

Stereotactic body radiation therapy: The report of AAPM Task Group 101

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Task Group 101 of the AAPM has prepared this report for medical physicists, clinicians, and therapists in order to outline the 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 a 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. © 2010 American Association of Physicists in Medicine. [DOI: 10.1118/1.3438081]

Key words: stereotactic body radiation therapy, SBRT, BED, patient safety, 4DCT, immobilization, IGRT, hypofractionation

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IV.C. Imaging artifacts.....	4082	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. <i>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.</i>	
IV.D. Treatment planning.....	4082	In addition to these major features, there are other characteristics that distinguish SBRT from conventional radiation therapy (Table I). These include a general increase in the number of beams used for treatment, the frequent use of noncoplanar 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.	
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TABLE I. Comparison of typical characteristics of 3D/IMRT radiotherapy and SBRT.

Characteristic	3D/IMRT	SBRT
Dose/fraction	1.8–3 Gy	6–30 Gy
No. of 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	Multimodality: 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

comes of SBRT for both primary and metastatic diseases compare favorably to 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 the 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 antitumoral 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}

III. 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 as 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 in-

clude 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-institutional 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.

IV. 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.

IV.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 positron emission tomography (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}

¹⁸F-fluorodeoxyglucose (¹⁸FDG) PET greatly enhances the specificity and sensitivity in diagnosis and staging compared to CT.^{67,68} Combined PET-CT systems can reduce image registration/fusion uncertainties to less than 2 mm due to inherent coregistration, 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 noncoplanar 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 at risk should be included and covered by the selected scan length so they can be considered by the treatment planning system (TPS) and evaluated with dose-volume histograms.⁷² Scan parameters such as the slice thickness, interslice 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}

IV.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 Planning target volumes (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} Multislice 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 [gross tumor volume/clinical target volume (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, 4DCT used in conjunction with maximum-intensity projection,^{95,96} minimum-intensity projection,⁹⁷ and respiration-correlated PET-CT.⁷⁹

IV.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 Jara⁹⁹ have described some general clinical guidelines for motion control in body MR imaging. 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 a 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.

IV.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 GTV, CTV, PTV, and 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 in CTV size and position due to respiratory motion or organ filling is generally accounted for by an internal margin added to the CTV, resulting in the internal target volume (ITV).¹¹³ The magnitude of this margin depends on whether motion compensation is employed during delivery. The PTV addresses all the possible geometrical variations by adding a variable margin for setup uncertainties, machine tolerances, and intratreatment 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 affect the accuracy of traditional margin recipes,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.

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

Dose prescriptions in SBRT are often specified at low isodoses (e.g., 80% isodose) 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 fall-off outside of the targeted volume and help spare nearby organs at risk. This practice increases dose heterogeneity 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 radioresistant hypoxic cells that might be more likely located there.¹²⁰ While the locations of hypoxic subregions 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 nonoverlapping 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}

IV.D.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 five to eight coplanar or noncoplanar 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 isotropic 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 11 posterior and posterior-oblique beams equally spaced 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

IV.D.3. Calculation grid size

The calculation grid resolution used in the 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 $\pm 5\%$ for an isotropic grid resolution of 4 mm.¹³⁴ Chung *et al.*¹³⁵ found 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 4 mm grids. Their conclusion is that 2 mm grids are required for IMRT procedures, especially in high-dose gradient areas.

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.

TABLE II. Summary of normalized tissue doses estimated using an α/β -ratio of 10 (late complications) and 3 Gy (early complications) for various SBRT fractionation schemes used in NSCLC.

Total physical dose (Gy)	Reference	NTD ₁₀ (Gy)	Log ₁₀ cell kill	Estimated 30-mo. local progression-free survival ^a	NTD ₃ (Gy)
30 × 2 = 60 ^b in 6 weeks	Estimated from Martel, 1999; ^c Fowler 2004 ^d	65	9.9	17.7% ^b with repopulation	60
35 × 2 = 70 ^b in 7 weeks	Estimated from Martel, 1999; ^c Fowler 2004 ^d	72	10.9	28.4% ^b with repopulation	70
4 × 12 = 48	Nagata, 2002 ^e	83	12.6	78.9% no repopulation	144
3 × 15 = 45	Nyman, 2006 ^f	94	14.2	90.8% no repopulation	162
5 × 12 = 60	Hodge, 2006 ^g	110	16.7	97.1% no repopulation	180
3 × 20 = 60	McGarry, 2005; ^h Timmerman 2003 ⁱ	150	22.7	>99% no repopulation	276
3 × 22 = 66	McGarry, 2005; ^h Timmerman 2003 ⁱ	176	26.7	>99% no repopulation	330

^aProgression-free survival at 30 months has been estimated using the following dose response model: $LPF_{30\text{m}} = 1 / (1 + (NTD_{10}^{50} / NTD_{10})^{4\gamma_{50}})$ using the following parameter values: $NTD_{10}^{50} = 84$ Gy; $\gamma_{50} = 1.5$ (cf. Ref. 143) when repopulation is included and $NTD_{10}^{50} = 70$ Gy; $\gamma_{50} = 1.94$ (cf. Ref. 120) when repopulation is not included.

^bThe progression-free survival of patients with NSCLC at 30 months was estimated from Martel *et al.* (Ref. 143) for the schedules marked with “b” and from Fowler *et al.* (Ref. 120) when rapid proliferation can be neglected.

^cReference 143.

^dReference 120.

^eReference 37.

^fReference 255.

^gReference 256.

^hReference 49.

ⁱReference 32.

IV.D.4. Bioeffect-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 a 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 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 a 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 on which fractionation schedule is employed (cf. Refs. 120 and 142 and Ref. 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 equieffective doses delivered at the standard dose per fraction of 2 Gy, generating numbers that can be more

easily compared to the dose levels of standard treatment schedules. Table II 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 “b” and from Fowler *et al.*¹²⁰ when rapid proliferation can be neglected.

The comparisons in Table II 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}

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

Table III summarizes tolerance doses from the University of Texas Southwestern⁸ 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.²⁶⁶ 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 follow-up for SBRT, it should be recognized that the data in both Table III 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 I protocols, critical organ tolerance doses based on the SBRT experience in the evolving peer-reviewed literature must be respected.

IV.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 to PTV or a conformity index 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, and
- Dose to organs at risk (dose to 1% and 5% volumes and mean doses).

V. 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 in 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 (Ref. 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

TABLE III. Summary of suggested dose constraints for various critical organs. Note that for serial tissues, the volume-dose constraints are given in terms of the critical maximum tissue volume that should receive a dose equal or greater than the indicated threshold dose for the given number of fractions used. For parallel tissue, the volume-dose constraints are based on a critical minimum volume of tissue that should receive a dose equal to or less than the indicated threshold dose for the given number of fractions used.

Serial tissue	Max critical volume above threshold	One fraction		Three fractions		Five fractions		End point (≥Grade3)
		Threshold dose (Gy)	Max point dose (Gy) ^a	Threshold dose (Gy)	Max point dose (Gy) ^a	Threshold dose (Gy)	Max point dose (Gy) ^a	
Optic pathway	<0.2 cc	8	10	15.3 (5.1 Gy/fx)	17.4 (5.8 Gy/fx)	23 (4.6 Gy/fx)	25 (5 Gy/fx)	Neuritis Hearing loss
Cochlea			9		17.1 (5.7 Gy/fx)		25 (5 Gy/fx)	Cranial neuropathy
Brainstem (not medulla)	<0.5 cc	10	15	18 (6 Gy/fx)	23.1 (7.7 Gy/fx)	23 (4.6 Gy/fx)	31 (6.2 Gy/fx)	Myelitis
Spinal cord and medulla	<0.35 cc	10	14	18 (6 Gy/fx)	21.9 (7.3 Gy/fx)	23 (4.6 Gy/fx)	30 (6 Gy/fx)	
Spinal cord subvolume (5–6 mm above and below level treated per Ryu)	<1.2 cc	7		12.3 (4.1 Gy/fx)		14.5 (2.9 Gy/fx)		
	<10% of subvolume	10	14	18 (6 Gy/fx)	21.9 (7.3 Gy/fx)	23 (4.6 Gy/fx)	30 (6 Gy/fx)	Myelitis
Cauda equina	<5 cc	14	16	21.9 (7.3 Gy/fx)	24 (8 Gy/fx)	30 (6 Gy/fx)	32 (6.4 Gy/fx)	Neuritis
Sacral plexus	<5 cc	14.4	16	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	30 (6 Gy/fx)	32 (6.4 Gy/fx)	Neuropathy
Esophagus ^b	<5 cc	11.9	15.4	17.7 (5.9 Gy/fx)	25.2 (8.4 Gy/fx)	19.5 (3.9 Gy/fx)	35 (7 Gy/fx)	Stenosis/fistula
Brachial plexus	<3 cc	14	17.5	20.4 (6.8 Gy/fx)	24 (8 Gy/fx)	27 (5.4 Gy/fx)	30.5 (6.1 Gy/fx)	Neuropathy
Heart/pericardium	<15 cc	16	22	24 (8 Gy/fx)	30 (10 Gy/fx)	32 (6.4 Gy/fx)	38 (7.6 Gy/fx)	Pericarditis
Great vessels	<10 cc	31	37	39 (13 Gy/fx)	45 (15 Gy/fx)	47 (9.4 Gy/fx)	53 (10.6 Gy/fx)	Aneurysm
Trachea and large bronchus ^b	<4 cc	10.5	20.2	15 (5 Gy/fx)	30 (10 Gy/fx)	16.5 (3.3 Gy/fx)	40 (8 Gy/fx)	Stenosis/fistula Stenosis with atelectasis
Bronchus-smaller airways	<0.5 cc	12.4	13.3	18.9 (6.3 Gy/fx)	23.1 (7.7 Gy/fx)	21 (4.2 Gy/fx)	33 (6.6 Gy/fx)	Pain or fracture
Rib	<1 cc	22	30	28.8 (9.6 Gy/fx)	36.9 (12.3 Gy/fx)	35 (7 Gy/fx)	43 (8.6 Gy/fx)	
	<30 cc			30.0 (10.0 Gy/fx)				
Skin	<10 cc	23	26	30 (10 Gy/fx)	33 (11 Gy/fx)	36.5 (7.3 Gy/fx)	39.5 (7.9 Gy/fx)	Ulceration
Stomach	<10 cc	11.2	12.4	16.5 (5.5 Gy/fx)	22.2 (7.4 Gy/fx)	18 (3.6 Gy/fx)	32 (6.4 Gy/fx)	Ulceration/fistula
Duodenum ^b	<5 cc	11.2	12.4	16.5 (5.5 Gy/fx)	22.2 (7.4 Gy/fx)	18 (3.6 Gy/fx)	32 (6.4 Gy/fx)	Ulceration
	<10 cc	9		11.4 (3.8 Gy/fx)		12.5 (2.5 Gy/fx)		
Jejunum/ileum ^b	<5 cc	11.9	15.4	17.7 (5.9 Gy/fx)	25.2 (8.4 Gy/fx)	19.5 (3.9 Gy/fx)	35 (7 Gy/fx)	Enteritis/ obstruction
Colon ^b	<20 cc	14.3	18.4	24 (8 Gy/fx)	28.2 (9.4 Gy/fx)	25 (5 Gy/fx)	38 (7.6 Gy/fx)	Colitis/fistula
Rectum ^b	<20 cc	14.3	18.4	24 (8 Gy/fx)	28.2 (9.4 Gy/fx)	25 (5 Gy/fx)	38 (7.6 Gy/fx)	Proctitis/fistula
Bladder wall	<15 cc	11.4	18.4	16.8 (5.6 Gy/fx)	28.2 (9.4 Gy/fx)	18.3 (3.65 Gy/fx)	38 (7.6 Gy/fx)	Cystitis/fistula
Penile bulb	<3 cc	14	34	21.9 (7.3 Gy/fx)	42 (14 Gy/fx)	30 (6 Gy/fx)	50 (10 Gy/fx)	Impotence
Femoral heads (right and left)	<10 cc	14		21.9 (7.3 Gy/fx)		30 (6 Gy/fx)		Necrosis
Renal hilum/vascular trunk	<2/3 volume	10.6	18.6 (6.2 Gy/fx)			23 (4.6 Gy/fx)		Malignant hypertension

TABLE III. (Continued.)

