Chapter 2
The Physics of Hypofractionation and SRS/SBRT

Jason Matney, Alex Price, and Leith Rankine

The practice of SRS/SBRT and other hypofractionated radiation treatments relies on the accurate delivery of large doses in a limited number of fractions. To minimize normal tissue toxicities, radiation treatment is typically required to be highly conformal with rapid falloff of dose outside of the target volume. In SRS/SBRT cases, this requirement is achieved through a combination of specialized simulation, treatment planning, imaging, positional setup, motion management and delivery technologies. Since SRS/SBRT requires a hypofractionated regimen with little tolerance for error, establishing and following guidelines for rigorous quality assurance (QA) and quality control is extremely important. The quality of a SRS/SBRT program depends on the coordinated interactions of a team of skilled health care professionals.

This chapter outlines the physics of hypofractionation by starting with definitions, basic premise and reviewing some currently available delivery systems. This chapter includes a discussion of the basic SRS/SBRT strategy for simulation, motion management, treatment planning, and treatment delivery. Finally, the chapter concludes with a discussion of physics considerations for commissioning a clinical program and developing a comprehensive quality assurance program.

- In the mid-twentieth century, stereotactic radiosurgery (SRS) was developed to treat intracranial sites [1].
- Stereotaxis is a method in neurosurgery for locating points within the brain using an external, three-dimensional frame of reference usually based on the Cartesian coordinate system.

J. Matney · A. Price · L. Rankine (✉)
Department of Radiation Oncology, University of North Carolina School of Medicine, Chapel Hill, NC, USA
e-mail: matneyje@sutterhealth.org; alex.price@wustl.edu; Leith_Rankine@med.unc.edu

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- The earliest use of the term "stereotactic radiosurgery" was reported by Lars Leksell in 1951 [2]. Typically, SRS is used to describe single fraction radiotherapy to intracranial targets, initially used as an alternative to neurosurgery.
- Stereotactic radiotherapy (SRT) is a term for fractionated SRS to localized sites within the brain or spine.
- The first combined use of x-rays with a stereotactic device (or frame) for immobilization and localization occurred in 1950 [2].
- SRS was first developed using orthovoltage X-rays, followed by protons, heavy charged particles, and gamma rays from Cobalt-60 treatment machines.
- Two broad categories have been used to immobilize and localize intracranial targets: Invasive and noninvasive systems [3].
  - Historically, skull fixation frames were used to immobilize and localize the head prior to simulation and treatment planning. These devices would remain in place until completion of treatment. These systems often used a physical frame affixed to the patient's skull, commonly using pins or screws.
  - Recently, frameless systems have been developed that uses radiographic imaging to verify and monitor patient alignment.
- The combination of clinical experience of SRS combined with developments in technology led to similar techniques over the past two decades in extracranial sites, stereotactic ablative radiation therapy (SABR) or stereotactic body radiation therapy (SBRT) [4].
- Both techniques (SRS/SBRT) differ from traditional radiotherapy in that large doses are delivered in 1–5 fractions.
- The goal of SRS/SBRT is to deliver a high biologically effective dose while minimizing dose to normal tissues using highly conformal treatment beams to achieve rapid dose fall-off outside the target.
- To achieve such highly conformal dose deliveries, it is imperative that the entire treatment process achieves accuracy and precision beyond that of conventional radiation therapy.
- Clinical patient outcomes of SBRT were first published in 1995, initially focusing on lung, liver and retroperitoneal disease sites [5].
- A 2011 survey of physicians found over 63% of physicians using SBRT, and over half had adopted SBRT in 2008 or later. Among SBRT users, the most common disease sites treated were lung (89.3%), spine (67.5%), and liver (54.5%) tumors. Overall, 76.0% of current users planned to increase their SBRT use, while 66.5% of nonusers planned to adopt the technology in the future [6].
- The clinical implementation recommendations including protocols, equipment, resources and QA procedures has been outlined in AAPM Task Group 101 publication [7]. Major features of SRS/SBRT adapted from AAPM TG-101 are summarized in Table 2.1.

Table 2.1 General Comparison of conventional (3D/IMRT) to stereotactic (SRS/SBRT) radiotherapy

Treatment	Conventional 3D/IMRT	SRS/SBRT
Dose/fraction	1.8–3 Gy	5–30 Gy
Fractions	10–30	1–5
Target definition	CTV/PTV (gross disease + subclinical extent). Tumor may not have sharp boundary	GTV/CTV/ITV/PTV Well defined tumors: GTV=CTV
Prescription Isodose line	~90–95%	~50–90%
Dose gradient outside PTV	Moderate falloff	Very steep falloff
Margin	~Centimeter	Millimeters
Beam arrangement	Typically coplanar beams	Typically include non-coplanar beams
Physics/dosimetry involvement & monitoring	Indirect	Direct
Primary imaging modality	Multi-modality: CT/MR/PET	Multi-modality: CT/MR/PET
Redundancy in geometric verification	No	Yes, imaging prior to each treatment, possibly during
Maintenance of target accuracy throughout treatment	Moderate patient positioning control and monitoring	High; strict immobilization and high frequency position monitoring
Need for respiratory motion management	Potentially	Necessary in sites with potential for respiratory motion
Staff training requirements	High	High + additional SBRT training

2.1 Treatment Systems for SRS/SBRT

2.1.1 GammaKnife

- The GammaKnife® Perfexion [8] system (Elekta, Crowley, UK) treats cranial sites with 192 Cobalt-60 sources in a conical configuration Older models used over 200 sources that were arranged in a hemispherical pattern and a helmet-type collimation system
- Primary and secondary collimation in the GammaKnife Perfexion® system is achieved by a single 12-cm thick tungsten collimator array, in which collimators are arranged in a series of five concentric rings around the patient, divided into independently moving eight regions.
- The collimation device produces individual beams of 4, 8 and 16 mm converging at the isocenter. Beam diameters are changed by moving the source tray over the selected collimator set.
  - Due to the pattern of source placements, the source to focus distance ranges from 374 to 433 mm.

