenosis with atelectasis
Rib	<1 cc <30 cc	22 Gy	30 Gy	28.8 Gy (9.6 Gy/fx) 30.0 Gy (10.0 Gy/fx)	36.9 Gy (12.3 Gy/fx)	35 Gy (7 Gy/fx)	43 Gy (8.6 Gy/fx)	Pain or fracture
Skin	<10 cc	23 Gy	26 Gy	30 Gy (10 Gy/fx)	33 Gy (11 Gy/fx)	36.5 Gy (7.3 Gy/fx)	39.5 Gy (7.9 Gy/fx)	ulceration
Stomach	<10 cc	11.2 Gy	12.4 Gy	16.5 Gy (5.5 Gy/fx)	22.2 Gy (7.4 Gy/fx)	18 Gy (3.6 Gy/fx)	32 Gy (6.4 Gy/fx)	ulceration/fistula
Duodenum*	<5 cc <10 cc	11.2 Gy 9 Gy	12.4 Gy	16.5 Gy (5.5 Gy/fx) 11.4 Gy (3.8 Gy/fx)	22.2 Gy (7.4 Gy/fx)	18 Gy (3.6 Gy/fx) 12.5 (2.5 Gy/fx)	32 Gy (6.4 Gy/fx)	ulceration
Jejunum/Ileum*	<5 cc	11.9 Gy	15.4 Gy	17.7 Gy (5.9 Gy/fx)	25.2 Gy (8.4 Gy/fx)	19.5 Gy (3.9 Gy/fx)	35 Gy (7 Gy/fx)	enteritis/obstruction
Colon*	<20 cc	14.3 Gy	18.4 Gy	24 Gy (8 Gy/fx)	28.2 Gy (9.4 Gy/fx)	25 Gy (5 Gy/fx)	38 Gy (7.6 Gy/fx)	colitis/fistula
Rectum*	<20 cc	14.3 Gy	18.4 Gy	24 Gy (8 Gy/fx)	28.2 Gy (9.4 Gy/fx)	25 Gy (5 Gy/fx)	38 Gy (7.6 Gy/fx)	proctitis/fistula
Bladder wall	<15 cc	11.4 Gy	18.4 Gy	16.8 Gy (5.6 Gy/fx)	28.2 Gy (9.4 Gy/fx)	18.3 Gy (3.65 Gy/fx)	38 Gy (7.6 Gy/fx)	cystitis/fistula

Penile bulb	<3 cc	14 Gy	34 Gy	21.9 Gy (7.3 Gy/fx)	42 Gy (14 Gy/fx)	30 Gy (6 Gy/fx)	50 Gy (10 Gy/fx)	impotence
Femoral Heads (Right & Left)	<10 cc	14 Gy		21.9 Gy (7.3 Gy/fx)		30 Gy (6 Gy/fx)		necrosis
Renal hilum/vascular trunk	<2/3 volume	10.6 Gy	18.6 Gy (6.2 Gy/fx)			23 Gy (4.6 Gy/fx)		malignant hypertension
		One Fraction		**Three Fractions**		**Five Fractions**		
Parallel Tissue	**Minimum critical volume below threshold**	**Threshold dose (Gy)**	**Max point dose (Gy)****	**Threshold dose (Gy)**	**Max point dose (Gy)****	**Threshold dose (Gy)**	**Max point dose (Gy)****	**Endpoint (≥Grade 3)**
Lung (Right & Left)	1500 cc	7 Gy	NA - Parallel tissue	11.6 Gy (2.9 Gy/fx)	NA - Parallel tissue	12.5 Gy (2.5 Gy/fx)	NA - Parallel tissue	Basic Lung Function
Lung (Right & Left)	1000 cc	7.4 Gy	NA – Parallel tissue	12.4 Gy (3.1 Gy/fx)	NA – Parallel tissue	13.5 Gy (2.7 Gy/fx)	NA - Parallel tissue	Pneumonitis
Liver	700 cc	9.1 Gy	NA – Parallel tissue	19.2 Gy (4.8 Gy/fx)	NA – Parallel tissue	21 Gy (4.2 Gy/fx)	NA - Parallel tissue	Basic Liver Function
Renal cortex (Right & Left)	200 cc	8.4 Gy	NA - Parallel tissue	16 Gy (4 Gy/fx)	NA - Parallel tissue	17.5 Gy (3.5 Gy/fx)	NA - Parallel tissue	Basic renal function