Serial tissue	Max critical volume above threshold	One fraction		Three fractions		Five fractions		End point (\geq Grade3)
		Threshold dose (Gy)	Max point dose (Gy) ^a	Threshold dose (Gy)	Max point dose (Gy) ^a	Threshold dose (Gy)	Max point dose (Gy) ^a	
Parallel tissue	Minimum critical volume below threshold	One fraction	One fraction	Three fractions	Three fractions	Five fractions	Five fractions	End point (\geq Grade 3)
Lung (right and left)	1500 cc	Threshold dose (Gy)	Max point dose (Gy) ^a	Threshold dose (Gy)	Max point dose (Gy) ^a	Threshold dose (Gy)	Max point dose (Gy) ^a	End point (\geq Grade 3)
Lung (right and left)	1000 cc	7	NA-Parallel tissue	11.6 (2.9 Gy/tx)	NA-Parallel tissue	12.5 (2.5 Gy/tx)	NA-Parallel tissue	Basic lung function
Liver	700 cc	7.4	NA-Parallel tissue	12.4 (3.1 Gy/tx)	NA-Parallel tissue	13.5 (2.7 Gy/tx)	NA-Parallel tissue	Pneumonitis
Renal cortex (right and left)	200 cc	9.1	NA-Parallel tissue	19.2 (4.8 Gy/tx)	NA-Parallel tissue	21 (4.2 Gy/tx)	NA-Parallel tissue	Basic liver function
		8.4	NA-Parallel tissue	16 (4 Gy/tx)	NA-Parallel tissue	17.5 (3.5 Gy/tx)	NA-Parallel tissue	Basic renal function

^aPoint defined as 0.035 cc or less.

^bAvoid circumferential irradiation.

TABLE IV. Achievable accuracies reported in the literature categorized by body site and immobilization/repositioning device.

Author, year	Site	Immobilization/repositioning	Reported accuracy
Lax, 1994 ^a	Abdomen	Wood frame/stereotactic coordinates on box to skin marks	3.7 mm Lat, 5.7 mm Long
Hamilton, 1995 ^b	Spine	Screw fixation of spinous processes to box	2 mm
Murphy, 1997 ^c	Spine	Frameless/implanted fiducial markers with real-time imaging and tracking	1.6 mm radial
Lohr, 1999 ^d	Spine	Body cast with stereotactic coordinates	≤3.6 mm mean vector
Yenice, 2003 ^e	Spine	Custom stereotactic frame and in-room CT guidance	1.5 mm system accuracy, 2–3 mm positioning accuracy
Chang, 2004 ^f	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	5 mm
Nakagawa, 2000 ^g	Thoracic	MVCT on linac	Not reported
Wulf, 2000 ^h	Lung, liver	Elekta™ body frame	3.3mm lat, 4.4 mm long
Fuss, 2004 ⁱ	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 ^j	Liver	Leibinger body frame	1.8–4.4 mm
Nagata, 2002 ^k	Lung	Elekta™ body frame	2 mm
Fukumoto, 2002 ^l	Lung	Elekta™ body frame	Not reported
Hara, 2002 ^m	Lung	Custom bed transferred to treatment unit after confirmatory scan	2 mm
Hof, 2003 ⁿ	Lung	Leibinger body frame	1.8–4 mm
Timmerman, 2003 ^o	Lung	Elekta™ body frame	Approx. 5 mm
Wang, 2006 ^p	Lung	Medical Intelligence body frame stereotactic coordinates/CT on rails	0.3 ± 1.8 mm AP, -1.8 ± 3.2 mm Lat, 1.5 ± 3.7 mm SI

^aReference 109.^bReference 257.^cReference 258.^dReference 252.^eReference 131.^fReference 42.^gReference 259.^hReference 260.ⁱReference 160.^jReference 28.^kReference 37.^lReference 34.^mReference 35.ⁿReference 31.^oReference 117.^pReference 88.

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.

V.A. 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 IV 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 define 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}

V.B. 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 (Ref. 164) or kV (Refs. 165–167) cone beam scanning, n MV fan beam using a tomographic acquisition,¹⁶⁸ and in-the-vault CT systems.^{131,163} Dual^{169,170} or multiple¹⁷¹ 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 intrafractional 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 an 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.^{180,181} Implanting fiducials percutaneously in to the lung poses a high risk of pneumothorax.^{182,183} Ultrasound (U.S.) 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 U.S. in SBRT for a variety of sites has been described by Meeks *et al.*,¹⁸⁴ Fuss,¹⁸⁵ and reviewed by Kuban and co-workers.¹⁸⁶

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.¹⁸⁷

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.

V.C. 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.”¹⁸⁸ They are mentioned here briefly for the sake of completeness.

V.C.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.^{189,190} 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.¹⁹¹

Cone beam imaging is increasingly being used for localization of lung tumors.^{192–194} Cone beam scans can have an acquisition time 60 s 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

ITV (Ref. 113) as obtained from 4DCT.^{195,196} 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 min) 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.¹⁹⁷ 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.

V.C.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 infrared cameras and video photogrammetry, are used to track the 3D coordinates of points on the patient’s skin in real time.

Infrared tracking systems use either active infrared light emitting diodes (IRLEDs) 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 infrared cameras are used to track the IRLEDs or reflectors in 3D during treatment.¹⁹⁸ Several optical tracking systems have been developed for stereotactic radiation therapy.^{111,199–204} 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.²⁰⁵ 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 2 mm in certain situations.^{206–208}

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.²⁰⁹ 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.

V.C.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.^{210–212} 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 nongated treatments; published duty cycles (ratio of beam on to total beam delivery time) range from 30% to 50%.^{213–215} 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.^{119,210,216}

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

- Determine if the patient's treatment would likely benefit from techniques such as respiratory gating;
- To quantify the residual motion expected during the respiratory gated delivery if such delivery is used;
- To design margins for treatment planning; and
- 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.

V.D. Delivery data reporting

It is important that a 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 resimulation 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.

VI. SPECIAL DOSIMETRY CONSIDERATIONS

VI.A. 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,²¹⁷ volume averaging,^{217–220} detector-interface artifacts, collimator effects,^{221–224} and detector position-orientation effects.^{94,220,225}

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 (or relative output factor), tissue-maximum ratio, and off-axis ratios. 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).^{218,226–228} MLC-shaped fields have more geometry and dosimetry uncertainties than those of the circular cones. Li *et al.*²²⁹ 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.*²³⁰ demonstrated a simple approach to unfolding the chamber size artifact from measured small-beam profiles using typical cylindrical chambers by deconvolving 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.

VI.B. 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 in the central axis dose beyond the cavity and potentially an underdosage of the tumor.^{231–233} Heterogeneity correction becomes extremely important in situations where the target is surrounded by low-density tis-

sue 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 precalculated 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.^{232,234} The Radio-logical 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.²³⁵

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.²³⁶ 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 (Ref. 236) 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) 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.²³⁷ For site-specific recommendations, the clinical user should refer to Report 85 of Task Group 65.²³⁶

VII. 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.) 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.

VII.A. 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.²³⁸

VII.A.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 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 85,²³⁶ the use of pencil-beam algorithms is not recommended for lung SBRT applications.

VII.A.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^{239,240} (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 h, respectively, vs 2.0 h 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 than that required for a standard 3D conformal procedure. The guidelines published by ASTRO/ACR (Ref. 238) includes provisions for SBRT personnel and clearly specifies 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.

VII.B. 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.^{241,242} 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),^{243,244} imaging equipment,^{243,245,246} treatment planning systems (TG-53),²⁴⁷ and IMRT.²⁴⁸ TG-142 provides an update to TG-40 and includes specific recommendations for SBRT.²⁴² In addition, a recent QA supplement published in the International Journal of Radiation Oncology Biology Physics²⁴⁹ 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 V).

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.*²⁵⁰ The integral use of on-board imaging in SBRT makes it critical to also verify the coincidence of the imaging isocenter.²⁵¹ Nonisocentric 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.^{252,253} 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

TABLE V. Summary of published QA recommendations for SBRT and SBRT-related techniques.

Source	Purpose	Proposed test	Reported achievable tolerance	Proposed frequency
Ryu <i>et al.</i> , 2001 ^a	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 <i>et al.</i> , 2001 ^a	Intrafraction targeting variability	Stereo x ray/DRR fusion	0.2 mm average, 1.5 mm maximum	Daily (during treatment)
Verellen <i>et al.</i> , 2003 ^b	End-to-end localization accuracy	Hidden target (using stereo x ray/DRR fusion)	0.41 ± 0.92 mm	Initial commissioning and annually thereafter
Verellen <i>et al.</i> , 2003 ^b	End-to-end localization accuracy	Hidden target (using implanted fiducials)	0.28 ± 0.36 mm	Initial commissioning and annually thereafter
Yu <i>et al.</i> , 2004 ^c	End-to-end localization accuracy	Dosimetric assessment of hidden target (using implanted fiducials)	0.68 ± 0.29 mm	Initial commissioning and annually thereafter
Sharpe <i>et al.</i> , 2006 ^d	CBCT mechanical stability	Constancy comparison to MV imaging isocenter (using hidden targets)	0.50 ± 0.5 mm	Baseline at commissioning and monthly thereafter
Galvin <i>et al.</i> , 2008 ^e	Overall positioning accuracy, including image registration (frame-based systems)	Winston–Lutz test modified to make use of the in-room imaging systems	≤ 2 mm for multiple couch angles	Initial commissioning and monthly thereafter
Palta <i>et al.</i> , 2008 ^f	MLC accuracy	Light field, radiographic film, or EPID	< 0.5 mm (especially for IMRT delivery)	Annually
Solberg <i>et al.</i> , 2008 ^g	End-to-end localization accuracy	Hidden target in anthropomorphic phantom	1.10 ± 0.42 mm	Initial commissioning and annually thereafter
Jiang <i>et al.</i> , 2008 ^h	Respiratory motion tracking and gating in 4D CT	Phantoms with cyclical motion	N/A	N/A
Bissonnette <i>et al.</i> , 2008 ⁱ	CBCT geometric accuracy	Portal image vs CBCT image isocenter coincidence	± 2 mm	daily

^aReference 159.^bReference 170.^cReference 253.^dReference 261.^eReference 262.^fReference 241.^gReference 263.^hReference 264.ⁱReference 265.

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 six 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.

VII.C. 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 intrafractional 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.

VII.D. 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.²⁵⁴

VIII. 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 bioeffect 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 therapy and chemotherapy 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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¹D. W. Andrews, C. B. Scott, P. W. Sperduto, A. E. Flanders, L. E. Gaspar,