- Each exposure is referred to as a "shot" of radiation where the circular beams intersect to produce a roughly spherical dose distribution.
  - Multiple spherical shots can be combined to "pack" a volume, leading to the term "sphere packing" to describe the method of treatment planning in GammaKnife.
- The patient is moved into the treatment unit using the couch. The only other main moving part on the GammaKnife unit is the drive which moves the source tray into position over the desired beam collimator holes.
- Patients are affixed in a head frame which is attached to the patient's skull with screws. This remains in place during imaging, planning and treatment.
  - This provides a rigid frame around the patient, but traditionally limits the GammaKnife to a single fraction, to avoid repeated placement of the head frame on to the patient.
  - The more recent GammaKnife® Icon (shown in Fig. 2.1) enables on-board CBCT and thus allows for frameless radiosurgery using a thermoplastic mask.
- Plans on the GammaKnife system are prescribed to the 50% isodose line. Thus, the maximum dose point is twice the prescription value.
- Advantages of GammaKnife include sharp penumbra and treatment planning with the ability to easily use multiple isocenters.

Fig. 2.1 Elekta GammaKnife® Icon unit, which collimates 192 Cobalt-60 sources to deliver multiple beams simultaneously

- Disadvantageous of GammaKnife include the need for source replacement approximately every 7 years due to the 5.26 year half-life of Cobalt-60, the ability to treat only intracranial lesions, and the limited field size/shaping available.

2.1.2 CyberKnife

- The CyberKnife system (Accuray, Sunnyvale, CA) shown in Fig. 2.2 is comprised of a 6 MV flattening filter free (FFF) linear accelerator mounted on a robotic arm and a robotic couch [9].
- The robotic arm can manipulate the accelerator into hundreds of predefined positions, called nodes. From each node, the system can produce non-coplanar, non-isocentric beams.
- Radiographic image guidance is performed with a two planar X-ray systems for patient alignment and intrafractional tracking.
- Initial CyberKnife treatments used fixed circular stereotactic cones with sizes 5–60 mm fields as measured at a reference source-to-axis distance of 800 mm.
- A variable aperture (IRIS) was later developed that can reproduce each of the fixed cones [10]. This allows for more field sizes to be used in a plan without the therapist needing to enter the room to physically exchange cones.

Fig. 2.2 Accuray CyberKnife system with a linear accelerator mounted on a robotic arm. Also shown are the ceiling and in-floor X-ray imaging system and robotic treatment couch

- Recently, a multileaf collimator system (InCise) was added that allows for MLC-defined step-and-shoot field shapes to be used.
  - This compact MLC is designed to achieve a maximum field size of 120×102.5 mm^2, using 41 leaf pairs with a width of 2.5 mm at the reference source-axis-distance (SAD) of 800 mm [11].
- Depending on the type/location of tumor, the CyberKnife allows for multiple frameless patient setup and tracking methods.
  - 6D skull tracking system: A frameless system using orthogonal x-rays to determine translation and rotation to align bony skull anatomy to the planned position using a series of digitally reconstructed radiographs (DRR).
  - Xsight Spine Alignment system: Similar to 6D skull tracking, spine tracking aligns the spine to the planned position using the X-ray imaging system and a series of DRRs from the treatment plan.
    - Options exist to treat patients in both prone and supine positions.
  - Synchrony Tracking System: The system synchronizes the beam delivery with the motion of internal fiducials.
    - The system continuously monitors external reflective markers placed on the patient's chest/abdomen.
    - By observing the fiducials through intermittent stereoscopic x-ray imaging, the system correlates the motion of the external reflective markers with the internal fiducials.
    - The CyberKnife system adjusts the treatment beam to track the position of the moving target in real time using the correlation model between the external markers and internal fiducials.

2.1.3 Linear Accelerators

- Two of the largest manufacturers, Varian and Elekta, have similar system configurations for their linear accelerators.
  - Both offer 6 and 10 MV beam energies, which are common for SRS/SBRT. Future versions of machines are likely to remain very similar in characteristics.
- Varian (Palo Alto, CA) accelerators that may be used for SRS/SBRT include the TrueBeam®, Trilogy®, and Clinac® platforms when used with the Varian On-Board Imaging® (OBI) kV imaging system.
- Elekta (Crowley, UK) accelerators that may be used for SRS/SBRT include the VersaHD®, Infinity®, and Synergy® platforms when used with the Elekta X-ray Volumetric Imaging (XVI) kV imaging system.

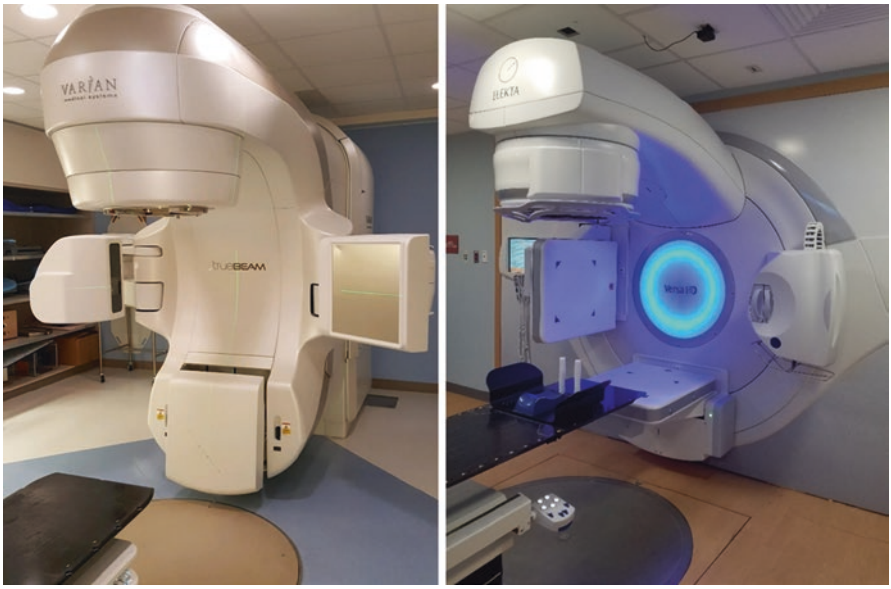

Fig. 2.3 Images of a two standard modern linear accelerators with IGRT capabilities: Varian TrueBeam® and Elekta VersaHD® which show the kV imaging source and panels, and carbon fiber couches on both systems

- A few design differences between Varian and Elekta linear accelerators, summarized in Table 2.2 and shown for comparison in Fig. 2.3:
  - Elekta uses a magnetron and a travelling wave guide to accelerate electrons, in contrast to Varian's klyston and standing wave guide.
  - Varian features a gridded triode electron gun. This grid allows the user to rapidly terminate the injection of electrons to the waveguide, which allows faster termination of the beam. This is an important feature for gated deliveries.
  - Recent Elekta machines are designed without x-direction jaws, instead using the MLC carriage with backup diaphragm to replace as the jaws.
  - Varian machines are designed with tertiary MLCs. Two sets of x-direction and y-direction jaws are still used.
- Both manufacturers offer high dose rate flattening filter free (FFF) modes. These modes remove the flattening filter from the beam. A cross-profile comparison of a flattened and FFF beam is shown in Fig. 2.4.
- For SRS & SBRT planning, the target dose is not meant to be uniform, thus FFF modes lend well to such treatments.
- The removal of the flattening filter for FFF mode results in a peaked profile, lower average photon energy (no beam hardening from the flattening filter), faster dose rate, lower head leakage, reduced scatter and less neutron production for 10+ MV beams.