*Avoid circumferential irradiation

** “point” defined as 0.035cc or less

6

7

8 Table 4

9

Author / year	Site	Immobilization / Repositioning	Reported accuracy
Lax-1994[109]	Abdomen	Wood frame / stereotactic coordinates on box to skin marks	3.7mm Lat 5.7mm Long
Hamilton-1995[258]	Spine	Screw fixation of spinous processes to box	2mm
Murphy-1997[259]	Spine	Frameless / Implanted fiducial markers with real time imaging and tracking	1.6mm radial
Lohr-1999[253]	Spine	Body cast with stereotactic coordinates	≤ 3.6mm mean vector
Yenice – 2003[131]	Spine	Custom stereotactic frame and in-room CT guidance	1.5mm system accuracy, 2-3mm positioning accuracy
Chang-2004[42]	Spine	MI™ BodyFix with Stereotactic Frame / linac / CT on rails with 6D robotic couch	1 mm system accuracy
Tokuuye-1997	Liver	Prone position Jaw and arm straps	5mm
Nakagawa-2000[260]	Thoracic	MVCT on linac	Not reported
Wulf-2000[261]	Lung, Liver	Elekta™ body frame	3.3mm lat 4.4 mm long.
Fuss-2004[160]	Lung, liver	MI™ BodyFix	Bony anatomy translation 0.4, 0.1, 1,6 mm (mean X, Y, Z); Tumor translation before image guidance 2.9, 2.5, 3.2 mm (mean X, Y, Z)
Herfarth-2001[28]	Liver	Leibinger body frame	1.8-4.4 mm
Nagata-2002[37]	Lung	Elekta™ body frame	2mm
Fukumoto-2002[34]	Lung	Elekta™ body frame	Not reported
Hara-2002[35]	Lung	Custom bed transferred to treatment unit after confirmatory scan	2mm
Hof-2003[117]	Lung	Leibinger body frame	1.8 – 4 mm
Timmerman-2003[32]	Lung	Elekta™ body frame	Approx. 5mm

Wang-2006[88]	Lung	Medical Intelligence Body Frame stereotactic coordinates / CT on rails	0.3 ± 1.8mm AP -1.8 mm±3.2mm Lat 1.5 mm ± 3.7 mm SI

Table 5

Source	Purpose	Proposed Test	Reported Achievable Tolerance	Proposed Frequency
Ryu et al, 2001[327]	End-to-end localization accuracy	Stereo x-ray/DRR fusion	1.0 to 1.2 mm root mean square	Initial commissioning and annually thereafter
Ryu et al, 2001[327]	Intrafraction targeting variability	Stereo x-ray/DRR fusion	0.2 mm average, 1.5 mm maximum	Daily (during treatment)
Verellen et al, 2003[170]	End-to-end localization accuracy	Hidden target (using stereo x-ray/DRR fusion)	0.41 ± 0.92 mm	Initial commissioning and annually thereafter
Verellen et al, 2003[170]	End-to-end localization accuracy	Hidden target (using implanted fiducials)	0.28 ± 0.36 mm	Initial commissioning and annually thereafter
Yu et al, 2004[254]	End-to-end localization accuracy	Dosimetric assessment of hidden target (using implanted fiducials)	0.68 ± 0.29 mm	Initial commissioning and annually thereafter
Sharpe et al, 2006[262]	CBCT mechanical stability	Constancy comparison to MV imaging isocenter (using hidden targets)	0.50±0.5mm	Baseline at commissioning and monthly thereafter
Galvin et al., 2008[263]	Overall positioning accuracy, including image registration	Winston-Lutz test modified to make use of the in-room	<=2mm for multiple couch angles	Initial commissioning and monthly thereafter

	(frame-based systems)	imaging systems		
Palta et al, 2008[242]	MLC accuracy	Light field, radiographic film, or EPID	<0.5mm (especially for IMRT delivery)	Annually
Solberg et al, 2008[264]	End-to-end localization accuracy	Hidden target in anthropomorphic phantom	1.10 ± 0.42 mm	Initial commissioning and annually thereafter
Jiang et al, 2008[265]	Respiratory motion tracking and gating in 4D CT	Phantoms with cyclical motion	N/A	N/A
Bissonnette et al, 2008[266]	CBCT geometric accuracy	Portal image vs. CBCT image isocenter coïncidence	±2mm	daily

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