- M. C. Schell, M. Werner-Wasik, W. Demas, J. Ryu, J. P. Bahary, L. Souhami, M. Rotman, M. P. Mehta, and W. J. Curran, Jr., "Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases: Phase III results of the RTOG 9508 randomised trial," *Lancet* **363**, 1665–1672 (2004).
- ²J. C. Flickinger, D. Kondziolka, A. Niranjan, and L. D. Lunsford, "Results of acoustic neuroma radiosurgery: An analysis of 5 years' experience using current methods," *J. Neurosurg.* **94**, 1–6 (2001).
- ³J. C. Flickinger *et al.*, "An analysis of the clinical radiobiology of arteriovenous malformation obliteration by radiosurgery," *Int. J. Radiat. Oncol., Biol., Phys.* **48**, 255 (2000).
- ⁴M. Izawa, M. Hayashi, K. Nakaya, H. Satoh, T. Ochiai, T. Hori, and K. Takakura, "Gamma knife radiosurgery for pituitary adenomas," *J. Neurosurg.* **93**, 19–22 (2000).
- ⁵S. L. Stafford, B. E. Pollock, R. L. Foote, M. J. Link, D. A. Gorman, P. J. Schomberg, and J. A. Leavitt, "Meningioma radiosurgery: Tumor control, outcomes, and complications among 190 consecutive patients," *Neurosurgery* **49**, 1029–1038 (2001).
- ⁶B. E. Pollock, L. K. Phuong, D. A. Gorman, R. L. Foote, and S. L. Stafford, "Stereotactic radiosurgery for idiopathic trigeminal neuralgia," *J. Neurosurg.* **97**, 347–353 (2002).
- ⁷R. F. Young, A. Shumway-Cook, S. S. Vermeulen, P. Grimm, J. Blasko, A. Posewitz, W. A. Burkhart, and R. C. Goiney, "Gamma knife radiosurgery as a lesioning technique in movement disorder surgery," *J. Neurosurg.* **89**, 183–193 (1998).
- ⁸R. D. Timmerman, "An overview of hypofractionation and introduction to this issue of seminars in radiation oncology," *Semin. Radiat. Oncol.* **18**, 215–222 (2008).
- ⁹I. S. Grills, V. S. Mangona, R. Welsh, G. Chmielewski, E. McInerney, S. Martin, J. Wloch, H. Ye, and L. L. Kestin, "Outcomes after stereotactic lung radiotherapy or wedge resection for stage I non-small-cell lung cancer," *J. Clin. Oncol.* **28**, 928–935 (2010).
- ¹⁰R. D. Timmerman, C. S. Bizakis, H. I. Pass, Y. Fong, D. E. Dupuy, L. A. Dawson, and D. Lu, "Local surgical, ablative, and radiation treatment of metastases," *Ca-Cancer J. Clin.* **59**, 145–170 (2009).
- ¹¹Y. Fong, A. M. Cohen, J. G. Fortner, W. E. Enker, A. D. Turnbull, D. G. Coit, A. M. Marrero, M. Prasad, L. H. Blumgart, and M. F. Brennan, "Liver resection for colorectal metastases," *J. Clin. Oncol.* **15**, 938–946 (1997).
- ¹²R. A. Patchell, P. A. Tibbs, J. W. Walsh, R. J. Dempsey, Y. Maruyama, R. J. Kryscio, W. R. Markesbery, J. S. Macdonald, and B. Young, "A randomized trial of surgery in the treatment of single metastases to the brain," *N. Engl. J. Med.* **322**, 494–500 (1990).
- ¹³K. E. Rusthoven, S. F. Hammerman, B. D. Kavanagh, M. J. Birtwhistle, M. Stares, and D. R. Camidge, "Is there a role for consolidative stereotactic body radiation therapy following first-line systemic therapy for metastatic lung cancer? A patterns-of-failure analysis," *Acta Oncol.* **48**, 578–583 (2009).
- ¹⁴S. Hellman and R. R. Weichselbaum, "Oligometastases," *J. Clin. Oncol.* **13**, 8–10 (1995).
- ¹⁵S. Hellman and R. R. Weichselbaum, "Importance of local control in an era of systemic therapy," *Nat. Reviews Clin. Oncol.* **2**, 60–61 (2005).
- ¹⁶M. T. Milano, A. W. Katz, A. G. Muhs, A. Philip, D. J. Buchholz, M. C. Schell, and P. Okunieff, "A prospective pilot study of curative-intent stereotactic body radiation therapy in patients with 5 or fewer oligometastatic lesions," *Cancer* **112**, 650–658 (2008).
- ¹⁷U. Pastorino, M. Buyse, G. Friedel, R. J. Ginsberg, P. Girard, P. Goldstraw, M. Johnston, P. McCormack, H. Pass, and J. B. Putnam, Jr., "Long-term results of lung metastasectomy: Prognostic analyses based on 5206 cases," *J. Thorac. Cardiovasc. Surg.* **113**, 37–49 (1997).
- ¹⁸P. J. Wersäll, H. Blomgren, I. Lax, K. M. Kalkner, C. Linder, G. Lundell, B. Nilsson, S. Nilsson, I. Naslund, P. Pisa, and C. Svedman, "Extracranial stereotactic radiotherapy for primary and metastatic renal cell carcinoma," *Radiother. Oncol.* **77**, 88–95 (2005).
- ¹⁹J. K. Salama, S. J. Chmura, N. Mehta, K. M. Yenice, W. M. Stadler, E. E. Vokes, D. J. Haraf, S. Hellman, and R. R. Weichselbaum, "An initial report of a radiation dose-escalation trial in patients with one to five sites of metastatic disease," *Clin. Cancer Res.* **14**, 5255–5259 (2008).
- ²⁰J. C. Yang, J. Abad, and R. Sherry, "Treatment of oligometastases after successful immunotherapy," *Semin. Radiat. Oncol.* **16**, 131–135 (2006).
- ²¹R. Simon and L. Norton, "The Norton-Simon hypothesis: Designing more effective and less toxic chemotherapeutic regimens," *Nat. Reviews Clin. Oncol.* **3**, 406–407 (2006).
- ²²J. E. Chang, D. Khuntia, H. I. Robins, and M. P. Mehta, "Radiotherapy and radiosensitizers in the treatment of glioblastoma multiforme," *Clin. Adv. Hematol. & Oncol.* **5**, 894–902 (2007).
- ²³C. Nieder, M. Adam, M. Molls, and A. L. Grosu, "Therapeutic options for recurrent high-grade glioma in adult patients: Recent advances," *Crit. Rev. Oncol. Hematol.* **60**, 181–193 (2006).
- ²⁴H. Joensuu, "Novel cancer therapies: More efficacy, less toxicity and improved organ preservation," *Ann. Med.* **32**, 31–33 (2000).
- ²⁵H. Joensuu and M. Tenhunen, "Physical and biological targeting of radiotherapy," *Acta Oncol.* **38**, 75–83 (1999).
- ²⁶H. Blomgren, I. Lax, I. Naslund, and R. Svanstrom, "Stereotactic high dose fraction radiation therapy of extracranial tumors using an accelerator. Clinical experience of the first thirty-one patients," *Acta Oncol.* **34**, 861–870 (1995).
- ²⁷K. K. Herfarth, J. Debus, F. Lohr, M. L. Bahner, P. Fritz, A. Hoss, W. Schlegel, and M. F. Wannemacher, "Extracranial stereotactic radiation therapy: Set-up accuracy of patients treated for liver metastases," *Int. J. Radiat. Oncol., Biol., Phys.* **46**, 329–335 (2000).
- ²⁸K. K. Herfarth, J. Debus, F. Lohr, M. L. Bahner, B. Rhein, P. Fritz, A. Hoss, W. Schlegel, and M. F. Wannemacher, "Stereotactic single-dose radiation therapy of liver tumors: Results of a phase I/II trial," *J. Clin. Oncol.* **19**, 164–170 (2001).
- ²⁹K. K. Herfarth, J. Debus, F. Lohr, M. L. Bahner, and M. Wannemacher, "Stereotactic irradiation of liver metastases," *Radiologe* **41**, 64–68 (2001).
- ³⁰K. K. Herfarth, J. Debus, and M. Wannemacher, "Stereotactic radiation therapy of liver metastases: Update of the initial phase-I/II trial," *Front. Radiat. Ther. Oncol.* **38**, 100–105 (2004).
- ³¹J. Wulf, U. Hadinger, U. Oppitz, W. Thiele, R. Ness-Dourdoumas, and M. Flentje, "Stereotactic radiotherapy of targets in the lung and liver," *Strahlenther. Onkol.* **177**, 645–655 (2001).
- ³²R. Timmerman, L. Papiez, R. McGarry, L. Likes, C. DesRosiers, S. Frost, and M. Williams, "Extracranial stereotactic radioablation: Results of a phase I study in medically inoperable stage I non-small cell lung cancer," *Chest* **124**, 1946–1955 (2003).
- ³³R. I. Whyte, R. Crownover, M. J. Murphy, D. P. Martin, T. W. Rice, M. M. DeCamp, Jr., R. Rodebaugh, M. S. Weinhaus, and Q. T. Le, "Stereotactic radiosurgery for lung tumors: Preliminary report of a phase I trial," *Ann. Thorac. Surg.* **75**, 1097–1101 (2003).
- ³⁴S. Fukumoto, H. Shirato, S. Shimzu, S. Ogura, R. Onimaru, K. Kitamura, K. Yamazaki, K. Miyasaka, M. Nishimura, and H. Dosaka-Akita, "Small-volume image-guided radiotherapy using hypofractionated, coplanar, and noncoplanar multiple fields for patients with inoperable stage I nonsmall cell lung carcinomas," *Cancer* **95**, 1546–1553 (2002).
- ³⁵R. Hara, J. Itami, T. Kondo, T. Aruga, Y. Abe, M. Ito, M. Fuse, D. Shinohara, T. Nagaoka, and T. Kobiki, "Stereotactic single high dose irradiation of lung tumors under respiratory gating," *Radiother. Oncol.* **63**, 159–163 (2002).
- ³⁶S. W. Lee, E. K. Choi, H. J. Park, S. D. Ahn, J. H. Kim, K. J. Kim, S. M. Yoon, Y. S. Kim, and B. Y. Yi, "Stereotactic body frame based fractionated radiosurgery on consecutive days for primary or metastatic tumors in the lung," *Lung Cancer* **40**, 309–315 (2003).
- ³⁷Y. Nagata, Y. Negoro, T. Aoki, T. Mizowaki, K. Takayama, M. Kokubo, N. Araki, M. Mitsumori, K. Sasai, Y. Shibamoto, S. Koga, S. Yano, and M. Hiraoka, "Clinical outcomes of 3D conformal hypofractionated single high-dose radiotherapy for one or two lung tumors using a stereotactic body frame," *Int. J. Radiat. Oncol., Biol., Phys.* **52**, 1041–1046 (2002).
- ³⁸H. Onishi *et al.*, "Stereotactic hypofractionated high-dose irradiation for stage I nonsmall cell lung carcinoma: Clinical outcomes in 245 subjects in a Japanese multiinstitutional study," *Cancer* **101**, 1623–1631 (2004).
- ³⁹M. Uematsu *et al.*, "Computed tomography (CT)-guided stereotactic radiation therapy (SRT) for stage I non-small cell lung cancer (NSCLC): 8-year results of 50 initial patients," *Int. J. Radiat. Oncol., Biol., Phys.* **57**, S281 (2003).
- ⁴⁰D. L. Benzil, M. Saboori, A. Y. Mogilner, R. Rocchio, and C. R. Moothy, "Safety and efficacy of stereotactic radiosurgery for tumors of the spine," *J. Neurosurg.* **101**, 413–418 (2004).
- ⁴¹M. H. Bilsky, Y. Yamada, K. M. Yenice, M. Lovelock, M. Hunt, P. H. Gutin, and S. A. Leibel, "Intensity-modulated stereotactic radiotherapy of paraspinal tumors: A preliminary report," *Neurosurgery* **54**(3), 823–830 (2004).
- ⁴²E. L. Chang, A. S. Shiu, M. F. Lii, L. D. Rhines, E. Mendel, A. Mahajan, J. S. Weinberg, L. A. Mathews, B. W. Brown, M. H. Maor, and J. D. Cox,