Table 2.2 Comparison of two recent accelerator models from Varian and Elekta

Machine	Varian TrueBeam	Elekta VersaHD
Years of manufacture	2010-current	2013-current
Photon energy available	6&10/15/18	6&10/15/18
RF power source	Klystron	Magnetron
Maximum dose rate	6 MV FFF: 1400 MU/min 10 MV FFF: 2400 MU/min	6 MV FFF: 1400 MU/min 10 MV FFF: 2400 MU/min
Maximum field size	40×40 cm^2	40×40 cm^2
MLC	120 MLC 5 mm leaf width at isocenter 10 mm width on outside leaves at isocenter	160 MLC 5 mm leaf thickness at isocenter
Portal imager	Amorphous silicon: aS1000	Amorphous silicon: iViewGT
Treatment delivery	3D/IMRT/SRS/SBRT/Arc	3D/IMRT/SRS/SBRT/Arc
Arc therapy	Yes: RapidArc	Yes: VMAT
IGRT	OBI system with CBCT: kV planar Fluoroscopy Fiducial tracking algorithms	XVI system with CBCT: kV planar Fluoroscopy Online 4D CBCT
Couch	3D: Exact IGRT table or 6D: PerfectPitch	3D: Precise table or 6D: HexaPOD

- Both manufacturers include IGRT systems that incorporate both MV and kV energies. This includes the ability to acquire fluoroscopic studies for motion assessment and volumetric imaging which includes both CBCT and 4D CBCT capabilities.
  - Typical imaging kV energies range from 70–150 kVp.
- BrainLab Novalis™ Radiosurgery system features a high-definition MLC with 2.5 mm central leaves on a Varian linear accelerator with a 6D robotic couch and the ExacTrac® system that incorporates an infrared guidance with a stereoscopic X-ray system.
  - The combined kV/optical system allows for continuous monitoring of optical markers on the patient with x-ray verification of internal positioning.
- The Varian Edge™ radiosurgery system is the most recent SRS/SBRT machine by Varian. The machine has 6, 6 FFF & 10 FFF MV energies only, and 120 MLCs with 2.5 mm leaf width as isocenter with a maximum field size of 40×22 cm^2. This system also incorporates an optical surface monitoring system.
- Magnetic Resonance guided Radiation Therapy (MRgRT) is a recent development that combines MR imaging into patient setup and treatment delivery.
  - Cobalt therapy can be combined with MR guidance during treatment. One example is the ViewRay MRIdian® system (ViewRay, Oakwood Village, Ohio) that incorporates three independent, high activity cobalt sources mounted on a ring

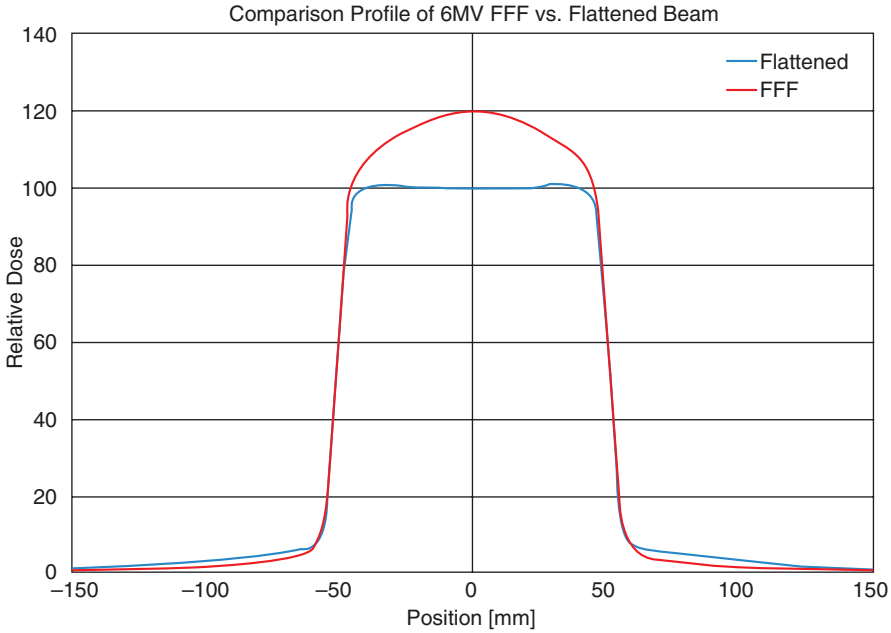

Fig. 2.4 Profile comparison of a 6 MV flattened beam (blue) with a flattening filter free (red) beam for a 10 × 10 cm^2 field at a depth of 10 cm in water

gantry with 120° separation with a 0.35 T MR system [12]. Each source has an independent MLC. The MR and cobalt therapy systems share a common isocenter, enabling simultaneous and continuous MRI during treatment delivery.

– The inclusion of MR imaging allows for continuous, non-ionizing imaging during treatment with superior soft tissue contrast.
– Disadvantages include the currently low MR field strength. Also with Cobalt-60 therapies, there is increased penumbra due to the source size and a limited dose rate: maximum 600 cGy/min which decays over time.
– Several institutions are commissioning recently designed linear accelerators with MR imaging capabilities. One example is the Elekta MR-linac which combines a 1.5 T Philips MRI with a ring based gantry system that houses a 6 MV accelerator [13].

2.1.4 Brachytherapy

- High Dose Rate Brachytherapy is a short course of radiation, usually ≤10 fractions where a high-activity Iridium-192 (5–10 Curies) source is placed into or near the tumor site using a remote afterloader to position the source.
- High dose rate is usually quantified as greater than 12 Gy/hr [14].