- "Phase I clinical evaluation of near-simultaneous computed tomographic image-guided stereotactic body radiotherapy for spinal metastases," *Int. J. Radiat. Oncol., Biol., Phys.* **59**, 1288–1294 (2004).
- ⁴³S. Ryu, F. F. Yin, J. Rock, J. Zhu, A. Chu, E. Kagan, L. Rogers, M. Ajlouni, M. Rosenblum, and J. H. Kim, "Image-guided and intensity-modulated radiosurgery for patients with spinal metastasis," *Cancer* **97**, 2013–2018 (2003).
- ⁴⁴S. Ryu, J. Rock, M. Rosenblum, and J. H. Kim, "Patterns of failure after single-dose radiosurgery for spinal metastasis," *J. Neurosurg.* **101**, 402–405 (2004).
- ⁴⁵J. Bradley, M. V. Graham, K. Winter, J. A. Purdy, R. Komaki, W. H. Roa, J. K. Ryu, W. Bosch, and B. Emami, "Toxicity and outcome results of RTOG 9311: A phase I-II dose-escalation study using three-dimensional conformal radiotherapy in patients with inoperable non-small-cell lung carcinoma," *Int. J. Radiat. Oncol., Biol., Phys.* **61**, 318–328 (2005).
- ⁴⁶P. C. Gerszten, S. A. Burton, and C. Ozhasoglu, "CyberKnife radiosurgery for spinal neoplasms," *Prog. Neurol. Surg.* **20**, 340–358 (2007).
- ⁴⁷P. C. Gerszten, S. A. Burton, C. Ozhasoglu, and W. C. Welch, "Radiosurgery for spinal metastases: Clinical experience in 500 cases from a single institution," *Spine* **32**, 193–199 (2007).
- ⁴⁸L. A. Dawson, D. Normolle, J. M. Balter, C. J. McGinn, T. S. Lawrence, and R. K. Ten Haken, "Analysis of radiation-induced liver disease using the Lyman NTCP model," *Int. J. Radiat. Oncol., Biol., Phys.* **53**, 810–821 (2002).
- ⁴⁹R. C. McGarry, L. Papiez, M. Williams, T. Whitford, and R. D. Timmerman, "Stereotactic body radiation therapy of early-stage non-small-cell lung carcinoma: Phase I study," *Int. J. Radiat. Oncol., Biol., Phys.* **63**, 1010–1015 (2005).
- ⁵⁰T. E. Scheffer, B. D. Kavanagh, R. D. Timmerman, H. R. Cardenes, A. Baron, and L. E. Gaspar, "A phase I trial of stereotactic body radiation therapy (SBRT) for liver metastases," *Int. J. Radiat. Oncol., Biol., Phys.* **62**, 1371–1378 (2005).
- ⁵¹G. R. Borst, M. Ishikawa, J. Nijkamp, M. Hauptmann, H. Shirato, R. Onimaru, M. M. van den Heuvel, J. Belderbos, J. V. Lebesque, and J. J. Sonke, "Radiation pneumonitis in patients treated for malignant pulmonary lesions with hypofractionated radiation therapy," *Radiother. Oncol.* **91**, 307–313 (2009).
- ⁵²M. Hoyer, H. Roed, L. Sengelov, A. Traberg, L. Ohlhuis, J. Pedersen, H. Nellesmann, A. Kiil Berthelsen, F. Eberholst, S. A. Engelholm, and H. von der Maase, "Phase-II study on stereotactic radiotherapy of locally advanced pancreatic carcinoma," *Radiother. Oncol.* **76**, 48–53 (2005).
- ⁵³M. Hoyer, H. Roed, A. Traberg Hansen, L. Ohlhuis, J. Petersen, H. Nellesmann, A. Kiil Berthelsen, C. Grau, S. Aage Engelholm, and H. Von der Maase, "Phase II study on stereotactic body radiotherapy of colorectal metastases," *Acta Oncol.* **45**, 823–830 (2006).
- ⁵⁴A. C. Koong, E. Christofferson, Q. T. Le, K. A. Goodman, A. Ho, T. Kuo, J. M. Ford, G. A. Fisher, R. Greco, J. Norton, and G. P. Yang, "Phase II study to assess the efficacy of conventionally fractionated radiotherapy followed by a stereotactic radiosurgery boost in patients with locally advanced pancreatic cancer," *Int. J. Radiat. Oncol., Biol., Phys.* **63**, 320–323 (2005).
- ⁵⁵H. U. Kauczor, C. P. Heussel, and M. Thelen, "Radiodiagnosis of the lung," *Radiology* **40**, 870–877 (2000).
- ⁵⁶R. Komaki, J. B. Putnam, Jr., G. Walsh, J. S. Lee, and J. D. Cox, "The management of superior sulcus tumors," *Semin Surg. Oncol.* **18**, 152–164 (2000).
- ⁵⁷I. R. Kamel and E. K. Fishman, "Recent advances in CT imaging of liver metastases," *Cancer J.* **10**, 104–120 (2004).
- ⁵⁸I. R. Kamel, E. Liapi, and E. K. Fishman, "Multidetector CT of hepatocellular carcinoma," *Best Pract. Res. Clin. Gastroenterol.* **19**, 63–89 (2005).
- ⁵⁹M. Debois, R. Oyen, F. Maes, G. Verswijvel, G. Gatti, H. Bosmans, M. Feron, E. Bellon, G. Kutcher, H. van Poppel, and L. Vanuytsel, "The contribution of magnetic resonance imaging to the three-dimensional treatment planning of localized prostate cancer," *Int. J. Radiat. Oncol., Biol., Phys.* **45**, 857–865 (1999).
- ⁶⁰C. Rasch, I. Barillot, P. Remeijer, A. Touw, M. van Herk, and J. V. Lebesque, "Definition of the prostate in CT and MRI: A multi-observer study," *Int. J. Radiat. Oncol., Biol., Phys.* **43**, 57–66 (1999).
- ⁶¹S. F. Tanner, D. J. Finnigan, V. S. Khoo, P. Mayles, D. P. Dearnaley, and M. O. Leach, "Radiotherapy planning of the pelvis using distortion corrected MR images: The removal of system distortions," *Phys. Med. Biol.* **45**, 2117–2132 (2000).
- ⁶²D. J. Husband, K. A. Grant, and C. S. Romaniuk, "MRI in the diagnosis and treatment of suspected malignant spinal cord compression," *Br. J. Radiol.* **74**, 15–23 (2001).
- ⁶³T. Mizowaki, N. Araki, Y. Nagata, Y. Negoro, T. Aoki, and M. Hiraoka, "The use of a permanent magnetic resonance imaging system for radiotherapy treatment planning of bone metastases," *Int. J. Radiat. Oncol., Biol., Phys.* **49**, 605–611 (2001).
- ⁶⁴W. R. Webb, C. Gatsonis, E. A. Zerhouni, R. T. Heelan, G. M. Glazer, I. R. Francis, and B. J. McNeil, "CT and MR imaging in staging non-small cell bronchogenic carcinoma: Report of the Radiologic Diagnostic Oncology Group," *Radiology* **178**, 705–713 (1991).
- ⁶⁵R. Komaki, C. F. Mountain, J. M. Holbert, A. S. Garden, R. Shallemberger, J. D. Cox, M. H. Maor, V. F. Guinee, and B. Samuels, "Superior sulcus tumors: Treatment selection and results for 85 patients without metastasis (Mo) at presentation," *Int. J. Radiat. Oncol., Biol., Phys.* **19**, 31–36 (1990).
- ⁶⁶P. Günther, J. P. Schenk, R. Wunsch, J. Troger, and K. L. Waag, "Abdominal tumours in children: 3-D visualisation and surgical planning," *Eur. J. Pediatr. Surg.* **14**, 316–321 (2004).
- ⁶⁷S. S. Gambhir, J. Czernin, J. Schwimmer, D. H. Silverman, R. E. Coleman, and M. E. Phelps, "A tabulated summary of the FDG PET literature," *J. Nucl. Med.* **42**, 1S–93S (2001).
- ⁶⁸N. C. Gupta, G. M. Graeber, W. J. Tamim, J. S. Rogers, L. Irisari, and H. A. Bishop, "Clinical utility of PET-FDG imaging in differentiation of benign from malignant adrenal masses in lung cancer," *Clin. Lung Cancer* **3**, 59–64 (2001).
- ⁶⁹D. Lardinois, W. Weder, T. F. Hany, E. M. Kamel, S. Korom, B. Seifert, G. K. von Schulthess, and H. C. Steinert, "Staging of non-small-cell lung cancer with integrated positron-emission tomography and computed tomography," *N. Engl. J. Med.* **348**, 2500–2507 (2003).
- ⁷⁰A. M. Gharib, D. Thomasson, and K. C. Li, "Molecular imaging of hepatocellular carcinoma," *Gastroenterology* **127**, S153–S158 (2004).
- ⁷¹W. Y. Lin, S. C. Tsai, and G. U. Hung, "Value of delayed 18F-FDG-PET imaging in the detection of hepatocellular carcinoma," *Nucl. Med. Commun.* **26**, 315–321 (2005).
- ⁷²B. A. Fraass and D. L. McShan, in *Radiation Therapy Physics*, edited by A. R. Smith (Springer-Verlag, Berlin, 1995), pp. 139–154.
- ⁷³D. G. Disler, D. S. Marr, and D. I. Rosenthal, "Accuracy of volume measurements of computed tomography and magnetic resonance imaging phantoms by three-dimensional reconstruction and preliminary clinical application," *Invest. Radiol.* **29**, 739–745 (1994).
- ⁷⁴A. Somigliana, G. Zonca, G. Loi, and A. E. Sichirolli, "How thick should CT/MR slices be to plan conformal radiotherapy? A study on the accuracy of three-dimensional volume reconstruction," *Tumori* **82**, 470–472 (1996).
- ⁷⁵H. T. Winer-Muram, S. G. Jennings, C. A. Meyer, Y. Liang, A. M. Aisen, R. D. Tarver, and R. C. McGarry, "Effect of varying CT section width on volumetric measurement of lung tumors and application of compensatory equations," *Radiology* **229**, 184–194 (2003).
- ⁷⁶Q. S. Chen, M. S. Weinhaus, F. C. Deibel, J. P. Ciezki, and R. M. Macklis, "Fluoroscopic study of tumor motion due to breathing: Facilitating precise radiation therapy for lung cancer patients," *Med. Phys.* **28**, 1850–1856 (2001).
- ⁷⁷Y. Seppenwoolde, H. Shirato, K. Kitamura, S. Shimizu, M. van Herk, J. V. Lebesque, and K. Miyasaka, "Precise and real-time measurement of 3D tumor motion in lung due to breathing and heartbeat, measured during radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **53**, 822–834 (2002).
- ⁷⁸C. W. Stevens, R. F. Munden, K. M. Forster, J. F. Kelly, Z. Liao, G. Starkschall, S. Tucker, and R. Komaki, "Respiratory-driven lung tumor motion is independent of tumor size, tumor location, and pulmonary function," *Int. J. Radiat. Oncol., Biol., Phys.* **51**, 62–68 (2001).
- ⁷⁹C. B. Caldwell, K. Mah, M. Skinner, and C. E. Danjoux, "Can PET provide the 3D extent of tumor motion for individualized internal target volumes? A phantom study of the limitations of CT and the promise of PET," *Int. J. Radiat. Oncol., Biol., Phys.* **55**, 1381–1393 (2003).
- ⁸⁰G. T. Chen, J. H. Kung, and K. P. Beaudette, "Artifacts in computed tomography scanning of moving objects," *Semin. Radiat. Oncol.* **14**, 19–26 (2004).
- ⁸¹F. J. Lagerwaard, J. R. van Sornsen de Koste, M. R. Nijssen-Visser, R. H. Schuchhard-Schipper, S. S. Oei, A. Munne, and S. Senan, "Multiple 'slow' CT scans for incorporating lung tumor mobility in radiotherapy planning," *Int. J. Radiat. Oncol., Biol., Phys.* **51**, 932–937 (2001).
- ⁸²K. Takayama, Y. Nagata, Y. Negoro, T. Mizowaki, T. Sakamoto, M. Saka-

- moto, T. Aoki, S. Yano, S. Koga, and M. Hiraoka, "Treatment planning of stereotactic radiotherapy for solitary lung tumor," *Int. J. Radiat. Oncol., Biol., Phys.* **61**, 1565–1571 (2005).
- ⁸³M. Uematsu, A. Shioda, K. Tahara, T. Fukui, F. Yamamoto, G. Tsumatori, Y. Ozeki, T. Aoki, M. Watanabe, and S. Kusano, "Focal, high dose, and fractionated modified stereotactic radiation therapy for lung carcinoma patients: A preliminary experience," *Cancer* **82**, 1062–1070 (1998).
- ⁸⁴G. S. Mageras and E. Yorke, "Deep inspiration breath hold and respiratory gating strategies for reducing organ motion in radiation treatment," *Semin. Radiat. Oncol.* **14**, 65–75 (2004).
- ⁸⁵E. A. Barnes, B. R. Murray, D. M. Robinson, L. J. Underwood, J. Hanson, and W. H. Roa, "Dosimetric evaluation of lung tumor immobilization using breath hold at deep inspiration," *Int. J. Radiat. Oncol., Biol., Phys.* **50**, 1091–1098 (2001).
- ⁸⁶J. Hanley, M. M. Debois, D. Mah, G. S. Mageras, A. Raben, K. Rosenzweig, B. Mychalczak, L. H. Schwartz, P. J. Gloeggler, W. Lutz, C. C. Ling, S. A. Leibel, Z. Fuks, and G. J. Kutcher, "Deep inspiration breath-hold technique for lung tumors: The potential value of target immobilization and reduced lung density in dose escalation," *Int. J. Radiat. Oncol., Biol., Phys.* **45**, 603–611 (1999).
- ⁸⁷H. Onishi, K. Kuriyama, T. Komiyama, S. Tanaka, J. Ueki, N. Sano, T. Araki, S. Ikenaga, Y. Tateda, and Y. Aikawa, "CT evaluation of patient deep inspiration self-breath-holding: How precisely can patients reproduce the tumor position in the absence of respiratory monitoring devices?," *Med. Phys.* **30**, 1183–1187 (2003).
- ⁸⁸L. Wang, S. Feigenberg, L. Chen, K. Pasklev, and C. C. Ma, "Benefit of three-dimensional image-guided stereotactic localization in the hypofractionated treatment of lung cancer," *Int. J. Radiat. Oncol., Biol., Phys.* **66**, 738–747 (2006).
- ⁸⁹R. C. Frazier, F. A. Vicini, M. B. Sharpe, D. Yan, J. Fayad, K. L. Baglan, L. L. Kestin, V. M. Remouchamps, A. A. Martinez, and J. W. Wong, "Impact of breathing motion on whole breast radiotherapy: A dosimetric analysis using active breathing control," *Int. J. Radiat. Oncol., Biol., Phys.* **58**, 1041–1047 (2004).
- ⁹⁰V. M. Remouchamps, N. Letts, F. A. Vicini, M. B. Sharpe, L. L. Kestin, P. Y. Chen, A. A. Martinez, and J. W. Wong, "Initial clinical experience with moderate deep-inspiration breath hold using an active breathing control device in the treatment of patients with left-sided breast cancer using external beam radiation therapy," *Int. J. Radiat. Oncol., Biol., Phys.* **56**, 704–715 (2003).
- ⁹¹V. M. Remouchamps, N. Letts, D. Yan, F. A. Vicini, M. Moreau, J. A. Zielinski, J. Liang, L. L. Kestin, A. A. Martinez, and J. W. Wong, "Three-dimensional evaluation of intra- and interfraction immobilization of lung and chest wall using active breathing control: A reproducibility study with breast cancer patients," *Int. J. Radiat. Oncol., Biol., Phys.* **57**, 968–978 (2003).
- ⁹²V. M. Remouchamps, F. A. Vicini, M. B. Sharpe, L. L. Kestin, A. A. Martinez, and J. W. Wong, "Significant reductions in heart and lung doses using deep inspiration breath hold with active breathing control and intensity-modulated radiation therapy for patients treated with locoregional breast irradiation," *Int. J. Radiat. Oncol., Biol., Phys.* **55**, 392–406 (2003).
- ⁹³J. W. Wong, M. B. Sharpe, and D. A. Jaffray, "The use of active breathing control (ABC) to minimize breathing motion during radiation therapy," *Int. J. Radiat. Oncol., Biol., Phys.* **39**, 164 (1997).
- ⁹⁴F. F. Yin, J. Zhu, H. Yan, H. Gaun, R. Hammoud, S. Ryu, and J. H. Kim, "Dosimetric characteristics of Novalis shaped beam surgery unit," *Med. Phys.* **29**, 1729–1738 (2002).
- ⁹⁵B. J. Slotman, F. J. Lagerwaard, and S. Senan, "4D imaging for target definition in stereotactic radiotherapy for lung cancer," *Acta Oncol.* **45**, 966–972 (2006).
- ⁹⁶R. W. Underberg, F. J. Lagerwaard, B. J. Slotman, J. P. Cuijpers, and S. Senan, "Use of maximum intensity projections (MIP) for target volume generation in 4DCT scans for lung cancer," *Int. J. Radiat. Oncol., Biol., Phys.* **63**, 253–260 (2005).
- ⁹⁷K. S. Cover, F. J. Lagerwaard, and S. Senan, "Color intensity projections: A rapid approach for evaluating four-dimensional CT scans in treatment planning," *Int. J. Radiat. Oncol., Biol., Phys.* **64**, 954–961 (2006).
- ⁹⁸J. H. Lewis and S. B. Jiang, "A theoretical model for respiratory motion artifacts in free-breathing CT scans," *Phys. Med. Biol.* **54**, 745–755 (2009).
- ⁹⁹M. A. Barish and H. Jara, "Motion artifact control in body MR imaging," *Magn. Reson Imaging Clin. N. Am.* **7**, 289–301 (1999).
- ¹⁰⁰R. T. Constable, "MR physics of body MR imaging," *Radiol. Clin. North Am.* **41**, 1–15 (2003).
- ¹⁰¹S. Eustace, R. Goldberg, D. Williamson, E. R. Melhem, O. Oladipo, E. K. Yucel, and H. Jara, "MR imaging of soft tissues adjacent to orthopaedic hardware: Techniques to minimize susceptibility artefact," *Clin. Radiol.* **52**, 589–594 (1997).
- ¹⁰²A. Guermazi, Y. Miaux, S. Zaim, C. G. Peterfy, D. White, and H. K. Genant, "Metallic artefacts in MR imaging: Effects of main field orientation and strength," *Clin. Radiol.* **58**, 322–328 (2003).
- ¹⁰³S. H. Kolind, A. L. MacKay, P. L. Munk, and Q. S. Xiang, "Quantitative evaluation of metal artifact reduction techniques," *J. Magn. Reson Imaging* **20**, 487–495 (2004).
- ¹⁰⁴S. A. Nehmeh, Y. E. Erdi, C. C. Ling, K. E. Rosenzweig, O. D. Squire, L. E. Braban, E. Ford, K. Sidhu, G. S. Mageras, S. M. Larson, and J. L. Humm, "Effect of respiratory gating on reducing lung motion artifacts in PET imaging of lung cancer," *Med. Phys.* **29**, 366–371 (2002).
- ¹⁰⁵S. A. Nehmeh, Y. E. Erdi, T. Pan, A. Pevsner, K. E. Rosenzweig, E. Yorke, G. S. Mageras, H. Schoder, P. Vernon, O. Squire, H. Mostafavi, S. M. Larson, and J. L. Humm, "Four-dimensional (4D) PET/CT imaging of the thorax," *Med. Phys.* **31**, 3179–3186 (2004).
- ¹⁰⁶S. A. Nehmeh, Y. E. Erdi, T. Pan, E. Yorke, G. S. Mageras, K. E. Rosenzweig, H. Schoder, H. Mostafavi, O. Squire, A. Pevsner, S. M. Larson, and J. L. Humm, "Quantitation of respiratory motion during 4D-PET/CT acquisition," *Med. Phys.* **31**, 1333–1338 (2004).
- ¹⁰⁷S. A. Nehmeh, Y. E. Erdi, K. E. Rosenzweig, H. Schoder, S. M. Larson, O. D. Squire, and J. L. Humm, "Reduction of respiratory motion artifacts in PET imaging of lung cancer by respiratory correlated dynamic PET: Methodology and comparison with respiratory gated PET," *J. Nucl. Med.* **44**, 1644–1648 (2003).
- ¹⁰⁸H. Cardenes, R. Timmerman, and L. Papiez, "Extracranial stereotactic radioablation: Review of biological basis, technique and preliminary clinical experience," *Oncologica* **25**, 193–199 (2002).
- ¹⁰⁹I. Lax, H. Blomgren, I. Naslund, and R. Svanstrom, "Stereotactic radiotherapy of malignancies in the abdomen. Methodological aspects," *Acta Oncol.* **33**, 677–683 (1994).
- ¹¹⁰L. Papiez, "Leaf sweep algorithm for immobile and moving target as an optimal control problem," *Math. Comput. Modell.* **37**, 735–745 (2003).
- ¹¹¹R. M. Cardinale, Q. Wu, S. H. Benedict, B. D. Kavanagh, E. Bump, and R. Mohan, "Determining the optimal block margin on the planning target volume for extracranial stereotactic radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **45**, 515–520 (1999).
- ¹¹²ICRU, "Prescribing, recording, and reporting photon beam therapy," *ICRU Report No. 50*, 1993.
- ¹¹³ICRU, "Prescribing, recording and reporting photon beam therapy (supplement to ICRU Report No. 50)," *ICRU Report No. 62*, 1999.
- ¹¹⁴I. S. Grills, D. L. Fitch, N. S. Goldstein, D. Yan, G. W. Chmielewski, R. J. Welsh, and L. L. Kestin, "Clinicopathologic analysis of microscopic extension in lung adenocarcinoma: Defining clinical target volume for radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **69**, 334–341 (2007).
- ¹¹⁵L. Papiez, V. Moskvina, and R. D. Timmerman, in *Stereotactic Body Radiation Therapy*, edited by B. D. Kavanagh and R. D. Timmerman (Lippincott Williams and Wilkins, Philadelphia, 2004), p. 160.
- ¹¹⁶U. Hadinger, W. Thiele, and J. Wulf, "Extracranial stereotactic radiotherapy: Evaluation of PTV coverage and dose conformity," *Z. Med. Phys.* **12**, 221–229 (2002).
- ¹¹⁷H. Hof, K. K. Herfarth, M. Munter, A. Hoess, J. Motsch, M. Wannenmacher, and J. J. Debus, "Stereotactic single-dose radiotherapy of stage I non-small-cell lung cancer (NSCLC)," *Int. J. Radiat. Oncol., Biol., Phys.* **56**, 335–341 (2003).
- ¹¹⁸J. Wulf, U. Hadinger, U. Oppitz, W. Thiele, G. Mueller, and M. Flentje, "Stereotactic radiotherapy for primary lung cancer and pulmonary metastases: A noninvasive treatment approach in medically inoperable patients," *Int. J. Radiat. Oncol., Biol., Phys.* **60**, 186–196 (2004).
- ¹¹⁹J. J. Sonke, M. Rossi, J. Wolthaus, M. van Herk, E. Damen, and J. Belderbos, "Frameless stereotactic body radiotherapy for lung cancer using four-dimensional cone beam CT guidance," *Int. J. Radiat. Oncol., Biol., Phys.* **74**, 567–574 (2009).
- ¹²⁰J. F. Fowler, W. A. Tome, J. D. Fenwick, and M. P. Mehta, "A challenge to traditional radiation oncology," *Int. J. Radiat. Oncol., Biol., Phys.* **60**, 1241–1256 (2004).
- ¹²¹Z. Lin, J. Mechalakos, S. Nehmeh, H. Schoder, N. Lee, J. Humm, and C. C. Ling, "The influence of changes in tumor hypoxia on dose-painting treatment plans based on 18F-FMISO positron emission tomography,"