Fig. 2.5 Images of two common remote afterloaders for HDR brachytherapy: Varian Varisource® iX and Elekta MicroSelectron®. Both allow for the controlled placement of a sealed Iridium-192 source into a variety of applicators placed inside/on a patient

- Remote HDR afterloaders are an application of the "As Low as Reasonably Achievable" (ALARA) principle in radiation protection. By removing the need to hand place sources, remote afterloaders reduce exposure to all staff. Remote afterloading also allows for optimization of the source dwell time and position to optimize the dose distribution.
- Two common remote afteloaders are shown in Fig. 2.5.
- Various applicators are used to direct and separate the source from the patient. Different applicators exists for lung/bronchial, skin, gynecological, and breast treatments.

2.2 Patient Simulation

(a) Computed tomography (CT) is typically used for treatment planning. Recommendations from AAPM's Task Group 101 include:
   - Scan extent should include target and all relevant OARs.
   - Scan at least 5–10 cm in the superior-inferior direction beyond the OARs.
   - When using non coplanar beams, scan upwards to 15 cm in the superior-inferior direction to accurately model dose within the patient.
   - Slice thickness should be 1–3 mm.
   - Deep inspiration breath-hold CT scans can help reduce normal tissue dose during treatment for highly mobile tumors [15].

(b) Simulation for Respiratory Motion:

- Tumors in the thorax (lung, rib) or abdomen (liver, pancreas, kidney) can be affected by respiratory motion.
- Respiratory motion can induce artifacts in free-breathing planning CT, leading to target/normal-tissue delineation errors.
- Breath hold CT scans can be used to limit motion during a simulation/treatment.
- 4DCTs take advantage of time-resolved information of couch position and breathing motion to reconstruct a 4DCT.
- Inahle and exhale breath hold CTs may over-estimate tumor motion compared to 4DCTs as the patients may breathe more than normal tidal breathing.
- 4DCTs are imperative when treating free breathing treatment sites since it will demonstrate the extent of tumor motion to help aid in creating treatment margins [16].
- 4DCT should be acquired in addition to the planning CT at time of simulation
  - External surrogates often used to monitor breathing
    - Surface tracking (e.g. AlignRT®, Catalyst® systems)
    - Bellows device
    - Infra-red/optical reflective marker tracking
    - Spirometry
  - Breathing wave consistency and tag placement should be checked for errors by physics prior to reconstruction.
  - 4DCT imaging typically sorts CT images into ten different phases.
  - Amplitude-binning is generally less artifact-prone than phase-binning [17], but is only supported on modern CT scanners. Typically, amplitude values range from full-exhale (0%) to full-inhale (100%).
  - Maximum intensity projections (MIP) can be useful for lung planning; minimum intensity projections (MinIP) can be useful for liver planning; both projection images can cause target delineation errors if used near diaphragm
  - Most robust planning information is obtained by using all reconstructed 4DCT phases. Using only end-inhale and end-inhale imaging may underestimate respiratory motion due to tissue hysteresis.
- Inhale breath-hold and exhale breath-hold CT scans can be additionally attained to estimate extent of tumor motion; may over-estimate tumor motion compared to free-breathing motion 4DCT
- Some systems permit treatment during breath hold. However, variation in tumor location between breath holds should be quantified and included in margins.

(c) Immobilization devices

- Minimize inter-fraction and intra-fraction motion
- Currently available commercial immobilization systems include:

- Vacuum bag immobilization devices: (e.g. Vac-Lok Bag, Alpha Cradle)
  - Vacuum sealed bag with plastic beads or foam that conform to patient.
  - Patient in bag which hardens around patient to immobilize.
- Thermo-plastic masks and molds:
  - Plastic that is pliable when heated and formed to the patient where it is locked into anchors and hardens around patient.
- Compression belt/paddles:
  - Abdominal compression is used for lower lobe lung lesions or liver lesions to help reduce the respiratory motion.
- Body frames: (e.g. Elekta BodyFIX system)
  - Similar to a vacuum bag systems but also has a plastic wrap that suctions around the patient to help decrease motion of body areas not in contact with the bag.
- Full Body SBRT Frames:
  - Several vendors offer a complete body immobilization system that attaches to the simulation CT couch and accelerator couch that includes an immobilization bag, wingboard, head sponge, handles, abdominal compression device, knee sponge, and leg specific immobilization.

2.3 Image Registration

- Image registration has an important role in target delineation. Many different imaging modalities have been used in SRS/SBRT planning.
  - Magnetic Resonance Imaging (MRI) has better soft tissue and cerebral tissue delineation compared to CT. Task Group 101 considered MRI to be the gold standard for brain imaging.
  - When registering MRI and CT, one should be careful about:
    - The two scans are not always a complete match due to different patient positions between MR scan and simulation scan.
    - MRI does not provide electron density needed for the calculation of dose as is the case for CT.
    - One must be aware that MRI is prone to geometric distortions, especially at the periphery of a scan, which could cause limitations in the quality of a registration [18].
    - MRI can also have "ghost" artifacts which are the representation of more than one of the same object due to motion [18]

- Positron Emission Tomography (PET) scans are used in conjunction with CT scans to add biological information provided in the PET scan.
  - PET has attenuation corrections utilizing the CT taken concurrently and the attenuation corrected PET scan should be used for registration.
  - Fuse CT from PET/CT to planning CT to limit error since the PET/CT should already be registered. One must verify that the patient did not move between the CT and PET acquisitions.
  - Some disadvantages of a PET scan include [19]:

    PET is quantified in terms of standard uptake value of the PET radionuclide. One must work with standard update value (SUV) cautiously as visual appearance can change greatly from window and level, and SUV may not be reproducible from one scan to the next.

    Since PET scans take a longer time compared to CT, the PET scan is more prone to motion blurring and other artifacts.

2.4 Treatment Planning

(a) Unlike convention treatment planning, SRS/SBRT planning does not seek to achieve a uniform target dose coverage. Hot spots within the target volume are often considered acceptable as long as normal tissues are spared. This may have the benefit of delivering higher dose to what may be hypoxic regions at the center of some tumors.

(b) In SRS and SBRT, we continue to use GTV/CTV/ITV/PTV and OAR concepts that are covered in ICRU 50 [20] and ICRU 62 [21]. These margins are delineated by the radiation oncologist. Some anatomical sites may consider the GTV and CTV to be identical, due to well defined tumor edges.

(c) SRS: In cranial sites, the concept of PTV is not used. In such cases, plans are designed with GTV or CTV as the target.