- Int. J. Radiat. Oncol., Biol., Phys. **70**, 1219–1228 (2008).
- ¹²²R. McCammon, T. E. Schefter, L. E. Gaspar, R. Zaemisch, D. Gradvahl, and B. Kavanagh, "Observation of a dose-control relationship for lung and liver tumors after stereotactic body radiation therapy," Int. J. Radiat. Oncol., Biol., Phys. **73**, 112–118 (2009).
- ¹²³L. Papiez, R. Timmerman, C. DesRosiers, and M. Randall, "Extracranial stereotactic radioablation: Physical principles," Acta Oncol. **42**, 882–894 (2003).
- ¹²⁴Q. J. Wu, Z. Wang, J. P. Kirkpatrick, Z. Chang, J. J. Meyer, M. Lu, C. Huntzinger, and F. F. Yin, "Impact of collimator leaf width and treatment technique on stereotactic radiosurgery and radiotherapy plans for intra- and extracranial lesions," Radiat. Oncol. **4** (2009).
- ¹²⁵M. Ding, F. Newman, C. Chen, K. Stuhr, and L. E. Gaspar, "Dosimetric comparison between 3DCRT and IMRT using different multileaf collimators in the treatment of brain tumors," Med. Dosim. **34**, 1–8 (2009).
- ¹²⁶J. Y. Jin, F. F. Yin, S. Ryu, M. Ajlouni, and J. H. Kim, "Dosimetric study using different leaf-width MLCs for treatment planning of dynamic conformal arcs and intensity-modulated radiosurgery," Med. Phys. **32**, 405–411 (2005).
- ¹²⁷J. E. Monk, J. R. Perks, D. Doughty, and P. N. Plowman, "Comparison of a micro-multileaf collimator with a 5-mm-leaf-width collimator for intracranial stereotactic radiotherapy," Int. J. Radiat. Oncol., Biol., Phys. **57**, 1443–1449 (2003).
- ¹²⁸L. Papiez, M. Langer, and X. Lu, "On the isotropic distribution of beam directions," Math. Models Meth. Appl. Sci. **10**, 991–1000 (2000).
- ¹²⁹H. Blomgren *et al.*, "Radiosurgery for tumors in the body: Clinical experience using a new method," J Radiosurg **1**, 63–74 (1998).
- ¹³⁰M. M. Matuszak, D. Yan, I. Grills and A. Martinez, "Clinical applications of volumetric modulated arc therapy," Int. J. Radiat. Oncol., Biol., Phys. **77**, 608–616.
- ¹³¹K. M. Yenice, D. M. Lovelock, M. A. Hunt, W. R. Lutz, N. Fournier-Bidoz, C. H. Hua, J. Yamada, M. Bilsky, H. Lee, K. Pfaff, S. V. Spirou, and H. I. Amols, "CT image-guided intensity-modulated therapy for paraspinal tumors using stereotactic immobilization," Int. J. Radiat. Oncol., Biol., Phys. **55**, 583–593 (2003).
- ¹³²K. Yenice, "Advanced treatment techniques II," in *A Practical Guide to Intensity-Modulated Radiation Therapy* (Medical Physics Publishing, Madison, 1993), p. 450.
- ¹³³J. F. Dempsey, H. E. Romeijn, J. G. Li, D. A. Low, and J. R. Palta, "A Fourier analysis of the dose grid resolution required for accurate IMRT fluence map optimization," Med. Phys. **32**, 380–388 (2005).
- ¹³⁴J. L. Bedford, P. J. Childs, V. Nordmark Hansen, M. A. Mosleh-Shirazi, F. Verhaegen, and A. P. Warrington, "Commissioning and quality assurance of the Pinnacle(3) radiotherapy treatment planning system for external beam photons," Br. J. Radiol. **76**, 163–176 (2003).
- ¹³⁵H. Chung, H. Jin, J. Palta, T. S. Suh, and S. Kim, "Dose variations with varying calculation grid size in head and neck IMRT," Phys. Med. Biol. **51**, 4841–4856 (2006).
- ¹³⁶B. G. Douglas and J. F. Fowler, "The effect of multiple small doses of x rays on skin reactions in the mouse and a basic interpretation," Radiat. Res. **66**, 401–426 (1976).
- ¹³⁷J. V. Lebesque and R. B. Keus, "The simultaneous boost technique: The concept of relative normalized total dose," Radiother. Oncol. **22**, 45–55 (1991).
- ¹³⁸H. R. Withers, H. D. Thames, Jr., and L. J. Peters, "A new isoeffect curve for change in dose per fraction," Radiother. Oncol. **1**, 187–191 (1983).
- ¹³⁹A. Niemierko, "Reporting and analyzing dose distributions: A concept of equivalent uniform dose," Med. Phys. **24**, 103–110 (1997).
- ¹⁴⁰B. D. Kavanagh, R. D. Timmerman, S. H. Benedict, Q. Wu, T. E. Schefter, K. Stuhr, S. McCourt, F. Newman, R. M. Cardinale, and L. F. Gaspar, "How should we describe the radiobiologic effect of extracranial stereotactic radiosurgery: Equivalent uniform dose or tumor control probability?," Med. Phys. **30**, 321–324 (2003).
- ¹⁴¹H. Suit, S. Skates, A. Taghian, P. Okunieff, and J. T. Efrid, "Clinical implications of heterogeneity of tumor response to radiation therapy," Radiother. Oncol. **25**, 251–260 (1992).
- ¹⁴²W. A. Tome, J. D. Fenwick, and M. P. Mehta, "How can tumor effects and normal tissue effects be balanced in stereotactic body radiotherapy?," Radiosurgery **6**, 86–97 (2005).
- ¹⁴³M. K. Martel, R. K. Ten Haken, M. B. Hazuka, M. L. Kessler, M. Strawderman, A. T. Turrisi, T. S. Lawrence, B. A. Fraass, and A. S. Lichter, "Estimation of tumor control probability model parameters from 3-D dose distributions of non-small cell lung cancer patients," Lung Cancer **24**, 31–37 (1999).
- ¹⁴⁴M. Guckenberger, J. Wulf, G. Mueller, T. Krieger, K. Baier, M. Gabor, A. Richter, J. Wilbert, and M. Flentje, "Dose-response relationship for image-guided stereotactic body radiotherapy of pulmonary tumors: Relevance of 4D dose calculation," Int. J. Radiat. Oncol., Biol., Phys. **74**, 47–54 (2009).
- ¹⁴⁵R. Onimaru, M. Fujino, K. Yamazaki, Y. Onodera, H. Taguchi, N. Katoh, F. Hommura, S. Oizumi, M. Nishimura, and H. Shirato, "Steep dose-response relationship for stage I non-small-cell lung cancer using hypofractionated high-dose irradiation by real-time tumor-tracking radiotherapy," Int. J. Radiat. Oncol., Biol., Phys. **70**, 374–381 (2008).
- ¹⁴⁶H. Onishi *et al.*, "Hypofractionated stereotactic radiotherapy (HypoFX-SRT) for stage I non-small cell lung cancer: Updated results of 257 patients in a Japanese multi-institutional study," J. Thorac. Oncol. **2**, S94–S100 (2007).
- ¹⁴⁷J. P. Kirkpatrick, J. J. Meyer, and L. B. Marks, "The linear-quadratic model is inappropriate to model high dose per fraction effects in radio-surgery," Semin. Radiat. Oncol. **18**, 240–243 (2008).
- ¹⁴⁸D. Lea and D. Catcheside, "The mechanism of induction by radiation of chromosome aberrations in *tradesantia*," Genetics **44**, 216–245 (1942).
- ¹⁴⁹C. Park, L. Papiez, S. Zhang, M. Story, and R. D. Timmerman, "Universal survival curve and single fraction equivalent dose: Useful tools in understanding potency of ablative radiotherapy," Int. J. Radiat. Oncol., Biol., Phys. **70**, 847–852 (2008).
- ¹⁵⁰B. D. Kavanagh and F. Newman, "Toward a unified survival curve: In regard to Park *et al.* [Int. J. Radiat. Oncol., Biol., Phys. **70**, 847–852 (2008) and Krueger *et al.*, Int. J. Radiat. Oncol., Biol., Phys. **69**, 1262–1271 (2007)]," Int. J. Radiat. Oncol., Biol., Phys. **71**, 958–959 (2008).
- ¹⁵¹N. E. Dunlap, J. Cai, G. B. Biedermann, W. Yang, S. H. Benedict, K. Sheng, T. E. Schefter, B. D. Kavanagh and J. M. Lerner, "Chest wall volume receiving >30 Gy predicts risk of severe pain and/or rib fracture after lung stereotactic body radiotherapy," Int. J. Radiat. Oncol., Biol., Phys. **76**, 796–801 (2009).
- ¹⁵²R. Timmerman, R. McGarry, C. Yiannoutsos, L. Papiez, K. Tudor, J. DeLuca, M. Ewing, R. Abdulrahman, C. DesRosiers, M. Williams, and J. Fletcher, "Excessive toxicity when treating central tumors in a phase II study of stereotactic body radiation therapy for medically inoperable early-stage lung cancer," J. Clin. Oncol. **24**, 4833–4839 (2006).
- ¹⁵³R. D. Timmerman, B. D. Kavanagh, L. C. Cho, L. Papiez, and L. Xing, "Stereotactic body radiation therapy in multiple organ sites," J. Clin. Oncol. **25**, 947–952 (2007).
- ¹⁵⁴J. D. Murphy, S. Dieterich, D. T. Chang, and A. C. Koong, "duodenal toxicity in single-fraction stereotactic body radiotherapy," Int. J. Radiat. Oncol., Biol., Phys. **75**, S29–S30 (2009).
- ¹⁵⁵L. J. Hazard, B. Wang, T. B. Skidmore, S. S. Chern, B. J. Salter, R. L. Jensen, and D. C. Shrieve, "Conformity of LINAC-based stereotactic radiosurgery using dynamic conformal arcs and micro-multileaf collimator," Int. J. Radiat. Oncol., Biol., Phys. **73**, 562–570 (2009).
- ¹⁵⁶F. F. Yin, S. Ryu, M. Ajlouni, J. Zhu, H. Yan, H. Guan, K. Faber, J. Rock, M. Abdalhak, L. Rogers, M. Rosenblum, and J. H. Kim, "A technique of intensity-modulated radiosurgery (IMRS) for spinal tumors," Med. Phys. **29**, 2815–2822 (2002).
- ¹⁵⁷M. Guckenberger, J. Meyer, J. Wilbert, K. Baier, O. Sauer, and M. Flentje, "Precision of image-guided radiotherapy (IGRT) in six degrees of freedom and limitations in clinical practice," Strahlenther. Onkol. **183**, 307–313 (2007).
- ¹⁵⁸G. Soete, D. Verellen, K. Tournel, and G. Storme, "Setup accuracy of stereoscopic x-ray positioning with automated correction for rotational errors in patients treated with conformal arc radiotherapy for prostate cancer," Radiother. Oncol. **80**, 371–373 (2006).
- ¹⁵⁹S. I. Ryu, S. D. Chang, D. H. Kim, M. J. Murphy, Q. T. Le, D. P. Martin, and J. R. Adler, Jr., "Image-guided hypo-fractionated stereotactic radio-surgery to spinal lesions," Neurosurgery **49**, 838–846 (2001).
- ¹⁶⁰M. Fuss, B. J. Salter, P. Rassiah, D. Cheek, S. X. Cavanaugh, and T. S. Herman, "Repositioning accuracy of a commercially available double-vacuum whole body immobilization system for stereotactic body radiation therapy," Technol. Cancer Res. Treat. **3**, 59–67 (2004).
- ¹⁶¹L. Wang, R. Jacob, L. Chen, C. Ma, B. Movsas, S. Feigenberg, and A. Kanski, "Stereotactic IMRT for prostate cancer: Setup accuracy of a new stereotactic body localization system," J. Appl. Clin. Med. Phys. **5**, 18–28 (2004).
- ¹⁶²D. M. Lovelock, C. Hua, P. Wang, M. Hunt, N. Fournier-Bidoz, K. Yenice, S. Toner, W. Lutz, H. Amols, M. Bilsky, Z. Fuks, and Y. Yamada,