(d) SBRT: The PTV concept, as in conventional radiotherapy, is a geometrical concept that is meant to account for all possible geometric variations of the CTV/GTV. Margins depend on treatment site, patient motion, and delivery system.

(e) To achieve a high dose gradient outside of the target, dose prescriptions in SRS/SBRT are often specified at a lower isodose, typically 50–90%. Often, little to no margin is used for block edge or beam penumbra.

- Typical brain isodose lines are around 80%, and spine/lung/liver are typically prescribed to the 60–80% isodose line. GammaKnife treatments (brain) are always prescribed to the 50% isodose line.

(f) Due to the high dose per fraction that is used in these treatments, the volume of normal tissue receiving high dose must be limited. Thus, the dose falloff around the target structure must be high.

(g) Non-coplanar beams are often used, and essentially required in some modalities such as GammaKnife and CyberKnife treatments.

(h) Beam selection: The use of multiple, non-overlapping beams and tight collimation is the primary means of achieving a high dose gradient outside the target. This practice increases the dose heterogeneity within the target.
(i) The use of multiple beams will also help to decrease the skin dose. One downside is the increased treatment time with more beams.
(j) Beam energy also affects the dose falloff around the target. For small beams, such as those used in SRS/SBRT, high energy photons will cause higher lateral scatter of secondary electrons. Thus, the beam penumbra will increase at high energy. This is why most SRS/SBRT accelerators use 6 MV, and 15–18+ MV is not used.

- For brain and thorax sites, 6 MV is used. For deep-seated sites outside of the thorax and head, 10 MV may be considered.

(k) The resolution of the beam shaping devices also affects the penumbra. Cones provide the sharpest penumbra, but are limited to discrete circular field sizes. The use of finer MLC leaves improves the conformity around the target. Several manufacturers now provide smaller MLC leaf sizes (<5mm) on linear accelerators, specifically designed for SRS/SBRT.
(l) Arc therapy: A single arc can be considered a collection of multiple beam angles. Thus, arc techniques are an excellent choice for SRS/SBRT delivery. The use of arc therapy has been supported in literature and can significantly improve delivery efficiency of lung and spine SBRT [22].

- In our experience, volumetric modulated arc therapy (VMAT) is useful for SBRT when respiratory motion is minimal (<5 mm). Planning methods that produce dynamic conformal arcs (or that limit beam modulation to low levels) provide plans that are equal to static beam plans, and can be delivered in the same, if not shorter, time frame.

(m) Isocenter placement is important to consider for treatments on conventional linear accelerators. At the time of simulation, it is important to understand the characteristics of the system that the patient is to be treated on. Accelerators used for SRS/SBRT will have imaging panels that may collide with the patient. This is especially important to consider when using couch kicks to deliver non-coplanar beams. The selection of the isocenter is important to minimize the potential for patient-machine collisions.
(n) The size of the TPS dose calculation grid will affect the accuracy of the calculation. For small targets with large dose gradients, a large dose grid may not be sufficient. For SRS/SBRT planning, AAPM Task Group 101 recommends an isotropic dose calculation grid size of 2 mm or less.
(o) Pencil beam or path-length-based algorithms accounting for one dimensional scatter are not recommended by Task Group 101 for accurate dose estimation in the lung. Furthermore, AAPM Task Group 65 [23] describes 1D algorithms as inaccurate in areas of electron disequilibrium, e.g. near lung-tumor interfaces or in beam penumbra regions, and recommends either superposition-convolution or Monte Carlo for lung dose calculation. More recent algorithms

that directly solve the Boltzmann Transport Equation (BTE) have been shown to have a high level of heterogeneity calculation accuracy and are suitable for lung SBRT [24].

(p) Planning for Respiratory Motion:

- Internal Target Volume (ITV):
  - From ICRU 62: Delineate CTV motion encompassing all phases of breathing cycle [21]
  - Results in a larger PTV compared to Mid-Position, gated, and breath-hold [25]
  - Abdominal compression has been shown to decrease motion (on average) in lower lung and liver targets; should be decided on a per-patient basis based on imaging with and without compression device [26, 27]
- Mid-Position with statistically generated PTV-margin [28]
  - Use 4DCT data to generate a Mid-Position CT for planning
  - Combine 4DCT estimate of respiratory motion with other uncertainties (i.e. target delineation uncertainty, machine mechanical tolerances, inter-treatment setup errors, intra-treatment baseline shifts) to create custom PTV margin
- Breath-hold, active breathing control, or free-breathing gated treatments are the most common methods to deliver gated therapy.
  - Free breathing gating: Requires minimal effort for patient as breathing should remain normal. Treatment beam typically enabled at exhale position of cycle due to increased duty cycle and more stable tumor position.
  - Breath-hold delivery is possible at full-inhale or full-exhale:
    - Inhale: larger lung volume and therefore better lung dosimetry; patients may be able to hold breath for longer than in exhale; less repeatable tumor positioning at inhale.
    - Exhale: stable and repeatable tumor baseline positioning; more difficult to hold breath for extended periods of time in exhale; smaller lung volume and therefore slightly worse DVH values
  - Active breathing control involves use of systems to limit or force respiration to desired state.
  - Respiratory gating is often not during a single phase, but over a finite period of time in which the tumor may be moving. Motion during the radiation delivery should be considered. One method is to generate partial-breathing-phase ITV to account for gating duty-cycle or differences in breath-hold position; can use phases of 4DCT surrounding inhale or exhale for free-breathing gated treatments.
- Dynamic tumor tracking

  - Active fiducial tracking via fluoroscopy and external surrogate (e.g. CyberKnife)
  - Must ensure that implanted fiducials move with tumor; i.e. provide a good surrogate for tumor motion

- For ITV or mid-Position treatments, IMRT/VMAT should be used with caution, as overly modulated fields may be subject to target/MLC interplay effects, which could result in hot/cold spots in the PTV

2.5 Patient Setup and Treatment Delivery

- Current SBRT systems rely on image guidance for patient setup before every fraction. The details of the IGRT available depend on the treatment machine.
- Typically simulation CT images or DRR are transferred to the treatment console to perform registration with kV and/or MV images acquired with the in-room imaging systems.
- It is important to consider the potential imaging dose to the patient over the course of SRS/SBRT. The management of imaging dose during IGRT is discussed in AAPM Task Group 75 [29].
  - The dose is dependent on technique of imaging. Overall kV imaging dose depends on many factors, such as energy
    - Planar imaging will deposit the high dose at the imaged entrance skin surface.
    - Volumetric imaging (e.g. CBCT) will deliver roughly uniform dose throughout the imaged volume.
  - To achieve ALARA, collimate radiographic imaging studies to the areas of interest to reduce imaging dose to the patient.
  - The imaging dose for a given imaging technique should be quantified by a qualified medical physicist.
- Resulting IGRT offsets in the co-registration signify setup shifts required to bring the patient into the planned position.
  - All SRS/SBRT systems have methods to align the patient after image guidance, typically by moving the treatment couch.
- In our clinic, after any patient shift, we repeat the imaging study to ensure that the patient positioning system performed as intended.
  - While all patient positioning systems should undergo daily quality assurance procedures, the high dose and limited number of fractions in SBRT/SRS warrant additional imaging to ensure proper patient alignment.
- Prior to the first treatment, our clinic's policies state that the in-room images must be reviewed by a physician.
- Additional delivery considerations to account for tumor motion

- Magnitude and frequency of tumor motion can vary [30]:
    - between simulation and treatment
    - day-to-day between treatments
    - during a treatment fraction
- For all approaches (ITV, Mid-Position, gating, breath-hold) daily pre-treatment dynamic imaging is vital to confirm estimated tumor motion and correlation with any external surrogates [31].
- Examples of pre-treatment respiratory motion assessment includes:
    - 4D-CBCT
    - CBCT or on-board fluoroscopy fiducial tracking
    - MRI (e.g. MRgRT real-target imaging)
- For extended treatment times encountered in SBRT, periodic monitoring of internal motion is recommended as patient respiration can vary over during a fraction.

2.6 Quality Assurance

2.6.1 Patient-Specific Physics Quality Assurance

- In our clinic, several additional tasks are performed for SBRT/SRS beyond that of conventional radiotherapy treatments.
- A physician and physicist is present throughout the simulation to assist with selection and usage of immobilization devices. The immobilization devices for SRS/SBRT are often more complex than traditional radiotherapy.
- A pretreatment physics chart check is performed to check relevant parameters such as treatment intent, simulation images, contouring, image registration, isocenter location (if applicable), and overall plan quality. An important check is the comparison of parameters in the patient's electronic chart against the TPS.
- A secondary monitor unit (MU) calculation is performed for every patient. Typically the second check and TPS MU are within 5% agreement per beam and 3% overall calculation point dose.
- Any patient treated with intensity modulated or arc therapy will have a measurement based QA performed. Often, this is similar to QA measurements performed for standard fractionation arc plans. This also serves to verify that the leaf position/sequencing from the TPS was correctly transferred to the record and verify system and the treatment machine control station.
- For cone defined fields (such as Cyberknife), our clinic does not perform patient-specific beam measurements. Each cone has been thoroughly measured and quantified during linear accelerator commissioning.
    - Beam data for a selection of cones is verified during annual QA

- For SBRT/SRS treated with MLC-based 3D conformal radiotherapy, the combination of irregular treatment field shapes and small treatment field areas (e.g. usually less than 4 cm × 4 cm) are an indication for individual field ion chamber output measurements. An ion chamber with small collecting volume dimensions must be used, so as not to succumb to partial volume effects. Additionally, we check the MLC transfer (from TPS to TMS to the linac) and positioning accuracy by way of diode array measurements or EPID-based port films of each field.
- Similarly, for VMAT/IMRT, with many irregular and small segments, the dose output is measured using a small ion chamber, and the relative dose distributions of each field/arc are measured through one plane of the treatment field, using either film or diode array.
  - Note: ion chamber and diode array measurements seldom test the accuracy of the dose calculation algorithm in heterogeneous media; this test should be performed during commissioning, and validated by way of a third-party heterogeneous phantom measurement (e.g. Imaging and Radiation Oncology Core [IROC], MD Anderson Cancer Center, Houston, TX).
- AAPM Task Group 101 [7] recommends that:
  - At least one qualified medical physicist is present from beginning to end of the first fraction and is available for therapists to consult for any subsequent fractions
  - A radiation oncologist approves the results of image guidance and verifies portal imaging before every fraction.
  - All systems to align the patient must be checked with specific quality assurance procedures. Daily imaging isocenter checks and simple localization checks are performed as part of routine morning QA in our clinic.

2.6.2 Machine-Specific Physics Quality Assurance

- Quality assurance programs for SRS/SBRT should be an extension of already existing tests.
  - The same format of daily, monthly and annual testing procedures is recommended.
  - These procedures should be designed to detect any deviations from the baseline performance determined at acceptance and commissioning
    - Daily QA should be designed to verify the basic functionality and safe usage of all delivery and IGRT systems.
    - Monthly QA should be designed to detect trends in performance away from the baseline and focus on tests most likely to affect patient treatment.
    - Annual QA should be a thorough retesting of all individual and combined systems used and sets a baselines for monthly comparisons.

- Our departmental linac quality assurance policies and procedures have been developed based on the following AAPM Task Group Reports:
  - TG-40 - Comprehensive QA for Radiation Oncology: This older report provides a comprehensive list of test, testing frequencies, and tolerance for linear accelerator based quality assurance [32].
  - TG-142 - Quality assurance of medical accelerators: This report is an update to TG-40 with increased testing recommendations for accelerators used for IGRT and SRS/SBRT techniques [33].
  - TG-104 - The Role of In-Room kV X-Ray Imaging for Patient Setup and Target Localization: This report outlines the different types of planar X-ray imaging systems available and recommends quality assurance tests for these systems [34].
  - TG-179 - Quality assurance for image-guided radiation therapy utilizing CT-based technologies: This report outlines available technology and general quality assurance testing and frequency of tests for kV CBCT and MV CBCT, and CT-on-rails units used for patient positioning [35].
  - TG-147 - Quality Assurance for nonradiographic localization and positioning systems: This report summarizes various systems and outlines quality assurance test and testing frequencies for non-radiographic systems used to align patients [16].
  - QA of robotic radiosurgery devices is covered by AAPM Task Group 135 [36]
  - AAPM Task Group 142 recommends daily, monthly and annual quality assurance tests that should be performed for all linear accelerators and additional tests for SRS/SBRT units.
  - In addition, an ASTRO executive summary recommended additional tests not mentioned in the earlier report [37].
  - Table 2.3 summarizes recommendations from ASTRO and Task Group 142.
  - Additional tests or more frequent testing may be appropriate depending on the treatment machine and technologies used.
- The Winston Lutz test is an important test of a linear accelerator used for SRS/SBRT.
  - This test was developed by Lutz et al., where a metal sphere is placed at isocenter. A film was acquired of the treatment beam, and the center of the sphere is compared to the center of the treatment field [38].
  - This test checks the gantry, table and collimator isocenter alignments in various angles.
    - Mechanical flex in the system as the gantry angles changes or variation in the center of the couch or collimator rotation can all be detected using this test.
  - Winston-Lutz films can now be acquired using the EPID imagers of most linear accelerators.
  - Typically, this test is performed daily to verify the imaging isocenter aligns to the treatment (MV) isocenter.