- "Accurate setup of paraspinal patients using a noninvasive patient immobilization cradle and portal imaging," *Med. Phys.* **32**, 2606–2614 (2005).
- ¹⁶³A. S. Shiu, E. L. Chang, J. S. Ye, M. Lii, L. D. Rhines, E. Mendel, J. Weinberg, S. Singh, M. H. Maor, R. Mohan, and J. D. Cox, "Near simultaneous computed tomography image-guided stereotactic spinal radiotherapy: An emerging paradigm for achieving true stereotaxy," *Int. J. Radiat. Oncol., Biol., Phys.* **57**, 605–613 (2003).
- ¹⁶⁴J. Pouliot, A. Bani-Hashemi, J. Chen, M. Svatos, F. Ghelmsarai, M. Mitschke, M. Aubin, P. Xia, O. Morin, K. Bucci, M. Roach III, P. Hernandez, Z. Zheng, D. Hristov, and L. Verhey, "Low-dose megavoltage cone-beam CT for radiation therapy," *Int. J. Radiat. Oncol., Biol., Phys.* **61**, 552–560 (2005).
- ¹⁶⁵D. A. Jaffray, "Emergent technologies for 3-dimensional image-guided radiation delivery," *Semin. Radiat. Oncol.* **15**, 208–216 (2005).
- ¹⁶⁶D. A. Jaffray, "Kilovoltage volumetric imaging in the treatment room," *Front. Radiat. Ther. Oncol.* **40**, 116–131 (2007).
- ¹⁶⁷D. A. Jaffray, J. H. Siewerdsen, J. W. Wong, and A. A. Martinez, "Flat-panel cone-beam computed tomography for image-guided radiation therapy," *Int. J. Radiat. Oncol., Biol., Phys.* **53**, 1337–1349 (2002).
- ¹⁶⁸T. R. Mackie *et al.*, "Image guidance for precise conformal radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **56**, 89–105 (2003).
- ¹⁶⁹S. D. Chang, W. Main, D. P. Martin, I. C. Gibbs, and M. P. Heilbrun, "An analysis of the accuracy of the CyberKnife: A robotic frameless stereotactic radiosurgical system," *Neurosurgery* **52**, 140–147 (2003).
- ¹⁷⁰D. Verellen, G. Soete, N. Linthout, S. Van Acker, P. De Roover, V. Vinh-Hung, J. Van de Steene, and G. Storme, "Quality assurance of a system for improved target localization and patient set-up that combines real-time infrared tracking and stereoscopic X-ray imaging," *Radiother. Oncol.* **67**, 129–141 (2003).
- ¹⁷¹H. Shirato, S. Shimizu, T. Kunieda, K. Kitamura, M. van Herk, K. Kagei, T. Nishioka, S. Hashimoto, K. Fujita, H. Aoyama, K. Tsuchiya, K. Kudo, and K. Miyasaka, "Physical aspects of a real-time tumor-tracking system for gated radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **48**, 1187–1195 (2000).
- ¹⁷²J. M. Balter, H. M. Sandler, K. Lam, R. L. Bree, A. S. Lichter, and R. K. ten Haken, "Measurement of prostate movement over the course of routine radiotherapy using implanted markers," *Int. J. Radiat. Oncol., Biol., Phys.* **31**, 113–118 (1995).
- ¹⁷³P. W. Chung, T. Haycocks, T. Brown, Z. Cambridge, V. Kelly, H. Alasti, D. A. Jaffray, and C. N. Catton, "On-line aSi portal imaging of implanted fiducial markers for the reduction of interfraction error during conformal radiotherapy of prostate carcinoma," *Int. J. Radiat. Oncol., Biol., Phys.* **60**, 329–334 (2004).
- ¹⁷⁴E. Vigneault, J. Pouliot, J. Laverdiere, J. Roy, and M. Dorion, "Electronic portal imaging device detection of radioopaque markers for the evaluation of prostate position during megavoltage irradiation: A clinical study," *Int. J. Radiat. Oncol., Biol., Phys.* **37**, 205–212 (1997).
- ¹⁷⁵R. E. Wurm, F. Gum, S. Erbel, L. Schlegler, D. Scheffler, D. Agaoglu, R. Schild, B. Gebauer, P. Rogalla, M. Plotkin, K. Ocran, and V. Budach, "Image guided respiratory gated hypofractionated stereotactic body radiation therapy (H-SBRT) for liver and lung tumors: Initial experience," *Acta Oncol.* **45**, 881–889 (2006).
- ¹⁷⁶J. de Mey, J. Van de Steene, F. Vandenbroucke, D. Verellen, L. Trappeniens, M. Meysman, H. Everaert, M. Noppen, G. Storme, and A. Bossuyt, "Percutaneous placement of marking coils before stereotactic radiation therapy of malignant lung lesions," *J. Vasc. Interv. Radiol.* **16**, 51–56 (2005).
- ¹⁷⁷M. Imura, K. Yamazaki, H. Shirato, R. Onimaru, M. Fujino, S. Shimizu, T. Harada, S. Ogura, H. Dosaka-Akita, K. Miyasaka, and M. Nishimura, "Insertion and fixation of fiducial markers for setup and tracking of lung tumors in radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **63**, 1442–1447 (2005).
- ¹⁷⁸H. Shirato, K. Suzuki, G. C. Sharp, K. Fujita, R. Onimaru, M. Fujino, N. Kato, Y. Osaka, R. Kinoshita, H. Taguchi, S. Onodera, and K. Miyasaka, "Speed and amplitude of lung tumor motion precisely detected in four-dimensional setup and in real-time tumor-tracking radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **64**, 1229–1236 (2006).
- ¹⁷⁹T. R. Willoughby, A. R. Forbes, D. Buchholz, K. M. Langen, T. H. Wagner, O. A. Zeidan, P. A. Kupelian, and S. L. Meeks, "Evaluation of an infrared camera and x-ray system using implanted fiducials in patients with lung tumors for gated radiation therapy," *Int. J. Radiat. Oncol., Biol., Phys.* **66**, 568–575 (2006).
- ¹⁸⁰P. M. Medin, T. D. Solberg, A. A. De Salles, C. H. Cagnon, M. T. Selch, J. P. Johnson, J. B. Smathers, and E. R. Cosman, "Investigations of a minimally invasive method for treatment of spinal malignancies with LINAC stereotactic radiation therapy: Accuracy and animal studies," *Int. J. Radiat. Oncol., Biol., Phys.* **52**, 1111–1122 (2002).
- ¹⁸¹M. J. Murphy, S. Chang, I. Gibbs, Q. T. Le, D. Martin, and D. Kim, "Image-guided radiosurgery in the treatment of spinal metastases," *Neurosurg. Focus* **11** (2001).
- ¹⁸²T. Naruke, T. Goya, R. Tsuchiya, and K. Suemasu, "Prognosis and survival in resected lung carcinoma based on the new international staging system," *J. Thorac. Cardiovasc. Surg.* **96**, 440–447 (1988).
- ¹⁸³M. Uematsu, A. Shioda, A. Suda, T. Fukui, Y. Ozeki, Y. Hama, J. R. Wong, and S. Kusano, "Computed tomography-guided frameless stereotactic radiotherapy for stage I non-small cell lung cancer: A 5-year experience," *Int. J. Radiat. Oncol., Biol., Phys.* **51**, 666–670 (2001).
- ¹⁸⁴S. L. Meeks, J. M. Buatti, L. G. Bouchet, F. J. Bova, T. C. Ryken, E. C. Pennington, K. M. Anderson, and W. A. Friedman, "Ultrasound-guided extracranial radiosurgery: Technique and application," *Int. J. Radiat. Oncol., Biol., Phys.* **55**, 1092–1101 (2003).
- ¹⁸⁵M. Fuss, J. Boda-Heggemann, N. Papanikolaou, and B. J. Salter, "Image-guidance for stereotactic body radiation therapy," *Med. Dosim.* **32**, 102–110 (2007).
- ¹⁸⁶D. A. Kuban, L. Dong, R. Cheung, E. Strom, and R. De Crevoisier, "Ultrasound-based localization," *Semin. Radiat. Oncol.* **15**, 180–191 (2005).
- ¹⁸⁷J. M. Balter, J. N. Wright, L. J. Newell, B. Friemel, S. Dimmer, Y. Cheng, J. Wong, E. Vertatschitsch, and T. P. Mate, "Accuracy of a wireless localization system for radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **61**, 933–937 (2005).
- ¹⁸⁸P. J. Keall, G. S. Mageras, J. M. Balter, R. S. Emery, K. M. Forster, S. B. Jiang, J. M. Kapatoes, D. A. Low, M. J. Murphy, B. R. Murray, C. R. Ramsey, M. B. Van Herk, S. S. Vedam, J. W. Wong, and E. Yorke, "The management of respiratory motion in radiation oncology report of AAPM Task Group 76," *Med. Phys.* **33**, 3874–3900 (2006).
- ¹⁸⁹T. Zhang, N. P. Orton, and W. A. Tome, "On the automated definition of mobile target volumes from 4D-CT images for stereotactic body radiotherapy," *Med. Phys.* **32**, 3493–3502 (2005).
- ¹⁹⁰J. W. Wolthaus, C. Schneider, J. J. Sonke, M. van Herk, J. S. Belderbos, M. M. Rossi, J. V. Lebesque, and E. M. Damen, "Mid-ventilation CT scan construction from four-dimensional respiration-correlated CT scans for radiotherapy planning of lung cancer patients," *Int. J. Radiat. Oncol., Biol., Phys.* **65**, 1560–1571 (2006).
- ¹⁹¹F. Casamassima, C. Cavedon, P. Francescon, J. Stancanello, M. Avanzo, S. Cora, and P. Scalchi, "Use of motion tracking in stereotactic body radiotherapy: Evaluation of uncertainty in off-target dose distribution and optimization strategies," *Acta Oncol.* **45**, 943–947 (2006).
- ¹⁹²G. R. Borst, J. J. Sonke, A. Betgen, P. Remeijer, M. van Herk, and J. V. Lebesque, "Kilo-voltage cone-beam computed tomography setup measurements for lung cancer patients; first clinical results and comparison with electronic portal-imaging device," *Int. J. Radiat. Oncol., Biol., Phys.* **68**, 555–561 (2007).
- ¹⁹³T. G. Purdie, J. P. Bissonnette, K. Franks, A. Bezjak, D. Payne, F. Sie, M. B. Sharpe, and D. A. Jaffray, "Cone-beam computed tomography for on-line image guidance of lung stereotactic radiotherapy: Localization, verification, and intrafraction tumor position," *Int. J. Radiat. Oncol., Biol., Phys.* **68**, 243–252 (2007).
- ¹⁹⁴M. Guckenberger, J. Meyer, J. Wilbert, K. Baier, G. Mueller, J. Wulf, and M. Flentje, "Cone-beam CT based image-guidance for extracranial stereotactic radiotherapy of intrapulmonary tumors," *Acta Oncol.* **45**, 897–906 (2006).
- ¹⁹⁵G. D. Hugo, J. Liang, J. Campbell, and D. Yan, "On-line target position localization in the presence of respiration: A comparison of two methods," *Int. J. Radiat. Oncol., Biol., Phys.* **69**, 1634–1641 (2007).
- ¹⁹⁶Z. Wang, Q. J. Wu, L. B. Marks, N. Larrier, and F. F. Yin, "Cone-beam CT localization of internal target volumes for stereotactic body radiotherapy of lung lesions," *Int. J. Radiat. Oncol., Biol., Phys.* **69**, 1618–1624 (2007).
- ¹⁹⁷J. J. Sonke, L. Zijp, P. Remeijer, and M. van Herk, "Respiratory correlated cone beam CT," *Med. Phys.* **32**, 1176–1186 (2005).
- ¹⁹⁸S. L. Meeks, W. A. Tome, T. R. Willoughby, P. A. Kupelian, T. H. Wagner, J. M. Buatti, and F. J. Bova, "Optically guided patient positioning techniques," *Semin. Radiat. Oncol.* **15**, 192–201 (2005).
- ¹⁹⁹G. Baroni, G. Ferrigno, and A. Pedotti, "Implementation and application of real-time motion analysis based on passive markers," *Med. Biol. Eng.*