Table 2.3 Combined AAPM Task Group 142 and ASTRO Recommended Minimum Quality Assurance Testing Specifically for SRS/SBRT Linear Accelerators

Test Type	Procedure	Tolerance for SRS/SBRT accelerator
Daily tests (in addition to TG 142 guidelines)		
Dosimetric	X-ray output Constancy	3%
Mechanical	Laser localization	1 mm
	Optical distance indicator at isocenter	2 mm
	Collimator/jaw size indicator	1 mm
	Winston Lutz MV-kV isocenter coincidence (single angle)	≤1 mm, <0.75 mm average
	IGRT system couch positioning/repositioning	1 mm
Safety	Stereotactic interlocks/lockouts	Functional
	Collisional interlocks of kV/MV systems	Functional
	Imaging system interlocks	Functional
Monthly tests (in addition to TG 142 guidelines)		
Dosimetric	X-ray output	2%
	Dose rate output constancy	2%
Mechanical	Treatment couch positioning indicators	1 mm & 0.5°
	MV-kV isocenter coincidence (cardinal angles)	1 mm
Imaging	Hidden target test using frame or IGRT system	≤1 mm
	Planar kV and MV geometrical scaling	≤1 mm kV ≤2 mm MV
	CBCT contrast, spatial resolution, HU constancy, uniformity and noise	Baseline
	CBCT geometrical accuracy	≤1 mm
Annual tests (in addition to TG 142 guidelines)		
Dosimetric	SRS arc rotation	1 MU or 2%
	MU linearity	≤5% or 2–4 MU
	Spot check of small field beam data including output factors, depth dose and off-axis factors	≤1% from baseline
Mechanical	MV-kV isocenter coincidence	1 mm
Imaging	CBCT imaging dose	Baseline
	Planar kV or MV imaging dose	Baseline
	KV beam quality and energy	Baseline
	Imager position of full range of travel	±5 mm
	End-to-end localization assessment	≤1 mm
	End-to-end dosimetric measurement	≤2%

  - Figure 2.6 demonstrates typical Winston Lutz images.

- One recommended monthly QA addition is use of "hidden target" end-to-end test of the IGRT systems, in which the user aligns a phantom with an internal spherical target to the machine isocenter using the IGRT capabilities, and then verifies the target position using kV and MV imaging.

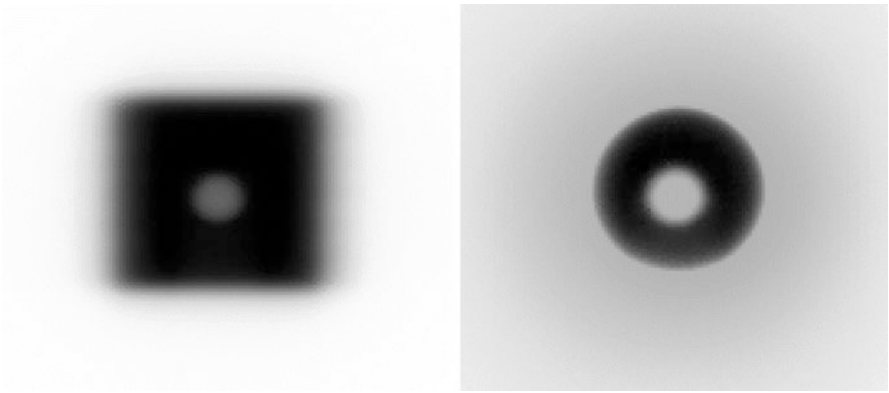

Fig. 2.6 Examples of Winston-Lutz tests for a MLC-defined field (left) and a cone-defined field (right) on a linear accelerator. The test compares the center of the radiation field to the center of a metal sphere placed at isocenter. In the image on the right, a small variation in the radiation field relative to the sphere is easily detected by the human eye

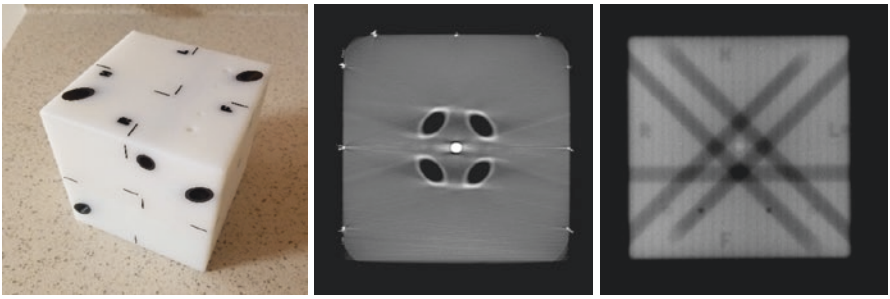

Fig. 2.7 A "hidden object" end-to-end test can be performed with commercial phantoms. Shown here are the MIMI phantom (left) and its resulting CBCT (center), which is used to align its central Winston-Lutz-style metal sphere to the kV isocenter. Finally, an MV portal image (right) can be taken to verify alignment of the metal sphere with the MV isocenter

- Intentionally misaligning the phantom initially by a known off-set, and then testing the IGRT system's ability to adequately correct the position, is a more thorough version of this recommended test.
- Several vendors have designed phantoms to facilitate this test for a variety of systems. These phantoms are able to test alignment of the laser, kV and MV isocenters.
- In our clinic, the "hidden target" test is performed using the "Multiple Imaging Modality Isocentricity" (MIMI) phantom (Fig. 2.7) from Standard Imaging (Middleton, WI)

    - The phantom has a hidden, metal sphere embedded at the center for Winston-Lutz testing and multiple open air columns assist with image registration.
    - Marked on the outside of the phantom are off-center lines to align the phantom with a known offset from the central sphere.
    - A CBCT of the phantom is acquired. The IGRT system automated registration algorithm aligns the phantom's center to isocenter and performs the couch shift. This tests the couch alignment capabilities of the system and should equal the known offset from sphere to external laser marking.
    - The previous step aligned the central sphere to the kV imaging isocenter. MV portal imaging is used to verify the central sphere aligns with the central axis of the radiation field.
  - Any ancillary imaging system isocenter, such as an optical surface tracking system, can also be tested with the hidden target test once the phantom is aligned to the MV isocenter.

2.7 Clinical Implementation and Commissioning

- AAPM Task Group 101 outlines the critical steps for initiating a clinical SBRT program
  - Establish the scope of the program including and goals for each treatment site.
  - Determine the treatment modality, dose, fractionation scheme, and treatment planning goals that support the clinical goals for each treatment site
  - Determine the equipment requirements for patient positioning, treatment delivery, and positional verification
  - Determine the personnel needs for implementation, including additional requirements on therapists, dosimetrists, physicists, and physicians.
  - Establish and perform acceptance testing and commissioning test procedures for all SBRT equipment
  - Establish quality assurance procedures for simulation, treatment planning, treatment delivery, and IGRT verification guidelines. Include reporting methodologies and action levels for these guidelines.
  - Conduct personnel training for all new equipment, procedures and guidelines.
- Acceptance testing is not the same as commissioning, but is only the first step of the process for physics.

  - Acceptance testing is generally performed with the vendor's personnel to ensure that the system is functional, operates within intended specifications, and in compliance with all regulatory requirements.

- Commissioning testing should be developed by the institution's physics team to establish a comprehensive baseline characterization of the SRS/SBRT system's performance. A time consuming but crucial portion of the commissioning process is the measurement and characterization of the radiation from the machine.
  - AAPM Task Group 106 provides guidelines and recommendations on standard linear accelerator beam data commissioning [39].
  - SBRT/SRS commonly use small treatment fields to achieve the necessary conformality. Accurate dosimetric measurement of small fields is complicated by several issues:
    - Detector volume averaging
    - Loss of lateral electronic equilibrium
    - Collimator effects (e.g. MLC leakage, leaf end transmission)
    - Detector position uncertainty
  - AAPM TG 101 recommends that the active diameter of the detector should be less than half of the full-width half maximum of the smallest beam measured.
- The TPS must be commissioned using beam data to ensure accurate calculation of dose and monitor units. This includes a systematic comparison of calculation and measurement ranging from simple configurations such as a single beam to sophisticated arrangements of beams replicating all potential SRS/SBRT clinical scenarios [37].
- There are large potential clinical consequences for incorrect beam data and machine calibration, especially in SRS/SBRT.
  - Due to the increased potential for errors, commissioning data should be compared to published data (often termed "golden data") and any inconsistencies should be investigated.
- Acceptance testing and commissioning should characterize each step of the SRS/SBRT process. Once the individual components of the SRS/SBRT planning and treatment technique are commissioned, it is recommended to perform an all-encompassing "end-to-end" test of the entire system [40].
  - The testing should mimic actual patient treatment and should use all of the same equipment used for treating the patient.

Table 2.4 Recommendations of comprehensive quality control measures from ASTRO

Appendix 1 – Recommendations to Guard Against Catastrophic Failures in SRS and SBRT			
Procedure and tests	Principal	Primary review	Secondary review
1. Commissioning Treatment Devices and Planning Systems			
Machine output calibrations and factors in accordance with relevant guidelines (TG-51, TG-101, TG-142).	Physicist	2nd Physicist	Independent assessment (RPC, etc.)
Treatment planning system commissioning should, include test cases similar to those encountered in SBRT (TG-53).	Physicist	2nd Physicist	Physicists and Dosimetrists
2. Patient Selection			
Patient selection should be in accordance with an approved clinical protocol.	Physician	Physicians and Physicists	ALL
3. Patient Simulation			
Patient simulated in accordance with approved protocol (immobilization and respiratory management) and supervised by physician.	Simulation Therapist	Physician	Physicists and Dosimetrists
4. Patient Treatment Planning			
Verify the patient information, treatment site, and prescription.	Dosimetrist	Physician	ALL
Verify correct positioning of the high dose and intermediate regions of isodose plan relative to targets.	Dosimetrist	Physician	Physicist
Verily the reference images and any shift information - physician determines KRT technique.	Dosimetrist	Physicist	ALL
5. Pre-Treatment Quality Assurance			
Verify that the correct version of the patient*s treatment plan is approved, sent to treatment management system, and used for patient-specific QA.	Dosimetrist	Physicist	ALL
Perform a thorough chart review.	Therapist	Physicist	ALL
Perform a complete chart check including review of information in treatment management system, field apertures in treatment management system, and check of dose to verify TPS calculation.	Dosimetrist	Physicist	ALL
Before the first treatment or for any change in treatment perform patient-specific QA to guarantee that data transfer between systems is correct before patient treatment begins.	Physicist	Physicist	ALL
6. Treatment Delivery			
Halt a procedure if the operator is unclear a bout what is being done.	ALL	ALL	ALL
Perform a check of treatment parameters before start of each treatment against a fixed version of the treatment plan.	Therapist	2nd Therapist	ALL

Table 2.4 (continued)

Appendix 1 – Recommendations to Guard Against Catastrophic Failures in SRS and SBRT			
Procedure and tests	Principal	Primary review	Secondary review
Perform a time out prior to treatment delivery.	Therapist	2nd Therapist	ALL
Assess patient clinically during course of SBRT to identify any acute effects	Physician, Therapist, and Nurse	Physician, Therapist, and Nurse	
7. Quality Performs nee and Improvement			
Perform end-to-end testing to guarantee transfer of data among all systems involved in imaging, planning and dose delivery (annually and after any software or hardware changes)	Physicist	2nd Physicist	Physicists and Dosimetrists

  - "End-to-end" testing using anthropomorphic phantoms is a recommended procedure prior to final commissioning and as part of on-going quality assurance.

- Prior to releasing the machine for clinical usage, it is recommended to independently verify the absolute machine calibration utilizing a remote dosimetric monitoring service.
  - One example is the MD Anderson IROC Houston Quality Assurance Center which provides dosimeters and phantoms via mail order service [41].
- Table 2.4 outlines recommendations of comprehensive quality control measures from ASTRO [37].

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