- Comput. **36**, 693–703 (1998).
- ²⁰⁰F. J. Bova, J. M. Buatti, W. A. Friedman, W. M. Mendenhall, C. C. Yang, and C. Liu, “The University of Florida frameless high-precision stereotactic radiotherapy system,” *Int. J. Radiat. Oncol., Biol., Phys.* **38**, 875–882 (1997).
- ²⁰¹H. D. Kubo, P. M. Len, S. Minohara, and H. Mostafavi, “Breathing-synchronized radiotherapy program at the University of California Davis Cancer Center,” *Med. Phys.* **27**, 346–353 (2000).
- ²⁰²M. Menke, F. Hirschfeld, T. Mack, O. Pastyr, V. Sturm, and W. Schlegel, “Photogrammetric accuracy measurements of head holder systems used for fractionated radiotherapy,” *Int. J. Radiat. Oncol., Biol., Phys.* **29**, 1147–1155 (1994).
- ²⁰³R. D. Rogus, R. L. Stern, and H. D. Kubo, “Accuracy of a photogrammetry-based patient positioning and monitoring system for radiation therapy,” *Med. Phys.* **26**, 721–728 (1999).
- ²⁰⁴L. T. Wang, T. D. Solberg, P. M. Medin, and R. Boone, “Infrared patient positioning for stereotactic radiosurgery of extracranial tumors,” *Comput. Biol. Med.* **31**, 101–111 (2001).
- ²⁰⁵C. Bert, K. G. Metheany, K. Doppke, and G. T. Chen, “A phantom evaluation of a stereo-vision surface imaging system for radiotherapy patient setup,” *Med. Phys.* **32**, 2753–2762 (2005).
- ²⁰⁶A. Muacevic, C. Drexler, B. Wowra, A. Schweikard, A. Schlaefel, R. T. Hoffmann, R. Wilkowski, H. Winter, and M. Reiser, “Technical description, phantom accuracy, and clinical feasibility for single-session lung radiosurgery using robotic image-guided real-time respiratory tumor tracking,” *Technol. Cancer Res. Treat.* **6**, 321–328 (2007).
- ²⁰⁷A. Schweikard, G. Glosser, M. Bodduluri, M. J. Murphy, and J. R. Adler, “Robotic motion compensation for respiratory movement during radiosurgery,” *Comput. Aided Surg.* **5**, 263–277 (2000).
- ²⁰⁸A. Schweikard, H. Shiomi, and J. Adler, “Respiration tracking in radiosurgery,” *Med. Phys.* **31**, 2738–2741 (2004).
- ²⁰⁹D. Ionascu, S. B. Jiang, S. Nishioka, H. Shirato, and R. I. Berbeco, “Internal-external correlation investigations of respiratory induced motion of lung tumors,” *Med. Phys.* **34**, 3893–3903 (2007).
- ²¹⁰M. Guckenberger, T. Krieger, A. Richter, K. Baier, J. Wilbert, R. A. Sweeney, and M. Flentje, “Potential of image-guidance, gating and real-time tracking to improve accuracy in pulmonary stereotactic body radiotherapy,” *Radiother. Oncol.* **91**, 288–295 (2009).
- ²¹¹H. D. Kubo and B. C. Hill, “Respiration gated radiotherapy treatment: A technical study,” *Phys. Med. Biol.* **41**, 83–91 (1996).
- ²¹²R. W. Underberg, F. J. Lagerwaard, B. J. Slotman, J. P. Cuijpers, and S. Senan, “Benefit of respiration-gated stereotactic radiotherapy for stage I lung cancer: An analysis of 4DCT datasets,” *Int. J. Radiat. Oncol., Biol., Phys.* **62**, 554–560 (2005).
- ²¹³E. C. Ford, G. S. Mageras, E. Yorke, K. E. Rosenzweig, R. Wagman, and C. C. Ling, “Evaluation of respiratory movement during gated radiotherapy using film and electronic portal imaging,” *Int. J. Radiat. Oncol., Biol., Phys.* **52**, 522–531 (2002).
- ²¹⁴H. D. Kubo and L. Wang, “Introduction of audio gating to further reduce organ motion in breathing synchronized radiotherapy,” *Med. Phys.* **29**, 345–350 (2002).
- ²¹⁵G. S. Mageras, E. Yorke, K. Rosenzweig, L. Braban, E. Keatley, E. Ford, S. A. Leibel, and C. C. Ling, “Fluoroscopic evaluation of diaphragmatic motion reduction with a respiratory gated radiotherapy system,” *J. Appl. Clin. Med. Phys.* **2**, 191–200 (2001).
- ²¹⁶S. S. Korreman, T. Juhler-Nottrup, and A. L. Boyer, “Respiratory gated beam delivery cannot facilitate margin reduction, unless combined with respiratory correlated image guidance,” *Radiother. Oncol.* **86**, 61–68 (2008).
- ²¹⁷B. E. Bjärngard, J. S. Tsai, and R. K. Rice, “Doses on the central axes of narrow 6-MV x-ray beams,” *Med. Phys.* **17**, 794–799 (1990).
- ²¹⁸J. Y. Cheung, K. N. Yu, R. T. Ho, and C. P. Yu, “Monte Carlo calculated output factors of a Leksell Gamma Knife unit,” *Phys. Med. Biol.* **44**, N247–N249 (1999).
- ²¹⁹W. U. Laub and T. Wong, “The volume effect of detectors in the dosimetry of small fields used in IMRT,” *Med. Phys.* **30**, 341–347 (2003).
- ²²⁰Y. Yang and L. Xing, “Using the volumetric effect of a finite-sized detector for routine quality assurance of multileaf collimator leaf positioning,” *Med. Phys.* **30**, 433–441 (2003).
- ²²¹C. Martens, C. De Wagter, and W. De Neve, “The value of the PinPoint ion chamber for characterization of small field segments used in intensity-modulated radiotherapy,” *Phys. Med. Biol.* **45**, 2519–2530 (2000).
- ²²²K. A. Paskalev, J. P. Seuntjens, H. J. Patrocinio, and E. B. Podgorsak, “Physical aspects of dynamic stereotactic radiosurgery with very small photon beams (1.5 and 3 mm in diameter),” *Med. Phys.* **30**, 111–118 (2003).
- ²²³S. C. Prasad, “Effects of collimator jaw setting on dose output for treatments with multileaf collimator,” *Med. Dosim.* **23**, 296–298 (1998).
- ²²⁴S. Webb, T. Bortfeld, J. Stein, and D. Convery, “The effect of stair-step leaf transmission on the ‘tongue-and-groove problem’ in dynamic radiotherapy with a multileaf collimator,” *Phys. Med. Biol.* **42**, 595–602 (1997).
- ²²⁵A. Mack, S. G. Scheib, J. Major, S. Gianolini, G. Pazmandi, H. Feist, H. Czempel, and H. J. Kreiner, “Precision dosimetry for narrow photon beams used in radiosurgery-determination of Gamma Knife output factors,” *Med. Phys.* **29**, 2080–2089 (2002).
- ²²⁶K. De Vlaminck, H. Palmans, F. Verhaegen, C. De Wagter, W. De Neve, and H. Thierens, “Dose measurements compared with Monte Carlo simulations of narrow 6 MV multileaf collimator shaped photon beams,” *Med. Phys.* **26**, 1874–1882 (1999).
- ²²⁷T. C. Zhu and B. E. Bjärngard, “The head-scatter factor for small field sizes,” *Med. Phys.* **21**, 65–68 (1994).
- ²²⁸X. R. Zhu, J. J. Allen, J. Shi, and W. E. Simon, “Total scatter factors and tissue maximum ratios for small radiosurgery fields: Comparison of diode detectors, a parallel-plate ion chamber, and radiographic film,” *Med. Phys.* **27**, 472–477 (2000).
- ²²⁹S. Li, A. Rashid, S. He, and D. Djajaputra, “A new approach in dose measurement and error analysis for narrow photon beams (beamlets) shaped by different multileaf collimators using a small detector,” *Med. Phys.* **31**, 2020–2032 (2004).
- ²³⁰P. D. Higgins, C. H. Sibata, L. Siskind, and J. W. Sohn, “Deconvolution of detector size effect for small field measurement,” *Med. Phys.* **22**, 1663–1666 (1995).
- ²³¹E. R. Epp, A. L. Boyer, and K. P. Doppke, “Underdosing of lesions resulting from lack of electronic equilibrium in upper respiratory air cavities irradiated by 10MV x-ray beams,” *Int. J. Radiat. Oncol., Biol., Phys.* **2**, 613–619 (1977).
- ²³²C. Martens, N. Reynaert, C. De Wagter, P. Nilsson, M. Coghe, H. Palmans, H. Thierens, and W. De Neve, “Underdosage of the upper-airway mucosa for small fields as used in intensity-modulated radiation therapy: A comparison between radiochromic film measurements, Monte Carlo simulations, and collapsed cone convolution calculations,” *Med. Phys.* **29**, 1528–1535 (2002).
- ²³³A. K. Rustgi, A. Samuels, and S. N. Rustgi, “Influence of air inhomogeneities in radiosurgical beams,” *Med. Dosim.* **22**, 95–100 (1997).
- ²³⁴M. K. Woo and J. R. Cunningham, “The validity of the density scaling method in primary electron transport for photon and electron beams,” *Med. Phys.* **17**, 187–194 (1990).
- ²³⁵E. K. Lee, T. Fox, and I. Crocker, “Simultaneous beam geometry and intensity map optimization in intensity-modulated radiation therapy,” *Int. J. Radiat. Oncol., Biol., Phys.* **64**, 301–320 (2006).
- ²³⁶N. Papanikolaou, J. Battista, A. Boyer, C. Kappas, E. Klein, T. Mackie, M. Sharpe, and J. Van Dyke, AAPM Report No. 85: Tissue Inhomogeneity Corrections for Megavoltage Photon Beams, American Association of Physicists in Medicine (2004).
- ²³⁷S. E. Davidson, R. A. Pople, G. S. Ibbott, and D. S. Followill, “Technical note: Heterogeneity dose calculation accuracy in IMRT: Study of five commercial treatment planning systems using an anthropomorphic thorax phantom,” *Med. Phys.* **35**, 5434–5439 (2008).
- ²³⁸L. Potters, M. Steinberg, C. Rose, R. Timmerman, S. Ryu, J. M. Hevezi, J. Welsh, M. Mehta, D. A. Larson, and N. A. Janjan, “American Society for Therapeutic Radiology and Oncology and American College of Radiology practice guideline for the performance of stereotactic body radiation therapy,” *Int. J. Radiat. Oncol., Biol., Phys.* **60**, 1026–1032 (2004).
- ²³⁹M. D. Mills, “Analysis and practical use: The ABT study of medical physicist work values for radiation oncology physics services—Round II,” *J. Am. Coll. Radiol.* **2**, 782–789 (2005).
- ²⁴⁰I. ABT Associates, 2008.
- ²⁴¹J. R. Palta, C. Liu, and J. G. Li, “Quality assurance of intensity-modulated radiation therapy,” *Int. J. Radiat. Oncol., Biol., Phys.* **71**, S108–S112 (2008).
- ²⁴²E. E. Klein, J. Hanley, J. Bayouth, F.-F. Yin, W. Simon, S. Dresser, C. Serago, F. Aguirre, L. Ma, B. Arjomandy, and C. Liu, “AAPM Task Group 142 report: Quality assurance of medical accelerators,” *Med. Phys.* **36**, 4197–4212 (2009).
- ²⁴³G. J. Kutcher *et al.*, “Comprehensive QA for radiation oncology: Report

- of AAPM Radiation Therapy Committee Task Group 40," *Med. Phys.* **21**, 581–618 (1994).
- ²⁴⁴R. Nath, P. J. Biggs, F. J. Bova, C. C. Ling, J. A. Purdy, J. van de Geijn, and M. S. Weinhaus, "AAPM code of practice for radiotherapy accelerators: Report of AAPM Radiation Therapy Task Group No. 45," *Med. Phys.* **21**, 1093–1121 (1994).
- ²⁴⁵P. Lin *et al.*, "Specification and acceptance testing for computed tomography scanners," AAPM Report No. 39, Vol. 95 (American Institute of Physics, Inc., 1993).
- ²⁴⁶J. G. Och, G. D. Clarke, W. T. Sobol, C. W. Rosen, and S. K. Mun, "Acceptance testing of magnetic resonance imaging systems: Report of AAPM Nuclear Magnetic Resonance Task Group No. 6," *Med. Phys.* **19**, 217–229 (1992).
- ²⁴⁷B. Fraass, K. Doppke, M. Hunt, G. Kutcher, G. Starkschall, R. Stern, and J. Van Dyke, "American Association of Physicists in Medicine Radiation Therapy Committee Task Group 53: Quality assurance for clinical radiotherapy treatment planning," *Med. Phys.* **25**, 1773–1829 (1998).
- ²⁴⁸G. A. Ezzell, J. M. Galvin, D. Low, J. R. Palta, I. Rosen, M. B. Sharpe, P. Xia, Y. Xiao, L. Xing, and C. X. Yu, "Guidance document on delivery, treatment planning, and clinical implementation of IMRT: Report of the IMRT Subcommittee of the AAPM Radiation Therapy Committee," *Med. Phys.* **30**, 2089–2115 (2003).
- ²⁴⁹Quality assurance for radiation therapy, quality assurance of radiation therapy: The challenges of advanced technologies symposium," *Int. J. Radiat. Oncol., Biol., Phys.* **71**, S1–S214 (2008).
- ²⁵⁰W. Lutz, K. R. Winston, and N. Maleki, "A system for stereotactic radiosurgery with a linear accelerator," *Int. J. Radiat. Oncol., Biol., Phys.* **14**, 373–381 (1988).
- ²⁵¹J. P. Bissonnette, "Quality assurance of image-guidance technologies," *Semin. Radiat. Oncol.* **17**, 278–286 (2007).
- ²⁵²F. Lohr, J. Debus, C. Frank, K. Herfarth, O. Pastyr, B. Rhein, M. L. Bahner, W. Schlegel, and M. Wannenmacher, "Noninvasive patient fixation for extracranial stereotactic radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **45**, 521–527 (1999).
- ²⁵³C. Yu, W. Main, D. Taylor, G. Kuduvalli, M. L. Apuzzo, and J. R. Adler, Jr., "An anthropomorphic phantom study of the accuracy of Cyberknife spinal radiosurgery," *Neurosurgery* **55**, 1138–1149 (2004).
- ²⁵⁴F. Rath, "Tools for developing a quality management program: Proactive tools (process mapping, value stream mapping, fault tree analysis, and failure mode and effects analysis)," *Int. J. Radiat. Oncol., Biol., Phys.* **71**, S187–S190 (2008).
- ²⁵⁵J. Nyman, K. A. Johansson, and U. Hulten, "Stereotactic hypofractionated radiotherapy for stage I non-small cell lung cancer—Mature results for medically inoperable patients," *Lung Cancer* **51**, 97–103 (2006).
- ²⁵⁶W. Hodge, W. A. Tome, H. A. Jaradat, N. P. Orton, D. Khuntia, A. Traynor, T. Weigel, and M. P. Mehta, "Feasibility report of image guided stereotactic body radiotherapy (IG-SBRT) with tomotherapy for early stage medically inoperable lung cancer using extreme hypofractionation," *Acta Oncol.* **45**, 890–896 (2006).
- ²⁵⁷A. J. Hamilton, B. A. Lulu, H. Fosmire, B. Stea, and J. R. Cassady, "Preliminary clinical experience with linear accelerator-based spinal stereotactic radiosurgery," *Neurosurgery* **36**, 311–319 (1995).
- ²⁵⁸M. J. Murphy, "An automatic six-degree-of-freedom image registration algorithm for image-guided frameless stereotactic radiosurgery," *Med. Phys.* **24**, 857–866 (1997).
- ²⁵⁹K. Nakagawa, Y. Aoki, M. Tago, A. Terahara, and K. Ohtomo, "Mega-voltage CT-assisted stereotactic radiosurgery for thoracic tumors: Original research in the treatment of thoracic neoplasms," *Int. J. Radiat. Oncol., Biol., Phys.* **48**, 449–457 (2000).
- ²⁶⁰J. Wulf, U. Hadinger, U. Oppitz, B. Olshausen, and M. Flentje, "Stereotactic radiotherapy of extracranial targets: CT-simulation and accuracy of treatment in the stereotactic body frame," *Radiother. Oncol.* **57**, 225–236 (2000).
- ²⁶¹M. B. Sharpe, D. J. Moseley, T. G. Purdie, M. Islam, J. H. Siewerdsen, and D. A. Jaffray, "The stability of mechanical calibration for a kV cone beam computed tomography system integrated with linear accelerator," *Med. Phys.* **33**, 136–144 (2006).
- ²⁶²J. M. Galvin and G. Bednarz, "Quality assurance procedures for stereotactic body radiation therapy," *Int. J. Radiat. Oncol., Biol., Phys.* **71**, S122–S125 (2008).
- ²⁶³T. D. Solberg, P. M. Medin, J. Mullins, and S. Li, "Quality assurance of immobilization and target localization systems for frameless stereotactic cranial and extracranial hypofractionated radiotherapy," *Int. J. Radiat. Oncol., Biol., Phys.* **71**, S131–S135 (2008).
- ²⁶⁴S. B. Jiang, J. Wolfgang, and G. S. Mageras, "Quality assurance challenges for motion-adaptive radiation therapy: Gating, breath holding, and four-dimensional computed tomography," *Int. J. Radiat. Oncol., Biol., Phys.* **71**, S103–S107 (2008).
- ²⁶⁵J. P. Bissonnette, D. Moseley, E. White, M. Sharpe, T. Purdie, and D. A. Jaffray, "Quality assurance for the geometric accuracy of cone-beam CT guidance in radiation therapy," *Int. J. Radiat. Oncol., Biol., Phys.* **71**, S57–S61 (2008).
- ²⁶⁶R. Timmerman, personal communication (26 October 2009).